NCC-WCH

Version 2.0

Diabetes in pregnancy

Management of diabetes and its complications from preconception to the postnatal period

NICE guideline 3

Appendices A – G, I – N

Wednesday February 25th, 2015

Final

Commissioned by the National Institute for Health and Care Excellence

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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Contents

Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period

1.1 Short title

Diabetes in pregnancy

2 The remit

This is an update of Diabetes in pregnancy (NICE clinical guideline 63). See section 4.3.1 for details of which sections will be updated. We will also carry out an editorial review of all recommendations to ensure that they comply with NICE's duties under equalities legislation.

This update is being undertaken as part of the guideline review cycle.

This is the scope for 1 of 4 NICE clinical guidelines being developed that address diabetes care. Included below is a summary of the content for each guideline and of the NICE steering committee.

Guideline 1 – Diabetes in children and young people (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update Type 1 diabetes in children, young people and adults (NICE clinical guideline 15) It will cover the diagnosis and management of type 1 and type 2 diabetes in children and young people (younger than 18 years). It will include: structured education programmes, behavioural interventions to improve adherence, glucose monitoring strategies, ketone monitoring, insulin regimens for type 1 diabetes and metformin monotherapy for type 2 diabetes.

Guideline 2 – Diabetes in pregnancy (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update Diabetes in pregnancy (NICE clinical guideline 63). It will cover women of reproductive age who have pre-existing diabetes or who develop diabetes during pregnancy and it will also cover their newborn babies. It will include: target glucose ranges in the preconception period and during pregnancy, glucose monitoring strategies during pregnancy, screening, diagnosis and treatment of gestational diabetes, and postnatal testing for type 2 diabetes.

Guideline 3 – Type 1 diabetes in adults (developed by the National Clinical Guideline Centre)

This guideline will update Type 1 diabetes in children, young people and adults (NICE clinical guideline 15). It will cover adults (18 years or older) with type 1 diabetes. It will include: tests to differentiate type 1 diabetes from type 2 diabetes, structured education programmes, clinical monitoring of glucose control, insulin regimens, ketone monitoring, dietary advice on carbohydrate counting and glycaemic index, and treatment and monitoring of specific complications.

Guideline 4 –Type 2 diabetes in adults (developed by the Internal Clinical Guidelines Programme, Centre for Clinical Practice, NICE)

This guideline will update Type 2 diabetes (NICE clinical guideline 66) and Type 2 diabetes: newer agents (NICE clinical guideline 87). It will cover adults (18 years or older) with type 2 diabetes. It will include: pharmacological management of blood glucose levels, target values for blood glucose control, self-monitoring of blood glucose levels for blood glucose control, antithrombotic therapy and drug therapy for erectile dysfunction.

NICE steering committee

NICE has set up a steering committee to oversee the production of these clinical guidelines. The group, which includes the Guideline Development

Groups' chairs, together with staff from the 3 guidance-producing centres and NICE, will identify and act on any gaps or overlaps across the different guidance topics to ensure that the final guidelines are complementary and consistent. It is intended that the guidance-producing centres will share systematic reviews and cross-refer to recommendations in the other guidelines where appropriate. This update is being undertaken as part of the guideline review cycle.

3 Clinical need for the guideline

3.1 Epidemiology

a) Diabetes is a disorder of carbohydrate metabolism that requires immediate changes in lifestyle. People who have diabetes for many years can develop long-term microvascular complications, including retinopathy, nephropathy and neuropathy as well as macrovascular complications of cardiovascular disease.

b) Diabetes that complicates pregnancy is becoming more common worldwide. Up to 5% of the approximately 700,000 women who give birth in England and Wales each year have pre-existing or gestational diabetes.

c) Less than 1% of pregnant women have pre-existing diabetes. Within this 1%, around 75% have type 1 diabetes, 25% have type 2 diabetes and a small number have secondary diabetes (for example, cystic fibrosis-related or monogenic diabetes). The proportion of women with type 1 or type 2 diabetes varies depending on the ethnic origins of the population. The duration of diabetes before conception also varies but is increasing because the average age of onset of type 1 diabetes is declining and more women are developing type 2 diabetes at an earlier age. This is important because duration of diabetes is one of the strongest factors associated with microvascular complications and it is, therefore, more likely that women with diabetes will enter

pregnancy with established retinopathy, nephropathy and neuropathy.

d) In the UK, at least 4% of women have gestational diabetes but this figure will vary greatly depending on the local population. The incidence of gestational diabetes is increasing due to higher rates of obesity in the general population and more pregnancies in older women. Most of the risks of gestational diabetes occur in the second half of pregnancy because the majority of women affected are normoglycaemic at the time of conception.

e) Gestational diabetes is defined as any degree of glucose intolerance that is detected for the first time during pregnancy. This includes women whose glucose intolerance resolves after pregnancy and up to 20% whose glucose intolerance persists, including women who had undiagnosed pre-existing type 2 diabetes (or in small numbers, type 1 diabetes) before pregnancy. Women with gestational diabetes are at increased risk of developing type 2 diabetes in the future.

f) Maternal risks of pre-existing diabetes include recurrent hypoglycaemia, progression of retinopathy, nephropathy, increased incidence of pre-eclampsia (especially in women with microvascular disease) and operative delivery.

g) Fetal risks of pre-existing maternal diabetes include structural congenital abnormality, pathological fetal growth (macrosomia) and 'unexplained' fetal death. Neonatal complications include premature delivery, respiratory distress syndrome, transient tachypnoea, birth trauma, hypoglycaemia, hypomagnesaemia, hypocalcaemia, polycythaemia and neonatal death.

3.2 Current practice

a) The additional care of women with diabetes in pregnancy, as set out in Diabetes in pregnancy (NICE clinical guideline 63), can be considered according to the stage of the pregnancy.

b) Preconception care aims to enable women with established diabetes to have a positive experience of pregnancy and childbirth and to minimise the risk of structural abnormalities in the baby. It includes information-giving and education, and emphasises the importance of planning pregnancy; offering assessment for, and management of, diabetes complications; improving blood glucose control; high-dose folic acid supplementation and changing potentially teratogenic medications are also important components of this stage of care.

c) Identification of gestational diabetes is a routine element of antenatal care for all women, as set out in Antenatal care (NICE clinical guideline 62). A risk factor based screening approach is recommended to identify women with gestational diabetes in a healthy population.

d) Antenatal care of women with diabetes follows a multidisciplinary approach characterised by an increased schedule of appointments. Care includes:

- regular blood glucose testing (fasting or preprandial, and 1-hour postprandial)
- treating diabetes with diet, insulin and/or oral hypoglycaemic drugs to maintain blood glucose profiles in the normal range
- use of concentrated glucose solutions or glucagon to treat hypoglycaemic episodes
- vigilance for diabetic ketoacidosis
- regular ophthalmic review and, if necessary, specialist referral
- review of renal function and, if necessary, specialist referral
- vigilance for pre-eclampsia.

e) Antenatal care for the baby includes offering screening for fetal abnormality and monitoring fetal growth and wellbeing. In special cases, monitoring may need to be individualised.

f) Care during labour includes offering elective birth after 38 completed weeks of pregnancy, maintaining blood glucose levels in the normal range and continuous electronic fetal heart rate monitoring.

g) Postnatal care for women with diabetes includes:

- resuming pre-pregnancy diabetes treatment in women with pre-existing diabetes
- stopping all diabetic treatment initiated during pregnancy in women with gestational diabetes and monitoring their blood glucose levels to confirm euglycaemia
- monitoring women with gestational diabetes who have persistently high blood glucose levels after birth to detect type 2 diabetes
- offering advice about the importance of contraception.

h) Additional postnatal and neonatal care for women and their babies includes encouraging breastfeeding and vigilance to prevent neonatal hypoglycaemia.

i) Since the publication of Diabetes in pregnancy (NICE clinical guideline 63), new evidence has been published on levels of hyperglycaemia in pregnancy. The blood glucose level at which intervention becomes cost effective and the importance that should be given to different outcomes remain issues for debate.

j) Consideration is also being given to early screening in pregnancy to identify and treat women with gestational diabetes who may have undiagnosed pre-existing diabetes and be unaware of the risks associated with diabetes in pregnancy.

k) New evidence has also been identified that may alter recommendations on:

- target ranges for preconception care
- continuous glucose monitoring
- the appropriate test to undertake at the postnatal check-up to diagnose type 2 diabetes in women who had gestational diabetes in pregnancy but who are euglycaemic on discharge to community care.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

For the topic of screening for gestational diabetes:

a) All pregnant women who do not have previously diagnosed non-gestational diabetes (new 2012).

For all other topics:

b) Women of reproductive age who have pre-existing diabetes or who develop diabetes during pregnancy, and their newborn babies.

c) Where the evidence supports it, the following subgroups will be given special consideration:

- Women of reproductive age with type 1 or type 2 diabetes.
- Women with gestational diabetes or a history of gestational diabetes.
- Young women of reproductive age with diabetes whose care has not yet transferred from paediatric to adult services
- Women with an ethnicity associated with a high prevalence of diabetes.

4.1.2 Groups that will not be covered

For the topic of screening for gestational diabetes:

a) Women of reproductive age who are not pregnant (new 2012).

b) Women who have previously diagnosed type 1 or type 2 diabetes (new 2012).

For all other topics:

c) Women of reproductive age who do not have diabetes.

4.2 Healthcare setting

a) All healthcare settings in which NHS care is received or commissioned.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Areas from the original guideline that will be updated

a) Target ranges for haemoglobin A_{1c} (HbA_{1c}) and blood glucose for women with type 1 or type 2 diabetes who are planning pregnancy

and for women with type 1, type 2 or gestational diabetes during pregnancy.

b) The effectiveness of blood ketone monitoring when compared with urine ketone monitoring in women with type 1 or type 2 diabetes who are planning pregnancy and in women with type 1, type 2 or gestational diabetes during pregnancy.

c) The effectiveness of the following screening procedures to detect gestational diabetes between 24–28 weeks:

- risk factor based screening
- urine testing for glycosuria
- random blood glucose test
- 50 g oral glucose challenge test
- fasting blood glucose test
- HbA_{1c} test.

d) The criteria that should be used to diagnose gestational diabetes using the 75 g oral glucose tolerance test (OGTT). There are two options:

- World Health Organization (WHO)
- International Association of Diabetes and Pregnancy Study Groups (IADPSG).

e) The effectiveness of the following interventions (alone or in combination) in women with gestational diabetes:

- non-pharmacological interventions (diet and/or exercise)
- pharmacological interventions (metformin, glibenclamide and insulin).

f) The effectiveness of continuous glucose monitoring in pregnant women with diabetes when compared with intermittent capillary blood glucose monitoring.

g) The effectiveness of specialist teams for pregnant women with diabetes.

h) The gestational age specific risk of intrauterine death in pregnancies with type 1, type 2 or gestational diabetes and the optimal timing of birth.

i) The effectiveness of the following tests in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care):

- fasting plasma glucose test
- HbA_{1c} test
- 75 g OGTT.

j) The optimal timing of postnatal testing for the detection of glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care).

Areas not in the original guideline that will be included in the update

k) The effectiveness of oral hormonal contraceptives in women with diabetes compared with women without diabetes.

l) The effectiveness of the following screening procedures to detect glucose intolerance in the first trimester:

- risk factor based screening
- urine test for glycosuria
- random blood glucose test
- 50 g oral glucose challenge test
- fasting blood glucose test
- HbA_{1c} test.

4.3.2 Clinical issues that will not be covered

Areas from the original guideline that will not be updated

The following areas addressed in Diabetes in pregnancy (NICE clinical guideline 63) will not be updated (the existing recommendations will remain as current guidance):

a) All aspects of preconception care, gestational diabetes, antenatal care, intrapartum care, postnatal care that are not listed in section 4.3.1.

b) Neonatal care.

Areas not covered by the original guideline or the update

c) Aspects of routine antenatal, intrapartum and postnatal care that apply equally to women with or without diabetes.

d) Aspects of routine care for women with diabetes that do not change during the preconception, antenatal, intrapartum and postnatal periods.

e) Investigation, management and treatment of comorbidities, for example fertility problems or pre-eclampsia.

f) Management of morbidity in newborn babies of women with diabetes beyond initial assessment and diagnosis.

4.4 Main outcomes

Outcomes will vary by the type of clinical question and systematic review undertaken. No more than seven outcomes will normally be prioritised for each topic.

a) Diagnostic accuracy:

- sensitivity and specificity.

b) Quality of life:

- health-related quality of life (validated questionnaire) – for example, diabetes-specific health-related quality of life.

c) Neonatal outcomes:

- admission to a neonatal intensive care unit, special care baby unit, or transitional care unit
- miscarriage, stillbirth (fetal death), neonatal or infant death
- macrosomia, large for gestational age, small for gestational age and intrauterine growth restriction
- neonatal hypoglycaemia requiring active management
- respiratory distress
- shoulder dystocia and birth trauma (bone fracture or nerve palsy)
- other neonatal complications (jaundice, polycythaemia, sepsis, hypocalcaemia or hypoxic ischaemic encephalopathy)
- congenital abnormality.

d) Maternal outcomes:

- maternal death
- perineal trauma
- preterm birth
- mode of birth (spontaneous vaginal, instrumental, or caesarean section)
- mode of infant feeding
- diabetic complications (hypoglycaemia, diabetic ketoacidosis, retinopathy, nephropathy, or macrovascular disease)
- antenatal and intrapartum complications in the unborn baby
- development of type 2 diabetes
- obstetric complications (haemorrhage, infection, thrombosis, admission to critical care, or incontinence)
- diabetes control (HbA_{1c}, fructosamine or mean glucose)
- postnatal mental health

- maternal satisfaction.

4.5 Review questions

These are draft review questions and the final questions will be agreed by the Guideline Development Group during development.

4.5.1 Preconception care

- What is the effectiveness of oral oestrogen-containing contraceptives in women with diabetes compared with women without diabetes?
- What is the effectiveness of oral progestogen-containing contraceptives in women with diabetes compared with women without diabetes?
- What is the target value for HbA_{1c} in women with type 1 or type 2 diabetes who are planning pregnancy?
- What are the target ranges for blood glucose in women with type 1 or type 2 diabetes who are planning pregnancy?
- What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1 or type 2 diabetes who are planning pregnancy?

4.5.2 Gestational diabetes

- What is the effectiveness of the following procedures in detecting glucose intolerance in the first trimester:
  - risk factor based screening
  - urine test for glycosuria
  - random blood glucose test
  - 50 g oral glucose challenge test
  - fasting blood glucose test
  - HbA_{1c} test?

- What is the effectiveness of the following procedures in detecting glucose intolerance in the second trimester:
  - risk factor based screening
  - urine test for glycosuria
  - random blood glucose test

  - 50 g oral glucose challenge test
  - fasting blood glucose test
  - HbA_{1c} test?

- Which criteria should be used to diagnose gestational diabetes using the 75 g OGTT:
  - WHO or
  - IADPSG?

- What is the effectiveness of the following interventions (alone or in combination) in women with gestational diabetes:
  - non-pharmacological interventions (diet and/or exercise)
  - pharmacological interventions (metformin, glibenclamide and insulin)?

4.5.3 Antenatal care

- What is the effectiveness of HbA_{1c} monitoring in predicting adverse outcomes in women with type 1 or type 2 diabetes during pregnancy?
- What is the effectiveness of blood glucose monitoring in predicting adverse outcomes in women with type 1 or type 2 diabetes during pregnancy?
- What is the target value for HbA_{1c} in women with type 1, type 2 or gestational diabetes during pregnancy?
- What are the target ranges for blood glucose in women with type 1, type 2 or gestational diabetes during pregnancy?
- What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1, type 2 or gestational diabetes during pregnancy?
- What is the effectiveness of continuous glucose monitoring in pregnant women with diabetes compared with intermittent capillary blood glucose monitoring?
- What is the effectiveness of specialist teams for pregnant women with diabetes?

4.5.4 Intrapartum care

- What is the gestational age-specific risk of intrauterine death in pregnancies with type 1, type 2 or gestational diabetes, and the optimal timing of birth?

4.5.5 Postnatal care

- What is the effectiveness of the following tests in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care):
  - fasting plasma glucose test
  - HbA_{1c} test
  - 75 g OGTT?

- What is the optimal timing of postnatal testing in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care)?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

4.7.1 Scope

This is the final scope.

4.7.2 Timing

The development of the guideline recommendations is expected to begin in October 2012.

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

Depending on the evidence, this guideline might update and replace parts of the following NICE guidance (in relation to gestational diabetes only):

- Antenatal care. NICE clinical guideline 62 (2008).

5.1.2 Related NICE guidance

- Preventing type 2 diabetes – risk identification and interventions for individuals at high risk. NICE public health guidance 38 (2012).
- Patient experience in adult NHS services. NICE clinical guideline 138 (2012).
- Caesarean section. NICE clinical guideline 132 (2011).
- Multiple pregnancy. NICE clinical guideline 129 (2011).
- Diabetic foot problems. NICE clinical guideline 119 (2011).
- Preventing type 2 diabetes: population and community-level interventions in high-risk groups and the general population. NICE public health guidance 35 (2011).
- Hypertension in pregnancy. NICE clinical guideline 107 (2010).
- Dietary interventions and physical activity interventions for weight management before, during and after pregnancy. NICE public health guidance 27 (2010).
- Type 2 diabetes: newer agents. NICE clinical guideline 87 (2009).
- Induction of labour. NICE clinical guideline 70 (2008).
- Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. NICE technology appraisal guidance 151 (2008).
- Intrapartum care. NICE clinical guideline 55 (2007).

- Antenatal and postnatal mental health. NICE clinical guideline 45 (2007).
- Routine postnatal care of women and their babies. NICE clinical guideline 37 (2006).
- Smoking cessation services. NICE public health guidance 10 (2008).
- Obesity. NICE clinical guideline 43 (2006).
- Nutrition support in adults. NICE clinical guideline 32 (2006).
- Four commonly used methods to increase physical activity. NICE public health guidance 2 (2006).
- Type 1 diabetes. NICE clinical guideline 15 (2004).
- Type 2 diabetes: prevention and management of foot problems. NICE clinical guideline 10 (2004).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Type 1 diabetes (update). NICE clinical guideline. Publication expected 2014.
- Type 2 diabetes (update). NICE clinical guideline. Publication expected 2014.
- Diabetes in children and young people (update). NICE clinical guideline. Publication expected 2014.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'.

Information on the progress of the guideline will also be available from the NICE website.

Appendix B: Declarations of interests

B.1 Declarations of interest from guideline development group for original (2008) guideline

Table 1: 2008 GDG members' declarations of interest

GDG member	Interest
Dominique Acolet	No interests declared
Lynne Carney	Personal non-pecuniary interests: Speaker at Welsh CEMACH conference Non-current interests – planned: Teacher on specialist antenatal course for women with diabetes
Anne Dornhorst	Personal pecuniary interests – specific: Consultancy for GlaxoSmithKline, Novo Nordisk and Takeda; UK principal investigator for PREDICTIVE post-marketing surveillance study for treatment of type 1 and type 2 diabetes using insulin detemir and insulin aspart funded by Novo Nordisk; conference expenses and/or lecture fees from Aventis, GlaxoSmithKline, Merck Sharp & Dohme Limited, Novo Nordisk and Servier Personal non-pecuniary interests: Officer of the Royal College of Physicians; Member of the Working Lives intercollegiate committee Non-personal pecuniary interests – specific: Hospital department receives funding from Novo Nordisk in connection with the PREDICTIVE study and insulin detemir in pregnancy study
Robert Fraser	No interests declared
Roger Gadsby	Personal pecuniary interests – specific: Adviser to Bristol-Myers Squibb, Colgate-Palmolive, Merck Pharma, Merck Sharp & Dohme Limited, Novo Nordisk, Osaki, Pfizer, Sanofi Aventis and Takeda Personal non-pecuniary interests: Medical adviser to Warwick Diabetes Care, University of Warwick; Chairman of Trustees of Pregnancy Sickness Support, Nuneaton, Warwickshire; Honorary Treasurer of the Primary Care Diabetes Society Non-personal pecuniary interests – specific: Warwick Diabetes Care receives sponsorship for educational programmes from the British In Vitro Diagnostics Association (BIVDA), Eli Lilly, GlaxoSmithKline, Lifescan, Novo Nordisk, Pfizer, Sanofi Aventis and Servier; the Primary Care Diabetes Society receives sponsorship for educational programmes from Eli Lilly, GlaxoSmithKline, Merck Pharma, Novo Nordisk, Roche Diagnostics, Sanofi Aventis, Servier and Takeda

GDG member	Interest
	Non-current interests – previous: Consultancy, conference expenses and/or lecture fees from Bristol-Myers Squibb, GlaxoSmithKline, Merck, Novartis, Novo Nordisk, Roche, Roche Diagnostics, Sanofi Aventis, Servier and Takeda; Warwick Diabetes Care received start-up sponsorship from Aventis, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Lifescan, Novo Nordisk, Owen Mumford, Pfizer and Takeda
Jane Hawdon	Personal non-pecuniary interests: Chair of neonatal working group for the CEMACH Diabetes in Pregnancy Enquiry; adviser and speaker for Baby Friendly Initiative, BLISS and CEMACH
Richard Holt	Personal pecuniary interests – specific: Investigator for insulin aspart and insulin detemir in pregnancy studies funded by Novo Nordisk; conference expenses and/or lecture fees from Eli Lilly and GlaxoSmithKline Personal pecuniary interests – non-specific: Consultancy, lecture fees and educational grants from Astra-Zeneca, Eli Lilly, GlaxoSmithKline, Merck Sharp & Dohme Limited, Novo Nordisk, Roche and Takeda Non-personal pecuniary interests – specific: Investigator for Softsense blood glucose meter in pregnancy study funded by Abbott Laboratories and insulin aspart and insulin detemir in pregnancy studies funded by Novo Nordisk; research funding from GlaxoSmithKline to examine the role of insulin resistance in gestational diabetes Personal non-pecuniary interests: Chair of the Professional Advisory Council of Diabetes UK
Anne Parker	No interests declared
Nickey Tomkins	No interests declared
Stephen Walkinshaw	No interests declared
Jackie Webb	Personal pecuniary interests – specific: Conference/meeting expenses and/or lecture fees from Abbot Diabetes Care, Bayer, Becton and Dickenson, Eli Lilly, GlaxoSmithKline, Lifescan, Menarini, Novartis, Novo Nordisk, Roche Diagnostics, Sanofi Aventis and the Centre for Pharmacy Postgraduate Education, University of Manchester; funded by Novo Nordisk to work on an out-of-hours helpline and to attend related update meetings Personal non-pecuniary interests: Member of Diabetes UK and Royal College of Nursing; participation in CEMACH meetings; attended a meeting of the Management of Diabetes for Excellence (MODEL) group Non-personal pecuniary interests – specific: Adviser on patient education literature for Eli Lilly; adviser on GlucoGel for British BioCell;

GDG member	Interest
	Department Trust fund receives funding to support attendance at conferences, courses, study days, meetings and patient-support events and meetings from Abbot Diabetes Care, Bayer, Becton and Dickenson, Diabetes UK, Eli Lilly, GlaxoSmithKline, Lifescan, Menarini, Novo Nordisk, Roche Diagnostics and Sanofi Aventis; insulin detemir study funded by Novo Nordisk
Saiyyidah Zaidi	No interests declared

B.2 Declarations of interest from guideline development group for updated (2015) guideline

All guideline development group members' interests were recorded on declaration forms provided by NICE. The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. Guideline development group members' interests are listed in this section. Where conflicts were identified, guideline development group members were asked not to participate in the relevant discussions. Details are available from the guideline development group minutes available on the NICE website. Note that the guideline development group chair, members and expert advisers were appointed under NICE's April 2007 Code of Practice for Declaring and Dealing with Conflicts of Interest.

