Screening, Diagnosis and Management of Gestational Diabetes in New Zealand

A clinical practice guideline

2014

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Executive summary

This guideline provides evidence-based recommendations for the diagnosis of probable undiagnosed diabetes in early pregnancy and of gestational diabetes mid-trimester in order to improve maternal and infant outcomes. It also provides recommendations of the treatment and subsequent management of women diagnosed with gestational diabetes.

General healthy lifestyle

All pregnant women should be advised to eat a healthy, balanced diet with appropriate calorific intake and be encouraged to be physically active for at least 30 minutes per day most days of the week (as per The New Zealand Physical Activity Guidelines 2001). Women with risk factors for diabetes or gestational diabetes should be offered additional advice. Women should avoid excessive weight gain during their pregnancy (Ministry of Health 2014). The healthy approach to diet and lifestyle should continue after birth.

Early pregnancy

Universal screening using glycated haemoglobin (HbA1c), as part of 'booking' antenatal blood tests (ideally before 20 weeks), will identify women with probable undiagnosed diabetes or prediabetes. Women with an HbA1c ≥ 50 mmol/mol should be under the care of a service that specialises in diabetes in pregnancy. Women with HbA1c values in the range of 41–49 mmol/mol should be offered the diagnostic oral glucose tolerance test at 24–28 weeks as they are at an increased risk of gestational diabetes. Some local policies currently treat women with HbA1c values in the range of 41–49 mmol/mol.

At 24–28 weeks' gestation

At 24–28 weeks' gestation, all women not previously diagnosed with diabetes who are at high risk of gestational diabetes (HbA1c of 41–49 mmol/mol) should be offered the diagnostic two-hour, 75 g oral glucose tolerance test. (If fasting glucose ≥ 5.5 mmol/L or two-hour value ≥ 9.0 mmol/L, refer to services that specialise in diabetes in pregnancy.) All other women should be offered screening for gestational diabetes using the one-hour, 50 g, oral glucose challenge test known as the polycose test. (If glucose ≥ 11.1 mmol/L, refer directly to services that specialise in diabetes in pregnancy without further testing; if glucose ≥ 7.8–11.0 mmol/L, arrange a 75 g, two-hour oral glucose tolerance test (OGTT) without delay). Offer enrolment in the randomised trial of different diagnostic criteria. For further details of the New Zealand GEMS Trial contact gems@auckland.ac.nz or go to www.ligginstrials.org/GEMS.

After diagnosis of gestational diabetes

All women diagnosed with gestational diabetes should be offered ongoing treatment provided by health professionals. That treatment should include specialised dietary advice, lifestyle advice and educational material that is culturally and ethnically appropriate.

Women with poor glycaemic control (meeting < 10% of treatment targets in a week), including those who do not respond to dietary and lifestyle interventions, should be offered pharmacological therapy with oral hypoglycaemics and/or insulin. Treatment targets should be fasting ≤ 5.0 mmol/L; one-hour post-prandial ≤ 7.4 mmol/L and two-hour postprandial ≤ 6.7 mmol/L. A specialist review of treatment is required (which can be a remote consultation) where more than 10% of blood glucose values exceed these targets in one week. Treatment decisions should not be based solely on fetal ultrasound.

At the time of birth

Pharmacological treatment should cease at the time of birth. Vaginal birth is the preferred mode of birth. Elective delivery prior to 40 weeks' gestational age is not recommended in women who have no obstetric complications (including hypertension, pre-eclampsia, large for gestational age infant ≥ 90th centile, maternal age > 40 years) and who have had good glucose control (> 90% of glucose readings within glucose treatment targets) throughout their pregnancy.

Women with poor glucose control (> 10% of glucose readings outside of treatment targets per week) or other obstetric complications (including hypertension, pre-eclampsia, large for gestational age infant > 90th centile, maternal age > 40 years) should be assessed individually by an obstetrician.

Breastfeeding should be encouraged as soon as possible after delivery. Maternal monitoring of blood glucose should continue for 24 hours after birth to confirm the absence of hyperglycaemia. Neonatal blood sugar should be tested within one to two hours of birth for neonatal hypoglycaemia (< 2.6 mmol/L).

Contraception and family planning should be discussed in the early postnatal period.

Follow-up of women with gestational diabetes

Women with gestational diabetes should be informed of their increased risk of having gestational diabetes in another pregnancy and of the lifelong risk of developing type 2 diabetes. The importance of returning for postpartum screening and ongoing surveillance should be emphasised and encouraged.

Screening for diabetes and impaired glucose tolerance using HbA1c is recommended at three months postpartum (41–49 mmol/mol repeat test in three months; ≥ 50 mmol/mol confirms diabetes). This conforms with detection of diabetes outside of pregnancy and appears to be a preferable test to the woman. A reminder system should be introduced to increase the uptake of the postpartum screening test. Unless symptomatic of diabetes, women should return annually for HbA1c screening with their primary care provider.

The oral glucose tolerance test at 6–12 weeks postpartum is no longer recommended.

Implications for planning services for women with gestational diabetes

Workforce development, especially for specialised dietetic and laboratory services, and midwifery and general practitioner education are priorities.

Flow chart for diabetes in pregnancy

All pregnant women —— Known diabetes (type 1 and 2) ——→ *(IMMEDIATE REFERRAL)*

↓

HbA1c with booking bloods < 20 weeks for diagnosed diabetes ① ——→ **Probable undiagnosed diabetes** / HbA1c ≥ 50 mmol/mol

↓ Normal HbA1c < 40 mmol/mol

At 24 to 28 weeks arrange screening or diagnostic testing for gestational diabetes ②

↓

- Offer enrolment in randomised trial of different diagnostic criteria*
- If HbA1c at booking ≤ 40 mmol/mol
- If HbA1c at booking 41 to 49 mmol/mol

↓

Glucose challenge test (GCT) ③ ≥ 7.8 mmol/L —— Yes ——→ Oral Glucose Tolerance Test (OGTT) ④ fasting ≥ 5.5 mmol/L or 2-hour ≥ 9.0 mmol/L —— Yes ——→ **Diabetes in pregnancy pathway** ⑤

No ↓   No ↓

Routine antenatal care and delivery

Diabetes in pregnancy pathway ⑤
- Specialist services for diabetes in pregnancy
- Weight and lifestyle advice
- Ultrasound scan at the time of diagnosis
- Glucose targets fasting ≤ 5.0 mmol/L; 1-hour post-prandial ≤ 7.4 mmol/L; 2-hour post-prandial ≤ 6.7 mmol/L
- Metformin and/or insulin

36 to 37 weeks ⑥ ultrasound scan and plan timing of delivery

—— Normal growth and no comorbidity ——→ Plan delivery at 40+ weeks

↓

Comorbidities present OR

Glucose levels not in target range

↓

Delivery 38 to 39 weeks

Plan delivery at 40+ weeks ↓ → All women with gestational diabetes have HbA1c 3-months postpartum and annually thereafter ⑦ ←—— Delivery 38 to 39 weeks

* For further details of the New Zealand GEMS Trial contact: Email: gems@auckland.ac.nz or go to www.ligginstrials.org/GEMS.

① **What is HbA1c?**

- HbA1c (glycated haemoglobin) indicates the average blood glucose levels over the previous six to eight weeks.
- It is a reliable method of detecting probable undiagnosed diabetes in the first 20 weeks of pregnancy.
- An HbA1c of ≥50 mmol/mol suggests probable undiagnosed diabetes. Refer these women to specialist services for diabetes in pregnancy.
- An HbA1c of 41 to 49 mmol/mol suggests prediabetes. Give these women dietary and lifestyle advice. In some local policies, they are also referred to specialist services.

② **At 24 to 28 weeks gestation**

- Women with a booking HbA1c of 41 to 49 mmol/mol should be offered a 75 g, two-hour oral glucose tolerance test (OGTT) due to an increased risk of gestational diabetes (some women with risk factors might be considered for OGTT based on local policies/prevalence levels) OR
- All other women should be offered a 50 g, 1 hour oral glucose challenge test (polycose test) OR
- Offer enrolment in the randomised trial of different diagnostic criteria. For details of the New Zealand GEMS Trial contact gems@auckland.ac.nz or go to www.ligginstrials.org/GEMS.

③ **Screening thresholds for gestational diabetes**

- A value of the non-fasting oral glucose challenge test of ≥ 7.8 to 11.0 mmol/L requires a confirmatory oral glucose tolerance test for diagnosis of gestational diabetes.
- If value ≥ 11.1 mmol/L refer to specialist services for diabetes in pregnancy.

④ **Diagnostic thresholds for gestational diabetes**

- Values of the oral glucose challenge test of fasting ≥ 5.5 mmol/L or two hour post-prandial ≥ 9.0 mmol/L requires referral to specialist services for diabetes in pregnancy.

⑤ **Diabetes in pregnancy pathway**

- Care is provided in consultation (including virtual clinics) with an obstetrician, a physician and a dietician as well as by the lead maternity carer (LMC).
- Weight and lifestyle advice is ideally provided by a dietician or appropriately trained health professional.
- Glucose targets during treatment are to achieve fasting ≤5.0 mmol/L; one hour post-prandial ≤ 7.4 mmol/L and two hour post-prandial < 6.7 mmol/L for more than 90% of readings during a week. Failure to meet these targets requires further consultation.
- Metformin and/or insulin may be required where blood glucose treatment targets are unmet.
- Fetal growth assessed by ultrasound should not be used to guide treatment as it is not reliable.

⑥ **Timing of delivery**

- If ultrasound at 36 to 37 weeks reports normal fetal growth (< 90th percentile) and there are no maternal or fetal comorbidities plan delivery at 40[+] weeks.
- If growth is > 90th percentile or there are maternal and/or fetal comorbidities plan delivery for 38 to 39 weeks.

⑦ **Postpartum follow-up**

- Women with gestational diabetes are at increased risk of type 2 diabetes.
- At three months postpartum and annually thereafter, all women with gestational diabetes should have an HbA1c. The oral glucose tolerance test at six weeks postpartum is no longer required. This is consistent with screening of type 2 diabetes in adults in the New Zealand Primary Care Handbook (New Zealand Guidelines Group 2012).

Scope and purpose of the guideline

Purpose

The purpose of this guideline is to provide an evidence-based summary of best practice in the screening, diagnosis and management of gestational diabetes in pregnancy. This includes the early detection of probable undiagnosed diabetes, and the detection, treatment and follow-up of gestational diabetes in order to promote best clinical practice for these women and their infants.

Definitions for terms used for this guideline

The following terms are used throughout the document based on these definitions.

Diabetes in pregnancy – Any diagnosis of diabetes (type 1, type 2 or gestational diabetes) during a pregnancy.

Gestational diabetes – Diabetes that is first detected in pregnancy and resolves following the birth of the baby.

Probable undiagnosed diabetes – Diabetes (type 1 or type 2) that is first detected in pregnancy and that has often been referred to as gestational diabetes. However, blood glucose levels do not return to normal ranges following the birth and diabetes is confirmed following postpartum screening (HbA1c value of ≥ 50 mmol/mol).

Prediabetes – A state in which some but not all of the criteria are met for a diagnosis of diabetes (type 1 or type 2). It is often termed 'borderline diabetes' (HbA1c value of 41–49 mmol/mol). Abnormal glucose levels are likely to continue after pregnancy.

Borderline gestational diabetes – A state first identified in pregnancy in which some but not all of the criteria are met for a diagnosis of gestational diabetes. Blood sugar levels are likely to be controlled by diet and lifestyle alone and usually return to within normal ranges after birth.

Hyperglycaemia/glucose intolerance – 'Glucose intolerance' is used as an umbrella term for metabolic conditions resulting in higher than normal blood glucose levels – hyperglycaemia.

Type 1 diabetes – Usually diagnosed in childhood but can develop in adulthood. This is an autoimmune condition in which the body is unable to make insulin (or very little) and requires treatment with insulin.

Type 2 diabetes – Usually diagnosed in adulthood and is due to insufficient insulin being made by the body. Depending on the severity of the condition, treatment can include diet alone or in combination with oral hypoglycaemic drugs and/or insulin.

The need for the guideline

The New Zealand Ministry of Health identified a need for evidence-based guidance on the screening, diagnosis and management of gestational diabetes. The need for the guideline was also identified as a priority by the Maternity Quality Initiative Expert Working Group. The Virtual Diabetes Register recorded 225,731 individuals with diabetes in New Zealand as of 31 December 2012. Of these 14% are Māori, 11.5% are Pacific peoples and 5.6% are Indian (www.nzssd.org.nz/documents/misc/13%2006%20Virtual%20Diabetes%20Register%20release %2031%20Dec%202012%20(2).pdf).

Between 3000 and 4000 women per annum are diagnosed with gestational diabetes or recurrence in New Zealand (Auckland District Health Board 2012).[1] The New Zealand Diabetes Workforce Service Review (2011) reported on the increasing prevalence of diabetes in New Zealand (mean 8–9% compounded per annum). The prevalence was greater among Māori (5–10%), Pacific peoples (4–8%) and Asian Indians (4%) compared with New Zealand Europeans (3%). Approximately 90% of individuals with diabetes have type 2 diabetes and the prevalence of gestational diabetes is increasing (Diabetes Workforce Service Review 2011).

There are national and international differences of opinion especially on diagnosis and screening of women for hyperglycaemia in pregnancy which includes gestational diabetes. In New Zealand, opinions differ on where it is best to treat women and what is the best way of following up both the women and their infants after delivery due to the increased risk of developing type 2 diabetes.

Variations in international diagnostic criteria mean that prevalence of hyperglycaemia in pregnancy can range from 7.9% (Canadian Diabetes Association criteria) to 24.9% (Australian Diabetes in Pregnancy Society criteria) in the same group of women using the two-hour, 75 g oral glucose tolerance test (Agarwal 2005b). This highlights the need for evidence-based guidance on screening and diagnosis for gestational diabetes in New Zealand.

Scope of the guideline

This guideline covers the early screening of women for probable undiagnosed diabetes and screening, diagnosis and management of women with gestational diabetes. It also includes recommendations for follow-up of women with gestational diabetes to detect type 2 diabetes after birth.

Although the early detection of women with probable undiagnosed diabetes (type 1 and type 2) and the appropriate referral pathway for these women are covered, their subsequent treatment and management during pregnancy are excluded from this guideline.

Women with type 1 and type 2 diabetes diagnosed before pregnancy are not covered in this guideline. This guideline does not cover all clinical scenarios or medical and obstetric emergencies. It does not include drugs that have been withdrawn from the market.

The Guideline Development Team recommends that monitoring of adherence to the guideline recommendations should be an integral aspect of the implementation process.

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[1]   Provisional data also extracted from National Maternity Collection 2013, Ministry of Health.

Target audience

This guideline is intended for the providers of care to pregnant women and providers of care to women with gestational diabetes. It is also anticipated that this guideline will have implications for health service provider organisations, funders of maternity services and funders in primary and secondary care, and may be accessed by women with gestational diabetes and their families and whānau.

The Guideline Development Team has been committed to including consumers in the guideline development process. Consumers are an integral part of the Guideline Development Team and have helped with the evaluation of the evidence and the development of the recommendations.

Treaty of Waitangi

The Guideline Development Team acknowledges the importance of the Treaty of Waitangi to New Zealand, and considers the Treaty principles of partnership, participation and protection to be central to improving Māori health. As part of its commitment to the Treaty, it has involved a Māori consumer and Māori health care practitioners in its work and Māori are represented on the Guideline Development Team.

The Guideline Development Team has specifically considered Māori health issues that are pertinent to the guideline and its implementation. It has considered specific barriers in the guideline development process where Māori health must be considered and addressed. Māori health has been considered at all points in the guideline in a less explicit manner.

Guideline development process

The Guideline Development Team followed a structured process for guideline development. This process is outlined in Appendix A.

In summary, the multidisciplinary Guideline Development Team was comprised of members nominated by key stakeholder groups who had been identified from the Ministry of Health and the research group (Appendix B). There were four, one day, face-to-face meetings of the Guideline Development Team, where evidence was presented by the research team on 21 clinical questions. The Guideline Development Team reviewed this evidence and recommendations were developed. The 21 clinical questions were used to guide systematic and narrative reviews of the evidence. The different levels of evidence that were searched included (but were not limited to) existing clinical practice guidelines, systematic reviews, randomised controlled trials and observational studies. For continuity of the document, the Guideline Development Team has incorporated New Zealand–specific evidence or data (where available) into each relevant chapter.

For the clinical questions and maternal and infant outcomes, refer to Appendices C and D.

The adapted Grading of Recommendations Assessment, Development and Evaluation (GRADE) method allows for the development of clinical practice recommendations to be STRONG or CONDITIONAL based on the balance of benefits to harms. Recommendations can be made for or against clinical practice. Where there is insufficient evidence to make a recommendation, or in areas where a narrative review has been conducted, a good practice point (GPP) is made based on expert opinion/consensus. Where there is a lack of high-quality evidence on which to make a recommendation, the Guideline Development Team has made a research recommendation.

Funding of the guideline

Summary of recommendations

The evidence-based recommendations developed by the Guideline Development Team are summarised below.

Diagnosis of probable undiagnosed diabetes in early pregnancy

	Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
1	Offer all women an HbA1c test in their 'booking' antenatal bloods to detect undiagnosed diabetes.	CONDITIONAL	Chapter 2
2a	Women with HbA1c ≥ 50 mmol/mol should be under the care of a service that specialises in diabetes in pregnancy.	CONDITIONAL	Chapter 2
2b	All women with HbA1c 41–49 mmol/mol should receive dietary and lifestyle advice and have an oral glucose tolerance test at 24–28 weeks.	GPP	Chapter 2
3	Do not offer an HbA1c as a diagnostic test for gestational diabetes as it is not sensitive enough to detect gestational diabetes.	CONDITIONAL	Chapter 2
Research recommendation: Randomised controlled trial comparing dietary and lifestyle advice with pharmacotherapy for women whose HbA1c at booking is in the range of 41–49 mmol/mol, in terms of their impact on maternal and infant outcomes and development of gestational diabetes.			
Research recommendation: Studies that investigate whether early diagnosis and treatment lead to improved maternal and infant outcomes.			

Diagnosis of gestational diabetes at 24–28 weeks

Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
At 24–28 weeks	GPP	Chapter 3
4 For all women not previously diagnosed with diabetes who are at high risk of gestational diabetes (HbA1c of 41–49 mmol/mol), offer a two-hour, 75 g oral glucose tolerance test. • If fasting glucose is ≥ 5.5 mmol/L or two-hour value is ≥ 9.0 mmol/L, refer the woman to a diabetes in pregnancy clinic. Offer all other women a one-hour, 50 g, oral glucose challenge test. • If glucose is ≥ 11.1 mmol/L, refer directly to diabetes in pregnancy clinic without further testing. • If glucose ≥ 7.8 mmol/L to < 11.0 mmol/L, then arrange a 75 g, two-hour oral glucose tolerance test without delay. Consider enrolment in the randomised trial of different diagnostic criteria*	GPP	
5 If the fasting or two-hour values are borderline and there are risk factors for gestational diabetes, consider self-monitoring of blood glucose levels weekly.	GPP	Chapter 2 (section 2.3) – risk factors Chapter 3
Research recommendation: A randomised controlled trial that compares current New Zealand screening and diagnostic criteria with those proposed by the International Association of Diabetes and Pregnancy Study Groups in terms of their impact on maternal and infant outcomes is required.		

* For further details of the New Zealand GEMS Trial contact gems@auckland.ac.nz or go to www.ligginstrials.org/GEMS.

Prevention of gestational diabetes

Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
6 Encourage all women and their families to eat a balanced, healthy diet with appropriate calorie intake to prevent the onset of gestational diabetes prior to and during pregnancy. Discuss how they could make their diet healthier, taking account of their needs, preferences and individual circumstances.	CONDITIONAL	Chapter 4
7 Encourage all women to be physically active for at least 30 minutes most days of the week (this can be in 10-minute blocks) in the absence of medical contra-indications.	GPP	Chapter 4
8 Measure and record maternal weight at routine antenatal visits.*	GPP	Chapter 4

Note: * Refer to Ministry of Health guidelines in Appendix K, Table 33.

Treatment of women with gestational diabetes

	Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
9	Offer all women diagnosed with gestational diabetes ongoing treatment by health professionals, including specialised dietary advice, lifestyle advice and educational material that is culturally and ethnically appropriate.	STRONG	Chapter 5 (section 5.2)
10	Advise pregnant women with gestational diabetes that their dietary recommendations could include: • consuming a minimum of 175 g carbohydrate per day • spreading carbohydrates evenly throughout the day between meals and snacks • reducing intake of saturated fats • consuming lean protein • keeping weight gain in pregnancy in line with Ministry of Health recommendations.* This recommendation is dependent on individual requirements.	GPP	Chapter 5 (section 5.4)
11	Where women who have gestational diabetes and poor glycaemic control (above treatment targets) in spite of dietary and lifestyle interventions, offer oral hypoglycaemics (metformin or glibenclamide) and/or insulin therapy. In deciding whether to use oral therapy or insulin, take account of the clinical assessment and advice, and the woman's preferences and her ability to adhere to medication and self-monitoring.	STRONG	Chapter 5 (section 5.5)
12	Treatment targets for capillary glucose are: • fasting glucose ≤ 5.0 mmol/L • one-hour post-prandial** ≤ 7.4 mmol/L • two-hour post-prandial** ≤ 6.7 mmol/L.	GPP	Chapter 5 (section 5.6)
13a	Women with 10% of readings (three to four readings) above the treatment targets should have their treatment reassessed.	GPP	Chapter 5 (section 5.8)
13b	Discuss high postprandial blood glucose levels with the woman to establish what she had eaten for that meal.		
14	Offer women with gestational diabetes an ultrasound scan at the time of diagnosis and at 36–37 weeks. Further ultrasound scans should be based on clinical indications. Treatment decisions should not be based solely on fetal ultrasound.	CONDITIONAL	Chapter 5 (section 5.7)
Research recommendation: A randomised controlled trial to compare tight with less tight glycaemic control in women diagnosed with gestational diabetes in terms of their impact on maternal and infant outcomes.			
Research recommendation: A randomised controlled trial comparing more intensive ultrasound scanning with usual care in women with gestational diabetes in terms of their impact on maternal and infant outcomes.			
Research recommendation: A randomised controlled trial of leisure activity interventions for the treatment of gestational diabetes.			

Note: * Ministry of Health (2014)
 ** After the start of eating.

Timing and mode of birth

	Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
15	Recommend vaginal birth for women with gestational diabetes whose pregnancy is progressing well, with good glycaemic control (≥ 90% of glucose readings within treatment targets), normal fetal growth (≥ 10th to ≤ 90th percentile) and no obstetric complications.	CONDITIONAL	Chapter 6 (section 6.2)
16	Planned delivery before 40 weeks is not recommended for women with gestational diabetes who have good glucose control (≥ 90% of blood glucose readings within treatment targets) unless there are other complications present.	GPP	Chapter 6 (section 6.3)
17	Assess timing of birth individually where women have poorly controlled gestational diabetes (< 90% of blood glucose readings within treatment targets) or there are other maternal or infant comorbidities (including hypertension, pre-eclampsia, large for gestational age infant > 90th centile, maternal age > 40 years).	GPP	Chapter 6
18	Advise women to report any reduction or change in fetal movements from 28 weeks' gestational age onwards.	GPP	Chapter 6

Immediate postpartum care

	Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
19	Encourage women diagnosed with gestational diabetes to start breastfeeding and have skin to skin contact as early as possible after birth (preferably within one hour).	GPP	Chapter 7 (section 7.2)
20	Encourage mothers diagnosed with gestational diabetes to feed their infants frequently (every two to three hours) during the first 48 hours after birth.	GPP	Chapter 7 (section 7.2)
21	Measure the infant's plasma glucose at one to two hours of age, four hours, and then four hourly, preferably before feeds, until there have been three consecutive readings > 2.6 mmol/L.*	GPP	Chapter 7 (section 7.3)
22	For infants with blood glucose levels < 2.6 mmol/L: • offer supplementary breastfeeds where possible • if blood sugar levels remain < 2.6 mmol/L for two consecutive readings one hour apart, refer the infant to the neonatal team • if any reading is ≤ 2.0 mmol/L, refer immediately to the neonatal team.	GPP	Chapter 7 (section 7.3)
23	Monitor the blood glucose of women who have been diagnosed with gestational diabetes before breakfast (fasting blood sugar) and two hours after meals for 24 hours after delivery. Refer to the medical team if values are between 7 mmol/L and ≥ 11 mmol/L on two consecutive occasions. If blood glucose levels are within normal range, stop monitoring after 24 hours.	GPP	Chapter 7 (section 7.4)
24	Discontinue diabetes medication for women with a diagnosis of gestational diabetes at birth.	GPP	Chapter 7 (section 7.5)

Note: * An appropriately sensitive method, such as the glucose oxidase method, should be used to test for neonatal hypoglycaemia. Accucheck is not sensitive enough and should not be used to measure neonatal blood glucose.

Information and follow-up

Recommendation		Strength of recommendation or good practice point (GPP)	Where to refer in guideline
25	Encourage and support women with gestational diabetes to exclusively breastfeed for a minimum of six months.	GPP	Chapter 8 (section 8.2)
26	Encourage women who are unable to breastfeed, or do not wish to breastfeed, to use donor breast milk before formula milk. The decision should be based on maternal preference.	GPP	Chapter 8 (section 8.2)
27	There is currently insufficient evidence to recommend the use of antenatal breast milk expression for women with gestational diabetes.	GPP	Chapter 8
28	Discuss methods of contraception agreeable with the woman and her partner and prescribe contraceptives based on maternal risk factors for cardiovascular disease, in the early postnatal period.	GPP	Chapter 8 (section 8.3)
29	Inform women diagnosed with gestational diabetes of the increased risk of gestational diabetes in a subsequent pregnancy and the increased risk for developing type 2 diabetes.	GPP	Chapter 8
30	Inform women (in particular those who are obese or overweight) that they can reduce their risk of recurrent gestational diabetes or type 2 diabetes by maintaining a healthy, balanced diet and increasing physical activity at moderate levels.	GPP	Chapter 8 (section 8.4)

Postpartum screening

	Recommendation	Strength of recommendation or good practice point (GPP)	Where to refer in guideline
31	For all women diagnosed with gestational diabetes, their lead maternity carer or diabetes clinic in the postnatal review should provide printed information about the importance of postpartum screening and the risk of developing type 2 diabetes.	CONDITIONAL	Chapter 9
32	Remind all women with gestational diabetes and their primary care provider (at the time of hospital discharge) of the need to participate in screening at three months after birth and annually thereafter.	CONDITIONAL	Chapter 9
33	The primary care provider of women with gestational diabetes should offer screening for type 2 diabetes at three months postpartum using HbA1c. If the value is: • ≤ 40 mmol/mol, the result is normal. Repeat the test in one year • 41–49 mmol/mol (prediabetes or impaired fasting glucose), advise on diet and lifestyle modification. If the woman is over 35 years, a full cardiovascular risk assessment and appropriate management are indicated. Repeat test after six months • ≥ 50 mmol/mol and symptomatic 'diabetes', refer to medical specialist • ≥ 50 mmol/mol and asymptomatic, repeat HbA1c or fasting plasma glucose.*	GPP	Chapter 9 (section 9.3)
34	The primary health organisation performance programme should be used to encourage primary care practitioners to record postpartum gestational diabetes screening.	GPP	Chapter 9

Note: * Two results above the diagnostic cut-offs are required for diagnosis of diabetes if the woman is asymptomatic.

Gestational diabetes and risk of type 2 diabetes

Recommendation		Strength of recommendation or good practice point (GPP)	Where to refer in guideline
35	Consider metformin in women (with previous gestational diabetes) who have HbA1c 41–49 mmol/mol and who are not successful with lifestyle modification (in particular those planning another pregnancy).	CONDITIONAL	Chapter 10
36	Provide women diagnosed with gestational diabetes with lifestyle and dietary advice and advise on how to maintain a healthy weight.	CONDITIONAL	Chapter 10
37	Inform women with a previous diagnosis of gestational diabetes and/or prediabetes of the risk of gestational diabetes and offer early pre-pregnancy screening for diabetes when they are planning future pregnancies.	GPP	Chapter 10
Research recommendation: Randomised controlled trials that evaluate the outcomes of lifestyle versus pharmacological interventions to prevent type 2 diabetes in women with a previous history of gestational diabetes.			

Chapter 1: Introduction

The World Health Organization (WHO) defines gestational diabetes as 'carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy' (WHO and Department of Noncommunicable Disease Surveillance 1999). This definition currently includes those women with previously undiagnosed diabetes.

1.1   Epidemiology of gestational diabetes in New Zealand

Several sources report evidence on the rates and trends of gestational diabetes in New Zealand (Auckland District Health Board 2012; Drury et al 2013; Winnard et al 2013).[2]

Gestational diabetes is a growing problem in New Zealand and rates have been increasing over the last five years, in particular over the last two years (Appendix E, Figure 1). The district health boards with the highest prevalence of gestational diabetes are Auckland (8.2%), Waitemata (7.1%) and Counties Manukau (7.1%). The lowest rates are found in Tairawhiti (2.2%) and Wairarapa (1.4%).[3]

The number of pregnancies (in New Zealand) associated with gestational diabetes has increased from 1.3% in 2001 to 2% in 2006 to 4.9% in 2012, equating to an annual increase of 13.9% ($p < 0.01$) (Drury et al 2013). Similar data are reported by several district health boards (Auckland District Health Board 2012; Winnard et al 2013; refer to Appendix E, Figures 2 and 3). The increased rates of gestational diabetes over the last two years may reflect changes in local policy for the diagnosis of gestational diabetes.

Estimated rates of gestational diabetes vary by ethnicity (Appendix E, Table 1). The highest rates are identified in Asian (median 8.1%), Pacific (median 7.2%), and Middle Eastern, Latin American and African (median 7.5%) ethnicities.[4] Lower rates for Māori (median 3.3%) may be a reflection of low rates of screening attendance rather than lower rates of gestational diabetes.

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[2]   Data also extracted from National Maternity Collection 2012, Ministry of Health.

[3]   National Maternity Collection 2012, Ministry of Health.

[4]   National Maternity Collection 2012, Ministry of Health.

1.2 Adverse outcomes associated with gestational diabetes

Hyperglycaemia in pregnancy, including gestational diabetes, is associated with an increased risk of maternal and infant adverse outcomes (The HAPO Study Cooperative Research Group 2008; Wendland et al 2012; Wang et al 2013).

Adverse outcomes for women with gestational diabetes	
Pregnancy associated hypertension	Caesarean section
3rd and 4th degree perineal tear	Operative vaginal birth
Type 2 diabetes in later life	Preterm labour
Postpartum haemorrhage	Polyhydramnios
Adverse outcomes for infants born to women with gestational diabetes	
Shoulder dystocia	Bone fractures, nerve palsy
Macrosomia	Large for gestational age
Hypoglycaemia	Hyperbilirubinaemia
Congenital malformation	Small for gestational age
Respiratory distress syndrome	Stillbirth
Overweight and childhood obesity	Type 2 diabetes in later life
Metabolic syndrome in later life	

1.3 Guidelines and position statements

Twenty international and national guidelines and position statements were identified and critically appraised using the AGREE II tool. They are summarised in Appendix E, Table 2. These guidelines are referred to throughout this document.

1.4 Women's perspectives on gestational diabetes

Where possible, a woman-centred perspective has been taken in this guideline. Chapter 13 summarises interviews with women with gestational diabetes conducted by the Guideline Development Team and other organisations.

Women considering being screened for gestational diabetes need to understand the reason for being screened and what will happen as they go through the care pathway from screening and diagnosis to treatment and follow-up.

Some women will feel significant anxiety when they learn they have gestational diabetes, but most studies reported that this feeling is not sustained in the antepartum or postpartum period. There is evidence that the treatment of gestational diabetes may improve a woman's health-related quality of life and reduce the incidence of depression after birth (Crowther et al 2005).

Given that their views, needs and expectations are as varied as women themselves, women need a responsive and flexible service. They need to be informed of and understand the importance of adhering to treatment for the health of both themselves and their baby. Effective and satisfactory communication between these pregnant women and their health care providers may reduce anxiety and facilitate adherence to screening and treatment regimens.

Barriers to treatment include personal costs (time off work and travel to appointments) which may place additional pressure on pregnant women with gestational diabetes and their partners, family and whānau. Increased physical activity often requires social support from multiple sources to assist with child care arrangements.

Woman-centred care focuses on the woman's unique needs, expectations and aspirations; recognises her right to self-determination in terms of choice, control and continuity of care; and addresses her social, emotional, physical, psychological, spiritual and cultural needs and expectations. It also acknowledges that a woman and her unborn baby do not exist independently of the woman's social and emotional environment, and incorporates this understanding in assessment and provision of health care (Australian Health Ministers' Advisory Council 2012).

Recently published clinical practice antenatal guidelines provide a summary of the World Health Organization principles of antenatal care and include a series of principles regarding the provision of woman-centred care (refer to Appendix F).

1.5   Summary

Rates of gestational diabetes are increasing in New Zealand, particularly in centres in the greater Auckland region and Northland (reflecting high-risk ethnic groups). Rates are likely to continue to increase as the obesity epidemic spreads. Probable undiagnosed or untreated gestational diabetes poses a significant potential health risk to the mother and the infant. Timely diagnosis, treatment and continued follow-up are essential to prevent or minimise these adverse outcomes.

Chapter 2: Who should be screened for hyperglycaemia in pregnancy and how?

2.1 Background

Increasing rates of diabetes in the general population are mirrored by an increase in the number of women with diabetes in pregnancy. Probable undiagnosed diabetes may result in maternal hyperglycaemia being present at the time of conception. This poses a threat to the developing fetus (increased risk of congenital abnormalities) and the mother (risk of diabetes-associated complications requiring therapy during pregnancy) and will require treatment to normalise glycaemic control during pregnancy (IADPSG 2010). Women with type 2 diabetes require immediate treatment and management and are outside the scope of this clinical guideline.

2.2 Prevalence of probable undiagnosed diabetes in New Zealand

The overall prevalence of (diagnosed and undiagnosed) diabetes in the adult general population, as identified by survey data (2008/09 New Zealand Adult Nutrition Survey), was 7%, and for prediabetes was 18.6% (Coppell et al 2013). Probable undiagnosed diabetes was highest in Pacific peoples (6.4%) compared with Māori (2.2%) and Europeans and others (1.5%) (Coppell et al 2013).

In women, the prevalence of undiagnosed diabetes was 1.5%. For women aged 25–34 years the incidence was 1.1% and for women aged 35–44 years it was 2%. Prevalence was much higher in women who were obese (4.1%) compared with those who were normal weight (0.5%) or overweight (0.6%) (Coppell et al 2013).

2.3 Risk factors associated with probable undiagnosed diabetes and gestational diabetes

The risk factors identified from clinical guidelines and professional bodies for the screening of probable undiagnosed diabetes and for gestational diabetes are listed in Appendix G, Tables 3 and 4.

A total of six systematic reviews and 58 additional observational studies were identified. Overall the quality of the evidence is very low (refer to Appendix G, Tables 5–14). A systematic review of 49 observational studies, which included New Zealand studies, identified indigenous women as being at higher risk of having undiagnosed type 2 diabetes (Chamberlain et al 2013).

It is likely that interactions between risk factors, rather than any single risk factor, predispose a woman to gestational diabetes.

Summary of risk factors associated with probable undiagnosed diabetes and gestational diabetes

- Increasing maternal age (in particular > 40 years)
- Family history of diabetes in first-degree relative
- High-risk ethnic group (Indo-Asian, Māori, Pacific peoples, Middle Eastern)
- Elevated body mass index: ≥ 27 kg/m² in Indo-Asian, ≥ 30 kg/m² in other ethnicities
- Previous macrosomic infant (> 4000 g)
- Previous history of gestational diabetes mellitus
- Previous history of impaired fasting glucose or impaired glucose tolerance
- Women with polycystic ovary syndrome
- Known cardiovascular disease, persistent hypertension (> 135/80 mmHg), elevated triglycerides/cholesterol
- Advancing age: ≥ 35 years for Māori, Indo-Asian and Pacific peoples; ≥ 45 years for other ethnicity
- Acanthosis nigricans
- Long-term use of steroids/antipsychotic medication
- Physical inactivity/sedentary lifestyle

Some women with no known risk factors may still be diagnosed with gestational diabetes. Risk factor screening would fail to identify these women. For women with probable undiagnosed diabetes, the risk of adverse outcomes for mother and infant from waiting until 24–28 weeks' gestation for screening and diagnosis for gestational diabetes (as currently recommended) is unknown. Identification of women with diabetes early in pregnancy allows preventive measures to be commenced earlier.

2.4 Screening for undiagnosed diabetes in New Zealand

A New Zealand study screened for asymptomatic type 2 diabetes in a population of 2130 Europeans, Māori and Pacific peoples (aged 40–79 years) in South Auckland (Simmons et al 2004). Risk factor screening (family history of diabetes, known hypertension, and past history of gestational diabetes) was compared with a random glucose test, which was positive if the value was ≥ 6.5 mmol/L at less than two hours, or ≥ 6.0 mmol/L at more than two hours postprandial. In addition, 28% of those who had a negative random glucose test also underwent an oral glucose tolerance test (OGTT). Obesity (body mass index ≥ 30 kg/m²) was identified as a risk factor in 80% of those with newly diagnosed type 2 diabetes and 34% had a first-degree relative with diabetes. A high proportion of Polynesians had risk factors. The authors report that a quarter of newly diagnosed Europeans with type 2 diabetes had no known risk factors for diabetes.

In a non-pregnant population, random glucose and glycated haemoglobin (HbA1c) were comparable when screening for dysglycaemia. HbA1c was superior for detecting diabetes alone and HbA1c screening (threshold ≥ 34.4 mmol/mol) was superior to risk factor screening. Risk factor screening alone would have missed 18% of all subjects and a third of Europeans who had an HbA1c ≥ 8% (Simmons et al 2004).

2.5 HbA1c to detect previously undiagnosed diabetes or prediabetes in early pregnancy (< 20 weeks' gestation)

2.5.1 Background

The Guideline Development Team assessed the evidence for screening with HbA1c in early pregnancy (< 20 weeks). No published randomised controlled trial evidence was found. The recommendations and statements on early screening in the guidelines and reports generally appear to be derived from consensus; where the statements or recommendations are graded, the evidence supporting the grading is frequently unreported (refer to Appendix G, Table 15).

2.5.2 Observational studies

Three observational studies assessed HbA1c as an early screening tool in pregnant women (Maegawa et al 2003; Moore et al 2013; Hughes et al 2014). One study screened 296 women with an HbA1c test at the first antenatal visit (all prior to 20 weeks) (Moore et al 2013). Those with an HbA1c ≥ 48 mmol/mol (group 1) were considered to have diabetes and were instructed on diet and daily self-monitoring of blood glucose. Those with an HbA1c between 39 and 47 mmol/mol (group 2) were considered to have glucose intolerance and were tested immediately for gestational diabetes and if necessary again at 24–28 weeks. Women with an HbA1c < 39 mmol/mol (group 3) were tested at 24–28 weeks for gestational diabetes.

The authors concluded that HbA1c testing at the first antenatal visit can be used to optimise the timing of later screening for gestational diabetes. The study did not have a control group so it was unable to determine whether screening early in pregnancy was associated with beneficial outcomes for pregnant women (Moore et al 2013).

A Japanese study assessed four different approaches to detecting gestational diabetes (50 g oral glucose challenge test (also known as the polycose test), random plasma glucose measurement, HbA1c and fasting blood glucose) and compared screening in the first and second trimesters of pregnancy (Maegawa et al 2003). Gestational diabetes was confirmed with a 75 g oral glucose tolerance test within four weeks of being screened. The glucose challenge test was found to be the optimal test for gestational diabetes screening based on assessments of different thresholds of the tests used. The authors conclude that first trimester screening for glucose intolerance was important as it suggests that the problem was probably present before pregnancy (Maegawa et al 2003).

The New Zealand STEP (Screening for type 2 diabetes in Early Pregnancy) or gestational diabetes in early pregnancy. Women (*n* = 16,122) were screened with an HbA1c and random blood glucose measured with the first antenatal blood tests. Women with HbA1c ≥ 38 mmol/mol or a random blood glucose ≥ 5.5 mmol/L and a consecutive series of 1000 women with results below these thresholds (control group) were invited to have a two-hour, 75 g OGTT before 20 weeks' gestation. Diabetes in pregnancy and gestational diabetes were diagnosed by WHO glucose criteria. The uptake of the diagnostic invitation (OGTT) was very low: 16.4% of the control group and 21.3% of those women above the threshold participated. An early OGTT was performed for only 983 women; however, the analysis weighted the results to adjust for the discrepancy in the number of women with low and high screening test results (Hughes et al 2014).

Only 0.6% (99 out of 16,122) of the study population had probable undiagnosed diabetes. The authors conclude that the HbA1c test was superior to random blood glucose for detecting probable undiagnosed diabetes in pregnancy. They also state that HbA1c is likely to be a cost-effective addition to the first antenatal screen, especially in a population with a high prevalence of diabetes. The authors note the need for studies confirming that earlier treatment improves pregnancy outcomes (Hughes et al 2014).

2.5.3 Summary

There is minimal evidence to determine if all pregnant women at less than 20 weeks' gestation should be offered an HbA1c to detect previously undiagnosed type 2 diabetes. Recommendations from guidelines and position statements for HbA1c testing of all women or women with risk factors prior to 20 weeks appear to have been mostly derived from consensus. No evidence was identified to link screening using HbA1c early in pregnancy with later maternal or fetal outcomes.

2.6 HbA1c thresholds to identify probable undiagnosed diabetes or prediabetes in pregnant women at less than 20 weeks' gestation

2.6.1 Background

Measurement of HbA1c is currently recommended by many international diabetes societies as a legitimate diagnostic test for diabetes in a non-pregnant population using a threshold of 48 mmol/mol (American Diabetes Association 2011; Goldenberg et al 2011; WHO 2011a). The New Zealand Society for the Study of Diabetes Working Party recommends regarding a value of ≤ 40 mmol/mol as normal glucose tolerance and a value of ≥ 50 mmol/mol as diagnostic of diabetes, with values of 41–49 mmol/mol representing prediabetes or dysglycaemia (Braatvedt et al 2012). The Working Party recommends that individuals with intermediate values (41–49 mmol/mol) have repeat HbA1c screening in 6–12 months. However, these thresholds have not yet been recommended for identification of pre-gestational or probable undiagnosed diabetes in pregnancy.

One rationale for investigating alternative thresholds required for the HbA1c test in pregnant women (as compared with current thresholds for use of HbA1c in a non-pregnant population) is provided by the drop in the reference range for HbA1c during early pregnancy due to a reduced fasting glucose level and changes in erythrocyte turnover (Nielsen et al 2004; Moses 2012a, b). It has been suggested that the upper reference range for HbA1c may be about 0.6% lower than in the non-pregnant state (Mosca et al 2006).

2.6.2   Observational studies

Two studies with direct evidence from women early in pregnancy were identified (Hughes et al 2009; Burlingame et al 2012; Hughes et al 2014).

The Burlingame study (conference abstract) was a retrospective cohort of women diagnosed with gestational diabetes. The women had an antepartum HbA1c test (at different gestational weeks) and a postpartum 75 g oral glucose tolerance test to diagnose probable undiagnosed type 2 diabetes. Almost 8% of 403 women who had an HbA1c test result ≥ 48 mmol/mol were diagnosed with diabetes postpartum (Burlingame et al 2012; refer to Appendix G, Table 16).

The authors were unable to demonstrate a clinically useful positive predictive value for defining type 2 diabetes using the HbA1c threshold of ≥ 48 mmol/mol. Numbers of participants were limited and 87% had their HbA1c test after 20 weeks.

In the STEP study, the areas under the receiver operating characteristic (ROC) curves for HbA1c versus random blood glucose for detecting probable undiagnosed diabetes were 0.99 versus 0.81 and for detecting early gestational diabetes were 0.72 versus 0.66, respectively (Hughes et al 2009; Hughes et al 2014). The optimal threshold for detecting probable undiagnosed diabetes was 41 mmol/mol (sensitivity 100%, specificity 97.4%). In this population (which had a low prevalence for diabetes) the positive predictive value of an HbA1c ≥ 41 mmol/mol for probable undiagnosed diabetes was 18.8%. No random blood glucose threshold had an adequate sensitivity and specificity combination for screening purposes.

The HbA1c threshold ≥ 41 mmol/mol was seen in 2.9% of the women screened. This threshold was also highly specific for 'early gestational diabetes' (98.4%) which was considered to be a useful finding as these women do not require an oral glucose tolerance test to confirm their gestational diabetes diagnosis. The positive predictive value of an HbA1c ≥ 41 mmol/mol for early gestational diabetes was 52.9% and in total 74% of women with an HbA1c above this threshold developed OGTT criteria for gestational diabetes at some stage in pregnancy. Women with an HbA1c value < 41 mmol/mol require further testing for gestational diabetes in later pregnancy (24–28 weeks' gestation). The authors suggest that further studies are required to assess how earlier treatment influences pregnancy outcomes (Hughes et al 2014).

2.6.3   Summary

Guidelines and position statements have suggested two thresholds for the screening and/or diagnosis of diabetes using the HbA1c test (either 42 or 48 mmol/mol) but these recommendations appear to have been derived from consensus. One primary study had insufficient numbers to adequately assess thresholds in pregnant women. However, a recent New Zealand study has reported both high sensitivity and high specificity using an HbA1c threshold of > 40 mmol/mol for detecting probable undiagnosed diabetes in a pregnant population.

2.7 Screening principles applied to first trimester screening for undiagnosed diabetes

For a full summary addressing the requirements of a screening programme, refer to Appendix H.

Screening protocols, together with the appropriate management subsequently, can affect health outcomes and ideally should be evaluated with randomised controlled trials. No randomised controlled trials were identified. Screening recommendations in guidelines vary widely and most are based on consensus statements. A study of 296 women concluded that HbA1c was useful to optimise the timing of screening for gestational diabetes, allowing for treatment at any earlier stage of pregnancy, but that this finding needs confirmation by larger studies (Moore et al 2013).

In regard to screening thresholds (for early identification of probable undiagnosed type 2 diabetes), the only relevant direct evidence was from the STEP study, which reported high sensitivity and specificity with an HbA1c threshold of 41 mmol/mol (> 40 mmol/L). The positive predictive value was 18.8% in this low-prevalence population (Hughes et al 2014). Additional research is required to confirm these findings.

The New Zealand STEP study has suggested thresholds for the use of HbA1c early in pregnancy that maximise the chance of identifying women with diabetes or prediabetes, who are then referred to a different management pathway. Although it is unclear how outcomes are impacted, these women may benefit from increased surveillance and intervention throughout their pregnancy. High-quality randomised controlled trials are needed to provide stronger evidence on the impact of this approach.

It is important to distinguish between HbA1c testing in early pregnancy (< 20 weeks) and testing between 24 and 28 weeks to identify gestational diabetes.

HbA1c measurements later in pregnancy do not adequately separate women with normal pregnancy from those with gestational diabetes as HbA1c levels decline during pregnancy (Kurishita et al 1992). The Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study assessed whether HbA1c could be used as an alternative to measurement of glucose in pregnant women and reported that, at an average of 28 weeks' gestation, HbA1c was not associated as strongly with adverse pregnancy outcomes as the oral glucose tolerance test (Lowe et al 2012). Another study evaluated HbA1c as a screening test between 24 and 28 weeks for gestational diabetes mellitus in a high-risk population in India (Agarwal et al 2005a). HbA1c would eliminate the need for an oral glucose tolerance test in 25% of this population, of whom 27% would be misclassified. At any HbA1c threshold with an acceptable sensitivity, the false positive rate remained high, making it necessary for too many healthy women to undergo the confirmatory oral glucose tolerance test. The authors concluded that HbA1c was a poor test to screen for gestational diabetes later in pregnancy.

> **Key points**
> - HbA1c is used to diagnose diabetes and prediabetes in the non-pregnant population.
> - It is important to identify and treat women with probable undiagnosed diabetes early in pregnancy to prevent maternal and fetal adverse events.
> - The sensitivity of HbA1c to detect gestational diabetes declines during pregnancy.

2.8 Evidence to recommendations

The Guideline Development Team took into consideration the high prevalence of previously undiagnosed diabetes and gestational diabetes in certain areas of New Zealand and the high chance that many women would have one or more risk factors. It decided that using universal screening at booking would be more appropriate in the New Zealand context than risk-based screening in early pregnancy.

The Guideline Development Team accepted that HbA1c is used to diagnose diabetes in the non-pregnant population and, although the evidence is mostly indirect, it felt that there was sufficient emerging evidence to support the use of HbA1c in early pregnancy for the detection of probable undiagnosed diabetes and prediabetes. The current thresholds recommended by the New Zealand Society for the Study of Diabetes are ≥ 50 mmol/mol to suggest diabetes and 41–49 mmol/mol for prediabetes in non-pregnant adults. Values less than 40 mmol/mol are considered to be in the normal range (www.nzssd.org.nz).

There was some debate within the Guideline Development Team regarding the management of pregnant women with HbA1c of 41–49 mmol/mol at booking. The consensus of the group was that these women should be provided with appropriate dietary and lifestyle advice and should be offered a one-step diagnostic test for gestational diabetes at 24–28 weeks. The Guideline Development Team acknowledges that, in some areas of New Zealand, services that specialise in diabetes in pregnancy review women with HbA1c of 41–49 mmol/mol at booking and that this practice can continue although randomised controlled trials are lacking.

Diagnosis of probable undiagnosed diabetes in early pregnancy

	Recommendation	Strength of recommendation or good practice point (GPP)
1	Offer all women an HbA1c test in their 'booking' antenatal bloods to detect undiagnosed diabetes.	CONDITIONAL
2a	Women with HbA1c ≥ 50 mmol/mol should be under the care of a service that specialises in diabetes in pregnancy.	CONDITIONAL
2b	All women with HbA1c 41–49 mmol/mol should receive dietary and lifestyle advice and have an oral glucose tolerance test at 24–28 weeks.	GPP
3	Do not offer an HbA1c as a diagnostic test for gestational diabetes as it is not sensitive enough to detect gestational diabetes.	CONDITIONAL

Research recommendation: Randomised controlled trial comparing dietary and lifestyle advice with pharmacotherapy for women whose HbA1c at booking is in the range of 41–49 mmol/mol, in terms of their impact on maternal and infant outcomes and development of gestational diabetes.

Research recommendation: Studies that investigate whether early diagnosis and treatment lead to improved maternal and infant outcomes.

Chapter 3: Screening and diagnosis of gestational diabetes at 24–28 weeks

3.1 Background

The Guideline Development Team examined the accuracy of commonly used screening and diagnostic tests for gestational diabetes. Different methods and diagnostic criteria have been suggested (O'Sullivan et al 1964; National Diabetes Data Group 1979; Carpenter et al 1982; Sacks et al 1989; IADPSG 2010).

The International Association of Diabetes and Pregnancy Study Groups (IADPSG 2010) proposed diagnostic thresholds based on the incidence of adverse perinatal outcomes reported in the Hyperglycaemia and Adverse Pregnancy Outcomes study (The HAPO Study Cooperative Research Group 2008). Refer to Appendix I, Table 17.

Because of the evidence showing beneficial effects of treating gestational diabetes (Chapter 5), accurately identifying women with gestational diabetes in order to provide appropriate and effective treatment has become more important.

3.2 Systematic review evidence

The screening and diagnostic values recommended by various international organisations are shown in Appendix I, Table 17.

The Guideline Development Team has drawn its evidence from a recent technology assessment and systematic review conducted by the Agency for Healthcare Research and Quality (Hartling et al 2012). Some of the following data have been taken directly from the Agency for Healthcare Research and Quality report. Appropriate permission for reproductions has been obtained. Units are converted to mmol/L where possible.

The included studies lack an agreed reference standard, although most studies have used the oral glucose tolerance test. Due to their differences in diagnostic criteria, studies have produced different prevalence rates which makes it difficult to compare studies internationally.

3.2.1 Screening using 50 g oral glucose challenge test; gestational diabetes confirmed using a 100 g, three-hour oral glucose tolerance test

Nine studies provided test accuracy data for a 50 g oral glucose challenge test (threshold ≥ 7.8 mmol/L); gestational diabetes was confirmed using a 100 g, 3-hour oral glucose tolerance test (Carpenter et al criteria). Six studies reported results for a lower threshold of ≥ 7.2 mmol/L on the 50 g oral glucose challenge test and one study used a threshold of ≥ 11.1 mmol/L. Sensitivity and specificity were both high (Hartling et al 2012). Refer to Appendix I, Figure 6.

The 50 g oral glucose challenge test with the ≥ 7.2 mmol/L threshold had higher sensitivity when compared with ≥ 7.8 mmol/L, although specificity was lower. Both thresholds have high negative predictive values but variable positive predictive values across a range of data on gestational diabetes prevalence. The Toronto Trihospital study found evidence to support the use of the lower screening threshold for higher-risk patients, and the higher screening threshold for lower-risk patients. Refer to Appendix I, Figure 6 (Hartling et al 2012).

Seven studies assessed a 50 g oral glucose challenge test with a ≥ 7.8 mmol/L threshold where gestational diabetes was confirmed using the National Diabetes Data Group criteria. Three studies reported on a lower threshold of ≥ 7.2 mmol/L and one study used a threshold of > 11.1 mmol/L. Sensitivity and specificity were both high (Hartling et al 2012). Refer to Appendix I, Figure 7.

3.2.2 Screening using 50 g oral glucose challenge test; gestational diabetes confirmed using 75 g oral glucose tolerance test

Three studies assessed a one-hour 50 g oral glucose challenge test (different thresholds); gestational diabetes was confirmed using the American Diabetes Association (2000–2010) 75 g, two-hour criteria. One Canadian study confirmed diagnosis using the Canadian Diabetes Association 75 g, two-hour criteria (Hartling et al 2012). Refer to Appendix I, Figure 8.

Three studies assessed a 50 g oral glucose challenge test (≥ 7.8 mmol/L) with gestational diabetes confirmed using the World Health Organization 75 g criteria (Hartling et al 2012). There was a wide range in diagnostic accuracy. Refer to Appendix I, Figure 9.

3.2.3 Fasting plasma glucose

Seven studies assessed fasting plasma glucose to screen for gestational diabetes which was confirmed using Carpenter and Coustan criteria. For the joint estimates of sensitivity and specificity for the different fasting plasma glucose threshold values, refer to Appendix I, Figure 10 (Hartling et al 2012).

3.2.4 Other screening criteria and screening tests

The results of studies using other criteria are summarised in Appendix I, Figure 11 (Hartling et al 2012). For the diagnostic accuracy of other screening tests, refer to Appendix I, Table 18. Limited data support the use of HbA1c as a screening test at 24–28 weeks. One study conducted in the United Arab Emirates using an HbA1c value of ≥ 37 mmol/mol lacked specificity (21%) despite good sensitivity (82%). A Turkish study showed that an HbA1c threshold of ≥ 55 mmol/mol had 64% sensitivity and specificity. HbA1c does not perform as well as the 50 g oral glucose challenge test as a screening test for gestational diabetes later in pregnancy except when HbA1c is markedly elevated (Hartling et al 2012).

3.2.5 Effect of prevalence on diagnostic test accuracy

Appendix I, Table19 presents a series of scenarios that demonstrate the changes in positive and negative predictive values for three levels of prevalence (7%, 15% and 25%). The higher the prevalence of gestational diabetes, the higher the positive predictive value (that is, the more likely it is that a positive result is able to predict the presence of gestational diabetes). When the prevalence of gestational diabetes is low, the positive predictive value is also low, even when the test has high sensitivity and specificity. Generally the negative predictive value (which rules out gestational diabetes) is very high – 98% or better at a gestational diabetes prevalence of 7% (Hartling et al 2012).

Differences in prevalence associated with different diagnostic criteria were identified in five observational studies (refer to Appendix I, Table 20).

3.3 Optimal diagnostic threshold for maternal and infant outcomes

3.3.1 The Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study

The HAPO study reported no obvious thresholds at which risks for adverse pregnancy outcomes increased. The study found strong, continuous associations of maternal glucose levels below those diagnostic of diabetes with increased birthweight and increased cord-blood serum C-peptide levels (The HAPO Study Cooperative Research Group 2008).

3.3.2 Evaluating the new International Association of Diabetes and Pregnancy Study Groups' (IADPSG) criteria

Based on the HAPO data, the IADPSG panel made a consensus-based recommendation for diagnostic thresholds based on the average glucose values at which odds for adverse neonatal outcomes reached 1.75 times the estimated odds of these outcomes (Hadar et al 2010). Refer to Appendix I, Table 17.

A systematic review of eight studies (44,829 women) evaluated the association of gestational diabetes as diagnosed by different criteria with adverse pregnancy outcomes in untreated women (Wendland et al 2012). Statistically significant associations were reported between WHO and the International Association of Diabetes and Pregnancy Study Groups' diagnostic criteria for fetal macrosomia and large for gestational age births. There was no statistical association between the two sets of criteria for perinatal mortality. For maternal outcomes, statistically significant associations were reported between World Health Organization diagnostic criteria and International Association of Diabetes and Pregnancy Study Groups' criteria for pre-eclampsia and caesarean delivery. The authors concluded that both sets of criteria identified women with gestational diabetes at a slightly increased risk for adverse pregnancy outcomes (Wendland et al 2012).

Five studies compared the outcomes of women who would have been diagnosed with gestational diabetes using the International Diabetes and Pregnancy Study Groups' criteria with the outcomes of women without gestational diabetes (refer to Appendix I, Table 21).

3.3.3 National Diabetes Data Group's criteria compared with Carpenter and Coustan criteria

Two retrospective cohorts compared perinatal outcomes among women diagnosed with gestational diabetes by the National Diabetes Data Group criteria with women meeting only Carpenter et al criteria (Appendix I, Table 22). One study concluded that women who meet the more inclusive Carpenter and Coustan criteria (Appendix I, Table 17) would potentially benefit from treatment, but acknowledged the resource difficulties associated with the increased prevalence (Berggren et al 2011). The second study concluded that the more stringent National Diabetes Data Group criteria may miss a subgroup of women still at risk for complications (Cheng et al 2009).

3.4 Risk factor versus universal screening

3.4.1 Background

There is a variety of screening approaches, including universal routine screening of all pregnant women, selective screening based on various risk factors, and a mixed approach involving both of these methods. The most common selective screening criteria are: previous history or family history of gestational diabetes, family history of diabetes, previous poor obstetric history (including previous unexplained perinatal death, history of infant with congenital malformations, history of preeclampsia) and body mass index (Jiwani et al 2012). Section 2.3 of this guideline has identified important risk factors.

3.4.2 Systematic review evidence

One systematic review summarising the evidence for screening for gestational diabetes was identified (Tieu et al 2010b). Among the trials included in the review there was one quasi-randomised trial that compared risk factor screening with universal screening (50 g oral glucose challenge test) in terms of their impact on health outcomes (Tieu et al 2010b).

The risk factor group received glucose testing by a 100 g oral glucose tolerance test at 32 weeks' gestation if they were found to have any of the risk factors listed (having a first-degree relative with diabetes mellitus, weighing more than 100 kg in the current pregnancy, having a previous baby heavier than 4.5 kg, previous unexplained stillbirth or intrauterine death, previous major malformation, previous gestational diabetes, glycosuria in second fasting urine sample, macrosomia in the current pregnancy and polyhydramnios in the current pregnancy). The universal screening group underwent a one-hour, 50 g glucose challenge test at 26–28 weeks' gestation. A positive screening test ($\geq$ 7.8 mmol/L) was an indication for a full 100 g oral glucose tolerance test using the National Diabetes Data Group's criteria for diagnosis. The 50 g glucose challenge test was repeated in those with a negative test and with risk factors for gestational diabetes 4–6 weeks after the initial glucose challenge test (Tieu et al 2010b).