This appendix includes all interests declared on or before 19th November 2014.

Table 2: 2015 guideline development group members' declarations of interest

Guideline development group member	Interest
Rudolf Bilous	Personal pecuniary: Speaker fees from Boehringer Ingelheim, Novo Nordisk and Roche diagnostics (no ongoing links with any of these companies in terms of topics covered by the guideline update); consultancy for Roche diagnostics and Roche Pharma (to advise on a peroxisome proliferator-activated receptor (PPAR) alpha and gamma agonists for type 2 diabetes and renal disease); meeting expenses from Animas (insulin pumps), Boehringer Ingelheim, Johnson and Johnson (insulin pumps); invited to act as Principal Investigator on a study of a new insulin pump being developed by Roche, honorarium and meeting expenses from the Cordelier Research Center (Paris). Personal non-pecuniary: Member of the Medicines and Healthcare products Regulatory Agency (MHRA) Cardiovascular, Diabetes, Renal, Respiratory and Allergy Expert Advisory Group (CDDRAEG) of the Commission on Human Medicines and the MHRA Insulin Use group; guideline development group member for the National Kidney Foundation guideline on chronic kidney disease and diabetic kidney disease; published research on diabetes and pregnancy based on the

Guideline development group member	Interest
	Northern Regional Diabetes Database of the Regional Maternity Survey Office (RMSO); member of data monitoring safety boards of the Adolescent type 1 Diabetes cardio-renal Intervention Trial (AdDIT) and the atrasentan trial (not related to diabetes in pregnancy). Non-personal pecuniary: Department receives funding from Diabetes UK; department participates in a clinical trial on diabetes and hypertension through the Comprehensive Clinical Research Network (CCRN).
Jacqueline Berry	Personal pecuniary: £100 towards Diabetes UK Conference fees for one day admission to the conference from Novo Nordisk. Personal non-pecuniary: Member of the Royal College of Nursing; seconded to King's College London; speaker at a Diabetes UK meeting (sensor-augmented pump therapy in diabetes in pregnancy); Spoke at SETDiG (South East London Diabetes Specialist Nurses about practical management of diabetes in pregnancy). Did not receive payment or expenses.
Anne Dornhorst	Personal pecuniary: Meeting expenses from Reata Pharmaceuticals (clinical trial of bardoxolone methyl; the meetings were also funded by Eli Lilly) and from European Association for the Study of Diabetes (EASD). Personal non-pecuniary: Seeking funding from Boehringer Ingelheim and Eli Lilly for a randomised controlled trial (RCT) of asymptomatic hypoglycaemia in people with type 2 diabetes and chronic kidney disease using glicazide (a sulfonylurea) and linagliptin (a dipeptidyl peptidase-4 (DPP4) inhibitor); honoraria for speaking about diabetic renal guidelines at North West Thames consultants and general practitioners (GPs) meetings funded by Boehringer Ingelheim and Eli Lilly; honorarium and expenses for speaking about diabetes in pregnancy at a diabetes symposium in Bristol funded by NovoNordisk. Personal family: Husband is employed by Quintiles, which undertakes clinical trials for pharmaceutical companies (involves contact with scientific advisors at various companies). Non-personal pecuniary: Co-applicant for funding from the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme for research relating to hyperglycaemia in pregnancy Personal non-pecuniary:

Guideline development group member	Interest
	Board member of the NovoNordisk Foundation and the International Association of Diabetes and Pregnancy Study Groups (IADPSG).
Stacia Smales Hill	No interest declared
Aderonke Kuti	No interest declared
Michael Maresh	Personal pecuniary: Speaker expenses from Diabetes UK; expenses to attend annual steering group re HAPO follow up study funded by NIH (US). Non-personal pecuniary: Department is funded by Diabetes UK to develop a test for fetal wellbeing in pregnancies complicated by type 1 diabetes (the test was not available during development of the guideline); department funded by Bridges for an RCT using a DVD for women with gestational diabetes; department funded by the National Institutes of Health (NIH), USA, for a follow-up of women and children from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study; co-applicant for funding from the NIHR HTA programme for research relating to hyperglycaemia in pregnancy. Personal non-pecuniary: Paper published on Glycemic targets in the second and third trimester of pregnancy for women with type 1 diabetes in Diabetes care Spoke about non-applicability of the World Health Organization diagnostic criteria for gestational diabetes, advantages of centralisation of care for type 1 diabetes, individualisation of decision making for timing and mode of birth, and results of the HAPO study. Paper accepted for publication on “Stillbirth rates in pre-gestational diabetic women” in Diabetic Medicine; Papers published on Timing of delivery and stillbirth rate in type 1 & 2 diabetes and Post natal follow up of GDM – full GTT or fasting glucose; is submitting a paper on Perinatal outcomes and Glycaemic control in pregnancy.
Judy Shakespeare	No interest declared
Katharine Stanley	Personal pecuniary: Honorarium and meeting expenses from Diabetes UK. Non-personal pecuniary: Department received a midwifery research grant from NovoNordisk.
Elizabeth Stenhouse	Personal pecuniary: Received payment for a manuscript in Practical Diabetes.
Diane Todd	Personal non-pecuniary: Member of the Diabetes UK conference organising committee, the NHS Diabetes Pregnancy Audit Group and Diabetes in Pregnancy Network Steering Group.

Guideline development group member	Interest
	Personal pecuniary: Novonordisk paid registration fee for Diabetes UK annual professional conference 5-7 March 2014.

B.3 Declarations of interest from expert advisors

Table 3: Expert advisors' declarations of interest

Expert	Interest
Rhona Hughes	Personal non-pecuniary: Published research on comparison of American Diabetes Association and the American College of Obstetricians and Gynecologists Guidelines with the UK National Institute for Health and Clinical Excellence guidelines; published research on the cost-effectiveness of different screening strategies for gestational diabetes.
William Lamb	Personal non-pecuniary: Volunteer for Diabetes UK, JDRF, charity fund-raising;Professional member of Diabetes UK Member British Society of Endocrinology and Diabetes Member of International Society for Paediatric and Adolescent Diabetes Member of Association Of Children's Diabetes Clinicians Associate editor Clinical Diabetes Attended a variety of diabetes and paediatric related meetings which have attracted varying amounts of sponsorship from a very wide variety of sources
Chris Patterson	Personal family: Spouse holds stock in GlaxoSmithKline (GSK) Plc

B.4 Declarations of interest from NCC-WCH staff

Table 4: NCC-WCH staff's declarations of interest

NCC-WCH staff member	Interest
Sarah Bailey	No interest declared
Frauke Becker	No interest declared
Shona Burman-Roy	No interest declared
Anne Carty	No interest declared
Ella Fields	No interest declared
Paul Jacklin	Personal non-pecuniary: Published research on comparison of American Diabetes Association and the American College of Obstetricians and Gynecologists Guidelines with the UK National Institute for Health and Clinical Excellence guidelines; published

NCC-WCH staff member	Interest
	research on the cost-effectiveness of different screening strategies for gestational diabetes.
David James	No interest declared
Juliet Kenny	No interest declared
Rosalind Lai	No interest declared
Hugh McGuire	No interest declared
Paul Mitchell	No interest declared
Moira Mugglestone	Non-personal pecuniary: Co-applicant for funding from the NIHR HTA programme for research relating to hyperglycaemia in pregnancy.
Nitara Prasannan	No interest declared
Cristina Visintin	No interest declared

Appendix C: List of review questions

Number	Review question
Preconception care	
1	What is the effectiveness of oral oestrogen-containing contraceptives in women with diabetes compared with women without diabetes?
2	What is the effectiveness of oral progestogen-containing contraceptives in women with diabetes compared with women without diabetes?
3	What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1 or type 2 diabetes who are planning pregnancy?
4	What are the target ranges for blood glucose in women with type 1 or type 2 diabetes who are planning pregnancy?
5	What is the target value for haemoglobin A1c (HbA1c) in women with type 1 or type 2 diabetes who are planning pregnancy?
Gestational diabetes	
6	What is the effectiveness of the following procedures in detecting glucose intolerance in the first trimester diagnosed using a 75g OGTT: • risk factor based screening • urine test for glycosuria • random blood glucose test • 50 g oral glucose challenge test • fasting blood glucose test • HbA1c test?
7	What is the effectiveness of the following procedures in detecting glucose intolerance in the second trimester diagnosed using a 75g OGTT: • risk factor based screening • urine test for glycosuria • random blood glucose test • 50 g oral glucose challenge test • fasting blood glucose test • HbA1c test?
8	Which criteria should be used to diagnose gestational diabetes using the 75 g oral glucose tolerance test (OGTT): • World Health Organization (WHO) or • International Association of Diabetes and Pregnancy Study Groups (IADPSG)?
9	What is the effectiveness of the following interventions (alone or in combination) in women with gestational diabetes: • non-pharmacological interventions (diet and/or exercise) • pharmacological interventions (metformin, glibenclamide and insulin)?
Antenatal care	
10	What is the effectiveness of blood glucose monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?
11	What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1, type 2 or gestational diabetes during pregnancy?
12	What are the target ranges for blood glucose in women with type 1, type 2 or gestational diabetes during pregnancy?
13	What is the effectiveness of HbA1c monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?
14	What is the target value for HbA1c in women with type 1, type 2 or gestational diabetes during pregnancy?

Number	Review question
15	What is the effectiveness of continuous glucose monitoring in pregnant women with diabetes compared with intermittent capillary blood glucose monitoring?
16	What is the effectiveness of specialist teams for pregnant women with diabetes?
Intrapartum care	
17	What is the gestational age-specific risk of intrauterine death in pregnancies with type 1, type 2 or gestational diabetes, and the optimal timing of birth?
Postnatal care	
18	What is the effectiveness of the following tests in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care): • fasting plasma glucose test • HbA1c test • 75 g OGTT?
19	What is the optimal timing of postnatal testing in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care)?

Appendix D: Review protocols

D.1 Oral contraceptives containing oestrogen and/or progestogen

Questions 1 and 2		
Existing recommendation (s) in 2008 guideline	Women with diabetes who are planning to become pregnant should be advised: • that the risks associated with pregnancies complicated by diabetes increase with the duration of diabetes • to use contraception until good glycaemic control (assessed by HbA_{1c})† has been established • that glycaemic targets, glucose monitoring, medications for diabetes (including insulin regimens for insulin-treated diabetes) and medications for complications of diabetes will need to be reviewed before and during pregnancy • that additional time and effort is required to manage diabetes during pregnancy and that there will be frequent contact with healthcare professionals. Women should be given information about the local arrangements for support, including emergency contact numbers. † Diabetes Control and Complications Trial (DCCT)-aligned haemoglobin A_{1c} (HbA_{1c}) test.	
Review questions for update	What is the effectiveness of oral oestrogen-containing contraceptives in women with diabetes compared with women without diabetes? What is the effectiveness of oral progestogen-containing contraceptives in women with diabetes compared with women without diabetes?	NCC-WCH technical team to note alternative spelling of progestogen is progestogen – NICE style is to use progestogen, and this spelling should be used in all documents, even if source articles use the spelling progestogen (the only exception is the full guideline reference list where the titles of cited articles should match the wording in the source publications).
Objectives	To determine whether the use of oral contraceptives containing oestrogen and/or progestogen is associated with any risks in women with pre-existing (type 1 or type 2) diabetes, especially those with vascular complications of diabetes. Risks of interest include the risk of pregnancy despite contraceptive use, and the risk of adverse effects in the woman as a result of using the contraceptives. Since all oral oestrogen-	There is existing NICE guidance on the topic of long-acting reversible contraception (Clinical Guideline 30), which includes recommendations about certain forms of contraception not being contraindicated in

Questions 1 and 2		
	containing contraceptives also contain progestogen, the review questions can be interpreted as follows. What is the effectiveness of oral combined oestrogen and progestogen contraceptives in women with diabetes compared with women without diabetes? What is the effectiveness of oral progestogen-only contraceptives in women with diabetes compared with women without diabetes? The guideline development group agreed that the evidence identified in the searches for the above questions should also be used to evaluate the risk of adverse effects of using oral contraceptives in women with diabetes compared with women with diabetes using other forms of contraception, or compared with women with diabetes using no contraception. Where the evidence allows it, the systematic review will include comparison of effectiveness according to: • whether the woman has type 1 diabetes or type 2 diabetes • whether the woman does or does not have diabetes-related complications • the dosage of oestrogen and/or progestogen.	women with diabetes The UK Medical Eligibility Criteria for Contraceptive Use (UKMEC 2009, available at http://www.fsrh.org/pdfs/UKMEC2009.pdf) also provides guidance that may assist the guideline development group in formulating recommendations.
Language	English	
Study design	• Systematic reviews • Randomised controlled trials • Comparative observational studies (cohort and case-control studies)	
Status	Published articles (no limitation on year of publication)	The topic of whether oral contraceptives containing oestrogen and/or progestogen are effective in women with diabetes was not addressed in the 2008 guideline, and so the search should not be restricted by year of publication. However, studies relating to use of a 50 microgram dose of ethinyloestradiol should be excluded because this dose is not currently used in contraceptive practice.
Population	Women with and without type 1 or type 2 diabetes wishing to use contraception	The population should be interpreted as being broad enough to include young women wishing to use contraception (there

Questions 1 and 2		
		is no age limit on this search).
Intervention or index test	Oral contraceptives containing oestrogen and progestogen Oral contraceptives containing progestogen only	Systematic search to include the terms: • ethinyloestradiol, mestranol and oestradiol (oestrogens) • estradiol as a synonym for oestradiol • dienogest, desogestrel, etynodiol, gestodene, levonorgestrel, norethisterone, norgestimate and progesterone (progestogens) • progestagen as a synonym for progestogen (see notes above)
Comparator or reference standard	Main comparisons will be between: women with diabetes using oral contraceptives and women without diabetes using oral contraceptives women with diabetes using oral contraceptives and women with diabetes not using oral contraceptives Consider subgroup analyses by: • type of diabetes (type 1 or type 2) • presence of vascular disease (micro- and macrovascular) • dosage of oestrogen and/or progestogen • age • body mass index • smoking	
Clinical outcomes	For the comparison of women with diabetes using oral contraceptives and women without diabetes using oral contraceptives (to document the risk of pregnancy): Pregnancy rate (preferably using the Pearl Index) For the comparison of women with diabetes using oral contraceptives and women with diabetes not using oral contraceptives (to document the risk of adverse effects): • Worsening of retinopathy and/or nephropathy (as indicators of severity of diabetic microvascular disease) • Change in HbA_{1c} (as an indicator of glycaemic control)	The guideline development group selected up to 7 outcomes for presentation in GRADE, plus mortality in the woman or baby if relevant. For this question, mortality in the woman was prioritised as an important adverse event to consider. The NICE long-acting reversible

Questions 1 and 2		
	• Incidence of dyslipidaemia (also an indicator of glycaemic control) • Venous thromboembolic disease • Arterial thromboembolic disease (as an indicator of macrovascular disease) • Hypertension • Mortality	contraception guideline (clinical guideline 30) includes evidence for pregnancy rate based on the Pearl Index. The guideline development group noted that neuropathy would be difficult to evaluate in studies with short-term follow-up, and so it was not prioritised as an outcome. The guideline development group also noted that hypoglycaemia is unlikely to occur as a result of using oral hormonal contraceptives because the homeones would tend to exacerbate hyperglycaemia, and so it was not prioritised as an outcome.
Health economic outcomes	These questions were not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	• Exclude results relating to use of a 50 microgram dose of ethinyloestradiol (see note above) • Exclude parenteral (including 'depot') administration of progestogen (medroxyprogesterone, norethisterone and etonogestrel) • Exclude intra-uterine devices for administration of progestogen (levonorgestrel)	NCC-WCH to outline for the guideline development group what is identified in the search results to inform completion of the review. NCC-WCH to note that subgroup analysis for the age group 14-24 years would be useful if the evidence identified for inclusion allows this.
Search strategies	See separate document	
Review strategies	• Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.2 Ketone monitoring in the preconception and antenatal periods

Questions 3 and 11		
Existing recommend-ations in 2008 guideline	Women with type 1 diabetes who are planning to become pregnant should be offered ketone testing strips and advised to test for ketonuria or ketonaemia if they become hyperglycaemic or unwell. Women with type 1 diabetes who are pregnant should be offered ketone testing strips and advised to test for ketonuria or ketonaemia if they become hyperglycaemic or unwell.	
Review questions for update	What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1 or type 2 diabetes who are planning pregnancy? What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1, type 2 or gestational diabetes during pregnancy?	There are two separate review questions but the difference between them relates only to the timing at which monitoring is performed, and they will probably be addressed via a single search for evidence. These questions are solely about self-monitoring of ketones (not monitoring of ketones by healthcare professionals during clinic visits).
Objectives	To determine the effectiveness of ketone monitoring in: • women with pre-existing diabetes who are planning pregnancy • women with pre-existing diabetes or gestational diabetes during pregnancy The aim of ketone monitoring is early detection of impending or actual diabetic ketoacidosis, which is associated with poor maternal and fetal or neonatal outcomes. Both reviews should consider: • frequency of monitoring • maternal and fetal or neonatal outcomes associated with specific ketone targets or concentrations Urine ketone monitoring is the historical comparator, and is recommended in the 2008 guideline as an alternative to blood ketone monitoring	
Language	English	

Questions 3 and 11		
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational studies (cohort and case-control studies)	Although RCTs are unlikely, there may be observational studies comparing outcomes of different monitoring strategies (although there may be very little evidence at all).
Status	Articles indexed after the searches for the 2008 guideline were completed	This is an update of a review conducted for the 2008 guideline, although no evidence was identified for inclusion in the 2008 guideline (see the questions 'How should blood glucose and ketones be monitored in the preconception period?' and 'How should blood glucose and ketones be monitored during pregnancy?' in the 2008 guideline).
Population	Women with type 1 or type 2 diabetes who are planning pregnancy Pregnant women with type 1 diabetes, type 2 diabetes or gestational diabetes	The populations differ according to the timing of monitoring (before or during pregnancy) in the two questions.
Intervention or index test	Blood ketone monitoring	Ketoacidosis, ketosis and pregnancy may be useful as search terms.
Comparator or reference standard	Urine ketone monitoring	
Outcomes	Maternal • Preterm birth (birth before 37^{+0} weeks' gestation; take dichotomous or continuous data) • Non-routine hospital contact or assessment for ketosis (ketonaemia or ketonuria, however defined), including phone contact • Hospital admission for diabetic ketoacidosis • Maternal satisfaction Fetal/Neonatal • Mortality - perinatal and neonatal death • Neonatal intensive care unit length of stay greater than 24 hours	The guideline development group selected up to 7 outcomes for presentation in GRADE, plus mortality in the woman or baby if relevant. For these questions, maternal mortality in association with diabetic ketoacidosis was recognised as a possibility but maternal mortality is unlikely to occur often, and so it was not prioritised. Even if these questions were prioritised for health economic analysis, the risk of perinatal or neonatal death with diabetic ketoacidosis would be more likely to influence the cost effectiveness of monitoring than would the risk of maternal mortality, and so the omission of maternal mortality is unlikely to present problems during any health

Questions 3 and 11		
		economic analysis Also, shoulder dystocia was recognised as being an important outcome, but because it might be defined differently in different studies it was not prioritised as an outcome. If shoulder dystocia is needed for health economic analysis it may be necessary to extrapolate from large-for-gestational-age (for example, using data from CEMACH). Non-routine hospital contact or assessment for ketosis is specified as an outcome because pregnant women with diabetes will be tested routinely for ketones.
Health economic outcomes	These questions were not selected as priorities for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	
Search strategies	See separate document	It is likely that a single search will be conducted to cover both review questions.
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.3 Blood glucose target values in the preconception and antenatal periods

Questions 4 and 12		
Existing recommendations in 2008 guideline	Women with diabetes who are planning to become pregnant should be advised: • that the risks associated with pregnancies complicated by diabetes increase with the duration of diabetes • to use contraception until good glycaemic control (assessed by HbA_{1c})† has been established • that glycaemic targets, glucose monitoring, medications for diabetes (including insulin regimens for insulin-treated diabetes) and medications for complications of diabetes will need to be reviewed before and during pregnancy • that additional time and effort is required to manage diabetes during pregnancy and that there will be frequent contact with healthcare professionals. Women should be given information about the local arrangements for support, including emergency contact numbers. Individualised targets for self-monitoring of blood glucose should be agreed with women with diabetes in pregnancy, taking into account the risk of hypoglycaemia. Recommendations for target ranges for blood glucose during pregnancy If it is safely achievable, women with diabetes should aim to keep fasting blood glucose between 3.5 and 5.9 mmol/litre and 1 hour postprandial blood glucose below 7.8 mmol/litre during pregnancy. † Diabetes Control and Complications Trial (DCCT)-aligned haemoglobin A1c (HbA1c) test.	HbA1c is haemoglobin A1c
Review questions for update	What are the target ranges for blood glucose in women with type 1 or type 2 diabetes who are planning pregnancy? What are the target ranges for blood glucose in women with type 1, type 2 or gestational diabetes during pregnancy?	Note that there are six inter-related review questions about the effectiveness of monitoring HbA1c and blood glucose during pregnancy, and target values or ranges for HbA1c and blood glucose before and during pregnancy (questions 3, 4, 10, 11, 12 and 13).