Significantly more women were diagnosed with gestational diabetes in the universal screening group than the risk factor screening group. Infants of mothers in the risk factor group were born earlier but the difference is unlikely to be of clinical significance. Although women who were routinely screened by 50 g glucose challenge test were more likely to be diagnosed with gestational diabetes than those screened by their risk factors, effects of subsequent management on health outcome are unclear (Tieu et al 2010b).

3.4.3   Observational studies

One retrospective cohort study evaluated a selective screening strategy for gestational diabetes based on the presence of body mass index $\geq$ 25 kg/m², age $\geq$ 35 years, family history of diabetes, personal history of gestational diabetes, or birth of a child with macrosomia (Cosson et al 2013).

Gestational diabetes screening at 24–28 weeks was diagnosed using WHO criteria. Women were screened at 15 weeks if they had a history of gestational diabetes or two or more risk factors. At least one risk factor was present in 59% of women, who represented 65% of all those with gestational diabetes. The presence of risk factors was significantly associated with gestational diabetes (p = 0.001) and with gestational diabetes-related events (pre-eclampsia, large for gestational age infant, shoulder dystocia) (p = 0.001). With selective screening, one-third of the women with gestational diabetes would have been missed and these women, even without risk factors, had more events than women without gestational diabetes (Cosson et al 2013). Refer to Appendix I, Table 23.

The prevalence of gestational diabetes was particularly high when there were three or more risk factors, although only 3% of the cohort were in this category. It was suggested that women with gestational diabetes, but no risk factors, would have a good prognosis and therefore missing their diagnosis would be of minimal consequence. The incidence of gestational diabetes-related events was found to be very high when four or more risk factors were identified. This is restricted to multiparous women, as two risk factors (macrosomia and gestational diabetes) depend on a previous pregnancy (Cosson et al 2013).

Key points

- It is difficult to compare screening tests and diagnostic thresholds because of the variety of populations and tests.

- Prevalence of gestational diabetes varies across studies and the diagnostic criteria used.

- The 50 g oral glucose challenge test with the 7.2 mmol/L threshold has higher sensitivity than the 7.8 mmol/L threshold; however, specificity is lower. Both thresholds have high negative predictive value but variable positive predictive value across a range of data on gestational diabetes prevalence.

- Fasting plasma glucose at a threshold of ≥ 4.7 mmol/L has similar sensitivity to 50 g oral glucose challenge test; specificity is lower.

- The prevalence of gestational diabetes ranged from 1.4–50% when a 75 g load was compared with a 100 g load (reference standard). Median sensitivity and positive predictive value were low; median specificity and negative predictive value were high.

- One study compared a one-step with a two-step strategy. Prevalence of gestational diabetes was 13% with one-step strategy and 9.6% with the two-step strategy. Positive and negative predictive values were 61% and 98%, respectively (Hartling et al 2012).

- Risk factor-based screening has the potential to miss up to one-third of women with gestational diabetes.

3.5 Evidence to recommendations

While evidence supports a positive association between increasing plasma glucose on a 75 g or 100 g oral glucose tolerance test and macrosomia and primary caesarean section, clear thresholds for increased risk were not found. The 50 g oral glucose challenge test has high negative predictive value but variable positive predictive value (Hartling et al 2012).

The International Association of Diabetes and Pregnancy Study Groups' criteria (one-step strategy) identify women who have significantly worse outcomes compared with women without gestational diabetes, particularly among women who have a caesarean section. What remains unclear is the effectiveness of treatment for these women.

Risk factor-based screening has the potential to miss up to one-third of women with gestational diabetes. Universal screening will identify more women with gestational diabetes than risk factor-based screening but the effects of subsequent management on health outcome are unclear.

When considering risk factor screening versus universal screening for gestational diabetes, it is important to take account of women's views of the two forms of screening. Some women may find the tests inconvenient and unpleasant. The National Institute for Health and Care Excellence (NICE) cost-effectiveness model for diabetes in pregnancy assumed that women were more likely to accept a test if they had already been identified as being at higher risk, either by risk factors or a previous screening test (NICE 2008).

The Guideline Development Team felt that, although some observational data suggested that the International Association of Diabetes and Pregnancy Study Groups' criteria (one-step strategy) may identify women and infants with worse outcomes who may benefit from treatment, there was no randomised controlled trial evidence to support this. There was concern that recommending a change in diagnostic thresholds that may then be overturned by emerging new evidence could result in the thresholds being changed again. This would further reduce consistency of practice throughout New Zealand as well as having huge workforce and financial implications that could not be sustained currently in many areas of New Zealand.

The Guideline Development Team agreed that there was an urgent need for a high-quality randomised control trial that compared current practice in New Zealand with the International Association of Diabetes and Pregnancy Study Groups' criteria. The trial outcomes should include both maternal and infant outcomes and also report on cost-effectiveness. In the absence of trial evidence to indicate that using the one-step strategy produces greater benefits, the Guideline Development Team decided to recommend no change to the current two-step diagnostic thresholds of the oral glucose tolerance test.

The Guideline Development Team decided that women considered at high risk for gestational diabetes (HbA1c at booking 41–49 mmol/mol) should be offered the one-step diagnostic oral glucose tolerance test at 24–28 weeks' gestation. All other women should be offered screening for gestational diabetes with the one-hour, 50 g oral glucose challenge test followed by the oral glucose tolerance test (if the challenge test is positive), a process known as a two-step strategy.

The Guideline Development Team noted that women should be informed that:

- the glucose challenge test can be falsely normal in approximately 20% of women with gestational diabetes
- if the screening test is elevated, they will still be asked to go for an oral glucose tolerance test to diagnose gestational diabetes.

Some women will have 'borderline' results – that is, they have met some but not all of the criteria for diagnosis of gestational diabetes. These women should be considered for self-monitoring of glucose levels, especially if risk factors for gestational diabetes are present (section 2.3). The Guideline Development Team also acknowledges that there are other risk factors for gestational diabetes (section 2.3) and health professionals may consider these when discussing gestational diabetes screening options with pregnant women.

As there is a lack of good-quality evidence for the optimal screening strategy at 24–28 weeks' gestation, the Guideline Development Team was only able to make good practice points.

Recommendation	Strength of recommendation or good practice point (GPP)
At 24–28 weeks	GPP
4 For all women not previously diagnosed with diabetes who are at high risk of gestational diabetes (HbA1c of 41–49 mmol/mol), offer a two-hour, 75 g oral glucose tolerance test.	
• If fasting glucose is ≥ 5.5 mmol/L or two-hour value is ≥ 9.0 mmol/L, refer the woman to a diabetes in pregnancy clinic.	
Offer all other women a one-hour, 50 g, oral glucose challenge test.	GPP
• If glucose is ≥ 11.1 mmol/L, refer directly to diabetes in pregnancy clinic without further testing.	
• If glucose ≥ 7.8 mmol/L to < 11.0 mmol/L, then arrange a 75 g, two-hour oral glucose tolerance test without delay.	
Consider enrolment in the randomised trial of different diagnostic criteria.*	
5 If the fasting or two-hour values are borderline and there are risk factors for gestational diabetes, consider self-monitoring of blood glucose levels weekly.	GPP
Research recommendation: A randomised controlled trial that compares current New Zealand screening and diagnostic criteria with those proposed by the International Association of Diabetes and Pregnancy Study Groups in terms of their impact on maternal and infant outcomes is required.	

* For further details of the New Zealand GEMS Trial contact gems@auckland.ac.nz or go to www.ligginstrials.org/GEMS.

Chapter 4: Prevention of gestational diabetes

4.1 Background

The Guideline Development Team examined the evidence for the primary prevention of gestational diabetes. Its scope included dietary counselling, exercise programmes, and programmes that combine dietary and exercise interventions.

Historically, exercise and weight loss during pregnancy have been discouraged due to concerns that exercise-induced injury would have adverse fetal and maternal outcomes (Han et al 2012). A recent health technology assessment report from the United Kingdom found no evidence of significant adverse effects from exercise in pregnancy (Thangaratinam et al 2012).

4.2 Dietary interventions alone

Two systematic reviews of dietary interventions were identified, which together covered seven randomised controlled trials and 813 women (Tieu et al 2008; Oostdam et al 2011; refer to Appendix J, Table 24). Systematic review evidence advises reducing energy intake or weight gain but is based on heterogeneous populations with varying levels of risk for gestational diabetes and different methods for screening and diagnosis of gestational diabetes. Dietary counselling is more effective than usual care in reducing the risk of gestational diabetes (Oostdam et al 2011).

A randomised controlled trial examined the effectiveness of a single (two-hour) dietary education session in early pregnancy (< 20 weeks), led by a research dietician, and follow-up sessions at 28 and 34 weeks' gestation compared with routine antenatal care. There was no statistical difference between the groups in the incidence of diabetes. A formal glucose tolerance test was not carried out on all participants which may have limited the number of cases diagnosed (Walsh et al 2012).

Another randomised controlled trial comparing a multidisciplinary approach (maternity carer, dietary advice, clinical psychologist) to the management of obese pregnant women with routine antenatal care (n = 124) found a significant reduction in the incidence of gestational diabetes (6% versus 29% respectively, p = 0.04) (Quinlivan et al 2011).

A systematic review identified three trials (n = 127 women) of a high versus low glycaemic index diet (Oostdam et al 2011). In all studies, the participants started the dietary intervention in the first half of their pregnancy and continued until 36 weeks' gestation. A low glycaemic index diet is more effective than a high glycaemic index diet in reducing the risk of having a large for gestational age infant (Oostdam et al 2011).

4.3 Exercise interventions alone

Two systematic reviews were identified (Oostdam et al 2011; Han et al 2012). Interventions included exercise training programmes of varying durations (Oostdam et al 2011) and any types of exercise and lifestyle management such as exercise advice or providing exercise sessions for pregnant women for the prevention of gestational diabetes before screening tests (Han et al 2012). Neither review found a significant difference in the gestational diabetes incidence between women receiving additional exercise intervention and those having routine antenatal care. Refer to Appendix J, Table 25.

A single-centre randomised controlled trial (n = 510 women) recruited sedentary (not exercising > 20 minutes on > 3 days/week) women with an uncomplicated singleton pregnancy who were not at risk for preterm birth (Barakat et al 2013). A moderate-intensity training programme, consisting of three days per week in sessions of 50–55 minutes each from weeks 10–12 of pregnancy through to the end of the third trimester (weeks 38–39), was compared with usual care including general advice about the benefits of exercise during pregnancy. The intervention did not reduce the risk of developing gestational diabetes. Refer to Appendix J, Table 25.

No evidence on the impact of exercise on large for gestational age was identified.

4.4 Combined dietary and exercise interventions and gestational diabetes diagnosis

Five randomised controlled trials of combined dietary and exercise interventions were identified. Refer to Appendix J, Table 26. The four randomised controlled trials found no statistically significant difference between intervention and control groups in the diagnosis of gestational diabetes (Korpi-Hyovalti et al 2011; Phelan et al 2011; Vinter et al 2011; Hui et al 2012).

A multicentre cluster randomised controlled trial of a combined dietary and exercise intervention was identified (Luoto et al 2011). The participants of the trial (n = 399 women) had a normal blood glucose level at 8–12 weeks gestation but at least one risk factor for gestational diabetes. The trial found a significant reduction in the incidence of gestational diabetes (6% versus 29% respectively, p = 0.04) (Luoto et al 2011). The proportion of large for gestational age infants was lower in the intervention than in the usual care group (12.1% versus 19.7% respectively, p = 0.042) (Luoto et al 2011).

Key points

- Exercise alone does not appear to be effective in preventing gestational diabetes.

- Lifestyle interventions may help to reduce the incidence of large for gestational infants.

4.5 Evidence to recommendations

In general the evidence was of low quality. The available evidence on this topic will always be limited because the participants of these trials cannot be blinded from the lifestyle intervention.

Exercise alone does not appear to be an effective intervention. There is some limited evidence that dietary interventions are effective at reducing the risk of gestational diabetes and having large for gestational age infants.

Combined dietary and exercise interventions did not appear to be effective in reducing the incidence of gestational diabetes. The evidence for lifestyle interventions reducing the risk of a woman having a large for gestational age infant is limited in quality and volume but shows such interventions may have some benefit.

The Guideline Development Team evaluated the evidence and decided that all pregnant women should be encouraged to maintain a healthy lifestyle throughout their whole pregnancy. This should be done through advice on a healthy, balanced diet and being physically active according to current Ministry of Health guidelines. Limiting excessive weight gain was viewed as an important factor and the Guideline Development Team therefore felt that routine monitoring of maternal weight is of high importance. The Ministry of Health provides guidelines on weight gain during pregnancy that should be used alongside good clinical judgement and should include discussion between the woman and her care provider about diet and exercise (Ministry of Health 2014). The Guideline Development Team acknowledges the potentially beneficial role of green prescriptions for women at high risk.

	Recommendation	Strength of recommendation or good practice point (GPP)
6	Encourage all women and their families to eat a balanced, healthy diet with appropriate calorie intake to prevent the onset of gestational diabetes prior to and during pregnancy. Discuss how they could make their diet healthier, taking account of their needs, preferences and individual circumstances.	CONDITIONAL
7	Encourage all women to be physically active for at least 30 minutes most days of the week (this can be in 10-minute blocks) in the absence of medical contra-indications.	GPP
8	Measure and record maternal weight at routine antenatal visits.*	GPP

Note: * Refer to Ministry of Health guidelines in Appendix K, Table 33.

Ongoing trials

Two trials in progress were identified:

- a randomised controlled trial comparing the effectiveness of a telephone-based behavioural change programme with usual care in reducing the incidence of gestational diabetes in overweight and obese women (ACTRN12613000125729)
- probiotics for the prevention of gestational diabetes in overweight and obese women (ACTRN12611001208998).

Chapter 5: Treatment for women with gestational diabetes

5.1 Background

The type of treatment an individual has for gestational diabetes is dependent on her ability to maintain glycaemic control within target ranges. Some women with gestational diabetes may be adequately controlled with lifestyle interventions whereas others may require supplementary pharmacological interventions. The Guideline Development Team has examined the evidence for dietary and lifestyle advice, exercise alone, head-to-head dietary interventions, oral hypoglycaemic drugs and insulin, glycaemic treatment targets and the use of ultrasound to modify treatment.

5.2 Combined diet and lifestyle interventions

The interventions include any treatment package for gestational diabetes such as a programme of diet and/or exercise, other educational media and supplementary pharmacological intervention (if required) compared with usual or standard care.

A Cochrane review (Alwan et al 2009) was being updated in 2014 to include 11 randomised controlled trials (n = 3134 women). Two other systematic reviews were identified (Horvath et al 2010; Falavigna et al 2012).

This review of the evidence has included the 11 randomised trials identified in the updated Cochrane systematic review, which include the thresholds for diagnosing gestational diabetes. Refer to Appendix K, Tables 27 and 28. The components of the packages of treatment are identified in Appendix K, Table 29.

5.2.1 Maternal outcomes

The relative risk of pre-eclampsia was significantly reduced (by 48%) in the women in the treatment group (p < 0.0001; refer to Appendix K, Figure 12). In 2012 women with International Classification of Diseases (ICD) coding for both gestational diabetes and pre-eclampsia accounted for 0.5% of all pregnancies and 9.5% of gestational diabetes pregnancies.[5]

The rate of caesarean sections was significantly lower (13%) in the treated women compared with those who received usual care (p = 0.01). One trial reported no statistically significant differences in type of caesarean section (emergency or elective) between intervention and control groups (Appendix K, Figure 13).

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[5] National Maternity Collection 2012, Ministry of Health.

The relative risk of induction of labour was significantly higher (19%) in the treatment group than in the usual care group (p = 0.008). This is probably a reflection of local policy for elective delivery but does not adversely affect the caesarean section rate in the intervention groups. Refer to Appendix K, Figure 14.

Gestational weight gain was significantly lower in treated women compared with usual care (p < 0.00001) but heterogeneity was high. The differences are probably due to different definitions of the timing around when the weight measurements were first taken.

There were no statistically significant differences between groups for perineal trauma, diagnosis of postpartum type 2 diabetes or preterm birth. Supplementary insulin was required by 16.6% of women in the intervention groups and 4.2% of women in the control groups (Alwan et al 2009). Meta-analysis of the data could not be conducted due to heterogeneity. The differences may be attributed to differing treatment targets specified in the trial protocols or to intensified monitoring in the intervention groups.

5.2.2   Infant outcomes

The risk for large for gestational age (> 90th percentile) was significantly lower (45%) in infants born to mothers who had received treatment compared with those whose mothers receiving usual care (p < 0.00001; refer to Appendix K, Figure 15).

Infants whose mothers received treatment were 25% less likely to have hyperbilirubinaemia than those whose mothers received usual care (p = 0.02) and the relative risk of shoulder dystocia was significantly less (62%) in infants whose mothers had been treated compared with those receiving usual care (p = 0.0006). Refer to Appendix K, Figures 16 and 17.

There were no significant differences in bone fractures or nerve palsy between infants whose mothers had received a specific package of treatment and those who had received usual care. There was no statistically significant difference between groups for neonatal hypoglycaemia, respiratory distress syndrome, admission to neonatal intensive care, perinatal deaths, stillbirths or neonatal deaths or childhood obesity.

Key points

- Providing dietary and lifestyle interventions +/- pharmacotherapy for women with gestational diabetes has clear maternal and infant benefits.

- It is important to initiate treatment as soon as possible after diagnosis.

5.3   Exercise versus control

A systematic review included four small randomised trials (114 women) diagnosed with gestational diabetes (NICE 2008). Interventions included exercising on a cycle ergometer, an arm ergometer, circuit-type resistance training, and cycling. Outcomes were not consistently reported by the trials and it is difficult to make inferences based on the results. There were no preterm deliveries in either the exercise alone or control arms in two of the trials (refer to Appendix K, Table 30).

Another systematic review of 13 studies of mixed design (refer to Appendix K, Table 30) found insufficient evidence to determine the effectiveness of exercise alone as an intervention to treat women diagnosed with gestational diabetes (DiNallo et al 2008).

One randomised controlled trial compared a structured resistance exercise programme with usual care in women diagnosed with gestational diabetes. Resistance exercise significantly decreased requirements for supplementary insulin (2.9% versus 56.3% respectively, p = 0.005), and significantly increased (p = 0.006) the percentage of weeks spent within the target range of glycaemic control. There were no significant differences in any of the other maternal or infant outcomes reported (de Barros et al 2010). Refer to Appendix K, Table 30.

Key points

- Exercise alone is not an effective intervention to treat gestational diabetes.

- Exercise as a component of lifestyle advice is important.

5.4 Dietary interventions for gestational diabetes

Dietary recommendations for women with gestational diabetes from clinical guidelines and professional bodies are summarised in Appendix K, Table 31.

A Cochrane systematic review evaluated different types of dietary interventions offered to women with gestational diabetes (Han et al 2013). There were three main types of dietary advice offered and the review included nine randomised controlled trials (refer to Appendix K, Table 32).

There were no differences between interventions for caesarean section, induction of labour, preterm birth, pre-eclampsia, need for pharmacotherapy or developing type 2 diabetes in the mother and no statistical differences in the incidence of large for gestational age infants (refer to Appendix K, Table 32).

Two trials reported gestational weight gain. One of the comparisons identified no significant differences in gestational weight gain between a standard and a high-fibre diet. Women who had a high-monounsaturated fat diet had a significantly higher body mass index at time of birth compared with those on a high-carbohydrate diet (Han et al 2013).

Dieticians New Zealand (2011) provides culturally appropriate, effective nutritional advice to women with gestational diabetes. It bases the recommended weight gain in pregnancy on the Ministry of Health (2014) guidelines (Table A).

Table A: Ministry of Health recommendations on weight gain in pregnancy

Pre-pregnancy body mass index	Body mass index (kg/m²)*	Total weight gain range (kg)
Underweight	< 18.5	13–18
Normal weight	18.5–24.9	11–16
Overweight	25.0–29.9	7–11
Obese (all classes)	≥ 30.0	5–9

Source: Institute of Medicine (2009), cited in Ministry of Health (2014)

5.5 Oral hypoglycaemics and insulin

Seven systematic reviews comparing oral hypoglycaemic agents with insulin were identified (NICE 2008; Alwan et al 2009; Nicholson et al 2009, 2011; Wensel 2009; Dhulkotia et al 2010; Waugh et al 2010).

The Guideline Development Team included 13 trials identified in the Cochrane systematic review currently being updated in 2014 (Alwan et al 2009). Seven randomised trials used glibenclamide (n = 821 women), six trials used metformin (n = 1319) and one trial compared acarbose with insulin. All trials compared oral hypoglycaemics with insulin. Tables 34 and 35 in Appendix K provide details of screening/diagnostic criteria and demographic details of the participants in these randomised trials.

5.5.1 Maternal outcomes

No trials reported any cases of maternal mortality. There were no statistically significant differences between women treated with oral hypoglycaemics or insulin in the occurrence of pre-eclampsia or caesarean section rate, induction of labour or diagnosis of type 2 diabetes postpartum. Supplementary insulin was required by 6.9% of participants treated with glibenclamide, 34% of those treated with metformin and 42% of those treated with acarbose.

Gestational weight gain was reported in five trials. Due to the high levels of heterogeneity (probably due to the different definitions used), it was inappropriate to combine the data in a meta-analysis. Women who received metformin had significantly less weight gain (kg) during pregnancy compared with those who received insulin. One of the trials reported the greatest difference with a mean of 0.4 ± 2.9 kg weight gain in the women receiving metformin and 2.0 ± 3.3 kg weight gain in the women receiving insulin.

Overall the trials have an insufficient duration of follow-up to ascertain the long-term consequences of treating gestational diabetes on maternal and infant health.

5.5.2 Neonatal outcomes

Overall there were no statistical differences between oral hypoglycaemics and insulin for infants born large for gestational age. Subgroup analysis found that women who had been treated with glibenclamide were 54% more likely (relative risk) to have a large for gestational age infant (p = 0.04).

Overall there was no difference observed in the occurrence of neonatal hypoglycaemia between infants whose mothers were treated with oral hypoglycaemics and those whose mothers were treated with insulin. However, the risk of neonatal hypoglycaemia was two times higher in infants whose mothers had received glibenclamide compared with infants whose mothers had received insulin (p = 0.003).

There were significantly more infants delivered before 37 weeks in the oral hypoglycaemic group compared with those whose mothers had received insulin (p = 0.03). Subgroup analysis only found the difference to be observed in the trials comparing metformin and insulin; the difference is, however, not clinically significant (refer to Appendix K, Figure 18).

There were no statistically significant differences in perinatal death, fetal deaths or stillbirths between women who had received oral hypoglycaemics and those who had received insulin. Nor were there any differences in rates of hyperbilirubinaemia or respiratory distress syndrome, shoulder dystocia or admission to neonatal intensive care.

One trial (metformin versus insulin) reported childhood follow-up at two years of age. There was no difference in childhood weight, childhood fat-free mass, or childhood total fat percentage. The biceps skinfold thickness (mm) was statistically significantly more in the group whose mothers had been treated with metformin (p = 0.05). The difference is less than 0.5 mm and may not be of clinical significance.

5.5.3 Ongoing trials

A randomised controlled trial (comparing metformin and insulin) was identified that was published after the search for this guideline had been conducted. The findings agree with the evidence presented above and would not alter the results of the meta-analysis (Spaulonci et al 2013).

Several other randomised trials currently in recruitment phase plan to compare metformin and insulin:

- Efficacy of metformin in achieving glycaemia goals as recommended for the treatment of gestational diabetes in non-obese women (www.clinicaltrials.gov/ct2/show/NCT01756105)
- Metformin versus in insulin in gestational diabetes (www.clinicaltrials.gov/ct2/show/NCT01240785)
- Gestational diabetes: Insulin or oral hypoglycaemic agents? (www.clinicaltrials.gov/ct2/show/NCT01215331)
- Metformin in gestational diabetes mellitus (MetGDM) (www.clinicaltrials.gov/ct2/show/NCT00681460)

- Probiotics in Pregnancy Study (ProP Study) (ISRCTN97241163) – a randomised controlled trial of probiotics in pregnancy to reduce maternal glucose in obese and gestational diabetic women.

Key points

- Metformin appears to be as effective as insulin in treating women with gestational diabetes for maternal and infant outcomes.

- Glibenclamide is more likely to result in a large for gestational age baby and there is an increased risk of neonatal hypoglycaemia.

- Some women with gestational diabetes may prefer the option of oral hypoglycaemics to insulin therapy.

5.6 Treatment targets for managing glycaemic control in women with gestational diabetes

5.6.1 Recommendations from guidelines and professional bodies for treatment targets

Appendix K, Table 36 details the treatment targets for managing glycaemic control in women with gestational diabetes proposed by guidelines and professional bodies. The evidence on which these recommendations are based is generally unclear and does not compare different blood glucose thresholds at which to initiate treatment.

5.6.2 Randomised controlled trial evidence

A secondary outcome of the Metformin in Gestational Diabetes trial (including New Zealand sites) was to determine how glucose control in women with gestational diabetes treated with metformin and/or insulin influenced pregnancy outcomes (Rowan et al 2010; refer to Appendix K, Table 37). A baseline oral glucose tolerance test did not predict outcomes, but HbA1C predicted large for gestational age infants ($p = 0.003$). During treatment, fasting capillary glucose predicted neonatal complications ($p < 0.001$) and postprandial glucose predicted pre-eclampsia ($p < 0.016$) and large for gestational age infants ($p = 0.001$). There were increased rates of respiratory distress in the infants of women in the higher glucose tertile measured by postprandial glucose ($p < 0.01$) compared with lower tertiles (Rowan et al 2010). Obesity did not influence outcomes. There were no observed effects on birth trauma. The authors suggest that targets for fasting and postprandial capillary glucose may need to be lower than currently recommended (Rowan et al 2010).

5.6.3   Observational studies

Refer to Appendix K, Table 37 for details of the observational studies identified. A population-based cohort study compared conventional with intensified management. A significant linear relationship between the level of glycaemia and rate of large for gestational age/macrosomic infants was demonstrated in the intensified management group only. The authors concluded that level of glycaemia is clearly related to pregnancy outcome in gestational diabetes (Langer et al 1994).

A matched case-control study identified three groups based on mean blood glucose throughout pregnancy (low, ≤ 4.77 mmol/L; mid, 4.83–5.77 mmol/L; and high, ≥ 5.83 mmol/L). The incidence of large for gestational age infants was 21-fold higher in the 'low' mean blood glucose category (24% versus 1.4%, $p < 0.0001$) and two-fold higher in the 'high' mean blood glucose category compared with the control group ($p < 0.03$). There were no significant differences between groups for other glucose categories (Langer et al 1989).

A retrospective cohort study looked at groups of women with gestational diabetes and pre-eclampsia based on the severity of gestational diabetes. Women were grouped by fasting glucose in the oral glucose tolerance test into mild hyperglycaemia and severe hyperglycaemia (fasting plasma glucose < 5.83 mmol/L and > 5.83 mmol/L respectively). The rate of pre-eclampsia increased significantly in the severe hyperglycaemia group. The authors conclude that the rate of pre-eclampsia is influenced by the severity of gestational diabetes and pre-pregnancy body mass index and suggest that optimising glucose control during pregnancy may decrease the rate of pre-eclampsia, even in those with more severe gestational diabetes (Yogev et al 2004).

Acceptable control (fasting plasma glucose 3.9–5.3 mmol/L, two-hour postprandial plasma glucose 5.6–6.7 mmol/L, HbA1c 6.5–7.5%) had the best outcomes for the incidence of large for gestational age infants compared with tight control (fasting plasma glucose < 3.88 mmol/L, postprandial plasma glucose < 5.6 mmol/L and HbA1c < 6.5%) women (0% versus 12.5% respectively) or uncontrolled (fasting plasma glucose > 5.3 mmol/L, postprandial plasma glucose > 6.7 mmol/L and HbA1c > 7.5%) women (0% versus 22.2% respectively) ($p < 0.01$).

Perinatal mortality and neonatal hypoglycaemia were significantly decreased in patients who were tightly controlled. For women with gestational diabetes, outcomes may not be uniformly affected by the same degree of glycaemic control (Banerjee et al 2004).

Key points

- Women with gestational diabetes who have high blood sugars during pregnancy are at increased risk of pre-eclampsia and having large babies.

- Current glycaemic treatment targets during pregnancy for women with gestational diabetes may not be tight enough.

- Tighter treatment targets are often more difficult for women to achieve and there may be increased risk of maternal hypoglycaemia and having smaller babies.

5.7 Ultrasound guided treatment for the management of gestational diabetes

A National Institute for Health and Care Excellence guideline included six randomised controlled trials investigating ultrasound guided treatment and recommended that 'hypoglycaemic therapy should be considered for women with gestational diabetes if ultrasound investigation suggests incipient fetal macrosomia (abdominal circumference above the 70th percentile) at diagnosis' (NICE 2008).

The decision-making process was unclear and appeared not to consider the quality of the included trials. The Guideline Development Team has therefore reviewed five of the trials published after 1990. Two studies were well conducted and judged to be at low risk of bias and three trials were judged to be at unclear risk of bias, mainly due to lack of reporting (NICE 2008). Refer to Appendix K, Table 38.

5.7.1 Maternal outcomes

One study, judged to be at low risk of bias, showed a significantly higher rate of caesarean section in the intervention group. Three studies showed no differences between groups for rates of caesarean section (NICE 2008). No significant differences were reported for any other outcomes. Refer to Appendix K, Table 38.

5.7.2 Infant outcomes

Two trials judged to be at low risk of bias found no significant differences in the incidence of babies who were large for gestational age between women receiving more intensive and women receiving less intensive ultrasound evaluations. Three studies (in women who had abdominal circumference measurements > 75th percentile) found women randomised to the intervention groups (treatment based on more intensive ultrasound measurement) were significantly less likely to have an infant who was large for gestational age (NICE 2008). No significant differences were reported for any other outcomes. Refer to Appendix K, Table 39.

Key point

- There is no evidence to suggest that intensified ultrasound guided treatment for women with gestational diabetes has beneficial maternal or infant outcomes. Serial ultrasound scans for obstetric indications are still appropriate.

5.8 Overall evidence to recommendations for treatment of women with gestational diabetes

Randomised controlled trial evidence suggests a clear benefit in maternal outcomes (reduced rates of pre-eclampsia and caesarean section) and infant outcomes (reduced incidence of large for gestational age, hyperbilirubinaemia; reduced rates of shoulder dystocia) when women with gestational diabetes are treated with dietary and lifestyle advice.

Randomised controlled trial evidence suggests that oral hypoglycaemic drugs (in particular metformin) are as effective as, and have no greater harms than, insulin therapy in women with gestational diabetes. The use of oral hypoglycaemic medication may be preferable to many women when compared with the option of injecting insulin. The adverse effects associated with oral hypoglycaemics and insulin were not adequately discussed in the trials.

The evidence for exercise alone as an intervention to treat women diagnosed with gestational diabetes is limited in quality and volume. The type of exercise was mainly 'supervised' exercise (resistance training and use of equipment not readily available to most women). There was a lack of trials that examined the effect of 'unsupervised' or leisure time activity (www.health.govt.nz/your-health/healthy-living/food-and-physical-activity/physical-activity).

There is an overall lack of long-term follow-up in both women and their infants for glucose tolerance and childhood obesity in the treatment intervention trials and cost implications are rarely described.

Overall, the evidence for optimal glucose targets is limited and of varying quality. It appears that women who have lower blood glucose or who are more tightly controlled are less likely to develop pre-eclampsia, have babies that are large for gestational age, have neonatal hypoglycaemia or experience perinatal mortality. The Guideline Development Team decided to lower the fasting blood glucose value to ≤ 5.0 mmol/L. The Guideline Development Team felt that a two-hour postprandial blood glucose level of ≤ 6.7 mmol/L was acceptable and concurred with the recent Australasian Diabetes in Pregnancy Society (Nankervis et al 2013) and American Diabetes Association (2013) recommendations. Additional high-quality, adequately powered randomised controlled trials are required.

Feedback during consultation highlighted the issues around accuracy of self-monitoring of blood glucose. The Guideline Development Team acknowledges that women's recording of blood glucose readings may be inaccurate for a number of reasons. Health professionals should not rely on self-reported readings but should download data from blood glucose meters (where possible).

Overall, the evidence for treating gestational diabetes according to fetal ultrasound measurement is unclear. There was no evidence to support intensified ultrasound scanning to guide treatment in gestational diabetes.

Recommendation	Strength of recommendation or good practice point (GPP)
9 Offer all women diagnosed with gestational diabetes ongoing treatment by health professionals, including specialised dietary advice, lifestyle advice and educational material that is culturally and ethnically appropriate.	STRONG
10 Advise pregnant women with gestational diabetes that their dietary recommendations could include: • consuming a minimum of 175 g carbohydrate per day • spreading carbohydrates evenly throughout the day between meals and snacks • reducing intake of saturated fats • consuming lean protein • keeping weight gain in pregnancy in line with Ministry of Health recommendations.* This recommendation is dependent on individual requirements.	GPP
11 Where women who have gestational diabetes and poor glycaemic control (above treatment targets) in spite of dietary and lifestyle interventions, offer oral hypoglycaemics (metformin or glibenclamide) and/or insulin therapy. In deciding whether to use oral therapy or insulin, take account of the clinical assessment and advice, and the woman's preferences and her ability to adhere to medication and self-monitoring.	STRONG
12 Treatment targets for capillary glucose are: • fasting glucose ≤ 5.0 mmol/L • one-hour post-prandial** ≤ 7.4 mmol/L • two-hour post-prandial** ≤ 6.7 mmol/L.	GPP
13a Women with 10% of readings (three to four readings) above the treatment targets should have their treatment reassessed. 13b Discuss high postprandial blood glucose levels with the woman to establish what she had eaten for that meal.	GPP
14 Offer women with gestational diabetes an ultrasound scan at the time of diagnosis and at 36–37 weeks. Further ultrasound scans should be based on clinical indications. Treatment decisions should not be based solely on fetal ultrasound.	CONDITIONAL
Research recommendation: A randomised controlled trial to compare tight with less tight glycaemic control in women diagnosed with gestational diabetes in terms of their impact on maternal and infant outcomes.	
Research recommendation: A randomised controlled trial comparing more intensive ultrasound scanning with usual care in women with gestational diabetes in terms of their impact on maternal and infant outcomes.	
Research recommendation: A randomised controlled trial of leisure activity interventions for the treatment of gestational diabetes.	

Note: * Ministry of Health (2014)
  ** After the start of eating.

Chapter 6: Timing of birth in women with gestational diabetes

6.1 Background

A significant obstetric complication associated with gestational diabetes is fetal macrosomia or large for gestational age which places the fetus at increased risk for birth trauma (shoulder dystocia, bone fractures and brachial plexus injury) (Boulvain et al 2009). The rationale behind a planned birth (elective caesarean section or induction of labour) for a woman with gestational diabetes is to avoid these complications (Boulvain et al 2009).

6.2 Mode of birth for women with gestational diabetes

Three systematic reviews identified one randomised trial published in 1993 by Kjos (NICE 2008; Nicholson et al 2008; Witkop et al 2009). Women (n = 200) with insulin-dependent gestational diabetes (13 women had a diagnosis of diabetes before their pregnancy) were randomised to induction of labour or expectant management at 38 weeks' gestation. Women had no evidence of obstetric complications and the estimated fetal weight was < 3800 g. Thirty women in the induction of labour group had spontaneous delivery or caesarean section prior to the planned induction, and 56 women in the expectant group had induction of labour or caesarean section prior to the onset of spontaneous labour for medical indications.

The National Institute for Health and Care Excellence guideline (2008) identified a quasi-randomised study that found no advantage to preterm caesarean section in women with gestational diabetes.

A retrospective cohort study (Alberico et al 2010) compared induction of labour at 38 weeks with expectant management (which included fetal ultrasound at 40–41 weeks and caesarean section if estimated fetal weight was ≥ 4250 g).

6.2.1 Maternal outcomes

There was no evidence of a statistical difference in caesarean section rates for induction of labour compared with expectant management, and no differences between groups for shoulder dystocia (NICE 2008; Nicholson et al 2008; Witkop et al 2009; Alberico et al 2010).

6.2.2   Infant outcomes

The rate of large for gestational age infants was significantly higher in the expectant management group (23% versus 10%, p = 0.02) (NICE 2008; Nicholson et al 2008; Witkop et al 2009). This may be attributable to the later gestational age at delivery in the expectant management group.

There were no significant differences between induction of labour and expectant management groups for admission to the neonatal intensive care unit (Alberico et al 2010). There were no cases of neonatal hypoglycaemia or perinatal deaths in the randomised controlled trial (NICE 2008; Nicholson et al 2008; Witkop et al 2009). The observational study reported a single stillbirth in the expectant management group only, at 41 weeks' gestational age (Alberico et al 2010).

6.3   Timing of birth for women with gestational diabetes

The evidence is based on the single randomised controlled trial by Kjos in 1993 or on low-quality observational studies. The evidence either recommends delivery before 40 weeks or recommends that, as long as there has been good glycaemic control (unspecified) during the pregnancy and there are no known obstetric complications, the pregnancy should be allowed to continue to 40 weeks without induction of labour or elective caesarean section (refer to Appendix L, Table 40).

6.3.1   Ongoing studies

A protocol was identified for a multicentre, randomised, open label trial comparing induction of labour with expectant management in women with gestational diabetes (GINEXMAL) (Maso et al 2011).

Key points

- Vaginal birth is preferable to elective caesarean section when the mother has maintained glycaemic treatment targets and there are no maternal or fetal complications.

- Some evidence suggests that, as long as the mother has maintained glycaemic treatment targets and there are no maternal or fetal complications, there is no need to induce labour before 40 weeks' gestation.

6.4　Evidence to recommendations

The evidence is considered to be of very low quality and mainly based on a single randomised trial conducted in the 1990s. The trial suggested that active induction of labour at 38 weeks' gestation resulted in reduced birthweight and a lower incidence of macrosomia and large for gestational age infants. There was no evidence of an adverse effect on the mother as measured by caesarean section rate. Very low-quality evidence from observational studies also suggested that induction of labour resulted in decreased rates of macrosomia and shoulder dystocia when compared with elective caesarean. There was insufficient evidence to suggest the gestational age at which elective delivery should be considered.

There is no evidence on the cost-effectiveness of induction of labour or expectant management for women with gestational diabetes. Given that the number of women with gestational diabetes is increasing, there would be additional costs if these women underwent elective delivery rather than spontaneous birth in the absence of obstetric complications. Reducing the number of unnecessary elective caesarean sections would benefit the mother and the health service provider and would reduce obstetric risks in subsequent pregnancies.

The available evidence has substantive heterogeneity with serious flaws in study design and methodology. There was insufficient evidence to draw any conclusions on optimal timing and mode of delivery in women with gestational diabetes. The Guideline Development Team therefore made good practice points based on the available data.

	Recommendation	Strength of recommendation or good practice point (GPP)
15	Recommend vaginal birth for women with gestational diabetes whose pregnancy is progressing well, with good glycaemic control (≥ 90% of glucose readings within treatment targets), normal fetal growth (≥ 10th to ≤ 90th percentile) and no obstetric complications.	CONDITIONAL
16	Planned delivery before 40 weeks is not recommended for women with gestational diabetes who have good glucose control (≥ 90% of blood glucose readings within treatment targets) unless there are other complications present.	GPP
17	Assess timing of birth individually where women have poorly controlled gestational diabetes (< 90% of blood glucose readings within treatment targets) or there are other maternal or infant comorbidities (including hypertension, pre-eclampsia, large for gestational age infant > 90th centile, maternal age > 40 years).	GPP
18	Advise women to report any reduction or change in fetal movements from 28 weeks' gestational age onwards.	GPP

Chapter 7: Immediate postpartum care for women and infants

7.1 Background

The information in this chapter is based on clinical guidelines and local practice guidelines throughout New Zealand. Local policies on care for gestational diabetes, including intra-partum and postpartum care, were requested from representatives of district health boards. The Guideline Development Team has addressed the initiation of breastfeeding, monitoring of maternal and neonatal blood glucose levels in the immediate postpartum period, diabetic medication and maternal diet after delivery.

7.2 Breastfeeding initiation

Evidence on early breastfeeding initiation for the prevention of neonatal hypoglycaemia was identified from three clinical guidelines (Health Service Executive 2010; Negrato et al 2010; SIGN 2010) and four local New Zealand policies. Two district health boards emphasised the importance of frequent feeding (two- to three-hourly) in the first 48 hours after birth.

A small pilot study found that early breastfeeding (within 30 minutes of birth) could facilitate glycaemic control in infants whose mothers had gestational diabetes. There was a significantly lower rate of borderline hypoglycaemia compared with infants who were not breastfed in the early postnatal period (10% versus 28%) or those who received formula as their first feed (9% versus 46%, $p = 0.001$) (Chertok et al 2009).

7.3 Monitoring of neonatal blood glucose levels postpartum

The generally accepted international definition of neonatal hypoglycaemia is < 2.6 mmol/L. In the local policies that were examined, five district health boards recommended that the blood sugar of the neonate should be checked one hour after birth. One district health board recommended checking blood sugars of the neonate two hours after birth. Where there was evidence of neonatal hypoglycaemia, one of the local policies suggested giving a small supplemental feed (breast milk if possible). Intravenous dextrose should be considered with recurrent levels < 2.3 mmol/L in conjunction with a paediatric decision in the neonatal intensive care unit. Two policies recommended that monitoring should continue for about 12–24 hours until three consecutive pre-feed readings > 2.6 mmol/L are made.

New Zealand–based evidence from the Sugar Babies trial (Harris et al 2012) indicated that 49% of women with diabetes (any type) met criteria for hypoglycaemia (< 2.6 mmol/L). The incidence of hypoglycaemia may have been higher had there not been an early breastfeeding initiative in place. International recommendations from the Canadian Paediatric Society and the Committee on Fetus Newborn both suggest that monitoring of the infant should be discontinued 12 hours after birth in babies of diabetic mothers if neonatal blood sugars are ≥ 2.6 mmol/L (Harris et al 2012).

7.4 Monitoring of maternal blood glucose levels postpartum

There were local differences in monitoring and thresholds of maternal blood glucose after delivery. The majority of the district health boards that provided policies suggest monitoring of blood glucose before and two hours after meals for 24 hours after delivery. There was a lack of consistency around the definitions of normal thresholds and when a referral to the medical team should be made (refer to Appendix M, Table 41).

7.5 Diabetic medication – oral hypoglycaemics and insulin

Evidence from eight local New Zealand policies agreed that diabetic medication (oral hypoglycaemics and insulin) should stop immediately after delivery and should not be recommenced without referral to the medical or diabetic team.

7.6 Maternal diet

Three local district health board policies were identified that recommended the women could return to a 'normal diet' (not defined) after delivery.

7.7 Evidence to recommendations

Evidence supports early initiation of breastfeeding in women with gestational diabetes to prevent neonatal hypoglycaemia as well as to promote maternal infant bonding. The Guideline Development Team felt it was important to emphasise the need to encourage early skin to skin contact in women with gestational diabetes to promote bonding and lactation initiation.

The current internationally accepted definition of neonatal hypoglycaemia is < 2.6 mmol/L. Where blood glucose monitoring suggests neonatal hypoglycaemia, frequent breastfeeding (as a first option) should be commenced and a referral made to the neonatal team. Feedback during consultation suggested a need to emphasise that methods sensitive enough to detect low glucose levels in neonatal blood (such as glucose oxidase methods) should be used. The Guideline Development Team agreed with this.

After birth, ongoing pharmacological intervention in women with gestational diabetes should not be required. Capillary monitoring of maternal fasting and postprandial blood glucose should continue until values normalise. If there are continuing abnormal blood glucose values, the Guideline Development Team felt that it would be appropriate to refer to the medical team. The Guideline Development Team considered that following birth the woman should continue with a healthy, balanced diet and physical activity as recommended in early pregnancy.

Recommendation	Strength of recommendation or good practice point (GPP)
19 Encourage women diagnosed with gestational diabetes to start breastfeeding and have skin to skin contact as early as possible after birth (preferably within one hour).	GPP
20 Encourage mothers diagnosed with gestational diabetes to feed their infants frequently (every two to three hours) during the first 48 hours after birth.	GPP
21 Measure the infant's plasma glucose at one to two hours of age, four hours, and then four hourly, preferably before feeds, until there have been three consecutive readings > 2.6 mmol/L.*	GPP
22 For infants with blood glucose levels < 2.6 mmol/L: • offer supplementary breastfeeds where possible • if blood sugar levels remain < 2.6 mmol/L for two consecutive readings one hour apart, refer the infant to the neonatal team • if any reading is ≤ 2.0 mmol/L, refer immediately to the neonatal team.	GPP
23 Monitor the blood glucose of women who have been diagnosed with gestational diabetes before breakfast (fasting blood sugar) and two hours after meals for 24 hours after delivery. Refer to the medical team if values are between 7 mmol/L and ≥ 11 mmol/L on two consecutive occasions. If blood glucose levels are within normal range, stop monitoring after 24 hours.	GPP
24 Discontinue diabetes medication for women with a diagnosis of gestational diabetes at birth.	GPP

Note: * An appropriately sensitive method, such as the glucose oxidase method, should be used to test for neonatal hypoglycaemia. Accucheck is not sensitive enough and should not be used to measure neonatal blood glucose.

Chapter 8: Information women with gestational diabetes should receive after birth

8.1 Background

The evidence presented here is a narrative review. It covers breastfeeding, contraception and family planning, lifestyle and dietary advice and postpartum screening.

8.2 Breastfeeding

8.2.1 Benefits for the infant/child

The benefits to the infant gained from breastfeeding from women with gestational diabetes and/or diabetes are globally recognised (Canadian Diabetes Association 2008; NICE 2008; International Diabetes Federation 2009; Health Service Executive 2010; SIGN 2010; Wisconsin Department of Health Services 2012).

Cohort studies have found an association between fetal exposure to gestational diabetes and later development of type 2 diabetes in adulthood which can be ameliorated by breastfeeding (Gunderson 2007; Canadian Diabetes Association 2008; International Diabetes Federation 2009). Early breastfeeding is associated with the prevention of neonatal hypoglycaemia and stimulation of lactation (NICE 2008; Chertok et al 2009; Health Service Executive 2010; SIGN 2010).

A systematic review of observational studies could not draw any conclusions on the association between breastfeeding and risk of metabolic disorders in the offspring due to the limited and low-quality evidence (Kerlan 2010). Due to the population characteristics, including that participants were mainly Pima Indians, the findings are unlikely to be generalisable to the New Zealand setting.

Breastfeeding appears to reduce the risk of being overweight in the child and the adolescent (Gunderson 2007). Breastfeeding for six months or more (in infants exposed to diabetes in utero) appears to be protective against childhood adiposity (Crume et al 2011, 2012).

A national strategic document on breastfeeding promotes exclusive breastfeeding for the first six months of life to improve infant health, including by reducing the risk of obesity and of developing type 2 diabetes in later life (National Breastfeeding Advisory Committee of New Zealand 2009). The document summarises legislative, policy and national strategic initiatives and interventions to improve breastfeeding in New Zealand (National Breastfeeding Advisory Committee of New Zealand, undated). Currently the New Zealand Ministry of Health does not recommend baby-led weaning and the introduction of solids is not recommended before six months of age (www.health.govt.nz/your-health/healthy-living/food-and-physical-activity/nutrition/baby-led-weaning) (National Breastfeeding Advisory Committee of New Zealand, undated).

8.2.2 Benefits for the mother

A systematic review of observational studies reported equivocal evidence, with some studies showing a decreased risk of type 2 diabetes associated with breastfeeding and others showing no difference (Kerlan 2010). The included studies were limited by their design and, due to the population characteristics including that participants were mainly Latina women, the findings are unlikely to be generalisable to the New Zealand setting.

Three studies identified a protective effect of breastfeeding on the development of type 2 diabetes in women who had been diagnosed with gestational diabetes (O'Reilly et al 2011; Gunderson et al 2012a, 2012b; Ziegler et al 2012). A reduced risk for developing metabolic syndrome was associated with longer duration breastfeeding and was stronger in women with gestational diabetes than for women without gestational diabetes (Gunderson et al 2010).

8.2.3 Antenatal breast milk expression

There is controversy regarding the safety and effectiveness of antenatal breast milk expression. The advantages include the avoidance of using formula milk and reduced risk of neonatal hypoglycaemia (Chapman et al 2013). Infants can still receive colostrum even if they are separated from their mother for clinical reasons in the immediate postnatal period. However, antenatal breast milk expression has been associated with the initiation of preterm labour (Chapman et al 2013).

A systematic review identified two relevant studies (Chapman et al 2013). A low-quality retrospective cohort study reported borderline statistical significance for timing of delivery between the antenatal breast milk expression group and the controls, and for admission to the neonatal nursery. A small randomised pilot study reported that the infants of the antenatal breast milk expression group were more likely to be admitted to the neonatal nursery than controls (30% versus 17%) and of those admitted, 64% of the antenatal breast milk expression group infants were admitted for neonatal hypoglycaemia (Chapman et al 2013). The pilot work concluded that antenatal breast milk expression should not be recommended until an appropriately powered randomised trial has been conducted.

There is a Cochrane systematic review protocol on 'Antenatal breast milk expression by women with diabetes for improving infant outcomes' (East et al) and an ongoing randomised trial 'Diabetes and antenatal milk expressing (DAME): a randomised controlled trial' (ACTRN12611000217909).

8.3 Contraception and family planning

Women with a history of gestational diabetes are at increased risk of gestational diabetes in a subsequent pregnancy and are also at risk for developing persistent abnormal glucose tolerance or type 2 diabetes. Planning of subsequent pregnancies or prevention of unplanned pregnancies is therefore important for the management and health of these women.

There is no evidence of contra-indication to the use of most contraceptive methods (Damm et al 2007) and the World Health Organization reports no restrictions on contraceptives in women with a history of gestational diabetes (Kerlan 2010). Subsequent pregnancies in women with a history of gestational diabetes should be planned where possible in discussion with a health professional (Canadian Diabetes Association 2008) or with pre-conception counselling (NICE 2008; SIGN 2010).

> **Key points**
>
> - There are short- and long-term maternal and infant benefits from breastfeeding.
> - There is currently insufficient evidence for the use of antenatal breast milk expression in women with gestational diabetes.
> - Contraception and family planning are important for maternal health and the wellbeing of future pregnancies.

8.4 Lifestyle and diet

Providing lifestyle and dietary advice is important for the subsequent management and health of women with a history of gestational diabetes due to the increased risk of recurrent gestational diabetes, persistent abnormal glucose tolerance or type 2 diabetes.

Postpartum lifestyle interventions, including advice on weight control, diet and exercise, have been recommended for women who have been diagnosed with gestational diabetes (NICE 2008, 2012; Paulweber et al 2010; SIGN 2010). Effective interventions are resource-intensive, typically involving one-to-one sessions delivered by specialists including highly qualified exercise physiologists, dieticians and behavioural psychologists (NICE 2012).

> **Key points**
>
> - Lifestyle and dietary interventions have been found to prevent or delay the onset of type 2 diabetes in adults at high risk.
> - Weight reduction of 5–7% is sufficient to lower the risk of type 2 diabetes in adults at high risk.
> - Increasing the amount of physical activity done for 30–60 minutes per day reduces the risk of type 2 diabetes in adults at high risk.
> - Increasing dietary fibre intake and reducing fat intake (particularly saturated fat) can help reduce the chances of developing type 2 diabetes.

8.5 Evidence to recommendations

The evidence supports early breastfeeding for beneficial maternal and infant outcomes. The Guideline Development Team recognises that the practice of antenatal breast milk expression is taught by some health professionals in New Zealand. However, some of the members felt there was insufficient evidence to recommend the practice at present. The consensus was that there is currently insufficient evidence to recommend the use of antenatal breast milk expression in women with gestational diabetes outside the clinical trial setting.

Family planning is important in the planning of future pregnancies and ensuring that appropriate monitoring of pregnancies can be initiated for the health of the mother and infant.

The Guideline Development Team recognises that information on lifestyle (diet, exercise and appropriate weight gain) is important throughout the pregnancy and into the postpartum period.

Recommendation		Strength of recommendation or good practice point (GPP)
25	Encourage and support women with gestational diabetes to exclusively breastfeed for a minimum of six months.	GPP
26	Encourage women who are unable to breastfeed, or do not wish to breastfeed, to use donor breast milk before formula milk. The decision should be based on maternal preference.	GPP
27	There is currently insufficient evidence to recommend the use of antenatal breast milk expression for women with gestational diabetes.	GPP
28	Discuss methods of contraception agreeable with the woman and her partner and prescribe contraceptives based on maternal risk factors for cardiovascular disease, in the early postnatal period.	GPP
29	Inform women diagnosed with gestational diabetes of the increased risk of gestational diabetes in a subsequent pregnancy and the increased risk for developing type 2 diabetes.	GPP
30	Inform women (in particular those who are obese or overweight) that they can reduce their risk of recurrent gestational diabetes or type 2 diabetes by maintaining a healthy, balanced diet and increasing physical activity at moderate levels.	GPP

Chapter 9: Postpartum screening in women diagnosed with gestational diabetes

9.1 Background

Postpartum screening allows women with continuing dysglycaemia after birth to be identified (Keely 2012). It has been suggested that only half of women receive any postnatal glucose screening (Keely 2012). Refer to Appendix N, Table 42 for postpartum screening and diagnostic recommendations from guidelines and position statements.

9.2 Systematic review evidence

One systematic review investigated postpartum screening tests for type 2 diabetes in women who had recently been diagnosed with gestational diabetes. The studies were often heterogeneous based on risk of developing type 2 diabetes, time to postpartum testing and different ethnic populations (Bennett et al 2011).

Three studies compared different fasting plasma glucose thresholds as part of the two-hour, 75 g oral glucose tolerance test. They reported a specificity of 98–99% for the oral glucose tolerance test using fasting plasma glucose ≥ 7.0 mmol/L compared with fasting plasma glucose ≥ 7.8 mmol/L as the reference (Bennett et al 2011).

Five studies compared fasting plasma glucose ≥ 7.0 mmol/L with a two-hour, 75 g oral glucose tolerance test (reference standard). The sensitivity for the single fasting plasma glucose ranged from 16–89%. The specificity was fixed at 100%, as all the oral glucose tolerance tests with negative results will necessarily have a fasting blood glucose < 7.0 mmol/L, and it is therefore not possible to have a false positive.

Five studies comparing the fasting plasma glucose ≥ 7.0 mmol/L with a two-hour, 75g oral glucose tolerance test with a fasting threshold of ≥ 7.8 mmol/L and a two-hour plasma glucose > 11.1 mmol/L. These studies consistently reported high specificity of the fasting plasma glucose (range 94–99%) with very few false positives. However, the sensitivities of the fasting plasma glucose alone ranged from 14–100% (Bennett et al 2011).

9.3 Diagnostic cohort studies of HbA1c

In addition to the systematic review, three diagnostic cohort studies investigated the diagnostic accuracy of HbA1c (Appendix N, Tables 43 and 44). There were differences in the conclusions of the three studies. The HbA1c test (alone or in combination with fasting glucose test) lacked diagnostic test accuracy in detecting abnormal carbohydrate metabolism in women who have had gestational diabetes at a mean follow-up of 13 months postpartum (Picon et al 2012). Another cohort study reported that the sensitivity and specificity for HbA1c to diagnose diabetes was 16.7% and 100% at one-year follow-up (Megia et al 2012). The third study reported that at a threshold ≥ 39 mmol/mol, HbA1c was a fair test for detection of abnormal glucose tolerance among women with histories of gestational diabetes (Kim et al 2011).

9.4 Interventions to increase postpartum glucose screening in women who had gestational diabetes

Studies have reported postpartum screening rates in women with gestational diabetes as low as 3–30% (Almario et al 2008; Blatt et al 2011; Hale et al 2012). Screening uptake was found to be lowest in White (14.8%) and African American (16.2%) women and highest in Asian women (19.1%) (Blatt et al 2011). The lack of postpartum screening has also been associated with the test not being requested by the physician (Dietz et al 2008).

Available evidence suggests that postpartum testing by oral glucose tolerance test or HbA1c was conducted in only 63% of women resident in the three district health boards in the greater Auckland region (Winnard and Anderson 2013). Up to 40% or more of women are not receiving adequate postpartum follow-up.

9.4.1 Randomised controlled trial

A single-centre, randomised Canadian trial of 256 women compared sending a postal reminder to the patient, their physician or both with usual care (no reminder). This simple intervention increased screening for diabetes postpartum compared with usual care ($p < 0.05$) from 14.3% to 60.5%. Five times as many women returned for postpartum screening when both they and their physician received a reminder. There were still approximately 40% of women (mainly who had moved out of area) who were not screened (Clark et al 2009).

An implementation study compared a reminder protocol using a letter or telephone call in routine care with no reminder. The proportion of women undergoing postpartum screening was lower than in the randomised trial (28% versus 60%) but the reminder system doubled the screening rate (14% usual care, 28% with reminder) (Shea et al 2011).

9.4.2 Observational studies

A checklist (placed in the woman's notes to remind health care providers to give the laboratory requisition for postpartum screening to the woman, and provide additional written information on the importance of postpartum screening and risk of type 2 diabetes) resulted in a three-fold increase in the odds of being screened postpartum ($p < 0.0001$) although less than half returned for postpartum screening (Lega et al 2012).

A brief (5- to 10-minute) educational counselling session provided by a nurse educator (at 37–38 weeks' gestation) significantly increased the postpartum screening rate (53% versus 33%, $p < 0.001$) compared with a time period when the service was not offered (Stasenko et al 2011).

9.4.3 New Zealand-specific research

Exploratory interviews with practice nurses in Waikato found a lack of understanding of the importance of postnatal screening in women who had been diagnosed with gestational diabetes and a lack of an efficient recall system in primary care. For women with gestational diabetes, the barriers to attending screening were lack of motivation and the need for constant encouragement to complete the oral glucose tolerance test. Laboratory forms were misplaced and women often did not have access to child care at the time of the test.

Simple initiatives were used to increase awareness and uptake of postpartum screening such as a sticker stating 'My mum had GDM' attached to the vaccination records of the Well Child book, a telephone call to the relevant practice nurse to suggest postnatal follow-up, or a letter sent to both the practice nurse and the general practitioner to add the woman's details to the recall register (George 2011).

A follow-up study on 110 women in Northland treated for gestational diabetes found almost one-third (32%) had abnormal glucose results at follow-up (mean 2.4 years) and 60% of those women had diabetes. Uptake of postpartum screening was very low (30%) and the diagnosis of diabetes in half of the women was as a direct result of the study. Of those with abnormal results, 66% were Māori and 95% of those diagnosed with diabetes had required insulin during pregnancy (McGrath et al 2007). After four years' follow-up there had been an increase in the community for testing blood glucose levels one to two years after pregnancy (McGrath and Baldwin 2012). The study highlights the increasing problem of type 2 diabetes following gestational diabetes, in particular for Māori women.

9.4.4 Ongoing studies

A protocol for a randomised trial was identified that aims to compare a Promotora (who will provide education, address barriers to follow-up, remind subjects of their appointments, and call them to reschedule if they miss appointments) with standard postpartum care in the follow-up and prevention of type 2 diabetes in women with gestational diabetes (www.clinicaltrials.gov/ct2/show/NCT00998595).

The DIAMIND trial will use SMS text reminders for women who have had gestational diabetes to return for a test for type 2 diabetes or impaired glucose tolerance at either six weeks or six months postpartum (www.anzctr.org.au ACTRN12612000621819).