Questions 4 and 12		
		The six questions will probably be addressed via a single search for evidence. The two questions addressed in this protocol differ only in the timing at which targets apply (before or during pregnancy).
Objectives	To define clinically important and achievable blood glucose target ranges in: women with type 1 or type 2 diabetes who are planning pregnancy pregnant women with type 1, type 2 or gestational diabetes To consider whether target ranges in the preconception period and/or during pregnancy should be aligned with target ranges that apply outside pregnancy (as defined in the NICE guidelines for type 1 diabetes in adults, type 2 diabetes in adults, and type 1 and type 2 diabetes in children and young people) The review relating to the target range for blood glucose in women planning pregnancy should include consideration of pregnancy outcomes (especially congenital abnormality rates) associated with particular blood glucose values in and around the preconception period Both reviews should consider: • the trade-off between the increased risk of hypoglycaemia with tighter glycaemic control and the benefits of improved pregnancy outcomes • setting individualised targets • setting different targets for type 1, type 2 and gestational diabetes to reflect different risks associated with the different types of diabetes	Liaison with the guideline development group s and/or technical teams for the NICE guidelines on type 1 diabetes in adults, type 2 diabetes in adults, and type 1 and type 2 diabetes in children and young people will be important for aligning prepregnancy target values and ranges for HbA1c and blood glucose, or justifying the need for different targets in the different guidelines.
Language	English	
Study design	• Systematic reviews • Randomised controlled trials (RCTs) • Comparative observational studies (cohort and case-control studies) • Non-comparative studies	Although RCTs evaluating different degrees of control are unlikely, there may be observational studies relating different degrees of control to clinical outcomes, preferably through predictive accuracy measures. Other relevant comparative study designs would be those which report

Questions 4 and 12		
		associations between blood glucose values and pregnancy outcomes, such as the Hyperglycemia and Pregnancy Outcome (HAPO) study. Non-comparative studies will be considered for inclusion only if no comparative studies are identified for inclusion.
Status	Articles indexed after the searches for the 2008 guideline were completed	This is an update of two reviews conducted for the 2008 guideline. Studies included in the 2008 guideline will need to be considered against the current protocol and data will be extracted for presentation in evidence profiles where relevant (see the questions 'What are the target ranges for blood glucose in the preconception period?' and 'What are the target ranges for blood glucose during pregnancy?' in the 2008 guideline).
Population	Women with type 1 or type 2 diabetes who are planning pregnancy Pregnant women with type 1 diabetes, type 2 diabetes or gestational diabetes	The populations differ according to the timing at which targets apply (before or during pregnancy) in the two questions.
Intervention or index test	Specified target ranges for blood glucose or blood glucose values achieved (recorded) in women planning pregnancy Specified target values for blood glucose or blood glucose values achieved (recorded) in women with type 1 diabetes, type 2 diabetes or gestational diabetes during pregnancy	It may be difficult to disentangle effects (or associations) with blood glucose targets for the preconception period and during pregnancy. In RCTs look for intention-to-treat analysis based on targets set (rather than post hoc analysis based on values achieved) and downgrade retrospective analyses based on what was achieved in groups randomised to treatment. Include highest quality evidence available for each type of diabetes when considered separately, and extend to lower levels for any types of diabetes for which the highest-quality evidence is not available. NCC-WCH to refine approach to inclusion/exclusion in

Questions 4 and 12		
		consultation with guideline development group when the results of search are available.
Comparator or reference standard	Comparisons to be made between outcomes according to target ranges for blood glucose and/or blood glucose values achieved (recorded)	
Clinical outcomes	For the question relating to targets when planning pregnancy Maternal outcomes: • HbA1c values in the first trimester • Hypoglycaemic episodes before pregnancy or in the first trimester • Spontaneous miscarriage • Acceptability of targets (covers concordance and implications of hypoglycaemia) Neonatal outcomes: • Any congenital abnormality, regardless of gestational age *Mortality For the question relating to targets during pregnancy Maternal outcomes: • **Mode of birth (spontaneous vaginal, operative vaginal, caesarean section (elective or emergency)) • Pre-eclampsia • HbA1c values at any time during pregnancy • Hypoglycaemic episodes at any time during pregnancy Neonatal outcomes: • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • Neonatal intensive care unit length of stay greater than 24 hours • Shoulder dystocia (as a specific example of birth trauma) • *Mortality	The guideline development group selected up to 7 outcomes plus mortality (where relevant) for each review question Evidence tables should document: the types of congenital abnormality and how many resulted in planned termination of pregnancy in the question relating to targets when planning pregnancy the indication for mode of birth (if reported) in the question relating to targets during pregnancy any treatment administered in response to monitoring in the question relating to targets during pregnancy the definition of maternal hypoglycaemic episodes The guideline development group noted that: presence of pre-eclampsia was of interest for the question on targets during pregnancy, and the studies should provide data on this there would be some overlap between neonatal intensive care unit length of stay greater than 24 hours and presence of neonatal hypoglycaemia neonatal hypoglycaemia was less important than the other outcomes selected for the question relating to targets during pregnancy, although it may be important in defining future research priorities presence of congenital abnormality was not a

Questions 4 and 12		
	*The definition of mortality includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth) **If neither of these outcomes is available, onset of labour (spontaneous, induced, or no labour) should be considered and the GDG advised about available evidence	priority for the question relating to targets during pregnancy because such abnormalities arise very early in pregnancy
Health economic outcomes	These questions were not prioritised for health economic analysis	This question will not be a priority for health economic analysis even if the effectiveness of blood glucose monitoring is prioritised
Other criteria for inclusion/ exclusion of studies	None	
Search strategies	See separate document	NCC-WCH technical team to consider whether one search across the two questions addressed in this protocol, or even across all six questions relating to target values and ranges and monitoring during pregnancy, would be appropriate
Review strategies	• Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.4 HbA1c target values in the preconception and antenatal periods

Questions 5 and 14		
Existing recommendations in 2008 guideline	Women with diabetes who are planning to become pregnant should be advised: • that the risks associated with pregnancies complicated by diabetes increase with the duration of diabetes • to use contraception until good glycaemic control (assessed by HbA1c)† has been established • that glycaemic targets, glucose monitoring, medications for diabetes (including insulin regimens for insulin-treated diabetes) and medications for complications of diabetes will need to be reviewed before and during pregnancy • that additional time and effort is required to manage diabetes during pregnancy and that there will be frequent contact with healthcare professionals. Women should be given information about the local arrangements for support, including emergency contact numbers. If it is safely achievable, women with diabetes who are planning to become pregnant should aim to maintain their HbA1c below 6.1%. Women should be reassured that any reduction in HbA1c towards the target of 6.1% is likely to reduce the risk of congenital malformations. Women with diabetes whose HbA1c is above 10% should be strongly advised to avoid pregnancy. Recommendations for target ranges for blood glucose during pregnancy HbA1c should not be used routinely for assessing glycaemic control in the second and third trimesters of pregnancy. † Diabetes Control and Complications Trial (DCCT)-aligned haemoglobin A_{1c} (HbA1c) test.	HbA1c is haemoglobin A_{1c}. The 2008 guideline did not include targets for HbA1c during pregnancy because the guideline recommended that HbA1c should not be used routinely for assessing glycaemic control in the second and third trimesters (note that there were no recommendations that explicitly recommended what to do in terms of HbA1c monitoring in the first trimester). The reasons for reconsidering targets for HbA1c in the update include a need to re-evaluate the effectiveness of HbA1c monitoring during pregnancy, which is being addressed by a separate review question (question 10). Setting targets for HbA1c during pregnancy will only become relevant if the guideline development group concludes that monitoring HbA1c during pregnancy is effective – the guideline development group may, however, need to consider the evidence identified for inclusion in this question to reach a conclusion (for example, if no evidence is identified for the effectiveness of pre-specified monitoring strategies, there may still be evidence relating pregnancy outcomes to HbA1c values achieved or recorded during pregnancy that would support setting targets and, therefore, specifying a monitoring strategy)
Review questions for update	What is the target value for HbA1c in women with type 1 or type 2 diabetes who are planning pregnancy? What is the target value for HbA1c in women with type 1, type 2 or gestational diabetes during pregnancy?	Note that there are six inter-related review questions about the effectiveness of monitoring HbA1c and blood glucose during pregnancy, and target values or ranges for

Questions 5 and 14		
		HbA1c and blood glucose before and during pregnancy (questions 3, 4, 10, 11, 12 and 13). The six questions will probably be addressed via a single search for evidence. The two questions addressed in this protocol differ only in the timing at which targets apply (before or during pregnancy).
Objectives	To define clinically important and achievable HbA1c target values in: women with type 1 or type 2 diabetes who are planning pregnancy pregnant women with type 1, type 2 or gestational diabetes To consider whether target values in the preconception period and/or during pregnancy should be aligned with target values that apply outside pregnancy (as defined in the NICE guidelines for type 1 diabetes in adults, type 2 diabetes in adults, and type 1 and type 2 diabetes in children and young people) The review relating to the target value for HbA1c in women planning pregnancy should include consideration of pregnancy outcomes (especially congenital abnormality rates) associated with particular HbA1c values in and around the preconception period The review relating to the target value for HbA1c during pregnancy should include consideration of the rate of reduction of HbA1c (towards a target value) in women who enter pregnancy with very high values (for example, HbA1c above 10%) Both reviews should consider:* • the trade-off between the increased risk of hypoglycaemia with tighter glycaemic control and the benefits of improved pregnancy outcomes • setting individualised targets • setting different targets for type 1, type 2 and gestational diabetes to reflect different risks associated with the different types of diabetes	Liaison with the guideline development group s and/or technical teams for the NICE guidelines on type 1 diabetes in adults, type 2 diabetes in adults, and type 1 and type 2 diabetes in children and young people will be important for aligning prepregnancy target values and ranges for HbA1c and blood glucose, or justifying the need for different targets in the different guidelines. * Targets for HbA1c should take account of physiological changes (reductions and sometimes later increases) in HbA1c during pregnancy, regardless of diabetes (document in evidence tables whether or not included studies have adapted normal ranges to take account of pregnancy, for example, specific to a particular trimester).

Questions 5 and 14		
Language	English	
Study design	• Systematic reviews • Randomised controlled trials (RCTs) • Comparative observational studies (cohort and case-control studies) • Non-comparative studies	Although RCTs evaluating different degrees of control are unlikely, there may be observational studies relating different degrees of control to clinical outcomes, preferably through predictive accuracy measures. Other relevant comparative study designs would be those which report associations between blood glucose values and pregnancy outcomes, such as the Hyperglycemia and Pregnancy Outcome (HAPO) study. Non-comparative studies will be considered for inclusion only if no comparative studies are identified for inclusion. Include highest quality evidence available for each type of diabetes when considered separately, and extend to lower levels for any types of diabetes for which the highest-quality evidence is not available. NCC-WCH to refine approach to inclusion/exclusion in consultation with guideline development group when the results of search are available.
Status	Articles indexed after the searches for the 2008 guideline were completed	This is an update of two reviews conducted for the 2008 guideline. Studies included in the 2008 guideline will need to be considered against the current protocol and data will be extracted for presentation in evidence profiles where relevant (see the questions 'What are the target ranges for blood glucose in the preconception period?' and 'What are the target ranges for blood glucose during pregnancy?' in the 2008 guideline; these questions were broad enough to cover targets for HbA1c).

Questions 5 and 14		
Population	• Women with type 1 or type 2 diabetes who are planning pregnancy • Pregnant women with type 1 diabetes, type 2 diabetes or gestational diabetes	The populations differ according to the timing at which targets apply (before or during pregnancy) in the two questions.
Intervention or index test	• Specified target values for HbA1c or HbA1c values achieved (recorded) in women planning pregnancy • Specified target values for HbA1c or HbA1c values achieved (recorded) in women with type 1 diabetes, type 2 diabetes or gestational diabetes during pregnancy	It may be difficult to disentangle effects (or associations) with HbA1c targets for the preconception period and during pregnancy.
Comparator or reference standard	Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded)	
Clinical outcomes	For the question relating to targets when planning pregnancy Maternal outcomes: • Hypoglycaemic episodes before pregnancy or in the first trimester • Spontaneous miscarriage • Acceptability of targets (covers concordance and implications of hypoglycaemia) Neonatal outcomes: • Any congenital abnormality, regardless of gestational age • *Mortality For the question relating to targets during pregnancy Maternal outcomes: • **Mode of birth (spontaneous vaginal, operative vaginal, caesarean section (elective or emergency)) • Pre-eclampsia • Hypoglycaemic episodes at any time during pregnancy Neonatal outcomes: • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms;	The guideline development group selected up to 7 outcomes plus mortality (where relevant) for each review question Evidence tables should document: the types of congenital abnormality and how many resulted in planned termination of pregnancy in the question relating to targets when planning pregnancy the indication for mode of birth (if reported) in the question relating to targets during pregnancy any treatment administered in response to monitoring in the question relating to targets during pregnancy the definition of maternal hypoglycaemic episodes. The guideline development group noted that: presence of pre-eclampsia was of interest for the question on targets during pregnancy, and there should be data on this there would be some overlap between neonatal intensive care unit length of stay greater than 24 hours and presence of

Questions 5 and 14		
	dichotomous data preferred) • Neonatal intensive care unit length of stay greater than 24 hours • Shoulder dystocia (as a specific example of birth trauma) • Neonatal hypoglycaemia (however defined) • *Mortality *The definition of mortality includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth) **If neither of these outcomes is available, onset of labour (spontaneous, induced, or no labour) should be considered and the guideline development group advised about available evidence	neonatal hypoglycaemia neonatal hypoglycaemia was more important for the question relating to targets during pregnancy than the presence of neonatal hyperinsulinaemia or hyper C-peptide-aemia, although the latter may be important in defining future research priorities presence of congenital abnormality was not a priority for the question relating to targets during pregnancy because such abnormalities arise very early in pregnancy.
Health economic outcomes	These questions were not prioritised for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	
Search strategies	See separate document	NCC-WCH technical team to consider whether one search across the two questions addressed in this protocol, or even across all six questions relating to target values and ranges and monitoring during pregnancy, would be appropriate.
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.5 Screening for gestational diabetes in the first trimester

Question 6		
	Screening for gestational diabetes using fasting plasma glucose, random blood glucose, glucose challenge test and urinalysis for glucose should not be undertaken. The 2 hour 75 g oral glucose tolerance test (OGTT) should be used to test for gestational diabetes and diagnosis made using the criteria defined by the World Health Organization. Women who have had gestational diabetes in a previous pregnancy should be offered early self-monitoring of blood glucose or OGTT at 16–18 weeks, and a further OGTT at 28 weeks if the results are normal. Women with any of the other risk factors for gestational diabetes should be offered an OGTT at 24–28 weeks.	OGTT is oral glucose tolerance test The recommendations listed are from the NICE 2008 routine antenatal care guideline. This guideline update covers first and second-trimester screening for gestational diabetes, and the routine antenatal care guideline will be updated in accordance with any changes to the recommendations listed
Review question for update	What is the effectiveness of the following procedures in detecting glucose intolerance in the first trimester diagnosed using a 75g OGTT: • risk factor based screening • urine test for glycosuria • random blood glucose test • 50 g oral glucose challenge test • fasting blood glucose test • HbA1c test	The term glucose intolerance covers: • impaired fasting glucose (IFG) • impaired glucose tolerance (IGT) and diabetes.
Objectives	To examine if a 'test' or combination of 'tests' in the first trimester identifies women with gestational diabetes Whether this identification improves the outcome	A 'test' is shorthand for 'screening procedure' as defined above. First trimester is defined as up to and including 13 weeks + 6 days
Language	English	
Study design	• Systematic reviews • Randomised controlled trials (RCTs) • Comparative observational cohort studies (of more than one of these tests in same population would be ideal) • Observational cohort studies (of tests in different populations only to be considered if no comparative data available	
Status	Published articles (no limitation on year of publication)	
Population	Pregnant women in the first trimester who do not have a pre-existing diagnosis of diabetes	Ideally the whole population should have a 75g OGTT to determine the predictive

Question 6		
		accuracy of the individual screening tests for an abnormal OGTT but that is unlikely to be done.
Intervention or index test	• Risk factor based screening (which could be either risk factor screening alone to predict gestational diabetes, or risk factor plus a subsequent biochemical test to predict gestational diabetes) • Urine test for glycosuria • Random blood glucose test • 50 g oral glucose challenge test • Fasting blood glucose test • HbA1c test	The risk factors detailed in the 2008 diabetes in pregnancy guideline are : • body mass index (BMI) above 30 kg/m2 previous macrosomic baby weighing 4.5 kg or above • previous gestational diabetes) • family history of diabetes (first-degree relative with diabetes) • 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).
Comparator or reference standard	75g OGTT	Interpreted using the World Health Organization (WHO) 1999 or International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria, or diagnostic criteria with thresholds equivalent to WHO 1999.
Clinical outcomes	Incidence of gestational diabetes • Comparative incidence of diagnosis of gestational diabetes in the first and second trimesters Diagnostic test accuracy • Sensitivity, specificity and likelihood ratios for diagnosis of gestational diabetes Maternal outcomes • Mode of birth: spontaneous vaginal , operative vaginal, caesarean section (elective/emergency)	

Question 6		
	• Treatment such as diet, oral hypoglycaemic agents and/or insulin • Acceptability/take-up of testing regimen Neonatal outcomes • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • All mortality - includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth) • Neonatal intensive care unit length of stay (greater than 24 hours) • Shoulder dystocia (no permanent damage, neurological injury (brachial plexus and cerebral palsy)	
Health economic outcomes	Prevalence of gestational diabetes in the first trimester Diagnostic test accuracy • Sensitivity, specificity Neonatal outcomes • Stillbirth, shoulder dystocia, perinatal death, birth trauma ('serious perinatal complications') Maternal outcomes • From the clinical outcomes above, although these predominantly affect 'downstream costs' rather than health-related quality of life Health-related quality of life • EQ5D, SF36	
Other criteria for inclusion/ exclusion of studies	Exclusions Studies comparing incidence of gestational diabetes by applying different diagnostic criteria without presenting relevant diagnostic data or outcomes data Studies where the screening test (e.g. glucose challenge test) is examined for prediction of maternal/neonatal outcomes	
Search strategies	See separate document	A single search will be conducted for the questions relating to first- and second-

Question 6		
		trimester screening.
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	Note that the QUADAS methodology checklist for diagnostic test accuracy studies (NICE guidelines manual January 2009) has been used for this question for consistency with the question relating to diagnosis of gestational diabetes. All other aspects of the review are consistent with the 2012 edition of the manual.
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.6 Screening for gestational diabetes in the second trimester

Question 7		
Existing recommendation(s) in 2008 guideline	Screening for gestational diabetes using fasting plasma glucose, random blood glucose, glucose challenge test and urinalysis for glucose should not be undertaken. The 2 hour 75 g oral glucose tolerance test (OGTT) should be used to test for gestational diabetes and diagnosis made using the criteria defined by the World Health Organization. Women who have had gestational diabetes in a previous pregnancy should be offered early self-monitoring of blood glucose or OGTT at 16–18 weeks, and a further OGTT at 28 weeks if the results are normal. Women with any of the other risk factors for gestational diabetes should be offered an OGTT at 24–28 weeks.	OGTT is oral glucose tolerance test The recommendations listed are from the NICE 2008 routine antenatal care guideline. This guideline update covers first and second-trimester screening for gestational diabetes, and the routine antenatal care guideline will be updated in accordance with any changes to the recommendations listed Screening in the first trimester was not recommended in the 2008 antenatal care guideline, but the recommendations listed may change depending on outcome of this review
Review question for update	What is the effectiveness of the following procedures in detecting glucose intolerance in the second trimester diagnosed using a 75g OGTT: • risk factor based screening • urine test for glycosuria • random blood glucose test • 50 g oral glucose challenge test • fasting blood glucose test • HbA1c test	The term glucose intolerance covers: • impaired fasting glucose (IFG) • impaired glucose tolerance (IGT) and • diabetes.
Objectives	To examine if a ‘test’ or combination of ‘tests’ in the second trimester identifies women with gestational diabetes Whether this identification improves the outcome	A ‘test’ is shorthand for ‘screening procedure’ as defined above. Second trimester is the period between 14 weeks + 0 days and 28 weeks + 6 days.
Language	English	

Question 7		
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational cohort studies (of more than one of these tests in same population would be ideal) Observational cohort studies (of tests in different populations if comparative studies unavailable – only to be considered if no comparative data)	
Status	Published articles (no limitation on year of publication)	
Population	Pregnant women in the second trimester who do not have a pre-existing diagnosis of diabetes	Ideally the whole population should have a 75g OGTT to determine the predictive accuracy of the individual screening tests for an abnormal OGTT.
Intervention or index test	• Risk factor based screening (which could be either risk factor screening alone to predict gestational diabetes, or risk factor plus a subsequent biochemical test to predict gestational diabetes) • Urine test for glycosuria • Random blood glucose test • 50 g oral glucose challenge test • Fasting blood glucose test • HbA1c test	The risk factors detailed in the 2008 diabetes in pregnancy guideline are : body mass index (BMI) above 30 kg/m2 previous macrosomic baby weighing 4.5 kg or above previous gestational diabetes) family history of diabetes (first-degree relative with diabetes) 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).
Comparator or reference standard	75g OGTT	Interpreted using the World Health Organization (WHO) 1999 or International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria, or diagnostic criteria with thresholds equivalent to WHO 1999.