Key points

- Women often perceive the 6- to 12-week postpartum oral glucose tolerance test as unpleasant and inconvenient.

- At three months postpartum the diagnosis of diabetes can be made with the HbA1c (single, non-fasting test) as in the general adult population.

- Reminders for women and primary care providers increase the attendance at postpartum screening in women with gestational diabetes.

9.5   Evidence to recommendations

A 75 g oral glucose tolerance test is the most accurate test for diagnosing glucose intolerance (including diabetes) in the first year following a diagnosis of gestational diabetes. HbA1c with a fasting glucose has a reasonable sensitivity and specificity and HbA1c alone has a low sensitivity but good specificity.

However, the postpartum oral glucose tolerance test may not be acceptable for some women (especially breastfeeding mothers) as it requires a fasting blood sugar, an unpleasant tasting glucose drink and up to two hours of waiting with multiple blood samples. Between 30% and 70% of women will not perform the test.

The American Diabetes Association (2012) did not recommend the use of HbA1c as the 6- to 12-week postpartum screening test due to the influence of antepartum treatment of hyperglycaemia. It is more logical to perform the test at approximately three months postpartum.

The use of HbA1c may miss a number of women with lower levels of hyperglycaemia, but will detect women with the highest glucose levels who will require immediate assessment. A fasting glucose can be added (on an individual basis) to increase the sensitivity of the test.

HbA1c is currently used to screen for diabetes in New Zealand in the non-pregnant population. It is likely that more appropriate follow-up and continuing surveillance will be undertaken by the general practitioner if an initial HbA1c is performed. The progression of HbA1c over time is an important concept that is not captured by cross-sectional studies. The initial test is a one-step method that is likely to engage the woman and her general practitioner in the process of regular follow-up testing and review of healthy lifestyle interventions (+/- metformin). The majority of guidelines recommended annual follow-up testing in women with a history of gestational diabetes.

When women are planning another pregnancy, the HbA1c is a useful way of identifying which women are at increased risk of miscarriage or congenital anomaly, because of elevated glucose levels, and who may benefit from pre-pregnancy counselling.

Although interventions to increase postpartum screening are successful, the rates of postpartum screening remain suboptimal. In order to detect and treat women who develop diabetes or impaired glucose tolerance, it is important that they are identified in a timely fashion to prevent future complications associated with the condition. There may be a number of barriers for attendance at postnatal screening and some of these have been identified through qualitative research. Refer to Appendix N, Table 45.

Postpartum screening in women with gestational diabetes provides an opportunity to identify women with undiagnosed diabetes and to commence surveillance of a specific group of individuals at increased risk of developing diabetes in the future. Women should be informed through a variety of media about the importance of postpartum screening for diabetes following gestational diabetes. The reasons for non-adherence to postpartum screening in New Zealand may need further exploration.

All health care providers involved in a woman's care should relay consistent messages regarding the need for postnatal screening. A health professional should be identified who is responsible for ensuring that the information is received and that the appropriate laboratory requisition is given to the woman with information about the requirements of the diagnostic test. Reminder systems appear to be a useful method for increasing postpartum screening rates.

	Recommendation	Strength of recommendation or good practice point (GPP)
31	For all women diagnosed with gestational diabetes, their lead maternity carer or diabetes clinic in the postnatal review should provide printed information about the importance of postpartum screening and the risk of developing type 2 diabetes.	CONDITIONAL
32	Remind all women with gestational diabetes and their primary care provider (at the time of hospital discharge) of the need to participate in screening at three months after birth and annually thereafter.	CONDITIONAL
33	The primary care provider of women with gestational diabetes should offer screening for type 2 diabetes at three months postpartum using HbA1c. If the value is: • ≤ 40 mmol/mol, the result is normal. Repeat the test in one year • 41–49 mmol/mol (prediabetes or impaired fasting glucose), advise on diet and lifestyle modification. If the woman is over 35 years, a full cardiovascular risk assessment and appropriate management are indicated. Repeat test after six months • ≥ 50 mmol/mol and symptomatic 'diabetes', refer to medical specialist • ≥ 50 mmol/mol and asymptomatic, repeat HbA1c or fasting plasma glucose.*	GPP
34	The primary health organisation performance programme should be used to encourage primary care practitioners to record postpartum gestational diabetes screening.	GPP

Note: * Two results above the diagnostic cut-offs are required for diagnosis of diabetes if the woman is asymptomatic.

Chapter 10: Type 2 diabetes in women diagnosed with gestational diabetes

10.1   Background

There is an increased risk for women with a history of gestational diabetes to develop diabetes over time. Women with a history of gestational diabetes comprise an increasing proportion of the population. Identification of potentially modifiable risk factors that are indicative of significantly increased risk of developing type 2 diabetes may be useful in targeting prevention strategies.

10.2   Prevalence of type 2 diabetes in women diagnosed with gestational diabetes

Evidence is based on systematic reviews within two clinical guidelines and 20 additional observational studies. Refer to Appendix O, Table 46.

The risk of recurrence of gestational diabetes in subsequent pregnancies ranges between 30% and 84% following the index pregnancy (75% for women who were treated with insulin). The risk of developing type 2 diabetes ranges from 2.6–70% over time with the greatest risk occurring within five years of the index pregnancy (NICE 2008).

One of the strongest predictors of type 2 diabetes postpartum was elevated intrapartum fasting plasma glucose levels. Lean women (under 30 years of age) who received insulin therapy during pregnancy were more likely to develop type 1 diabetes postpartum (Canadian Diabetes Association 2008).

10.3   Prevalence of type 2 diabetes in early postpartum period (5–16 weeks)

Abnormal glucose tolerance in the early postpartum period (up to four months after delivery) was reported in six observational studies (refer to Appendix O, Table 46). The incidence of diabetes ranged from 1.3% (Ogonowski and Miazgowski 2009) to 18.8% (Rivas et al 2007). The percentage of women with impaired fasting glucose or impaired glucose tolerance ranged from 2.2% (Ogonowski et al 2009) to 44.8% (Kim et al 2011). The studies vary in the diagnostic criteria used, populations and the percentage of women that returned for postpartum screening.

10.4 Prevalence of type 2 diabetes (six months to five years)

Abnormal glucose tolerance from six months to five years after delivery was reported in six observational studies (Appendix O, Table 46). The incidence of type 2 diabetes ranged from 1.1% (Lawrence et al 2010) to 37% (Oldfield et al 2007); the incidence of impaired glucose tolerance or impaired fasting glucose ranged from 16.3% (Lawrence et al 2010) to 22% (Madarasz et al 2009). There is variation in diagnostic criteria, the populations included and the percentage of women that returned for postpartum screening.

10.5 Prevalence of type 2 diabetes after five or more years' follow-up

Abnormal glucose tolerance of any type after five or more years of follow-up was reported in seven observational studies (Appendix O, Table 46). The incidence of type 2 diabetes ranged from 1.3% (Pirkola et al 2010) to 33% (in a migrant population) (Girgis et al 2012). The incidence of impaired fasting glucose or impaired glucose tolerance ranged from 15% (in a migrant population) (Girgis et al 2012) to 48.1% (Malinowski-Polubiec et al 2012).

Two studies reported an increased risk of developing diabetes even in women who had abnormal glucose tolerance during pregnancy but did not meet the diagnostic criteria for gestational diabetes (Carr et al 2008; Retnakaran et al 2010).

10.6 Gestational diabetes as a risk factor for developing type 2 diabetes

The evidence is based on three systematic reviews (Canadian Diabetes Association 2008; NICE 2008; Bellamy 2009) and 21 observational studies (Oldfield et al 2007; Rivas et al 2007; Carr et al 2008; Hossein-Nezhad et al 2009; Madarasz et al 2009; Ogonowski et l 2009; Schaefer-Graf et al 2009; Chodick et al 2010; Ekelund et al 2010; Lawrence et al 2010; McClean et al 2010; Pirkola et al 2010; Retnakaran et al 2010, 2011; Kim et al 2011; Lee et al 2011; Girgis et al 2012; Malinowski-Polubiec et al 2012; Mukerji et al 2012; Tehrani et al 2012; Wang et al 2013).

The risk estimate for developing type 2 diabetes in women with a history of gestational diabetes ranged from 1.16–7.7 (Carr et al 2008; Bellamy et al 2009; Chodick et al 2010; Lee et al 2011; Retnakaran et al 2011; Wang et al 2013).

10.7 Other risk factors associated with developing type 2 diabetes in women diagnosed with gestational diabetes

The evidence is based on three systematic reviews (NICE 2008; Nicholson et al 2008; Golden et al 2009) and 20 additional observational studies (Appendix O, Table 47). Data are not pooled in a meta-analysis due to the high likelihood of heterogeneity from different populations and diagnostic thresholds.

The limited evidence suggests later development of type 2 diabetes in women diagnosed with gestational diabetes is associated with:

- overweight/obesity before, during and after pregnancy
- insulin requirement during the index pregnancy (risk estimates range between OR 1.57 and 4.67)
- high diagnostic test levels for gestational diabetes in the index pregnancy
- an abnormal postpartum glucose tolerance test (effect estimates < 2.5)
- increasing parity or short inter-pregnancy intervals (a four-fold increased risk; women aged 30 years and over had a five-fold increased risk)
- a family history of diabetes (estimates ranged from a four- to nine-fold increased risk)
- other risk factors that were identified in a limited number of studies.

There is growing evidence to suggest that the risk of developing type 2 diabetes is increased for women with an abnormal screening glucose but normal oral glucose tolerance test ($p < 0.0001$) (Retnakaran et al 2010, 2011). In particular, women who are overweight have up to an almost 13-fold increased risk (Pirkola et al 2010).

10.8 Summary of evidence

The cumulative risk of developing type 2 diabetes has been estimated to be as high as 50% depending on ethnicity and time from index pregnancy. The risk of developing type 2 diabetes in women with a history of gestational diabetes is estimated to be 6–8 times higher than it is in those with no history of gestational diabetes. The evidence identified a number of key risk factors for developing type 2 diabetes in women diagnosed with gestational diabetes.

Continued intensive surveillance of women with a history of gestational diabetes is important for early detection and treatment of diabetes. Identification of women with risk factors is important in initiating any prevention or surveillance intervention. A lack of long-term follow-up in women with gestational diabetes may mean that a high proportion of women have undiagnosed diabetes.

Risk factors contributing to development of type 2 diabetes in women with gestational diabetes are:

- previous or current history of gestational diabetes
- postpartum overweight or obesity
- disease severity in index pregnancy
- increasing maternal age
- family history of diabetes.

Other risk factors contributing to development of type 2 diabetes in women with gestational diabetes are:

- pre-pregnancy overweight or obesity
- high diagnostic glucose levels
- high glucose levels during pregnancy
- early gestational age at diagnosis of gestational diabetes
- elevated postpartum oral glucose tolerance test.

Chapter 11: Prevention of type 2 diabetes in women diagnosed with gestational diabetes

11.1 Background

As identified in Chapter 10, women with a history of gestational diabetes are at increased risk of gestational diabetes in a subsequent pregnancy and at risk for developing persistent abnormal glucose tolerance or diabetes. This chapter looks at the evidence for preventing type 2 diabetes in women with previous gestational diabetes using lifestyle and/or pharmacological interventions. Population- and community-level interventions were not included in the literature search.

11.2 Lifestyle interventions

The evidence identified is mainly indirect. The American Diabetes Association (2013) recommends lifestyle interventions to be targeted towards people at high risk for developing type 2 diabetes. The Diabetes Prevention Program randomised participants to either standard lifestyle and placebo, or metformin (an oral hypoglycaemic) or an intensive lifestyle intervention (Ratner et al 2008; refer to Appendix P, Table 48). The authors estimate that only five to six women would need to be treated over three years with either metformin or intensive lifestyle intervention to prevent one case of diabetes. In women without a history of gestational diabetes, the estimated numbers needed to treat to prevent a single case of diabetes over three years are 24 for metformin and 9 for intensive lifestyle intervention (Ratner et al 2008).

Women with a history of gestational diabetes were less able to sustain the prescribed level of physical activity, resulting in a significantly lower weight loss over time than women without a history of gestational diabetes. Weight loss was strongly associated with a reduced risk of diabetes in the Diabetes Prevention Program trial (Ratner et al 2008).

There is a reduction of over 50% in the risk of type 2 diabetes following structured lifestyle interventions in the high-risk groups (refer to Appendix P, Table 49; for details of the goals in the included trials, refer to Appendix P, Table 50). The interventions used behaviour-change strategies to increase physical activity, encourage healthy eating and maintain healthy body weight (NICE 2012). Interventions were resource-intensive and relied on specialised health professionals (NICE 2012).

The evidence highlighted the importance of identifying people at risk of developing type 2 diabetes using a stepped approach (validated risk-assessment score and a blood test); and providing those at high risk with a quality-assured, evidence-based, intensive lifestyle change programme to prevent or delay the onset of type 2 diabetes (NICE 2012).

The European evidence-based guideline for the prevention of type 2 diabetes (EURO) provides advice about public health strategies to prevent type 2 diabetes; the recommendations include advice on screening and interventions (Paulweber et al 2010). The guideline provides recommendations on lifestyle interventions for all adults with a high risk of developing type 2 diabetes (gestational diabetes is one risk factor). Refer to Appendix P, Box 1.

Systematic review evidence found that combined exercise and dietary interventions reduced the risk of diabetes compared with standard recommendations by 37%. No statistically significant effects on diabetes incidence were observed when comparing exercise-only interventions either with standard recommendations or with diet-only interventions (Orozco et al 2008).

A pilot trial found no significant differences in fasting plasma glucose and two-hour glucose values between the control (written information) and intervention (web-based pedometer) groups (Kim et al 2012).

Two trials focused on reducing risk factors. A small, multicentre, pilot randomised controlled trial from Australia compared telephone-based motivational interviewing with standard care in 28 rural-based women with previous gestational diabetes. The intervention group significantly reduced total fat intake, total carbohydrate intake and glycaemic load. They increased leisure physical activity, although there was no significant change in total physical activity levels, and significantly reduced their body mass index compared with the control group (Reinhardt et al 2012). A second pilot trial examined a postpartum lifestyle intervention adapted from the Diabetes Prevention Program (Ferrara et al 2011). The proportion of women who reached the postpartum weight goal was higher in the intervention condition, although not to a level of statistical significance, than among usual care (absolute difference 16.1%). The intervention was more effective among women who did not exceed the recommended gestational weight gain. The intervention significantly decreased dietary fat intake more than the usual care (p = 0.002). No differences in postpartum physical activity were observed between conditions.

A one-year (interim) report on the feasibility of a lifestyle intervention programme found no significant differences in changes in fasting glucose and two-hour glucose after an oral glucose tolerance test. During the first year, average body weight loss was significantly higher in the intervention group compared with the control group (p = 0.001), and the decrease was more significant among baseline overweight women in the intervention (body mass index ≥ 24 kg/m^2) compared with that in the control group (p < 0.001) (Hu et al 2012).

Key point

- Lifestyle interventions may be useful in preventing type 2 diabetes in women who have had gestational diabetes but they require motivation from the individual and are resource intense.

11.3 Pharmacological treatment to prevent type 2 diabetes

The Guideline Development Team has not considered any pharmacological interventions that have been withdrawn from the market.

Five systematic reviews (indirect evidence) reported on pharmacological interventions for preventing type 2 diabetes. The Diabetes Prevention Program trial (Appendix P, Table 48) reported that both intensive lifestyle and metformin therapy reduced the incidence of diabetes by approximately 50% compared with the placebo group, whereas this reduction was 49% for intensive lifestyle intervention and 14% for metformin therapy in parous women without gestational diabetes (Ratner et al 2008).

Meta-analyses of pharmacological treatments for people with impaired glucose tolerance (refer to Appendix P, Table 51) found benefits in the reduction of type 2 diabetes using oral diabetes drugs and anti-obesity drugs (Jones et al 2011; NICE 2012).

Metformin was recommended for adults at high risk of type 2 diabetes whose blood glucose measure (fasting plasma glucose or HbA1c) showed progression towards type 2 diabetes, despite their participation in an intensive lifestyle-change programme, and for those who were unable to participate in lifestyle-change programmes because of a disability or for medical reasons. Orlistat was recommended in those with a body mass index > 28 kg/m² (NICE 2012).

EURO provides recommendations on pharmacological interventions for all adults with a high risk of developing type 2 diabetes (Paulweber et al 2010). Refer to Appendix P, Box 2.

A mixed-treatment comparison meta-analysis of oral anti-diabetic agents for the prevention of type 2 diabetes in high-risk individuals (including 20 trials) found that thiazolidinediones, alpha-glucosidase inhibitors and biguanides significantly reduced the relative risk of developing diabetes by 64%, 40% and 27%, respectively, compared with control. Thiazolidinediones significantly reduced the relative risk of diabetes by 50% compared with biguanides and trended towards a 40% risk reduction compared with alpha-glucosidase inhibitors (Phung et al 2011).

A Cochrane systematic review of oral anti-diabetic agents for women with pre-existing diabetes mellitus/impaired glucose tolerance or previous gestational diabetes failed to identify any suitable trials, highlighting a large gap in the research available to guide clinical practice (Tieu et al 2010a).

Key point

- Metformin may be a useful treatment in women who have had gestational diabetes and who continue to have impaired glucose tolerance despite lifestyle interventions, especially if they are planning another pregnancy.

11.4 Ongoing studies

The following trials in progress were identified:

- Metformin in the prevention of gestational diabetes: The MPG Trial (ACTRN12610000157077)
- The effect of a group behaviour intervention program on preventing diabetes pregnancy from progressing to type 2 diabetes: macrolevel system change in South Australia and Victoria (ACTRN12610000338066)
- Walking for Exercise and Nutrition to prevent Diabetes for You (WENDY) (ACTRN12611000075987, NCT01247753)
- An evaluation of Croí MyAction community lifestyle modification programme compared with standard care to reduce progression to diabetes/prediabetes in women with prior gestational diabetes mellitus (GDM): study protocol for a randomised controlled trial (Trials ISRCTN41202110).

11.5 Evidence to recommendations

The risk of developing type 2 diabetes can be reduced by either lifestyle or pharmacological interventions. However, evidence is based on a general population at risk of developing diabetes rather than women who have been diagnosed with gestational diabetes.

The direct evidence of lifestyle and pharmacological interventions in women with a history of gestational diabetes is limited to one trial (Ratner et al 2008).

More research is needed to guide clinical practice, particularly in regard to pharmacological treatment and any potential for harm. Randomised controlled trials with long-term follow-up are required to determine the effectiveness of lifestyle interventions for women with a history of gestational diabetes.

The Guideline Development Team agreed that the primary focus for preventing type 2 diabetes needs to be on lifestyle interventions and acknowledged the potential role of green prescriptions in women with high risk of developing diabetes.

Recommendation	Strength of recommendation or good practice point (GPP)
35 Consider metformin in women (with previous gestational diabetes) who have HbA1c 41–49 mmol/mol and who are not successful with lifestyle modification (in particular those planning another pregnancy).	CONDITIONAL
36 Provide women diagnosed with gestational diabetes with lifestyle and dietary advice and advise on how to maintain a healthy weight.	CONDITIONAL
37 Inform women with a previous diagnosis of gestational diabetes and/or prediabetes of the risk of gestational diabetes and offer early pre-pregnancy screening for diabetes when they are planning future pregnancies.	GPP
Research recommendation: Randomised controlled trials that evaluate the outcomes of lifestyle versus pharmacological interventions to prevent type 2 diabetes in women with a previous history of gestational diabetes.	

Chapter 12: Cost-effectiveness of screening, diagnosis and treatment of gestational diabetes

12.1 Background

Health care decisions are made within a constrained health care budget. The decision to fund a screening programme or treatment uses scarce resources which have competing uses. Cost-effectiveness analysis is a form of economic analysis that compares the relative costs and outcomes (effects) of two or more courses of action.

12.2 Systematic review evidence

A systematic review of the cost-effectiveness literature was used to develop a single cost-effectiveness model addressing screening, diagnosis and treatment for gestational diabetes in the United Kingdom (NICE 2008).

The review included one French study that recommended high-risk screening and an Italian study that found universal screening was more costly than the selective screening approach per case of gestational diabetes diagnosed. No incremental analysis was reported and the review authors concluded that screening using either strategy was justified.

A cost analysis study recommended the use of universal fasting plasma glucose or giving an oral glucose challenge test to those over the age of 25 years and with risk factors. Fasting plasma glucose detected an additional 6009 cases at a cost of £489 per additional case detected when compared with oral glucose challenge test. A strategy of universal oral glucose tolerance test was predicted to detect an additional 1493 cases compared with the universal fasting plasma glucose, at a cost per additional case detected of £4,665.

Four studies reported the estimated cost per case of gestational diabetes detected. One of the studies recommended risk factor-based screening; it involved screening women aged over 25 years using a 50 g, one-hour oral glucose challenge test. Another study recommended universal screening in a high-prevalence population, with a cost per case diagnosed of US$80.56. These two studies did not report incremental analysis. Two studies made no conclusion on the cost-effectiveness of either approach.

12.2.1   Cost-effectiveness models for screening

The National Institute for Health and Care Excellence diabetes in pregnancy and antenatal guideline development group developed a single cost-effectiveness model addressing screening, diagnosis and treatment for gestational diabetes. All screening methods, including risk factor-based screening, screening blood tests and universal diagnostic tests, were considered (in isolation and combinations of tests). Twenty-one screening strategies were considered in total (NICE 2008).

Costs appear to be based on 2006 prices and were based on outcomes from an Australian treatment trial of mild gestational diabetes (Crowther et al 2005). Additional probabilities, costs and utilities were derived from National Health Service data and other identified literature. The model is based on a disease prevalence of 3.5% which is lower than the prevalence in New Zealand.

The model was analysed from a National Health Service perspective and assumes that women are more likely to accept a test if they have already been identified as being at higher risk, either by risk factors or a previous screening test. The model included an assumption that the two-hour oral glucose tolerance test is 100% sensitive and specific. Cost-effectiveness was measured as the incremental cost-effectiveness ratio which is the amount we are willing to pay for each unit of improved quality of life.

The model favoured two screening strategies on dominance grounds. Screening for gestational diabetes based on risk factors other than age was recommended. The consensus view was that advanced maternal age should not be used as a risk factor because this would result in most pregnant women receiving a diagnostic test. The two-hour 75 g oral glucose tolerance diagnostic test was recommended using the criteria defined by the World Health Organization (NICE 2008).

A United States study analysed the cost-effectiveness of adopting the International Association of Diabetes and Pregnancy Study Groups' diagnostic criteria (Appendix I, Table 17) (Werner et al 2012).The model compared the cost-utility of three strategies to diagnose gestational diabetes. The International Association of Diabetes and Pregnancy Study Groups' diagnostic criteria are cost-effective only when postpartum care reduces diabetes incidence. The proposed International Association of Diabetes and Pregnancy Study Groups' diagnostic criteria are expected to increase costs by US$125.6 million (Werner et al 2012).

Another cost analysis study from the United States investigated the cost-effectiveness of gestational diabetes screening using the International Association of Diabetes and Pregnancy Study Groups' guidelines from a societal perspective (Mission et al 2012). The United States model compared routine screening using a two-hour oral glucose tolerance test with the one-hour oral glucose challenge test. All probabilities, costs and benefits were derived from the literature. This study found that screening with the two-hour oral glucose tolerance test was more expensive, more effective, and cost-effective at US$61,503 per quality adjusted life year. The more inclusive diagnostic approach of the International Association of Diabetes and Pregnancy Study Groups remained cost-effective as long as ≥ 2% of women were diagnosed and treated for gestational diabetes.

One study extended the National Institute for Health and Care Excellence (2008) guidance (Round et al 2011). This study estimated the cost-effectiveness of eight strategies for screening for gestational diabetes (including no screening) with respect to the level of individual patient risk from a National Health Service perspective. When gestational diabetes risk is < 1%, then the no screening/treatment strategy is cost-effective; where risk is between 1.0% and 4.2% fasting plasma glucose followed by oral glucose tolerance test is most likely to be cost-effective; and where risk is > 4.2%, universal oral glucose tolerance test is most likely to be cost-effective. However, acceptability of the test alters the most cost-effective strategy.

The best screening strategy for gestational diabetes is dependent on individual risk and the acceptability of the tests used. If a woman's individual risk of gestational diabetes could be accurately predicted, then health care resource allocation could be improved by providing an individualised screening strategy (Round et al 2011).

12.2.2   Cost-effectiveness models for treatment

The cost-effectiveness model for screening informed the probabilities attached to given patient treatment pathways for gestational diabetes in the National Institute for Health and Care Excellence guideline. The cost analysis of different treatment options (analogue insulin, glibenclamide and metformin) for gestational diabetes utilised a cost minimisation approach (NICE 2008). This approach was considered appropriate given that the interventions have been shown to be equally efficacious.

Costs were based on the same trial as the screening model (Crowther et al 2005). The model assumes that women start with dietary treatment, and those who do not achieve adequate glycaemic control after 10 days would be started on pharmacological therapy. The model addresses a possible differential in the hypoglycaemic risk between the different treatments. Oral hypoglycaemics were considerably cheaper than analogue insulin (NICE 2008).

A study from the United States investigated the cost-effectiveness of treating mild gestational diabetes (Ohno et al 2011). The model simulated a cohort of women with mild gestational diabetes and divided them into a treatment and no treatment arm. The model was based on data derived from an American trial (Landon et al 2009). Treating gestational diabetes is more expensive at US$12,623 than US$12,167 for no treatment but is more effective as shown by higher-quality adjusted life years at 56.891002 versus 56.868753 for no treatment. The incremental cost per quality adjusted life year is cost-effective (below the cost-effectiveness threshold of US$100,000 per quality adjusted life year) at US$20,412 per quality adjusted life year (Ohno et al 2011).

A cost analysis of the Australian trial of treatment for mild gestational diabetes (Moss et al 2007) took the perspective of the health system and its patients (direct and indirect costs). For every 100 women offered treatment for mild gestational diabetes in addition to routine obstetric care, AU$53,985 additional direct costs were incurred at the obstetric hospital, AU$6,521 additional charges were incurred by women and their families, 9.7 additional women experienced induction of labour and 8.6 more babies were admitted to a neonatal nursery. However, 2.2 fewer babies experienced serious perinatal complication and 1.0 fewer babies experienced perinatal death. The incremental cost per additional serious perinatal complication prevented was AU$27,503, per perinatal death prevented was AU$60,506 and per discounted life-year gained was AU$2,988. The authors concluded that over the whole lifespan, the incremental cost per extra life-year gained was highly favourable.

12.2.3 Cost-effectiveness of screening and treatment

Another study (piloted in India and Israel) assessed the cost-effectiveness of gestational diabetes screening and lifestyle change for the prevention of type 2 diabetes (Lohse et al 2011). The costs evaluated included direct service delivery costs and indirect costs such as general administration activities. The model calculated the cost-effectiveness ratio per disability adjusted life year.

The authors concluded that gestational diabetes screening and postpartum lifestyle management are either cost saving or have a net cost but an attractive cost-effectiveness ratio. Universal screening of pregnant women followed by postpartum lifestyle management yielded net savings of US$78 per woman with gestational diabetes in India and US$1,945 per woman in Israel. The estimated disability adjusted life years averted were 2.33 in India and 3.10 in Israel. With lower gestational diabetes prevalence, intervention efficacy and type 2 diabetes incidence, the intervention had a net cost in India, with a cost per disability adjusted life year averted, of US$11.32. This was below the WHO definition of 'very cost-effective', set at annual gross domestic product per capita.

12.3   Summary of evidence

Three of the cost-effectiveness studies that were identified favoured risk factor-based screening, four studies recommended a universal approach and two studies recommended either strategy. A cost-effectiveness analysis from the United Kingdom concluded that the best strategy of screening for gestational diabetes is dependent on the underlying risk of each individual and the acceptability of the tests used.

When considering universal versus risk factor-based screening, the cost of detecting the additional cases needs to be considered alongside the incremental benefit. The more women that are screened for gestational diabetes, the higher the number of false positives. It is necessary to consider the cost of providing treatment and the potential for unnecessary anxiety experienced by women falsely diagnosed with gestational diabetes. Section 3.4 highlighted the concerns about potentially missing women with gestational diabetes when risk factor screening was used in New Zealand. This strategy is of particular concern where women with previously undiagnosed diabetes but no apparent risk factors are not screened.

The results of international cost-effectiveness studies are not immediately generalisable to the New Zealand context. Setting-specific differences in price weights and medical service use are important, and different morbidity and mortality patterns also justify consideration.

Another issue to consider is the generalisability of the modelling to the New Zealand demographic. The gestational diabetes prevalence of the National Institute for Health and Care Excellence model was estimated at 3.5%. New Zealand's prevalence is thought to be approximately 5.1%.[6] The prevalence of gestational diabetes also varies in different regions of New Zealand (Appendix E, Table 1) and the prevalence is affected by the screening practices of those regions. This is potentially important as it influences the trade-off between the detection of gestational diabetes and false positives. The results suggested that varying the prevalence over a range of three percentage points (to 5% prevalence) had little impact on the cost-effectiveness conclusions of the model (NICE 2008).

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[6]   National Maternity Collection 2012, Ministry of Health.

The United States cost-effectiveness model found a one-step screening process was only cost-effective as compared with no screening when postpartum care reduces the incidence of diabetes. Two of the United States cost-effectiveness studies modelled the benefits of lifestyle changes alongside the benefits of screening for gestational diabetes. These benefits were often derived from intensive lifestyle modification programmes, which are not currently offered to women with gestational diabetes in New Zealand.

Chapter 13: Interviews with women with gestational diabetes

Interviews were conducted with women diagnosed with gestational diabetes during a pregnancy in order to find out more about the experience of having gestational diabetes. The results of these interviews are described below. Also summarised are the findings from similar studies recently conducted in New Zealand.

A narrative review of a limited number of qualitative studies was undertaken to summarise the literature describing women's perception of gestational diabetes. The studies were not critically appraised or summarised in evidence tables.

13.1 Interviews with women diagnosed with gestational diabetes

Interviews were conducted as part of the guideline development process to provide the consumer perspective on:

- knowledge about gestational diabetes
- experiences of diagnosis and treatment
- what could be improved
- where women got their information from.

The data from the interviews were non-identifying. Two women were interviewed from the rural North Island and five women from Auckland City. There were four Māori women and one European, one Samoan and one Asian woman. Three women were having their first pregnancy and one woman was in her sixth pregnancy.

13.1.1 Knowledge of gestational diabetes

When a pregnant woman is diagnosed with gestational diabetes, there is a lot of new information to try to understand including the causes of gestational diabetes, and the effects on the mother and infant. The women that were interviewed showed varying levels of understanding about gestational diabetes (Table B).

Table B: Participants' knowledge of gestational diabetes

Gestational diabetes is caused by …	Gestational diabetes isn't good for mothers because …	Gestational diabetes isn't good for babies because …
• Diet and family history • Sugar levels • Too much sugar is not good • Not clear why the body develops more insulin • Not really sure	• It isn't good for the baby • You can't have a home birth • It makes the baby too big • When my blood sugar goes up, the baby's goes up too • I can't eat whatever I want	• Problems with brain development • Baby could stop growing OR get too fat • The sugar increases their insulin and they could go into shock • Baby gets too big too quickly

Women were asked if there was anything about gestational diabetes that they did not understand. Most of the women felt comfortable with what they knew, and felt that they had learnt a lot during their pregnancy. One person made the comment that she had enough information and knew there were some things she was doing that were 'wrong'. Another woman continued to pretend she didn't have gestational diabetes.

There were some additional responses that highlight potential gaps in care. One woman did not know whether the medication during pregnancy would have any long-term effects on her children. Another woman felt that the whole picture of treatment and the care pathway were not clearly described:

> No one explains the whole picture about what could happen and what sort of monitoring is required. So you have to go away and read about it at home. They give you an information pack but it is pretty baffling. It was easier to go home and find out more on the internet.

13.1.2 Experience of diagnosis

Most of the women were diagnosed with gestational diabetes at 20 weeks, one woman was diagnosed at 28 weeks, and one woman was diagnosed 6 weeks before the birth. Overall, the women found that the diagnostic tests were easy to do, but one woman stated that they 'took a long time' (two hours) and another stated that the glucose drink 'tasted awful'.

The diagnosis changed everything for a couple of women. They felt more isolated and different, forced into a separate channel away from other pregnant women.

On the whole, most felt there was no judgement or negativity from the person providing the diagnosis. One woman thought that the midwife saw her as more of a nuisance because she was more complicated to manage. Another woman was pleased to have a team of people caring for her and supporting her.

13.1.3 Experience with appointments

Attending appointments for gestational diabetes takes a lot of extra time for the women. The time commitment reported ranged from one day a fortnight to an afternoon a fortnight. This means more time off work, reduced income, and increased costs of travel to appointments and of child care. This is especially an issue for women living in rural areas.

Some district health boards have multidisciplinary team appointments. Here the woman with gestational diabetes is present while several health practitioners discuss her options for treatment or care. One woman found this experience unpleasant and would have felt more supported if her midwife had been present:

> … When I got there I went into a room with about five or six people – it was really unfriendly – they talked about me not to me. They tell you what to do but spend most of the time talking to each other. You don't get told you can take along a support person and your midwife isn't always there.

13.1.4   Experience of treatment

Women with gestational diabetes are often required to keep a food diary and monitor their blood glucose levels using finger-prick testing (self-monitoring). Self-monitoring was described as easy, but sometimes painful:

> … After several weeks of finger-prick testing your fingers get really sore – so sore you hate doing the tests. Plus you don't want to do the finger-prick tests because it might give you an answer you don't want.

One person experienced additional personal costs as she purchased the needles for finger-prick testing. Another person was not clear what to do if she got consecutively high readings.

The treatment for gestational diabetes often involves taking oral hypoglycaemic drugs and/or insulin injections. Two people described the oral hypoglycaemic agent metformin as easy to take. Insulin injections were described as unpleasant:

> I have to inject the insulin into my tummy. It is very unpleasant and it is hard to do and my stomach gets covered in bruises.

> Using insulin is sore and it is embarrassing using it at work – you need to do it in private but it isn't always possible.

13.1.5   Lifestyle interventions

Women with gestational diabetes are encouraged to change their dietary and exercise habits. The women generally knew which foods to eat and which ones to avoid; two women also discussed the importance of portion size. There was some concern about how much to eat and some anxiety about not undernourishing the baby. Two women observed that making changes to diet was easier than increasing physical activity. Some of the women were already very busy and had other children to care for, making it hard for them to get out and about. One woman had been going swimming but found that she was getting very tired. Two women who were already very active continued their high levels of activity.

13.1.6   Information and follow-up

During the interviews, women with gestational diabetes were asked if there was any information that would have made things easier for them, and if there was anything that could have been done differently that would have improved their experience.

The women suggested they would like to receive advice regarding reliable internet sites and educational videos that explained what to expect along the treatment and care pathway. One woman spoke English as a second language and would have found it easier to read about the condition in her own language. Another woman mentioned text messaging as a useful way to remind her to watch what she was eating.

13.2   New Zealand health literacy report

Workbase recently conducted a health literacy research project for the Ministry of Health (Workbase 2014). The final report for the project has not been completed and these interim results are subject to change. The objective was to identify interventions or approaches that are effective in strengthening health literacy to enable better understanding and management of gestational diabetes in New Zealand.

Māori women, particularly young women aged up to 24 years, were the focus for the project. Screening rates for gestational diabetes are extremely low for Māori women, at 30% nationally compared with 70% for non-Māori, even though Māori women are at higher risk of gestational diabetes (Yappa and Simmons 2000).

Interviews were carried out with nine midwife lead maternity carers, five maternity service and diabetes specialists, as well as 26 Māori women and their whānau. There were also 114 responses to a survey of midwife lead maternity carers associated with the New Zealand College of Midwives and nine responses to a survey of primary health organisations and district health boards.

13.2.1   Interviews with women receiving antenatal care

Pregnant or recently pregnant women were interviewed about their experiences of antenatal care, their decision to be screened for gestational diabetes, their knowledge of gestational diabetes and their experiences of managing gestational diabetes. The majority of women interviewed were Māori and under 24 years of age. Of these women, 21 had completed a glucose challenge test, and five had also completed an oral glucose tolerance test, with four being confirmed with gestational diabetes. Five women had not been screened.

Women who were screened for gestational diabetes did so based on advice from their lead maternity carer. Unless they had experienced gestational diabetes in a previous pregnancy, the women had little understanding of gestational diabetes before or after being tested, but understood they might be at risk for a variety of reasons, such as a family history of diabetes.

Women discussed their reasons for not being tested and their attitudes towards testing and pregnancy. Two women reported avoiding or declining every test during pregnancy because they considered tests to be largely unnecessary. They had experienced healthy pregnancies before and felt their current pregnancies to be similar. These women did not complete other second trimester blood tests. Each woman was monitoring the size and growth of their baby as the main indicator of baby health.

Two women who consented to, but did not complete, screening could not describe the consequences of gestational diabetes. These women made no explicit decision not be tested, but testing never became a priority for them. One young woman did not have the test because her mother (who was also pregnant at the same time) declined the test.

Within the population of young Māori women who are not being screened for gestational diabetes, there are those choosing not to be screened, nor to access antenatal care, based on their experience and knowledge of pregnancy. However, there is also a substantial proportion of young women who do not know enough about gestational diabetes when deciding whether to be screened.

People with low health literacy are less likely to ask questions, or to independently seek health information online or through publications. They are more likely to rely on trusted personal advisors, such as mothers and grandmothers. This makes it especially important for a lead maternity carer to involve this wider group in their discussions with a woman.

The report concludes that a woman's decision to be screened is influenced by the approach that her lead maternity carer takes to screening, as well as by the knowledge, confidence and beliefs of the woman and her support network. Table C summarises the factors contributing to low screening rates for gestational diabetes.

Table C: Factors contributing to low screening rates for gestational diabetes

Lead maternity carer knowledge and practice	Women's knowledge and action
• Providing little encouragement for screening beyond making the offer	• Having little or no knowledge of gestational diabetes or why screening is important
• Assessing risk factors to determine whether to recommend screening	• Lack of confidence in unfamiliar health settings (reluctance to participate)
• Not explaining the consequences of gestational diabetes	• Influential family or friends dismiss the need for screening
• Providing little explanation of the screening process	• Young women in denial about pregnancy and various aspects of the pregnancy
• Not contacting women when screening is not completed when planned	• Past negative results for glucose challenge test or oral glucose tolerance test
• Concern about upsetting the relationship with a woman by questioning why she hasn't completed screening	• Past negative experiences with gestational diabetes specialist support services
• Concern about the specialist diabetes support and advice provided once gestational diabetes is diagnosed	• Fear of diagnosis of diabetes mellitus
• Gestational diabetes is one of many health concerns during pregnancy and other things may take priority	• Perception that pregnancy is being over-medicalised
• Not offering screening (non-New Zealand College of Midwives lead maternity carers)	• Not accessing antenatal care

Systemic issues
• No nationally agreed guidelines for screening and diagnosing gestational diabetes
• Poor public awareness and understanding of gestational diabetes
• Poor service coordination resulting in low rate of postpartum testing for gestational diabetes
• Lack of accessible, comprehensive, clear information about gestational diabetes, consequences and screening

Source: Reproduced from Workbase (2014)

13.3 Additional evidence on women's perceptions of gestational diabetes

13.3.1 Indigenous women

A systematic review of literature on screening for diabetes in pregnancy for indigenous women in Australia, Canada, New Zealand and the United States was identified (Chamberlain et al 2013). There were a limited number of publications reported on the preferences and values of indigenous women related to diabetes in pregnancy more generally. Three qualitative studies, appraised as providing a moderate level of evidence, described mixed levels of understanding of the risks and causes of diabetes in pregnancy among both indigenous women and their care providers. They outlined the importance of family ties, preserving cultural values and adapting resources, and ensuring access to blood sugar data as a means of control; and described the perceptions of weight gain and the challenges in losing weight after pregnancy. There were no publications reporting on the acceptability of gestational diabetes screening for indigenous women. There were no studies evaluating potential risks of early gestational diabetes diagnosis for indigenous women, including psychological stress or negative self-esteem, social dislocation or physical outcomes as a result of increased intervention (Chamberlain et al 2013).

A qualitative study conducted in Tonga investigated the perceptions of 11 women who had developed gestational diabetes in the previous 12 months (Doran and Davis 2010). Women participating in the study were influenced by education and had an increased awareness of the need for behaviour change as a result of a diagnosis of gestational diabetes. The difficulties involved in making the required behavioural changes were a common theme. Two factors that were found to motivate behavioural change were concerns for the health of the baby and a fear of developing diabetes.

13.3.2 Views of pregnant women with gestational diabetes

A narrative review of studies focusing on women's perception of gestational diabetes included seven studies from Australia, Sweden and the United States. Most of the studies were small qualitative studies (Lawrence 2011). Some women will experience significant anxiety when they learn that they have gestational diabetes, but most studies reported that this was not sustained in the antepartum or postpartum period. Furthermore, women who were diagnosed with gestational diabetes perceived their health status as worse than did women who did not have gestational diabetes. Women's perception of having gestational diabetes was influenced by sociodemographic and cultural factors, the women's experience during any prior pregnancies and interactions with their health-care provider. Most women reported a positive perception of the gestational diabetes screening process, regardless of the outcome of their tests, and wanted to be tested for gestational diabetes in any future pregnancies (Lawrence 2011).

In contrast to the above qualitative studies, one randomised controlled trial investigated the effect of treatment of gestational diabetes and found that treatment may improve the woman's health-related quality of life (Crowther et al 2005). Maternal psychological outcomes included measures of anxiety, depression and health-related quality of life. All measures of the health state utility showed trends in favour of the intervention group, although not all were significant. At three months postpartum, fewer women in the intervention than in the routine care group had a score on the Edinburgh Postnatal Depression Scale suggestive of depression (8% versus 17%). The level of anxiety was similar in the two groups.

As part of the Diabetes Attitudes, Wishes and Needs (DAWN) study framework, a survey across 10 centres evaluated the needs and wishes of Italian and immigrant women affected by gestational diabetes (Lapolla et al 2012). The diagnosis of gestational diabetes caused anxiety. One-third of the women feared their child could contract diabetes at delivery and/or have congenital malformations. Some women had trouble in following treatment regimens, with their main concerns being dietary advice and blood glucose testing. Effective and satisfactory communication between pregnant women with gestational diabetes and their health care providers may reduce the level of anxiety.

A study conducted in Italian diabetic clinics evaluated the quality of life of 245 pregnant women with diabetes (Dalfrà et al 2012). Pregnancy was associated with a perception of poor general health in women with gestational diabetes. After delivery, significantly worse depressive symptoms were documented.

A cross-sectional survey conducted in an Australian hospital examined the attitudes and beliefs towards gestational diabetes among a multiethnic sample (Carolan et al 2010). Questionnaires were returned from 143 pregnant women who had gestational diabetes and were from Vietnamese, Indian, Filipino and Caucasian backgrounds. This study found that lower educational level, though not English language fluency, was associated with less appreciation of gestational diabetes as a serious condition and also with a lower value placed on tight glucose control. This effect was irrespective of ethnic group. Indian and Vietnamese women indicated a lower valuing of patient autonomy and also reported fewer negative psychological effects than Caucasian and Filipino women (Carolan et al 2010).

Another qualitative study, also from Australia, explored the experiences and understandings of South Asian women after diagnosis with gestational diabetes. Face-to-face interviews with 17 immigrant women found that before the diagnosis of gestational diabetes, women's knowledge and awareness of any type of diabetes was low. Women and their partners were upset by the diagnosis. Women reported feeling 'upset', 'shocked' and 'disappointed'. Dietary advice received was seen to be challenging in the context of culturally different food habits and, consequently, managing diet after diagnosis proved difficult. Different attitudes to exercise in pregnancy also raised issues for women, such as the perception that too much physical activity might put a strain on the baby (Bandyopadhyay et al 2011).

A telephone survey conducted in Sydney, Australia, examined patterns of postpartum physical activity and psychosocial factors among women with recent gestational diabetes. This study found that self-efficacy and social support were strongly related to physical activity. Practical support, through help with child care and undertaking other responsibilities, appeared to be particularly important (Smith et al 2005).

One qualitative study from the United States explored barriers to management of diabetes among women with a history of diabetes in pregnancy (Collier et al 2011). This study found examples of barriers related to finance, social support, communication, knowledge deficit and attitudes.

Another United States qualitative study focused on how pregnant and postpartum Latino women perceived diabetes, physical activity and health (Kieffer et al 2002). This study identified barriers and facilitators to physical activity. The facilitators to physical activity included social support from family and friends, community safety, learning to drive and to speak English, exercise guidance and education, and child care.

13.4 Summary

The evidence from interviews and other literature describing women's experiences of gestational diabetes highlights a number of key issues for implementation.

- Women needed clear and meaningful information about what gestational diabetes meant for their health and for the health of their baby.
- They needed information on the clinical pathway and what they could expect at various stages of the journey up to the birth of their baby and beyond.
- Women needed clarity and good examples of what to eat and how much to eat.
- They found it difficult to adhere to lifestyle interventions.
- Clinic appointments were difficult at a number of different levels in terms of time and personal costs. Such difficulties were exacerbated for women living in rural areas.
- There were issues around the acceptability of screening test and pharmacological treatment.
- Women wanted access to more resources through a variety of media.

Chapter 14: Implementation plan

This guideline has provided specific recommendations for clinical practice in the screening, diagnosis, management and follow-up of women with gestational diabetes in New Zealand. It has also made a number of key research recommendations in areas where evidence is insufficient.

A full implementation plan has been submitted to the Ministry of Health. It includes:

- a dissemination plan for the full guideline and summary versions
- a PowerPoint presentation describing the key recommendations of the guideline, which can be downloaded
- recommendations for promoting the recommendations to key stakeholder groups including pregnant woman, Māori and Pacific communities, health care workers and maternity service providers
- an algorithm for health professionals, which can be downloaded
- suggestions for incorporating the guideline recommendations into a range of contexts such as conference programmes, journal articles, continuing education programmes and online quizzes
- an evaluation strategy to assess the extent to which the recommendations have been adopted into routine practice.

When developing an evaluation strategy, the Guideline Development Team recommends, and emphasises the importance of, considering ways to identify those changes in practice that are likely to have the most significant impact on the health outcomes of women with gestational diabetes and their babies, and to identify what data are already being collected relating to these recommendations and how they can be used to monitor changes in practice.

In evaluating the implementation of this guideline, the suggested indicators for success are:

- the percentage of women offered an HbA1c as part of the routine pregnancy blood tests at < 20 weeks
- the percentage of women having the oral glucose tolerance test or oral glucose challenge test at 24–28 weeks
- the percentage of women with gestational diabetes who are then offered an HbA1c 12 weeks after the birth of their child
- the number of green prescriptions issued to women with diabetes in pregnancy
- results from monitoring levels of labour inductions, caesarean sections and Neonatal Intensive Care Unit admissions for women with gestational diabetes and their babies.

In addition, to assess uptake of the guidelines, information could be collected on the number of:

- people who download or order copies of the guidelines and summaries
- health practitioners attending education sessions and workshops and successfully completing online quizzes
- people downloading tools such as apps.

14.1   Updating the guideline

It is proposed that the guideline is updated in a minimum of three years. At this point the Guideline Development Team would focus on any new randomised controlled trial evidence of screening and diagnostic regimens and their effect on maternal and infant outcomes.

Chapter 15: Research recommendations

To address areas where it found evidence gaps or inconsistent evidence, the Guideline Development Team has made the following research recommendations.

Research recommendations
Randomised controlled trial comparing dietary and lifestyle advice with pharmacotherapy for women whose HbA1c at booking is in the range of 41–49 mmol/mol, in terms of their impact on maternal and infant outcomes and development of gestational diabetes.
Studies that investigate whether early diagnosis and treatment lead to improved maternal and infant outcomes.
A randomised controlled trial that compares current screening and diagnostic criteria with those proposed by the International Association of Diabetes and Pregnancy Study Groups in terms of their impact on maternal and infant outcomes is required.
A randomised controlled trial to compare tight with less tight glycaemic control in women diagnosed with gestational diabetes in terms of their impact on maternal and infant outcomes.
A randomised controlled trial comparing more intensive ultrasound scanning with usual care in women with gestational diabetes in terms of their impact on maternal and infant outcomes.
A randomised controlled trial of leisure activity interventions for the treatment of gestational diabetes.
Randomised controlled trials that evaluate the outcomes of lifestyle versus pharmacological interventions to prevent type 2 diabetes in women with a previous history of gestational diabetes.

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Glossary

Adverse event	An adverse outcome that occurs during or after the use of a drug or other intervention but is not necessarily caused by it.
Antenatal/ antepartum	Occurring before birth; concerned with the care and treatment of the unborn child and pregnant women.
Applicability	The degree to which a body of evidence is relevant to a particular health care context.
Bias	Systematic (as opposed to random) deviation of the results of a study from the 'true' results.
Body mass index (BMI)	The body's weight in kilograms divided by the square of the height in metres, used in the assessment of obesity.
Case control study	A study that compares people who have a specific disease or outcome of interest (cases) with people from the same population who do not have that disease or outcome (controls), and that seeks to find associations between the outcome and prior exposure to particular risk factors. This design is particularly useful where the outcome is rare and past exposure can be reliably measured. Case control studies are usually retrospective.
Clinical effectiveness	The extent to which a specific treatment or intervention, when used under usual or everyday conditions, has a beneficial effect on the course or outcome of disease compared with no treatment or other routine care.
Cochrane Library	A regularly updated electronic collection of evidence-based health care databases, including the Cochrane Database of Systematic Reviews.
Cochrane Review / Cochrane Systematic Review	A systematic review of the evidence usually from randomised controlled trials relating to a particular health problem or health care intervention, produced by the Cochrane Collaboration. Available electronically as part of the Cochrane Library.
Cohort study	An observational study that takes a group (cohort) of patients and follows their progress over time in order to measure outcomes such as disease or mortality rates and make comparisons according to the treatments or interventions that another group of patients received.
	Cohorts can be assembled in the present and followed into the future (a 'concurrent' or 'prospective' cohort study) or identified from past records and followed forward from that time up to the present (a 'historical' or 'retrospective' cohort study).
Confidence interval	A range of values for an unknown population outcome estimated from a study. It will depend on the number of study recruits and the variation in the outcome data. A 95% confidence interval (CI) means that if the study was repeated 100 times with a different sample of recruits and a CI calculated each time, the interval would contain the 'true' value of the population outcome 95 times.
Considered judgement	The application of the collective knowledge of a guideline development group to a body of evidence, to assess its applicability to the target population and the strength of any recommendation that it would support.
Control group	A group of patients that receives no treatment, a treatment of known effect or a placebo (dummy treatment) as part of a study, in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.

Cost-effectiveness	Value for money. A specific health care treatment is said to be 'cost-effective' if it gives a greater health gain than could be achieved by using the resources in other ways.
Cost-effectiveness analysis	A type of economic evaluation comparing the costs and the health effects of different treatments. Health effects are measured in 'health-related units'; for example, the cost of preventing one additional patient from a condition.
Cross-sectional study	The observation of a defined set of people at a single point in time or specific time period – a snapshot. This type of study contrasts with a longitudinal study, which follows a set of people over a longer period of time.
Diabetic ketoacidosis	A state of absolute or relative insulin deficiency characterised by hyperglycaemia, dehydration, acidosis and ketosis.
Diagnostic study	A study to assess the effectiveness of a test or measurement in terms of its ability to accurately detect or exclude a specific disease.
Epidemiology	Study of diseases within a population, covering the causes and means of prevention.
Evidence-based	The best available evidence gained from the scientific method to inform medical decision-making. It seeks to assess the quality of evidence of the risks and benefits of treatments (including lack of treatment).
Evidence level	A code (eg, 1++, 1+) linked to an individual study, indicating where it fits into the hierarchy of evidence and how well it has adhered to recognised research principles. Also called level of evidence.
Evidence statement	A statement summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.
Evidence table	A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.
Fetal	Of or pertaining to a fetus or to the period of its development.
Gestation	The time from conception to birth. The duration of gestation is measured from the first day of the last normal menstrual period.
Gestational age	The period of time between last menstrual period and birth.
Gestational diabetes	Carbohydrate intolerance of varying severity which is diagnosed in pregnancy and may or may not resolve after pregnancy.
Glycaemic control targets	Recommended levels of blood glucose.
Glycated haemoglobin (HbA1c)	A test that measures the amount of glucose-bound haemoglobin and reflects how well the blood glucose level has been controlled over the previous six to eight weeks.
Harms	Adverse effects.
Heterogeneity	Also termed lack of homogeneity. The term is used in meta-analyses and systematic reviews when the results or estimates of effects of treatment from separate studies seem to be very different in terms of the size of treatment effects or even to the extent that some indicate beneficial and others suggest adverse treatment effects. Such results may occur due to differences between studies in terms of the patient populations, outcome measures, definition of variables or duration of follow-up.

Hierarchy of evidence	An established hierarchy of study types, based on the degree of certainty that can be attributed to the conclusions that can be drawn from a well-conducted study. Well-conducted randomised controlled trials (RCTs) are at the top of this hierarchy (for example, several large, statistically significant RCTs that are in agreement represent stronger evidence than one small RCT). Well-conducted studies of patients' views and experiences would appear at a lower level in the hierarchy of evidence.
Homogeneity	Where the results of studies included in a systematic review or meta-analysis are similar and there is no evidence of heterogeneity. Results are usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance.
Hyperglycaemia	Elevated blood sugar levels.
Hypoglycaemic agents	Pharmacological agents that are used to control blood sugar.
Hypertension	High blood pressure.
Hypoglycaemia	Low blood glucose level.
Interquartile range	Difference between the first quartile (25th percentile) and the third quartile (75th percentile) of an ordered range of data.
Macrosomia	A condition in which a baby is large, often defined as having a birthweight above the 90th centile for gestation or a birthweight of 4000 g or more.
Methodological quality	The extent to which a study has conformed to recognised good practice in the design and execution of its research methods.
Necrotising enterocolitis	A medical condition primarily seen in premature infants, where portions of the bowel undergo tissue death (necrosis).
Negative predictive value (NPV)	The proportion of people with a negative test result who do not have the disease (where not having the disease is indicated by the 'gold standard' test being negative).
Neonatal	Pertaining to the neonatal period, which is the first four weeks after birth.
Neonate	An infant in the first four weeks of life.
Number needed to treat to benefit	The number of patients who need to be treated with the new or intervention treatment (rather than the control treatment) for one patient to benefit from the new treatment.
Observational studies	A study in which the investigators do not seek to intervene, and simply observe the course of events. Changes or differences in one characteristic (eg, whether or not people received the intervention of interest) are studied in relation to changes or differences in other characteristic(s) (eg, whether or not they died), without action by the investigator. There is greater risk of selection bias than in experimental studies.
Odds ratio (OR)	The odds of the outcome in the intervention group to the odds of an outcome in the control group.
Parity	The number of times a woman has given birth to a fetus with a gestational age of 20 weeks or more, regardless of whether the child was born alive or was stillborn.
Placebo	An inactive substance or preparation used as a control in an experiment or test to determine the effectiveness of a medicinal drug.
Positive predictive value	The proportion of people with a positive test result who have the disease (where having the disease is indicated by the 'gold standard' test being positive).

Pre-eclampsia	A pregnancy-induced condition that can occur in the second half of pregnancy. It is characterised by high blood pressure, swelling that happens suddenly along with rapid weight gain due to fluid retention, and protein in the urine.
Preterm birth	The birth of a baby of less than 37 weeks' gestation.
Prevalence	The proportion of individuals in a population having a disease.
***p*-value**	Used in hypothesis testing where initially it is assumed that there is no difference between two treatments. The *p*-value is the probability that the difference observed in a study between the two treatments might have occurred by chance. Small *p*-values indicate evidence against an assumption of no difference. Large *p*-values indicate insufficient evidence against the assumption of no difference between treatments, **not** that there is actually no difference between treatments. A *p*-value will depend on study size; large studies can detect small differences, for example.
Postnatal	Occurring after birth; concerned with the care and treatment of the baby and pregnant women after birth.
Postpartum	The period of time after birth.
Postprandial	After a meal.
Randomised controlled trial	A comparative study in which participants are randomly allocated to intervention and control groups and followed up to examine differences in outcomes between the groups.
Reference standard	A method, procedure or measurement that is widely accepted as being the best available. Also called a gold standard.
Regimen	A pattern of treatment, eg, dose, frequency of a drug.
Risk of bias	The extent to which the reported outcomes of a study are at risk of bias, which may be caused by an inadequacy in the way the study is designed or conducted. For example, if any of the following aspects of the trial were not conducted properly then the trial may be said to have an increased risk of bias: the random allocation of the treatments, allocation concealment, blinding of researchers during intervention and measurement of outcomes, missing outcome data, selective outcome reporting.
Risk ratio (RR)	The ratio of risks in two treatment groups. In intervention studies, it is the ratio of the risk in the intervention group to the risk in the control group. A risk ratio of 1 indicates no difference between comparison groups. For undesirable outcomes, a risk ratio that is less than 1 indicates that the intervention was effective in reducing the risk of that outcome. (Also called relative risk).
Sample size	The number of units (people, animals, patients, specified circumstances, etc) in a population to be studied. The sample size should be big enough to have a high likelihood of detecting a true difference between two groups.
Sensitivity	The proportion of true positive results that are correctly identified as positive by the test. 100% sensitivity means that all those with a negative test result do not have the disease. Specificity should be considered alongside sensitivity to fully judge the accuracy of a test.
Shoulder dystocia	Any documented evidence of difficulty with delivering the shoulders after delivery of the baby's head.
Sliding scale	Intravenous insulin and dextrose infusions with a set of instructions for adjusting the dose of insulin on the basis of blood glucose test results.

Specificity	The proportion of true negative results that are correctly identified as negative by the test. 100% specificity means that all those with a positive test result have the disease. Sensitivity should be considered alongside specificity.
Stillbirth	Death in a fetus ≥ 400 g or at least 20 weeks' gestational age.
Study population	All of the people who have been identified as the subjects of a study.
Systematic review	A review of a clearly formulated question using systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods may or may not be used to analyse the results.
Trimester	One of the three-month periods into which pregnancy is divided. The first trimester is 0–13 weeks of gestation, the second trimester is 14–26 weeks of gestation, and the third trimester is 27 weeks of gestation until birth.
Type 1 diabetes mellitus	An absolute deficiency of insulin production. It accounts for 5–15% of all people with diabetes.
Type 2 diabetes mellitus	A relative deficiency of insulin production, and/or the insulin produced is not effective (insulin resistance). It accounts for 85–95% of all people with diabetes.

Appendices

Appendix A: Methods and searching

This appendix details the methodology used for the development of this guideline.

Electronic searching

Search strategies were developed by an information specialist in conjunction with the research team or were rerun from previous guidelines and systematic reviews where available.

Date of searches was limited from 2007 to present unless otherwise stated based on the search dates of the National Institute for Health and Care Excellence 2008 guideline and from 2008 for the screening questions as determined by the Health Technology Assessment screening guideline (Waugh et al 2010).

The databases that were searched were:
- Medline
- Embase
- Cinahl
- CENTRAL
- Cochrane Database of Systematic Reviews
- HTA database
- National Guideline Clearing House
- Guidelines International Network Database
- Te Puna
- Clinical Trials Register
- Specialised register of the Pregnancy and Childbirth Cochrane Group.

New Zealand-specific data were identified via government and professional body websites, personal contacts and Google searches.

Population

The target population was women who develop hyperglycaemia during pregnancy, alternatively referred to as gestational diabetes. Women with a diagnosis of type 1 or type 2 diabetes made prior to pregnancy were excluded. The Guideline Development Team did include women with undiagnosed diabetes identified in early pregnancy and women diagnosed with type 2 diabetes in the postpartum period.