Question 7		
Clinical outcomes	Incidence of gestational diabetes • Comparative incidence of diagnosis of gestational diabetes in the first and second trimesters Diagnostic test accuracy • Sensitivity, specificity and likelihood ratios for diagnosis of gestational diabetes Maternal outcomes • Mode of birth: spontaneous vaginal , operative vaginal, caesarean section (elective/emergency) • Treatment such as diet, oral hypoglycaemic agents and/or insulin • Acceptability/take-up of testing regimen Neonatal outcomes • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • All mortality - includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth Neonatal intensive care unit length of stay (greater than 24 hours) • Shoulder dystocia (no permanent damage, neurological injury (brachial plexus and cerebral palsy)	
Health economic outcomes	Prevalence of gestational diabetes in the second trimester Diagnostic test accuracy • Sensitivity, specificity Neonatal outcomes • Stillbirth, shoulder dystocia, perinatal death, birth trauma (‘serious perinatal complications’) Maternal outcomes • From the clinical outcomes above, although these predominantly affect ‘downstream costs’ rather than health-related quality of life	

Question 7		
	Health-related quality of life • EQ5D, SF36	
Other criteria for inclusion/ exclusion of studies	Studies that overlap 28 weeks + 6 into the third trimester, or screen later than 28 weeks + 6 will be excluded Studies that do not use IADPSG or WHO 1999 (or equivalent) diagnostic criteria will be excluded Studies where the screening test (eg GCT) is examined for prediction of maternal/neonatal outcomes will be excluded	
Search strategies	See separate document	A single search will be conducted for the questions relating to first- and second-trimester screening.
Review strategies	• Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence	Note that the QUADAS methodology checklist for diagnostic test accuracy studies (NICE guidelines manual January 2009) has been used for this question for consistency with the question relating to diagnosis of gestational diabetes. All other aspects of the review are consistent with the 2012 edition of the manual.
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.7 Diagnostic criteria for gestational diabetes

Question 8		
Existing recommendation(s) in 2008 guideline	The 2 hour 75 g oral glucose tolerance test (OGTT) should be used to test for gestational diabetes and diagnosis made using the criteria defined by the World Health Organization.* Women who have had gestational diabetes in a previous pregnancy should be offered early self-monitoring of blood glucose or OGTT at 16–18 weeks, and a further OGTT at 28 weeks if the results are normal. Women with any of the other risk factors for gestational diabetes should be offered an OGTT at 24–28 weeks. * Fasting plasma venous glucose concentration greater than or equal to 7.0 mmol/litre or 2 hour plasma venous glucose concentration greater than or equal to 7.8 mmol/litre. World Health Organization Department of Non communicable Disease Surveillance (1999) Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO consultation. Part 1: diagnosis and classification of diabetes mellitus. Geneva: World Health Organization.	OGTT is oral glucose tolerance test
Review question for update	Which criteria should be used to diagnose gestational diabetes using the 75 g OGTT: World Health Organization (WHO) (1999) or International Association of Diabetes and Pregnancy Study Groups (IADPSG)?	This is a new topic for the update to investigate use of the new (IADPSG) criteria against WHO 1999 as recommended in the 2008 guideline.
Objectives	To investigate whether using IADPSG criteria rather than WHO (1999) criteria would improve: clinical diagnostic effectiveness and cost effectiveness of diagnosis for women who are diagnosed with gestational diabetes. The evaluation of cost effectiveness should take account of any increase in the number of women who would be diagnosed with gestational diabetes using the IADPSG criteria rather than the WHO criteria.	During the course of the development of the Guideline in 2014, WHO updated their criteria for diagnosing gestational diabetes. So these critieria were considered alongside the IADPSG and WHO (1999) criteria.
Language	English	
Study design	Comparison of the two sets of criteria using: • systematic reviews • randomised controlled trials (RCTs) • cohort studies	
Status	Published articles (no limitation on year of publication)	Although no limitation on year of publication will be applied in the search, the relevant evidence is expected to have been published since the 2008

Question 8		
		guideline because the IADPSG criteria were published after that guideline.
Population	Pregnant women who do not have pre-existing diabetes	
Intervention or index test	A 75 g OGTT interpreted using the IADPSG diagnostic criteria (based on an odds ratio (OR) for adverse outcomes of 1.5, 1.75 or 2.0) in the first or second trimester	Health economic analysis might incorporate interpretation at different thresholds (ORs for adverse outcomes).
Comparator or reference standard	A 75 g OGTT interpreted using the WHO 1999 diagnostic criteria in the first or second trimester	
Clinical outcomes	Incidence of gestational diabetes • Comparative incidence of diagnosis of diabetes with the two sets of criteria Diagnostic test accuracy • Sensitivity, specificity and likelihood ratios for positive and negative test results in the diagnosis of gestational diabetes using and comparing the IADPSG and WHO 1999 criteria Maternal and neonatal outcomes • Prioritised maternal outcomes: • *Mode of birth (spontaneous vaginal, operative vaginal, caesarean section (elective or emergency)) • *Preterm birth (birth before 37 + 0 weeks' gestation; take dichotomous or continuous data) • Need for treatment for gestational diabetes, such as diet, oral hypoglycaemic agents or insulin Prioritised neonatal outcomes: • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • Neonatal intensive care unit length of stay greater than 24 hours • Shoulder dystocia • Neonatal hyperinsulinaemia or hyper C-peptide-aemia (raised neonatal blood concentrations of insulin or C-peptide)	

Question 8		
	• **Mortality *If neither of these outcomes is available, onset of labour (spontaneous, induced, or no labour) should be considered and the guideline development group advised about available evidence **The definition of mortality includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth)	
Health economic outcomes	Prevalence of gestational diabetes • Estimated prevalence of gestational diabetes using the IADPSG and WHO criteria Diagnostic test accuracy • Sensitivity and specificity for diagnosis of gestational diabetes using the IADPSG and WHO criteria Maternal and neonatal outcomes • Mortality (defined as above; maternal mortality will not be considered)	
Other criteria for inclusion/ exclusion of studies	Include studies that report test and outcome results from a single population of women (and their babies) according to a diagnosis of gestational diabetes made by applying the IADPSG and WHO 1999 criteria Include studies that do not report IADPSG valuesfor 1 hour in the OGTT results, but downgrade such evidence in the evidence profiles Exclude studies that do not use the WHO 1999 criteria as defined above (for example, studies that use only 2-hour plasma glucose concentrations and not fasting plasma glucose (FPG) concentrations, or that apply different threshold values to WHO 1999 criteria)	
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	Note that the QUADAS methodology checklist for diagnostic test accuracy studies (NICE guidelines manual January 2009) has been used for this question because the majority of the systematic reviewing was undertaken when the 2009 edition of the manual

Question 8		
		was still in use. All other aspects of the review are consistent with the 2012 edition of the manual.
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.8 Interventions for gestational diabetes

Question 9		
Existing recommendation(s) in 2008 guideline	Women with gestational diabetes should be offered information covering: • the role of diet, body weight and exercise • the increased risk of having a baby who is large for gestational age, which increases the likelihood of birth trauma, induction of labour and caesarean section • the importance of maternal glycaemic control during labour and birth and early feeding of the baby in order to reduce the risk of neonatal hypoglycaemia • the possibility of transient morbidity in the baby during the neonatal period, which may require admission to the neonatal unit • the risk of the baby developing obesity and/or diabetes in later life. Women with gestational diabetes should be advised to choose, where possible, carbohydrates from low glycaemic index sources, lean proteins including oily fish and a balance of polyunsaturated fats and monounsaturated fats. Women with gestational diabetes whose pre-pregnancy body mass index was above 27 kg/m2 should be advised to restrict calorie intake (to 25 kcal/kg/day or less) and to take moderate exercise (of at least 30 minutes daily). Hypoglycaemic therapy should be considered for women with gestational diabetes if diet and exercise fail to maintain blood glucose targets during a period of 1–2 weeks. 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. Hypoglycaemic therapy for women with gestational diabetes (which may include regular insulin, rapid-acting insulin analogues [aspart and lispro] and/or hypoglycaemic agents [metformin and glibenclamide] should be tailored to the glycaemic profile of, and acceptability to, the individual woman.	.
Review question for update	What is the effectiveness of the following interventions (alone or in combination) in women with gestational diabetes: non-pharmacological interventions (diet and/or exercise) pharmacological interventions (metformin, glibenclamide and insulin)?	

Question 9		
Objectives	To examine the effectiveness of: • Diet strategies • Exercise regimens • Different pharmacological interventions (metformin, glibenclamide and insulin) as first line pharmacological treatment in the management of gestational diabetes in the second and third trimesters	
Language	English	
Study design	Systematic reviews Randomised controlled trials (RCTs)	It is anticipated that there will be a large number of RCTs and studies of other designs will, therefore, not be considered.
Status	Published articles	
Population	Pregnant women with gestational diabetes (however the study defines gestational diabetes), but who are presumed to not have pre-existing diabetes	
Intervention or index test	Diet strategy/advice (including strategies to increase intake of vitamins, minerals and micronutrients), with or without insulin use Exercise regimen with or without diet strategy/advice 3a) Metformin 3b) Glibenclamide 3c) Metformin	Non-pharmacological comparisons a) Diet strategy/advice vs standard care or no diet strategy/advice b) Insulin + Diet strategy/advice vs Diet strategy/advice c) Exercise regimen + Diet strategy/advice vs Exercise regimen d) Diet A vs Diet B e) Exercise regimen vs standard care or no exercise regimen f) Exercise regimen + Diet strategy/advice vs Diet strategy/advice g) Intense exercise regimen vs exercise regimen h) Exercise regimen A vs Exercise regime B. Consider cultural dietary practices including food types and dietary observances.

Question 9		
		Pharmacological comparisons i)Metformin vs Insulin j)Glibenclamide vs Insulin k)Metformin vs Glibenclamide. Note that glibenclamide is usually referred to as 'glyburide' in US studies.
Comparator or reference standard	Standard care, Diet strategy /advice, Exercise regimen Standard care, Exercise regimen, Diet strategy/advice 3a) Insulin 3b) Insulin 3c) Glibenclamide	
Clinical outcomes	Maternal outcomes • Mode of birth: spontaneous vaginal , operative vaginal, caesarean section (elective/emergency) • Treatment such as diet, oral hypoglycaemic agents and/or insulin • Acceptability/take-up of treatment (including hypoglycaemic episodes where insulin is used, if reported) Neonatal outcomes • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • Neonatal intensive care unit length of stay (greater than 24 hours) • Shoulder dystocia (no permanent damage, neurological injury (brachial plexus and cerebral palsy) • Neonatal hyperinsulinaemia/ hyper C-peptide-aemia* • All mortality - includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth *Neonatal hypoglycaemia (which can be further subdivided by (biochemical or symptomatic) diagnosis alone, extra complementary formula milk, oral glucose (extra feeds), need for intravenous glucose) is to be used when there is no data on neonatal hyperinsulinaemia/hyper C-peptide aemia available	

Question 9		
Health economic outcomes	Neonatal outcomes • Stillbirth, shoulder dystocia, perinatal death, neonatal death, birth trauma (thus focussing on 'serious perinatal complications') Maternal outcomes • From the clinical outcomes above, although these predominantly affect 'downstream costs' rather than health-related quality of life Health-related quality of life • EQ5D, SF36	
Other criteria for inclusion/ exclusion of studies	Non-randomised comparative studies will be excluded No limitation on year of publication	
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.9 Antenatal blood glucose monitoring

Question 10		
Existing recommendations in 2008 guideline	Women with diabetes who are planning to become pregnant should be advised: • that the risks associated with pregnancies complicated by diabetes increase with the duration of diabetes • to use contraception until good glycaemic control (assessed by HbA1c)† has been established • that glycaemic targets, glucose monitoring, medications for diabetes (including insulin regimens for insulin-treated diabetes) and medications for complications of diabetes will need to be reviewed before and during pregnancy • that additional time and effort is required to manage diabetes during pregnancy and that there will be frequent contact with healthcare professionals. Women should be given information about the local arrangements for support, including emergency contact numbers. Women with diabetes who are planning to become pregnant should be offered a meter for self-monitoring of blood glucose. Women with diabetes who are planning to become pregnant and who require intensification of hypoglycaemic therapy should be advised to increase the frequency of self-monitoring of blood glucose to include fasting and a mixture of pre- and postprandial levels. Women with diabetes should be advised to test fasting blood glucose levels and blood glucose levels 1 hour after every meal during pregnancy. Women with insulin-treated diabetes should be advised to test blood glucose levels before going to bed at night during pregnancy. † Diabetes Control and Complications Trial (DCCT)-aligned haemoglobin A1c (HbA1c) test.	HbA1c is haemoglobin A1c The recommendations in the 2008 guideline relating to monitoring blood glucose in women who are planning pregnancy are not being updated, but are included here for context
Review question for update	What is the effectiveness of blood glucose monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?	Note that there are six inter-related review questions about the effectiveness of monitoring HbA1c and blood glucose during pregnancy, and target values or ranges for HbA1c and

Question 10		
		blood glucose before and during pregnancy (questions 3, 4, 10, 11, 12 and 13). The six questions will probably be addressed via a single search for evidence.
Objectives	To evaluate the effectiveness of monitoring blood glucose in pregnant women with type 1, type 2 or gestational diabetes This review question relates specifically to intermittent capillary blood glucose self-monitoring (continuous glucose monitoring during pregnancy is addressed in a separate question). The review should specifically focus on the frequency of monitoring blood glucose and timing relative to meals (for example, to include testing blood glucose before meals and adjusting insulin accordingly), since this is likely to reflect practice outside pregnancy The effectiveness of monitoring blood glucose in women with type 1 or type 2 diabetes who are planning pregnancy has already been established and the corresponding section of the 2008 guideline is not being updated	Liaison with the GDGs and/or technical teams for the NICE guidelines on type 1 diabetes in adults, type 2 diabetes in adults, and type 1 and type 2 diabetes in children and young people will be important for aligning monitoring strategies for HbA1c and blood glucose, or justifying the need for different strategies in the different guidelines. However, alignment of recommendations during pregnancy with other guidelines for non-pregnant individuals is unlikely to be as important as in the preconception period.
Language	English	
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational studies (cohort and case-control studies)	RCTs evaluating monitoring strategies may be limited in number (a few RCTs comparing different monitoring strategies were included in the 2008 guideline, but no RCTs compared monitoring with no monitoring). There may, however, be more evidence from observational studies relating different strategies to clinical outcomes.
Status	Articles indexed after the searches for the 2008 guideline were completed	This is an update of a review conducted for the 2008 guideline. Studies included in the 2008 guideline will need to be considered against the current protocol and data will be extracted for presentation in evidence profiles where

Question 10		
		relevant (see the question 'How should blood glucose and ketones be monitored during pregnancy?' in the 2008 guideline).
Population	Pregnant women with type 1 diabetes, type 2 diabetes or gestational diabetes	
Intervention or index test	Specified monitoring strategies for blood glucose	The way in which blood glucose was monitored, including the frequency and timing of monitoring, should be documented for each included study. Studies that report outcomes associated with different levels of blood glucose but without documenting a particular monitoring strategy are not eligible for inclusion in this question – they should instead be considered for the corresponding questions on blood glucose target ranges.
Comparator or reference standard	Comparisons to be made between outcomes according to monitoring strategies used	The ideal study would be one which allowed a direct comparison between two or more monitoring strategies (including before-and-after comparisons in the same cohort of women).
Clinical outcomes	Maternal outcomes: • *Mode of birth (spontaneous vaginal, operative vaginal, caesarean section (elective or emergency)) • HbA1c % (as a measure of glycaemic control during pregnancy) • Hypoglycaemic episodes during pregnancy (another measure of glycaemic control during pregnancy) Neonatal outcomes: • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • Neonatal intensive care unit length of stay greater than 24 hours	The GDG selected up to 7 outcomes plus mortality (where relevant); maternal mortality was not considered to be a priority for blood glucose monitoring during pregnancy Evidence tables should document: the indication for mode of birth (if reported) any treatment administered in response to monitoring the definition of maternal and/or neonatal hypoglycaemic episodes

Question 10		
	• Shoulder dystocia (as a specific example of birth trauma) • Neonatal hypoglycaemia (however defined) • **Mortality *If neither of these outcomes is available, onset of labour (spontaneous, induced, or no labour) should be considered and the GDG advised about available evidence **The definition of mortality includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth)	(results for neonatal hypoglycaemia may be difficult to compare between studies because of different definitions). The GDG noted that: presence of pre-eclampsia was of interest for this question, but was less of a priority than the other outcomes selected maternal hypoglycaemia was an important outcome that would not be covered by HbA1c there would be some overlap between neonatal intensive care unit length of stay greater than 24 hours and presence of neonatal hypoglycaemia respiratory distress would be covered by admission to neonatal intensive care neonatal hypoglycaemia was more important than the presence of neonatal hyperinsulinaemia or hyper C-peptide-aemia, although the latter may be important in defining future research priorities presence of a congenital abnormality is not relevant during pregnancy.
Health economic outcomes	This question was not prioritised for health economic analysis	Availability of testing strips for blood glucose monitoring might be a cost issue and reviewing health economic priorities if time allows (and if relevant evidence is identified) and considering differences between planning pregnancy, during pregnancy and women with pre-existing diabetes who are not planning pregnancy (for example, type 2 diabetes in adults guideline update) might be undertaken.

Question 10		
Other criteria for inclusion/ exclusion of studies	None	
Search strategies	See separate document	NCC-WCH technical team to consider whether one search across all six questions relating to target values and ranges and monitoring during pregnancy would be appropriate.
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.10 Antenatal HbA1c monitoring

Question 13		
Existing recommendations in 2008 guideline	Women with diabetes who are planning to become pregnant should be advised: • that the risks associated with pregnancies complicated by diabetes increase with the duration of diabetes • to use contraception until good glycaemic control (assessed by HbA1c)† has been established • that glycaemic targets, glucose monitoring, medications for diabetes (including insulin regimens for insulin-treated diabetes) and medications for complications of diabetes will need to be reviewed before and during pregnancy • that additional time and effort is required to manage diabetes during pregnancy and that there will be frequent contact with healthcare professionals. Women should be given information about the local arrangements for support, including emergency contact numbers. Women with diabetes who are planning to become pregnant should be offered monthly measurement of HbA1c. HbA1c should not be used routinely for assessing glycaemic control in the second and third trimesters of pregnancy. † Diabetes Control and Complications Trial (DCCT)-aligned haemoglobin A1c (HbA1c) test.	HbA1c is haemoglobin A1c The 2008 guideline is not explicit about whether or not to monitor HbA1c in the first trimester, although this is implicitly acceptable. The GDG may want to address this as part of the update The recommendation in the 2008 guideline relating to monitoring HbA1c in women who are planning pregnancy is not being updated, but is included here for context. Note that 'routinely' does not rule out monitoring if clinically indicated
Review question for update	What is the effectiveness of HbA1c monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?	Note that there are six inter-related review questions about the effectiveness of monitoring HbA1c and blood glucose during pregnancy, and target values or ranges for HbA1c and blood glucose before and during pregnancy (questions 3, 4, 10, 11, 12 and 13). The six questions will probably be addressed via a single search for evidence.

Question 13		
Objectives	To evaluate the effectiveness of monitoring HbA1c in pregnant women with type 1, type 2 or gestational diabetes, specifically in the context of whether the 2008 guideline recommendation not to monitor HbA1c routinely in the second and third trimesters of pregnancy should be changed The review should include consideration of: the frequency of monitoring HbA1c whether monitoring HbA1c is more effective that monitoring blood glucose alone whether different monitoring strategies are appropriate in women with type 1, type 2 and gestational diabetes The effectiveness of monitoring HbA1c in women with type 1 or type 2 diabetes who are planning pregnancy has already been established and the corresponding section of the 2008 guideline is not being updated	Liaison with the GDGs and/or technical teams for the NICE guidelines on type 1 diabetes in adults, type 2 diabetes in adults, and type 1 and type 2 diabetes in children and young people will be important for aligning monitoring strategies for HbA1c and blood glucose, or justifying the need for different strategies in the different guidelines. However, alignment of recommendations during pregnancy with other guidelines for non-pregnant individuals is unlikely to be as important as in the preconception period. Include evidence based on HbA1c monitoring in any trimester.
Language	English	
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational studies (cohort and case-control studies)	RCTs evaluating monitoring strategies may be limited in number (a few RCTs comparing different monitoring strategies were included in the 2008 guideline, but no RCTs compared monitoring with no monitoring). There may, however, be more evidence from observational studies relating different strategies to clinical outcomes.
Status	Articles indexed after the searches for the 2008 guideline were completed	This is an update of a review conducted for the 2008 guideline. Studies included in the 2008 guideline will need to be considered against the current protocol and data will be extracted for presentation in evidence profiles where relevant (see the question ‘How should blood glucose and ketones be monitored during pregnancy?’ in the 2008 guideline; this question was broad

Question 13		
		enough to cover monitoring HbA1c).
Population	Pregnant women with type 1 diabetes, type 2 diabetes or gestational diabetes	
Intervention or index test	Specified monitoring strategies for HbA1c (with or without monitoring of blood glucose)	The way in which HbA1c (and blood glucose if relevant) was monitored, including the frequency of monitoring, should be documented for each included study, as should the gestational age or trimester at which HbA1c monitoring was performed. Studies that report outcomes associated with different levels of HbA1c but without documenting a particular monitoring strategy are not eligible for inclusion in this question – they should instead be considered for the corresponding questions on HbA1c target values.
Comparator or reference standard	Comparisons to be made between outcomes according to monitoring strategies used Comparison with monitoring based on blood glucose alone	The ideal study would be one which allowed a direct comparison between two or more monitoring strategies (including before-and-after comparisons in the same cohort of women). The GDG noted that there may be evidence relating to comparison between HbA1c monitoring and monitoring based on blood glucose alone for women with gestational diabetes.
Clinical outcomes	Maternal outcomes: • *Mode of birth (spontaneous vaginal, operative vaginal, caesarean section (elective or emergency)) • Pre-eclampsia (HbA1c may predict this)	The GDG selected up to 7 outcomes plus mortality (where relevant); maternal mortality was not considered to be a priority for HbA1c monitoring during pregnancy.

Question 13		
	Neonatal outcomes: • Large for gestational age (however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) • Neonatal intensive care unit length of stay greater than 24 hours • Shoulder dystocia (as a specific example of birth trauma) • Neonatal hypoglycaemia (however defined) • Any congenital abnormality, regardless of gestational age • **Mortality *If neither of these outcomes is available, onset of labour (spontaneous, induced, or no labour) should be considered and the GDG advised about available evidence **The definition of mortality includes perinatal mortality (stillbirth and neonatal death up to 7 days after birth) and neonatal mortality (neonatal death up to 28 days after birth)	Evidence tables should document: the indication for mode of birth (if reported) any treatment administered in response to monitoring the definition of neonatal hypoglycaemic episodes (results for neonatal hypoglycaemia may be difficult to compare between studies because of different definitions) the types of congenital abnormality and how many resulted in planned termination of pregnancy. The GDG noted that: preterm birth was not selected as a priority for this question because the presence of a congenital abnormality was considered a greater priority there would be some overlap between neonatal intensive care unit length of stay greater than 24 hours and presence of neonatal hypoglycaemia neonatal hypoglycaemia was more important than the presence of neonatal hyperinsulinaemia or hyper C-peptide-aemia, although the latter may be important in defining future research priorities presence of a congenital abnormality is relevant during pregnancy because although such abnormalities arise very early in pregnancy, HbA1c represents a retrospective average measure of glycaemic control and this (especially first-trimester HbA1c) could be useful (for example, for counselling, fetal

Question 13		
		monitoring during pregnancy and evaluating the likelihood of needing neonatal intensive care).
Health economic outcomes	This question was not prioritised for health economic analysis	Availability of testing strips for blood glucose monitoring might be a costissue and reviewing health economic priorities if time allows (and if relevant evidence is identified) and considering differences between planning pregnancy, during pregnancy and women with pre-existing diabetes who are not planning pregnancy (for example, type 2 diabetes in adults guideline update) might be undertaken.
Other criteria for inclusion/ exclusion of studies	None	
Search strategies	See separate document	NCC-WCH technical team to consider whether one search across all six questions relating to target values and ranges and monitoring during pregnancy would be appropriate.
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.11 Antenatal continuous glucose monitoring

Question 15		
Existing recommendations in 2008 guideline	Women with diabetes should be advised to test fasting blood glucose levels and blood glucose levels 1 hour after every meal during pregnancy. Women with insulin-treated diabetes should be advised to test blood glucose levels before going to bed at night during pregnancy.	When the 2008 guideline was developed, there was insufficient evidence to evaluate the effectiveness of continuous blood glucose monitoring. The 2008 guideline did, however, include a research recommendation to evaluate the effectiveness of (ambulatory) continuous blood glucose monitoring in pregnancies complicated by diabetes
Review question for update	What is the effectiveness of continuous glucose monitoring in pregnant women with diabetes compared with intermittent capillary blood glucose monitoring?	
Objectives	To assess whether continuous glucose monitoring during pregnancy is more effective than intermittent capillary blood glucose monitoring for improving: glycaemic control maternal and fetal/neonatal outcomes	
Language	English	
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational studies if RCTs not available	Details of discussions about including Cochrane reviews are included in the 'Email repository' folder on the V drive. In summary, two Cochrane review protocols were published when reviewing started in May 2013, but the full reviews were unlikely to be published in the near future, and so the protocols were excluded from the current review.
Status	Articles indexed after the searches for the 2008 guideline were completed	The searches for the 2008 guideline included up to 21st March 2007. The first run of the searches for the updated guideline started from October 2007. Therefore, the rerun searches need to include March 2007 to October 2007 (this has been agreed with RL).