Type of studies

Where possible, the highest possible level of evidence was used to inform clinical practice recommendations. This meant, where possible, restricting evidence to clinical guidelines, systematic reviews, randomised controlled trials (for intervention questions), diagnostic studies and economic modelling studies. The Guideline Development Team acknowledges that the studies in some areas, such as epidemiology, do not meet these criteria and a lower level of evidence was accepted.

Where studies were identified within existing systematic reviews or guidelines, they were not critically appraised nor was an evidence table created.

Only evidence published in peer-reviewed journals was included in the systematic reviews. The evidence was limited to those published in the English language.

The following types of publication were excluded from the systematic reviews: case series studies, editorials and commentaries, publications in abstract form (including conference proceedings), book chapters, personal communications and news items.

Evidence tables

Evidence has been summarised in risk of bias or evidence tables depending on the level of evidence. These have been provided to the Ministry of Health in a separate document.

Assessment of quality of included studies

A number of internationally recognised tools are available to critically appraise studies. In these systematic reviews, guidelines have been appraised using the AGREE II tool; systematic reviews have been appraised using an adapted Grading of Recommendations Assessment, Development and Evaluation (GRADE) method which has been developed by the Scottish Intercollegiate Guidelines Network (SIGN). Randomised and non-randomised studies were appraised using the Review Manager program (Cochrane Collaboration) and diagnostic studies using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) (http://publications.nice.org.uk/the-guidelines-manual-appendices-bi-pmg6b/appendix-f-methodology-checklist-the-quadas-2-tool-for-studies-of-diagnostic-test-accuracy).

The AGREE tool (www.agreetrust.org) evaluates the quality of clinical practice guidelines and either recommends the guideline, recommends with provisos or does not recommend the guideline. The adapted GRADE (www.gradeworkinggroup.org) method details the volume of evidence, the methodological risk of bias, evidence of heterogeneity, directness of evidence, precision of the evidence and publication bias. Cochrane (www.cochrane.org) methodology appraises evidence based on method of randomisation, allocation concealment, blinding of participants, researchers and outcome assessors, selection and reporting bias.

The following search strategies are taken from MEDLINE and have been adapted when used with other search engines.

Risk factors

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
----
1 pregnant women/ (4665)
2 pregnancy/ (653624)
3 pregnan$.tw. (336429)
4 or/1-3 (723933)
5 pregnancy in diabetes/ (9442)
6 or/4-5 (723963)
7 exp diabetes mellitus/ (284883)
8 diabetes, mellitus type 1/ (56570)
9 diabetes, mellitus type 2/ (72971)
10 diabetes mellitus, lipoatrophic/ (171)
11 diabetes insipidus/ (5624)
12 diabetes, gestational/ (4733)
13 diabet$.tw. (358743)
14 or/7-13 (409632)
15 and/6,14 (22551)
16 exp risk/ (728523)
17 risk$.tw. (1108951)
18 or/16-17 (1413855)
19 and/15,18 (7631)
20 epidemiological studies/ (5442)
21 exp case control studies/ (563363)
22 exp cohort studies/ (1193155)
23 case control.tw. (64621)
24 (cohort adj (study or studies)).tw. (66238)
25 cohort analy$.tw. (2932)
26 (follow up adj (study or studies)).tw. (34231)
27 (observational adj (study or studies)).tw. (34224)
28 longitudinal.tw. (119058)
29 retrospective.tw. (227811)
30 cross sectional.tw. (134214)
31 cross-sectional studies/ (143704)
32 or/20-31 (1634776)
33 and/19,32 (2956)
34 animal/ not (human/ or (human/ and animal/)) (3666161)
35 33 not 34 (2953)
36 limit 35 to yr="2007 – 2012" (1315)
37 limit 36 to english language (1227)

Induction of labour

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
----
1 exp Diabetes, Gestational/ (6152)
2 (pregnan$ adj5 diabet$).tw. (7868)
3 (hyperglyc$ adj5 pregnan$).tw. (368)
4 GDM.tw. (2407)
5 (insulin resistance adj5 pregnan$).tw. (377)
6 (glucose intoleran$ adj5 pregnan$).tw. (207)
7 (gestation$ adj5 diabet$).tw. (6931)
8 (gestation$ adj5 weight gain).tw. (1047)
9 (gestation$ adj5 obes$).tw. (409)
10 maternal obes$.tw. (803)
11 (maternal adj5 weight gain).tw. (1499)
12 or/1-11 (17064)
13 exp cesarean section/ or exp cesarean section, repeat/ or exp labor, induced/ (39389)
14 (induc$ adj5 labo?r).tw. (6598)
15 c?esarean$.tw. (38712)
16 C-section$.tw. (585)
17 (active adj3 induction$).tw. (759)
18 (elective$ adj3 induc$).tw. (479)
19 (timing adj3 induc$).tw. (451)
20 delivery.tw. (239266)
21 delivered.tw. (94733)
22 (deliver or delivering).tw. (52200)
23 or/13-22 (377580)
24 randomized controlled trial.pt. (343003)
25 controlled clinical trial.pt. (85733)
26 randomized.ab. (259617)
27 placebo.tw. (146234)
28 clinical trials as topic.sh. (163875)
29 randomly.ab. (189192)
30 trial.ti. (111700)
31 (crossover or cross-over or cross over).tw. (55734)
32 or/24-31 (842723)
33 exp animals/ not humans.sh. (3813901)
34 32 not 33 (777552)
35 Meta-Analysis as Topic/ (12621)
36 meta analy$.tw. (48571)
37 metaanaly$.tw. (1210)
38 Meta-Analysis/ (38026)
39 (systematic adj (review$1 or overview$1)).tw. (40683)
40 exp Review Literature as Topic/ (6633)
41 Review/ (1760390)
42 or/35-41 (1810442)
43 cochrane.ab. (24190)
44 embase.ab. (21912)
45 (psychlit or psyclit).ab. (874)
46 (psychinfo or psycinfo).ab. (8375)
47 (cinahl or cinhal).ab. (8081)

48 science citation index.ab. (1748)
49 bids.ab. (338)
50 cancerlit.ab. (568)
51 or/43-50 (39707)
52 reference list$.ab. (8367)
53 bibliograph$.ab. (10633)
54 hand-search$.ab. (3445)
55 relevant journals.ab. (610)
56 manual search$.ab. (2004)
57 or/52-56 (22420)
58 Comment/ (527572)
59 Letter/ (786066)
60 Editorial/ (323245)
61 animal/ (5098239)
62 human/ (12720842)
63 61 not (61 and 62) (3721468)
64 or/58-60,63 (4899891)
65 42 or 51 or 57 (1820731)
66 65 not 64 (1661128)
67 34 or 66 (2329282)
68 12 and 23 and 67 (680)
69 (2007$ or 2008$ or 2009$ or 2010$ or 2011$ or 2012$).ed. (5464646)
70 68 and 69 (297)

Follow-up

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
----
1 pregnant women/ (4669)
2 pregnancy/ (653981)
3 pregna$.tw. (337064)
4 or/1-3 (724682)
5 pregnancy in diabetics/ (9444)
6 or/4-5 (724712)
7 exp diabetes mellitus/ (285217)
8 diabetes, mellitus type 1/ (56611)
9 diabetes, mellitus type 2/ (73142)
10 diabetes mellitus, lipoatrophic/ (171)
11 diabetes insipidus/ (5625)
12 diabetes, gestational/ (4744)
13 diabetes$.tw. (282751)
14 or/7-13 (386068)
15 and/6,14 (20647)
16 postnatal care/ (3477)
17 ((postnatal or postpartum) adj (care or period)).tw. (9624)
18 or/16-17 (12590)
19 aftercare/ (6239)
20 after?care.tw. (1959)
21 or/19-20 (7447)
22 follow up.tw. (531657)

23 follow?up.tw. (15451)
24 or/22-23 (546097)
25 or/18,21,24 (563688)
26 and/15,25 (978)
27 animal/ not (human/ and animal/) (3668019)
28 26 not 27 (964)
29 limit 28 to (english language and yr="2007 – 2012") (349)

Cost effectiveness

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R)
Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
----
1 (costs and cost analysis).mp. [mp=title, abstract, original title, name of substance word,
subject heading word, protocol supplementary concept, rare disease supplementary concept,
unique identifier] (41112)
2 cost of illness/ (15285)
3 exp economics/ (459496)
4 (pharmacoeconomic$ or pharmaco-economic$ or cost$ or economic$).tw. (408042)
5 exp quality-adjusted life years/ (5792)
6 (qaly$ or EQ5D or EQ-5D or euroqol or euro-qol).tw. (6729)
7 6 or 4 or 1 or 3 or 2 or 5 (748255)
8 exp diabetes, gestational/ (5867)
9 (gestation* adj2 diabetes*).tw. (5973)
10 exp hyperglycemia/ (23109)
11 exp pregnancy/ (670623)
12 11 and 10 (1336)
13 ((hyperglycemia or hyperglycaemia) adj4 pregnan$).tw. (263)
14 13 or 8 or 9 or 12 (8883)
15 ((glucose tolerance or impaired fasting glucose) adj3 pregnan*).tw. (433)
16 diabet$adj2 pregnan$.m_titl. (0)
17 15 or 14 or 16 (9042)
18 7 and 17 (310)
19 limit 18 to english language (279)
20 limit 19 to yr="2009 – 2012" (88)

Prevention of diabetes

Database: Embase <1980 to 2012 Week 44>
Search Strategy:
----
1 exp pregnancy diabetes mellitus/ (17371)
2 (pregnan$ adj5 diabet$).tw. (9751)
3 (hyperglyc$ adj5 pregnan$).tw. (503)
4 GDM.tw. (3550)
5 (insulin resistance adj5 pregnan$).tw. (484)
6 (glucose intoleran$ adj5 pregnan$).tw. (258)
7 (gestation$ adj5 diabet$).tw. (9572)
8 (gestation$ adj5 weight gain).tw. (1277)
9 (gestation$ adj5 obes$).tw. (625)
10 maternal obes$.tw. (1213)

11 (maternal adj5 weight).tw. (6635)

12 or/1-11 (30268)

13 exp lifestyle/ (63323)

14 life*style.tw. (51852)

15 exp diet therapy/ or exp low carbohydrate diet/ or exp diet/ or exp diabetic diet/ or exp low fat diet/ or exp diet restriction/ or exp Mediterranean diet/ or exp low calory diet/ (351610)

16 diet$.tw. (407610)

17 (food adj3 intake).tw. (39241)

18 calor$.tw. (61907)

19 nutrition$.tw. (199321)

20 exp weight reduction/ or exp body weight/ (347235)

21 (weight adj3 reduc$).tw. (26363)

22 (weight adj3 los$).tw. (71696)

23 loose weight.tw. (96)

24 (body mass index adj3 reduc$).tw. (605)

25 (body mass index adj3 decreas$).tw. (796)

26 (body mass index adj2 loss).tw. (226)

27 exp muscle exercise/ or aerobic exercise/ or exp dynamic exercise/ or exp stretching exercise/ or aquatic exercise/ or exp exercise/ (180252)

28 exercise$.tw. (215829)

29 (run$ or jog$).tw. (137079)

30 (sport$ or walk$).tw. (123365)

31 (swim$ or cycling).tw. (60481)

32 (training or bicycling).tw. (258884)

33 fit$.tw. (202036)

34 yoga.tw. (1985)

35 aerobic$.tw. (60083)

36 physical therap$.tw. (15308)

37 exp running/ or exp swimming/ or exp walking/ or exp fitness/ (96177)

38 exp Yoga/ (2891)

39 or/13-38 (2019336)

40 exp health promotion/ (62935)

41 (Health$ adj2 Promot$).tw. (31732)

42 exp health education/ (212877)

43 (Health adj2 Educat$).tw. (31144)

44 exp behavior therapy/ or exp Cognitive Therapy/ (52987)

45 (motivation$ adj2 therap$).tw. (583)

46 exp psychotherapy/ (168640)

47 Psychotherapy.tw. (32635)

48 behavio?r therap$.tw. (6210)

49 (cognitive adj3 therap$).tw. (14022)

50 exp directive counseling/ (453)

51 Counse?ling.tw. (66432)

52 exp social support/ (50442)

53 Social Support.tw. (22632)

54 exp self concept/ (112567)

55 self efficacy.tw. (12426)

56 (motivation$ adj3 therap$).tw. (784)

57 or/40-56 (596619)

58 exp prebiotic agent/ or exp probiotic agent/ or exp synbiotic agent/ or exp diet supplementation/ (69851)

59 prebiotic$.tw. (3621)

60 probiotic$.tw. (10898)

61 synbiotic$.tw. (529)
62 bifidobacteri$.tw. (5778)
63 lactic acid bacteri$.tw. (6112)
64 Lactobacill$.tw. (19822)
65 Saccharomyces boulardii.tw. (524)
66 Streptococcus thermophilus.tw. (1212)
67 Enterococcus faecium.tw. (3842)
68 exp Leuconostoc/ or exp lactic acid bacterium/ (4789)
69 exp Enterococcus faecium/ (4202)
70 Leuconostoc.tw. (1866)
71 exp antioxidant/ (87591)
72 Antioxidant$.tw. (120535)
73 exp fish oil/ (11279)
74 (Fish adj2 Oil$).tw. (8639)
75 exp vitamin D/ (77399)
76 Vitamin D.tw. (41430)
77 exp inositol/ (8226)
78 (mesoinositol or myoinositol).tw. (1198)
79 (chiro-inositol$ or myo-inositol).tw. (5478)
80 exp thiamine/ or thiamin$.tw. (18855)
81 or/58-80 (359796)
82 39 or 57 or 81 (2733053)
83 12 and 82 (14222)
84 Clinical Trial/ (873672)
85 Randomized Controlled Trial/ (332138)
86 exp randomization/ (59934)
87 Single Blind Procedure/ (16606)
88 Double Blind Procedure/ (111711)
89 Crossover Procedure/ (35428)
90 Placebo/ (207567)
91 Randomi?ed controlled trial$.tw. (80572)
92 Rct.tw. (10348)
93 random allocation.tw. (1193)
94 randomly allocated.tw. (17891)
95 allocated randomly.tw. (1845)
96 (allocated adj2 random).tw. (712)
97 Single blind$.tw. (12733)
98 Double blind$.tw. (131840)
99 ((treble or triple) adj blind$).tw. (287)
100 placebo$.tw. (181223)
101 prospective study/ (218076)
102 or/84-101 (1286597)
103 case study/ (17571)
104 case report.tw. (234064)
105 abstract report/ or letter/ (849577)
106 or/103-105 (1096413)
107 102 not 106 (1251029)
108 exp Meta Analysis/ (66936)
109 ((meta adj analy$) or metaanalys$).tw. (61975)
110 (systematic adj (review$1 or overview$1)).tw. (47873)
111 review.ti. (261772)
112 or/108-111 (351225)
113 107 or 112 (1521145)

114 83 and 113 (1984)
115 (2007$ or 2008$ or 2009$ or 2010$ or 2011$ or 2012$).em. (6315759)
116 114 and 115 (1207)

Different intensities of glycaemic control/treatment targets

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R)
Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 exp Diabetes, Gestational/ (6056)
2 (pregnan$ adj5 diabet$).tw. (7796)
3 (hyperglyc$ adj5 pregnan$).tw. (361)
4 GDM.tw. (2355)
5 (insulin resistance adj5 pregnan$).tw. (373)
6 (glucose intoleran$ adj5 pregnan$).tw. (203)
7 (gestation$ adj5 diabet$).tw. (6835)
8 (gestation$ adj5 weight gain).tw. (1004)
9 (gestation$ adj5 obes$).tw. (397)
10 maternal obes$.tw. (778)
11 (maternal adj5 weight gain).tw. (1469)
12 (glucose toleran$ adj5 pregnan$).tw. (732)
13 (maternal adj3 hyperglycemi$).tw. (275)
14 (maternal adj3 hyperglycaemi$).tw. (83)
15 (pregestational adj3 diabet$).tw. (340)
16 maternal glyc?emi$.tw. (202)
17 or/1-16 (17191)
18 glyc?emic status.tw. (399)
19 (glycemic adj3 control$).tw. (11565)
20 (glycaemic adj3 control$).tw. (4789)
21 (monitor$ adj3 glucose).tw. (6070)
22 (monitor$ adj3 glyc?em$).tw. (419)
23 (metabolic adj3 control$).tw. (10554)
24 (glucose adj3 control$).tw. (11585)
25 (metabolic adj3 manag$).tw. (796)
26 (normoglyc?emi$ adj3 control$).tw. (456)
27 (intens$ adj3 manag$).tw. (3534)
28 (tight$ adj3 manag$).tw. (114)
29 (strict adj3 manag$).tw. (272)
30 (level$ adj3 glyc?emi$).tw. (1635)
31 (intens$ adj3 control$).tw. (4223)
32 (intens$ adj3 treat$).tw. (15946)
33 (tight adj3 control$).tw. (3377)
34 (tight adj3 treat$).tw. (133)
35 (strict adj3 control$).tw. (3347)
36 (strict adj3 treat$).tw. (450)
37 or/18-36 (68433)
38 17 and 37 (1801)
39 randomized controlled trial.pt. (339054)
40 controlled clinical trial.pt. (85098)
41 randomized.ab. (256457)
42 placebo.tw. (144132)

43 clinical trials as topic.sh. (162088)
44 randomly.ab. (187749)
45 trial.ti. (109412)
46 (crossover or cross-over or cross over).tw. (55285)
47 or/39-46 (833381)
48 exp animals/ not humans.sh. (3754079)
49 47 not 48 (768269)
50 Meta-Analysis as Topic/ (12380)
51 meta analy$.tw. (47545)
52 metaanaly$.tw. (1196)
53 Meta-Analysis/ (36981)
54 (systematic adj (review$1 or overview$1)).tw. (39972)
55 exp Review Literature as Topic/ (6505)
56 Review/ (1739624)
57 or/50-56 (1788851)
58 cochrane.ab. (23227)
59 embase.ab. (21144)
60 (psychlit or psyclit).ab. (845)
61 (psychinfo or psycinfo).ab. (8271)
62 (cinahl or cinhal).ab. (7751)
63 science citation index.ab. (1619)
64 bids.ab. (332)
65 cancerlit.ab. (548)
66 or/58-65 (38655)
67 reference list$.ab. (7972)
68 bibliograph$.ab. (10392)
69 hand-search$.ab. (3348)
70 relevant journals.ab. (584)
71 manual search$.ab. (1982)
72 or/67-71 (21718)
73 Comment/ (520330)
74 Letter/ (777608)
75 Editorial/ (319765)
76 animal/ (5004352)
77 human/ (12551760)
78 76 not (76 and 77) (3663527)
79 or/73-75,78 (4830271)
80 57 or 66 or 72 (1799057)
81 80 not 79 (1641401)
82 49 or 81 (2301809)
83 38 and 82 (531)

Treatment of gestational diabetes:

The search strategy for this topic was conducted by the Cochrane Pregnancy and Childbirth Group and is available through the trials search co-ordinator of this group.

Early screening with HbA1c

Database: Embase <1980 to 2013 March 29>
Search Strategy:

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1 exp non insulin dependent diabetes mellitus/ or exp pregnancy diabetes mellitus/ (138815)
2 diabet$ type 2.tw. (1278)
3 diabet$ type II.tw. (416)
4 noninsulin-dependent diabet$.tw. (1495)
5 diabet$ type two.tw. (2)
6 maturity onset diabetes mellitus.tw. (109)
7 diabet$ non insulin dependent.tw. (72)
8 diabetes mellitus adult onset.tw. (3)
9 or/1-8 (139826)
10 HbA1C.tw. (24464)
11 Hb A1C.tw. (404)
12 glycosylated hemoglobin/ (14312)
13 glycoh?emoglobin.tw. (937)
14 glycosyl h?emoglobin.tw. (8)
15 glycosylh?emoglobin.tw. (1)
16 hb a 1.tw. (11)
17 hb a1.tw. (141)
18 H?emoglobin A1.tw. (638)
19 glucose tolerance test/ (18994)
20 glucose challenge.tw. (2266)
21 Glucose Tolerance.tw. (36962)
22 or/10-21 (81915)
23 Pregnan$.tw. (402066)
24 9 and 22 and 23 (3208)
25 limit 24 to (human and english language) (2338)
26 exp "SENSITIVITY AND SPECIFICITY"/ (186605)
27 sensitivity.tw. (575062)
28 specificity.tw. (348268)
29 ((pre-test or pretest) adj probability).tw. (1639)
30 post-test probability.tw. (407)
31 predictive value$.tw. (81088)
32 likelihood ratio$.tw. (9652)
33 *Diagnostic Accuracy/ (4007)
34 or/26-33 (902132)
35 25 and 34 (391)

Diagnostic test accuracy (randomised controlled trials)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 exp Diabetes Mellitus, Type 2/ (76314)
2 (diabet$ adj5 type 2).tw. (61768)
3 (diabet$ adj5 type II).tw. (7327)
4 maturity onset diabetes mellitus.tw. (118)
5 (diabet$ adj3 non-insulin-dependent).tw. (10065)
6 (diabet$ adj5 type ii).tw. (7327)
7 stable diabetes mellitus.tw. (16)
8 niddm.tw. (6742)
9 noninsulin-dependent diabet$.tw. (1245)
10 non insulin-dependent diabet$.tw. (9674)
11 diabetes mellitus adult onset.tw. (3)
12 ketosis-resistant diabetes mellitus.tw. (1)
13 (diabet$ adj5 type two).tw. (35)
14 or/1-13 (102243)
15 fasting plasma glucose.tw. (6679)
16 exp Blood Glucose/ (121244)
17 fasting blood glucose.tw. (5446)
18 fasting glucose.tw. (8934)
19 fpg.tw. (2918)
20 random blood glucose.tw. (253)
21 HbA1C.tw. (11908)
22 Hb A1C.tw. (332)
23 exp Hemoglobin A, Glycosylated/ (20399)
24 hb a1c.tw. (332)
25 hb a1b.tw. (7)
26 hba1.tw. (1562)
27 H?emoglobin A1.tw. (494)
28 H?emoglobin A 1.tw. (38)
29 glycohemoglobin a.tw. (14)
30 glycated hemoglobins.tw. (28)
31 (glycated adj3 h?emoglobin$).tw. (4050)
32 hb a1.tw. (92)
33 Random glucose.tw. (119)
34 RBG.tw. (210)
35 exp Glucose Tolerance Test/ (27817)
36 glucose challenge test.tw. (378)
37 Glucose Tolerance Test.tw. (12791)
38 or/15-37 (161311)
39 14 and 38 (32862)
40 exp Pregnancy/ (681069)
41 exp Pregnancy in Diabetics/ (10739)
42 Pregnan$.tw. (345732)
43 gestation$.tw. (136196)
44 or/40-43 (787032)
45 39 and 44 (1166)
46 exp animals/ not humans.sh. (3784287)
47 45 not 46 (1070)

Appendix B: Guideline Development Team

Member	Organisation
Ken Clark	Chair
Norma Campbell Nicholette Emerson	New Zealand College of Midwives
Ross Lawrenson	National Screening Advisory Committee
Rose Elder	Royal Australian and New Zealand College of Obstetrics and Gynaecology
Michelle Downie	New Zealand Society for the Study of Diabetes
Janet Rowan*	Australasian Diabetes in Pregnancy Society
Karl Cole	Royal New Zealand College of General Practitioners
Diana McNeill	Diabetes New Zealand Consumer Māori
Malcolm Battin	Perinatal Society of New Zealand Pediatric Society
Kara Okesene-Gafa	Pacific peoples representative
Mary Meendering	Clinical Nurse Specialist diabetes
Kelsey Coster	Consumer
Tim Cundy	National Diabetes Service Improvement Group
Anna Jackson	Dietician
No representative	Royal Australasian College of Physicians
Leona Dann/Kass Ozturk (Ministry of Health)	Ex officio member
Cindy Farquhar	Ex officio member
Catherine Marshall (implementation)	Ex officio member
Caroline Crowther	Ex officio member
Julie Brown	Ex officio member
Catherine Coop	Ex officio member
Anita Fitzgerald	Ex officio member
Anne Lethaby	Ex officio member
Philippa Middleton	Ex officio member
Vicki Masson	Ex officio member

Note: * Dr Janet Rowan withdrew from the Guideline Development Team following the last team meeting due to conflicts with some of the recommendations. She was, however, present at all meetings and contributed to the guideline development process. We thank her for her valuable contribution.

Appendix C: Clinical questions

Epidemiology and early screening

1a   Who should be screened for hyperglycaemia in pregnancy?

1b   Should all pregnant women less than 20 weeks' gestation be offered HbA1c to diagnose type 2 diabetes?

1c   What thresholds should be used to diagnose type 2 diabetes in pregnant women less than 20 weeks' gestation?

2   What risk factors are associated with increased risk of gestational diabetes?

Prevention of gestational diabetes

3   How effective are lifestyle interventions for the prevention of gestational diabetes (pre-conception and during pregnancy)?

24- to 28-week screening and diagnosis

4   What is the diagnostic accuracy of commonly used screening and diagnostic tests for gestational diabetes?

5   What is the optimal diagnostic threshold for diagnosing gestational diabetes?

6   Which screening/diagnostic regimen is optimal for maternal and infant outcomes?

7   What is the evidence for referral pathways following screening for gestational diabetes?

8   What is the effectiveness of risk factor versus universal screening on maternal and infant outcomes?

9   What is the cost-effectiveness of commonly used screening/diagnostic strategies?

Treatment/management

10   What is the safety and effectiveness of dietary and lifestyle interventions versus usual care on maternal and infant outcomes in women with gestational diabetes?

11   What is the safety and effectiveness of oral hypoglycaemic versus insulin therapy on maternal and infant outcomes in women with gestational diabetes?

12   What is the optimal timing and mode of delivery for women with gestational diabetes?

13   What are the optimal glucose targets for managing hyperglycaemia in pregnancy?

14   What is the safety and effectiveness of treatment of gestational diabetes targeted according to foetal ultrasound measurement?

15   What is the cost-effectiveness of treatments for gestational diabetes?

Follow-up

16   What information and follow-up should be offered to women with gestational diabetes after birth? (Diet and lifestyle information/interventions, breastfeeding, contraception)

17   What is the best practice for immediate postpartum care for women and infants?

18   What is the risk of developing type 2 diabetes and what are the risk factors for developing type 2 diabetes in women with gestational diabetes?

19   What is the diagnostic test accuracy of postpartum screening test for diabetes in women who have been diagnosed with gestational diabetes?

20   What interventions are useful in increasing the uptake of postnatal glucose screening in women who had gestational diabetes?

21   Can type 2 diabetes be prevented in women with a diagnosis of gestational diabetes?

Appendix D: Maternal and infant outcomes

The following maternal and infant outcomes were identified by the Guideline Development Team. These outcomes were used to inform the evidence base for the clinical questions listed in Appendix C.

Maternal

- Gestational weight gain
- Pre-eclampsia
- Induction of labour/caesarean section
- Maternal mortality
- Gestational diabetes
- Perineal trauma
- Acceptability
- Type 2 diabetes
- Maternal morbidity, eg, wound infection

Infant

- Neonatal hypoglycaemia
- Admission to neonatal intensive care
- Large for gestational age
- Respiratory distress syndrome
- Hyperbilirubinaemia
- Laboratory measures
- Gestational age at delivery (< 37/40 weeks)
- Birth trauma
- Perinatal mortality
- Stillbirth
- Perinatal asphyxia
- Obesity in older age
- Type 2 diabetes in childhood
- Neurodevelopment

Appendix E: Supporting evidence for Chapter 1

Figure 1: Percentage of women with gestational diabetes in New Zealand (2008–2012)
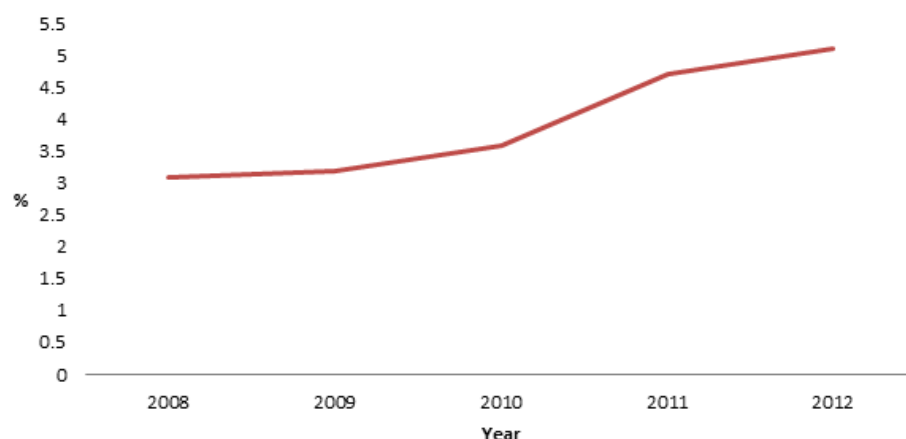
Source: National Maternity Collection, Ministry of Health, 2012

Figure 2: Incidence of gestational diabetes at National Women's Hospital (2002–2011)
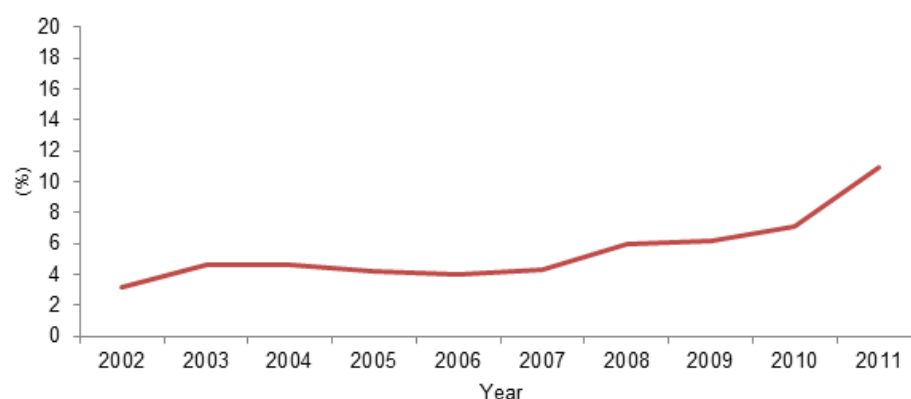
Source: Auckland District Health Board (2012)

Figure 3: Incidence of gestational diabetes for Counties Manukau District Health Board (2006/07–2011/12)
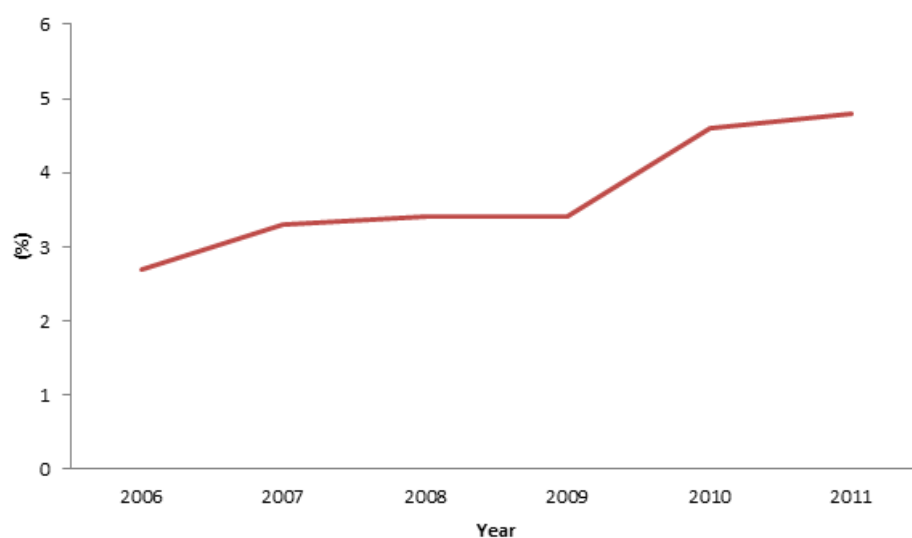
Source: Winnard and Anderson (2013)

Table 1: Percentage of women flagged with gestational diabetes mellitus by ethnicity in New Zealand (2012)

District health board	Ethnicity					Total
	Asian	European	Māori	Pacific	MELAA	
Auckland	13.8	3.3	5.0	11.8	7.4	8.2
Waitemata	12.6	4.1	4.9	12.2	7.9	7.1
Counties Manukau	13.3	4.3	3.9	8.3	5.9	7.1
Canterbury	10.3	4.7	4.4	10.6	7.5	5.6
Waikato	1.2	3.9	3.5	5.5	15.8	4.7
Capital & Coast	9.8	3.0	4.5	7.2	7.0	4.7
Taranaki	9.8	4.2	4.1	–	7.7	4.5
Hawke's Bay	4.4	4.5	3.6	7.5	4.6	4.2
Southern	8.1	3.7	2.9	7.8	1.9	3.9
Bay of Plenty	15.3	2.9	3.0	4.8	3.1	3.7
South Canterbury	6.5	3.6	3.0	–	17.0	3.7
Northland	11.4	3.3	3.3	5.6	10	3.6
West Coast	23.1	2.5	3.3	14.3	–	3.5
Hutt Valley	4.9	2.6	2.3	3.6	8.2	3.4
Nelson Marlborough	6.2	3.0	3.6	5.0	9.1	3.4
Lakes	6.3	3.8	2.5	7.3	–	3.3
Mid Central	4.9	3.1	2.5	6.9	8.3	3.3
Whanganui	4.0	3.2	2.3	–	50.0	2.8
Tairawhiti	5.6	0.5	1.7	37.5	–	2.2
Wairarapa	–	1.6	1.2	–	–	1.4
Median	**8.1**	**3.3**	**3.3**	**7.2**	**7.5**	**3.7**
Range	**0–23.1**	**0.5–4.7**	**1.2–5.0**	**0–37.5**	**0–50**	**1.4–8.2**

Note: MELAA = Middle Eastern, Latin American and African.

Data refer to a single woman who is only counted once although she may have given birth to more than one infant in the year.

Source: National Maternity Collection, Ministry of Health, 2012

Table 2: Summary of appraisals of national and international guidelines using the AGREE II tool

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
Standards of Medical Care in Diabetes (American Diabetes Association 2013)	Type 1 and type 2 diabetes, and gestational diabetes mellitus	United States 2013	Recommended with provisos or alterations	This guideline provides advice on the components of diabetes care, general treatment goals, and tools to evaluate quality of care. It covers a wide range of clinical scenarios and provides monitoring/audit criteria. The guideline has some methodological weaknesses. There is a lack of clarity around the criteria for selecting the evidence and a limited discussion on the strengths and limitations of the evidence. The guideline includes some discussion on cost-effectiveness. People with diabetes do not appear to have been involved or consulted during guideline development.
Diabetes in Pregnancy	Diabetes in pregnancy	New Zealand 2012	Not recommended	This guideline provides advice on the detection and management of diabetes in pregnancy. The guideline has some serious methodological weaknesses. Although the report cites relevant clinical studies, the recommendations were not formed on the basis of a systematic search of the literature, introducing a risk of selection bias. The guideline provides useful advice on general treatment goals and detailed clinical guidelines for managing diabetes and glucose intolerance in pregnancy. There are checklists and an algorithm that may be useful for clinicians. The resource implications of the recommendations are not discussed.
Preventing Type 2 Diabetes: Risk identification and interventions for individuals at high risk (NICE 2012)	Prevention of type 2 diabetes mellitus	United Kingdom 2012	Recommended	This report provides high-quality guidance focusing on identifying people at high risk of type 2 diabetes. The methods included quantitative and qualitative methods; evidence review, economic modelling, considering the testimony of experts and commissioned reports, considering stakeholder comments and fieldwork. The report provides recommendations on the provision of effective, cost-effective and appropriate interventions for people at high risk. The method of development was rigorous; the evidence was gathered systematically using a variety of sources. The guideline development group incorporated a number of relevant areas of expertise. A number of tools to aid implementation are available on the website.

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
Screening and Diagnosing Gestational Diabetes Mellitus (Hartling 2012)	Gestational diabetes mellitus	United States 2012	Recommended with provisos or alterations	Overall this is a high-quality summary of the evidence. It provides advice on screening for and treatment of gestational diabetes. The method of development was rigorous; the criteria for selecting evidence are well described; and the link between the evidence and the conclusions is explicitly described. As this review is intended for use in producing guidelines, it contains no recommendations or implementation tools for use in practice. The technical advisory panel included people with relevant clinical and methodological expertise. Women with hyperglycaemia in pregnancy were not involved in developing the report. The guideline is primarily aimed at public health officials. The report extracted cost-related data but did not search for cost-effectiveness studies or conduct cost-effectiveness analysis.
Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	Diabetes mellitus	United States 2012	Not recommended	Overall, this guideline has some serious limitations. It covers a wide range of issues concerned with the diagnosis and treatment of diabetes mellitus. There is a lack of clarity around the quality of the evidence, or the strength of the evidence on which the recommendations are based. There is no description of how the guideline development group used the evidence to form recommendations. There is also a lack of clarity around the criteria for selecting the evidence and the search strategies are not described, introducing a strong possibility of selection bias. The guideline provides a lot of tools for use in practice but they do not appear to have been derived from the evidence or the main recommendations.
Australasian Diabetes In Pregnancy Society (ADIPS) Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia (Nankervis 2013)	Gestational diabetes mellitus	Australia 2012	Not recommended	This guideline provides advice on the testing and diagnosis of gestational diabetes. There are also recommendations on suggested treatment targets and postpartum management. The guideline has some serious methodological weaknesses. Although the report cites relevant clinical studies, the recommendations were not formed on the basis of a systematic search of the literature, introducing a risk of selection bias. The included studies were not formally appraised for quality. The guideline recommends lowering the diagnostic threshold but does not examine the potential resource implications or discuss the balance between the risks and benefits. Women with diabetes were not involved or consulted during guideline development.

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
WHO Recommendations for Induction of Labour (WHO 2011b)	Induction of labour	World Health Organization 2011	Recommended	Overall this is a high-quality guideline providing advice on the induction of labour. The method of development was rigorous; Cochrane systematic reviews formed the basis of the evidence and updates were undertaken as required. There is good discussion of the strengths and limitations of the evidence supporting the recommendations. The recommendations are clear and concise. Suggestions for monitoring and evaluating guideline implementation are made. Service users were involved in reviewing the guideline and the guideline development team comprised a range of health professionals and practitioners. Although there is no discussion of the influence of the funding body, it is unlikely to have had an impact on the guideline. The resource implications are briefly discussed but there is no economic analysis.
Screening for Hyperglycaemia in Pregnancy: A rapid update for the National Screening Committee (Waugh 2010)	Hyperglycaemia in pregnancy	United Kingdom 2010	Recommended with provisos or alterations	Overall this is a high-quality, well-conducted systematic review. This review will inform the update of the NICE guideline. It analyses multiple treatments for hyperglycaemia in pregnancy and examines selected screening studies. The issue of cost-effectiveness has been fully considered and the report provides clear guidance on future economic modelling. The method of development was rigorous; systematic methods were used to search for the evidence and the strengths and limitations of the body of evidence are clearly described. As this is not a guideline, it does not include recommendations or implementation details.
Obesity in Pregnancy	Obesity in pregnancy	Canada 2010	Not recommended	This guideline provides advice on the counselling and management of obese pregnant women. The guideline has some methodological weaknesses. The link between the recommendations and the supporting evidence is sometimes unclear. There is a lack of clarity around the quality of the included studies and the method used to form recommendations is not described. The resource implications of the recommendations are not fully examined and women with obesity were not involved in the development of the guideline. The guideline was based on a good literature search and the involvement of the relevant health professional expertise.

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
A European Evidence-based Guideline for the Prevention of Type 2 Diabetes (Paulweber 2010)	Type 2 diabetes	Europe 2010	Recommended with provisos or alterations	Overall this is a good-quality guideline providing advice about public health strategies to prevent type 2 diabetes and its comorbidities. The guideline provides recommendations to prevent type 2 diabetes in numerous populations, including those at high risk. The guideline development group included a wide range of stakeholders. The recommendations are clearly linked to the evidence. The guideline is supported by a published toolkit for the prevention of type 2 diabetes. The methodology is mostly well reported and appears to have been rigorous. There is a lack of clarity around the specific clinical questions and the method of addressing any potential conflicts of interest.
International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy (IADPSG 2010)	Hyperglycaemia in pregnancy	United States 2010	Not recommended	Overall this guideline does not meet the best standards for guideline development. It provides advice on the diagnosis and classification of hyperglycaemia in pregnancy. The clinical question at the centre of the guideline (diagnostic accuracy and screening) is not clearly defined and the literature on the topic was not systematically searched. The guideline presents two tables summarising the recommendations, which could be a useful implementation tool. Women with diabetes were not involved in developing the guideline and the resource implications of the recommendations have not been fully considered.
Guidelines for the Management of Pre-gestational and Gestational Diabetes Mellitus from Pre-conception to the Postnatal Period (Health Service Executive 2010)	Type 1 and type 2 diabetes and gestational diabetes mellitus	Ireland 2010	Not recommended	Overall this guideline does not meet the best standards for guideline development. It provides advice on the care of women with diabetes (type 1 and type 2) and gestational diabetes. There is a lack of clarity on the criteria for selecting the evidence. Although the recommendations are clearly graded related to the strength of the evidence, the link between the evidence and the recommendations is unclear and not discussed at all. Women with diabetes were not involved in developing the guideline. The resource implications of the recommendations do not appear to have been considered.

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
Dysglycemias in Pregnancy: From diagnosis to treatment. Brazilian consensus statement (Negrato 2010)	Hyperglycaemia in pregnancy	Brazil 2010	Recommended with provisos or alterations	This guideline aims to standardise diagnosis and clinical management of pregnant women with any degree of dysglycaemia. It appears that the evidence has been considered carefully but the reporting of the methodology is weak in some areas, making it difficult to understand the link between the evidence and the recommendations. There is a lack of clarity on the criteria for selecting the evidence and the quality appraisal process is not described. The algorithm and tables summarising the evidence may enhance effective implementation in clinical practice. Women with diabetes were not involved in developing the guideline and the resource implications of the recommendations have not been fully considered.
Management of Diabetes (SIGN 2010)	Type 1 and type 2 diabetes, and gestational diabetes mellitus	United Kingdom 2010	Recommended	Overall this is a high-quality guideline providing advice for health care professionals involved in the care of people with diabetes. Consumers were involved in the development of the guideline, and the guideline development team comprised a range of health professionals and practitioners. The recommendations are clearly linked to the evidence. Helpful tools for implementation are provided. The process for forming the recommendations is not well described. Although there is no discussion of the influence of the funding body, it is unlikely to have had an impact on the guideline. The resource implications are briefly discussed but there is no economic analysis.
Pregnancy and Diabetes	Diabetes in pregnancy	Belgium 2009	Not recommended	This guideline provides broad advice on identifying women with hyperglycaemia in pregnancy and providing care for women with known diabetes during pregnancy. The guideline has some serious methodological weaknesses. There is a lack of clarity around the criteria for selecting the evidence and the search strategies are not provided, introducing a strong possibility of selection bias. The target users and the setting for the guideline are not well defined. The resource implications of the recommendations are not fully examined. Women with hyperglycaemia/diabetes were not involved in the development of the guideline.

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
Therapeutic Management, Delivery, and Postpartum Risk Assessment and Screening in Gestational Diabetes (Nicholson 2008)	Gestational diabetes mellitus	United States 2008	Recommended with provisos or alterations	Overall this is a high-quality summary of the evidence primarily aimed at public health officials. It provides advice on glucose management, labour management, postpartum risk assessment, and screening of women with gestational diabetes. The method of development was rigorous; criteria for selecting evidence are well described; and the link between the evidence and the conclusions is explicit. Due to insufficient evidence, the guideline team was unable to provide clear recommendations. The guideline development group includes the relevant clinical and methodological expertise. The views and preferences of the target population have not been incorporated.
Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada (Canadian Diabetes Association 2008)	Type 1 and type 2 diabetes, diabetes in special groups (including diabetes in pregnancy)	Canada 2008	Recommended	Overall this is a methodologically sound guideline providing advice on the management of diabetes. The method of development was well described and appears to have been rigorous. The data to support some of the recommendations could have been presented in table format to provide a clearer link between the recommendations and the supporting evidence. The guideline development group includes the relevant clinical and methodological expertise; however, the views and preferences of the target population have not been incorporated. The resource implications of applying the recommendations are not discussed. A number of useful tools are provided to aid implementation, including algorithms and checklists within the guideline. There are also online educational tools for people with diabetes and health professionals. Conflicts of interests have been reported and addressed appropriately.
Diabetes in Pregnancy: Management of diabetes and its complications from preconception to the postnatal period (NICE 2008)	Diabetes in pregnancy	United Kingdom 2008	Recommended	Overall this is a high-quality guideline providing advice on the management of diabetes and its complications in pregnancy, from preconception to the postnatal period. The method of development was rigorous; the recommendations are clear and linked to the evidence. Service users were involved in the development of the guideline and the guideline development team comprised a range of health professionals and practitioners. A number of tools to aid implementation are available on the website. Although there is no discussion of the influence of the funding body, it is unlikely to have had an impact on the guideline.

Guideline title	Main topic area covered	Country, date of publication	Guideline appraisal outcome	Guideline appraisal summary
American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus (Blonde 2007)	Type 1 and type 2 diabetes, and gestational diabetes mellitus	United States 2007	Recommended with provisos or alterations	Overall this is a methodologically sound guideline providing advice on the prevention, diagnosis, screening and management of diabetes. The method of development is well described and there is a clear link between the evidence and the recommendations. The specific objective of the guideline and the health questions is not clearly defined and there is a lack of clarity around the criteria for selecting the evidence. The guideline development group includes the relevant clinical and methodological expertise; however, the views and preferences of the target population have not been incorporated. Conflicts of interests are reported, although the procedure for dealing with them during the recommendation phase is not detailed.
Managing Diabetes in Primary Care in the Caribbean (Caribbean Health Research Council 2006)	Type 2 diabetes	Caribbean 2006	Not recommended	This guideline provides evidence-based advice on the management of diabetes in primary care with a focus on type 2 diabetes. The guideline has some serious methodological weaknesses. There is a lack of clarity around the criteria for selecting the evidence and the search strategies are not provided, introducing a strong possibility of selection bias. The resource implications of the recommendations are not fully examined. People with diabetes were not involved in the development of the guideline.

Appendix F: Principles of woman-centred care

Understanding the woman's context

- Every woman has a right to antenatal care that takes into account her individual social and emotional situation.
- The experience of pregnancy differs for each woman (for example, the stability of woman's relationships and social environment).
- Referral to other services should also be considered, in partnership with the woman, if necessary.

Cultural safety in antenatal care

- Optimise communication (for example, by using interpreters).
- Build sound relationships.
- Acknowledge women's cultural preferences.
- Reflect on and analyse how power relationships and history have affected the health of individuals.

Providing information and support so that woman can make decisions

- In health interactions, women have the protection of the Code of Rights.
- Health professionals and women need to communicate and collaborate in a team approach.
- The woman's input (and the input of her family, if she chooses) is an important part of the process.
- Women have the right to decline care/advice if they choose, or withdraw consent at any time and have their choice respected. The level of care provided should not alter.
- Documenting decisions and discussions is important.
- Shared and reciprocal information is recommended.

Involving the woman's family

- Woman-centred care encompasses the needs of the baby, the woman's family, significant others and the community, as identified and negotiated by the woman herself.
- Each woman should be asked about who she would like to be involved in her care.
- Involving fathers/partners in antenatal care enables them to participate in decision-making and be informed about the care pathway and environmental factors that may influence the health of the baby during pregnancy (for example, exposure to passive smoking or domestic violence).
- Involving fathers/partners in antenatal care may also enable early intervention (for example, family support) for families requiring additional assistance.

Source: Adapted from Australian Health Ministers' Advisory Council (2012), pp 2–7.

Appendix G: Supporting evidence for Chapter 2

Summary of evidence for risk factors

There was variation in the diagnostic tests used between the studies and in the variables used in adjusted models.

Maternal age

Studies reported the risk of developing gestational diabetes increased with increasing maternal age (Gonzalez-Clemente et al 2007; Iqbal et al 2007; Ogonowski and Miazgowski 2010; Hoseini et al 2011; Ismail et al 2011; Kun et al 2011; Nanda et al 2011; Far et al 2012; Ramos-Levi et al 2012).

Two studies reported an increased risk of developing gestational diabetes in women aged 25 years or older at the time of conception (adj OR 1.34, 95%CI 1.04–1.73, p = 0.02) (Cypryk et al 2008; Lagerros et al 2012) and one of the studies reported a 50% increased risk for women aged 25–29 years compared with those aged 20–24 years (adj OR 1.5, 95%CI 1.3–1.7) (Lagerros et al 2012).

Two studies reported increased risk for women aged 30 years or older (Yang et al 2009; Makgoba et al 2012). One study reported an increased risk for women aged 30–33 years compared with those aged 20–24 years (Lagerros et al 2012); five studies reported increased risk for women aged 35 years and over (Hossein-Nezhad et al 2007; Aljohani et al 2008; Al-Kuwari and Al-Kubaisi 2011; Schneider et al 2011; Teede et al 2011). The risk appears to increase with maternal age such that the risk for women aged 40 years or older was seven times greater than that for women younger than 25 years (adj OR 7.0, 95%CI 2.9–17.2, p < 0.0001) (Teede et al 2011). Compared with women with normal glycaemic control in pregnancy, women aged 40 years or over also had a seven-fold increased risk of developing gestational diabetes (OR 7.0, 95%CI 2.9 –17.2, p < 0.001) (Teh et al 2011). A four-fold increased risk was reported for white European women aged over 40 years compared with those aged 20–24 years (OR 4.08, 95%CI 2.61–6.38, p < 0.001) (Makgoba et al 2012).

There is an increased risk for Black African, Black Caribbean and South Asian women at a younger age, compared with white European women (Makgoba et al 2012).

Ethnicity

Two systematic reviews and 15 observational studies were identified.

A systematic review of 49 observational studies identified indigenous women as being at an increased risk of developing gestational diabetes compared with other women in the same country (Chamberlain et al 2013).

Another systematic review of 24 observational studies (approximately 126,298 women) investigated migration and the development of gestational diabetes (Gagnon et al 2011). The following four migrant subgroups showed greater risk of gestational diabetes compared with receiving countries:

- Caribbean (RR 3.03, 95%CI 2.26–4.05; two studies)
- unspecified African (probably North African) (RR 2.46, 95%CI 2.12–2.85; four studies)
- European (RR 1.50, 95%CI 1.35–1.67; three studies)
- northern European (RR 1.21, 95%CI 1.03–1.42; two studies).

Due to heterogeneity, other data could not be pooled.

Three studies found an overall increased risk associated with being a migrant compared with being a national (born in the country) (Savitz et al 2008; Hedderson et al 2010b; Schneider et al 2011) and one study reported that being a national increased the risk of developing gestational diabetes (Al-Kuwari and Al-Kubaisi 2011).

Seven observational studies identified women from Asia and India as being at high risk of developing gestational diabetes (Savitz et al 2008; Hedderson et al 2010a; Ismail et al 2011; Nanda et al 2011; Teede et al 2011; Teh et al 2011; Makgoba et al 2012). Five studies identified Chinese women as being at high risk (Yang et al 2009; Hedderson et al 2010b; Ismail et al 2011; Teede et al 2011; Teh et al 2011; Winnard and Anderson 2013). Variation in ethnicity-associated risk was also reported within the same geographical region (Savitz et al 2008; Yang et al 2009). This variation further increases the difficulty in interpreting the evidence.

Women of Asian or Filipina backgrounds had a higher risk of gestational diabetes at lower body mass index levels (22–24.9 kg/m^2). The higher prevalence in other ethnicities was also detected at different body mass index values: Hispanic (28–30 kg/m^2), non-Hispanic White (34–36 kg/m^2) and African American ($\geq$ 37 kg/m^2). The estimated population-attributable risks suggested that 65% of cases of gestational diabetes in African American women and 23% in Asian women could be prevented if women were of normal body mass index (< 25 kg/m^2) (Hedderson et al 2012).

The risk of gestational diabetes being diagnosed in the third pregnancy for women who had already had two gestational diabetes pregnancies was OR 35.0 (95%CI 14.8–83.1) for non-Hispanic White, OR 158.4 (95%CI 22.8–897) for non-Hispanic Black, OR 17.3 (95%CI 9.9–30.1) for Hispanic and OR 36.1 (95%CI 14.7–89) for Asian/Pacific Islander. Hispanics and Asian/Pacific Islanders had a much higher recurrent risk of gestational diabetes compared with White women (Getahun et al 2010).

A number of inter-relationships were identified between race, body mass index and maternal age such that, for a non-white pregnant woman aged 25–29 years , the risk of developing gestational diabetes is similar to that of a White European woman of 40 years, and about three to four times greater than that of a White European aged 20–24 years. The odds for developing gestational diabetes were also significantly higher in other racial groups but at a younger age (older than 25 years if they were Black African or Black Caribbean and older than 20 years if they were South Asian) (Makgoba et al 2012).

Family history of diabetes

Ten out of thirteen observational studies reported risk estimates that ranged from 1.7–6.27. All of the studies reported an increased risk of developing gestational diabetes associated with having a positive family history of diabetes.

Previous history of gestational diabetes

Ten observational studies identified a positive association between previous gestational diabetes and recurrence of gestational diabetes in the index pregnancy.

Maternal weight or body mass index

One systematic review, a secondary analysis of a randomised trial and 29 observational studies were identified. Three distinct time frames were identified.

1. Pre-pregnancy weight was reported in 20 studies.

2. Early gestational weight gain was reported in four studies.

3. Body mass index during pregnancy or at point of screening was reported in 11 studies.

Pre-pregnancy body mass index

A number of different thresholds for pre-pregnancy body mass index were associated with increased risk of developing gestational diabetes. The range of levels was as follows: ≥ 24 kg/m² (Yang et al 2009), ≥ 25 kg/m² (Cypryk et al 2008; Makgoba et al 2012), 25–29 kg/m² (Bhat et al 2010; Kun et al 2011), > 30 kg/m² (Radesky et al 2008), ≥ 35 kg/m² (Torloni et al 2009; Schneider et al 2011; Teede et al 2011; Singh et al 2012) and > 40 kg/m² (Singh et al 2012).

In a systematic review (17 observational studies, including 395,338 women), maternal pre-pregnancy body mass index was directly associated with the risk of developing gestational diabetes, and the risk increased with increasing body mass index. The risk of gestational diabetes was twice as high for women with a body mass index of 25–29 kg/m² compared with women with a normal body mass index (Torloni et al 2009). For severely obese women, the risk was more than five times higher compared with women with a normal body mass index (Torloni et al 2009). An increased risk with increasing body mass index was reported in two observational studies and a systematic review (Gonzalez-Clemente et al 2007; Torloni et al 2009; Nanda et al 2011). A modest reduction in pre-pregnancy body mass index can have the potential to reduce the risk of gestational diabetes (Torloni et al 2009).

In a large cohort study including 323,083 women, the risk of gestational diabetes increased significantly with increasing body mass index (Lagerros et al 2012). The risk of gestational diabetes for women who were classified as obese was further amplified if they themselves had been born small for gestational age or large for gestational age compared with normal weight women (when compared with appropriate for gestational age: small for gestational age adj OR 2.3, 95%CI 1.8–2.9; large for gestational age adj OR 1.8, 95%CI 1.3–2.4). Compared with women who were born appropriate birthweight for gestational age and had normal adult early-pregnancy body mass index; women who were classified as obese had increased risk of developing gestational diabetes if they were small for gestational age (adj OR 28.7, 95%CI 17–48.6); if they had been large for gestational age the risk was adj OR 20.3 (95%CI 11.8–34.7); and if they had been born appropriate for gestational age, their risk of gestational diabetes was still 10 times higher (adj OR 10.4, 95%CI 8.4–13.0) (Lagerros et al 2012).

Lean or underweight women appear to have the lowest risk, or decreased risk, of developing gestational diabetes. The probability of developing gestational diabetes increased with increasing body mass index. With normal weight women as the reference group, underweight women (13–18.4kg/m²) had a reduced risk of developing gestational diabetes (adj RR 0.38, 95%CI 0.16–0.89). Women who were classified as overweight (25–29.9 kg/m²) had a two-fold increased risk of developing gestational diabetes (adj RR 2.17, 95%CI 1.58–2.97). The risk continued to rise for women classified as obese (30–34.9 kg/m²) adj RR 2.51 (95%CI 1.76–2.97),

and extremely obese (35–64.9kg/m²) who were reported to have a five-fold increased risk of developing gestational diabetes (adj RR 5.03, 95%CI 3.64–6.95) (Kim et al 2010). In another observational study there were significant relationships between pre-pregnancy body mass index and gestational diabetes in all body mass index categories except underweight women. Body mass index was the strongest predictor for requiring insulin therapy. The risk of gestational diabetes increased by 11.6% for each change in body mass index unit and was more pronounced in women who were treated with insulin compared with those treated with diet (19% and 8% respectively). The greatest risk occurred when there was a shift from normal weight to overweight and from overweight to obese categories (Ogonowski and Miazgowski 2009).

The risk of developing gestational diabetes was increased for women who were obese at the age of 18 years compared with women of normal weight at that age (RR 4.53, 95%CI 1.25–16.43). Adjusted analysis found a lower risk for women who were lean and a higher risk among obese women compared with normal weight women (RR 3.25, 95%CI 1.85–5.71). There was no association for overweight women (RR 0.74, 95%CI 0.23– 2.40). For women who gained 10 kg or more during adulthood, the risk of developing gestational diabetes was increased three-fold compared with women who had a weight change of 2.5 kg or less (RR 3.43, 95%CI 1.60–7.37). In an adjusted analysis, a 5 kg gain in weight between the age of 18 and pregnancy increased the risk of developing gestational diabetes by 20%. Where women had evidence of weight cycling (losing and then gaining weight), the adjusted relative risk was RR 1.46 (95%CI 0.87–2.43). Risk increased with repeated episodes of weight cycling, so that, for three or more cycles of weight change, the RR was 2.04 (95%CI 0.83–5.02) (Rudra et al 2007).

Compared with women with stable weight, women who gained weight at a rate of 1.1–2.2 kg per year had a small increased risk of gestational diabetes (adj OR 1.63, 95%CI 0.95–2.81) and women who gained weight at 2.3–10 kg per year had a 2.5-fold risk of developing gestational diabetes (adj OR 2.61, 95%CI 1.50–4.57). The association was stronger among women who were not overweight (body mass index < 25 kg/m²) at baseline (adj OR 2.81, 95%CI 1.33–5.93). Women who were overweight or obese at baseline had an increased risk of developing gestational diabetes (adj OR 2.14, 95%CI 1.41–3.25 and adj OR 1.93, 95%CI 1.20–3.10 respectively) (Hedderson et al 2008).

Increased percentage body fat was identified as a significant risk factor (OR 1.07, 95%CI 1.03–1.13) (Iqbal et al 2007).

Early gestational weight gain

Four studies agreed that there was an increased risk of developing gestational diabetes or impaired glucose tolerance with early increased gestational weight gain (Herring et al 2009; Hedderson et al 2010b; Carreno et al 2012; Gibson et al 2012).

A secondary analysis of a randomised trial reported that the odds of developing gestational diabetes were 43% higher in the group of women with excessive early gestational weight gain; particularly at risk were women with normal pre-pregnancy body mass index (adj OR 1.4, 95%CI 1.1–1.9). There was no effect observed for overweight or obese women with excessive early gestational weight gain (Carreno et al 2012).

Rapid increase in weight in early pregnancy, in particular the first trimester, resulted in an increased risk of gestational diabetes. Non-white women in the highest tertile for rate of weight gain had a 2.5-fold increased risk of developing gestational diabetes (OR 2.66, 95%CI 1.45–4.90) (Hedderson et al 2010b).

Body mass index/weight during pregnancy

Eight studies reported that there was an increased risk of developing gestational diabetes with increased body mass index or increased weight gain during pregnancy (Hossein-Nezhad et al 2007; Hedderson et al 2010b, 2012; Ogonowski et al 2009 Ismail et al 2011; Nanda et al 2011; Teh et al 2011; Far et al 2012).

Prevalence of gestational diabetes in Asian and Filipina women was higher at a lower body mass index category (22–24.9 kg/m²) whereas for Hispanic, non-Hispanic White and African American women the higher prevalence occurred with body mass index categories of 28–30, 34–36, and ≥ 37 kg/m² respectively. The estimated population attributable risks suggested that 65% of cases of gestational diabetes in African American women and 23% in Asian women could be prevented if women were of normal body mass index (< 25 kg/m²) (Hedderson et al 2012).

In an adjusted analysis, the risk of developing gestational diabetes increased with increasing rates of weight gain. Using the third tertile as a referent (less than 0.27 kg per week), rate gains of 0.27–0.4 kg per week (OR 1.43, 95%CI 0.96– 2.14) and 0.41 kg per week or more (OR 1.74, 95%CI 1.16–2.60) were associated with increased risks of gestational diabetes. The association was stronger in overweight or obese and non-white women. Non-white women in the highest tertile for rate of weight gain had a 2.5-fold increased risk of developing gestational diabetes (OR 2.66, 95%CI 1.45–4.90) compared with the risk for non-Hispanic White women of OR 1.56 (95%CI 0.90–2.68) (Hedderson et al 2010b).

Previous history of macrosomic or large for gestational age infant

A history of previous macrosomia/large for gestational age infants or current macrosomia was identified as a risk factor for developing gestational diabetes in six studies (Cypryk et al 2008; Bhat et al 2010). The risk of developing gestational diabetes ranged from 2.72–4.39 times higher for women with a macrosomic infant.

Parity

Nine studies reported on parity as a risk factor in the development of gestational diabetes. Seven studies reported the effect estimate which ranged from 0.6–2.7.

Nulliparous women were at increased risk of developing gestational diabetes (Hossein-Nezhad et al 2007; Cypryk et al 2008; Al-Kuwari and Al-Kubaisi 2011; Hoseini et al 2011; Kun et al 2011; Nanda et al 2011; Schneider et al 2011; Lagerros et al 2012; Singh et al 2012), but this was most likely due to probable undiagnosed diabetes (Singh et al 2012). Ten studies did not identify parity as a risk factor (Lagerros et al 2012: Hossein-Nezhad et al 2007; Cypryk et al 2008; Al-Kuwari and Al-Kabaisi 2011; Hoseini et al 2011; Kun et al 2011; Nanda et al 2011; Schneider et al 2011; Lagerros et al 2012; Singh et al 2012).

Dietary risk factors

Ten observational studies were identified. Increased consumption of red meat or processed meat was associated with an increased risk of developing gestational diabetes (Qiu et al 2011a; Bowers et al 2012; Ramos-Levi et al 2012). Compared with women with the lowest decile of heme iron intake (primarily obtained through red meat), women in the highest decile intake were three times more likely to develop gestational diabetes (adj RR 3.31, 95%CI 1.02–10.72) (Qiu et al 2011a). A 1 mg per day increase in heme iron was associated with a minimum of 51% increased risk of developing gestational diabetes (RR 1.51, 95%CI 0.99–2.36) (Qiu et al 2011a). With every 0.5 mg/day of increase in intake in heme iron, the adj RR was 1.22 (95%CI 1.1–1.36) (Bowers et al 2011). Consumption of red and/or processed meat more than six times per week

increased the risk of developing gestational diabetes but no risk estimates were provided (Ramos-Levi et al 2012). No significant relationships were identified between total dietary, non-heme, or supplemental iron intake and risk of gestational diabetes (Bowers et al 2011). Increased iron status was significantly higher in women with gestational diabetes compared with controls.

Monounsaturated fatty acid is a component of animal fat and red meat is a major source of animal fat. When dietary carbohydrates were substituted with mono-unsaturated fatty acid (per each 5% of total calories), risk of gestational diabetes was increased by 29% (RR 1.29, 95%CI 1.09−1.51, p = 0.003) (Bowers et al 2012). Replacing 5% of energy from carbohydrates with animal fat increased the risk of GDM by 13% (RR 1.13, 95%CI 1.08−1.18, p = 0.001). Conversely the substitution of vegetable fat for animal fat suggested a decrease in the risk of gestational diabetes. (RR 0.93, 95%CI 0.88−0.98, p = 0.01). The increased risk of developing gestational diabetes in women in the highest quintile of animal fat intake was about 90% (adj RR 1.88, 95%CI 1.36−2.60, p = 0.05) (Bowers et al 2012).

Other dietary risk factors included increased consumption of sugary drinks (more than four to five servings per week) (Chen et al 2009; Ramos-Levi et al 2012), high coffee intake (two to three times per day) and high intake of biscuits and pastries (more than four times per week) (Ramos-Levi et al 2012); increased egg consumption (seven or more eggs per week) was associated with an increased risk (OR 2.65, 95%CI 1.48−4.72) (Qiu et al 2011b). The relative risk of developing gestational diabetes for women with high cholesterol intake (≥ 294 mg per day) versus low cholesterol intake (< 151 mg per day) was 2.35 (95%CI 1.35−4.09) (Qiu et al 2011c).

Intake of n-3 fatty acids was associated with increased risk of gestational diabetes but not impaired glucose tolerance (OR 1.11, 95%CI 1.02−1.22, per 300 mg/day). The increased risk associated with n-3 fatty acid intake was limited to the group of women with pre-pregnancy body mass index < 25 kg/m^2 (adj OR 1.19, 95%CI 1.06−1.35) per 300 g per day compared with women with a body mass index of ≥ 25 kg/m^2 (adj OR 1.03, 95%CI 0.83−1.27) (Radesky et al 2008).

Increased intake of polyunsaturated fats and n-6 fatty acids was also associated with an increased risk of developing gestational diabetes in women with a pre-pregnancy body mass index < 25 kg/m^2 (Radesky et al 2008).

Increased intake of saturated and trans fat and decreased intake of fruit and fibre have been identified as a risk factor (Ley et al 2011). Development of gestational diabetes was associated with lower carbohydrate intake and higher total fat intake distributions as a percentage of energy (Ley et al 2011).

Each 50 mg per 1000 kcal increase in cholesterol intake was associated with an increase of 88% in the diagnosis of gestational diabetes (adj OR 1.88, 95%CI 1.09−3.23) but there was no relationship between the presence of gestational diabetes and the intake of saturated, monounsaturated, polyunsaturated or trans unsaturated fat (Gonzalez-Clemente et al 2007).

Vitamin D levels

One systematic review included seven observational studies of 2146 women, of whom 433 had gestational diabetes. Women with gestational diabetes had significantly lower vitamin D levels than women with normal glucose levels during pregnancy (MD -5.33 nmol/L, 95%CI -9.7 to -0.9, p = 0.02, I^2 = 69%). Caution is required in interpreting results due to significant heterogeneity. After adjustment for studies that reported on maternal age and obesity, the association remained significant (combined OR 1.57, 95%CI 1.11–2.22, I^2 = 17%) (Poel et al 2012).

Three additional observational studies were identified (Lau et al 2011; Burris et al 2012; Parlea et al 2012). A significant association was found between vitamin D < 73.5 nmol/L and risk of gestational diabetes (adj OR 2.21, 95%CI 1.19–4.13, p = 0.001) (Lau et al 2011). HbA1c levels were significantly lower at -0.41% (95%CI -0.16% to -0.66%, p = 0.001) in women who had 25(OH)D levels ≤ 50 nmol/L compared with women with levels of > 50 nmol/L. These women also had lower blood glucose readings at fasting (-0.4mmol/L (95%CI -0.1 to -0.7, p = 0.02) and one hour (-2.4mmol/L 95%CI -0.60 to -4.3, p = 0.013) oral glucose tolerance test (Lau et al 2011). Significantly increased odds of gestational diabetes in women with severe vitamin D deficiency (serum 25 hydroxyvitamin D 25(OH)D < 25nmol/L) compared with women with normal glucose tolerance adj OR 3.1 (95%CI 1.3–7.4) were also reported (Burris et al 2012).

These studies call for screening of vitamin D levels in early pregnancy (16–18 weeks) and to potentially use supplementation or lifestyle advice to increase vitamin D levels. The studies are, however, based on small sample sizes and may lack the power to detect true differences.

Maternal history of subfertility

Maternal history of subfertility was reported as a risk factor for developing gestational diabetes in one systematic review (Toulis et al 2009) and two observational studies (Bhat et al 2010; Reyes-Munoz et al 2012b). Criteria used to diagnose gestational diabetes varied between studies.

A three-fold increased risk of developing gestational diabetes in women with a history of subfertility was reported in both observational studies (Bhat et al 2010; Reyes-Munoz et al 2012b). The systematic review and one of the observational studies identified increased risk of developing gestational diabetes in women with subfertility associated with polycystic ovary syndrome (Toulis et al 2009; Reyes-Munoz et al 2012b). The systematic review also reported a three-fold increased risk of developing gestational diabetes (OR 2.89, 95%CI 1.68–4.98, p = 0.0001) in 15 observational studies (Toulis et al 2009). The effect was only apparent in the cohort studies, not in case control studies. Due to high levels of heterogeneity, caution was suggested in interpreting any association between polycystic ovary syndrome related subfertility and developing gestational diabetes (Toulis et al 2009).

Maternal height

Four studies reported an increased risk for women of short stature (Rudra et al 2007; Yang et al 2009; Ogonowski et al 2010; Lagerros et al 2012).

Socioeconomic status

Women with a low income were identified with a 16% increased risk of developing gestational diabetes (adj OR 1.16; 95%CI 1.05–1.3, p = 0.004), and women who were classified as housewives were at increased risk of developing gestational diabetes compared with skilled workers (adj OR 1.21, 95%CI 1.14–1.29) (Schneider et al 2011). In a Canadian study of First Nation indigenous people, there was an increased risk of developing gestational diabetes for women living in rural areas compared with those in urban areas (adj OR 0.78; 95%CI 0.74–0.82, p < 0.01) and this difference was particularly apparent in those living on First Nation reserves (Aljohani et al 2008).

Physical inactivity

Participation in sports for less than two days per week increased the risk of developing gestational diabetes. No risk estimates were provided (Ramos-Levi et al 2012). Women who were classified as 'inactive' before or during early pregnancy had OR 7.9 (95%CI 3.7–16.56) and OR 1.3 (95%CI 1.2 –1.4) respectively for developing gestational diabetes compared with those classified as 'minimally active' or 'active' women. There was a negative correlation between pre-pregnancy BMI and physical activity before pregnancy. Pregnancy resulted in a decrease in physical activity regardless of diagnosis (p < 0.001) (Harizopoulou et al 2010).

Obstetric history

Women with a history of spontaneous abortion had an increased risk of developing gestational diabetes adj OR 1.46 (95%CI 1.12–1.91, p = 0.03) (Yang et al 2009). Compared with women with a normal screening test, women with gestational diabetes were more likely to have had an abortion (not specified) (adj OR 3.12, 95%CI 1.98–4.91, p < 0.0001) (Hossein-Nezhad et al 2007). In an Iranian study previous pregnancy loss was not identified as a risk factor for gestational diabetes (Hoseini et al 2011).

Genetic variants

A systematic review of 22 studies (10,336 cases and 17,445 controls) identified eight polymorphisms strongly associated with developing gestational diabetes. The relative contribution of these genetic variants and their relevance in the development of gestational diabetes are yet to be established (Mao et al 2012).

Maternal comorbidity

Maternal comorbidity including hypothyroidism (Hoseini et al 2011), chronic hypertension (Hoseini et al 2011; Singh et al 2012) and candida infection (Yang et al 2009; Bhat et al 2010) were associated with increased risk of developing gestational diabetes.

Table 3: Risk factors for previously undiagnosed type 2 diabetes

Reference	Risk factors
American Diabetes Association (2012)	Body mass index ≥ 25 kg/m² and having one or more additional risk factors present. Those risk factors are: • physical inactivity • first-degree relative with diabetes • high-risk race/ethnicity (eg, African American, Latino, native American, Asian American, Pacific Islander) • women who delivered a baby weighing 4000 g or who were diagnosed with gestational diabetes • hypertension (blood pressure ≥ 140/90 mmHg) or on therapy for hypertension • high density lipoprotein cholesterol level <35 mg/dL (0.9 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L) • women with polycystic ovary syndrome • HbA1c ≥5.7%, impaired glucose tolerance, or impaired fasting glucose on previous testing • other clinical conditions associated with insulin resistance (eg, severe obesity, acanthosis nigricans) • history of cardiovascular disease.
Canadian Task Force on Preventative Health Care (2012)	• Age > 45 years • Body mass index > 25 kg/m² • Waist circumference > 80 cm • Physical inactivity < 30 minutes/day • No daily consumption of fruits, vegetables or berries • Any history of hyperglycaemia • Family history (first- or second-degree relative) of type 1 or 2 diabetes • History of hypertension requiring medication
National Institute for Health and Care Excellence (NICE 2012)	• Age ≥ 40 years • Age 25–39 years if South Asian, Chinese, African Caribbean, Black African or another high-risk black or minority group • People with conditions that increase the risk of type 2 diabetes (cardiovascular disease, hypertension, obesity, polycystic ovary syndrome, history of gestational diabetes, and people with mental health problems)
Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	• Body mass index ≥ 25 kg/m² • A1C ≥ 5.7%, impaired glucose tolerance or impaired fasting glucose or prediabetes • Race/ethnicity (Hispanic/Latino, African American, Native American, Asian American or Pacific Islander) (American College of Obstetricians and Gynecologists 2001) • Family history (first-degree relative with diabetes) • History of gestational diabetes, baby weighing more than 4000 g at birth, unexplained stillbirth, or malformed infant • Markers of insulin resistance (acanthosis nigricans and/or waist circumference > 35 inches (> 31 inches for Asian women) • Women with polycystic ovary syndrome • Medications that affect normoglycaemia • Physical inactivity • History of hypertension (> 140/90 mmHg) or on therapy for hypertension • History of cardiovascular disease • History of dyslipidaemia: high density lipoprotein < 35 mg/dL and/or triglycerides ≥ 250 mg/dL

Reference	Risk factors
New Zealand Society for the Study of Diabetes (2011)*	Adults > 25 years of age with the following risk factors: • ischaemic heart disease (angina or myocardial infarction), cerebrovascular disease or peripheral vascular disease • on long-term steroid or anti-psychotic treatment • obese (body mass index ≥ 30 kg/m²; or ≥ 27kg/m² for Indo-Asian peoples) • a family history of early age of onset type 2 diabetes in more than one first-degree relative • a past personal history of gestational diabetes mellitus. Young adults who are obese should be screened if : • there is a family history of early onset type 2 diabetes or • they are of Māori, Pacific or Indo-Asian ethnicity.
Scottish Intercollegiate Guidelines Network (SIGN 2010)	• Persistent glycosuria • Random glucose levels > 5.5 mmol/L 2 hours after food or > 7.0 mmol/L within 2 hours of food

European Guideline on Prevention of Type 2 Diabetes (Paulweber 2010)	a) White people aged over 40 years or people from Black, Asian and minority ethnic groups aged over 25 years with one or more of the following risk factors:
	    • a first-degree family history of diabetes
	    • body mass index over 25 kg/m²
	    • waist measurement of ≥ 94 cm for White and Black men, ≥ 80 cm for White, Black and Asian women and ≥ 90 cm for Asian men
	    • systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or treated hypertension
	    • high density lipoprotein cholesterol ≤ 0.35 g/L (0.9 mM) or triglycerides ≥ 2 g/L (2.2 mM) or treated dyslipidemia
	b) Women with a history of gestational diabetes or with a child weighing > 4 kg at birth
	c) People with history of temporarily induced diabetes, eg, steroids
	d) People who have ischaemic heart disease, cerebrovascular disease, peripheral vascular disease
	e) Women with polycystic ovary syndrome who have a body mass index ≥ 30 kg/m²
	f) People who have severe mental health problems and/or who are receiving long-term anti-psychotic drugs
	g) People with a history of impaired glucose tolerance or impaired fasting glucose

Reference	Risk factors
Canadian Diabetes Association (2008)	• Age ≥ 40 years • First-degree relative with type 2 diabetes • Member of high-risk population (Aboriginal, Hispanic, South Asian, Asian, or African descent) • History of impaired fasting glucose or impaired glucose tolerance • Presence of complications associated with diabetes • Vascular disease (coronary, cerebrovascular or peripheral) • History of gestational diabetes • History of delivery of a macrosomic infant • Hypertension • Dyslipidaemia • Overweight • Abdominal obesity • Polycystic ovary syndrome • Acanthosis nigricans • Schizophrenia • Other factors associated with some infections, therapeutic drug use, or genetic syndromes
US Preventive Services Task Force (Norris 2008)	Sustained blood pressure > 135/80 mmHg
Gestational Diabetes Mellitus Technical Working Party (2007)	• History of gestational diabetes or previous diagnosis of impaired fasting glucose or impaired glucose tolerance prior to pregnancy • Glycosuria • Polycystic ovary syndrome • Morbid obesity (ethnic specific body mass index: European ≥ 35 kg/m², Polynesian ≥ 37 kg/m², Indian and Asian ≥ 32 kg/m²) • Two first-degree relatives with diabetes • Previous unexplained stillbirth • Previous shoulder dystocia • Previous macrosomic baby (≥ 97th percentile based on customised birthweight chart. If there is no access to customised charts then ≥ 4700 g for Polynesian, ≥ 4400 g for European, ≥ 4000 g for Asians, including South Asians)
American Association of Clinical Endocrinologists (Blonde 2007)	• Family history • Cardiovascular disease • Overweight/obesity • Sedentary lifestyle • Latino/Hispanic, non-Hispanic Black, Asian American, Native American, Pacific Islander • Previously identified impaired glucose tolerance or impaired fasting glucose • Hypertension • Increased levels of triglycerides or low concentration of high density lipoprotein cholesterol, or both • History of gestational diabetes • History of an infant weighing 4000 g • Polycystic ovary syndrome • Psychiatric illness

Reference	Risk factors
Caribbean Health Research Council (2006)	• Overweight (body mass index ≥ 25 kg/m²) • Age 45 years and older • Physical inactivity • Diabetes in a first-degree relative • Prior gestational diabetes or history of delivering a baby > 4 kg • Polycystic ovary syndrome • History of impaired glucose tolerance or impaired fasting glucose • High density lipoprotein cholesterol level ≤ 35 mg/dL (≤ 0.90 mmol/L) and/or triglyceride level ≥250 mg/dL (≥ 2.82 mmol/L) • Race/ethnicity (eg, people of Asian and African descent) • Presence of coronary artery disease and/or hypertension (blood pressure ≥140/90 mm Hg) • Presence of other vascular complications

Note: * The New Zealand Society for the Study of Diabetes position statement on the diagnosis of and screening for type 2 diabetes (updated September 2011) (www.nzssd.org.nz/statements.html).

Table 4: Risk factors for gestational diabetes identified in clinical guidelines/position statements

Agency for Healthcare Research and Quality (Hartling 2012)	Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	Health Service Executive, Ireland (2010)	Brazilian Diabetes Society and the Brazilian Federation of Gynecology and Obstetrics Societies (Negrato 2010)	Scottish Intercollegiate Guidelines Network (SIGN 2010)	Canadian Diabetes Association (2008)	National Institute for Health and Care Excellence (NICE 2008)	Caribbean Health Research Council (2006)	American Association of Clinical Endocrinologists (Blonde 2007)	Australasian Diabetes in Pregnancy Society (Nankervis 2013)
Previous GDM	–	–	–	Previous GDM	Previous GDM	Previous GDM	Previous history of abnormal glucose metabolism	History of abnormal glucose metabolism	Previous GDM
Delivery of a previous macrosomic infant	Previous macrosomic infant	Previous macrosomic baby (> 4.5 kg)	Macrosomic or large for gestational age infant	Previous macrosomic baby (> 4.5 kg)	Delivery of a previous macrosomic infant	Previous macrosomic baby (> 4.5 kg)	Previous macrosomic baby (> 4.5 kg)	History of a delivered infant > 4 kg	Previous macrosomic baby (> 4.5 kg)
Member of an ethnic group at increased risk for development of type 2 diabetes mellitus (ie, Hispanic, African, Native American, South or East Asian, or Pacific Islands ancestry)	Ethnicity in high-risk population (American Indian, African American, Hispanic/Latino, Asian American)	Ethnicity associated with a high prevalence of diabetes: India, Pakistan, Bangladesh, Black Caribbean, Saudi Arabia, United Arab Emirates, Iraq, Jordan, Syria, Oman, Qatar, Kuwait, Lebanon, Egypt	–	Family origin with a high prevalence of diabetes: South Asian (specifically women whose country of family origin is India, Pakistan or Bangladesh); Black Caribbean; Middle Eastern (specifically women whose country of family origin is Saudi Arabia, United Arab Emirates, Iraq, Jordan, Syria, Oman, Qatar, Kuwait, Lebanon or Egypt)	Member of a high-risk population (Aboriginal, Hispanic, South Asian, Asian African)	Minority ethnic background – South Asian (specifically India, Pakistan, Bangladesh), Black Caribbean and Middle Eastern women	Ethnicity associated with high prevalence of GDM	Latino/Hispanic, non-Hispanic Black, Asian American, Native American, Pacific Islander	Ethnicity: Asian (including Indian), Aboriginal, Māori, Pacific Islander, Middle Eastern, non-white African

Agency for Healthcare Research and Quality (Hartling 2012)	Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	Health Service Executive, Ireland (2010)	Brazilian Diabetes Society and the Brazilian Federation of Gynecology and Obstetrics Societies (Negrato 2010)	Scottish Intercollegiate Guidelines Network (SIGN 2010)	Canadian Diabetes Association (2008)	National Institute for Health and Care Excellence (NICE 2008)	Caribbean Health Research Council (2006)	American Association of Clinical Endocrinologists (Blonde 2007)	Australasian Diabetes in Pregnancy Society (Nankervis 2013)
Higher BMI	Overweight/ obesity	BMI > 30 kg/m²	BMI ≥ 25 kg/m² before pregnancy or in first trimester and/or excessive weight gain in index pregnancy	BMI > 30 kg/m²	BMI ≥ 30 kg/m²	BMI > 30 kg/m²	Overweight	Overweight/obesity	Obesity, especially if BMI ≥ 35 kg/m²
Greater maternal age	Advanced age	Maternal age ≥ 40 years	Advanced maternal age ≥ 35 years	–	Age ≥ 35 years	Advanced maternal age	Age > 25 years	Age > 25 years	Maternal age ≥ 40 years
Polycystic ovary syndrome	–	Polycystic ovary syndrome	Polycystic ovary syndrome	–	Polycystic ovary syndrome	–	–	Polycystic ovary syndrome	Polycystic ovary syndrome
–	–	Long-term steroid use	Use of thiazidic diuretics, corticosteroids or high dose of thyroid hormone	–	Corticosteroid use	–	–	–	Corticosteroid use or anti-psychotic treatment
Type 2 diabetes in a first-degree relative	Family history of diabetes	Family history of diabetes in a first-degree relative	Family history of diabetes in a first-degree relative	Family history of diabetes in a first-degree relative	–	Family history of diabetes (first-degree relative)	Family history of diabetes (first-degree relative)	Family history of diabetes (first-degree relative)	Family history of diabetes (first-degree relative including a sister)
Metabolic syndrome	History of abnormal glucose tolerance	Current glycosuria	Polyhydramnios	–	Acanthosis nigrans	Current smoker	Glycosuria	Fasting plasma glucose > 85 mg/dL or 2-hour postprandial glucose concentration > 140 mg/dL	–

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Agency for Healthcare Research and Quality (Hartling 2012)	Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	Health Service Executive, Ireland (2010)	Brazilian Diabetes Society and the Brazilian Federation of Gynecology and Obstetrics Societies (Negrato 2010)	Scottish Intercollegiate Guidelines Network (SIGN 2010)	Canadian Diabetes Association (2008)	National Institute for Health and Care Excellence (NICE 2008)	Caribbean Health Research Council (2006)	American Association of Clinical Endocrinologists (Blonde 2007)	Australasian Diabetes in Pregnancy Society (Nankervis 2013)
Polyhydramnios	Previous poor obstetric outcome	Polyhydramnios and/or macrosomia in existing pregnancy	Previous poor obstetric history	–	–	Increased maternal weight gain in early adulthood	Previous poor obstetric history	Previous poor obstetric history	–
History of unexplained stillbirth		Previous unexplained perinatal death	Hypertension/pre-eclampsia in index pregnancy	–	–	–	–	–	–

Note: BMI = body mass index; GDM = gestational diabetes mellitus.

Table 5: Studies reporting on maternal age as a risk factor for developing hyperglycaemia in pregnancy

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Lagerros (2012)	Sweden 332,083	Cohort	No details on screening 75 g OGTT Fasting plasma ≥7.0 mmol/L, and/or 2-hour plasma ≥ 10.0 mmol/L, or manifest diabetes only diagnosed as fasting plasma ≥ 7.0 mmol/L and/or 2-hour plasma ≥ 12.2 mmol/L.	25–29 years compared with 20–24 years: adj OR 1.5 (95%CI 1.3–1.7) 30–33 years compared with 20–24 years (adj OR 1.8, 95%CI 1.5–2.2)	HIGH
Teede (2011)	Australia 4276	Retrospective cohort	50 g, 1-hour OGCT If positive, followed by a 75 g, 2-hour OGTT: • fasting ≥ 5.5 mmol/L • 2-hour ≥ 8 mmol/L.	35–39 years compared with < 25 years: adj OR 5.4 (95%CI 2.4–12.2) ≥ 40 years compared with < 25 years: adj OR 7.0 (95%CI 2.9–17.2, $p < 0.0001$)	HIGH
Aljohani (2008)	Canada 165,969	Retrospective cohort	**From 1992** 50 g OGCT If ≥ 7.8 mmol/L then 100 g, 3-hour OGTT with two or more abnormal results required from: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 9.2 mmol/L • 3-hour ≥ 8.1 mmol/L. **From 1998** 50 g OGCT If ≥ 7.8 but < 10.2 mmol/L, then a 75 g, 2-hour OGTT with two or more abnormal results required from: • fasting ≥ 5.3 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 8.9 mmol/L.	≥ 35 years compared with < 35 years: adj OR 2.38 (95%CI 2.24–2.54). Effect similar for both First Nation and non-First Nation women	HIGH
Far (2012)	Iran 711	Cohort	50 g, 1-hour OGCT If ≥ 140 mg/dL after 1 hour, then a 3-hour, 100 g OGTT (National Diabetes Data Group criteria).	Increasing maternal age OR 1.14 (95%CI 1.07–1.21, $p < 0.001$)	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Makgoba (2012)	United Kingdom 174,320	Retrospective cohort	Diagnosis and screening varied between the units (no details).	Women with GDM were significantly older than non-GDM women (29.6 ± 5.2 versus 26.8 ± 5.1 years, $p < 0.001$). White European women > 30 years had significantly higher risk of developing GDM compared with White European women age 20–24 years. Women > 40 years OR 4.08 (95%CI 2.61–6.38, $p < 0.001$)	MEDIUM
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose recorded at 24–28 weeks, if > 6.7 mmol/L, then conducted a 75 g OGTT within two weeks. GDM diagnosed if fasting plasma glucose ≥6mmol/L or 2-hour level is ≥ 7.8 mmol/L.	Compared with women without GDM, women with GDM were older and had an increased risk of developing GDM per year of maternal age (adj OR 1.06, 95%CI 1.03–1.08, $p < 0.0001$).	MEDIUM
Schneider (2011)	Germany 647,385	Cross-sectional	No details provided.	Compared with women < 20 years, women aged > 35 years had an almost four-fold increased risk (adj OR 4.69; 95%CI 3.9–5.6, $p < 0.001$).	MEDIUM
Teh (2011)	Australia 2880	Retrospective cohort	75 g OGCT Positive result (1-hour venous plasma glucose ≥ 8.0 mmol/L) proceeded to a 2-hour, 75 g OGTT. Fasting venous plasma glucose level ≥5.5 mmol/L or 2-hour level of ≥ 8.0 mmol/L.	Compared women with no GDM, women aged ≥40 at greater risk of GDM: OR 7.0 (95%CI 2.9–17.2, $p < 0.001$).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Ogonowski (2010)	Poland 1830 cases, 1011 controls	Retrospective case control	GCT of 50 g If > 180 mg/dL (10 mmol/L), then diagnosed as GDM. If 140–180 mg/dL, then a 75 g OGTT using the WHO criteria: • fasting ≥ 110 mg/dL (6.1 mmol/L) • 2-hour ≥ 140 (7.8 mmol/L). Also used the ADA criteria where two abnormal values are required from: • fasting ≥ 95 mg/dL (5.3 mmol/L) • 1-hour ≥ 180 mg/dL (10.0 mmol/L) • 2-hour ≥ 155 mg/dL (8.6 mmol/L).	Women with increasing age were more likely to have GDM: OR 1.09 (95%CI 1.07–1.11, p = 0.000001)	MEDIUM
Yang (2009)	China 16,286	Prospective cohort	50 g GCT OGTT (>11.1 mmol/L diagnosed as GDM) If 7.9–11.0 mmol/L, then 75 g, 3-hour OGTT where two or more abnormal values are required from: • fasting > 5.3 mmol/L • 1-hour > 10 mmol/L • 2-hour > 8.6 mmol/L.	adj OR 2.18 (95%CI 1.88–2.52, $p < 0.001$)	MEDIUM
Cypryk (2008)	Poland 1670	Cohort	GDM diagnosed using WHO and Polish Diabetes Association criteria (no other details).	Adj OR 1.34 (95%CI 1.04–1.73, p = 0.02) for age >25 years at conception	MEDIUM
Gonzalez-Clemente (2007)	Spain 335	Cohort	50 g GCT (≥ 7.8 mmol/L) 100 g, 3-hour OGTT NDDG criteria	Adj OR 1.12 (95%CI 1.04–1.21, p = 0.003) per year increase	MEDIUM

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Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Iqbal (2007)	Pakistan 750	Prospective cohort	75 g, 2-hour GCT (> 7.8 mmol/L) followed by a 100 g, 3-hour OGTT if abnormal value. Cut-off values of ADA: • fasting >5.3 mmol/L • 1-hour >10 mmol/L • 2-hour > 8.6 mmol/L • 3-hour > 7.8 mmol/L. This analysis included subjects with either one or two raised values.	Increased maternal age adj OR 1.13 (95%CI 1.06–1.21)	MEDIUM
Hossein-Nezhad (2007)	Iran 2416	Cross-sectional	Universal screening with 50 g, 1-hour OGCT at 24–28 weeks (women with known risk factors were screened at first antenatal visit). If result abnormal (≥ 130 mg/dL), then underwent a 100 g, 3-hour OGTT using the Carpenter and Coustan criteria. Women divided into four groups: 1. GDM; 2. IGT –impaired glucose tolerance; 3. IGCT impaired glucose challenge test; 4. normal.	Compared with women with a normal screening test, women with GDM were more likely to be older (35–45 years) adj OR 9.96 (95%CI 5.74–17.27, $p < 0.0001$).	MEDIUM
Ramos-Levi (2012)	Spain 2194	Observational cohort	Screened with ADA criteria	Increasing age increased risk of GDM (no risk data reported).	LOW
Al-Kuwari (2011)	Qatar 4295	Cross-sectional	1 hour GCT (no details) If ≥7.8mmol/L, then a 75 g OGTT: • fasting > 95 mg/dL • 1-hour >180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL	≥35 years (OR 3.8; 95%CI 2.4–6.4)	LOW

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Hoseini (2011)	Iran 114 cases, 113 controls	Retrospective cross-sectional	50 g, 1-hour OGCT If > 140 mg/dL, then a 100 g, 3-hour OGTT with two or more abnormal readings required from: • fasting >95 mg/dL • 1-hour >180 mg/dL • 2-hour> 155 mg/dL • 3-hour > 140 mg/dL	Risk of GDM increased with increasing age. Women aged 26+ years had a two-fold greater risk of GDM than women < 26 years (OR 2.1, 95%CI not reported, p = 0.03).	LOW
Ismail (2011)	Malaysia 616	Observational	75 g OGTT, fasting and 2-hour postprandial > 6 mmol/L or > 7.8 mmol/L respectively	Increasing age associated with increased risk (p < 0.001).	LOW
Kun (2011)	Hungary 2260	Observational	75g OGTT, 2-hour post-test Diagnosis based on WHO or IADPSG criteria	Older women had increased risk compared with normal women using both criteria (p < 0.001 and p = 0.004 respectively). According to the WHO criteria, the risk of GDM increased by 7% per year of ageing (OR 1.07, 95%CI 1.03–1.11).	LOW
Yogev (2010)	Israel 5483	Case control	50g OGCT (> 140 mg/dL) 100 g, 3-hour OGTT: • fasting ≥ 5.3 mmol/L • 1-hour ≥ 10 mmol/L • 2-hour ≥ 8.6 mmol/L • 3-hour ≥ 7.8 mmol/L	The incidence of GDM was significantly higher for women aged ≥ 45 years (17%) compared with women aged 20–29 years (1.4%), 30–39 years (4.2%) and 40–44 years (10.2%), p < 0.001.	LOW

Note: ADA = American Diabetes Association; CI = confidence interval; GCT = glucose challenge test; GDM = gestational diabetes mellitus; IADPSG = International Association of Diabetes and Pregnancy Study Groups; NDDG = National Diabetes Data Group; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test; OR = odds ratio; WHO = World Health Organization.

Table 6: Studies reporting on ethnicity as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Getahun (2010)	USA 540,956	Retrospective cohort	Used ICD codes to identify women with a diagnosis of GDM	Compared with women who had not been diagnosed with GDM in the first two pregnancies, the risk of GDM being diagnosed in the third pregnancy for women who had already had two GDM pregnancies was: • OR 35.0 (95%CI 14.8–83.1) for non-Hispanic White • OR 158.4 (95%CI 22.8–897) for non-Hispanic Black • OR 17.3 (95%CI 9.9–30.1) for Hispanic • OR 36.1 (95%CI 14.7–89) for Asian/Pacific Islander.	MEDIUM
Singh (2012)	USA 26,842	Retrospective cohort	Not clearly specified	All ethnicities examined had a higher risk of GDM compared with Whites (Caucasians).	LOW
Hedderson (2012)	USA 123,040	Cohort	50 g test and if abnormal underwent 3-hour, 100 g OGTT with two or more abnormal values required, using ADA criteria: • fasting 95 mg/dL • 1-hour 180 mg/dL • 2-hour 155 mg/dL • 3-hour 140 mg/dL.	Prevalence of GDM in Asian and Filipina women was higher at a lower BMI (22–24.9 kg/m²) whereas for Hispanic, non-Hispanic White and African American women the higher prevalence occurred with BMIs of 28–30, 34–36 and ≥37 kg/m² respectively.	LOW
Teh (2011)	Australia 2880	Retrospective cohort	Women screened with non-fasting 75 g glucose challenge test at 26–28 weeks' gestation. Positive result (1-hour venous plasma glucose ≥ 8.0 mmol/L) proceeded to a 2-hour, 75 g OGTT. Diagnosis based on: • fasting venous plasma glucose level ≥ 5.5 mmol/L or • a 2-hour level of ≥8.0 mmol/L	Specific ethnicities associated with increased risk: • Asian (mainland South East Asia) OR 5.0 (95%CI 3.0–8.3, $p \leq 0.001$) • maritime South East Asia OR 3.1 (95%CI 1.6–6.0, $p \leq 0.001$) • Chinese Asian OR 3.7 (95%CI 2.1–6.8, $p \leq 0.001$) • Southern Asian OR 2.8 (95%CI 1.7–4.6, $p \leq 0.001$) • Polynesian OR 2.7 (95%CI 1.1–6.5, $p = 0.02$).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Yang (2009)	China 16,286	Prospective cohort	50 g OGCT OGTT (> 11.1 mmol/L diagnosed as GDM) If 7.9–11.0 mmol/L then 75 g, 3-hour OGTT with two or more abnormal values required from: • fasting > 5.3 mmol/L • 1-hour > 10 mmol/L • 2-hour > 8.6 mmol/L.	South China had increased risk compared with North China by almost two-fold: adj OR 1.84 (95%CI 1.59–2.13, $p < 0.001$).	MEDIUM
Makgoba (2012)	United Kingdom 174,320	Retrospective cohort	Diagnosis and screening varied between the units (no details).	Women with GDM were more likely to be of non-white origin ($p < 0.001$).	LOW
Al-Kuwari (2011)	Qatar 4295	Cross-sectional	1-hour glucose challenge test (no details) If ≥ 7.8 mmol/L then a 75 g OGTT: • fasting > 95 mg/dL • 1-hour >180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Qatari national women compared with non-national women (OR 1.7; 95%CI 1.3–2.4).	MEDIUM
Schneider (2011)	Germany 647,385	Cross-sectional	No details provided.	Compared with German women, migrants had an increased risk of GDM (adj OR 1.77; 95%CI 1.69–1.86, $p < 0.001$).	MEDIUM
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose recorded at 24–28 weeks. If > 6.7 mmol/L, then conducted a 75 g OGTT within two weeks. GDM diagnosed if: • fasting plasma glucose ≥ 6 mmol/L or • 2-hour level is ≥ 7.8 mmol/L.	High risk for South Asian (adj OR 2.73, 95%CI 1.73–4.3, $p < 0.0001$) and East Asian (adj OR 2.43, 95%CI 1.20–4.93, $p = 0.01$) women.	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Hedderson (2010b)	USA 216,089	Cohort	50 g test. If abnormal underwent 3-hour, 100 g OGTT with two or more abnormal values required, using ADA criteria: • fasting 95 mg/dL • 1-hour 180 mg/dL • 2-hour 155 mg/dL • 3-hour 140 mg/dL.	Increased risk of GDM associated with being born outside the USA. Compared with those women born inside the USA, the risk was approximately: • 80% higher for Asian Indian (adj OR 1.84; 95%CI 1.02–3.34), Black and Filipina (adj OR 1.78 95%CI 1.47–2.17) women • 50% higher among Chinese women (adj OR 1.51; 95%CI 1.20–1.91) and Pacific Islanders (adj OR 1.58; 95%CI 1.07–2.32) • 35% higher among non-Hispanic White (adj OR 1.36; 95%CI 1.24–1.49) and Mexican (adj OR 1.34, 95%CI 1.23–1.46) women. Japanese and Korean women born outside the USA had a 50% decreased risk of developing GDM.	MEDIUM
Savitz (2008)	USA 951,920	Cohort	Different policies in different sites. No definitions provided.	Compared with non-Hispanic White women, Asians showed the highest risks: • adj RR 4.7 (95%CI 4.6–4.9) for South Central Asians • adj RR 2.8 (95%CI 2.7–3.0) for South East Asians and Pacific Islanders • adj RR 2.3 (95%CI 2.2–2.4) for East Asians. In South Central Asia the highest risks were for women from Bangladesh (adj RR 7.1, 95%CI 6.8–7.3), Pakistan (adj RR 4.6, 4.3–4.8), and India (adj RR 3.7, 95%CI 3.5–3.9). Migrant women from sub-Saharan Africa, South East Asia and South America had higher adj RR 1.5 to < 2.0 compared with USA-born women.	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Aljohani (2008)	Canada 165,969	Retrospective cohort	**From 1992** 50 g OGTT If ≥ 7.8 mmol/L then 100 g, 3-hour OGTT with two or more abnormal results required from: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 9.2 mmol/L • 3-hour ≥ 8.1 mmol/L. **From 1998** 50 g OGTT If ≥ 7.8 but < 10.2 mmol/L then a 75 g, 2-hour OGTT with two or more abnormal results required from: • fasting ≥ 5.3 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 8.9 mmol/L.	First Nation women at 2.6–3.8 times higher risk of GDM compared with non-First Nation women over a 20-year period (adj OR 2.2; 95%CI 2.0–2.42, $p < 0.01$).	HIGH
Teede (2011)	Australia 4276	Retrospective observational	ADIPS criteria A positive glucose challenge test was followed by a 75 g, 2-hour OGTT: • fasting ≥ 5.5mmol/L • 2-hour ≥ 8 mmol/L.	Compared with Anglo Australians, the groups at greatest risk were: • mainland South East Asians, adj OR 5.0 (95%CI 3.0–8.2, $p < 0.0001$) • Chinese Asians, adj OR 3.7 (95%CI 2.0–6.7, $p < 0.0001$) • maritime South East Asians, adj OR 3.1 (95%CI 1.6–6.0, $p = 0.001$).	HIGH
Ismail (2011)	Malaysia 616	Observational	75 g OGTT: fasting and 2-hour postprandial > 6 mmol/L and > 7.8 mmol/L respectively.	Chinese and Indian at increased risk ($p = 0.04$).	LOW
Chang (2010)	Hawaii 2303	Retrospective cohort	Details limited but it appears a 1-hour OGCT and a 3-hour OGTT were used, with two or more abnormal values required for diagnosis.	Increased risk for obese Micronesian women for developing GDM compared with their non-obese counterparts (OR 4.1, 95%CI 2.39–7.04).	LOW

Note: ADA = American Diabetes Association; ADIPS = Australasian Diabetes in Pregnancy Society; BMI = body mass index; CI = confidence interval; GDM = gestational diabetes mellitus; ICD = International Classification of Diseases; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test; OR = odds ratio; RR = risk ratio.

Table 7: Studies reporting on family history of diabetes as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Teh (2011)	Australia 2880	Retrospective cohort	Women screened with non-fasting 75 g glucose challenge test at 26–28 weeks' gestation. Positive result (1-hour venous plasma glucose ≥ 8.0 mmol/L) proceeded to a 2-hour, 75 g OGTT. Diagnosis based on fasting venous plasma glucose level ≥ 5.5 mmol/L or a 2-hour level of ≥ 8.0 mmol/L.	Family history of diabetes OR 1.7 (95%CI 1.3–2.3, $p < 0.001$)	MEDIUM
Lim-Uy (2010)	Philippines 668	Retrospective cross-sectional	Diagnosed with GDM using the Carpenter and Coustan criteria.	Adj OR 6.27 (95%CI 2.63–14.96, $p < 0.0001$)	MEDIUM
Cypryk (2008)	Poland 1670	Cohort	GDM diagnosed using WHO and Polish Diabetes Association criteria (no other details).	Adj OR 1.76 (95%CI 1.38–2.24, $p < 0.001$)	MEDIUM
Yang (2009)	China 16,286	Prospective cohort	50 g OGCT, OGTT (> 11.1 mmol/L diagnosed as GDM) If 7.9–11.0 mmol/L, then 75 g, 3-hour OGTT with two or more abnormal values required from: • fasting > 5.3 mmol/L • 1-hour > 10 mmol/L • 2-hour> 8.6 mmol/L.	Adj OR 2.15 (95%CI 1.78–2.61, $p < 0.001$)	MEDIUM
Gonzalez-Clemente (2007)	Spain 335	Cohort	50 g, 1-hour test. If abnormal value (≥ 7.8 mmol/L), an OGCT of ≥ 11.1 mmol/L was considered diagnostic of GDM. If results abnormal, women underwent a 100 g, 3-hour OGTT after one to two weeks using the criteria of the National Diabetes Data Group.	Family history of type 2 diabetes mellitus compared with no history (51.2% vs 40.0%, $p = 0.02$)	MEDIUM
Al-Kuwari (2011)	Qatar 4295	Cross-sectional	1-hour glucose challenge test (no details) If ≥ 7.8 mmol/L, then a 75 g OGTT with abnormal values from: • fasting > 95 mg/dL • 1-hour >180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Positive paternal history of diabetes (OR 2.0; 95%CI 1.4–2.8) Positive maternal history of diabetes (OR not reported)	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose recorded at 24–28 weeks. If > 6.7 mmol/L then conducted a 75 g OGTT within two weeks. GDM diagnosed if fasting plasma glucose ≥6 mmol/L or 2-hour level is ≥ 7.8 mmol/L.	OR 1.95 (95%CI 1.48–2.58, $p < 0.0001$)	MEDIUM
Ogonowski (2010)	Poland 1830 cases, 1011 controls	Retrospective case control	OGCT of 50 g If > 180 mg/dL (10 mmol/L), then diagnosed as GDM. If 140–180 mg/dL then a 75 g OGTT using the WHO criteria: • fasting ≥ 110 mg/dL (6.1 mmol/L) • 2-hour ≥ 140 (7.8 mmol/L). Also used the ADA criteria where two abnormal values are required from: • fasting ≥ 95 mg/dL (5.3 mmol/L) • 1-hour ≥ 180 mg/dL (10.0 mmol/L) • 2-hour ≥ 155 mg/dL (8.6 mmol/L).	OR 2.87 (95%CI 2.28–3.59, $p = 0.000001$)	MEDIUM
Bhat (2010)	India 300 cases, 300 controls	Case control	50 g Oral glucose challenge test at 24–28 weeks and 32–34 weeks or after development of risk factors. GDM confirmed with 100 g OGTT if > 130 mg/dL at 1 hour, with two or more abnormal values required from: • fasting > 105 mg/dL • 1-hour > 190 mg/dL • 2-hour > 165 mg/dL • 3-hour > 145 mg/dL.	Paternal history (11.3% versus 5.3%) and maternal history (21.3% versus 8.3%) higher risk in cases than controls: adj OR 4.5 (95%CI 2.0–10.1, $p < 0.001$).	MEDIUM
Hossein-Nezhad (2007)	Iran 2416	Cross-sectional	Universal screening with 50 g, 1-hour glucose challenge test at 24–28 weeks (women with known risk factors were screened at first antenatal visit). If result abnormal (≥ 130 mg/dL) then underwent a 100 g, 3-hour OGTT using the Carpenter and Coustan criteria. Women divided into four groups: 1. GDM; 2. IGT –impaired glucose tolerance; 3. IGCT impaired glucose challenge test; 4. normal.	Adj OR 4.34 (95%CI 2.86–6.60, $p < 0.0001$)	MEDIUM

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Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Teede (2011)	Australia 4276	Retrospective observational	ADIPS criteria A positive glucose challenge test was followed by a 75 g, 2-hour OGTT: • fasting ≥ 5.5 mmol/L • 2-hour ≥ 8mmol/L.	Adj OR 1.7 (95%CI 1.3–2.3, p = 0.001)	HIGH
Ismail (2011)	Malaysia 616	Observational	75 g OGTT: fasting and 2-hour postprandial > 6 mmol/L or > 7.8 mmol/L respectively.	Positive association for family history and GDM (p = 0.008)	LOW
Retnakaran (2007)	Canada 180	Cross-sectional	50 g OGCT (≥ 7.8 mmol/L) followed by a 100 g, 3-hour OGTT. Two abnormal values using NDDG criteria: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 9.2 mmol/L • 3-hour ≥ 8.1 mmol/L. Impaired glucose tolerance was defined as only meeting one of the criteria.	GDM risk factors reconciled 35% of the variance in the area under the curve with previous GDM (p = 0.0003), log adiponectin (p = 0.0008) and parity (p = 0.002) being identified as negative independent covariates. In women with no family history, the same multivariate model reconciled only 15% of the variance with no significant variables.	LOW

Note: ADA = American Diabetes Association; ADIPS = Australasian Diabetes in Pregnancy Study Group; CI = confidence interval; GDM = gestational diabetes mellitus; NDDG = National Diabetes Data Group; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test; OR = odds ratio; WHO = World Health Organization.

Table 8: Studies reporting on previous history of gestational diabetes as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Getahun (2010)	USA 540,956	Retrospective cohort	ICD coding	Compared with women without previous GDM in first pregnancy, women whose first pregnancy was associated with a diagnosis of GDM had a significantly increased risk of developing GDM in a second pregnancy (adj OR 13.2, 95%CI 12.0–14.6). Compared with women without GDM in first and second pregnancies, women who had GDM in first but not second pregnancy had an increased risk of developing GDM in their third pregnancy (adj OR 6.3, 95%CI 4.5–9.0). For women who had had GDM in both first and second pregnancies, the risk of GDM in the third pregnancy was adj OR 25.9 (17.4–38.4).	HIGH
Kwak (2008)	Korea 792	Retrospective cohort	50 g, 1-hour glucose challenge test. Plasma glucose ≥ 130 mg/dL was followed by a diagnostic test using the criteria of the Third International Workshop–Conference on Gestational Diabetes Mellitus: • fasting ≥ 105 mg/dL • 1-hour ≥ 190 mg/dL • 2-hour ≥ 165 mg/dL • 3-hour ≥ 145 mg/dL. All women with GDM had a 75 g, 2-hour OGTT at two months postpartum.	RR 2.31 (95%CI 1.24–4.30) for recurrence of GDM if postpartum screening test was abnormal compared with normal test	LOW
Radesky (2008)	USA 1733	Prospective cohort	50 g OGCT If ≥ 140 mg/dL, then 100 g, 3-hour OGTT: • fasting > 155 mg/dL • 1-hour >180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Impaired glucose tolerance (OR 4.33, 95%CI 1.17–16.0) GDM (OR 58.3, 95%CI 21.1–161)	MEDIUM

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Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
The (2011)	Australia 2880	Retrospective cohort	Women screened with non-fasting 75 g glucose challenge test at 26–28 weeks' gestation. Positive result (1-hour venous plasma glucose ≥ 8.0 mmol/L) proceeded to a 2-hour, 75 g OGTT. Diagnosis based on: • fasting venous plasma glucose level ≥ 5.5 mmol/L or • a 2-hour level of ≥ 8.0 mmol/L.	OR 10.7 (95%CI 5.4–21.1, $p < 0.001$)	MEDIUM
Aljohani (2008)	Canada 165,969	Retrospective cohort	**From 1992** 50 g OGTT If ≥ 7.8 mmol/L then 100g, 3 hour OGTT with 2 or more abnormal results from: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 9.2 mmol/L • 3-hour ≥ 8.1 mmol/L. **From 1998** 50 g OGTT If ≥7.8 but < 10.2 mmol/L, then a 75 g, 2-hour OGTT with two or more abnormal results required from: • fasting ≥ 5.3 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 8.9 mmol/L.	Recurrence rate of GDM in subsequent pregnancies was 44.4% (adj OR 25.1; 95%CI 23.1–27.2). The recurrence rate was higher in First Nation women compared with non-First Nation women.	HIGH
Teede (2011)	Australia 4276	Retrospective observational	ADIPS criteria A positive glucose challenge test was followed by a 75 g, 2-hour OGTT: • fasting ≥ 5.5 mmol/L • 2-hour ≥ 8 mmol/L.	This was the strongest predictor: adj OR 10.9 (95%CI 5.5–21.4, $p < 0.0001$).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose recorded at 24–28 weeks. If > 6.7 mmol/L, then conducted a 75 g OGTT within two weeks. GDM diagnosed if fasting plasma glucose ≥ 6 mmol/L or 2-hour level is ≥ 7.8 mmol/L.	Multiparous women with a previous history of GDM had an increased risk of developing GDM in a subsequent pregnancy (adj OR 41.37, 95%CI 26.82–63.83, $p < 0.0001$)	MEDIUM
Ogonowski (2010)	Poland 1830 cases, 1011 controls	Retrospective case control	GCT of 50 g If > 180 mg/dL (10 mmol/L), then diagnosed as GDM. If 140–180mg/dL, then a 75g OGTT using the WHO criteria: • fasting ≥ 110 mg/dL (6.1 mmol/L) • 2-hour ≥ 140 mg/dL (7.8 mmol/L). Also used the ADA criteria where two abnormal values are required from: • fasting ≥ 95 mg/dL (5.3 mmol/L) • 1-hour ≥ 180 mg/dL (10.0 mmol/L) • 2-hour ≥ 155 mg/dL (8.6 mmol/L).	Previous GDM OR 5.10 (95%CI 2.67–9.76, $p = 0.000001$)	MEDIUM
Gonzalez-Clemente (2007)	Spain 335	Cohort	50 g, 1-hour test. If abnormal value (≥ 7.8 mmol/L), an OGCT of ≥ 11.1 mmol/L was considered diagnostic of GDM. If results abnormal, women underwent a 100 g, 3-hour OGTT after one to two weeks using the criteria of the National Diabetes Data Group.	Positive history of previous GDM (14.6% vs 1.7%; adj OR 8.18, 95%CI 2.13–31.47, $p = 0.01$)	MEDIUM
Ramos-Levi (2012)	Spain 2194	Observational cohort	Screened with ADA criteria	History of GDM increased risk but no risk data presented.	LOW

Note: ADA = American Diabetes Association; ADIPS = Australasian Diabetes in Pregnancy Study Group; CI = confidence interval; GDM = gestational diabetes mellitus; ICD = International Classification of Diseases; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test; OR = odds ratio; RR = risk ratio; WHO = World Health Organization.