Question 15		
		This is an update of a review conducted for the 2008 guideline. Three studies involving continuous glucose monitoring during pregnancy were included in the 2008 guideline. These studies will need to be considered against the current protocol and data will be extracted for presentation in evidence profiles where relevant (see the question 'How should blood glucose and ketones be monitored during pregnancy?' in the 2008 guideline). Published systematic reviews on continuous glucose monitoring in general (not specifically during pregnancy) may be good sources of studies to consider for the update. One such study is a published meta-analysis of RCTs using individual patient data (Pickup JC, BMJ 2011, 343, d3805; see http://www.bmj.com/content/343/bmj.d3805)
Population	Pregnant women with type 1 diabetes, type 2 diabetes or gestational diabetes	Continuous glucose monitoring is sometimes use by women with type 2 diabetes or gestational diabetes, but its main use is in women with type 1 diabetes
Intervention or index test	Continuous glucose monitoring	Some (older) articles might use the term ambulatory continuous glucose monitoring. Duration of the use of continuous monitoring may vary from study to study – document in evidence tables.
Comparator or reference	Intermittent capillary blood glucose monitoring	Other relevant terms and abbreviations for intermittent capillary blood glucose

Question 15		
standard		monitoring might include: • capillary glucose series • ICGM • ICBGM • 'testing' instead of 'monitoring' spot testing • home glucose monitoring or testing • self-monitoring or self-testing
Clinical outcomes	Maternal Mode of birth: spontaneous vaginal delivery, , instrumental vaginal delivery, caesarean section Preterm birth (birth before 37 + 0 weeks' gestation; take dichotomous or continuous data) Glycaemic control in the pregnancy measured by HbA1c Severe hypoglycaemic episodes Maternal satisfaction Fetal/Neonatal Mortality - perinatal and neonatal death Large for gestational age (or however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred) Neonatal intensive care unit length of stay greater than 24 hours	The GDG selected up to 7 outcomes for presentation in GRADE, plus mortality in the woman or baby if relevant. For this question, mortality in the woman was not prioritised. Also, shoulder dystocia was recognised as being an important outcome, but because it might be defined differently in different studies it was not prioritised as an outcome. If shoulder dystocia is needed for health economic analysis it may be necessary to extrapolate from large-for-gestational-age (for example, using data from CEMACH). Similarly, although the GDG expected that neonatal hypoglycaemia might be reported in some studies considered for this question, admission to a neonatal intensive care unit would be a more important outcome, and so neonatal hypoglycaemia was not prioritised. A severe hypoglycaemic episode is an episode of hypoglycaemia requiring third-party assistance.

Question 15		
Health economic outcomes	This question was selected as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	None	
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.12 Antenatal specialist teams

Question 16		
Existing recommendation (s) in 2008 guideline	Women with diabetes who are pregnant should be offered immediate contact with a joint diabetes and antenatal clinic.	
Review question for update	What is the effectiveness of specialist teams for pregnant women with diabetes?	
Objectives	Women with diabetes sometimes have appointments with different teams on different sites. The aim of this question is to assess the benefits of concentrating care in one place for delivery by an integrated team. The term 'specialist team' is to be interpreted in this question to include specialist centres and centralisation of care, for example, offering women with type 1 diabetes access to insulin pumps. The question should consider: • adverse outcome rates associated with specialist care • maternal satisfaction (including ease of access to care, for example, in terms of travelling to or between diabetes and antenatal clinics) • models of care for women with gestational diabetes, for example, including community midwifery • equality of access to, for example, insulin pumps for all groups (especially ethnic minority women)	Separate analyses to be considered for type 1 diabetes, type 2 diabetes and gestational diabetes. The GDG may wish to refer to the National Service Framework (NSF) for diabetes. Note that the emphasis in this question is on integration of care.
Language	English	
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational studies (cohort and case-control studies) Qualitative studies	Although RCTs are unlikely, there may be observational studies comparing outcomes of care delivered under different team structures.
Status	Published articles (no limitation on year of publication)	This is an update of a review conducted for the 2008 guideline. However, no specific searches were undertaken for the relevant section of the 2008 guideline and so the search for the update will not be limited by date.
Population	Pregnant women with type 1, type 2 or gestational diabetes	

Question 16		
Intervention or index test	Integrated care in one location, offering access to all relevant members of a multidisciplinary team (this should be the norm already but it may not yet be available everywhere) Centralised regional care for women with pregnancy complicated by diabetes	The NSF for diabetes recommends that antenatal care for women with diabetes should be delivered by a multidisciplinary team consisting of an obstetrician, a diabetes physician, a diabetes specialist nurse, a midwife and a dietitian. In this question, interest focuses on whether centralised care is important for women with pre-existing diabetes rather than gestational diabetes (even specialist care may be unnecessary for women with gestational diabetes, that is, community based care may be appropriate for women with gestational diabetes). Consistency and continuity of advice/care may be more important for the woman than the geographical location in which care is delivered. Westminster City Council, the London Borough of Hammersmith & Fulham and the Royal Borough of Kensington and Chelsea are undertaking a tri-borough pilot of combined public services that might have some useful data (see, for example, http://www.lbhf.gov.uk/combinedservices). However, the pilot is not specific to healthcare for women with diabetes in pregnancy.
Comparator or reference standard	Divided care, possibly in more than one location (relevant comparator for both integrated care and centralised regional care) Integrated care between centres (comparator for centralised regional care only)	

Question 16		
Clinical outcomes	Maternal • Mode of birth: spontaneous vaginal, instrumental vaginal delivery, caesarean section, • Preterm birth (birth before 37 + 0 weeks' gestation; using dichotomous or continuous data) • Glycaemic control in the pregnancy measured using HbA1c • Maternal satisfaction Fetal/Neonatal • Mortality - perinatal and/or neonatal death • Large for gestational age (however defined in the study, dichotomous data preferred) • Neonatal intensive care unit length of stay greater than 24 hours • Initiation of breastfeeding (when started and exclusivity)	The GDG selected up to 7 outcomes for presentation in GRADE, plus mortality in the woman or baby if relevant and reported. For this question, mortality in the woman was not prioritised. Also, shoulder dystocia was recognised as being an important outcome, but because it might be defined differently in different studies it was not prioritised as an outcome. If shoulder dystocia is needed for health economic analysis it may be necessary to extrapolate from large-for-gestational-age (for example, using data from CEMACH). Exclusivity of breastfeeding means whether the baby was fed using breast milk only.
Health economic outcomes	This question was selected as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Nested case-control studies that have not adjusted for confounding variables will be excluded	
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.13 Timing of birth

Question 17		
Existing recommendation(s) in 2008 guideline	Pregnant women with diabetes who have a normally grown fetus should be offered elective birth through induction of labour, or by elective caesarean section if indicated, after 38 completed weeks.	
Review question for update	What is the gestational age-specific risk of intrauterine death in pregnancies with type 1, type 2 or gestational diabetes, and the optimal timing of birth?	For the purposes of this review question, intrauterine death (stillbirth) is defined as fetal death from 24 weeks' gestation. Whilst the timing of stillbirth can be used as the main pregnancy outcome others should be included to inform the GDG. In summary: Consequences of elective delivery (37-39 weeks has been suggested in the literature) are – neonatal problems especially respiratory disorders, admission to NNICU. Consequences of an expectant approach to care are – stillbirth, shoulder dystocia, increased CS rates, macrosomia.
Objectives	To determine the optimal timing of birth in women with pregnancies complicated by the three forms of diabetes (type 1, type 2 and gestational diabetes). The optimal timing of birth will be determined by the nadir (minimum) in perinatal mortality and morbidity rates in diabetic pregnancies. This may vary between the different types of diabetes The question should consider stratifying risk and associated interventions (such as elective birth) according to: • gestational age • type of diabetes (type 1, type 2 or gestational diabetes, with the further possibility of defining a continuum of risk within one or more of these types) • HbA1c as an individualised measure of glycaemic control.	The main focus of interest in terms of comparing types of diabetes, and making recommendations relating to timing of birth, is whether the evidence supports separate recommendaitons for gestational diabetes versus pre-existing diabetes (type 1 or type 2 diabetes).

Question 17		
	The question should also consider: • pregnancy complications (other than those already covered by NICE guidelines for routine maternity care, for example, pre-eclampsia) • diabetes complications (for example, accelerated retinopathy) • potential confounders, such as age, parity, smoking, and body mass index (BMI) Possible subquestions for the GDG to consider are as follows. What is the intrauterine death rate in spontaneous or uncomplicated deliveries in women with diabetes in pregnancy (type 1 diabetes, type 2 diabetes or gestational diabetes)? What is the effectiveness of elective birth in women with diabetes in pregnancy (type 1 diabetes, type 2 diabetes or gestational diabetes)?	
Language	English	
Study design	Systematic reviews Randomised controlled trials (RCTs) Comparative observational studies (cohort and case-control studies)	Although RCTs are unlikely, there may be observational studies comparing elective birth at a particular gestational age with expectant management (allowing pregnancy to continue).
Status	Articles indexed after the searches for the 2008 guideline were completed	This is an update of a review conducted for the 2008 guideline. Included studies from the 2008 guideline will need to be considered against the current protocol and data will be extracted for presentation in evidence profiles where relevant (see the question 'Does intervening in the timing and mode of birth improve outcomes for women with diabetes and their babies?' in the 2008 guideline).
Population	Pregnant women with type 1, type 2 or gestational diabetes	Ideally it would be useful to know about any clinical confounders (maternal comorbidities) in the study population, such as hypertension or obesity.
Intervention or index test	Descriptive studies of intrauterine death rates according to gestational age Elective birth at a particular gestational age (intervention studies)	Studies eligible for inclusion are those in which: • pregnancies complicated by diabetes

Question 17		
		have been allowed to go into spontaneous labour, or • intervention relating to timing of birth is performed at or before 41 weeks' gestation. Studies in which intervention relating to timing of birth occurs after 41 weeks' gestation will, therefore, be excluded. Document mode of birth in each included study
Comparator or reference standard	Intrauterine death rates at different gestational ages Expectant management (intervention studies)	
Clinical outcomes	For studies evaluating intrauterine death rates by gestational age, gestational age-specific risk of intrauterine death is the only relevant outcome For intervention studies comparing elective birth and expectant management the following outcomes were prioritised. Maternal • Mode of birth (spontaneous vaginal, operative vaginal, caesarean section (elective or emergency)) • Maternal complications of delivery (including wound infection, urinary infection, postpartum haemorrhage, psychological outcomes and other complications developing over a longer period) • Maternal satisfaction/experiences Foetal/Neonatal • Mortality - still birth and neonatal death (and other mortality outcomes if reported) • Admission to NICU (to include respiratory disease - respiratory distress syndrome and transient tachypnoea of the newborn- and neonatal hypoglycaemia where reported) NICU stay >24 hours	

Question 17		
	• Macrosomia • Shoulder dystocia (with and without consequences for the baby such as trauma, neuromuscular injury)	
Health economic outcomes	This question was selected as a priority for health economic analysis	
Other criteria for inclusion/ exclusion of studies	Exclude: • multiple pregnancies • pregnancies with known potentially lethal congenital abnormalities • pregnancies with any complications not exclusively associated with diabetes that would lead to elective preterm birth	'Hypertension in pregnancy' (NICE clinical guideline 107) includes recommendations on timing of birth for women with chronic hypertension, gestational hypertension and pre-eclampsia, but that guideline does not cover women with diabetes who have co-existent hypertension(such women fall within the scope of the diabetes in pregnancy guideline).
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.14 Diagnostic accuracy of postnatal testing

Question 18		
Existing recommendation(s) in 2008 guideline	Women who were diagnosed with gestational diabetes should be offered lifestyle advice (including weight control, diet and exercise) and offered a fasting plasma glucose measurement (but not an OGTT) at the 6 week postnatal check and annually thereafter.	OGTT stands for 'oral glucose tolerance test'
Review question for update	What is the effectiveness of the following tests in the detection of glucose intolerance after pregnancy in women who have had gestational diabetes (but are euglycaemic before they are transferred to community care): • fasting plasma glucose (FPG) test • HbA1c test • 75 g OGTT?	The term glucose intolerance covers: impaired fasting glucose (IFG) impaired glucose tolerance (IGT) and diabetes. Alternative terminology for type 1 diabetes for NCC-WCH technical team to be aware of: type 1 diabetes mellitus; type I diabetes mellitus; insulin-dependent diabetes. Alternative terminology for type 2 diabetes for NCC-WCH technical team to be aware of: type 2 diabetes mellitus; type II diabetes mellitus; non-insulin-dependent diabetes.
Objectives	The two review questions (18 & 19) relating to postnatal testing have the combined aims of: • identifying which test should be used in the postnatal period • identifying the optimal timing for testing	The need to update this topic in the guideline was partly prompted by concerns that the recommendation in the 2008 guideline was based on a single study, conducted using a small sample (122 OGTTs) in a single hospital. Although the review question and objectives refer to postnatal testing, it was agreed that the question should be interpreted more broadly than the standard 6-8 week postnatal period to allow consideration of studies that evaluate testing at 12 weeks or later. The guideline scope is broad enough to allow the GDG to consider

Question 18		
		recommending testing annually after pregnancy, as in the 2008 guideline.
Language	English	
Study design	Randomised controlled trials (RCTs) Comparative observational studies	
Status	Published articles (no limitation on year of publication)	The original intention was to search for articles published after the searches for the 2008 guideline were completed, but such a search identified a systematic review that included relevant articles published before the cut-off date for the 2008 guideline that were not included in the 2008 guideline and so a search was executed without any limitation on year of publication.
Population	Women who have had gestational diabetes	It will be important to record whether included studies document a return to euglycaemia in the immediate days following the birth and before discharge to community care. It is, however, recognised that many studies may not provide this information. The criteria used to define gestational diabetes should be documented if resported (there are many variations of this).
Intervention or index test	Postnatal FPG test Postnatal HbA1c test	In the first instance, include studies only if the WHO 1999 criteria (or equivalents) are used for diagnosing diabetes after delivery (GDG to consider relaxing this restriction if there is not enough evidence to allow a recommendation to be made) Note that glucose challenge tests (GCTs), random glucose measurements and urinalysis are not to be included.

Question 18		
		The type of OGTT used and where it is done (primary or secondary care) should be documented in the evidence tables.
Comparator or reference standard	Postnatal OGTT	
Clinical outcomes	Incidence of IFG, IGT and diabetes in women at different time intervals in the postnatal period Accuracy in detecting IFG, IGT or diabetes	The definitions of glucose intolerance should be documented in the evidence tables to allow consideration of different thresholds used
Health economic outcomes	This question was selected as a priority for health economic analysis (a combined analysis for the questions on accuracy and timing of postnatal testing for diabetes may be undertaken)	
Other criteria for inclusion/ exclusion of studies	Exclude results for diagnosis based on WHO 1985 criteria (because the 2008 guideline recommends diagnosis of gestational diabetes using WHO 1999 criteria)	
Search strategies	A single search will be conducted to cover both review questions relating to postnatal testing - see separate document for further details	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	Note that the QUADAS methodology checklist for diagnostic test accuracy studies (NICE guidelines manual January 2009) has been used for this question because the majority of the systematic reviewing was undertaken when the 2009 edition of the manual was still in use. All other aspects of the review are consistent with the 2012 edition of the manual.
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

D.15 Timing of postnatal testing

Question 19		
Existing recommendation(s) in 2008 guideline	Women who were diagnosed with gestational diabetes should be offered lifestyle advice (including weight control, diet and exercise) and offered a fasting plasma glucose measurement (but not an OGTT) at the 6 week postnatal check and annually thereafter.	OGTT stands for 'oral glucose tolerance test' The recommendation to offer a test coinciding with the postnatal check at 6 weeks appears to have been based on: • an existing National Service Framework (NSF) • obstetric and gynaecology specialist recommendations
Review question for update	What is the optimal timing of postnatal testing for the detection of glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care)?	The term glucose intolerance covers: • impaired fasting glucose (IFG) • impaired glucose tolerance (IGT) and • diabetes. The gold-standard reference test is a fasting plasma glucose (FPG) measurement and 2-hour OGTT using the diagnostic criteria defined by WHO 1999 for IFG, IGT and diabetes. A positive test result from either the FPG or the OGTT components is sufficient to diagnose 'impairedness' or diabetes. Many different criteria are used to specify thresholds for diagnosis. Some require only one test to be performed (for example, ADA 1997) while others require two tests (for example, WHO 1999) Studies report outcomes for impairedness as IFG alone, IGT alone, or IFG and IGT together.
Objectives	The two review questions (18 & 19) relating to postnatal testing have the combined aims of: • identifying which test should be used in the postnatal period • identifying the optimal timing for testing	Although the review question and objectives refer to postnatal testing, it was agreed that the question should be interpreted more broadly than the standard

Question 19		
		6-8 week postnatal period to allow consideration of studies that evaluate testing at 12 weeks or later. The guideline scope is broad enough to allow the GDG to consider recommending testing annually after pregnancy, as in the 2008 guideline.
Language	English	
Study design	Observational studies	
Status	Published articles (no limitation on year of publication)	The original intention was to search for articles published after the searches for the 2008 guideline were completed, but such a search identified a systematic review that included relevant articles published before the cut-off date for the 2008 guideline that were not included in the 2008 guideline and so a search was executed without any limitation on year of publication.
Population	Women who have had gestational diabetes	
Intervention	Postnatal FPG Postnatal HbA1c Postnatal OGTT	In the first instance, include studies only if the WHO 1999 criteria (or equivalents) are used for the diagnosis of diabetes after delivery (GDG to consider relaxing this restriction if there is not enough evidence to allow a recommendation to be made).
Comparator or reference standard	NA	
Clinical outcomes	Incidence of IFG, IGT and diabetes in women at different time intervals in the postnatal period	
Health economic outcomes	This question was selected as a priority for health economic analysis (a combined analysis for the questions on accuracy and timing of postnatal testing for diabetes may be undertaken)	
Other criteria for inclusion/	Exclude results for diagnosis based on WHO 1985 criteria (because the 2008 guideline recommends diagnosis of gestational diabetes using WHO 1999 criteria)	

Question 19		
exclusion of studies		
Search strategies	A single search will be conducted to cover both review questions relating to postnatal testing - see separate document for further details	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	Note that the QUADAS methodology checklist for diagnostic test accuracy studies (NICE guidelines manual January 2009) has been used for this question because the majority of the systematic reviewing was undertaken when the 2009 edition of the manual was still in use. All other aspects of the review are consistent with the 2012 edition of the manual.
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

Appendix E: Search strategies

E.1 Search 1: Oral contraceptives containing oestrogen and/or progestogen

A single search was conducted for 2 review questions.

Review question 1: What is the effectiveness of oral oestrogen-containing contraceptives in women with diabetes compared with women without diabetes?

Review question 2: What is the effectiveness of oral progestogen-containing contraceptives in women with diabetes compared with women without diabetes?

Database(s): Ovid MEDLINE(R) 1946 to March Week 2 2014
Search Strategy: **DiP_update_combined_oral_contraceptive_RERUN1_medline_200314**

#	Searches
1	exp DIABETES MELLITUS/
2	(T1DM or T2DM).ti,ab.
3	IDDM.ti,ab.
4	diabet$.ti.
5	PREDIABETIC STATE/
6	prediabet$.ti,ab.
7	impaired glucose tolerance.ti,ab.
8	IGT.ti,ab.
9	Impaired fasting glucose.ti,ab.
10	IFG.ti,ab.
11	Impaired glucose regulation.ti,ab.
12	IGR.ti,ab.
13	GLUCOSE INTOLERANCE/
14	or/1-13
15	CONTRACEPTIVES, ORAL/ or CONTRACEPTIVES, ORAL, COMBINED/ or CONTRACEPTIVES, ORAL, HORMONAL/ or CONTRACEPTIVES, ORAL, SEQUENTIAL/ or CONTRACEPTIVES, ORAL, SYNTHETIC/ or exp CONTRACEPTIVES, POSTCOITAL/
16	ETHINYL ESTRADIOL/ or ETHINYL ESTRADIOL-NORGESTREL COMBINATION/ or MESTRANOL/
17	ESTRADIOL/
18	ESTROGENS/ or ESTROGENS, NON-STEROIDAL/
19	PROGESTINS/
20	DESOGESTREL/
21	DRSP.ti,ab.
22	exp NORPREGNENES/
23	gestodene.ti,ab.
24	drospirenone.ti,ab.
25	levonorgestrel.ti,ab.
26	(norethisterone or norgestimate).ti,ab.
27	NANDROLONE/
28	dienogest.ti,ab.
29	etynodiol.ti,ab.