Table 9: Studies reporting on body mass index/weight gain as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Lagerros (2012)	Sweden 332,083	Cohort	No details on screening 75 g OGTT (fasting plasma ≥ 7.0 mmol/L, and/or 2-hour plasma ≥ 10.0 mmol/L, or manifest diabetes only diagnosed as fasting plasma ≥ 7.0 mmol/L and/or 2-hour plasma ≥ 12.2 mmol/L).	Small for gestational age compared with appropriate for gestational age (adj OR 2.3, 95%CI 1.8–2.9). Large for gestational age compared with appropriate for gestational age (adj OR 1.8, 95%CI 1.3–2.4). Underweight compared with normal weight (adj OR 1.1, 95%CI 0.7–1.8). Overweight compared with normal weight (adj OR 2.2, 95%CI 1.9–2.6). Obese compared with normal weight (adj OR 4.5, 95%CI 3.8–5.4). Morbidly obese compared with normal weight (adj OR 11.1, 95%CI 9.3–13.2).	HIGH
Hedderson (2012)	USA 123,040	Cohort	50 g test and if abnormal underwent 3-hour, 100 g OGTT with two or more abnormal values required, using ADA criteria: • fasting 95 mg/dL • 1-hour 180 mg/dL • 2-hour 155 mg/dL • 3-hour 140 mg/dL.	Prevalence of GDM in Asian and Filipina women was higher at a lower BMI (22–24.9 kg/m²) whereas for Hispanic, non-Hispanic White and African American women, the higher prevalence occurred with BMIs of 28–30, 34–36 and ≥ 37 kg/m² respectively. The estimated population attributable risks suggested that 65% of cases of GDM in African American women and 23% in Asian women could be prevented if women were of normal BMI (< 25 kg/m²).	LOW

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Carreno (2012)	USA 10,154	Secondary analysis of randomised trial	No details on how GDM was diagnosed.	Overall after adjusting for maternal age, smoking, ethnicity and treatment group, the odds of developing GDM were 43% higher in the excessive early gestational weight gain group (adj OR 1.4, 95%CI 1.1–1.9). The odds of developing GDM in overweight women was not associated with excessive early gestational weight gain (adj OR 1.6, 95%CI 1.0–2.6), nor was any effect observed in obese women.	MEDIUM
Singh (2012)	USA 26,842	Retrospective cohort	Not clearly specified.	Increased risk with increasing BMI > 35–39.99 kg/m² OR 4.77 (95%CI 4.26–5.34) BMI > 40 kg/m² OR 5.57 (95%CI 4.9–6.32). Adj OR for BMI was 1.08 (95%CI 1.08–1.09) for each unit increase of BMI and OR 1.48 (95%CI 1.45–1.51) for each five-unit increase.	HIGH
Heude (2012)	France 1884	Prospective cohort	1-hour, 50 g OGCT. If > 130 mg/dL in Nancy or > 140 mg/dL in Poitiers, then 3-hour, 100 g OGTT with two or more abnormal values required from: • fasting ≥ 95 mg/dL • 1-hour ≥ 180 mg/dL • 2-hour ≥ 155 mg/dL • 3-hour ≥ 140 mg/dL.	Compared with women with a normal pre-pregnancy BMI, women who were overweight had an increased risk of developing GDM (adj OR 2.43, 95%CI 1.52–3.89). The risk was also increased further for obese women (adj OR 4.07, 95%CI 2.34–7.09, $p < 0.0001$).	MEDIUM
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose recorded at 24–28 weeks. If > 6.7 mmol/L, then conducted a 75 g OGTT within two weeks. GDM diagnosed if: • fasting plasma glucose ≥ 6 mmol/L or • 2-hour level is ≥ 7.8 mmol/L.	Women with GDM had a higher BMI than non-GDM mothers and there was an increased risk of developing GDM per kg/m² (adj OR 1.12, 95%CI 1.10–1.14, $p < 0.0001$).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Teh (2011)	Australia 2880	Retrospective cohort	Women screened with non-fasting 75 g glucose challenge test at 26–28 weeks' gestation. Positive result (1-hour venous plasma glucose ≥ 8.0 mmol/L) proceeded to a 2-hour, 75 g OGTT. Diagnosis based on: • fasting venous plasma glucose level ≥ 5.5 mmol/L or • a 2-hour level of ≥ 8.0 mmol/L.	Compared with the referent of < 20 kg/m²: • 20–24.9 kg/m² adj OR 1.7 (95%CI 1.0–3.0, NS) • 25–26.9 kg/m² adj OR 2.0 (95%CI 1.0–3.9, NS) • 27–29.9 kg/m² adj OR 2.2 (95%CI 1.1–4.5, $p = 0.02$) • 30–34.9 kg/m² adj OR 3.5 (95%CI 1.7–7.3, $p = 0.001$) • ≥ 35 kg/m² adj OR 6.1 (95%CI 3.0–12.1, $p < 0.001$).	MEDIUM
Kim (2010)	USA 22,767	Prospective population-based cohort	Identified from birth certificate	Compared with women with normal BMI: • overweight (25–29.9 kg/m²) adj RR 2.17 (95%CI 1.58–2.97) • obese (30–34.9kg/m²) adj RR 2.51 (95%CI 1.76–2.97) • extremely obese (35–64.9 kg/m²) adj RR 5.03 (95%CI 3.64–6.95).	MEDIUM
Hedderson (2010b)	USA 345 cases, 800 controls	Nested case control	50 g, 1-hour OGCT and a 100 g, 3-hour OGTT using National Diabetes Data Group criteria at 24–28 weeks' gestation, with two or more abnormal values required from: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.5 mmol/L • 2-hour ≥ 9.1 mmol/L • 3-hours ≥ 8.0 mmol/L.	In an adjusted analysis, the risk of developing GDM increased with increasing rates of weight gain. Using the third tertile as a referent (less than 0.27 kg/week), a weight gain of 0.27–0.4 kg/week (OR 1.43, 95%CI 0.96–2.14) and 0.41 kg/week or more (OR 1.74, 95%CI 1.16–2.60) were associated with increased risks of GDM. The association of increased gestational weight and GDM was mainly attributed to the first trimester. The association was stronger in overweight or obese and non-white women. Non-white women in the highest tertile for rate of weight gain had a 2.5 times greater risk of developing GDM (OR 2.66, 95%CI 1.45–4.90) compared with the risk for non-Hispanic White women (OR 1.56, 95%CI 0.90–2.68).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Lim-Uy (2010)	Philippines 212	Retrospective cross-sectional	Diagnosed with GDM using the Carpenter and Coustan criteria.	Pre-pregnancy BMI: adj OR 1.54 (95%CI 1.06–2.24, p = 0.02).	MEDIUM
Bhat (2010)	India 300 cases, 300 controls	Case control	50 g oral glucose challenge test at 24–28 weeks and 32–34 weeks or after development of risk factors. If > 130 mg/dL at 1 hour, GDM confirmed with 100 g OGTT, requiring two or more abnormal values from: • fasting > 105 mg/dL • 1-hour > 190 mg/dL • 2-hour > 165 mg/dL • 3-hour > 145 mg/dL.	≥ 25 kg/m² had a significantly higher risk in the cases than in the controls (37.9% versus 14.3%; multivariate logistic regression OR 2.7, 95%CI 0.16–8.84, p = 0.02).	MEDIUM
Cypryk (2008)	Poland 1670	Cohort	GDM diagnosed using WHO and Polish Diabetes Association criteria (no other details).	Adj OR 4.14 (95%CI 3.17–5.42, p < 0.001) for pre-gestational BMI > 25kg/m²	MEDIUM
Yang (2009)	China 16,286	Prospective cohort	50 g OGCT OGTT (> 11.1 mmol/L diagnosed as GDM) If 7.9–11.0 mmol/L then 75 g, 3-hour OGTT with two or more abnormal values required from: • fasting > 5.3 mmol/L • 1 hour > 10 mmol/L • 2 hour > 8.6 mmol/L.	Increased risk with increased weight gain for women ≥ 2 8 kg/m² compared with women < 24 kg/m² (BMI of 28 is considered obese in China): adj OR 2.85 (95%CI 2.29–3.54, p < 0.001).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Herring (2009)	USA 1960	Cohort	1 hour after 50 g oral glucose challenge test. If ≥ 140 mg/dL, then 100 g, 3-hour OGTT taken. Diagnosed as GDM if two or more values abnormal: • baseline > 95 mg/dL • 1-hour > 180 mg/dL • 2-hour > 155 mg/dL • 3-hour >140mg/dL. Classified as impaired glucose tolerance (IGT) if failed OGCT with one high value on the 3-hour OGTT.	43% of women diagnosed with IGT had weight gain in the highest quartile before screening (adj OR 2.54, 95%CI 1.25–5.15) but not significant for diagnosis of GDM (adj OR 0.93, 95%CI 0.50–1.70). High weight gain in both early and mid-pregnancy was associated with an increased risk of IGT (adj OR 2.14, 95%CI 1.04–4.42) but was not associated with GDM.	MEDIUM
Gonzalez-Clemente (2007)	Spain 335	Cohort	50 g, 1-hour oral glucose challenge test. If abnormal value (≥ 7.8 mmol/L), an OGCT of ≥ 11.1 mmol/L was considered diagnostic of GDM. If results abnormal, women underwent a 100 g, 3-hour OGTT after one to two weeks using the criteria of the National Diabetes Data Group.	Women with GDM had a higher body mass index (27.3 ± 0.7 vs 24.3 ± 0.3 kg/m²; adj OR 1.09, 95%CI 1.02–1.17, p = 0.02 for each kg/m² increase) than women without GDM.	MEDIUM
Hedderson (2008)	USA 251 cases, 204 controls	Nested case control	50 g, 1-hour OGCT and a 100 g, 3-hour OGTT using National Diabetes Data Group criteria at 24–28 weeks' gestation, with two or more abnormal values required from: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.5 mmol/L • 2-hour ≥ 9.1 mmol/L • 3-hour ≥ 8.0mmol/L.	Women who gained weight at a rate of 1.1–2.2 kg/year had a small increased risk of GDM (adj OR 1.63, 95%CI 0.95–2.81) compared with women with stable weight. Women who gain weight at 2.3–10 kg/year had a 2.5 times greater risk of developing GDM (adj OR 2.61, 95%CI 1.50–4.57) compared with women with stable weight. The association was stronger among women who were not overweight (BMI < 25 kg/m²) at baseline (adj OR 2.81, 95%CI 1.33–5.93). Women who were overweight or obese at baseline had an increased risk of developing GDM (adj OR 2.14, 95%CI 1.41–3.25 and adj OR 1.93, 95%CI 1.20–3.10 respectively).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Makgoba (2012)	United Kingdom 585,291	Retrospective cohort	Diagnosis and screening varied between the units (no details).	Women with GDM had a significantly higher BMI than non-GDM women (26.6 ± 5.5 versus 23.7 ± 4.0 kg/m², $p < 0.001$). There was also an association between increasing BMI in all the racial groups ($p < 0.001$).	LOW
Gibson (2012)	USA 163 cases, 489 controls	Retrospective matched case control	1-hour, 50 g OGCT > 200 mg/dL or two or more abnormal results on a 3-hour, 100 g OGTT using Carpenter and Coustan criteria.	24 week gestational weight gain was 11.2 lb ± 10.8 in the control group and 14.8 lb ± 12.7 in the GDM group ($p < 0.001$). No risk estimate provided.	LOW
Radesky (2008)	USA 1733	Prospective cohort	50 g OGCT If ≥ 140 mg/dL, then 100 g, 3-hour OGTT: • fasting > 155 mg/dL • 1-hour > 180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Pre-pregnancy BMI (≥ 30 kg/m² vs < 25 kg/m²) was a strong predictor of GDM risk (OR 3.44, 95%CI 1.88–6.31).	LOW
Schneider (2011)	Germany 14,990	Cross-sectional	No details provided	Compared with women with a normal BMI (20–25 kg/m²), women with a pre-pregnancy BMI > 35 kg/m² were more likely to have GDM (adj OR 4.96; 95%CI 4.7–5.24, $p < 0.001$). There was no effect on risk associated with excessive weight gain during pregnancy.	MEDIUM
Teede (2011)	Australia 4276	Retrospective observational	ADIPS criteria A positive glucose challenge test was followed by a 75 g, 2-hour OGTT: • fasting ≥ 5.5mmol/L • 2-hour ≥ 8 mmol/L.	Compared with women with a BMI < 20 kg/m², obese women with a BMI > 30 kg/m² were 3.6 times more likely to have GDM (adj OR 3.6, 95%CI 1.7–7.4, $p = 0.001$), rising to 6.2 times more likely for women with a BMI ≥ 35 kg/m² (adj OR 6.2, 95%CI 3.1–12.3, $p < 0.0001$).	HIGH

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Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Far (2012)	Iran 711	Cohort	50 g OGCT If ≥ 140 mg/dL after 1 hour, then a 3-hour, 100 g OGTT based on the criteria of the National Diabetes Data Group.	Increasing pre-pregnancy BMI: OR 1.09 (95%CI 1.03–1.15, $p = 0.004$)	MEDIUM
				Weight gain in pregnancy prior to glucose challenge test: OR 1.13 (95%CI 1.04–1.22, $p = 0.001$)	MEDIUM
Ogonowski (2010)	Poland 1414 cases, 1011 controls	Retrospective case control	OGCT of 50 g If >180 mg/dL (10 mmol/L), then diagnosed as GDM. If 140–180mg/dL, then a 75 g OGTT using the WHO criteria: • fasting ≥ 110 mg/dL (6.1 mmol/L) • 2-hour ≥ 140 (7.8 mmol/L). Also used the ADA criteria where two abnormal values are required from: • fasting ≥ 95 mg/dL (5.3 mmol/L) • 1-hour ≥ 180 mg/dL (10.0 mmol/L) • 2-hour ≥155 mg/dL (8.6 mmol/L).	Pre-pregnancy BMI was associated with GDM compared with false positive results and the controls (OR 1.07, 95%CI 1.05–1.09, $p = 0.000001$).	MEDIUM
				Pregnancy weight gain: OR 1.05 (95%CI 1.3–1.07, $p = 0.000003$)	MEDIUM
Ogonowski et al (2009)	Poland 1121 cases, 1011 controls	Retrospective case control	50 g oral challenge test at 24–28 weeks' gestation followed by 75 g OGTT if results were abnormal (7.8–11.1 mmol/L). GDM diagnosed if: • fasting glucose ≥ 7.0 mmol/L (WHO criteria) or • 2-hour level was ≥ 7.8 mmol/L.	BMI was the strongest predictor for requiring insulin therapy. Compared with women with a BMI of 18.5–20.9 kg/m², women with a BMI of 30–34.9 kg/m² had an adj OR 3.51 (95%CI 2.21–5.39) and with a BMI > 35 kg/m² adj OR 9.01 (95%CI 3.47–23.3), $p = 0.03$. The risk of GDM increased by 11.6% for each change in BMI unit and was more pronounced in women who were treated with insulin compared with those treated with diet (19% and 8% respectively). The greatest risk occurred when there was a shift from normal weight to overweight and from overweight to obese.	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Iqbal (2007)	Pakistan 750	Prospective cohort	75 g, 2-hour OGCT (> 7.8 mmol/L) followed by a 100 g, 3-hour OGTT if abnormal value. Cut-off values of ADA: • fasting > 5.3 mmol/L • 1-hour > 10 mmol/L • 2-hour > 8.6 mmol/L • 3-hour > 7.8 mmol/L. This analysis included subjects with either one or two raised values.	Increased percentage body fat: OR 1.07, 95%CI 1.03–1.13	MEDIUM
Hossein-Nezhad (2007)	Iran 2416	Cross-sectional	Universal screening with 50 g, 1-hour oral glucose challenge test at 24–28 weeks (women with known risk factors were screened at first antenatal visit). If result abnormal (≥ 130 mg/dL), then underwent a 100 g, 3-hour OGTT using the Carpenter and Coustan criteria. Women divided into four groups: 1. GDM; 2. IGT –impaired glucose tolerance; 3. IGCT impaired glucose challenge test; 4. normal.	There was a significant difference in BMI between the women in the GDM group and the three other groups ($p < 0.0001$). Compared with women with a normal screening test, women with GDM were more likely to have a BMI >27kg/m^2 (adj OR 4.23, 95%CI 2.80–6.37, $p < 0.0001$).	MEDIUM
Ismail (2011)	Malaysia 616	Observational	75 g OGTT, fasting and 2-hour postprandial > 6 mmol/L and > 7.8 mmol/L respectively.	> 80 kg at time of screening associated with increased risk ($p < 0.001$).	LOW
Kun (2011)	Hungary 2260	Observational	75 g OGTT. 2-hour post-test. Diagnosis based on WHO or IADPSG criteria.	Higher pre-pregnancy BMI was associated with higher risk of GDM compared with normal BMI using both criteria ($p = 0.001$ in both cases). Risk especially high for women with BMI of 24.2 kg/m^2 but risk decreased for women with BMI ≥ 29.2 kg/m^2 compared with those with BMI of 26.1–29.1 kg/m^2.	LOW
Ramos-Levi (2012)	Spain 2194	Observational cohort	Screened with ADA criteria.	Higher pre-pregnancy weight/BMI was associated with increased risk of GDM but no risk data presented.	LOW

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Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Chang (2010)	Hawaii 2303	Retrospective cohort	Details limited but appear to use a 1-hour OGCT and a 3-hour OGTT with two or more abnormal values required for diagnosis.	Obese Micronesian women had a 4.1-fold increased risk of developing GDM compared with non-obese Micronesian women (95%CI 2.39–7.04).	LOW
Rudra (2007)	USA 1644	Cohort	50 g, 1-hour oral glucose challenge test. If value > 140 mg/dL, then undertook a 100 g, 3-hour OGTT. Classified as GDM if two or more abnormal values were found from: • fasting ≥ 105 mg/dL • 1-hour ≥ 190 mg/dL • 2-hour ≥ 165 mg/dL • 3-hour ≥ 145 mg/dL.	GDM risk was increased for women who were obese at 18 years of age compared with women of normal weight (RR 4.53, 95%CI 1.25–16.43). Higher risk among obese women compared with normal weight women (RR 3.25, 95%CI 1.85–5.71). There was no association for overweight women (RR 0.74, 95%CI 0.23–2.40). For women who gained 10 kg or more during adulthood, the risk of developing GDM was increased three-fold compared with women who had a weight gain of 2.5 kg or less (RR 3.43, 95%CI 1.60–7.37). In an adjusted analysis, a 5 kg gain in weight between age 18 and pregnancy increased the risk of developing GDM by 20%. Where women had evidence of weight cycling (ie, losing and then gaining weight), adj RR 1.46 (95%CI 0.87–2.43). Risk increased with repeated episodes of weight cycling so that, for three or more cycles of weight change, the RR was 2.04 (95%CI 0.83–5.02).	LOW

Note: ADA = American Diabetes Association; ADIPS = Australasian Diabetes in Pregnancy Study Group; BMI = body mass index; CI = confidence interval; GDM = gestational diabetes mellitus; IADPSG = International Association of Diabetes and Pregnancy Study Groups; IGT = impaired glucose tolerance; NS = not significant; OGCT = oral glucose challenge test; OGTT= oral glucose tolerance test; OR = odds ratio; RR = risk ratio; WHO = World Health Organization.

Table 10: Studies reporting on macrosomia/large for gestational age as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose recorded at 24–28 weeks. If > 6.7 mmol/L, then conducted a 75 g OGTT within two weeks. GDM diagnosed if: • fasting plasma glucose ≥ 6 mmol/L or • 2-hour level is ≥ 7.8 mmol/L.	Women with a previous large for gestational age baby were at increased risk for developing GDM (adj OR 1.97, 95%CI 1.36–2.84, $p < 0.0001$).	MEDIUM
Bhat (2010)	India 300 cases, 300 controls	Case control	50 g oral glucose challenge test at 24–28 weeks and 32–34 weeks or after development of risk factors. If > 130 mg/dL at 1 hour, GDM confirmed with 100 g OGTT, requiring two or more abnormal values from: • fasting > 105 mg/dL • 1-hour >190 mg/dL • 2-hour > 165 mg/dL • 3-hour > 145 mg/dL.	Adj OR 4.39 (95%CI 1.0–19.1, $p = 0.05$).	MEDIUM
Cypryk (2008)	Poland 1670	Cohort	GDM diagnosed using WHO and Polish Diabetes Association criteria (no other details).	Adj OR 2.72 (95%CI 1.60–4.65, $p < 0.001$).	MEDIUM
Hoseini (2011)	Iran 227	Retrospective cross-sectional	50 g, 1-hour oral glucose challenge test If > 140 mg/dL then a 100 g, 3-hour OGTT, with two or more abnormal readings required from: • fasting > 95 mg/dL • 1-hour > 180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Women with a previous neonate weighing > 3800 g were at a higher risk of GDM (OR 9.6; 95%CI not reported, $p < 0.001$).	LOW

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Ogonowski (2010)	Poland 1414 cases, 1011 controls	Retrospective case control	OGCT of 50 g If > 180 mg/dL (10 mmol/L), then diagnosed as GDM. If 140–180 mg/dL, then a 75 g OGTT using the WHO criteria: • fasting ≥ 110 mg/dL (6.1 mmol/L) • 2-hour ≥ 140 mg/dL (7.8 mmol/L). Also used the ADA criteria where two abnormal values are required from: • fasting ≥ 95 mg/dL (5.3 mmol/L) • 1 hour ≥ 180 mg/dL (10.0 mmol/L) • 2 hour ≥ 155 mg/dL (8.6 mmol/L).	OR 1.52 (95%CI 1.03–2.23, p = 0.004)	MEDIUM
Hossein-Nezhad (2007)	Iran 2416	Cross-sectional	Universal screening with 50 g, 1-hour oral glucose challenge test at 24–28 weeks (women with known risk factors were screened at first antenatal visit). If result abnormal (≥ 130 mg/dL), then underwent a 100 g, 3-hour OGTT using the Carpenter and Coustan criteria. Women divided into four groups: 1. GDM; 2. IGT –impaired glucose tolerance; 3. IGCT impaired glucose challenge test; 4. normal.	Compared with women with a normal screening test, women with GDM were more likely to have had a baby with macrosomia in a previous pregnancy (adj OR 9.58, 95%CI 5.8–15.6, p < 0.0001).	MEDIUM

Note: ADA = American Diabetes Association; CI = confidence interval; GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test; OR = odds ratio; WHO = World Health Organization.

Table 11: Studies reporting on parity as a risk factor for developing hyperglycaemia in pregnancy

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Lagerros (2012)	Sweden 332,083	Cohort	No details on screening. 75 g OGTT (fasting plasma ≥ 7.0 mmol/L, and/or 2-hour plasma ≥ 10.0 mmol/L, or manifest diabetes only diagnosed as fasting plasma ≥ 7.0 mmol/L and/or 2-hour plasma ≥12.2 mmol/L).	2–3 infants compared with 1 infant (adj OR 0.8, 95%CI 0.7–0.9). > 3 infants compared with 1 infant (adj OR 0.6, 95%CI 0.4–1.0).	HIGH
Singh (2012)	USA 26,842	Retrospective cohort	Not clearly specified.	Nulliparity associated with increased risk (OR 1.26; 95%CI 1.18–1.35).	MEDIUM
Schneider (2011)	Germany 647,385	Cross-sectional	No details provided.	Multiparous women were at an increased risk compared with nulliparous women (adj OR 0.83; 95%CI 0.8–0.86, $p < 0.001$).	MEDIUM
Nanda (2011)	United Kingdom 11,464	Prospective cohort	Random plasma glucose at 24–28 weeks. If > 6.7 mmol/L, then a 75 g OGTT. GDM diagnosed if: • fasting plasma glucose ≥6mmol/L or • 2-hour level is ≥ 7.8 mmol/L.	Multiparous women with no previous history of GDM had an increased risk of developing GDM (OR 1.30, 95%CI 1.0–1.69, $p = 0.05$).	MEDIUM
Cypryk (2008)	Poland 1670	Cohort	GDM diagnosed using WHO and Polish Diabetes Association criteria (no other details).	Adj OR 1.8 (95%CI 1.30–2.49, $p < 0.001$).	MEDIUM
Hossein-Nezhad (2007)	Iran 2416	Cross-sectional	Universal screening with 50 g, 1-hour glucose challenge test at 24–28 weeks (women with known risk factors were screened at first antenatal visit). If result abnormal (≥ 130 mg/dL), then underwent a 100 g, 3-hour OGTT using the Carpenter and Coustan criteria. Women divided into four groups: 1. GDM; 2. IGT – impaired glucose tolerance; 3. IGCT impaired glucose challenge test; 4. normal.	Compared with women with a normal screening test, women with GDM were more likely to be multiparous (adj OR 1.56, 95%CI 1.07–2.31, $p = 0.02$).	MEDIUM

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Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Al-Kuwari (2011)	Qatar 4295	Cross-sectional	1-hour glucose challenge test (no details) If ≥ 7.8 mmol/L, then a 7 5g OGTT: • fasting > 95 mg/dL • 1-hour >180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	≥ 4 pregnancies (OR 2.7; 95%CI 1.7–4.2).	LOW
Kun (2011)	Hungary 2260	Observational	75 g OGTT. 2-hour post-test. Diagnosis based on WHO or IADPSG criteria.	The more deliveries a woman had had, the higher the risk of GDM using both diagnostic criteria (p = 0.002 and p < 0.0001 respectively) for up to three deliveries but the risk decreased risk after that.	LOW
Hoseini (2011)	Iran 114 cases, 113 controls	Retrospective cross-sectional	50 g, 1-hour oral glucose challenge test If > 140 mg/dL, then a 100 g, 3-hour OGTT, with two or more abnormal readings required from: • fasting > 95 mg/dL • 1-hour > 180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Not significant.	LOW

Note: GDM = gestational diabetes mellitus; IADPSG = International Association of Diabetes and Pregnancy Study Groups; OGTT = oral glucose tolerance test; OR = odds ratio; WHO = World Health Organization.

Table 12: Studies reporting on dietary factors as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Radesky (2008)	USA 1733	Prospective cohort	50 g OGCT If ≥ 140 mg/dL then 100 g, 3-hour OGTT: • fasting > 155 mg/dL • 1-hour > 180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Intake of n-3 fatty acids was associated with increased risk of GDM (OR 1.11, 95%CI 1.02–1.22, per 300 mg/day). The increased risk associated with n-3 fatty acid intake was limited to the group of women with pre-pregnancy BMI < 25 kg/m² (adj OR 1.19, 95%CI 1.06–1.35) per 300 g/day compared with women with a BMI of ≥ 25 kg/m² (adj OR 1.03, 95%CI 0.83–1.27). Increased intake of polyunsaturated fats (OR 1.38, 95%CI 1.08–1.77 per 1% increase in calories) and n-6 fatty acids (OR 1.16, 95%CI 1.02–1.32 per 1 g/day) was also associated with an increased risk of developing GDM in women with a pre-pregnancy BMI < 25 kg/m².	HIGH
Bowers (2012)	USA 13,475	Prospective cohort	Self-reported GDM.	Individuals in the highest quintile of animal fat intake had an approximately 90% increased risk of GDM (adj RR 1.88, 95%CI 1.36–2.60, p = 0.05). Increased risk of highest compared with the lowest quintiles of cholesterol intake was significantly associated with GDM after (adj RR 1.45, 95%CI 1.11–1.89, p = 0.04).	HIGH
Bowers (2011)	USA 13,475	Prospective cohort	Self-reported diagnosis of GDM.	The age-adjusted RR between extreme quintiles of cumulative heme iron intake was adj RR 2.13 (95%CI 1.70–2.67, p < 0.0001).	HIGH
Chen (2009)	USA 13,475	Prospective cohort	Self-reported diagnosis of GDM.	Compared with women who consumed < 1 serving/month, those who consumed ≥ 5 servings/week of sugar-sweetened cola had a 22% increased risk of GDM (RR 1.22, 95%CI 1.01–1.47).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Ley (2011)	Canada 205	Cohort	50 g, 1-hour test. If plasma glucose ≥ 7.8 mmol/L, then underwent a 100 g, 3-hour OGTT. GDM diagnosed if two or more abnormal results from: • fasting ≥ 5.8 mmol/L • 1-hour ≥ 10.6 mmol/L • 2-hour ≥ 9.2 mmol/L • 3-hour ≥ 8.1 mmol/L.	GDM significantly associated with lower carbohydrate (OR per 1-SD change: 0.60; 95%CI: 0.40, 0.90) and higher total fat (OR per 1-SD change: 1.61; 95%CI: 1.06, 2.44) intake distributions as a percentage of energy.	MEDIUM
Ramos-Levi (2012)	Spain 2194	Observational cohort	Screened with ADA criteria	High red and processed meat consumption > 6 times/week, high coffee intake (2–3 times/day), high intake of biscuits and pastries (> 4 times/week), sugary drinks (> 4 servings/ week). No risk data were provided.	LOW
Qiu (2011c)	USA Cohort 3158, 185 cases, 411 controls	1 Cohort	1 Cohort study: 50 g, 1-hour oral glucose challenge test. If result was abnormal (≥ 7.8 mmol/L), it was followed one to two weeks later with a 100 g, 3-hour OGTT. Two or more abnormal results were required for a diagnosis from: • fasting ≥ 5.3 mmol/L • 1-hour ≥ 10 mmol/L • 2-hour ≥ 8.6 mmol/L • 3-hour ≥ 7.8 mmol/L.	1 Cohort study: Compared with no egg consumption, the relative risk of developing GDM increased with increasing egg consumption ≥ 10 eggs per week: adj RR 2.52 (95%CI 1.11–5.75, *p* = 0.008). Women with high egg consumption ≥ 7 eggs had a 1.77 fold increased risk compared with women with low egg consumption (95%CI 1.19–2.63). The relative risk of developing GDM for women with high cholesterol intake (≥ 294 mg/day) versus low cholesterol intake (< 151 mg/day) was 2.35 (95%CI 1.35–4.09).	MEDIUM
		2 Case control	2 Case control study: Women diagnosed using a 3-hour OGTT with National Diabetes Data Group criteria.	2 Case control study: The adjusted odds ratio for consuming ≥ 7 eggs/week compared with < 7 eggs/week was 2.65 (95%CI 1.48–4.72). The odds for developing GDM also increased with increasing cholesterol intake (*p* = 0.02).	

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Qiu (2011a)	USA 3158	Prospective cohort	50 g, 1-hour oral glucose challenge (≥ 7.8mmol/L). If failed, received a 100 g, 3-hour OGTT within one to two weeks: • fasting ≥ 5.3 • 1-hour ≥ 10.0 • 2-hour ≥ 8.6 • 3-hour ≥ 7.8mmol/L.	Risk increased with increasing levels of heme iron (adj RR 2.15; 95%CI 1.09–4.27, p = 0.04). Compared with those in the lowest intake decile, the women in the highest decile of intake were three times more likely to have GDM (adj RR 3.31; 95%CI 1.02–10.72). A 1 mg/day increase in heme iron was associated with a minimum of 51% increased risk of GDM (RR 1.51; 95%CI 0.99–2.36).	MEDIUM
Gonzalez-Clemente (2007)	Spain 335	Cohort	50 g, 1-hour test. If abnormal value (≥ 7.8 mmol/L), a OGCT of ≥ 11.1 mmol/L was considered diagnostic of GDM. If results abnormal, women underwent a 100 g, 3-hour OGTT after one to two weeks using the criteria of the National Diabetes Data Group.	Women with GDM had a higher cholesterol intake than women without GDM (145.3 ± 4.5 mg/1000 kcal vs 134.5 ± 1.6 mg/1000 kcal, p = 0.03). Adj OR = 1.88; 95%CI: 1.09–3.23 for each increase of 50 mg/1000 kcal . Each 50 mg/1000 kcal increase in cholesterol intake was associated with an increase of 88% in the diagnosis of GDM.	MEDIUM
Afkhami-Ardekani (2009)	Iran 34 cases, 34 controls	Case control	ADA criteria 100 g OGTT with two or more abnormal values for positive diagnosis.	Concentrations of serum ferritin (p < 0.001), iron (p < 0.001), transferrin saturation (p < 0.001) and haemoglobin (p < 0.001), mean corpuscular volume (p = 0.001) and mean corpuscular haemoglobin (p = 0.001) were significantly higher in women diagnosed with GDM than controls. Total iron binding capacity was significantly lower in women with GDM (p < 0.001).	LOW

Note: ADA = American Diabetes Association; BMI = body mass index; CI = confidence interval; GDM = gestational diabetes mellitus; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test; OR = odds ratio; RR = risk ratio; SD = standard deviation.

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Table 13: Studies reporting on vitamin D as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Poel (2012)	7 studies 2146	Systematic review of observational studies	Reported in individual studies	Women with GDM had significantly lower vitamin D levels (MD ⁻5.33 nmol/L, 95%CI ⁻9.7 to ⁻0.9, p = 0.02, I² = 69%). Adj OR 1.57 (95%CI 1.11–2.22, I² = 17%)	LOW
Burris (2012)	USA 1314	Cohort	1-hour, 50 g OGCT. If value ≥ 140 mg/dL then underwent 3-hour, 100 g OGTT with two or more abnormal results required from: • fasting > 95 mg/dL • 1-hour > 180 mg/dL • 2-hour > 155 mg/dL • 3-hour > 140 mg/dL.	Odds of GDM in women with severe vitamin D deficiency (serum 25 hydroxyvitamin D 25(OH)D < 25 nmol/L) compared with women with normal glucose tolerance: adj OR 3.1 (95%CI 1.3–7.4). Impaired glucose tolerance versus normal glucose tolerance (adj OR 1.6, 95%CI 0.7–3.5).	MEDIUM
Parlea (2012)	Canada 116 cases, 219 controls	Nested case control	50 g, 1-hour OGCT. GDM diagnosed if ≥ 10.3 mmol/L after 1 hour. If levels between 7.8 and 10.2 mmol/L, then underwent a 3-hour, 100 g OGTT (fasting ≥ 5.8 mmol/L; 1 hour ≥ 10.6 mmol/L; 2-hour ≥ 9.2 mmol/L; 3-hour ≥ 8.9 mmol/L) or a 2-hour, 75 g OGTT (fasting ≥ 5.3 mmol/L; 1 hour ≥ 10.6 mmol/L; 2 hour ≥ 8.9 mmol/L) depending on the physician. Diagnoses if two or more abnormal results.	The odds ratio for GDM was lowest for women in the highest quartile of serum 25(OH)D with each of the lower quartiles demonstrating a doubling in the odds. The three lower quartiles were combined. There was a significant association between vitamin D < 73.5 nmol/L and risk of GDM (adj OR 2.21, 95%CI 1.19–4.13, p = 0.001).	MEDIUM

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Lau (2011)	Australia 147	Retrospective cross-sectional	ADIPS criteria. Fasting ≥ 5.5 mmol/L, and/or a 2-hour ≥ 8 mmol/L using a 75 g OGTT following a positive 50 g OGCT.	25(OH)D levels were inversely associated with fasting and 2-hour blood glucose levels during the OGTT (p = 0.05). There was also a significant inverse association between 25(OH)D and log[HbA1c]. Compared with women who had 25(OH)D levels ≤ 50 nmol/L, those with 25(OH)D levels of > 50 nmol/L had HbA1c levels that were significantly lower: ⁻0.41% (95%CI ⁻0.16% to ⁻0.66%, p = 0.001). They also had lower blood glucose readings at fasting (⁻0.4 mmol/L, 95%CI ⁻0.1 to ⁻0.7, p = 0.02) and 1-hour (⁻2.4 mmol/L 95%CI ⁻0.60 to ⁻4.3, p = 0.013) OGTT.	LOW

Note: ADIPS = Australasian Diabetes in Pregnancy Study Group; CI = confidence interval; GDM = gestational diabetes mellitus; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test; OR = odds ratio.

Table 14: Studies reporting on maternal history of subfertility as a risk factor for developing gestational diabetes

Study	Country and sample size	Study type	Screening/diagnostic criteria	Main results	Quality of evidence
Bhat (2010)	India 300 cases, 300 controls	Case control	50 g oral glucose challenge test at 24–28 weeks and 32–34 weeks or after development of risk factors. If > 130 mg/dL at 1 hour, GDM confirmed with 100 g OGTT, requiring two or more abnormal values from: • fasting > 105 mg/dL • 1-hour > 190 mg/dL • 2-hour > 165 mg/dL • 3-hour > 145 mg/dL.	Adj OR 3.3 (95%CI 1.13–9.55, p = 0.03).	MEDIUM
Toulis (2009)	2263	Systematic review of 16 observational studies	Nine studies used the 3-hour, 100 g OGTT and seven studies used the 2-hour, 75 g OGTT. Four studies used universal screening, three specified risk factors and nine used the diagnostic test after a positive challenge test.	The incidence of GDM in women with PCOS (101 of 730 women) was significantly higher than in women without PCOS (284 of 4568 women): OR 2.89 (95%CI 1.68–4.98, I^2 = 59.3%, p = 0.0001; 15 studies). The effect was apparent in cohort studies but not case control studies.	LOW
Reyes-Munoz (2012b)	Mexico 104	Historical cohort	50 g load of glucose Diagnosis based on a 3-hour, 100 g oral glucose tolerance test performed during the second trimester using ADA criteria: • fasting ≥ 95 mg/dL • 1-hour ≥ 180 mg/dL • 2-hour ≥ 155 mg/dL • 3-hour ≥ 140 mg/dL. Women with one impaired value were classified as having impaired glucose tolerance.	The relative risk of developing GDM in women with a history of infertility and PCOS compared with those with no such history was 26.9% and 9.6% respectively (RR 2.8, 95%CI 1.08–7.2, p = 0.02).	LOW

Note: ADA = American Diabetes Association; CI = confidence interval; GDM= gestational diabetes mellitus; OGTT= oral glucose tolerance test; OR = odds ratio; PCOS = polycystic ovary syndrome; RR = risk ratio.

Table 15: Recommendations and statements on early screening for diabetes in pregnancy

Reference	Statement/recommendation	Other comment
International documents and reports		
American Diabetes Association (2013)	Screen for undiagnosed type 2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria (grade B). The diagnostic criteria include any one of the following: - HbA1c ≥ 48 mmol/mol (measured in a lab using a certified method and standardised assay) - fasting plasma glucose ≥ 7 mmol/L; OR 2-hour plasma glucose ≥ 11.1 mmol/L during an oral glucose tolerance test; OR - random plasma glucose ≥ 11.1 mmol/L (in patient with symptoms of hyperglycaemia).	
Clinical Practice Guidelines (Canadian Diabetes Association 2008)	All pregnant women should be screened for GDM (Grade C, Level 3). For most women, screening should be performed between 24 and 28 weeks' gestation (Grade D, Consensus). Women with multiple risk factors should be screened during the first trimester and, if negative, should be reassessed during subsequent trimesters (Grade D, Consensus).	
Diabetes in Pregnancy (NICE 2008)	Women who have had gestational diabetes in a previous pregnancy should be offered early self-monitoring of blood glucose or oral glucose tolerance test at 16–18 weeks and a further oral glucose tolerance test at 28 weeks if the results are normal. Women with any other risk factors should be offered an oral glucose tolerance test at 24–28 weeks.	Recommendation ungraded.
Management of Diabetes (SIGN 2010)	At booking, all women should be assessed for the presence of risk factors for gestational diabetes (good practice point). All women with risk factors should have HbA1c or fasting glucose measured. Women in early pregnancy with levels of HbA1c ≥ 48 mmol/mol, fasting ≥ 7.0 mmol/L or 2-hour ≥ 11.1 mmol/L glucose diagnostic of diabetes should be treated as having pre-existing diabetes. Women with intermediate levels of glucose (HbA1c 42–48 mmol/mol), fasting glucose 5.1–6.9 mmol/L or 2-hour glucose 8.6–11.0 mmol/L should be assessed to determine the need for immediate home glucose monitoring and, if the diagnosis remains unclear, assessed for gestational diabetes by 75 g oral glucose tolerance test at 24–28 weeks (good practice point).	The SIGN group based its recommendation on the IADPSG consensus document (IADPSG 2010).

Reference	Statement/recommendation	Other comment
Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	Same recommendations as American Diabetes Association.	
Brazilian Consensus Statement: Dysglycemias in pregnancy (Negrato 2010)	In order to simplify the diagnosis of GDM, a fasting glycaemia must be performed in the first antenatal visit. If glycaemic level is ≥ 85 mg/dL and the patient shows risk factors for GDM, a 75 g oral glucose tolerance test must be performed. If the test is normal, it must then be repeated between 24th and 28th gestation week (Grade A).	
International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy (IADPSG 2010)	First prenatal visit: Measure fasting plasma glucose, HbA1c or random plasma glucose on all women or only high-risk women. The consensus thresholds were: • fasting plasma glucose ≥ 7.0 mmol/L • HbA1c ≥ 48 mmol/mol or • random plasma glucose ≥ 11.1 mmol/L. If results indicate overt diabetes, treatment and follow-up as for pre-existing diabetes If results not diagnostic of overt diabetes and fasting plasma glucose are: 1. ≥ 5.1 mmol/L but < 7.0 mmol/L, diagnose as GDM, or 2. < 5.1 mmol/L, test for GDM from 24–28 weeks' gestation with 75 g oral glucose tolerance test.	Consensus that it was not feasible to recommend a single test to use exclusively. Concerns about cost and standardisation of A1c testing and haemoglobin variants in some populations. It was noted that if enrolment is at 24 weeks' gestation or later and overt diabetes is found, the initial test should be followed by a 75 g oral glucose tolerance test.
Global Guideline on Pregnancy and Diabetes (International Diabetes Federation 2009)	There is a general consensus that testing should be done at an early stage in pregnancy if risk factors are present, but only poor evidence that interventions initiated at this early stage are helpful.	

Reference	Statement/recommendation	Other comment
Australasian Diabetes in Pregnancy Society: Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia (Nankervis 2013)	Women not known to have pre-existing glucose abnormalities but at high risk of GDM should have a 75 g oral glucose tolerance test at the first opportunity after conception.	
Position statement: Australian Diabetes Society, Royal College of Pathologists of Australia and the Australasian Association of Clinical Biochemists (not dated)	Measurement of HbA1c level can be used as a diagnostic test for diabetes (with particular conditions listed), with an HbA1c level of 48 mmol/mol as the cut-off point in non-pregnant patients. The existing criteria, based on fasting and random glucose levels and on the oral glucose tolerance test, remain valid and are the diagnostic tests of choice for gestational diabetes, type 1 diabetes and in the presence of conditions that interfere with HbA1c measurement.	No mention of early screening and HbA1c not recommended for pregnant patients.
New Zealand guidelines and reports		
Gestational Diabetes Mellitus in New Zealand: Technical report (Gestational Diabetes Mellitus Technical Working Party 2007)	Women with known impaired fasting glucose or impaired glucose tolerance are considered to have at least a degree of hyperglycaemia that should be managed as GDM (and they may have progressed to type 2 diabetes). They should have an HbA1c requested at booking and be directly referred to the diabetes in pregnancy team for management. Women with previous GDM and 'probably undiagnosed type 2 diabetes' (ie, women who had this diagnosis during pregnancy but never had a postpartum glucose tolerance test or women with symptoms of diabetes or random finger-prick glucose > 11.1 mmol/L) should be directly referred to the diabetes in pregnancy team for management and have an HbA1c requested at booking. Other women with past GDM should have an HbA1c requested at booking (even if this previous non-pregnant oral glucose tolerance test was normal) and the reasons for this explained. If elevated 42 mmol/mol, the woman should be referred immediately to the diabetes in pregnancy team. If the HbA1c is < 6.0%, an oral glucose tolerance test should be undertaken at the earliest opportunity, typically 14–16 weeks. If oral glucose tolerance test normal, repeat at 24–28 weeks (or earlier if clinical suspicion occurs). Other high-risk women: a strategy for screening other high-risk women (risk factors listed) for underlying type 2 diabetes using an HbA1c instrument at booking should be initiated as a pilot.	

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Reference	Statement/recommendation	Other comment
HbA1c in Diagnosing Type 2 Diabetes (New Zealand Society for the Study of Diabetes 2011)*	HbA1c testing is not currently recommended for diagnosis of diabetes in pregnant women because glucose tolerance is altered in pregnancy; a separate glucose-based diagnostic algorithm is used.	
Diabetes in Pregnancy Guideline (Auckland District Health Board 2012)	Women who have risk factors for unrecognised glucose tolerance or type 2 diabetes should be tested when they book in early pregnancy (risk factors listed). When booking bloods, add HbA1c. • If HbA1c above reference range (42 mmol/mol), refer directly to diabetes in pregnancy clinic. • If HbA1c is 38–41 mmol/mol and/or oral glucose tolerance test is normal but clinical presentation is suggestive of GDM, discuss with clinic. • If HbA1c is normal, still do early 75 g oral glucose tolerance test (16 weeks). • If oral glucose tolerance test normal, repeat at 24–28 weeks. • Consider further oral glucose tolerance test at 30–32 weeks. All women who are not screened in early pregnancy should be offered routine screening for GDM between 24 and 28 weeks' gestation.	

Note: GDM = gestational diabetes mellitus; IADPSG = International Association of Diabetes and Pregnancy Study Groups; SIGN = Scottish Intercollegiate Guidelines Network.

* The New Zealand Society for the Study of Diabetes position statement on the diagnosis of and screening for type 2 diabetes (updated September 2011) (www.nzssd.org.nz/statements.html).

Table 16: Diagnostic accuracy of HbA1c test reported in the Burlingame study (2012)

Gestational age (weeks)	N	Sensitivity	Specificity	Positive predictive value	Negative predictive value
0–23	53	40% (2/5)	6.3% (3/48)	4.4% (2/47)	50% (3/6)
≥ 24	350	46.2% (12/26)	4.6% (15/324)	3.7% (12/321)	51.7% (15/24)

Source: Burlingame et al (2012)

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Appendix H: Screening principles applied to first trimester screening for undiagnosed diabetes

Considering that the evidence to answer questions on screening early in pregnancy with HbA1c is scarce, it is important nevertheless to consider whether the test meets any or all of the criteria for screening originally proposed by the World Health Organization and modified for use in New Zealand (National Health Committee 2003). There are several clinical questions implicit in these criteria and a narrative review of the evidence has been compiled.

The criteria are as follows.

1. The condition is a suitable candidate for screening.

2. There is a suitable test.

3. There is an effective and accessible treatment or intervention for the condition identified through early detection.

4. There is high-quality evidence, ideally from randomised controlled trials, that a screening programme is effective in reducing mortality or morbidity.

5. The potential benefit from the screening programme should outweigh the potential physical and psychological harm (caused by the test, diagnostic procedures and treatment).

6. The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation.

7. There is consideration of social and ethical issues.

8. There is consideration of cost–benefit issues.

Taking each of these criteria in turn, HbA1c will be evaluated as a screening test for type 2 diabetes early in pregnancy (prior to 20 weeks).

1   The condition is a suitable candidate for screening

Undiagnosed type 2 diabetes is a significant and growing problem in New Zealand. It has been suggested that pregnancy may be playing a major role in the epidemic of type 2 diabetes via intra-uterine fetal programming (Hughes et al 2014). Pregnant women with diabetes produce offspring with an increased risk of diabetes and obesity themselves, leading to a vicious cycle (Fetit et al 2006; McLean et al 2006), and so early detection and treatment may break this cycle of events. In the general population, an estimated 50% of people with type 2 diabetes (100,000 people in New Zealand) and many more with prediabetes are undiagnosed. Moreover, the incidence of type 2 diabetes in pregnancy appears to be increasing and is now greater than type 1 diabetes (Cheung et al 2005; Drury et al 2013).

Gestational diabetes, which may be detected by screening at 24–28 weeks' gestation, usually resolves after a woman has given birth, but undiagnosed type 2 diabetes does not. It has been estimated that the proportion of cases with gestational diabetes corresponding to undiagnosed type 2 diabetes ranges from 8–15% (Guedj 2010). Thus an early screening programme to identify possible cases of undiagnosed type 2 diabetes should pick up women earlier when interventions could be considered well before birth.

This first criterion is met, as undiagnosed type 2 diabetes in pregnancy is important and the prevalence is increasing.

2 There is a suitable test

Previously, HbA1c has not been considered a screening option on the grounds of insensitivity (Scott et al 2002). However, advances in the measurement of HbA1c have made it a more reliable and standardised test and it is now recommended for diagnosing type 2 diabetes in non-pregnant patients using a cut-off point of ≥ 48 mmol/mol (Braatvedt et al 2012; American Diabetes Association 2013). Although there is evidence on the use of HbA1c for this purpose, it has not been well evaluated as a screening test in women early in pregnancy.

Preliminary analyses in the recent Hughes study conducted in New Zealand found that the area under the ROC curves for HbA1c for detecting type 2 diabetes was 0.99 (versus 0.81 for random blood glucose). The optimal HbA1c threshold reported by this study for detecting type 2 diabetes was 41 mmol/mol, with 100% sensitivity and 97% specificity (Hughes et al 2013). The positive predictive value in this low prevalence population was 18.8%.

These findings regarding the performance of the HbA1c test are contradicted by indirect evidence from three cohort studies; these studies were conducted in women who had previously had gestational diabetes and were now in the postpartum period. Although there are a number of studies assessing test performance of HbA1c in the general non-pregnant population, indirect evidence from women who are postpartum is most likely to be relevant as this group is in a similar age bracket to women who are newly pregnant. A cohort study with unclear risk of bias of women with a previous diagnosis of gestational diabetes who were no longer pregnant (at 6 weeks to 36 months postpartum) found that HbA1c (at a level ≥ 39 mmol/mol) had 65% sensitivity and 68% specificity for identifying elevated fasting plasma or 2-hour oral glucose tolerance test and 75% sensitivity and 62% specificity for elevated fasting plasma glucose alone (Kim et al 2011). The authors recommended that the agreement between HbA1c and glucose levels was fair for detection of abnormal glucose tolerance among women with histories of gestational diabetes.

Another cohort study with low risk of bias evaluated the usefulness of HbA1c for the reassessment of carbohydrate metabolism in postpartum women with a history of gestational diabetes using levels of 39–47 mmol/mol to indicate prediabetes and ≥ 48 mmol/mol to indicate diabetes; it found that neither HbA1c alone nor HbA1c in combination with fasting plasma glucose provided a sensitive and specific diagnosis of abnormal carbohydrate metabolism in women who had had gestational diabetes (Picon et al 2012). Another observational study with unclear risk of bias found that the sensitivity and specificity for HbA1c at a threshold of 48 mmol/mol to diagnose diabetes were 16.7% and 100% respectively using the oral glucose tolerance test as a reference standard. However, the combination of a cut-off value of 36 mmol/mol for HbA1c and fasting plasma glucose identified 95.1% of women with any kind of glucose intolerance (Megia et al 2012).

Other indirect evidence regarding the performance of HbA1c was identified in dissimilar population groups. A study with a population of German participants ranging in age from 55–74 years found that the most effective screening strategy in terms of number of cases (54%) was HbA1c ≥ 38 mmol/mol combined with an oral glucose tolerance test but it was also the most expensive (Icks et al 2004). The sensitivity was 75.1% and specificity was 56.6%. In a population of 11,247 Australians aged 25 years and over, a threshold of HbA1c ≥ 34 mmol/mol in subjects with one risk factor for diabetes resulted in a sensitivity of 78.7% and specificity of 82.8% for diabetes and of 42.0% and 88.2% respectively for impaired glucose tolerance or impaired fasting glucose. The positive predictive values in this population were 15.5% and 43.2% respectively (Colagiuri et al 2004) and 19.5% of Australian adults would require an oral glucose tolerance test. These findings with HbA1c were similar to those using fasting plasma glucose alone (≥ 5.5 mmol/L) in a similar population. A South Auckland study among European, Māori and Pacific peoples aged 40–79 years reported that an HbA1c of ≥ 34 mmol/mol was the optimal screening cut-off with a sensitivity, specificity and positive predictive value for undiagnosed diabetes in those with at least one risk factor of 76.3%, 67.7% and 22.29%, respectively (Simmons et al 2004). Fasting blood glucose had better sensitivity, specificity and positive predictive value than HbA1c.

In addition to test performance, there are other issues to consider regarding the appropriateness of the test for screening. It is considered more convenient than fasting plasma glucose as fasting is not required. However, HbA1c may vary with patient's ethnicity and can inaccurately reflect glycaemia with certain anaemias and haemoglobinopathies (American Diabetes Association 2013).

Thus the evidence behind the test performance of HbA1c is scant and conflicting, possibly because of the different populations assessed. In regard to performance of this test in women early in their pregnancy, further confirmation is required from other studies, specifically in pregnant patients. There is insufficient evidence to indicate whether this criterion is met.

3 There is an effective and accessible treatment or intervention for the condition identified through early detection

Management of type 2 diabetes in pregnancy includes lifestyle interventions (nutrition and exercise), as well as insulin and other drugs. Self-monitoring enables a woman with diabetes to check her blood glucose concentrations. A randomised controlled trial found that women with type 1 or 2 diabetes randomised to continuous glucose monitoring compared with standard antenatal care had lower mean glycated haemoglobin concentrations at 32–36 weeks' gestation (5.8% vs 6.4%), decreased mean birthweight scores and reduced risk of macrosomia (Murphy et al 2008). Another study compared pregnancy outcomes retrospectively in women diagnosed with gestational diabetes (which included type 2 diabetes) either early (at the time of first antenatal visit) or later (24–28 weeks' gestation) with an oral glucose tolerance test (Bartha et al 2003). Early diagnostic testing avoided some diabetes-related complications, such as hydramnios, fetal anomalies and preterm deliveries. In another study, information gathered from continuous glucose monitoring systems altered clinical management decisions in 62% of cases (McLachlan et al 2007).

The American Diabetes Association recommends that women with diabetes receive nutrition counselling which involves a carbohydrate-controlled meal plan with specific dietary recommendations determined and regularly modified by individual assessment (American Diabetes Association 2013). Exercise is also recommended to minimise the complications of diabetes in pregnancy (at least 30 minutes of planned physical activity each day) (Jovanovic 2004). However, despite efforts to maintain euglycaemia with diet and exercise alone, many women with diabetes discover that hyperglycaemia persists, necessitating supplemental pharmacological therapy. Fine-tuned insulin therapy and safe antihypertensive therapy are often required.

Although there are recommendations for treatment when diabetes is diagnosed in pregnancy, it is still relatively unclear whether earlier treatment leads to improved outcomes and the starting point for screening needs to be taken into account. Most groups recommend undertaking early screening for undiagnosed type 2 diabetes at the time of the first antenatal visit, but as the timing of the first antenatal visit varies throughout the country, the efficacy of treatment is also likely to vary as it will be instituted at different times throughout gestation. The rationale for early screening is that there will be more time available for intervention, but it is not clear whether these interventions impact significantly on outcomes. Ideally, this should come from randomised controlled trials.

Thus it is unclear if this criterion is met.

4 There is high-quality evidence, ideally from randomised controlled trials, that a screening programme is effective in reducing mortality or morbidity

Mortality and morbidity outcomes are increased in pregnant women with unrecognised type 2 diabetes. In Auckland, the perinatal mortality rate was 46.1/1000 among women with type 2 diabetes compared with 12.1/1000 for both type 1 diabetes and the background population (Cundy et al 2000). In the subgroup of women with type 2 diabetes that had not been recognised until the woman was pregnant, the perinatal mortality was even higher (56.2/1000). Studies from other countries also confirm the excess mortality in this group of women; one study has reported that the mean perinatal mortality rate is 7.6% (Langer et al 2010). In addition, the rate of major congenital malformations (cardiac, musculoskeletal, genito-urinary and neurological defects) is considerably higher than in the background population (Cheung et al 2005; Langer et al 2010).

There are no randomised controlled trials comparing screening with no screening in pregnant women and it is unlikely that there will be any undertaken in the future as clinicians may be reluctant to randomise women to a no screening arm. One observational study undertaken in Ontario assessed the impact on gestational diabetes (which may have included type 2 diabetes) of implementing screening in some areas and not in others (Wen et al 2000). Although the prevalence of GDM in the screened areas was increased compared with unscreened areas, the proportions of macrosomia (based on birthweight alone) were similar at 12.7% and 12.5% respectively. No other studies that compared screening with no screening in terms of effects on outcomes were identified.

Indirect evidence from a UK multicentre cluster randomised trial did not find a significant benefit for screening in 20,184 non-pregnant participants aged 40–69 years who were at high risk of undiagnosed diabetes (Simmons et al 2012). The trial compared screening followed by intensive treatment, screening followed by routine care, and no screening. Screening comprised a multistage process including random capillary glucose, HbA1c and fasting capillary blood glucose followed by a diagnostic oral glucose tolerance test if the test was positive. The median follow-up was 9.6 years. There were no significant reductions in cardiovascular, cancer or diabetes-related mortality associated with screening compared with no screening (Simmons et al 2012). However, this strategy was in a non-pregnant population and could not answer questions on impact of diabetes-related outcomes in pregnancy.

Thus, although rates of morbidity and mortality are increased in women with type 2 diabetes, there is insufficient direct evidence that screening (compared with no screening) will reduce morbidity or mortality and this criterion is not met.

5 The potential benefit from the screening programme should outweigh the potential physical and psychological harm (caused by the test, diagnostic procedures and treatment)

The 2007 technical report on gestational diabetes in New Zealand reported, 'As there is no ideal simple, sensitive and specific screening test (as discussed below), it is essential that well women are not exposed to additional investigations that have a significant false positive rate, as this may lead to increased anxiety' (Gestational Diabetes Mellitus Technical Working Party 2007). The authors go on to suggest that it is reasonable to offer a screening test at booking to women who are more likely to have unrecognised type 2 diabetes.

The addition of an HbA1c blood test at the first antenatal visit is unlikely to inconvenience women (in comparison with other screening tests for type 2 diabetes) but other potential harms from screening, in particular the false positive rate, may be considerable. No research was identified to adequately assess the balance of benefits and harms for either all pregnant women or those with risk factors and this criterion has not been met.

6 The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation

The adoption of an early screening programme for type 2 diabetes would result in a larger number of women requiring diabetic services. The current diabetic services for pregnant women diagnosed with type 1, 2 or gestational diabetes may need to be bolstered to be able to deal with increased numbers of women. These women would otherwise have been identified at the 24–28 weeks' gestation screening and diagnostic test and would have been referred for treatment later in their pregnancy. Currently, it is not clear whether this criterion is met.

7   There is consideration of social and ethical issues

The New Zealand report on screening notes that:

> Potential participants in the screening programme should be given information that allows them to weigh up the probable benefits and harms, using their own values and preferences. Culturally appropriate, evidence-based information should be available for people offered screening to assist them in making an informed decision. This information should also explain the consequences of testing, the possibility and importance of false-negative and false-positives, investigation and treatment.

<div align="right">(National Health Committee 2003)</div>

Because of the scarcity of research addressing use of HbA1c, there is insufficient evidence-based information to share with participants. This criterion is not met.

8   There is consideration of cost–benefit issues

No New Zealand research was identified. The modelling for the National Institute for Health and Care Excellence guideline on gestational diabetes concluded that selective screening for gestational diabetes (rather than type 2 diabetes) would be cost-effective in the United Kingdom. The cost-effectiveness of the programme would improve if gestational diabetes became more common, if intervention costs fell, if intervention became more effective and if screening costs fell, but these conclusions are based on screening between 24–28 weeks to identify gestational diabetes (NICE 2008). Indirect evidence from a German study in a non-pregnant older population (55–74 years), where the prevalence of diabetes is likely to be much higher, suggested that a screening strategy of HbA1c followed by an oral glucose tolerance test was the most expensive option of all screening options that were compared (Icks et al 2004). In New Zealand, the cost of an HbA1c test is currently more than $20 but no cost-effectiveness analyses have been done in pregnant patients. Thus this criterion is not met.

Appendix I: Supporting evidence for Chapter 3

Table 17: Commonly used screening and diagnostic procedures

Organisation	Year	Screening or diagnostic	Testing schedule	Abnormal values required	Threshold equal to or greater than			
					Fasting	**1 hour**	**2 hours**	**3 hours**
Australasian Diabetes in Pregnancy Society	2013	Diagnostic	OGTT	1	5.1 mmol/L	10.0 mmol/L	8.5 mmol/L	–
		Diagnostic	HbA1c*	na	48 mmol/mol	–	–	–
American Diabetes Association	2013	Diagnostic	75 g OGTT	1	5.1 mmol/L	10.0 mmol/L	8.5 mmol/L	–
American College of Obstetricians and Gynecologists	2013	Screening	50 g GCT	1	–	7.2 mmol/L or 7.8 mmol/L	–	–
		Diagnostic** (Carpenter and Coustan)	100 g OGTT	2	5.3 mmol/L	10.0 mmol/L	8.6 mmol/L	7.8 mmol/L
		Diagnostic** (NDDG)	100 g OGTT	2	5.8 mmol/L	10.6 mmol/L	9.2 mmol/L	8.0 mmol/L
International Association of Diabetes and Pregnancy Study Groups	2010	Diagnostic	75 g OGTT	1	5.1 mmol/L	10.0 mmol/L	8.5 mmol/L	–
World Health Organization	1999	Diagnostic for diabetes	75 g OGTT	1	7.0 mmol/L	–	11.1 mmol/L	–
Canadian Diabetes Association	2008	Screening	50 g GCT	1	–	7.8 mmol/L	–	–
		Diagnostic	75 g OGTT	2	5.3 mmol/L	10.6 mmol/L	8.9 mmol/L	–

Note: GCT = glucose challenge test; OGTT = oral glucose tolerance test; NDDG = National Diabetes Data Group.

* In areas where the rate of undiagnosed type 2 diabetes is thought to be high, or in remote areas where the performance of an OGTT may be logistically difficult, a measurement of HbA1c can be considered.

** American College of Obstetricians and Gynecologists stipulates that either the Carpenter and Coustan or the National Diabetes Data Group thresholds are appropriate to use.

Figure 4: Sensitivity and specificity: 50 g oral glucose tolerance test by Carpenter and Coustan or American Diabetes Association (2000–2010) criteria
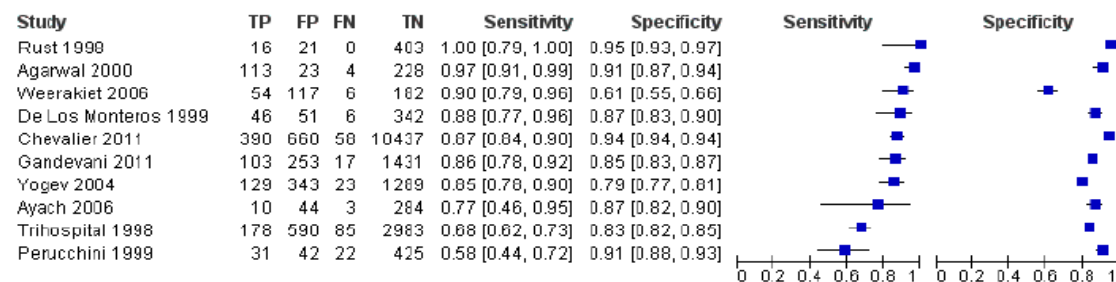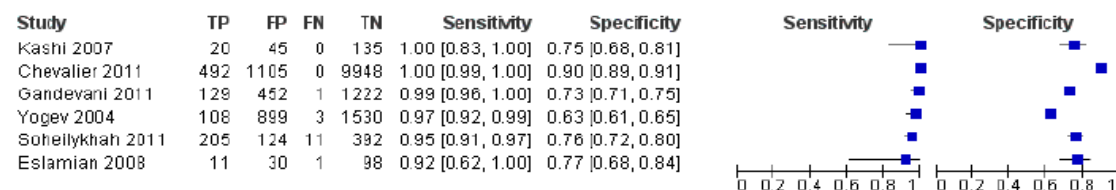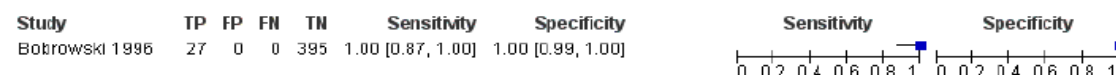
50 g oral glucose challenge test and 100 g, 3-hour oral glucose tolerance test (Carpenter and Coustan criteria)	Sensitivity	Specificity	Prevalence	Positive predictive value	Median negative predictive value	Number of studies
Threshold ≥ 7.8 mmol/L	85%	86%	3.8% to 31.9%	18% to 27% (Prevalence <10%) 32% to 83% (Prevalence ≥10%)	98%	9
Threshold ≥ 7.2 mmol/L	99%	77%	4.3% to 29.8%	11% to 27% (Prevalence <10%) 31% to 62% (Prevalence ≥10%)	100%	6
Threshold ≥ 11.1 mmol/L	100%	100%	6.4%	100%	100%	1

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and Diagnosing Gestational Diabetes Mellitus.* Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Figure 5: Forest plot of sensitivity and specificity: 50 g oral glucose challenge test by National Diabetes Data Group criteria

NDDG >140mg/dL

Study	TP	FP	FN	TN	Sensitivity	Specificity
Deerochanawong 1996	10	73	0	626	1.00 [0.69, 1.00]	0.90 [0.87, 0.92]
Perea-Carrasco 2002	36	151	1	454	0.97 [0.86, 1.00]	0.75 [0.71, 0.78]
De Los Monteros 1999	38	59	5	343	0.88 [0.75, 0.96]	0.85 [0.81, 0.89]
Lamar 1999	4	23	1	105	0.80 [0.28, 0.99]	0.82 [0.74, 0.88]
Trihospital 1998	111	657	34	3034	0.77 [0.69, 0.83]	0.82 [0.81, 0.83]
Uncu 1995	8	6	3	7	0.73 [0.39, 0.94]	0.54 [0.25, 0.81]
Cetin 1997	11	32	6	225	0.65 [0.38, 0.86]	0.88 [0.83, 0.91]

NDDG >130mg/dL

Study	TP	FP	FN	TN	Sensitivity	Specificity
Berkus 1995	19	20	2	39	0.90 [0.70, 0.99]	0.66 [0.53, 0.78]
Ardawi 2000	90	30	12	157	0.88 [0.80, 0.94]	0.84 [0.78, 0.89]
Uncu 1995	2	8	1	7	0.67 [0.09, 0.99]	0.47 [0.21, 0.73]

NDDG >200mg/dL

Study	TP	FP	FN	TN	Sensitivity	Specificity
Bobrowski 1996	27	0	0	395	1.00 [0.87, 1.00]	1.00 [0.99, 1.00]

50 g oral glucose challenge test and 100 g, 3-hour oral glucose tolerance test (National Diabetes Data Group criteria)	Sensitivity	Specificity	Prevalence	Positive predictive value	Median negative predictive value	Number of studies
Threshold ≥ 7.8 mmol/L	85%	83%	1.4% to 45.8%	12% to 39% (Prevalence <10%) 57% (Prevalence ≥10%)*	99%	7
Threshold ≥ 7.2 mmol/L	Data not pooled	Data not pooled	16.7% to 35.3%	20% to 75%	86% to 95%^	3
Threshold ≥ 11.1 mmol/L	100%	100%	Not stated	100%	100%	1

Note: * reported in one study, ^ range.

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and Diagnosing Gestational Diabetes Mellitus*. Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Figure 6: Forest plot of sensitivity and specificity: 50 g oral glucose challenge test (different thresholds) by American Diabetes Association (2000–2010) 75 g criteria

ADA 75g OGTT

Study	TP	FP	FN	TN	Sensitivity	Specificity
Buhling 2004	36	142	1	733	0.97 [0.86, 1.00]	0.84 [0.81, 0.86]
Yachi 2011	7	106	1	395	0.88 [0.47, 1.00]	0.79 [0.75, 0.82]
Maegawa 2003	19	95	3	632	0.86 [0.65, 0.97]	0.87 [0.84, 0.89]

CDA Criteria

Study	TP	FP	FN	TN	Sensitivity	Specificity
Rey 2004	17	29	4	66	0.81 [0.58, 0.95]	0.69 [0.59, 0.79]
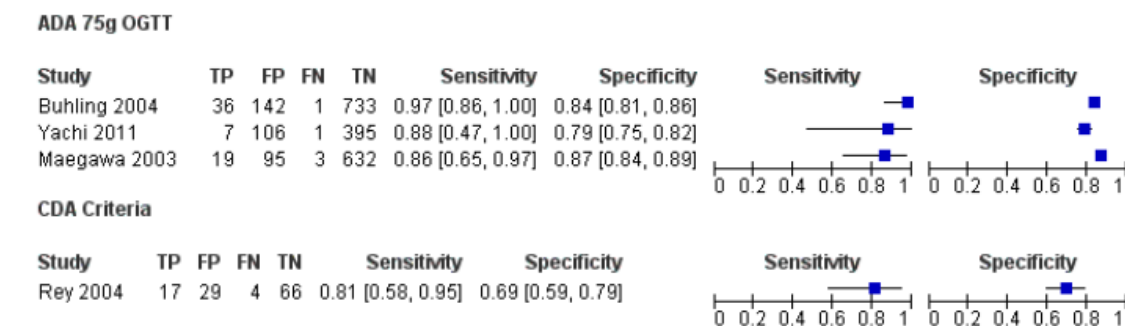
ADA = American Diabetes Association; CDA = Canadian Diabetes Association; OGCT = oral glucose challenge test; OGTT = oral glucose tolerance test

50 g oral glucose challenge test and 75 g, 2-hour oral glucose tolerance test (American Diabetes Association/Canadian Diabetes Association criteria)	Sensitivity	Specificity	Prevalence	Positive predictive value	Median negative predictive value	Number of studies
Various thresholds applied	86% to 97%	79% to 87%	1.6% to 4.1%	7% to 20%	99% to 100%	4

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Figure 7: Forest plot of sensitivity and specificity: 50 g oral glucose challenge test by World Health Organization criteria

>140 mg/dL

Study	TP	FP	FN	TN	Sensitivity	Specificity
Siribaddana 1998	40	185	7	489	0.85 [0.72, 0.94]	0.73 [0.69, 0.76]
van Leeuwen 2007	33	134	14	1100	0.70 [0.55, 0.93]	0.89 [0.87, 0.91]
Deerochanawong 1996	48	35	63	563	0.43 [0.34, 0.53]	0.94 [0.92, 0.96]

>137 mg/dL

Study	TP	FP	FN	TN	Sensitivity	Specificity
Tan 2007	166	256	14	85	0.92 [0.87, 0.96]	0.25 [0.20, 0.30]
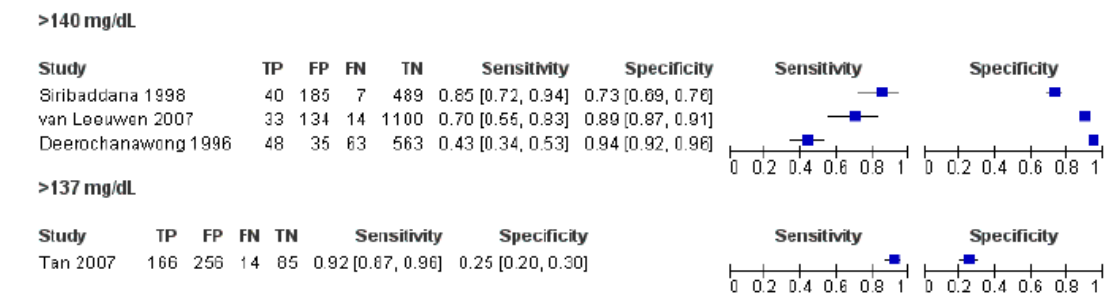
OGCT = oral glucose challenge test; WHO = World Health Organization

50 g oral glucose challenge test and 75 g, 2-hour oral glucose tolerance test (World Health Organization criteria)	Sensitivity	Specificity	Prevalence	Positive predictive value	Median negative predictive value	Number of studies
Threshold ≥ 7.8 mmol/L	43% to 85%	73% to 94%	3.7% to 15.7%	18% to 20% (Prevalence <10%) 58% (Prevalence ≥10%)*	99%	3

Note: * one study

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and diagnosing Gestational Diabetes Mellitus.* Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Figure 8: Forest plot of sensitivity and specificity: fasting plasma glucose by Carpenter and Coustan/American Diabetes Association (2000–2010) criteria
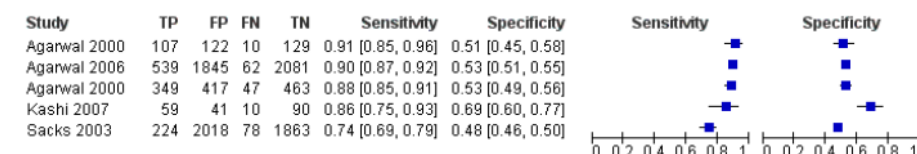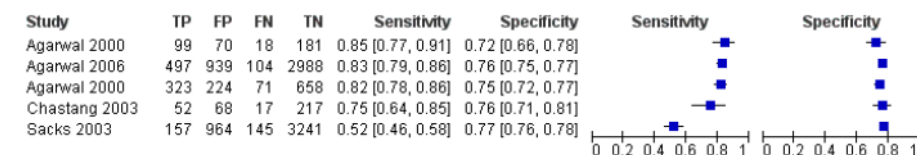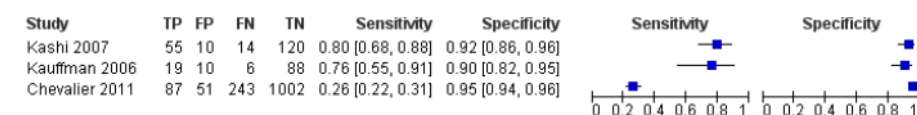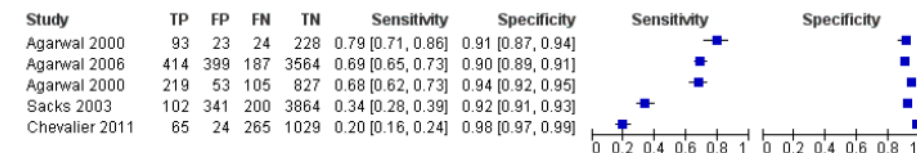
ADA = American Diabetes Association; CC = Carpenter-Coustan; OGCT = oral glucose challenge test

Fasting plasma glucose (Carpenter and Coustan and American Diabetes Association criteria)	Sensitivity	Specificity	Number of studies
Threshold ≥ 4.7 mmol/L	87%	52%	5
Threshold ≥ 5.0 mmol/L	77%	76%	5
Threshold ≥ 5.1 mmol/L	76%	92%	3
Threshold ≥ 5.3 mmol/L	54%	93%	5

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and Diagnosing Gestational Diabetes Mellitus*. Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Figure 9: Other screening criteria used to diagnose gestational diabetes

Criteria	Author, year, country	N*	Prevalence (%)	Sn (%) (95% CI)	Sp (%) (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy
WHO criteria	Reichelt, 1998, Brazil	4977	0.3	88 (62–98)	78 (77–79)	1.3 (0.8–2.1)	100	78
	Wjieyaratne, 2006, Sri Lanka**	853	16.9	92 (87–96)	71 68–75)	40 (35–45)	98 (96–99)	75
NDDG criteria	Kauffman, 2006, US	123	13.0	81 (54–96)	88 (80–93)	50 (32–68)	97 (92–99)	87
Other diagnostic criteria	Maegawa, 2003, Japan	749						
	(1st tri)		1.9	71 (68–79)	83 (78–87)	7 (4–13)	99 (98–100)	82
	(2nd tri)		2.9	77 (72–80)	91 (86–94)	20 (13–30)	99 (98–100)	90
	Rey, 2004, Canada*	122	17.2	90 (70–99)	46 (36–56)	22 (14–31)	94 (82–98)	42

CI = confidence interval; NDDG = National Diabetes Data Group; NPV = negative predictive value; PPV = positive predictive value; Sn = sensitivity; Sp = specificity; Tri = trimester; WHO = World Health Organization.

* Number of women in the analysis.

** Selective screening practice.

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and Diagnosing Gestational Diabetes Mellitus*. Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Table 18: Prevalence and characteristics of other screening tests by gestational diabetes diagnostic criteria

Screening test	Author, year, country	N*	Index test threshold	Reference standard	Prevalence (%)	Sn (%) (95% CI)	Sp (%) (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (%)
HbA1c	Uncu, 1995, Turkey	42	7.2%	CC	33.3	64 (35–87)	64 (44–81)	47 (27–68)	78 (59–87)	64
	Agarwal, 2005, UAE	442	7.5%	ADA (75 g)	19.0	82 (72–90)	21 (17–26)	20 (16–24)	83 (75–90)	33
	Agarwal, 2001, UAE	430	5.0%	CC	26.8	92 (86–96)	28 (23–33)	32 (27–37)	91 (83–95)	45
	Rajput, 2011, India	607	5.5%	ADA	7.1	86 (72–95)	61 (57–65)	15 (11–19)	98 (96–99)	63
			5.3%	IADPSG	23.7	12 (7–18)	97 (95–98)	57 (39–73)	78 (74–82)	77
Serum fructosamine	Agarwal, 2011, UAE	849	≥ 237 µmol/L	ADA (75 g)	13.3	86 (78–92)	23 (20–27)	15 (12–18)	92 (87–95)	32
	Uncu, 1995, Turkey	42	≥ 2.85 mmol/L	CC	33.3	71 (42–92)	46 (28–66)	40 (23–59)	77 (55–86)	55
	Agarwal, 2001, UAE	430	≥ 210 µmol/L	CC	26.7	92 (86–96)	23 (18–28)	31 (26–36)	89 (81–94)	42
Fasting plasma insulin	Kauffman, 2006, US	123	≥ 93 µmol/L	NDDG	13.0	56 (35–76)	71 (61–80)	33 (21–48)	86 (78–92)	68
	Yachi, 2007, Japan	509	≥ 3.66 mmol/L	JSOG (10-week)	2.0	48 (43–53)	72 (63–80)	86 (80–90)	29 (24–36)	53
Author defined (fructosamine/ total protein) – (glucose/100)	Perea-Carrasco, 2002, Spain	578	≥ 27.2	IWC, 2	7.0	98 (90–100)	89 (86–91)	44 (35–53)	100 (99–100)	90
Adiponectin	Weerakiet, 2006, Thailand	359	≥ 10 µg/mL	ADA	16.7	92 (82–97)	31 (26–36)	18 (14–23)	96 (91–98)	40

Screening test	Author, year, country	N*	Index test threshold	Reference standard	Prevalence (%)	Sn (%) (95% CI)	Sp (%) (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (%)
Capillary blood glucose	Agarwal, 2008, UAE	1662	≥ 88 mg/dL	ADA (FPG)	11.2	84 (78–89)	75 (73–77)	30 (26–34)	98 (96–98)	76
	Balaji, 2012, India	819	≥ 140 mg/dL	WHO	10.5	80 (70–88)	98 (97–99)	86 (77–92)	98 (96–99)	97
	Wijeyaratne, 2006, Sri Lanka	853	≥ 130 mg/dL	WHO	16.3	63 (54–70)	37 (34–41)	17 (14–20)	83 (79–87)	42
Glucose source	Estamian, 2008, Iran	138	50 g carb breakfast	ADA	8.6	83 (52–98)	86 (79–91)	36 (20–5)	98 (94–100)	86
	Lamar, 1999, US	136	50 g (28) jelly beans	NDDG	3.7	40 (5–85)	85 (78–91)	9 (3–28)	97 (93–99)	83
	Rust, 1998, US	448	100 g carb meal	ADA (20 week)	3.6	25 (7–52)	98 (96–99)	40 (17–69)	96 (93–98)	94

ADA = American Diabetes Association; carb = carbohydrate; CC = Carpenter-Coustan; CI = confidence interval; FPG = fasting plasma glucoase; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; IADPSG = International Association of Diabetes in Pregnancy Study Groups; IWC = International Workshop Conference; JSOG = Japan Society of Obstetrics and Gynecology; NDDG = National Diabetes Data Group; NPV = negative predictive value; PPV = positive predictive value; Sn = sensitivity; Sp = specificity; UAE = United Arab Emirates; WHO = World Health Organization.

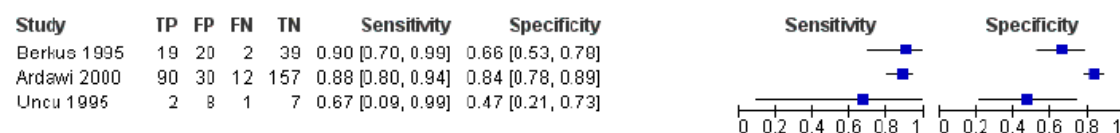* Number of women in the analysis.

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and Diagnosing Gestational Diabetes Mellitus.* Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Table 19: Effect of prevalence on positive and negative predictive values

	Screening test prevalence	Positive predictive value	Negative predictive value
50 g OGCT ≥ 140 mg/dL by CC/ADA (2000–2010) Sensitivity = 85% Specificity = 86%	7%	31%	99%
	15%	52%	97%
	25%	67%	95%
50 g OGCT ≥ 130 mg/dL by CC/ADA (2000–2010) Sensitivity = 99% Specificity = 77%	7%	24%	100%
	15%	43%	100%
	25%	59%	100%
50 g OGCT ≥ 140 mg/dL by NDDG Sensitivity = 85% Specificity = 83%	7%	27%	99%
	15%	47%	97%
	25%	63%	94%
50 g OGCT ≥ 130 mg/dL by NDDG Sensitivity = 88% Specificity = 66% (median)	7%	16%	99%
	15%	31%	97%
	25%	46%	94%
50 g OGCT ≥ 140 mg/dL by ADA 75 g Sensitivity = 88% Specificity = 84% (median)	7%	29%	99%
	15%	49%	98%
	25%	65%	95%
50 g OGCT ≥ 140 mg/dL by WHO Sensitivity = 78% Specificity = 81% (median)	7%	24%	98%
	15%	42%	95%
	25%	58%	92%
FPG (≥ 85 mg/dL) by CC/ADA (2000–2010) Sensitivity = 87% Specificity = 52%	7%	12%	98%
	15%	24%	96%
	25%	38%	92%
Risk factor screening by various criteria Sensitivity = 84% Specificity = 72% (median)	7%	21%	98%
	15%	38%	96%
	25%	54%	93%

ADA = American Diabetes Association; CC = Carpenter-Coustan; FPG = fasting plasma glucose; NDDG = National Diabetes Data Group; OGCT = oral glucose challenge test; WHO =World Health Organization.

Source: Reproduced from Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, Donovan L. 2012. *Screening and Diagnosing Gestational Diabetes Mellitus*. Evidence Report/Technology Assessment number 210 (Prepared by the University of Alberta Evidence-Based practice Center under contract No 290-2007-10021I). Rockville MD: AHRQ with permission of the Agency for Healthcare Research and Quality.

Table 20: Changes in prevalence of gestational diabetes based on diagnostic criteria

Study	Number of participants	Prevalence (%)
Moses (2011)	1272	IADPSG 13% versus ADIPS 9.6%
Agarwal (2010)	10,283	IADPSG 37.7% versus ADA 12.9%
Jenum (2012)	759	IADPSG 31.5% versus WHO 13%
Somani (2011)	291	WHO 4.8% versus Carpenter and Coustan 6.4% versus O'Sullivan 3.5%
Karcaaltincaba (2009)	21,531	Carpenter and Coustan 4.5% versus NDDG 3.2%

Note: ADA = American Diabetes Association; ADIPS = Australasian Diabetes in Pregnancy Society; IADPSG = International Association of Diabetes and Pregnancy Study Groups; NDDG = National Diabetes Data Group; WHO = World Health Organization.

Table 21: Outcomes for women who would have been diagnosed with gestational diabetes using the International Association of Diabetes and Pregnancy Study Groups' criteria compared with outcomes for women without gestational diabetes

| Reference	IADPSG criteria compared with:	n	Significant results
O'Sullivan (2011)	World Health Organization	258 newly diagnosed by IADPSG criteria vs. women with no GDM	Gestational hypertension (15% vs 7.5%, $p < 0.0001$) Pre-eclampsia (7.1% vs 4.0%, $p = 0.03$) Caesarean section (35.2% vs 24.9%, $p < 0.0001$) Macrosomia (28.8% vs 17.0%, $p = 0.02$) LGA (26.8% vs 16.2%, $p < 0.0001$) NICU admission (16.5% vs 9.1%, $p < 0.0001$)
Lapolla (2012)	Fourth International Workshop–Conference on Gestational Diabetes Mellitus criteria	112 newly diagnosed by IADPSG criteria vs 1815 women with no GDM	Caesarean section: 43.6% vs 31.1% ($p < 0.01$) Fetal morbidity: 16.5% vs. 7.3% ($p < 0.001$)
Morikawa (2010)	Japan Society of Obstetrics and Gynaecology criteria	43 newly diagnosed by IADPSG criteria vs 160 women with no GDM	Macrosomia (≥ 3600 g): 14% vs 3.8% ($p = 0.02$)
Benhalima (2013)	Carpenter and Coustan criteria	160 newly diagnosed by IADPSG criteria vs 6345 women with no GDM	Caesarean section: 30.5% vs 23.3% ($p = 0.001$) Shoulder dystocia: 3.9% vs 1.4% ($p = 0.007$)
Bodmer-Roy (2012)	Canadian Diabetes Association criteria	186 newly diagnosed by IADPSG criteria vs 372 women with no GDM	No significant differences

Note: GDM = gestational diabetes mellitus; IADPSG = -International Association of Diabetes and Pregnancy Study Groups, LGA = large for gestational age; NICU = neonatal intensive care unit.

Table 22: Outcomes for women who would have been diagnosed with gestational diabetes using the Carpenter and Coustan criteria compared with outcomes for women diagnosed with gestational diabetes using the National Diabetes Data Group criteria

Reference	Participants	Outcomes reported using criteria of Carpenter and Coustan versus National Diabetes Data Group Risk estimate (95% confidence interval)
Berggren (2011)	Total 33,179 screened Diagnosed by CC = 1542 Diagnosed by NDDG = 1082	Gestational hypertension aPR 1.54 (1.01–2.37) Pre-eclampsia aPR 1.70 (1.23–2.35) Caesarean section aPR 1.16 (1.04–1.30) Macrosomia > 4000 g aPR 1.25 (1.01–1.56) Admission to and length of stay in NICU > 48 hours, NS
Cheng (2009)	Total 14,693 screened Diagnosed by CC = 753 Diagnosed by NDDG = 480	Caesarean section OR 1.44 (1.01–2.07) Operative vaginal delivery OR 1.72 (1.20–2.46) Birthweight > 4500 g OR 4.47 (2.26–8.86) Shoulder dystocia OR 2.24 (1.03–4.88)

Note: aPR = adjusted prevalence ratio; CC = Carpenter and Coustan; NDDG = National Diabetes Data Group; NICU = neonatal intensive care unit; NS = not significant; OR = odds ratio.

Table 23: Maternal and infant outcomes according to the presence or absence of gestational diabetes and/or at least one risk factor

	No GDM		GDM		GDM effect (*p*-value)	Risk factor effect (*p*-value)
	No risk factors (%)	Risk factors (%)	No risk factors (%)	Risk factors (%)		
GDM-related events	8.8	11.1	16.7	18.2	< 0.0001	< 0.0001
Pre-eclampsia	1.9	2.2	3.2	3.1	< 0.05	NS
Large for gestational age	6.0	8.2	12.2	14.9	< 0.0001	< 0.0001
Shoulder dystocia	1.3	1.5	2.4	1.7	< 0.01	NS
Caesarean section	19.7	20.6	28.0	27.4	< 0.0001	NS
Preterm delivery	8.3	8.0	9.0	7.9	NS	NS
Intrauterine, fetal or neonatal death	1.2	1.1	0.7	0.5	NS	NS

Note: GDM = gestational diabetes mellitus; NS = not significant.

There were no significant interactions between GDM effect and risk factor effect.

Source: Cosson et al (2013)

Appendix J: Supporting evidence for Chapter 4

Table 24: Table of effects: dietary interventions to prevent gestational diabetes

Outcome	Number of studies and definitions	Author	Number of participants	Effect size (95% confidence interval) for diagnosis of gestational diabetes
Diagnosis of GDM	7 trials Various	Oostdam (2011)	813 Pregnant women	RD ⁻0.05 (⁻0.10 to ⁻0.01)
	1 trial Carpenter and Coustan, and American Diabetes Association criteria	Walsh (2012)	759 Pregnant women with history of delivering a macrosomic infant	Not significant
	1 trial 2-hour, 75 g oral glucose tolerance test	Quinlivan (2011)	124 Obese or overweight pregnant women	OR 0.17 (0.03–0.95) 6% versus 29%
	1 trial (probiotics)	Oostdam (2011)	256 Pregnant women	OR 0.27 (0.11–0.62)

Note: GDM = gestational diabetes mellitus; OR = odds ratio; RD = risk difference.

Table 25: Table of effects: exercise interventions to prevent gestational diabetes

Outcome	Number of studies and definitions	Author	Number of participants	Effect size (95% confidence interval) for diagnosis of gestational diabetes
Diagnosis of GDM	3 trials Various	Han (2012)	826 Pregnant women	1.10 (0.66–1.84), NS
	3 trials Various	Oostdam (2011)	238 Pregnant women	RD ⁻0.05 (⁻0.20 to 0.10), NS
	1 trial 2-hour OGTT at 24–26 weeks WHO and IADPSG criteria applied	Barakat (2013)	428 Sedentary*	OR 0.84 (0.50–1.40)

Note: GDM = gestational diabetes mellitus; IADPS = International Association for Diabetes and Pregnancy Study Groups; NS = not significant; OGTT = oral glucose tolerance test; OR = odds ratio; RD =risk difference; WHO = World Health Organization.

* Defined as not exercising > 20 min on > 3 days/week.

Table 26: Table of effects: dietary and exercise interventions to prevent gestational diabetes

Outcome	Number of studies and definitions	Reference	Type of intervention	Number of participants	Effect size (95% confidence interval) for diagnosis of gestational diabetes
Diagnosis of gestational diabetes	1 trial 1-hour OGTT	Hui (2012)	Combined dietary and exercise, community-based versus usual care	190 Pregnant women < 26 weeks	Incidence of GDM 1.8% in the intervention arm compared with 3% in the control arm NS
	1 trial 2-hour OGTT 26–28 weeks	Luoto (2011)	Intensified counselling on physical activity versus usual care	399 High risk of GDM	Absolute effect size 1.36 (0.71–2.62), NS
	1 trial 2-hour OGTT Modified WHO criteria	Korpi-Hyovalti (2011)	Individualised dietary and exercise advice versus usual care	54 High risk of GDM	Incidence of GDM 11.1% in the intervention arm compared with 3.7% in the control arm NS
	1 trial Not reported	Phelan (2011)	Exercise and nutrition information and behavioural counselling versus usual care	401 Pregnant women	OR 1.77 (0.65–4.82), NS
	1 trial 2-hour OGTT capillary blood glucose was ≥ 9 mmol/L	Vinter (2011)	Four dietary advice sessions, exercise advice, pedometer and aerobic exercise classes versus usual care	304 Obese pregnant women	Incidence of GDM 6% in the intervention arm compared with 5.2% in the control group (p = 0.760)
Large for gestational age	1 trial Birthweight above the 90th percentile adjusted gestational age	Luoto (2011)	Intensified counselling on physical activity versus usual care	399 High risk of GDM	Absolute effect size 0.58 (0.34–1.02)

Note: GDM = gestational diabetes mellitus; NS = not significant; OGTT = oral glucose tolerance test; OR = odds ratio; WHO = World Health Organization.

Appendix K: Supporting evidence for Chapter 5

Table 27: Details of screening/diagnostic criteria of interventions providing specific packages of treatment for women diagnosed with gestational diabetes

Reference	Screening	Loading dose of sugar	Fasting (mmol/L)	1-hour (mmol/L)	2-hour (mmol/L)	3-hour (mmol/L)
Ferrara (2011)	50 g oral glucose challenge test	100 g	≥ 5.1	≥ 10.0	≥ 8.5	–
Landon (2009)$	50 g, 1-hour oral glucose challenge test (values between 7.5 and 11.1 mmol/L)	100 g	< 5.3	> 10	> 8.6	> 7.8
Elnour (2008)	50 g, 1-hour oral glucose challenge test with cut-off of serum glucose > 7.2 mmol/L; plasma glucose > 7.8 mmol/L or risk factors	100 g	≥ 5.3	≥ 10	≥ 8.7	≥ 7.8
Crowther (2005)#	50 g glucose challenge test (≥ 7.8 mmol/L at 1 hour)	75 g	< 7.8	–	7.8–11	–
Gillen (2004)	High-risk women only	75 g	≥ 5.1	≥ 10.0	≥ 8.5	–
Yang (2003)	50 g, 1-hour oral glucose challenge test with cut-off of ≥ 7.8 mmol/L	75 g	≥ 7.0	–	≥ 7.8	–
Bancroft (2000)#	At discretion of physician	75 g	<7 .0	–	7.8–11	–
Garner (1997)^	75 g, 1-hour oral glucose challenge test with cut-off of ≥ 8 mmol/L	75 g	–	–	–	
Ford (1997)	No details	75 g	–	–	8.0–11.0	–
Thompson (1990)$	50 g, 1-hour oral glucose challenge test > 7.8 mmol/L	100 g	> 5.8	> 10.5	> 9.2	> 8.1
Langer (1989)*	50 g, 1-hour oral glucose challenge test (proceed if ≥ 7.2 mmol/L)	100 g	> 5.8	> 10.5	> 9.2	> 8.1

Note: * One or more abnormal values required; $ ≥2 abnormal values required; #2 abnormal values required; ^ Timing not specified but > 7.5 mmol/L in second trimester and > 9.6 mmol/L in third trimester.

Source: Alwan et al (2009)

Table 28: Demographic details of women included in randomised trials of specific packages of treatment for gestational diabetes

Reference	Country	Intervention/control	Mean age (years)	Mean BMI at booking (kg/m²)	Gestational age at diagnosis/study entry (weeks)	Ethnicity
Ferrara (2011)	Australia	Lifestyle, diet + exercise + breastfeeding (n = 96)	78.1% were > 30 years	57.3% were > 30 kg/m²	31.8 ± 5.6	19% Non-Hispanic White 52% Asian/Pacific Island 19% Hispanic 6% Other/missing
		Usual care (n = 101)	75.3% were > 30 years	52.5% were > 30 kg/m²	31.0 ± 6.1	
Landon (2009)	USA	Diet/insulin for mild GDM (n = 485)	29.2 ± 5.7	30.1 ± 5	28.8 ± 1.6	Black 11.5% White 25.3% Asian 5.2% Hispanic 57%
		Usual care (n = 473)	28.9 ± 5.6	30.2 ± 5.1	28.9 ± 1.5	
Elnour (2008)	United Arab Emirates	Lifestyle advice +/− insulin (n = 108)	31.1 (95%CI 30.2–32.1)	Not stated	< 20 weeks	United Arab Emirates nationals 100%
		Usual care (n = 72)	30.7 (95%CI 29.4–32.01)	Not stated	<20 weeks	
Crowther (2005)	Australia and UK	Diet/insulin (n = 490)	30.9 ± 5.4	26.8 (23.3–31.2)*	29.1 (28.2–30)*	White 73%, Asian 19%, Other 9%
		Usual care (n = 510)	30.1 ± 5.5	26 (22.9–30.9)*	29.2 (28.2–30)*	White 78%, Asian 14%, Other 8%
Gillen (2004)	Australia	Specific dietary advice (n = 16 Usual care (n = 16)	–	–	Approximately 28 weeks	–
Yang (2003)	China	Intensive Diabetes Management Plan (n = 95) Usual care (n = 55)	Not stated	Not stated	Not stated	Chinese women
Bancroft (2000)	UK	Diet/insulin (n = 32)	29.7 ± 6.23	31.2 ± 6.7	31 (24–38)	Caucasian 69%, Asian 31% in both groups
		Diet (n = 36)	31.9 ± 5.17	27.5 ± 6.1	32 (15–37)	
Garner (1997)	Canada	Dietary counselling (n = 149)	30.7 ± 4.6	Not stated	Not stated	Not stated
		Usual care (n = 150)	30.7 ± 4.8			
Ford (1997)	No details	Specific 'diabetic type' advice (n = 16) No specific advice (n = 13)	Not stated	Not stated	Not stated	Not stated

Reference	Country	Intervention/control	Mean age (years)	Mean BMI at booking (kg/m²)	Gestational age at diagnosis/study entry (weeks)	Ethnicity
Thompson (1990)	USA	Diet plus insulin (n = 45)	27 ± 5.4	192 lb ± 38	Not stated	51% Black
		Diet alone (n = 50)	26 ± 5.7	200 lb ± 47	Not stated	49% White
Langer (1989)	USA	Specific diet (n = 63)	31 ± 5	Not stated	31 ± 3	31.5% Black 33% Hispanic 34.5%White
		Usual care (n = 63)	28 ± 6	Not stated	31 ± 3	

Note: BMI = body mass index; CI = confidence interval; GDM = gestational diabetes mellitus.

* Median (interquartile ranges).

Source: Alwan et al (2009)

Table 29: Components of interventions using specific packages of treatment for women with gestational diabetes

Reference	Intervention	Control
Ferrara (2011)	Diet and exercise and breastfeeding intervention delivered by a dietician using social cognitive theory and transtheoretical model. Delivered prenatal, postpartum and maintenance based on one-to-one sessions and individual telephone counselling. Advised not to exceed 11.4 kg for obese women and to follow ADA diet and moderate physical activity (150 min/week). Also had lactation consultant and contact maintained for 6 weeks postpartum (n = 96).	Usual care. Printed material only in prenatal and postnatal period (n = 101).
Landon (2009)	Formal nutrition counselling and diet therapy +/− insulin and daily self-monitoring. Insulin was commenced if fasting glucose levels were predominantly at 5.3 mmol/L or greater or postprandial glucose was 6.7 mmol/L or greater (n = 485).	Usual prenatal care +/− insulin and self-monitoring. Insulin was commenced if fasting glucose levels were predominantly at 5.3 mmol/L or greater or postprandial glucose was 6.7 mmol/L or greater (n = 473).

Reference	Intervention	Control
Elnour (2008)	Structured pharmaceutical care for 10–30 minutes with a clinical pharmacist. Options of treatment explained and the woman was encouraged to participate in self-management. Structured education on GDM and management provided (diet and exercise, glycaemic control, self-monitoring, review of treatment if glycaemic control inadequate). Printed education booklet that contained general information on diabetes, aims of treatment, diet and exercise and action to take if hypoglycaemic or hyperglycaemic. Record plasma glucose at least five times per day for three to four days per week. Intervention took place at baseline and at monthly clinic visits. Encouraged to telephone pharmacist if any queries/concerns (n = 108).	Monthly clinic visits. Self-monitoring (n = 72).
Crowther (2005)	Usual obstetrical care with physician support. Individualised dietary advice from a qualified dietician, instructions on how to self-monitor glucose levels four times a day until fasting glucose levels of at least 3.5 mmol/L (63 mg/dL) and no more than 5.5 mmol/L (99 mg/dL), preprandial levels of no more than 5.5 mmol/L, and levels two hours postprandially that were no more than 7.0 mmol/L (126 mg/dL), followed by daily monitoring at rotating times during the day; and insulin therapy, with the dose adjusted based on glucose levels, if there were two capillary-blood glucose results during the two-week period in which the fasting level was at least 5.5 mmol/L or the postprandial level was at least 7.0 mmol/L at 35 weeks' gestation or earlier, if the postprandial level was at least 8.0 mmol per litre (144 mg per decilitre) at more than 35 weeks' gestation, or if one capillary-blood glucose result during the two-week period was at least 9.0 mmol/L (162 mg/dL) (n = 490).	Usual obstetrical care with physician support. Women and caregivers were not aware of the diagnosis of glucose intolerance, at the discretion of the attending clinician; if indications arose that were suggestive of diabetes, further assessment for GDM was permitted, with treatment as considered appropriate (n = 510).
Gillen (2004)	Standard clinical practice as on right, plus advice for targeted intakes of foods rich in unsaturated fats.	Standard clinical practice (individualised carbohydrate portion-controlled meal plan, with low-fat and low-glycaemic index dietary strategies and general advice about meeting nutritional requirements of pregnancy).
Yang (2003)	Intensive care with the Intensive Diabetes Management Plan. Diet and exercise advice, self-monitoring at home of blood glucose +/− insulin if required. Fortnightly specialist review. Low calorie intake prescribed according to pregravid BMI. Goal: to achieve fasting capillary blood glucose < 5.5 mmol/L and 1-hour postprandial < 7.0 mmol/L (n = 95).	Usual obstetric care (n = 55).

Reference	Intervention	Control
Bancroft (2000)	Care received in combined clinic with diabetologist and obstetrician. Standard dietary advice restricting carbohydrate intake to 185 g per day and a diet sheet listing calorific values of common foods. Capillary glucose measurements 5 days a week, HbA1c measured monthly (insulin was introduced if ≥ 5 capillary measurements > 7.0 mmol/L in 1 week), serial ultrasound for growth and amniotic fluid, Doppler studies, CTG monitoring (n = 32).	Care received in combined clinic with diabetologist and obstetrician. Dietary advice as for intervention group, HbA1c monthly but no capillary glucose measurements, serial ultrasound for growth and amniotic fluid, Doppler studies or CTG monitoring (n = 36).
Ford (1997)	Specific 'diabetic type' advice (ie, 'high fibre, high carbohydrate, low fat and appropriate energy'). Attended clinic weekly and performed plasma glucose profiles (n = 16).	No specific dietary advice. Attended clinic weekly and performed plasma glucose profiles (n = 13).
Garner (1997)	Care managed by obstetrician and endocrinologist. Dietary counselling, calories restricted diet (35 kcal/kg/day). Home glucose monitoring, if not controlled by diet alone then insulin supplementation, seen biweekly. Ultrasound assessment of fetal growth, amniotic fluid volume and cardiac size. Aim to maintain blood glucose within the target range of < 4.4 mmol/L fasting and < 7.8 mmol/L 1-hour postprandial (n = 149).	No dietary counselling but asked to continue unrestricted healthy diet for pregnancy as per Canada Food Guide. Managed by the primary obstetric provider and were not seen again in the teaching unit. Treatment failures were transferred to the treatment arm of the trial and treated with diet/insulin/monitoring (n = 150).
Thompson (1990)	A standard diet delivered by a nutritionist. 35 kcal/kg ideal body weight (50% carbohydrate, 30% fat, 20% protein) divided into three meals and two snacks per day with the addition of 20 units (NPH) and 10 units regular insulin 30 minutes before breakfast (n = 45).	A standard diet delivered by a nutritionist. 35 kcal/kg ideal body weight (50% carbohydrate, 30% fat, 20% protein) divided into three meals and two snacks per day. Supplementary insulin if glucose levels not maintained, 105 mg/dL fasting or < 120 mg/dL 2 hours postprandial (n = 50).
Langer (1989)	Managed according to diabetic protocol including dietary advice (determined by pre-pregnancy body mass index), insulin treatment based on 0.7 units per kg of body weight measured in pregnancy. All participants monitored capillary blood glucose seven times/day (n = 63).	Continued normal eating patterns. Monitored capillary blood glucose seven times/day for a four-week period for the untreated group (n = 63).

Note: ADA = American Diabetes Association; BMI = body mass index; CTG = cardiotocograph; GDM = gestational diabetes mellitus.

Source: Alwan et al (2009).

Figure 10: Pre-eclampsia in women with gestational diabetes receiving a specific package of treatment or usual care

Study or Subgroup	Specific treatment Events	Total	Routine ANC Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Crowther 2005	58	490	93	510	70.2%	0.65 [0.48, 0.88]
Elnour 2008	5	108	11	72	10.2%	0.30 [0.11, 0.84]
Landon 2009	12	476	25	455	19.7%	0.46 [0.23, 0.90]
Total (95% CI)		1074		1037	100.0%	0.58 [0.44, 0.75]
Total events	75		129			

Heterogeneity: Chi² = 2.57, df = 2 (P = 0.28); I² = 22%
Test for overall effect: Z = 4.06 (P < 0.0001)
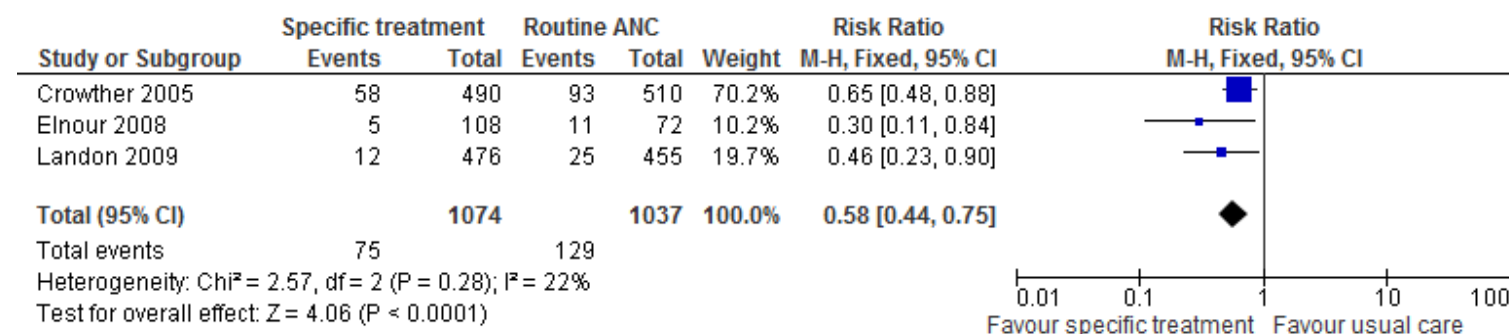
Source: Alwan et al (2009)

Figure 11: Caesarean section in women with gestational diabetes receiving a specific package of treatment or usual care

Study or Subgroup	Specific treatment Events	Total	Routine ANC Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bancroft 2000	10	32	11	36	2.3%	1.02 [0.50, 2.08]
Crowther 2005	152	490	164	510	35.7%	0.96 [0.80, 1.16]
Elnour 2008	7	108	12	72	3.2%	0.39 [0.16, 0.94]
Ford 1997	1	16	3	13	0.7%	0.27 [0.03, 2.31]
Garner 1997	30	149	28	150	6.2%	1.08 [0.68, 1.71]
Gillen 2004	1	16	1	16	0.2%	1.00 [0.07, 14.64]
Landon 2009	128	476	154	455	35.0%	0.79 [0.65, 0.97]
Langer 1989	9	63	11	63	2.4%	0.82 [0.36, 1.84]
Thompson 1990	8	50	8	45	1.9%	0.90 [0.37, 2.20]
Yang 2003	61	95	44	55	12.4%	0.80 [0.66, 0.98]
Total (95% CI)		1495		1415	100.0%	0.87 [0.78, 0.97]
Total events	407		436			

Heterogeneity: Chi² = 8.03, df = 9 (P = 0.53); I² = 0%
Test for overall effect: Z = 2.58 (P = 0.010)

Source: Alwan et al (2009)

Figure 12: Induction of labour in women with gestational diabetes receiving a specific package of treatment or usual care

Study or Subgroup	Specific treatment Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bancroft 2000	20	32	15	36	4.9%	1.50 [0.94, 2.40]
Crowther 2005	189	490	150	510	51.4%	1.31 [1.10, 1.56]
Landon 2009	130	476	122	455	43.6%	1.02 [0.82, 1.26]
Total (95% CI)		998		1001	100.0%	1.19 [1.05, 1.36]
Total events	339		287			

Heterogeneity: Chi² = 4.19, df = 2 (P = 0.12); I² = 52%
Test for overall effect: Z = 2.67 (P = 0.008)

Risk Ratio M-H, Fixed, 95% CI — scale 0.01, 0.1, 1, 10, 100. Favour usual care — Favour specific treatment
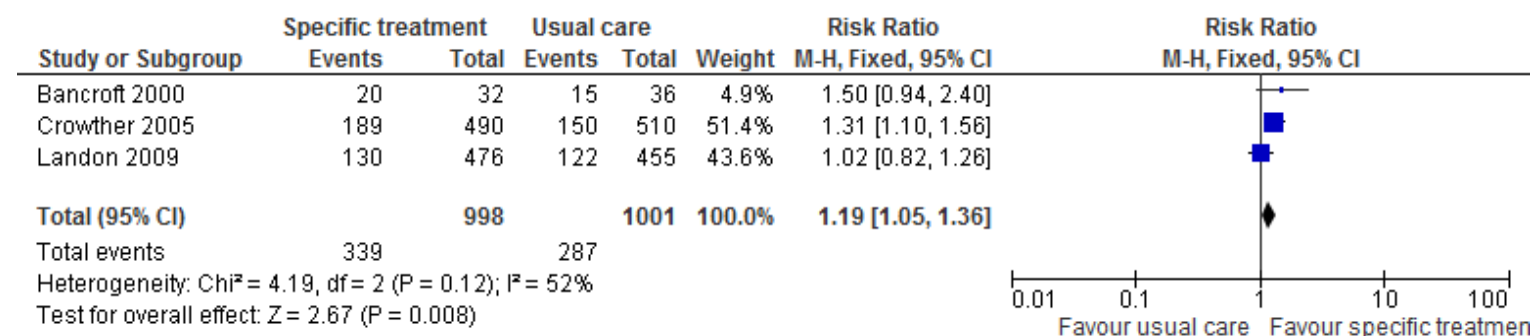
Source: Alwan et al (2009)

Figure 13: Large for gestational age in infants whose mothers were treated for gestational diabetes with a specific package of treatment or usual care

Study or Subgroup	Specific treatment Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bancroft 2000	8	32	7	36	2.9%	1.29 [0.53, 3.15]
Crowther 2005	68	506	115	524	50.3%	0.61 [0.47, 0.81]
Elnour 2008	9	108	15	72	8.0%	0.40 [0.19, 0.86]
Ford 1997	2	16	4	13	2.0%	0.41 [0.09, 1.88]
Landon 2009	34	477	66	454	30.1%	0.49 [0.33, 0.73]
Langer 1989	4	63	15	63	6.7%	0.27 [0.09, 0.76]
Total (95% CI)		1202		1162	100.0%	0.55 [0.45, 0.67]
Total events	125		222			

Heterogeneity: Chi² = 7.01, df = 5 (P = 0.22); I² = 29%
Test for overall effect: Z = 5.77 (P < 0.00001)

Risk Ratio M-H, Fixed, 95% CI — scale 0.01, 0.1, 1, 10, 100. Favour specific treatment — Favour usual care

Source: Alwan et al (2009)

Figure 14: Hyperbilirubinaemia in infants whose mothers were treated for gestational diabetes with a specific package of treatment or usual care

Study or Subgroup	Specific treatment Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Crowther 2005	44	506	48	524	35.8%	0.95 [0.64, 1.40]
Elnour 2008	1	99	8	66	7.3%	0.08 [0.01, 0.65]
Garner 1997	8	149	10	150	7.6%	0.81 [0.33, 1.98]
Landon 2009	43	450	54	418	42.5%	0.74 [0.51, 1.08]
Langer 1989	4	63	9	63	6.8%	0.44 [0.14, 1.37]
Thompson 1990	0	34	0	34		Not estimable
Total (95% CI)		1301		1255	100.0%	0.75 [0.59, 0.96]
Total events	100		129			

Heterogeneity: Chi² = 6.64, df = 4 (P = 0.16); I² = 40%
Test for overall effect: Z = 2.26 (P = 0.02)
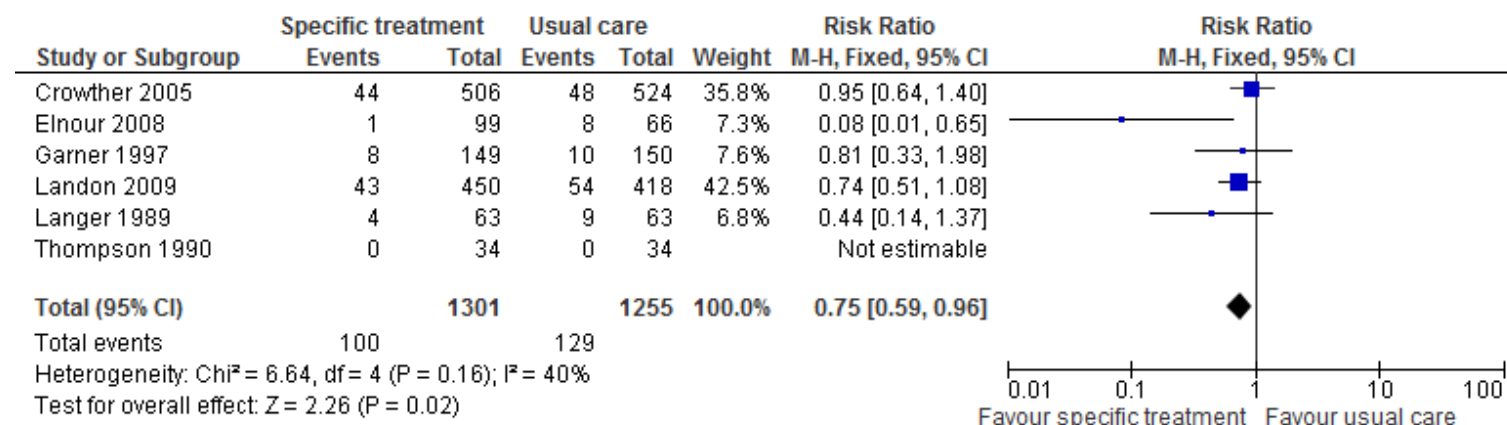
Source: Alwan et al (2009)

Figure 15: Shoulder dystocia in infants whose mothers were treated for gestational diabetes with a specific package of treatment or usual care

Study or Subgroup	Specific treatment Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bancroft 2000	0	32	1	36	3.3%	0.37 [0.02, 8.86]
Crowther 2005	7	506	16	524	36.8%	0.45 [0.19, 1.09]
Elnour 2008	2	108	6	72	16.8%	0.22 [0.05, 1.07]
Landon 2009	7	476	18	455	43.1%	0.37 [0.16, 0.88]
Thompson 1990	0	50	0	45		Not estimable
Total (95% CI)		1172		1132	100.0%	0.38 [0.21, 0.66]
Total events	16		41			

Heterogeneity: Chi² = 0.60, df = 3 (P = 0.90); I² = 0%
Test for overall effect: Z = 3.41 (P = 0.0006)
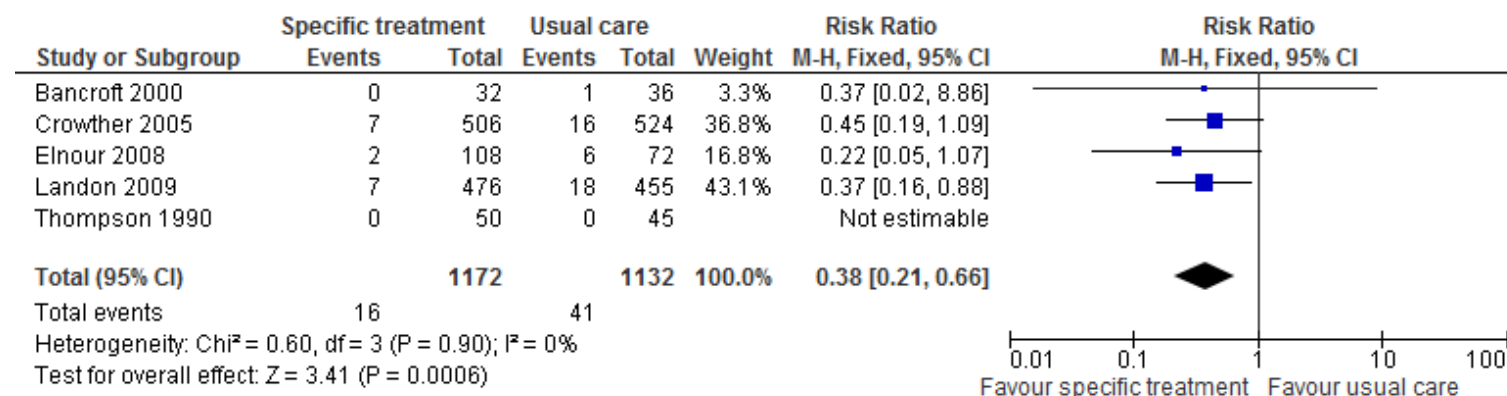
Source: Alwan et al (2009)

Table 30: Exercise alone versus control in women with gestational diabetes – clinical outcomes

Outcome	Reference	Number of trials and participants	Type of intervention	Results
Preterm birth	NICE (2008)	2 trials (n = 48)	Exercise + diet versus diet alone	No cases reported in either arm
	De Barros (2010)	2 trials (n = 34)	Exercise + diet versus diet + insulin	RR 0.50 (95%CI 0.05–5.01), NS
		1 trial (n = 64)	Resistance exercise versus usual care	Both groups had three cases of preterm birth
Caesarean section	NICE (2008)	1 trial (n = 29)	Exercise +diet versus diet alone	RR 0.93 95%CI 0.22–3.88)
	De Barros (2010)	1 trial (n = 34)	Exercise + diet versus diet + insulin	RR 0.67 (95%CI 0.13–3.50)
		1 trial (n = 64)	Resistance exercise versus usual care	65% versus 75%, NS
Stillbirth	NICE (2008)	2 trials (n = 48)	Exercise + diet versus diet alone	There were no stillbirths
		1 trial (n = 34)	Exercise + diet versus diet + insulin	
Induction of labour	NICE (2008)	1 trial (n = 34)	Exercise + diet versus diet + insulin	RR 0.50 (95%CI 0.05–5.01)
Neonatal hypoglycaemia	NICE (2008)	1 trial (n = 34)	Exercise + diet versus diet + insulin	RR 2.0 (95%CI 0.20–20.04)
Gestational weight gain	De Barros (2010)	1 trial (n = 64)	Resistance exercise versus usual care	NS
	DiNallo (2008)	1 trial (n = 96)	Exercise + diet versus diet alone	Effect size 0.50

Note: CI = confidence interval; NICE = National Institute for Health and Care Excellence; NS = not significant; RR = risk ratio.

Table 31: Recommendations for dietary interventions for women with gestational diabetes

Reference	Advice/recommendation
American Diabetes Association (2012)	Individualised Medical Nutrition Therapy should be provided to achieve treatment goals. This is optimally provided by a registered dietician who is familiar with the components of Medical Nutrition Therapy.
Canadian Diabetes Association (2008), Caribbean Health Research Council (2006) and Health Service Executive, Ireland (2010)	Women should be evaluated and followed by a registered dietician.
American Dietetic Association (2008)	Medical Nutrition Therapy should be initiated within one week of diagnosis of gestational diabetes. The same is appropriate for women with impaired glucose tolerance.
Scottish Intercollegiate Guidelines Network (SIGN 2010) and Brazilian Diabetes Society and Brazilian Federation of Gynecology and Obstetrics guideline (Negrato et al 2010)	Pregnant women with gestational diabetes should be offered dietary advice. These guidelines do not specify who should be responsible for the provision of the advice.
American Diabetes Association (2012)	The mixture of carbohydrates, protein and fat intake may be adjusted to meet individual metabolic goals and individual preferences of the person with diabetes.
Health Service Executive, Ireland (2010)	Adequate energy intake provides appropriate weight gain during pregnancy.
American Dietetic Association (2008)	Limited evidence regarding fibre, fat, protein and glycaemic index intake in women with gestational diabetes.
American Diabetes Association (2012), International Diabetes Federation (2009), Health Service Executive, Ireland (2010) and Brazilian Diabetes Society and Brazilian Federation of Gynecology and Obstetrics guideline (Negrato 2010)	Monitoring of carbohydrate intake is a key strategy for optimising glycaemic control.
American Dietetic Association (2008)	A registered dietician should encourage women with gestational diabetes to consume a minimum of 175 g of carbohydrates per day for the provision of glucose to the fetal brain and to prevent ketosis. The total carbohydrate intake should be < 45% of energy in women with gestational diabetes to prevent hyperglycaemia.
American Diabetes Association (2012)	Individualised meal planning should include optimisation of food choices to meet recommended daily allowance of all micronutrients.
Canadian Diabetes Association (2008)	There should be moderate carbohydrate restriction distributed over three meals and three snacks (one of which should be at bedtime).

Reference	Advice/recommendation
American Diabetes Association (2012)	There is no evidence for weight reduction in pregnant women with gestational diabetes as a specific subgroup.
Health Service Executive, Ireland (2010)	Did not recommend weight loss in women with gestational diabetes but did suggest that for overweight/obese women, modest energy and carbohydrate restriction may be required.
International Diabetes Federation (2009) and National Institute for Health and Care Excellence (NICE 2008)	In women with gestational diabetes who are overweight, reducing energy intake by no more than 30% of habitual intake is not associated with ketosis and does not cause harm.
National Institute for Health and Care Excellence (NICE 2008)	Women whose pre-pregnancy body mass index was > 27 kg/m^2 should be advised to restrict calories intake (to 25 kcal/kg/day or less) and to take moderate exercise (approximately 30 minutes per day).
American Dietetic Association (2008)	30 minutes of physical activity, at least three times per week (unless there were contra-indications).
Health Service Executive, Ireland (2010)	Starvation ketosis should be avoided in women with gestational diabetes.
Canadian Diabetes Association (2008)	Severe calorie-restricted diets should be avoided due to the risks of ketonaemia and small for gestational age infants. Hypocaloric diets were not recommended.

Table 32: Effects of dietary advice on maternal and infant outcomes

Outcome (values are risk estimate, 95%CI)	Low-moderate GI food versus moderate-high GI food	Low-GI diet versus high-fibre moderate-GI diet	Energy-restricted versus unrestricted diet	Low- versus high-carbohydrate diet	High monounsaturated fat diet versus high carbohydrate diet	Standard fibre diet versus high-fibre diet
LGA	RR 0.95 (0.27–3.36); 2 trials, 89 infants	RR 2.87 (0.61–13.50), 1 trial, 92 infants	RR 1.17 (0.65–2.12), 1 trial, 123 infants	–	RR 0.54 (0.21–1.37), 1 trial, 27 infants	–
Caesarean section	RR 0.66 (0.29–1.47), 1 trial, 63 women	RR 1.80 (0.66–4.94), 1 trial, 88 women	RR 1.18 (0.74–1.89), 1 trial, 121 women	RR 1.40 (0.57–3.43), 1 trial, 30 women	–	–
Induction of labour	RR 0.88 (0.33–2.34), 1 trial, 63 women	–	RR 1.02 (0.68–1.53), 1 trial, 114 women	–	–	–
Preterm birth	RR 0.52 (0.05–5.41), 1 trial, 63 infants	RR 0.96 (0.14–6.51), 1 trial, 92 infants	–	–	–	–
Gestational weight gain	–	MD ⁻1.20 kg (⁻3.43 to 1.03), 1 trial, 87 women	–	–	–	MD 2.40 kg (⁻2.20 to 7.00), 1 trial, 22 women
Pre-eclampsia	–	–	RR 1.00 (0.51–1.97), 1 trial, 117 women	–	–	–

Note: CI= confidence interval; GI = glycaemic index; LGA = large for gestational age; MD = mean difference; RR = risk ratio.

Source: Han et al (2013)

Table 33: Ministry of Health guidelines on weight gain during pregnancy

Pre-pregnancy body mass index	Body mass index (kg/m²)*	Total weight gain range (kg)
Underweight	< 18.5	12.7–18.1
Normal weight	18.5–24.9	11.3–15.9
Overweight	25.0–29.9	6.8–11.3
Obese (includes all classes)	≥ 30.0	5.0–9.0

Source: Institute of Medicine (2009), cited in Ministry of Health (2014)

Table 34: Details of screening/diagnostic criteria

Reference	Screening	Loading dose of sugar	Fasting mg/dL	1-hour mg/dL	2-hour mg/dL	3-hour mg/dL
Mukhopadhyay (2012)	Not stated	75 g	7.0 mmol/L	–	7.8 mmol/L	–
Niromanesh (2012)$	50 g GCT ≥ 130 mg/dL	100 g	5.3 mmol/L	10.0 mmol/L	8.6 mmol/L	7.8 mmol/L
Tertti (2012)	Risk criteria changed during trial	75 g	Pre-2008 ≥ 4.8 mmol/L; post-2008 ≥ 5.3 mmol/L	Pre- and post-2008 ≥ 10.0 mmol/L	Pre-2008 8.7 mmol/L Post-2008 8.6 mmol/L	–
Ijas (2011)*	Not stated	75 g	5.3 mmol/L	11 mmol/L	9.6 mmol/L	Not stated
Lain (2009)	50 g, 1-hour OGTT (> 7.5 mmol/L)	100 g#	> 5.3 mmol/L	> 10 mmol/L	> 8.6 mmol/L	> 7.8 mmol/L
Rowan (2008)	High-risk women only	75 g	≥ 5.1 mmol/L	≥ 10.0 mmol/L	≥ 8.5 mmol/L	–
Silva (2007)	Not stated	75 g	≥ 7.0 mmol/L	–	≥ 7.8 mmol/L	
Moore (2007)	50 g, 1-hour OGTT (proceed if ≥ 140 mg/dL)	100 g	> 5.8 mmol/L	> 10.6 mmol/L	> 9.2 mmol/L	> 8.1 mmol/L
Ogunyemi (2007)	50 g GCT (threshold not reported)	100 g	> 5.3 mmol/L	> 10.0 mmol/L	> 8.3 mmol/L	> 7.8 mmol/L
Anjalakshi (2006)	Not stated	75 g	7.0 mmol/L	–	7.8 mmol/L	–
Bertini (2005)	Not stated	75 g	≥ 6.1 mmol/L	–	≥ 7.8 mmol/L	–
Hague (2003)*	50 g GCT	75 g	≥ 5.5		≥ 8.0 mmol/L	
Langer (2000)	50 g OGTT (> 7.3 mmol/L at 1 hour)	100 g	> 5.3 to < 7.8 mmol/L	?	?	?

Note: GCT = glucose challenge test, OGTT = oral glucose tolerance test.