#	Searches
30	"combined oral contracepti$".ti,ab.
31	COCP.ti,ab.
32	mini?pill.ti,ab.
33	progest#gen$.ti,ab.
34	(Gedarel or Mercilon or Femodette or Millinette or Sunya or Loestrin or Marvelon or Yasmin or Katya or Levest or Microgynon, or Ovranette, or Rigevidon or Cilest or Brevinor or Ovysmen or Norimin or Norinyl or Femodene or Triadene or Logynon or Triregol or Binovum or Synphase or Trinovum or Qlaira).ti,ab.
35	(combined adj oral adj3 contracept$).ti,ab.
36	or/15-35
37	and/14,36
38	randomized controlled trial.pt.
39	controlled clinical trial.pt.
40	DOUBLE BLIND METHOD/
41	SINGLE BLIND METHOD/
42	RANDOM ALLOCATION/
43	or/38-42
44	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
45	clinical trial.pt.
46	exp CLINICAL TRIAL/
47	exp CLINICAL TRIALS AS TOPIC/
48	(clinic$ adj5 trial$).tw,sh.
49	PLACEBOS/
50	placebo$.tw,sh.
51	random$.tw,sh.
52	or/44-51
53	or/43,52
54	META ANALYSIS/
55	META ANALYSIS AS TOPIC/
56	meta analysis.pt.
57	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
58	(systematic$ adj5 (review$ or overview$)).tw,sh.
59	(methodologic$ adj5 (review$ or overview$)).tw,sh.
60	or/54-59
61	review$.pt.
62	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
63	((hand or manual$) adj2 search$).tw.
64	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
65	(pooling or pooled or mantel haenszel).tw,sh.
66	(peto or dersimonian or der simonian or fixed effect).tw,sh.
67	or/62-66
68	and/61,67
69	exp CASE-CONTROL STUDIES/
70	(case$ adj2 control$).tw.
71	exp COHORT STUDIES/

#	Searches
72	cohort$.tw.
73	or/69-72
74	comparative study.pt.
75	or/73-74
76	or/53,60,68,75
77	letter.pt.
78	comment.pt.
79	editorial.pt.
80	historical article.pt.
81	or/77-80
82	76 not 81
83	and/37,82
84	limit 83 to english language
85	limit 84 to animals
86	limit 84 to (animals and humans)
87	85 not 86
88	84 not 87
89	limit 88 to yr="2012 -Current"

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations March 19, 2014
Search Strategy: **DiP_update_combined_oral_contraceptive_RERUN1_mip_200314**

#	Searches
1	diabet$.ti,ab.
2	(T1DM or T2DM).ti,ab.
3	IDDM.ti,ab.
4	pre?diabet$.ti,ab.
5	((impaired or fasting) adj3 glucose).ti,ab.
6	IGT.ti,ab.
7	IFG.ti,ab.
8	Impaired glucose regulation.ti,ab.
9	IGR.ti,ab.
10	(glucose adj intoleran$).ti,ab.
11	or/1-10
12	((oral or combined or hormonal) adj3 (contracept$ or pill$)).ti,ab.
13	(estradiol or oestradiol or estrogen? or oestrogen?).ti,ab.
14	progestin?.ti,ab.
15	desogestrel.ti,ab.
16	DRSP.ti,ab.
17	norpregnenes.ti,ab.
18	gestodene.ti,ab.
19	drospirenone.ti,ab.
20	levonorgestrel.ti,ab.
21	(norethisterone or norgestimate).ti,ab.
22	nandrolone.ti,ab.
23	dienogest.ti,ab.

#	Searches
24	etynodiol.ti,ab.
25	(hormonal adj3 contracept$).ti,ab.
26	"combined oral contracepti$".ti,ab.
27	COCP.ti,ab.
28	mini?pill.ti,ab.
29	progest#gen$.ti,ab.
30	(Gedarel or Mercilon or Femodette or Millinette or Sunya or Loestrin or Marvelon or Yasmin or Katya or Levest or Microgynon, or Ovranette, or Rigevidon or Cilest or Brevinor or Ovysmen or Norimin or Norinyl or Femodene or Triadene or Logynon or Triregol or Binovum or Synphase or Trinovum or Logynon or Qlaira).ti,ab.
31	(combined adj oral adj3 contracept$).ti,ab.
32	or/12-31
33	and/11,32
34	limit 33 to yr="2012 -Current"

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials January 2014
Search Strategy: **DiP_update_combined_oral_contraceptive_RERUN1_cctr_200314**

#	Searches
1	exp DIABETES MELLITUS/
2	(T1DM or T2DM).ti,ab.
3	IDDM.ti,ab.
4	diabet$.ti.
5	PREDIABETIC STATE/
6	prediabet$.ti,ab.
7	impaired glucose tolerance.ti,ab.
8	IGT.ti,ab.
9	Impaired fasting glucose.ti,ab.
10	IFG.ti,ab.
11	Impaired glucose regulation.ti,ab.
12	IGR.ti,ab.
13	GLUCOSE INTOLERANCE/
14	or/1-13
15	CONTRACEPTIVES, ORAL/ or CONTRACEPTIVES, ORAL, COMBINED/ or CONTRACEPTIVES, ORAL, HORMONAL/ or CONTRACEPTIVES, ORAL, SEQUENTIAL/ or CONTRACEPTIVES, ORAL, SYNTHETIC/ or exp CONTRACEPTIVES, POSTCOITAL/
16	ETHINYL ESTRADIOL/ or ETHINYL ESTRADIOL-NORGESTREL COMBINATION/ or MESTRANOL/
17	ESTRADIOL/
18	ESTROGENS/ or ESTROGENS, NON-STEROIDAL/
19	PROGESTINS/
20	DESOGESTREL/
21	DRSP.ti,ab.
22	exp NORPREGNENES/
23	gestodene.ti,ab.
24	drospirenone.ti,ab.
25	levonorgestrel.ti,ab.

#	Searches
26	(norethisterone or norgestimate).ti,ab.
27	NANDROLONE/
28	dienogest.ti,ab.
29	etynodiol.ti,ab.
30	"combined oral contracepti$".ti,ab.
31	COCP.ti,ab.
32	mini?pill.ti,ab.
33	progest#gen$.ti,ab.
34	(Gedarel or Mercilon or Femodette or Millinette or Sunya or Loestrin or Marvelon or Yasmin or Katya or Levest or Microgynon, or Ovranette, or Rigevidon or Cilest or Brevinor or Ovysmen or Norimin or Norinyl or Femodene or Triadene or Logynon or Triregol or Binovum or Synphase or Trinovum or Qlaira).ti,ab.
35	(combined adj oral adj3 contracept$).ti,ab.
36	or/15-35
37	and/14,36
38	limit 37 to yr="2012 -Current"

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to February 2014, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2014
Search Strategy:
DiP_update_combined_oral_contraceptive_RERUN1_cdsrdare_200314

#	Searches
1	DIABETES MELLITUS.kw.
2	(T1DM or T2DM).tw,tx.
3	IDDM.tw,tx.
4	diabet$.ti.
5	PREDIABETIC STATE.kw.
6	prediabet$.tw,tx.
7	impaired glucose tolerance.tw,tx.
8	IGT.tw,tx.
9	Impaired fasting glucose.tw,tx.
10	IFG.tw,tx.
11	Impaired glucose regulation.tw,tx.
12	IGR.tw,tx.
13	GLUCOSE INTOLERANCE.kw.
14	or/1-13
15	(CONTRACEPTIVES, ORAL or CONTRACEPTIVES, ORAL, COMBINED or CONTRACEPTIVES, ORAL, HORMONAL or CONTRACEPTIVES, ORAL, SEQUENTIAL or CONTRACEPTIVES, ORAL, SYNTHETIC or CONTRACEPTIVES, POSTCOITAL).kw.
16	(ETHINYL ESTRADIOL or ETHINYL ESTRADIOL-NORGESTREL COMBINATION or MESTRANOL).kw.
17	ESTRADIOL.kw.
18	(ESTROGENS or ESTROGENS, NON-STEROIDAL).kw.
19	PROGESTINS.kw.
20	DESOGESTREL.kw.
21	DRSP.tw,tx.

#	Searches
22	NORPREGNENES.kw.
23	gestodene.tw,tx.
24	drospirenone.tw,tx.
25	levonorgestrel.tw,tx.
26	(norethisterone or norgestimate).tw,tx.
27	NANDROLONE.kw.
28	dienogest.tw,tx.
29	etynodiol.tw,tx.
30	(hormonal adj3 contracept$).tw,tx.
31	"combined oral contracepti$".tw,tx.
32	COCP.tw,tx.
33	mini?pill.tw,tx.
34	progest#gen$.tw,tx.
35	(Gedarel or Mercilon or Femodette or Millinette or Sunya or Loestrin or Marvelon or Yasmin or Katya or Levest or Microgynon, or Ovranette, or Rigevidon or Cilest or Brevinor or Ovysmen or Norimin or Norinyl or Femodene or Triadene or Logynon or Triregol or Binovum or Synphase or Trinovum or Qlaira).tw,tx.
36	(combined adj oral adj3 contracept$).tw,tx.
37	or/15-36
38	and/14,37
39	("2012" or "2013" or "2014").dp.
40	and/38-39

Database(s): EBM Reviews - Health Technology Assessment 1st Quarter 2014
Search Strategy: **DiP_update_combined_oral_contraceptive_RERUN1_hta_200314**

#	Searches
1	exp DIABETES MELLITUS/
2	(T1DM or T2DM).tw.
3	IDDM.tw.
4	diabet$.tw.
5	PREDIABETIC STATE/
6	prediabet$.tw.
7	impaired glucose tolerance.tw.
8	IGT.tw.
9	Impaired fasting glucose.tw.
10	IFG.tw.
11	Impaired glucose regulation.tw.
12	IGR.tw.
13	GLUCOSE INTOLERANCE/
14	or/1-13
15	CONTRACEPTIVES, ORAL/ or CONTRACEPTIVES, ORAL, COMBINED/ or CONTRACEPTIVES, ORAL, HORMONAL/ or CONTRACEPTIVES, ORAL, SEQUENTIAL/ or CONTRACEPTIVES, ORAL, SYNTHETIC/ or exp CONTRACEPTIVES, POSTCOITAL/
16	ETHINYL ESTRADIOL/ or ETHINYL ESTRADIOL-NORGESTREL COMBINATION/ or MESTRANOL/
17	ESTRADIOL/

#	Searches
18	ESTROGENS/ or ESTROGENS, NON-STEROIDAL/
19	PROGESTINS/
20	DESOGESTREL/
21	DRSP.tw.
22	exp NORPREGNENES/
23	gestodene.tw.
24	drospirenone.tw.
25	levonorgestrel.tw.
26	(norethisterone or norgestimate).tw.
27	NANDROLONE/
28	dienogest.tw.
29	etynodiol.tw.
30	"combined oral contracepti$".tw.
31	COCP.tw.
32	mini?pill.tw.
33	progest#gen$.tw.
34	(Gedarel or Mercilon or Femodette or Millinette or Sunya or Loestrin or Marvelon or Yasmin or Katya or Levest or Microgynon, or Ovranette, or Rigevidon or Cilest or Brevinor or Ovysmen or Norimin or Norinyl or Femodene or Triadene or Logynon or Triregol or Binovum or Synphase or Trinovum or Qlaira).tw.
35	(combined adj oral adj3 contracept$).tw.
36	or/15-35
37	and/14,36
38	limit 37 to yr="2012 -Current"

Database(s): Embase 1974 to 2014 March 19
Search Strategy: DiP_**update_combined_oral_contraceptive_RERUN1_embase_200314**

#	Searches
1	DIABETES MELLITUS/ or IMPAIRED GLUCOSE TOLERANCE/ or INSULIN DEPENDENT DIABETES MELLITUS/ or JUVENILE DIABETES MELLITUS/ or NON INSULIN DEPENDENT DIABETES MELLITUS/
2	(T1DM or T2DM).ti,ab.
3	(IDDM or NIDDM).ti,ab.
4	diabet$.ti.
5	pre?diabet$.ti,ab.
6	impaired fasting glucose.ti,ab.
7	(IGT or IFG).ti,ab.
8	IGR.ti,ab.
9	GLUCOSE INTOLERANCE/
10	or/1-9
11	exp ORAL CONTRACEPTIVE AGENT/
12	DIENOGEST PLUS ESTRADIOL VALERATE/
13	ESTRADIOL/
14	*ESTROGEN/
15	*GESTAGEN/
16	progestin?.ti,ab.

#	Searches
17	progest#gen$.ti,ab.
18	(hormonal adj3 contracept$).ti,ab.
19	"combined oral contracepti$".ti,ab.
20	COCP.ti,ab.
21	mini?pill.ti,ab.
22	(Gedarel or Mercilon or Femodette or Millinette or Sunya or Loestrin or Marvelon or Yasmin or Katya or Levest or Microgynon, or Ovranette, or Rigevidon or Cilest or Brevinor or Ovysmen or Norimin or Norinyl or Femodene or Triadene or Logynon or Triregol or Binovum or Synphase or Trinovum or Qlaira).ti,ab.
23	(combined adj oral adj3 contracept$).ti,ab.
24	or/11-23
25	and/10,24
26	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
27	(clinic$ adj5 trial$).tw,sh.
28	SINGLE BLIND PROCEDURE/
29	DOUBLE BLIND PROCEDURE/
30	RANDOM ALLOCATION/
31	CROSSOVER PROCEDURE/
32	PLACEBO/
33	placebo$.tw,sh.
34	random$.tw,sh.
35	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
36	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.
37	randomi?ed control$ trial$.tw.
38	or/26-37
39	META ANALYSIS/
40	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.
41	(systematic$ adj5 (review$ or overview$)).tw,sh.
42	(methodologic$ adj5 (review$ or overview$)).tw,sh.
43	or/39-42
44	review.pt.
45	(medline or medlars or embase).ab.
46	(scisearch or science citation index).ab.
47	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
48	((hand or manual$) adj2 search$).tw.
49	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
50	(pooling or pooled or mantel haenszel).tw.
51	(peto or dersimonian or "der simonian" or fixed effect).tw.
52	or/45-51
53	and/44,52
54	exp CASE CONTROL STUDY/
55	RETROSPECTIVE STUDY/
56	(case$ adj2 control$).tw.
57	COHORT ANALYSIS/
58	LONGITUDINAL STUDY/

#	Searches
59	FOLLOW UP/
60	PROSPECTIVE STUDY/
61	cohort$.tw.
62	or/54-61
63	or/38,43,53,62
64	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
65	63 not 64
66	COMPARATIVE STUDY/ or COMPARATIVE EFFECTIVENESS/ or DOSAGE SCHEDULE COMPARISON/ or exp DRUG COMPARISON/ or DRUG DOSAGE FORM COMPARISON/ or DRUG DOSE COMPARISON/ or INTERMETHOD COMPARISON/
67	and/25,65
68	and/25,66
69	or/67-68
70	limit 69 to english language
71	exp HORMONE SUBSTITUTION/
72	((hormone or oestrogen or estrogen) adj replacement therap?).ti,ab.
73	(HRT or EBHT).ti,ab.
74	or/71-73
75	70 not 74
76	limit 75 to yr="2012 -Current"

E.2 Search 2: Ketone monitoring in the preconception and antenatal periods

A single search was conducted for 2 review questions.

Review question 3: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1 or type 2 diabetes who are planning pregnancy?

Review question 11: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1, type 2 or gestational diabetes during pregnancy?

Database(s): Ovid MEDLINE(R) 1946 to February Week 2 2014
Search Strategy: **DiP_update_ketone_monitoring_RERUN1_medline_260214**

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	or/1-5
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
8	clinical trial.pt.
9	exp CLINICAL TRIAL/
10	exp CLINICAL TRIALS AS TOPIC/
11	(clinic$ adj5 trial$).tw,sh.
12	PLACEBOS/

#	Searches
13	placebo$.tw,sh.
14	random$.tw,sh.
15	or/7-14
16	or/6,15
17	META ANALYSIS/
18	META ANALYSIS AS TOPIC/
19	meta analysis.pt.
20	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21	(systematic$ adj5 (review$ or overview$)).tw,sh.
22	(methodologic$ adj5 (review$ or overview$)).tw,sh.
23	or/17-22
24	review$.pt.
25	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
26	((hand or manual$) adj2 search$).tw.
27	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
28	(pooling or pooled or mantel haenszel).tw,sh.
29	(peto or dersimonian or der simonian or fixed effect).tw,sh.
30	or/25-29
31	and/24,30
32	exp CASE-CONTROL STUDIES/
33	(case$ adj2 control$).tw.
34	exp COHORT STUDIES/
35	cohort$.tw.
36	or/32-35
37	or/16,23,31,36
38	exp PREGNANCY IN DIABETICS/
39	DIABETES, GESTATIONAL/
40	(diabet$ adj3 (gestat$ or pregnan$ or gravid$)).ti,ab.
41	GDM.ti,ab.
42	or/38-41
43	exp DIABETES MELLITUS/
44	exp DIABETES INSIPIDUS/
45	(T?1DM or T?2DM or IDDM or NIDDM).ti,ab.
46	diabet$.ti.
47	PREDIABETIC STATE/
48	(prediabet$ or pre diabet$).ti,ab.
49	impaired glucose tolerance.ti,ab.
50	IGT.ti,ab.
51	(impaired fasting glucose or impaired fasting glyc?emi$).ti,ab.
52	IFG.ti,ab.
53	Impaired glucose regulation.ti,ab.
54	IGR.ti,ab.
55	(Non diabetic hyperglyc?emi# or nondiabetic hyperglyc?emi#).ti,ab.
56	NDH.ti,ab.

#	Searches
57	GLUCOSE INTOLERANCE/
58	(glucose adj2 intoleran$).ti,ab.
59	or/43-58
60	PREGNANCY/
61	(pregnan$ or gestat$ or gravid$).ti,ab.
62	PREGNANT WOMEN/
63	or/60-62
64	and/59,63
65	or/42,64
66	KETONES/ or KETONE BODIES/
67	3-HYDROXYBUTYRIC ACID/
68	(keton?e$ or hyperketon?e$ or ketonuria or hyperketonuria).ti,ab.
69	(ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB).ti,ab,nm.
70	exp KETOSIS/
71	(diabet$ adj3 (ketogenesis or ketosis or ketoacido$)).ti,ab.
72	DKA.ti,ab.
73	or/66-72
74	MONITORING, PHYSIOLOGIC/ or BLOOD GLUCOSE SELF-MONITORING/ or exp FETAL MONITORING/ or SELF CARE/
75	(self monitor$ or monitor$ or meter$ or measur$ or test$ or screen$ or determin$ or assess$ or surveillance or check$).ti,ab.
76	or/74-75
77	and/73,76
78	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
79	or/77-78
80	and/65,79
81	and/37,80
82	LETTER/
83	EDITORIAL/
84	NEWS/
85	exp HISTORICAL ARTICLE/
86	ANECDOTES AS TOPIC/
87	COMMENT/
88	CASE REPORT/
89	(letter or comment* or abstracts).ti.
90	or/82-89
91	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
92	90 not 91
93	ANIMALS/ not HUMANS/
94	exp ANIMALS, LABORATORY/
95	exp ANIMAL EXPERIMENTATION/
96	exp MODELS, ANIMAL/

#	Searches
97	exp RODENTIA/
98	(rat or rats or mouse or mice).ti.
99	or/92-98
100	81 not 99
101	limit 100 to english language
102	limit 101 to yr="2013 -Current"

Database(s): **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations** March 22, 2013
Search Strategy: DiP_update_ketone_monitoring_mip_250313

#	Searches
1	(diabet$ adj3 (gestat$ or pregnan$ or gravid$)).ti,ab.
2	GDM.ti,ab.
3	or/1-2
4	(T?1DM or T?2DM or IDDM or NIDDM).ti,ab.
5	diabet$.ti.
6	(prediabet$ or pre diabet$).ti,ab.
7	impaired glucose tolerance.ti,ab.
8	IGT.ti,ab.
9	(impaired fasting glucose or impaired fasting glyc?emi$).ti,ab.
10	IFG.ti,ab.
11	Impaired glucose regulation.ti,ab.
12	IGR.ti,ab.
13	(Non diabetic hyperglyc?emi# or nondiabetic hyperglyc?emi#).ti,ab.
14	NDH.ti,ab.
15	(glucose adj2 intoleran$).ti,ab.
16	or/4-15
17	(pregnan$ or gestat$ or gravid$).ti,ab.
18	and/16-17
19	or/3,18
20	(keton?e$ or hyperketon?e$ or ketonuria or hyperketonuria).ti,ab.
21	(ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB).ti,ab.
22	(diabet$ adj3 (ketogenesis or ketosis or ketoacido$)).ti,ab.
23	DKA.ti,ab.
24	or/20-23
25	(self monitor$ or monitor$ or meter$ or measur$ or test$ or screen$ or determin$ or assess$ or surveillance or check$).ti,ab.
26	and/24-25
27	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
28	or/26-27
29	and/19,28

Database(s): **EBM Reviews - Cochrane Central Register of Controlled Trials** February 2013
Search Strategy: DiP_update_ketone_monitoring_cctr_250313

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(diabet$ adj3 (gestat$ or pregnan$ or gravid$)).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T?1DM or T?2DM or IDDM or NIDDM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	(prediabet$ or pre diabet$).ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	(impaired fasting glucose or impaired fasting glyc?emi$).ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	(Non diabetic hyperglyc?emi# or nondiabetic hyperglyc?emi#).ti,ab.
19	NDH.ti,ab.
20	GLUCOSE INTOLERANCE/
21	(glucose adj2 intoleran$).ti,ab.
22	or/6-21
23	PREGNANCY/
24	(pregnan$ or gestat$ or gravid$).ti,ab.
25	PREGNANT WOMEN/
26	or/23-25
27	and/22,26
28	or/5,27
29	KETONES/ or KETONE BODIES/
30	3-HYDROXYBUTYRIC ACID/
31	(keton?e$ or hyperketon?e$ or ketonuria or hyperketonuria).ti,ab.
32	(ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB).ti,ab.
33	exp KETOSIS/
34	(diabet$ adj3 (ketogenesis or ketosis or ketoacido$)).ti,ab.
35	DKA.ti,ab.
36	or/29-35
37	MONITORING, PHYSIOLOGIC/ or BLOOD GLUCOSE SELF-MONITORING/ or exp FETAL MONITORING/ or SELF CARE/
38	(self monitor$ or monitor$ or meter$ or measur$ or test$ or screen$ or determin$ or assess$ or surveillance or check$).ti,ab.