*   One or more abnormal value required; $ ≥ 2 abnormal values required; # 2 abnormal values required, an elevated fasting glucose level or 1-hour OGTT > 11.1 mmol/L.

Source: Alwan et al (2009)

Table 35: Demographic details of participants in randomised controlled trials comparing oral hypoglycaemics and insulin therapy for women with gestational diabetes

Reference	Country	Intervention/ control	Mean age (years)	Mean BMI at booking (kg/m²)	Gestational age at diagnosis/study entry (weeks)	Ethnicity
Mukhopadhyay (2012)	India	Glibenclamide (n = 30)	26.3 ± 4.6	23.7 ± 2.7	28.3 ± 2.2	Not stated
		Insulin (n = 30)	26 ± 4.3	23 ± 2.9	27.4 ± 2.7	
Niromanesh (2012)	Iran	Metformin (n = 86)	30.7 ± 5.5	28.1 ± 4.0	26.0 ± 3.5	Not stated
		Insulin (n = 86)	31.8 ± 5.1	27.1 ± 2.1	26.0 ± 3.7	
Tertti (2012)	Finland	Metformin (n = 111)	31.9 ± 5.0	29.4 ± 5.9	30.3 ± 2.0	Not stated
		Insulin (n = 110)	32.1 ± 5.4	28.9 ± 4.7	30.4 ± 1.8	
Ijas (2011)	Finland	Metformin (n = 50)	32.3 ± 5.6	31.5 ± 6.5	30 ± 4.9	Not stated
		Insulin (n = 50)	31.7 ± 6.1	30.8 ± 5.4	30 ± 4.0	
Lain (2009)	USA	Glibenclamide (n = 41)	32.2 ± 5	33.4 ± 12.9	30.8 ± 2.5	7.3% Black
		Insulin (n = 41)	31.2 ± 5.9	30.9 ± 5.7	30.6 ± 2.2	19.5% Black
Rowan (2008)	New Zealand and Australia	Metformin (n = 363)	33.5 ± 5.4	32.2 ± 8.2	30.2 ± 3.3	European/ White 46.8%
		Insulin (n = 370)	33.0 ± 5.1	31.9 ± 7.6	30.1 ± 3.2	Polynesian/ Māori 21.1% Chinese/ South East Asian 11.8% Other/ mixed 7.5%
Silva (2007)	Brazil	Glibenclamide (n = 32)	31.6 ± 4.2	27.5 ± 5.1	26.6 ± 4.3	Not stated
		Insulin (n = 36)	29.9 ± 6.0	27.9 ± 6.8	25.6 ± 5.9	
Moore (2007)	USA – New Mexico	Metformin (n = 32)	27.1 ± 4.7	NS	27.8 ± 6.5	49% African American
		Insulin (n = 31)	27.7 ± 6.7	NS	28.9 ± 5.0	44% Native American 5% Caucasian
Ogunyemi (2007)	USA	Glibenclamide (n = 48)	Not reported	32 ± 7.6	28.1 ± 7.6	80% Hispanic
		Insulin (n = 49)		30.8 ± 6.9	24.6 ± 8.0	15% African American
Anjalakshi (2006)	India	Glyburide (n = 10)	24.9 ± 3.73	22.82 ± 3.5	22.5 ± 4.72	Not stated
		Insulin (n = 13)	27.46 ± 5.83	25.32 ± 5.14	22.62 ± 5.62	

Reference	Country	Intervention/ control	Mean age (years)	Mean BMI at booking (kg/m²)	Gestational age at diagnosis/study entry (weeks)	Ethnicity
Bertini (2005)	Brazil	Insulin (n = 27)	28.7 ± 6	27 ± 7.2	11–33 weeks	Not stated
		Glyburide (n = 24)	31.2 ± 4.5	27.5 ± 5.8		
		Acarbose (n = 19)	31.5 ± 5.8	25.7 ± 4.2		
Hague (2003)	Australia	Metformin	33.7 ± 4.4	39.5 ± 6.9	29.8 ± 4.5	NS
		Insulin	34.1 ± 3.7	37.9 ± 6.9	30.4 ± 4.7	
Langer (2000)	USA	Glyburide (n = 201)	29 ± 7	Not reported	24 ± 7	Hispanic 83%
		Insulin (n = 208)	30 ± 6		25 ± 7	Non-Hispanic White 12% Black 5%

Note: BMI = body mass index.

Source: Alwan et al (2009)

Figure 16: Gestational age at delivery < 37 weeks in women being treated for gestational diabetes

	Oral hypoglycemics		Insulin			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.13.1 Glibenclamide							
Lain 2009	7	41	7	41	15.3%	1.00 [0.39, 2.60]	
Subtotal (95% CI)		41		41	15.3%	1.00 [0.39, 2.60]	
Total events	7		7				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.00 (P = 1.00)							
2.13.2 Metformin							
Ijas 2011	1	47	3	50	6.4%	0.35 [0.04, 3.29]	
Niromanesh 2012	9	86	4	86	8.8%	2.25 [0.72, 7.03]	
Rowan 2008	44	363	28	370	60.7%	1.60 [1.02, 2.51]	
Tertti 2012	6	111	4	110	8.8%	1.49 [0.43, 5.12]	
Subtotal (95% CI)		607		616	84.7%	1.56 [1.06, 2.30]	
Total events	60		39				
Heterogeneity: Chi² = 2.11, df = 3 (P = 0.55); I² = 0%							
Test for overall effect: Z = 2.26 (P = 0.02)							
Total (95% CI)		648		657	100.0%	1.48 [1.03, 2.11]	
Total events	67		46				
Heterogeneity: Chi² = 2.87, df = 4 (P = 0.58); I² = 0%							
Test for overall effect: Z = 2.14 (P = 0.03)							
Test for subgroup differences: Chi² = 0.72, df = 1 (P = 0.40), I² = 0%							

0.01 0.1 1 10 100

Insulin   Oral hypoglycaemic

Source: Alwan et al (2009)

Table 36: Treatment targets for glycaemic control recommended in clinical practice guidelines

Reference	Blood sugar level (mmol/L)		
	Fasting	**1-hour postprandial**	**2-hour postprandial**
Australasian Diabetes in Pregnancy Society (Nankervis 2013)	≤ 5.0	≤ 7.4	≤ 6.7
American Diabetes Association (2013)	≤ 5.3	≤ 7.8 or	≤ 6.7
Health Service Executive, Ireland (2010)	< 5.0	< 7.0	
Brazilian Diabetes Federation (Negrato 2010)	5.2	7.8	–
Scottish Intercollegiate Guidelines Network (SIGN 2010)	< 5.5	–	< 7.0
Canadian Diabetes Association (2008)	3.8–5.2	5.5–7.7	5.0–6.6
National Institute for Health and Care Excellence (NICE 2008)	3.5–5.9	< 7.8	–
Fifth International Workshop–Conference on Gestational Diabetes Mellitus (Metzger 2007)	5.0–5.5	< 7.8	< 6.7–7.1

Table 37: Trial characteristics for optimal glucose targets

Reference	Country	Participant characteristics	Inclusion criteria	Intervention/exposure	Comparison
Rowan (2010)	New Zealand and Australia	The mean gestation at recruitment was 30 ± 3 weeks. Approximately 47% of women were European, 21% Polynesian, 12% Indian, 11.5% Chinese or South East Asian and 7% mixed ethnicity.	Women were eligible for inclusion if they were between 18 and 45 years of age, had received a diagnosis of gestational diabetes mellitus according to ADIPS, were pregnant with a single fetus between 20 and 33 weeks of gestation, met the hospital's usual criteria for starting insulin treatment and, after lifestyle intervention consisting of advice about diet and exercise, had more than one capillary blood glucose measurement above 5.4 mmol/L (97.2 mg/dL) after an overnight fast or more than one 2-hour postprandial blood glucose measurement above 6.7 mmol/L (120.6 mg/dL).	Metformin was started at a dose of 500 mg once or twice daily with food and increased, typically over a period of one to two weeks, to meet glycaemic targets up to a maximum daily dose of 2500 mg. If the targets were not achieved with metformin alone, insulin was added. Metformin was stopped if maternal contra-indications (such as liver or renal impairment or sepsis) or fetal growth restriction developed.	Insulin was prescribed according to usual practice.
Langer (1989)	USA	Women with GDM were a mean of 31 (± 5) years old. 39% were White, 38% Black and 29% Hispanic.	Not specified	n = 334. Women with gestational diabetes receiving either restricted diet alone, or diet + insulin. The goal of treatment was to maintain a fasting blood glucose level of 60–80 mg/dL, preprandial levels of 70–90 mg/dL and postprandial levels of < 120 mg/dL (an overall mean of < 95 mg/dL).	n = 334. Non-diabetic controls

Reference	Country	Participant characteristics	Inclusion criteria	Intervention/exposure	Comparison
Langer (1994)	USA	A total of 2461 gestational diabetic women (10% of the screened population) participated. Approximately 83% were Hispanic (the vast majority were Mexican-American), 12% were non-Hispanic White, and 5% were Black.	Not specified.	(1) In the intensified management group (n = 1145) patients were assigned memory reflectance meters and were instructed by nurse-educators in self-monitoring blood glucose technique (seven times/day: fasting, preprandial, 2-hour postprandial, and at bedtime). (2) In the conventional management group (n = 1316) patients were instructed by a nurse-educator and were assessed weekly for fasting and 2-hour postprandial venous plasma glucose during clinic visits. The patients performed four daily self-monitored blood glucose determinations with glucose strips (fasting and 2 hours after breakfast, lunch and dinner).	Non-diabetic controls.
Yogev (2004)	USA	Patients had an approximate mean age of 28 years. Majority of patients (85%) were Mexican-American.	Women with singleton pregnancies and gestational diabetes first diagnosed in the current pregnancy before 33 weeks' gestation.	Patients who developed pre-eclampsia.	Patients who did not develop pre-eclampsia.

Reference	Country	Participant characteristics	Inclusion criteria	Intervention/exposure	Comparison
Banerjee (2004)	India	Mean age was 29.48 ± 4.23 years. Of the 176 GDM patients, 44 were detected before 24 weeks, 32 between 24 and 28 weeks, 72 between 29 and 34weeks and 28 beyond 34 weeks.	GDM cases (n = 176): On the basis of Carpenter and Coustan's modification of O'Sullivan-Mahan's criteria.	(1) Tight glycaemic control: Patients with fasting plasma glucose level < 70 mg/dL, 2-hour postprandial plasma glucose level < 100 mg/dL, and HbA1C < 6.5% following treatment. (2) Acceptable glycaemic control: Patients with fasting plasma glucose level between 70 and 95 mg/dL, 2-hour postprandial plasma glucose level between 100 and 120 mg/dL and HbA1C between 6.5% and 7.5% following treatment.	Uncontrolled glycaemic group: Patients with fasting plasma glucose level > 95 mg/dL, 2-hour postprandial plasma glucose level > 120 mg/dL and HbA1C > 7.5% in spite of treatment were included in this group.

Note: ADIPS = Australasian Diabetes in Pregnancy Society; GDM = gestational diabetes mellitus.

Table 38: Trial characteristics for ultrasound guided treatment

Reference	Country	Participant characteristics	Inclusion criteria	Intervention	Comparison
Buchanan (1994)	USA	Hispanic women between 29 and 33 weeks' gestation with otherwise uncomplicated singleton pregnancies.	Women who planned to deliver vaginally and whose fasting serum glucose concentrations were all < 5.8 mmol/L after the initiation of diet therapy with high-risk fetal abdominal circumference (> 75th percentile).	n = 30 Diet + insulin with strict glucose targets (4.4– 6.2 mmol/L).	n = 29. Diet alone.
Bonomo (2004)	Italy	All women diagnosed with GDM between 24 and 28 weeks of gestation, in each of the three hospitals taking part in the study, were considered eligible for enrolment.	Singleton pregnancies, without medical complications other than GDM potentially affecting fetal growth or neonatal outcome admitted.	n = 160. Modified management; the glycaemic target varied according to ultrasound measurement of the abdominal circumference centile performed every two weeks: 4.4–5.6 mmol/L if abdominal circumference ≥ 75th percentile, 5.6–7.8 mmol/L if abdominal circumference < 75th. Therapy was tailored to mean fasting and postprandial glycaemia. Ultrasound exams for fetal biometry were scheduled every two weeks.	n = 80. Conventional management; the glycaemic target was fixed at 90 fasting/120 postprandial mg/dL. Ultrasound exams for fetal biometry were scheduled at 34 and 38 weeks.

Reference	Country	Participant characteristics	Inclusion criteria	Intervention	Comparison
Kjos (2001)	USA	98 women with fasting plasma glucose concentrations of 105–120 mg/dL.	1 Diagnosis of GDM. 2 Fasting plasma glucose concentrations > 5.8 and < 6.7 mmol/L. 3 Gestational age > 14 and < 34 weeks at time of study entry. 4 Singleton pregnancy. 5 No medical complications (eg, hypertension or vascular disease, except GDM known to affect fetal growth or neonatal morbidity. 6 Reliable estimation of gestational age, with either the first clinical examination < 12 weeks or the first ultrasound examination < 20 weeks. 7 Literacy.	n = 49. Women were prescribed insulin immediately only if the fetal abdominal circumference was ≥ 70th percentile for gestational age. Initial doses were assigned as in the standard management group, but glycaemic targets were ≤ 4.4 mmol/L before meals and ≤ 6.2 mmol/L two hours after meals. After the baseline ultrasound, additional fetal abdominal circumference measurements were made at 20, 24, 28, 32 and 36 weeks gestation. Insulin therapy was prescribed using the initial doses and glycaemic targets described above if: 1 the fetal abdominal circumference at entry or any subsequent ultrasound examination was ≥ 70th percentile for gestational age 2 any fasting plasma glucose concentration measured during a clinic visit exceeded 6.7 mmol/L or 3 the subject failed to perform ≥ 50% of the recommended capillary glucose measurements.	n = 49. Women were prescribed NPH and regular insulin before breakfast and dinner. The initial daily dose (0.8, 0.9, 1.0, 1.1 or 1.2 units/kg body weight, respectively) was assigned according to the gestational age at entry. Insulin doses were adjusted to achieve preprandial capillary blood glucose concentrations ≤ 5.0 mmol/L and 2-hour postprandial concentrations ≤6.7 mmol/L.

Reference	Country	Participant characteristics	Inclusion criteria	Intervention	Comparison
Schaefer-Graf (2004)	Germany	Women with GDM who attained fasting capillary glucose < 6.7mmol/L and 2-hour postprandial capillary glucose < 11.1 mmol/L after 1 week of diet.	1 GDM, diagnosed by at least two abnormal values in a 75 g oral glucose tolerance test (fasting ≥ 5.0 mmol/L; 1 hour ≥ 9.1 mmol/L, 2 hour ≥ 8.0 mmol/L). 2 All capillary fasting glucose measurements ≤ 6.6 mmol/L and 2 hour postprandial capillary glucose measurements ≤ 11.1 mmol/L). 3 Singleton pregnancy 16 to 34 completed weeks confirmed by ultrasound performed before 20 weeks. 4 No maternal medical conditions known to affect fetal growth.	*n=99.* Insulin was initiated if capillary fasting glucose was 6.7 and 11.1 mmol/L, respectively, or a foetal abdominal circumference > 75th percentile. Insulin was started whenever the abdominal circumference exceeded the 75th percentile before 36 completed weeks. In this group, glucose targets were not discussed with patients, and glucose values were not used to guide management, unless any capillary fasting glucose was > 6.7 mmol/L and/or any 2 hour post prandial ≥ 11.1 mmol/L was measured, at which point insulin was prescribed irrespective of AC measurement. Because of the risk of maternal hypoglycaemia, insulin was not prescribed irrespective of foetal abdominal circumference when capillary fasting glucose was < 4.4 mmol/L and/or 2 hour post prandial value was < 15.6 mmol/L. Ultrasound examinations were performed at entry and thereafter at 4-week intervals at 20, 24, 28, 32, and 36 weeks of gestation.	n=100. Insulin was prescribed before 36 weeks gestation if two glucose profiles had two or more elevated values (capillary fasting glucose >5.0 mmol/L or 2 hour post prandial >6.7 mmol/L) or four profiles had at least one elevated value during a 2-week period.

Reference	Country	Participant characteristics	Inclusion criteria	Intervention	Comparison
Rossi (2000)	Italy	Women of all races, with otherwise uncomplicated singleton pregnancies.	Women who planned to deliver vaginally and whose diagnosis of GDM was established before 28 weeks' gestation were identified. In all cases, gestational age had been previously verified by first-trimester ultrasound. All these patients were prescribed an individual dietary regimen and instruction for daily multiple self-monitoring of capillary blood glucose levels.	$n = 73$. Fetal ultrasound was assessed at both 28 and 32 weeks' gestation. Insulin plus diet therapy was established as soon as fetal abdominal circumference exceeded 75th percentile. Women whose abdominal circumference was < 75th percentile were treated with diet alone.	$n = 68$. Fetal ultrasound was assessed at 32 weeks' gestation. Insulin plus diet therapy was established as soon as fetal abdominal circumference exceeded 75th percentile. Women whose abdominal circumference was < 75th percentile were treated with diet alone.

Note: GDM = gestational diabetes mellitus.

Source: National Institute for Health and Care Excellence (NICE 2008)

Table 39: Maternal and fetal outcomes for ultrasound guided treatment

Outcome	Buchanan (1994)	Bonomo (2004)	Kjos (2001)	Rossi (2000)	Schaefer-Graf (2004)
Neonatal outcomes					
Gestational age at delivery (weeks)	Intervention: 39.6 ± 0.2 Comparison: 39.5 ± 0.2	Intervention 39.0 ± 1.6 Comparison: 39.0 ± 1.5	Intervention 38.3 ± 1.2 Comparison: 38.2 ± 0.9	Intervention: 38.2 ± 1.4 Comparison: 38.5 ± 1.4	Intervention: 39.0 ±1.9 Comparison: 39.3 ± 1.3
Large for gestational age/macrosomia	–	Intervention: 12/151 (7.9%) Comparison: 14/78 (17.9%) $p < 0.05$	Intervention: 4/48 (8.3%) Comparison: 3/48 (6.3%)	Intervention: 8/73 (11.0%) Comparison: 12/68 (17.6%)	Intervention: 12.1% Comparison: 10.0%
Large for gestational age/macrosomia in women with abdominal circumference ≥ 75th centile	Intervention: 4/30 (13%) Comparison: 13/29 (45%) $p < 0.001$	Intervention: 5/62 (7.9%) Comparison: 12/39 (30.8%) $p < 0.001$	–	Intervention: 5/15 (33.3%) Comparison: 10/14 (71.4%) $p < 0.05$	–
Neonatal hypoglycaemia	Intervention: 4/30 (13%) Comparison: 5/29 (17%)	Intervention: 11/151 (7.3%) Comparison: 9/78 (11.5%)	Intervention: 5/48 (10.4%) Comparison: 5/48 (10.4%)	Intervention: 10/73 (13.7%) Comparison: 10/68 (14.7%)	Intervention: 17.0% Comparison: 16.0%
Hyperbilirubinaemia	–	Intervention: 10/151 (6.9%) Comparison: 8/78 (9.7%)	–	Intervention: 7/73 (9.5%) Comparison: 7/68 (10.3%)	–
Admission to neonatal intensive care unit	–	–	–	–	Intervention: 14.1% Comparison: 15.0%
Birth trauma (shoulder dystocia, bone fracture, nerve palsy)	–	–	Intervention: 2/48 (4.2%) Comparison: 1/48 (2.1%)	–	–
Maternal outcomes					
Induction of labour		–	Intervention: 38/49 (77.6%) Comparison:32/49 (65.3%)	–	Intervention: 23.2% Comparison: 23.0%
Caesarean section	–	Intervention: 62/151 (30.5%) Comparison: 24/78 (41.0%)	Intervention:16/49 (33.3%) Comparison: 7/49 (14.6%)	Intervention: 17/73 (23.3%) Comparison: 17/68 (25%)	Intervention: 18.2% Comparison: 19.0%
Maternal weight gain (kg)	Intervention: 2.9 ± 0.4 Comparison: 1.7 ± 0.4	Intervention: 11.2 ± 5.0 Comparison: 10.9 ± 4.5	–	–	–

Source: National Institute for Health and Care Excellence (NICE 2008)

Appendix L: Supporting evidence for Chapter 6

Table 40: Recommendations for the timing of delivery in women diagnosed with gestational diabetes

Reference	Evidence base	Recommendation/conclusion
Health Service Executive, Ireland (2010)	One randomised controlled trial Fifth International Workshop–Conference on Gestational Diabetes Mellitus	Where there had been excellent glycaemic control and adherence to therapy, and in the absence of maternal and fetal compromise, women with gestational diabetes could be allowed to wait for spontaneous labour up to 39–40 weeks' gestation. Fetal surveillance should increase if the pregnancy is allowed to continue beyond 40 weeks.
Scottish Intercollegiate Guidelines Network (SIGN 2010)	One randomised controlled trial	Women who require pharmacotherapy but are otherwise progressing normally should be assessed at 38 weeks' gestation and delivered shortly thereafter and certainly before 40 weeks (good practice point).
World Health Organization (WHO 2011)	One randomised controlled trial	'If gestational diabetes is the only abnormality, induction of labour before 41 weeks of gestation is not recommended.' However, induction of labour may be required in some women with diabetes such as those with placental insufficiency or uncontrolled diabetes.
National Institute for Health and Care Excellence (NICE 2008)	One observational study One case control study	Routine induction of labour at 38–39 weeks' gestation reduced the risk of stillbirth and shoulder dystocia in women with diabetes without increasing the caesarean section rate.
Agency for Healthcare Research and Quality guideline (Nicholson 2008)	Two observational studies	No differences in neonatal outcomes for ≥ 40 weeks versus 40 weeks.
Witkop (2009)	Three observational studies (including the two from the Agency for Healthcare Research and Quality guideline (2009))	Unclear.
American College of Obstetricians and Gynecologists (2001)	Unclear	'When glucose control is good and no other complications supervene, there is no good evidence to support routine delivery before 40 weeks of gestation.'

Reference	Evidence base	Recommendation/conclusion
American Diabetes Association (2004)	Unclear	'Gestational diabetes is not of itself an indication for caesarean delivery or for delivery before 38 completed weeks of gestation. Prolongation of gestation past 38 weeks increases the risk of fetal macrosomia without reducing caesarean rates so that delivery during the 38th week is recommended unless obstetric considerations dictate otherwise.'
Fifth International Workshop–Conference on Gestational Diabetes Mellitus (Metzger 2007)	Unclear	No data to support delivery in women with gestational diabetes prior to 38 weeks in the absence of clinical evidence of fetal or maternal compromise. No data to indicate if there was an increased risk of perinatal morbidity or mortality in infants whose mothers had well-controlled gestational diabetes and whose pregnancy was allowed to continue beyond 40 weeks' gestation. In these cases, increased fetal surveillance should be instigated.

Appendix M: Supporting evidence for Chapter 7

Table 41: Recommendations from local district health boards for the postpartum monitoring of blood glucose levels in women diagnosed with gestational diabetes

District health board	Timing of monitoring	Threshold
Southland Hospital (Southern DHB)	Monitor blood sugars hourly for four hours and then four-hourly until 12 hours postpartum.	Not specified.
South Canterbury DHB	Monitor blood sugar six-hourly for 24 hours.	If normal, stop monitoring (threshold not specified).
Auckland DHB	Monitor fasting and post-meal blood sugars for 24 hours after delivery	Not specified.
Waikato DHB	Monitor blood glucose levels fasting and two hours postprandial for 24 hours.	If blood glucose level > 8.0 mmol/L on two consecutive occasions, then inform diabetes or medical team.
Canterbury DHB Hawke's Bay DHB	Monitor blood sugar levels before breakfast and after all meals for 24 hours.	If blood sugar levels are fasting > 7 mmol/L and/or postprandial > 11.1 mmol/L, advise physician before discharge.
Northland DHB	Monitor blood glucose for at least one day or more.	If elevated fasting and 1-hour postprandial, refer to diabetes team.
Lakes DHB	Monitor blood sugars two-hourly until next meal for at least 48 hours.	Fasting, 2-hour postprandial and before bed. Call Obstetrics and Gynaecology senior house officer if glucose > 12 mmol/L for two consecutive readings. Monitor until glucose in normal range.
Hutt Valley DHB Capital & Coast DHB	Monitor blood sugar levels before meals and two hours after meals and at bedtime for several days after birth.	Monitor blood sugar levels until they normalise.

Note: DHB = district health board.

Appendix N: Supporting evidence for Chapter 9

Table 42: Recommendations for postpartum screening in women diagnosed with gestational diabetes

Organisation	Timing of postpartum test	Diagnostic method	Diagnostic criteria (glucose levels measured in mmol/L)	Subsequent testing	Additional comments or recommendations
American Diabetes Association (2012)	6–12 weeks	2-hour, 75 g OGTT HbA1c not recommended for immediate postpartum screening	Normal: FPG < 5.6 mmol/L and 2-hour PG < 7.8 mmol/L IFG: FPG ≥ 5.6 but < 7.0 mmol/L IGT: 2-hour PG ≥ 7.8 but < 11.1 mmol/L Type 2 diabetes: FPG ≥ 7.0 mmol/L or 2-hour PG ≥ 11.1 mmol/L or symptoms of type 2 diabetes and a random PG level ≥ 11.1 mmol/L	Annually using HbA1c, FPG or OGTT if IFG or IGT is detected postpartum. Otherwise minimum of three.	All patients with a history of GDM should be educated about lifestyle changes, including: 1 maintenance of normal body weight through healthy diet and physical activity 2 avoiding medications that worsen insulin resistance 3 awareness of symptoms of hyperglycaemia.
Wisconsin Diabetes Mellitus Essential Care Guidelines (Wisconsin Department of Health Services 2012)	6–12 weeks	–	–	3 yearly	–
Health Service Executive, Ireland (2010)	6 weeks	2-hour, 75 g OGTT	IFG: FPG 6.1–6.9 mmol/L and (if measured) 2-hour PG < 7.8 mmol/L IGT: FPG < 7.0 mmol/L and 2-hour PG ≥ 7.8–< 11.1 mmol/L Type 2 diabetes: FPG ≥ 7.0 mmol/L or 2-hour PG ≥ 11.1 mmol/L	Annually	Used WHO criteria.
Scottish intercollegiate Guidelines Network (SIGN 2010)	≥ 6 weeks	FPG and 75 g OGTT if clinically indicated	Values not stated	Annually FPG or HbA1c	–

Organisation	Timing of postpartum test	Diagnostic method	Diagnostic criteria (glucose levels measured in mmol/L)	Subsequent testing	Additional comments or recommendations
Brazilian Diabetes Association and Brazilian Federations of Gynecology and Obstetrics Consensus Group (Negrato 2010)	6 weeks	75 g OGTT	IFG: FPG 5.5–6.9 mmol/L and 2-hour PG ≥ 6.94 mmol/L IGT: 2-hour PG 7.8–11.06 mmol/L Type 2 diabetes: FPG ≥ 7 mmol/L or 2-hour PG ≥ 11.1 mmol/L HbA1c > 6.5%	Annual FPG. Women should be screened for diabetes when planning other pregnancies and have an OGTT early in pregnancy	Remind women of symptoms of hyperglycaemia
European Evidence-Based Guideline for the Prevention of Type 2 Diabetes (Paulweber 2010)	6–12 weeks	OGTT (no other details)	No details	1-year OGTT and then annually OGTT, FPG triannually	FPG should be conducted pre-pregnancy to establish glucose levels.
American College of Obstetricians and Gynecologists (2001, 2009)	6–12 weeks	75 g, 2-hour OGTT might be more advantageous than FPG as the initial test	IFG (FPG or OGTT): FPG is 100–125 mg/dL IGT: OGTT only 2-hour plasma glucose 140–199 mg/dL Type 2 diabetes: FPG ≥ 126mg/dL, or OGTT FPG ≥ 126 mg/dL or 2-hour plasma glucose ≥ 126 mg/dL-200 mg/dL	Annual follow-up FPG can be used in subsequent testing if both FPG and OGTT are normal postpartum	Individuals with IFG/IGT should be counselled about diet, exercise and weight reduction or maintenance. Metformin might be considered. For women with normal postpartum screening, glycaemic status should be assessed 3-yearly and counselled as necessary for weight loss and physical activity. Patients with IGT should be identified for future pregnancy counselling.

Organisation	Timing of postpartum test	Diagnostic method	Diagnostic criteria (glucose levels measured in mmol/L)	Subsequent testing	Additional comments or recommendations
World Health Organization (WHO 2006)	≥ 6 weeks	75 g OGTT	Normal: FPG < 6.1 and 2-hour PG < 7.8 IFG: FPG ≥ 6.1 and < 7.0 IGT: 2-hour PG ≥ 7.8 and < 11.1 Type 2 diabetes: FPG ≥ 7.0 or 2-hour PG ≥ 11.1 or both IFG and IGT	Not detailed	
Fifth International Workshop–Conference on Gestational Diabetes Mellitus (Metzger 2007)	FPG or random blood glucose after delivery (1–3 days) OGTT at 6 weeks to 1-year postpartum	75 g, 2 hour OGTT	Not stated	A 75 g, 2-hour OGTT should be performed at 1 year and thereafter a minimum of 3-yearly 75 g OGTT; annual FPG	Recommend implementation of the Diabetes Prevention Program lifestyle programme. A 75 g, 2-hour OGTT should be performed pre-pregnancy.
Canadian Diabetes Association (2008)	6 weeks to 6 months	FPG 5.6–6.0 mmol/L with more than one risk factor then 75 g, 2-hour OGTT	Normal: < 5.6 mmol/L IFG + IGT: FPG 6.1–6.9 mmol/L and 2-hour PG 7.8–11.0 mmol/L IFG: FPG 6.1–6.9 mmol/L and 2-hour PG < 7.8 mmol/L IGT: FPG < 6.1 mmol/L and 2-hour PG 7.8–11.0 mmol/L Type 2 diabetes: FPG ≥ 7.0 mmol/L or 2-hour PG ≥ 11.1 mmol/L	Maximum of 3-yearly or less	Pre-pregnancy screening for type 2 diabetes is also recommended.

Organisation	Timing of postpartum test	Diagnostic method	Diagnostic criteria (glucose levels measured in mmol/L)	Subsequent testing	Additional comments or recommendations
Australasian Diabetes in Pregnancy Society (Nankervis 2013)	6–12 weeks	2-hour, 75 g OGTT	–	75 g OGTT at least annually (if high risk or contemplating another pregnancy) and FPG every 1–2 years if lower risk	Frequency of continued testing is based on perceived risk of developing type 2 diabetes.
Caribbean Health Research Council (2006)	6 weeks	Not stated	Not stated	Not stated	–
International Diabetes Federation (2009)	Before hospital discharge to 6 weeks	OGTT (no details)	Not stated	If high risk then annual OGTT; if low risk then FPG every 2–3 years and an OGTT only if FPG ≥ 5.5 mmol/L (100 mg/dL)	Repeat OGTT prior to conception in other pregnancies or within first trimester.
American Association of Clinical Endocrinologists (Blonde 2007)	45–60 days	Not stated	Not stated	Annually	-

Note: FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; OGTT = oral glucose tolerance test; PG = plasma glucose.

Table 43: Demographic details of participants in diagnostic cohort study for postpartum screening

Reference	Country	Number	Age (years)	Body mass index	Follow-up time	HbA1c cut-off	OGTT (2hr, 75g)	Fasting plasma glucose
Picon (2012)	Spain	231	34.63 (± 4.65)	27.74 (± 5.95) kg/m²	Up to 12 months	≥ 6.5%	≥ 200 mg/dL	≥ 126 mg/dL
Megia (2012)	Spain	364	–	–	Up to 12 months	≥ 6.5%	≥ 200 mg/dL	–
Kim (2011)	USA	54	36 (± 4)	30.6 (± 7.0) kg/m²	6 weeks–36 months	≥ 5.7%	≥ 140 mg/dL	≥ 100 mg/dL

Note: OGTT = oral glucose tolerance test.

Table 44: Diagnostic accuracy outcomes in diagnostic cohort study for postpartum screening

Reference	Test	Reference standard	Prev	Sens	Spec	PPV	NPV	LR+	LR-
Picon (2012)	HbA1c	OGTT	45.89%	22.64%	84.0%	54.55%	56.15%	1.42	0.92
	FPG		45.89%	83.02%	100%	100%	87.41%	Not stated	0.17
	HbA1c + FPG		45.89%	83.02%	84.0%	81.48%	85.37%	5.19	0.20
Megia (2012)	HbA1c	OGTT	3.3%	16.7%	100%	100%	97.24%	Not stated	0.83
Kim (2011)	HbA1c	OGTT	22.2%	75.0%	61.9%	36.0%	89.7%	1.97	0.40

Note: FPG = fasting plasma glucose; LR- = likelihood ratio negative; LR+ = likelihood ratio positive; NPV = negative predictive value; OGTT = oral glucose tolerance test; PPV = positive predictive value; Prev = prevalence; Sens = sensitivity; Spec = specificity.

Table 45: Possible barriers and facilitators to attending postpartum screening

Barriers	Facilitators
Baby's health (morbidity)	Availability of child care
Emotional stress and fatigue, feeling overwhelmed with new baby	Health clearance provided
Demands of baby's schedule	Connecting with clinical and office staff again
Duration of test	Timing of appointment
Lack of time for self-care	Chance to ask specific questions
Privacy for breastfeeding	Health professional delivered individualised risk reduction advice
Transport and logistics	Written information provided after the birth
Child care needs	Being under the care of an obstetrician and diabetes educator during pregnancy
Lack of understanding of personal risk	
Poor communication from primary and secondary care providers	Good information about the need for screening
Fear of being diagnosed with diabetes	Family member with diabetes or gestational diabetes in previous pregnancy
Dissatisfaction with medical care and services	A postal, email or telephone reminder
Appropriate information about the requirements of the test	Oral glucose tolerance test conducted with other postpartum tests and checks
Poor communication between obstetric care providers and primary care providers	Need to know that they do not have diabetes
Dislike of the screening test (drink, blood tests, fasting)	

Source: Morrison (2009), Bennett et al (2011), Sterne et al (2011) and Stuebe et al (2010)

Appendix O: Supporting evidence for Chapter 10

Table 46: Prevalence of type 2 diabetes in women diagnosed with gestational diabetes

Reference	Country	Total number of participants	Incidence if reported	Postpartum follow-up time	Diagnostic criteria used	Quality
Ogonowski and Miazgowski (2009)	Poland	855	Only 37% (*n* = 318) returned for screening. Diabetes 1.3% IFG 2.5% IGT 7.5% Both IFG and IGT 2.2%	5–9 weeks	Diabetes: FPG ≥ 7.0 mmol/L or 2-hour value ≥ 11.1 mmol/L or symptoms of type 2 diabetes and a random plasma glucose level ≥ 11.1 mmol/L IFG: FPG ≥ 5.6 but < 7.0 mmol/L IGT: 2-hour plasma glucose ≥ 7.8 but < 11.1 mmol/L Normal: FPG < 5.6 and 2-hour plasma glucose < 7.8 mmol/L	MEDIUM
McClean (2010)	England	985	Diabetes 11.1%*	6 weeks	FPG > 6.1 mmol/L	LOW
Kim (2011)	Korea	381	Diabetes 5.2% IFG/IGT 44.8%	6–12 weeks	Diabetes: FPG ≥ 7.0 mmol/L, 2-hour glucose value ≥ 11.0 mmol/L IGT: FPG < 6.1 mmol/L and 2-hour glucose value 7.8–11.0 mmol/L IFG: FPG 6.1–6.9 mmol/L, 2-hour glucose value < 7.8 mmol/L	LOW
Schaefer-Graf (2009)	Germany	605	Diabetes 5.5% IFG 2.8% IGT 13.6%	6–12 weeks	Diabetes: FPG ≥ 7.0 mmol/L or 2-hour value ≥ 11.12 mmol/L IFG: fasting glucose > 6.1 mmol/L IGT: 2 hour glucose > 7.7 mmol/L	LOW
Hossein-Nezhad (2009)	Iran	2416 women of whom 114 had GDM	Diabetes 8.1% (95%CI 3.5–15.4%) IGT 21.4% (95%CI 13.7–30.8%)	6–12 weeks	75 g OGTT Diabetes: FPG ≥ 126 mg/dL IGT: 2-hour postprandial glucose between 140 and 199 mg/dL (7.8–11.0 mmol/L) IFG: FPG between 100 and 125 mg/dL (5.5 and 6.9 mmol/L).	LOW

Reference	Country	Total number of participants	Incidence if reported	Postpartum follow-up time	Diagnostic criteria used	Quality
Rivas (2007)	Venezuela	117	Diabetes 18.8% IGT 15.38% IFG 11.97%	2–4 months	75 g OGTT Diabetes: FPG ≥ 126 mg/dL IGT: 2-hour postprandial glucose between 140 and 199 mg/dL (7.8 and 11.0 mmol/L) IFG: FPG between 100 and 125 mg/dL (5.5 and 6.9 mmol/L)	LOW
Lawrence (2010)	USA	5939	Diabetes 1.1% IFG/IGT 16.3%	6 months	Diabetes: FPG ≥ 126 mg/dL, 2-hour plasma glucose ≥ 200 mg/dL IGT: 2-hour plasma glucose 140–199 mg/dL IFG: FPG 100–125 mg/dL	MEDIUM
Retnakaran (2010)	Canada	325/392 with normal glucose tolerance at 3 months postpartum	10% had progressed at one year to abnormal glucose tolerance. Diabetes 3% IFG 3% The remainder for IGT	1 year	2-hour OGTT (75 g) Diabetes: FPG ≥ 7.0 mmol/L or 2-hour ≥ 11.1 mmol/L IGT: fasting glucose < 6.1 mmol/L and 2-hour between 7.8 and 11.0 mmol/L IFG: fasting glucose between 6.1 and 6.9 mmol/L with 2-hour < 7.8mmol/L	MEDIUM
Madarasz (2009)	Hungary	68 cases 39 controls	Diabetes: 21% in cases and 0% in controls IGT: 16% in cases and 16% in controls IFG: 6% in cases and 0% in controls	4 years	Diabetes: FPG ≥ 7.0 mmol/L or 2-hour post-load glucose ≥ 11.0 mmol/L or reported doctor diagnosis or use of diabetic medication IGT: fasting glucose < 7.0 mmol/L and 2-hour between 7.8 and 11.0 mmol/L IFG: FPG between 6.1 and 6.9 mmol/L	LOW
Lee (2011)	Hong Kong	238	Diabetes 20% IGT 20%	Mean 52 ± 22 months	Diabetes: FPG ≥ 7mmol/L and/or 2-hour glucose ≥ 11.1 mmol/L IGT: FPG < 7.0 mmol/L and 2-hour glucose 7.8–11.1 mmol/L) IFG: FPG ≥ 5.6 but < 7.0 mmol/L	LOW

Reference	Country	Total number of participants	Incidence if reported	Postpartum follow-up time	Diagnostic criteria used	Quality
Oldfield (2007)	UK	73	Diabetes 37% IGT 19.2% IFG 2.7%	Mean 4.38 years	WHO criteria Diabetes: any plasma glucose level ≥ 11.1 mmol/L IGT: 2-hour value ≥ 7.8 mmol/L but < 11.1 mmol/L IFG: FPG between 6.1 and 7.0 mmol/L in the absence of a defining 2 hour value	LOW
Retnakaran (2011)	Canada	16,817	Diabetes 16.2%	Median 4.8 years	Not specified	MEDIUM
Ekelund (2010)	Sweden	174	Diabetes 30% IGT 19% IFG 2.8%	Up to 5 years	75 g OGTT, WHO (1999) criteria	MEDIUM
Girgis (2012)	Australia	73 migrants 28 Australians	Diabetes 33% (in migrants) IGT 15% (in migrants) Diabetes/IGT 39% (in Australians)	5.5 years	No details	LOW
Mukerji (2012)	Canada	>1,000,000	39.8 cases per 1000 person-years	Median 7.6 years	Recorded in the Ontario Diabetes Database	MEDIUM
Tehrani (2012)	Iran	29 cases 58 controls	Diabetes 27.3% Diabetes 9.5%	Up to 9 years	ADA criteria or using anti-diabetic drugs Diabetes: FPG ≥ 7 mmol/L or 2-hour plasma glucose ≥ 11.1 mmol/L IGT: 2-hour plasma glucose between 7.77 and 11.1 mmol/L IFG: fasting blood sugar between 5.6 and 6.9 mmol/L	LOW
Malinowski-Polubiec (2012)	Poland	155	Diabetes 23.2% IGT 30% IFG 18.1%	Up to 10 years	Diabetes: FPG ≥ 7.0 mmol/L or 2-hour OGTT ≥ 11.1 mmol/L IGT: 2-hour OGTT > 7.8 mmol/L but < 11.1 mmol/L IFG: fasting glucose > 6.1 mmol/L but < 7.0 mmol/L and normal 2-hour OGTT	LOW

Reference	Country	Total number of participants	Incidence if reported	Postpartum follow-up time	Diagnostic criteria used	Quality
Chodick (2010)	Israel	185,416	Diabetes 15.7%	Up to 10 years	Maccabi Healthcare Services Diabetes Registry	HIGH
Pirkola (2010)	Finland	9362	Diabetes 1.3%	20 years	National registry – diagnosed by doctor or by reimbursement for anti-diabetic drugs	MEDIUM

Note: ADA = American Diabetes Association; FPG = fasting plasma glucose; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test; WHO = World Health Organization.

* The study included some women with more than one pregnancy affected by hyperglycaemia.

Table 47: Risk factors associated with developing type 2 diabetes in women diagnosed with gestational diabetes

Risk factor	Reference	Country	Number of women	Risk estimate	Quality rating
Overweight/obesity					
High pre-pregnancy weight	Russell (2008)	Canada	1401	Adj RR 1.8, 95%CI 1.2–2.9	MEDIUM
	Oldfield (2007)	UK	73	Caucasian OR 1.02 (95%CI 1.01–1.05, $p < 0.01$), South Asian OR 1.04 (95%CI 1.03–1.08, $p = 0.04$)	LOW
BMI > 30 kg/m²	Chodick (2010)	Israel	185,416	Adj HR 5.12 (95%CI 4.38–5.97, $p < 0.001$)	HIGH
	Schaefer-Graf (2009)			OR 2.12 (95%CI 1.33–3.40, $p = 0.002$)	LOW
BMI > 25 kg/m²	Pirkola (2010)	Finland	6483	HR 47.24 (95%CI 25.53–87.40, $p < 0.001$)	MEDIUM
Obesity during pregnancy	Oldfield (2007)	UK	73	Caucasian OR 1.21 (95%CI 1.05–1.29, $p < 0.01$), South Asian OR 1.20 (95%CI 1.11–1.36, $p < 0.01$)	LOW
Pre-pregnancy BMI ≥ 27 kg/m²	Malinowski-Polubiec (2012)*	Poland	155	BMI ≥ 27 kg/m² versus BMI < 27 kg/m² RR 1.60 (no CIs provided)	LOW
	Kim (2011)	Korea	882	$\beta = 0.05$, $p = 0.03$	LOW
High postpartum BMI	Kim (2011)	Korea	882	$\beta = 0.06$, $p = 0.04$	LOW
	Retnakaran (2010)	Canada	325	Adj OR 1.09 (95%CI 1.03–1.17, $p = 0.007$)	MEDIUM
	Wang (2013)	USA	19,998	< 25 kg/m² HR 7.10 (95%CI 4.53–11.1) 25–29.9 kg/m² HR 5.64 (95%CI 3.93–8.09) 30–34.9 kg/m² HR 8.39 (95%CI 6.29–11.2) ≥ 35 kg/m² HR 6.03 (95%CI 5.31–7.48)	HIGH

Risk factor	Reference	Country	Number of women	Risk estimate	Quality rating
Disease severity					
Insulin therapy during index pregnancy	Chodick (2010)	Israel	185,416	Adj HR 2.77 (95%CI 2.39–3.20, $p < 0.001$)	HIGH
	Akinci (2011)	Turkey	195	Adj OR 4.67 (95%CI 1.66–13.18, $p = 0.004$)	MEDIUM
	Russell (2008)	Canada	1,401	Adj RR 4.1 (95%CI 2.1–7.9)	MEDIUM
	Ogonowski and Miazgowski (2009)	Poland	855	Adj OR 1.57 (95%CI 1.34–1.83, $p = 0.05$)	MEDIUM
	Lawrence (2010)	USA	11,825	Adj OR 3.30 (95%CI 2.15–5.05)	MEDIUM
	Schaefer-Graf (2009)	Germany	1184	OR 2.12 (95%CI 1.36–3.30, $p = 0.001$)	LOW
	Oldfield (2007)	UK	73	Caucasian OR 23.4 (95%CI 3.87–158.31, $p = 0.001$), South Asian (NS)	LOW
	Girgis (2012)*	Australia	101	Abnormal versus normal glucose tolerance OR 4.5 (95%CI 1.6–13.1, $p = 0.005$)	LOW
	Kim (2011)	Korea	882	$\beta = 1.1$, $p < 0.0001$	LOW
Insulin therapy after delivery	Malinowski-Polubiec (2012)*	Poland	155	RR 2.01 (no CIs provided)	LOW
Poor glycaemic control					
High diagnostic fasting glucose level	Akinci (2011)	Turkey	195	Adj OR 2.1 (95%CI 1.4–3.2, $p < 0.001$)	MEDIUM
	Ogonowski and Miazgowski (2009)	Poland	855	Adj OR 1.05 (95%CI 1.02–1.08, $p = 0.001$)	MEDIUM
	Schaefer-Graf (2009)	Germany	1184	OR 2.73 (95%CI 1.77–4.21, $p < 0.001$)	LOW
	Lee (2011)	Hong Kong	238	Adj HR 1.93 (95%CI 1.42–2.63, $p < 0.001$)	LOW
	Oldfield (2007)	UK	73	Caucasian OR 5.93 (95%CI 1.33–26.34, $p = 0.02$), South Asian OR 1.60 (95%CI 1.09–2.45, $p = 0.02$)	LOW
High glucose challenge test levels	Ogonowski and Miazgowski (2009)	Poland	855	Adj OR 1.03 (95%CI 1.01–1.08, $p = 0.007$)	MEDIUM

Risk factor	Reference	Country	Number of women	Risk estimate	Quality rating
High diagnostic 2-hour OGTT	Ogonowski and Miazgowski (2009)	Poland	855	Adj OR 1.02 (95%CI 1.01–1.04, p = 0.003)	MEDIUM
	Oldfield (2007)	UK	73	Caucasian OR 2.07 (95%CI 1.02–4.15, p = 0.04), South Asian (NS)	LOW
High HbA1c at diagnosis	Oldfield (2007)	UK	73	Caucasian OR 9.15 (95%CI 1.91–43.87, p = 0.006), South Asian OR 4.95 (95%CI 1.35–12.40, p = 0.01)	LOW
High HbA1C during pregnancy	Ekelund (2010)	Sweden	174	OR 2.6 (95%CI not stated, p = 0.01)	MEDIUM
	Ogonowski and Miazgowski (2009)	Poland	855	OR 2.36 (95%CI 1.19–4.68, p = 0.01)	MEDIUM
	Malinowski-Polubiec (2012)*	Poland	155	> 6.40% versus < 5.40% RR 2.65 (no CIs provided)	LOW
(High) fasting glucose levels during pregnancy	Ekelund (2010)	Sweden	174	OR 2.1 (95%CI not stated, p = 0.04)	MEDIUM
	Malinowski-Polubiec (2012)*	Poland	155	Fasting glucose ≥ 7.0 mmol/L RR 5.2 (no CIs provided)	LOW
	Girgis (2012)*	Australia	101	Abnormal versus normal glucose tolerance OR 2.8 (95%CI 1.2–6.6, p = 0.02)	LOW
High 2-hour OGTT values during pregnancy	Malinowski-Polubiec (2012)*	Poland	155	2-hour glucose ≥ 7.8 mmol/L RR 2.29 (no CIs provided)	LOW
	Girgis (2012)*	Australia	101	Abnormal versus normal glucose tolerance OR 2.1 (95%CI 1.3–3.3, p = 0.003)	LOW
High postpartum HbA1c	Kim (2011)	Korea	882	β = 1.2, p < 0.0001	LOW
Area under the glucose curve at 3-month OGTT	Retnakaran (2010)	Canada	310	Adj OR 1.37 (95%CI 1.13–1.65, p = 0.001)	MEDIUM
Sum of the glucose values at 3-month OGTT	Retnakaran (2010)	Canada	310	Adj OR 1.16 (95%CI 1.05–1.29, p = 0.004)	MEDIUM
Having a delayed blood glucose peak at 3-month OGTT (> 30 min post-load)	Retnakaran (2010)	Canada	310	Adj OR 2.89 (95%CI 1.29–6.45, p = 0.01)	MEDIUM

Risk factor	Reference	Country	Number of women	Risk estimate	Quality rating
Parity					
Previous pregnancy	Ekelund (2010)	Sweden	174	OR 4.3 (95%CI not stated, $p = 0.02$)	MEDIUM
Interval between first and second pregnancy of < 2 years	Russell (2008)	Canada	1401	Unadjusted RR 4.2 (95%CI 1.2–15.0)	MEDIUM
Maternal age					
Increasing age	Chodick (2010)	Israel	185,416	Adj HR 1.03 (95%CI 1.02–1.04, $p < 0.001$)	MEDIUM
	Oldfield (2007)	UK	73	Caucasian OR 1.31 (95%CI 1.1–1.59, $p = 0.007$), South Asian OR 1.13 (95%CI 1.02–1.25, $p = 0.02$)	LOW
	Wang (2013)	USA	19,998	Women aged 13–29.9 years (HR 8.97, 95%CI 7.57–10.6), compared with women aged 30–40 years (HR 5.27, 95%CI 4.27–6.51) and 40–50 years (HR 5.30, 95%CI 2.88–9.76)	HIGH
	Malinowski-Polubiec (2012)	Poland	155	Women aged < 25 years versus women aged 25–35 years RR 2.49 (no CIs provided); women aged > 35 years RR 3.30 (no CIs provided)	LOW
Gestational week at diagnosis					
Gestational week at diagnosis	Orgonowski and Miazgowski (2009)	Poland	855	Adj OR 0.91 (95%CI 0.86–0.96, $p = 0.001$)	MEDIUM
	Schaefer-Graf (2009)	Germany	1184	OR 1.81 (95%CI 1.16 –2.85, $p = 0.01$) (≤ 24 weeks)	LOW
	Malinowski-Polubiec (2012)	Poland	155	> 28 weeks RR 0.49 (no CIs provided)	LOW
Family history of diabetes					
Family history of diabetes	Kim (2011)	Korea	882	$\beta = 0.38$, $p = 0.05$	LOW
	Ekelund (2010)	Sweden	174	OR 4.1 (95%CI not stated, $p = 0.03$)	MEDIUM
	Oldfield (2007)	UK	73	Caucasian (NS), South Asian OR 9.0 (95%CI 2.50–32.67, $p = 0.001$)	LOW

Risk factor	Reference	Country	Number of women	Risk estimate	Quality rating
History of GDM					
Subsequent pregnancy with GDM	Russell (2008)	Canada	1401	Adj RR 2.3 (95%CI 1.6–3.4)	MEDIUM
	Retnakaran (2011)	Canada	16,817	Adj HR 1.16 (95%CI 1.01–1.34, p = 0.03)	MEDIUM
Previous GDM or GDM in index pregnancy	Chodick (2010)	Israel	185,416	Adj HR 7.70 (95%CI 7.05–8.41, p < 0.001)	HIGH
	Retnakaran (2010)	Canada	325	Adj OR 5.99 (95%CI 1.25–28.64, p = 0.03)	MEDIUM
	Pirkola (2010)	Finland	6483	HR 10.61 (95%CI 4.17–27.0, p < 0.001) (normal pre-pregnancy weight)	MEDIUM
				HR 47.24 (95%CI 25.53–87.40, p < 0.001) (pre-pregnancy weight > 25 kg/m²)	MEDIUM
	Girgis (2012)*	Australia	101	Abnormal versus normal glucose tolerance OR 2.2 (95%CI 1.0–4.8, p = 0.04)	LOW
Other factors					
Postpartum energy intake as a percentage of estimated energy requirement	Kim (2011)	Korea	882	β = 0.009, p = 0.05	LOW
Breastfeeding	Kim (2011)	Korea	882	β = ⁻0.016, p = 0.25	LOW
Ethnicity	Mukerji (2012)	Canada	1,050,108	Compared with White women, Chinese women (adj HR 0.6, 95%CI 0.6–0.7) and South Asian women (adj HR 1.4, 95%CI 1.3–1.5). Compared with women without GDM from the same ethnic group, women with GDM had significantly increased risk of developing diabetes (Chinese adj HR 9.2, 95%CI 8.1–10.3; South Asian adj HR 9.6, 95%CI 8.8–10.5; White adj HR 13.6, 95%CI 13.2–14.0)	MEDIUM HIGH
Polycystic ovary syndrome	Palomba (2012)	Italy	42 cases	Diabetes RR 4.0 (95%CI 0.37–42.86, NS)	LOW
			84 controls	Glucose metabolism impairment RR 3.45 (95%CI 1.82–6.58, p = 0.0002)	
Neonatal hypoglycaemia	Russell (2008)	Canada	1401	Adj RR 2.6 (95%CI 1.6–4.2)	MEDIUM

Note: BMI = body mass index; CI = confidence interval; GDM = gestational diabetes mellitus; HR = hazard ratio; NS = not significant; OGTT = oral glucose tolerance test; OR = odds ratio; RR = risk ratio.

* Data include impaired fasting glucose and impaired glucose tolerance as well as type 2 diabetes adjusted.

Appendix P: Supporting evidence for Chapter 11

Table 48: Effect of Diabetes Prevention Programme treatment on incidence of gestational diabetes

	Placebo		Metformin		Intensive lifestyle	
	GDM	**No GDM**	**GDM**	**No GDM**	**GDM**	**No GDM**
Incidence of diabetes (number of cases per 100 person-years)*	15.2[b]	8.9	7.8	7.8	7.4	4.7
Reduction in incidence (compared with placebo) %**			50.4[c]	14.4	53.4[c]	49.2[c]
Number needed to treat (to prevent one case in three years compared with placebo)^			6.1	24.0	5.3	9.0

Note: GDM = gestational diabetes mellitus.

*   Adjusted for age.

** $p < 0.05$ compared with non-GDM group.

^ $p < 0.05$ compared with placebo.

Source: Ratner et al (2008), p 4779

Table 49: Table of effects: Lifestyle interventions for the prevention of type 2 diabetes for people with impaired glucose tolerance

Intervention	Hazard ratio (95% confidence interval)
Lifestyle interventions	0.51 (0.43–0.62)
Diet	0.67 (0.49–0.92)
Exercise	0.53 (0.34–0.83)
Diet and exercise	0.47 (0.37–0.59)

Adapted from National Institute for Health and Care Excellence (NICE 2012)

Table 50: Goals of the major diabetes prevention trials

Trial	Goals					
	Physical activity	Weight loss	Increase fibre intake	Reduce total fat intake	Reduce saturated fat intake	Other dietary goals
Da-Qing study (China) (Pan 1997) Cluster-randomised	1–2 'units' a day. 1 unit = 30 minutes of slow walking or housework; or 20 minutes of fast walking/cycling or ballroom dancing; or 10 minutes of climbing stairs; or 5 minutes of swimming or basketball	Reduce body mass index to less than 24 kg/m² if body mass index over 25 kg/m²	–	Reduce to 25–30% of energy intake		Carbohydrate 55–65% of energy intake. Increase vegetable intake. Reduce sugar intake. Control alcohol intake
Diabetes prevention study (Finland) (Tuomilehto 2001)	More than 4 hours/week, moderate intensity	5% or more of initial body weight	Over 15 g per 1000 kcals	Reduce to less than 30% of energy intake	Less than 10% of energy intake	–
Diabetes prevention program (USA) (Diabetes Prevention Program Research Group 2002)	At least 150 minutes/week moderate intensity	7% of initial body weight	–	Adopt a low-fat diet	–	Low calorie
Diabetes prevention program (India) (Ramachandran 2006)	At least 30 minutes of brisk walking or cycling a day	–	Include fibre-rich foods	Reduce fats	–	Reduce total calorie and refined carbohydrate intake. Avoid sugar

Source: Reproduced from National Institute for Health and Care Excellence (NICE 2012)

Box 1: EURO guideline lifestyle interventions for the prevention of type 2 diabetes

EURO lifestyle interventions for preventing type 2 diabetes

- Intensive lifestyle interventions to encourage people to change their diet and to increase physical activity levels should be used to prevent or delay the onset of type 2 diabetes in adults with impaired glucose tolerance. The number needed to treat for prevention of one case of type 2 diabetes was 6.4 (95% CI 5.0–8.4) at mean follow-up ranging from 1.83 to 4.62 years. (A grade recommendation)

- Weight reduction is an essential element of prevention of type 2 diabetes prevention. Sustained weight reduction by 5–7% is sufficient to substantially lower the risk of type 2 diabetes. (A grade recommendation)

- An increase in physical activity even at a level of 30 minutes per day of moderate exercise reduces the risk of type 2 diabetes and is therefore recommended. (B grade recommendation)

- A diet with high fibre (≥ 15 g per 1000 kcal), moderate fat (≤ 10% of total energy) can lower body weight. (B grade recommendation)

- Comorbidities, particularly metabolic syndrome, should be monitored and taken into account while planning the diet. (C grade recommendation)

- Currently there is no evidence from long-term prevention studies that reducing total dietary carbohydrate prevents type 2 diabetes. Carbohydrate sources should mainly be wholegrain cereal, fruit, vegetables, and legumes. (C grade recommendation)

- There is no evidence from clinical trials of the effectiveness of interventions to prevent the onset of type 2 diabetes among children and adolescents. However, on the basis of physiological evidence and research in adults it can reasonably be assumed that maintaining a healthy weight through physical activity and balanced/healthy nutrition is the key factor and will be important to prevent or postpone the onset of type 2 diabetes among youth. (C grade recommendation)

Adapted from a European evidence-based guideline for the prevention of type 2 diabetes (Paulweber, 2010, page S17).

Table 51: Table of effects: pharmacological treatments for people with impaired glucose tolerance

Guideline	Outcome	Hazard ratio (95% confidence interval)
NICE: Preventing type 2 diabetes	Pharmacological treatments	0.64 (0.53–0.76)
	Oral diabetes drugs	0.60 (0.44–0.82)
	Anti-obesity drugs	0.67 (0.55–0.81)

Adapted from National Institute for Health and Care Excellence (NICE 2012)

Box 2. EURO guideline pharmacological interventions for the prevention of type 2 diabetes

- In people with impaired glucose tolerance, metformin and acarbose can be used as second-line strategies for prevention of type 2 diabetes, provided that the drugs are tolerated (gastrointestinal side-effects), and contra-indications to metformin therapy (kidney, liver diseases, hypoxic conditions) are considered. (A grade recommendation)

- In obese people with or without impaired glucose tolerance, carefully monitored anti-obesity treatment with orlistat, in addition to intensive lifestyle modification, can be used as a second-line strategy to prevent type 2 diabetes. (A grade recommendation)

- Glucose-lowering drugs such as glipizide or thiazolidendiones may reduce the risk of type 2 diabetes in certain high-risk groups, but either long-term efficacy or safety is unclear so these drugs cannot be recommended for diabetes prevention at present. (C grade recommendation)

- Antihypertensive and lipid-lowering drugs cannot be recommended for the prevention of type 2 diabetes at present. (C grade recommendation)

Source: Adapted from Paulweber et al (2010, p S17)