#	Searches
39	or/37-38
40	and/36,39
41	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
42	or/40-41
43	and/28,42
44	limit 43 to yr="2007 -Current"

Database(s): **EBM Reviews - Health Technology Assessment** 1st Quarter 2013
Search Strategy: DiP_update_ketone_monitoring_hta_250313

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(diabet$ adj3 (gestat$ or pregnan$ or gravid$)).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T?1DM or T?2DM or IDDM or NIDDM).tw.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	(prediabet$ or pre diabet$).tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	(impaired fasting glucose or impaired fasting glyc?emi$).tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	(Non diabetic hyperglyc?emi# or nondiabetic hyperglyc?emi#).tw.
19	NDH.tw.
20	GLUCOSE INTOLERANCE/
21	(glucose adj2 intoleran$).tw.
22	or/6-21
23	PREGNANCY/
24	(pregnan$ or gestat$ or gravid$).tw.
25	PREGNANT WOMEN/
26	or/23-25
27	and/22,26
28	or/5,27
29	KETONES/ or KETONE BODIES/
30	3-HYDROXYBUTYRIC ACID/
31	(keton?e$ or hyperketon?e$ or ketonuria or hyperketonuria).tw.
32	(ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B

#	Searches
	OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB).tw.
33	exp KETOSIS/
34	(diabet$ adj3 (ketogenesis or ketosis or ketoacido$)).tw.
35	DKA.tw.
36	or/29-35
37	MONITORING, PHYSIOLOGIC/ or BLOOD GLUCOSE SELF-MONITORING/ or exp FETAL MONITORING/ or SELF CARE/
38	(self monitor$ or monitor$ or meter$ or measur$ or test$ or screen$ or determin$ or assess$ or surveillance or check$).tw.
39	or/37-38
40	and/36,39
41	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.
42	or/40-41
43	and/28,42
44	limit 43 to yr="2007 -Current"

Database(s): Embase 1974 to 2014 February 25
Search Strategy: **DiP_update_ketone_monitoring_RERUN1_embase_260214**

#	Searches
1	CLINICAL TRIALS/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).tw,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.tw,sh.
9	random$.tw,sh.
10	RANDOMIZED CONTROLLED TRIALS/
11	((single or double or triple or treble) adj (blind$ or mask$)).tw,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).tw,sh.
16	(systematic$ adj5 (review$ or overview$)).tw,sh.
17	(methodologic$ adj5 (review$ or overview$)).tw,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online

#	Searches
	database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	19 and 27
29	COMPARATIVE STUDY/
30	(compar$ adj5 stud$).tw.
31	CASE-CONTROL STUDY/
32	RETROSPECTIVE STUDY/
33	PROSPECTIVE STUDY/
34	COHORT STUDY/
35	(case$ adj2 control$).tw.
36	or/29-35
37	or/13,18,28,36
38	abstract report.tw,sh.
39	note.tw,sh.
40	short survey.tw,sh.
41	letter.tw,sh.
42	editorial.tw,sh.
43	or/38-42
44	37 not 43
45	exp PREGNANCY DIABETES MELLITUS/
46	(diabet$ adj3 (gestation$ or pregnan$ or gravid$)).ti,ab.
47	GDM.ti,ab.
48	or/45-47
49	exp DIABETES MELLITUS/
50	exp DIABETES INSIPIDUS/
51	diabet$.ti.
52	(T?1DM or T?2DM).ti,ab.
53	(IDDM or NIDDM).ti,ab.
54	(prediabet$ or pre diabet$).ti,ab.
55	IMPAIRED GLUCOSE TOLERANCE/
56	IGT.ti,ab.
57	(impaired fasting glucose or impaired fasting glyc?emi$).ti,ab.
58	IFG.ti,ab.
59	impaired glucose regulat$.ti,ab.
60	IGR.ti,ab.
61	(Non diabetic hyperglyc?emi# or nondiabetic hyperglyc?emi#).ti,ab.
62	NDH.ti,ab.
63	GLUCOSE INTOLERANCE/
64	(glucose adj2 intoleran$).ti,ab.
65	or/49-62
66	PREGNANCY/ or FIRST TRIMESTER PREGNANCY/ or PREGNANT WOMAN/ or SECOND TRIMESTER PREGNANCY/ or THIRD TRIMESTER PREGNANCY/
67	(pregnan$ or gestation$ or gravid$).ti,ab.
68	or/66-67

#	Searches
69	and/65,68
70	or/48,69
71	KETOGENESIS/
72	KETONE/
73	KETONE BODY/
74	KETONURIA/
75	3 HYDROXYBUTYRIC ACID/
76	DIABETIC KETOACIDOSIS/
77	(keton?e$ or hyperketon?e$ or keton?ur$ or hyperketon?e$).ti,ab.
78	(hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or "B OHB" or 3OHB or "3 OHB" or BHB? or 3HB or "3 HB").ti,ab.
79	(diabet$ adj3 (ketogenesis or ketosis or ketoacido$)).ti,ab.
80	DKA.ti,ab.
81	or/71-80
82	PATIENT MONITORING/
83	FETUS MONITORING/
84	BLOOD GLUCOSE MONITORING/
85	SELF CARE/
86	(self monitor$ or monitor$ or meter$ or measure$ or test$ or assess$ or screen$ or determin$ or surveillance or check$).ti,ab.
87	or/82-86
88	and/81,87
89	((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (keton$ or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or "B OHB" or 3OHB or "3 OHB" or BHB? or 3HB or "3 HB")).ti,ab.
90	or/88-89
91	and/70,90
92	and/44,91
93	conference abstract.pt.
94	letter.pt. or LETTER/
95	note.pt.
96	editorial.pt.
97	CASE REPORT/ or CASE STUDY/
98	(letter or comment* or abstracts).ti.
99	or/93-98
100	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
101	99 not 100
102	ANIMAL/ not HUMAN/
103	NONHUMAN/
104	exp ANIMAL EXPERIMENT/
105	exp EXPERIMENTAL ANIMAL/
106	ANIMAL MODEL/
107	exp RODENT/
108	(rat or rats or mouse or mice).ti.
109	or/101-108

#	Searches
110	92 not 109
111	limit 110 to english language
112	limit 111 to yr="2013 -Current"

E.3 Blood glucose and HbA1c target values in the preconception period and antenatal monitoring and target values

A single search was conducted for six review questions:

Review question 4: What are the target ranges for blood glucose in women with type 1 or type 2 diabetes who are planning pregnancy?

Review question 5: What is the target value for HbA1c in women with type 1 or type 2 diabetes who are planning pregnancy?

Review question 10: What is the effectiveness of blood glucose monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?

Review question 12: What are the target ranges for blood glucose in women with type 1, type 2 or gestational diabetes during pregnancy?

Review question 13: What is the effectiveness of HbA1c monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?

Review question 14: What is the target value for HbA1c in women with type 1, type 2 or gestational diabetes during pregnancy?

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials March 2013
Search Strategy: DiP_update_HbA1c_blood_glucose_HbA1c_monitor_values_cctr_260413

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	GLUCOSE INTOLERANCE/

#	Searches
19	HYPERGLYCEMIA/
20	hyperglyc?emi?.ti,ab.
21	or/6-20
22	PREGNANCY/
23	(pregnan$ or gestation$).ti,ab.
24	PREGNANT WOMEN/
25	PRECONCEPTION CARE/
26	PRENATAL CARE/
27	pre?conception.ti,ab.
28	(pre adj conception).ti,ab.
29	pre?pregnancy.ti,ab.
30	(pre adj pregnancy).ti,ab.
31	(pre?natal$ or pre?conception or ante?natal$).ti,ab.
32	(pre adj natal$).ti,ab.
33	(pre adj conception).ti,ab.
34	(ante adj natal$).ti,ab.
35	or/22-34
36	and/21,35
37	or/5,36
38	BLOOD GLUCOSE/
39	(blood adj3 (glucose or sugar?)).ti,ab.
40	BLOOD GLUCOSE SELF-MONITORING/
41	BGSM.ti,ab.
42	(home glucose adj (test$ or monitor$)).ti,ab.
43	(self adj (test$ or monitor$)).ti,ab.
44	GLUCOSE TOLERANCE TEST/
45	OGTT.ti,ab.
46	(glucose adj (toleran$ or test$ or load$)).ti,ab.
47	(fasting adj plasma adj glucose).ti,ab.
48	FPG.ti,ab.
49	HEMOGLOBIN A, GLYCOSYLATED/
50	HbA1c.ti,ab.
51	(h?emoglobin? adj3 glycosylat$).ti,ab.
52	(glycated adj3 h?emoglobin?).ti,ab.
53	or/38-52
54	and/37,53
55	limit 54 to yr="2008 -Current"

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2013
Search Strategy:
DiP_update_HbA1c_blood_glucose_HbA1c_monitor_values_cdsrdare_260413

#	Searches
1	PREGNANCY IN DIABETICS.kw.
2	DIABETES, GESTATIONAL.kw.

#	Searches
3	(gestation$ adj3 diabet$).tw,tx.
4	GDM.tw,tx.
5	or/1-4
6	DIABETES MELLITUS.kw.
7	DIABETES INSIPIDUS.kw.
8	(T1DM or T2DM).tw,tx.
9	diabet$.tw,tx.
10	PREDIABETIC STATE.kw.
11	prediabet$.tw,tx.
12	impaired glucose tolerance.tw,tx.
13	IGT.tw,tx.
14	Impaired fasting glucose.tw,tx.
15	IFG.tw,tx.
16	Impaired glucose regulation.tw,tx.
17	IGR.tw,tx.
18	GLUCOSE INTOLERANCE.kw.
19	HYPERGLYCEMIA.kw.
20	hyperglyc?emi?.tw,tx.
21	or/6-20
22	PREGNANCY.kw.
23	(pregnan$ or gestation$).tw,tx.
24	PREGNANT WOMEN.kw.
25	PRECONCEPTION CARE.kw.
26	PRENATAL CARE.kw.
27	pre?conception.tw,tx.
28	(pre adj conception).tw,tx.
29	pre?pregnancy.tw,tx.
30	(pre adj pregnancy).tw,tx.
31	(pre?natal$ or pre?conception or ante?natal$).tw,tx.
32	(pre adj natal$).tw,tx.
33	(pre adj conception).tw,tx.
34	(ante adj natal$).tw,tx.
35	or/22-34
36	and/21,35
37	or/5,36
38	BLOOD GLUCOSE.kw.
39	(blood adj3 (glucose or sugar?)).tw,tx.
40	BLOOD GLUCOSE SELF-MONITORING.kw.
41	BGSM.tw,tx.
42	(home glucose adj (test$ or monitor$)).tw,tx.
43	(self adj (test$ or monitor$)).tw,tx.
44	GLUCOSE TOLERANCE TEST.kw.
45	OGTT.tw,tx.
46	(glucose adj (toleran$ or test$ or load$)).tw,tx.
47	(fasting adj plasma adj glucose).tw,tx.

#	Searches
48	FPG.tw,tx.
49	HEMOGLOBIN A, GLYCOSYLATED.kw.
50	HbA1c.tw,tx.
51	(h?emoglobin? adj3 glycosylat$).tw,tx.
52	(glycated adj3 h?emoglobin?).tw,tx.
53	or/38-52
54	and/37,53

Database(s): Embase 1974 to 2013 April 25
Search Strategy:
DiP_update_HbA1c_blood_glucose_HbA1c_monitor_values_embase_250413

#	Searches
1	PREGNANCY DIABETES MELLITUS/ or MATERNAL DIABETES MELLITUS/
2	(gestation$ adj3 diabet$).ti,ab.
3	or/1-2
4	DIABETES MELLITUS/ or IMPAIRED GLUCOSE TOLERANCE/ or INSULIN DEPENDENT DIABETES MELLITUS/ or JUVENILE DIABETES MELLITUS/ or NON INSULIN DEPENDENT DIABETES MELLITUS/
5	(T1DM or T2DM).ti,ab.
6	(IDDM or NIDDM).ti,ab.
7	diabet$.ti.
8	pre?diabet$.ti,ab.
9	impaired fasting glucose.ti,ab.
10	(IGT or IFG).ti,ab.
11	IGR.ti,ab.
12	GLUCOSE INTOLERANCE/
13	HYPERGLYCEMIA/
14	hyperglyc?emi?.ti,ab.
15	or/4-14
16	PREGNANCY/ or PREGNANT WOMAN/
17	(pregnan$ or gestation$).ti,ab.
18	MATERNAL CARE/
19	pre?conception.ti,ab.
20	(pre adj conception).ti,ab.
21	pre?pregnancy.ti,ab.
22	(pre adj pregnancy).ti,ab.
23	PRENATAL CARE/
24	(pre?natal$ or ante?natal$).ti,ab.
25	(pre adj natal$).ti,ab.
26	(ante adj natal$).ti,ab.
27	or/16-26
28	and/15,27
29	or/3,28
30	BLOOD GLUCOSE MONITORING/
31	(blood adj3 (glucose or sugar?)).ti,ab.

#	Searches
32	BGSM.ti,ab.
33	GLUCOSE BLOOD LEVEL/
34	(home glucose adj (test$ or monitor$)).ti,ab.
35	(self adj (test$ or monitor$)).ti,ab.
36	GLUCOSE TOLERANCE TEST/ or GLUCOSE CLAMP TECHNIQUE/ or INTRAVENOUS GLUCOSE TOLERANCE TEST/ or ORAL GLUCOSE TOLERANCE TEST/
37	(glucose adj (test$ or toleran$ or load?)).ti,ab.
38	(fasting adj plasma adj glucose).ti,ab.
39	FPG.ti,ab.
40	HEMOGLOBIN A1c/
41	HbA1c.ti,ab.
42	(h?emoglobin? adj3 glycosylat$).ti,ab.
43	(glycated adj3 h?emoglobin?).ti,ab.
44	or/30-43
45	and/29,44
46	conference abstract.pt.
47	letter.pt. or LETTER/
48	note.pt.
49	editorial.pt.
50	CASE REPORT/ or CASE STUDY/
51	(letter or comment* or abstracts).ti.
52	or/46-51
53	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
54	52 not 53
55	ANIMAL/ not HUMAN/
56	NONHUMAN/
57	exp ANIMAL EXPERIMENT/
58	exp EXPERIMENTAL ANIMAL/
59	ANIMAL MODEL/
60	exp RODENT/
61	(rat or rats or mouse or mice).ti.
62	or/54-61
63	45 not 62
64	limit 63 to english language
65	limit 64 to yr="2008 -Current"

Database(s): EBM Reviews - Health Technology Assessment 1st Quarter 2013
Search Strategy: DiP_update_HbA1c_blood_glucose_HbA1c_monitor_values_hta_260413

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/

#	Searches
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.tw.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	GLUCOSE INTOLERANCE/
19	HYPERGLYCEMIA/
20	hyperglyc?em?.tw.
21	or/6-20
22	PREGNANCY/
23	(pregnan$ or gestation$).tw.
24	PREGNANT WOMEN/
25	PRECONCEPTION CARE/
26	PRENATAL CARE/
27	pre?conception.tw.
28	(pre adj conception).tw.
29	pre?pregnancy.tw.
30	(pre adj pregnancy).tw.
31	(pre?natal$ or pre?conception or ante?natal).tw.
32	(pre adj natal$).tw.
33	(pre adj conception).tw.
34	(ante adj natal$).tw.
35	or/22-34
36	and/21,35
37	or/5,36
38	BLOOD GLUCOSE/
39	(blood adj3 (glucose or sugar?)).tw.
40	BLOOD GLUCOSE SELF-MONITORING/
41	BGSM.tw.
42	(home glucose adj (test$ or monitor$)).tw.
43	(self adj (test$ or monitor$)).tw.
44	GLUCOSE TOLERANCE TEST/
45	OGTT.tw.
46	(glucose adj (toleran$ or test$ or load$)).tw.
47	(fasting adj plasma adj glucose).tw.
48	FPG.tw.
49	HEMOGLOBIN A, GLYCOSYLATED/
50	HbA1c.tw.
51	(h?emoglobin? adj3 glycosylat$).tw.

#	Searches
52	(glycated adj3 h?emoglobin?).tw.
53	or/38-52
54	and/37,53

Database(s): Ovid MEDLINE(R) 1946 to April Week 3 2013
Search Strategy:
DiP_update_HbA1c_blood_glucose_HbA1c_monitor_values_medline_260413

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	GLUCOSE INTOLERANCE/
19	HYPERGLYCEMIA/
20	hyperglyc?emi?.ti,ab.
21	or/6-20
22	PREGNANCY/
23	(pregnan$ or gestation$).ti,ab.
24	PREGNANT WOMEN/
25	PRECONCEPTION CARE/
26	PRENATAL CARE/
27	pre?conception.ti,ab.
28	(pre adj conception).ti,ab.
29	pre?pregnancy.ti,ab.
30	(pre adj pregnancy).ti,ab.
31	(pre?natal$ or pre?conception or ante?natal$).ti,ab.
32	(pre adj natal$).ti,ab.
33	(pre adj conception).ti,ab.
34	(ante adj natal$).ti,ab.
35	or/22-34
36	and/21,35
37	or/5,36

#	Searches
38	BLOOD GLUCOSE/
39	(blood adj3 (glucose or sugar?)).ti,ab.
40	BLOOD GLUCOSE SELF-MONITORING/
41	BGSM.ti,ab.
42	(home glucose adj (test$ or monitor$)).ti,ab.
43	(self adj (test$ or monitor$)).ti,ab.
44	GLUCOSE TOLERANCE TEST/
45	(glucose adj (toleran$ or test$ or load$)).ti,ab.
46	OGTT.ti,ab.
47	(fasting adj plasma adj glucose).ti,ab.
48	FPG.ti,ab.
49	HEMOGLOBIN A, GLYCOSYLATED/
50	HbA1c.ti,ab.
51	(h?emoglobin? adj3 glycosylat$).ti,ab.
52	(glycated adj3 h?emoglobin?).ti,ab.
53	or/38-52
54	and/37,53
55	LETTER/
56	EDITORIAL/
57	NEWS/
58	exp HISTORICAL ARTICLE/
59	ANECDOTES AS TOPIC/
60	COMMENT/
61	CASE REPORT/
62	(letter or comment* or abstracts).ti.
63	or/55-62
64	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
65	63 not 64
66	ANIMALS/ not HUMANS/
67	exp ANIMALS, LABORATORY/
68	exp ANIMAL EXPERIMENTATION/
69	exp MODELS, ANIMAL/
70	exp RODENTIA/
71	(rat or rats or mouse or mice).ti.
72	or/65-71
73	54 not 72
74	limit 73 to english language
75	limit 74 to yr="2008 -Current"

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 25, 2013
Search Strategy: DiP_update_HbA1c_blood_glucose_HbA1c_monitor_values_mip_220413

#	Searches
1	((gestation$ or pregan$) adj3 diabet$).ti,ab.
2	(diabet$ or prediabet$ or pre?diabet$).ti,ab.
3	(T1DM or T2DM).ti,ab.

#	Searches
4	impaired glucose tolerance.ti,ab.
5	impaired fasting glucose.ti,ab.
6	impaired glucose regulation.ti,ab.
7	(IGT or IFG or IGR).ti,ab.
8	(glucose adj3 intoleran$).ti,ab.
9	hyperglyc?emi?.ti,ab.
10	or/2-9
11	(pregnan$ or gestation$).ti,ab.
12	(pre?natal$ or pre?conception or ante?natal$).ti,ab.
13	(pre adj natal$).ti,ab.
14	(pre adj conception).ti,ab.
15	(ante adj natal$).ti,ab.
16	or/11-15
17	and/10,16
18	or/1,17
19	(blood adj3 (glucose or sugar?)).ti,ab.
20	(glucose adj3 (test$ or monitor$ or assess$)).ti,ab.
21	OGTT.ti,ab.
22	(glucose adj (toleran$ or test$ or load$)).ti,ab.
23	fasting plasma glucose.ti,ab.
24	FPG.ti,ab.
25	(h?emoglobin? adj3 glycosylat$).ti,ab.
26	(glycated adj3 h?emoglobin?).ti,ab.
27	HbA1c.ti,ab.
28	or/19-27
29	and/18,28

E.4 Search 4: Screening for gestational diabetes in the first and second trimesters

A single search was conducted for 2 review questions.

Review question 6: What is the effectiveness of the following procedures in detecting glucose intolerance in the first trimester diagnosed using a 75g oral glucose tolerance test (OGTT):

- risk factor based screening
- urine test for glycosuria
- random blood glucose test
- 50g oral glucose challenge test
- fasting blood glucose test
- HbA1c test?

Review question 7: What is the effectiveness of the following procedures in detecting glucose intolerance in the second trimester diagnosed using a 75g oral glucose tolerance test (OGTT):

- risk factor based screening
- urine test for glycosuria
- random blood glucose test
- 50g oral glucose challenge test
- fasting blood glucose test
- HbA1c test?

Database(s): Ovid MEDLINE(R) 1946 to February Week 2 2014
Search Strategy: **DiP_update_diagnosis_1st_2nd_trimester_RERUN1_medline_240214**

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	Non?diabetic hyperglyc?emi#.ti,ab.
19	NDH.ti,ab.
20	GLUCOSE INTOLERANCE/
21	or/6-20
22	PREGNANCY/
23	(pregnan$ or gestation$).ti,ab.
24	PREGNANT WOMEN/
25	or/22-24
26	and/21,25
27	or/5,26
28	RISK ASSESSMENT/ or RISK FACTORS/
29	MASS tr/
30	screen$.ti,ab.
31	or/29-30
32	and/28,31
33	(risk adj2 factor? adj2 screen$).ti,ab.
34	or/32-33
35	exp GLYCOSURIA/
36	((glucose or sugar$) adj2 urine).ti,ab.
37	GLUCOSE TOLERANCE TEST/

#	Searches
38	BLOOD GLUCOSE/an [Analysis]
39	((random or fast$ or oral) adj2 blood glucose).ti,ab.
40	"oral glucose tolerance test".ti,ab.
41	(OGTT or FPG or IFG).ti,ab.
42	HEMOGLOBIN A, GLYCOSYLATED/
43	HbA1c.ti,ab.
44	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
45	MATERNAL SERUM SCREENING TESTS/
46	or/34-45
47	and/27,46
48	LETTER/
49	EDITORIAL/
50	NEWS/
51	exp HISTORICAL ARTICLE/
52	ANECDOTES AS TOPIC/
53	COMMENT/
54	CASE REPORT/
55	(letter or comment* or abstracts).ti.
56	or/48-55
57	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
58	56 not 57
59	ANIMALS/ not HUMANS/
60	exp ANIMALS, LABORATORY/
61	exp ANIMAL EXPERIMENTATION/
62	exp MODELS, ANIMAL/
63	exp RODENTIA/
64	(rat or rats or mouse or mice).ti.
65	or/58-64
66	47 not 65
67	limit 66 to english language
68	limit 67 to yr="2012 -Current"

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations June 13, 2014
Search Strategy:DiP_update_diagnosis_1st_2nd_trimester_mip_160614

#	Searches
1	((gestation$ or pregnan$) adj3 diabet$).ti,ab.
2	GDM.ti,ab.
3	or/1-2
4	(T1DM or T2DM).ti,ab.
5	diabet$.ti,ab.
6	prediabet$.ti,ab.
7	impaired glucose tolerance.ti,ab.
8	IGT.ti,ab.
9	Impaired fasting glucose.ti,ab.
10	IFG.ti,ab.

#	Searches
11	Impaired glucose regulation.ti,ab.
12	IGR.ti,ab.
13	Non?diabetic hyperglyc?emi#.ti,ab.
14	NDH.ti,ab.
15	(glucose adj (toleran$ or intoleran$)).ti,ab.
16	or/4-15
17	(pregnan$ or gestation$).ti,ab.
18	and/16-17
19	or/3,18
20	(risk adj2 factor? adj5 screen$).ti,ab.
21	glycosuria.ti,ab.
22	((glucose or sugar$) adj2 urine).ti,ab.
23	glucose tolerance test?.ti,ab.
24	((random or fast$ or oral) adj2 blood glucose).ti,ab.
25	"oral glucose tolerance test".ti,ab.
26	(OGTT or FPG or IFG).ti,ab.
27	HbA1c.ti,ab.
28	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).ti,ab.
29	or/20-28
30	and/19,29

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials January 2014
Search Strategy: **DiP_update_diagnosis_1st_2nd_trimester_RERUN1_cctr_240214**

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	Non?diabetic hyperglyc?emi#.ti,ab.
19	NDH.ti,ab.
20	GLUCOSE INTOLERANCE/
21	or/6-20

#	Searches
22	PREGNANCY/
23	(pregnan$ or gestation$).ti,ab.
24	PREGNANT WOMEN/
25	or/22-24
26	and/21,25
27	or/5,26
28	RISK ASSESSMENT/ or RISK FACTORS/
29	MASS SCREENING/
30	screen$.ti,ab.
31	or/29-30
32	and/28,31
33	(risk adj2 factor? adj2 screen$).ti,ab.
34	or/32-33
35	exp GLYCOSURIA/
36	((glucose or sugar$) adj2 urine).ti,ab.
37	GLUCOSE TOLERANCE TEST/
38	BLOOD GLUCOSE/an [Analysis]
39	((random or fast$ or oral) adj2 blood glucose).ti,ab.
40	"oral glucose tolerance test".ti,ab.
41	(OGTT or FPG or IFG).ti,ab.
42	HEMOGLOBIN A, GLYCOSYLATED/
43	HbA1c.ti,ab.
44	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).i,ab.
45	MATERNAL SERUM SCREENING TESTS/
46	or/34-45
47	and/27,46
48	limit 47 to yr="2012 -Current"

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to December 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2014
Search Strategy: **DiP_update_diagnosis_1st_2nd_trimester_RERUN1_cdsrdare_240214**

#	Searches
1	PREGNANCY IN DIABETICS.kw.
2	DIABETES, GESTATIONAL.kw.
3	(gestation$ adj3 diabet$).tw,tx.
4	GDM.tw,tx.
5	or/1-4
6	DIABETES MELLITUS.kw.
7	DIABETES INSIPIDUS.kw.
8	(T1DM or T2DM).tw,tx.
9	diabet$.ti.
10	PREDIABETIC STATE.kw.
11	prediabet$.tw,tx.
12	impaired glucose tolerance.tw,tx.
13	IGT.tw,tx.

#	Searches
14	Impaired fasting glucose.tw,tx.
15	IFG.tw,tx.
16	Impaired glucose regulation.tw,tx.
17	IGR.tw,tx.
18	Non?diabetic hyperglyc?emi#.tw,tx.
19	NDH.tw,tx.
20	GLUCOSE INTOLERANCE.kw.
21	or/6-20
22	PREGNANCY.kw.
23	(pregnan$ or gestation$).tw,tx.
24	PREGNANT WOMEN.kw.
25	or/22-24
26	and/21,25
27	or/5,26
28	(RISK ASSESSMENT or RISK FACTORS).kw.
29	MASS SCREENING.kw.
30	screen$.tw,tx.
31	or/29-30
32	and/28,31
33	(risk adj2 factor? adj2 screen$).tw,tx.
34	or/32-33
35	GlYCOSURIA.kw.
36	((glucose or sugar$) adj2 urine).ti,ab.
37	GLUCOSE TOLERANCE TEST.kw.
38	BLOOD GLUCOSE.kw.
39	((random or fast$ or oral) adj2 blood glucose).tw,tx.
40	"oral glucose tolerance test".tw,tx.
41	(OGTT or FPG or IFG).tw,tx.
42	HEMOGLOBIN A, GLYCOSYLATED.kw.
43	HbA1c.tw,tx.
44	((glycated or glycosylated) adj (haemoglobin or hemoglobin)).tw,tx.
45	MATERNAL SERUM SCREENING TESTS.kw.
46	or/34-45
47	and/27,46
48	("2012" or "2013" or "2014").dp.
49	and/47-48

Database(s): EBM Reviews - Health Technology Assessment 1st Quarter 2014
Search Strategy: **DiP_update_diagnosis_1st_2nd_trimester_RERUN1_hta_240214**

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4

#	Searches
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	Non?diabetic hyperglyc?emi#.tw.
19	NDH.tw.
20	GLUCOSE INTOLERANCE/
21	or/6-20
22	PREGNANCY/
23	(pregnan$ or gestation$).tw.
24	PREGNANT WOMEN/
25	or/22-24
26	and/21,25
27	or/5,26
28	RISK ASSESSMENT/ or RISK FACTORS/
29	MASS SCREENING/
30	screen$.tw.
31	or/29-30
32	and/28,31
33	(risk adj2 factor? adj2 screen$).tw.
34	or/32-33
35	exp GLYCOSURIA/
36	((glucose or sugar$) adj2 urine).ti,ab.
37	GLUCOSE TOLERANCE TEST/
38	BLOOD GLUCOSE/an [Analysis]
39	((random or fast$ or oral) adj2 blood glucose).tw.
40	"oral glucose tolerance test".tw.
41	(OGTT or FPG or IFG).tw.
42	HEMOGLOBIN A, GLYCOSYLATED/
43	HbA1c.tw.
44	((glycated or glycosylated) adj2 (haemoglobin or hemoglobin)).tw.
45	MATERNAL SERUM SCREENING TESTS/
46	or/34-45
47	and/27,46
48	("2012" or "2013" or "2014").dp.
49	nd 48

E.5 Search 5: Diagnostic criteria for gestational diabetes

Review question 8: Which diagnostic criteria should be used to diagnose diabetes in pregnant women using a 75g OGTT: WHO or IADPSG?

Database(s): Ovid MEDLINE(R) 1946 to June Week 2 2012
Search Strategy: **DiP_update_WHO_IADPSG_medline_250612**

#	Searches
1	"International Association of the Diabetes and Pregnancy Study Group$".ti,ab.
2	IADPSG.ti,ab.
3	or/1-2
4	LETTER/
5	EDITORIAL/
6	NEWS/
7	exp HISTORICAL ARTICLE/
8	ANECDOTES AS TOPIC/
9	COMMENT/
10	CASE REPORT/
11	(letter or comment* or abstracts).ti.
12	or/4-11
13	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
14	12 not 13
15	ANIMALS/ not HUMANS/
16	exp ANIMALS, LABORATORY/
17	exp ANIMAL EXPERIMENTATION/
18	exp MODELS, ANIMAL/
19	exp RODENTIA/
20	(rat or rats or mouse or mice).ti.
21	or/14-20
22	3 not 21
23	limit 22 to english language

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations June 25, 2012
Search Strategy: **DiP_update_WHO_IADPSG_mip_250612**

#	Searches
1	"International Association of the Diabetes and Pregnancy Study Group$".ti,ab.
2	IADPSG.ti,ab.
3	or/1-2

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials June 2012
Search Strategy: **DiP_update_WHO_IADPSG_cctr_250612**

#	Searches
1	"International Association of the Diabetes and Pregnancy Study Group$".ti,ab.
2	IADPSG.ti,ab.
3	or/1-2

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2012
Search Strategy: **DiP_update_WHO_IADPSG_cdsrdare_250612**

#	Searches
1	"International Association of the Diabetes and Pregnancy Study Group$".tw,tx.
2	IADPSG.tw,tx.
3	or/1-2

Database(s): EBM Reviews - Health Technology Assessment 2nd Quarter 2012
Search Strategy: **DiP_update_WHO_IADPSG_hta_270612**

#	Searches
1	"International Association of the Diabetes and Pregnancy Study Group$".tw,tx.
2	IADPSG.tw,tx.
3	or/1-2

Database(s): Embase 1974 to 2012 Week 25
Search Strategy: **DiP_update_WHO_IADPSG_embase_250612**

#	Searches
1	"International Association of the Diabetes and Pregnancy Study Group$".ti,ab.
2	IADPSG.ti,ab.
3	or/1-2
4	conference abstract.pt.
5	letter.pt. or LETTER/
6	note.pt.
7	editorial.pt.
8	CASE REPORT/ or CASE STUDY/
9	(letter or comment* or abstracts).ti.
10	or/4-9
11	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
12	10 not 11
13	ANIMAL/ not HUMAN/
14	NONHUMAN/
15	exp ANIMAL EXPERIMENT/
16	exp EXPERIMENTAL ANIMAL/
17	ANIMAL MODEL/
18	exp RODENT/
19	(rat or rats or mouse or mice).ti.
20	or/12-19
21	3 not 20
22	limit 21 to english language

E.6 Search 6: Interventions for gestational diabetes

Review question 9: What is the effectiveness of the following interventions (alone or in combination) in women with gestational diabetes:

- non-pharmacological interventions (diet and/or exercise)
- pharmacological interventions (metformin, glibenclamide and insulin)?

Database(s): Ovid MEDLINE(R) 1946 to March Week 3 2014 Search Strategy: DiP_update_GDM_interventions_RERUN1_medline_270314

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	or/1-5
7	((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
8	clinical trial.pt.
9	exp CLINICAL TRIAL/
10	exp CLINICAL TRIALS AS TOPIC/
11	(clinic$ adj5 trial$).tw,sh.
12	PLACEBOS/
13	placebo$.tw,sh.
14	random$.tw,sh.
15	or/7-14
16	or/6,15
17	META ANALYSIS/
18	META ANALYSIS AS TOPIC/
19	meta analysis.pt.
20	(metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21	(systematic$ adj5 (review$ or overview$)).tw,sh.
22	(methodologic$ adj5 (review$ or overview$)).tw,sh.
23	or/17-22
24	review$.pt.
25	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
26	((hand or manual$) adj2 search$).tw.
27	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
28	(pooling or pooled or mantel haenszel).tw,sh.
29	(peto or dersimonian or der simonian or fixed effect).tw,sh.
30	or/25-29
31	and/24,30
32	or/23,31
33	letter.pt.
34	case report.tw.
35	comment.pt.
36	editorial.pt.

#	Searches
37	historical article.pt.
38	or/33-37
39	32 not 38
40	16 not 38
41	32 not 38
42	or/40-41
43	DIABETES, GESTATIONAL/th, dh, dt [Therapy, Diet Therapy, Drug Therapy]
44	(diabet$ adj3 ("pregnancy induced" or gestat$ or gravid$)).ti,ab.
45	GDM.ti,ab.
46	or/43-45
47	exp LIFE STYLE/
48	((life style$ or life?style$) adj3 (modif$ or chang$ or advi$ or therap$)).ti,ab.
49	WEIGHT LOSS/
50	WEIGHT REDUCTION PROGRAMS/
51	DIABETIC DIET/
52	DIET THERAPY/
53	DIET, REDUCING/
54	CALORIC RESTRICTION/
55	(diet$ adj2 (therap$ or advi$ or modif$ or chang$)).ti,ab.
56	(diet$ adj5 (diabet$ or carbohydrat$ or fat$ or weigh$ or sugar$ or glyc?em$ or restrict$ or reduc$ or hypocalor$)).ti,ab.
57	(weigh$ adj3 (los$ or reduc$)).ti,ab.
58	((calori$ or calory) adj3 (restrict$ or reduc$ or low)).ti,ab.
59	exp EXERCISE/
60	exp EXERCISE THERAPY/
61	exp EXERCISE MOVEMENT TECHNIQUES/
62	exp "PHYSICAL EDUCATION AND TRAINING"/
63	PHYSICAL FITNESS/
64	exp SPORTS/
65	(exercis$ or sport$ or kinesi?therap$).ti,ab.
66	(physic$ adj5 (activ$ or fit$)).ti,ab.
67	METFORMIN/
68	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
69	GLYBURIDE/
70	(gl#bencl#mid? or gl#buride).ti,ab.
71	exp INSULIN/tu [Therapeutic Use]
72	exp INSULINS/tu [Therapeutic Use]
73	insulin$.ti,ab.
74	or/47-73
75	and/46,74
76	limit 75 to english language
77	LETTER/
78	EDITORIAL/
79	NEWS/
80	exp HISTORICAL ARTICLE/
81	ANECDOTES AS TOPIC/

#	Searches
82	COMMENT/
83	CASE REPORT/
84	(letter or comment* or abstracts).ti.
85	or/77-84
86	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
87	85 not 86
88	ANIMALS/ not HUMANS/
89	exp ANIMALS, LABORATORY/
90	exp ANIMAL EXPERIMENTATION/
91	exp MODELS, ANIMAL/
92	exp RODENTIA/
93	(rat or rats or mouse or mice).ti.
94	or/87-93
95	76 not 94
96	and/42,95
97	limit 96 to yr="2012 -Current"

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations June 20, 2012

DiP_update_GDM_interventions_mip_210612

#	Searches
1	(diabet$ adj3 ("pregnancy induced" or gestat$ or gravid$)).ti,ab.
2	GDM.ti,ab.
3	or/1-2
4	((life style$ or life?style$) adj3 (modif$ or chang$ or advi$ or therap$)).ti,ab.
5	(diet$ adj2 (therap$ or advi$ or modif$ or chang$)).ti,ab.
6	(diet$ adj5 (diabet$ or carbohydrat$ or fat$ or weigh$ or sugar$ or glyc?em$ or restrict$ or reduc$ or hypocalor$)).ti,ab.
7	(weigh$ adj3 (los$ or reduc$)).ti,ab.
8	((calori$ or calory) adj3 (restrict$ or reduc$ or low)).ti,ab.
9	(exercis$ or sport$ or kinesi?therap$).ti,ab.
10	(physic$ adj5 (activ$ or fit$)).ti,ab.
11	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
12	(gl#bencl#mid? or gl#buride).ti,ab.
13	insulin$.ti,ab.
14	or/4-13
15	and/3,14

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials June 2012

DiP_update_GDM_interventions_cctr_200612

#	Searches
1	DIABETES, GESTATIONAL/
2	(diabet$ adj3 (pregnan$ or gestat$)).kw.
3	(diabet$ adj3 ("pregnancy induced" or gestat$ or gravid$)).ti,ab.

#	Searches
4	GDM.ti,ab.
5	or/1-4
6	exp LIFE STYLE/
7	(life style$ or life?style$).kw.
8	((life style$ or life?style$) adj3 (modif$ or chang$ or advi$ or therap$)).ti,ab.
9	WEIGHT LOSS/
10	WEIGHT REDUCTION PROGRAMS/
11	DIABETIC DIET/
12	DIET THERAPY/
13	DIET, REDUCING/
14	CALORIC RESTRICTION/
15	(diet$ adj2 (therap$ or advi$ or modif$ or chang$)).ti,ab,kw.
16	(diet$ adj5 (diabet$ or carbohydrat$ or fat$ or weigh$ or sugar$ or glyc?em$ or restrict$ or reduc$ or hypocalor$)).ti,ab,kw.
17	(weigh$ adj3 (los$ or reduc$)).ti,ab,kw.
18	((calori$ or calory) adj3 (restrict$ or reduc$ or low)).ti,ab,kw.
19	exp EXERCISE/
20	exp EXERCISE THERAPY/
21	exp EXERCISE MOVEMENT TECHNIQUES/
22	exp "PHYSICAL EDUCATION AND TRAINING"/
23	PHYSICAL FITNESS/
24	exp SPORTS/
25	(exercis$ or sport$ or kinesi?therap$).ti,ab,kw.
26	(physic$ adj5 (activ$ or fit$)).ti,ab,kw.
27	physical education.kw.
28	METFORMIN/
29	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab,kw.
30	GLYBURIDE/
31	(gl#bencl#mid? or gl#buride).ti,ab,kw.
32	exp INSULIN/
33	exp INSULINS/
34	insulin$.ti,ab,kw.
35	or/6-34
36	and/5,35

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2012

DiP_update_GDM_interventions_cdsrdare_210612

#	Searches
1	(diabet$ adj3 (pregnan$ or gestat$)).kw.
2	(diabet$ adj3 ("pregnancy induced" or gestat$ or gravid$)).tw,tx.
3	GDM.tw,tx.
4	or/1-3
5	(life style$ or life?style$).kw.

#	Searches
6	((life style$ or life?style$) adj3 (modif$ or chang$ or advi$ or therap$)).tw,tx.
7	(diet$ adj2 (therap$ or advi$ or modif$ or chang$)).tw,tx.
8	(diet$ adj5 (diabet$ or carbohydrat$ or fat$ or weigh$ or sugar$ or glyc?em$ or restrict$ or reduc$ or hypocalor$)).tw,tx.
9	(weigh$ adj3 (los$ or reduc$)).tw,tx.
10	((calori$ or calory) adj3 (restrict$ or reduc$ or low)).tw,tx.
11	(exercis$ or sport$ or kinesi?therap$).tw,tx.
12	(physic$ adj5 (activ$ or fit$)).tw,tx.
13	physical education.kw.
14	(metformin or glucophage or glucient or metsol or bolamyn or metabet).tw,tx.
15	(gl#bencl#mid? or gl#buride).tw,tx.
16	insulin$.tw,tx.
17	or/5-16
18	and/4,17

Database(s): EBM Reviews - Health Technology Assessment 2nd Quarter 2012
DiP_update_GDM_interventions_hta_210612

#	Searches
1	DIABETES, GESTATIONAL/
2	(diabet$ adj3 ("pregnancy induced" or gestat$ or gravid$)).tw.
3	GDM.tw.
4	or/1-3
5	exp LIFE STYLE/
6	((life style$ or life?style$) adj3 (modif$ or chang$ or advi$ or therap$)).tw.
7	WEIGHT LOSS/
8	WEIGHT REDUCTION PROGRAMS/
9	DIABETIC DIET/
10	DIET THERAPY/
11	DIET, REDUCING/
12	CALORIC RESTRICTION/
13	(diet$ adj2 (therap$ or advi$ or modif$ or chang$)).tw.
14	(diet$ adj5 (diabet$ or carbohydrat$ or fat$ or weigh$ or sugar$ or glyc?em$ or restrict$ or reduc$ or hypocalor$)).tw.
15	(weigh$ adj3 (los$ or reduc$)).tw.
16	((calori$ or calory) adj3 (restrict$ or reduc$ or low)).tw.
17	exp EXERCISE/
18	exp EXERCISE THERAPY/
19	exp EXERCISE MOVEMENT TECHNIQUES/
20	exp "PHYSICAL EDUCATION AND TRAINING"/
21	PHYSICAL FITNESS/
22	exp SPORTS/
23	(exercis$ or sport$ or kinesi?therap$).tw.
24	(physic$ adj5 (activ$ or fit$)).tw.
25	METFORMIN/
26	(metformin or glucophage or glucient or metsol or bolamyn or metabet).tw.

#	Searches
27	GLYBURIDE/
28	(gl#bencl#mid? or gl#buride).tw.
29	exp INSULIN/
30	insulin$.tw.
31	or/5-30
32	and/4,31

Database(s): Embase 1974 to 2014 March 26
Search Strategy: **DiP_update_GDM_intervention_RERUN1_embase_270314**

#	Searches
1	CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2	(clinic$ adj5 trial$).ti,ab,sh.
3	SINGLE BLIND PROCEDURE/
4	DOUBLE BLIND PROCEDURE/
5	RANDOM ALLOCATION/
6	CROSSOVER PROCEDURE/
7	PLACEBO/
8	placebo$.ti,ab,sh.
9	random$.ti,ab,sh.
10	RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11	((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.
12	randomi?ed control$ trial$.tw.
13	or/1-12
14	META ANALYSIS/
15	((meta adj analy$) or metaanalys$ or meta-analy$).ti,ab,sh.
16	(systematic$ adj5 (review$ or overview$)).ti,sh,ab.
17	(methodologic$ adj5 (review$ or overview$)).ti,ab,sh.
18	or/14-17
19	review.pt.
20	(medline or medlars or embase).ab.
21	(scisearch or science citation index).ab.
22	(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23	((hand or manual$) adj2 search$).tw.
24	(electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25	(pooling or pooled or mantel haenszel).tw.
26	(peto or dersimonian or "der simonian" or fixed effect).tw.
27	or/20-26
28	and/19,27
29	or/18,28
30	(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31	13 not 30
32	29 not 30
33	or/31-32

#	Searches
34	exp PREGNANCY DIABETES MELLITUS/th, dt [Therapy, Drug Therapy]
35	(diabet$ adj3 ("pregnancy induced" or gestat$ or gravid$)).ti,ab.
36	GDM.ti,ab.
37	or/34-36
38	LIFESTYLE/
39	LIFESTYLE MODIFICATION/
40	((life style$ or life?style$) adj3 (modif$ or chang$ or advi$ or therap$)).ti,ab.
41	WEIGHT REDUCTION/
42	DIABETIC DIET/
43	DIET THERAPY/
44	DIET RESTRICTION/
45	LOW CALORY DIET/
46	CALORIC RESTRICTION/
47	(diet$ adj2 (therap$ or advi$ or modif$ or chang$)).ti,ab.
48	(diet$ adj5 (diabet$ or carbohydrat$ or fat$ or weigh$ or sugar$ or glyc?em$ or restrict$ or reduc$ or hypocalor$)).ti,ab.
49	(weigh$ adj3 (los$ or reduc$)).ti,ab.
50	((calori$ or calory) adj3 (restrict$ or reduc$ or low)).ti,ab.
51	exp EXERCISE/
52	exp PHYSICAL ACTIVITY/
53	FITNESS/
54	exp KINESIOTHERAPY/
55	PHYSICAL EDUCATION/
56	exp SPORT/
57	(exercis$ or sport$ or kinesi?therap$).ti,ab.
58	(physic$ adj5 (activ$ or fit$)).ti,ab.
59	METFORMIN/
60	(metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
61	GLIBENCLAMIDE/
62	(gl#bencl#mid? or gl#buride).ti,ab.
63	exp INSULIN DERIVATIVE/ct, dt [Clinical Trial, Drug Therapy]
64	insulin$.ti,ab.
65	or/38-64
66	and/37,65
67	limit 66 to english language
68	conference abstract.pt.
69	letter.pt. or LETTER/
70	note.pt.
71	editorial.pt.
72	CASE REPORT/ or CASE STUDY/
73	(letter or comment* or abstracts).ti.
74	or/68-73
75	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
76	74 not 75
77	ANIMAL/ not HUMAN/
78	NONHUMAN/

#	Searches
79	exp ANIMAL EXPERIMENT/
80	exp EXPERIMENTAL ANIMAL/
81	ANIMAL MODEL/
82	exp RODENT/
83	(rat or rats or mouse or mice).ti.
84	or/76-83
85	67 not 84
86	and/33,85
87	limit 86 to yr="2012 -Current"

E.7 Search 7: Antenatal continuous glucose monitoring

Review question 15: What is the effectiveness of continuous glucose monitoring in pregnant women with diabetes compared with intermittent capillary blood glucose monitoring?

Database(s): Ovid MEDLINE(R) 1946 to March Week 2 2013
Search Strategy:DiP update_CGM_medline_260313

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).ti,ab.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24
26	(continu$ adj2 glucose monitor$).ti,ab.
27	(ambulatory adj3 (glucose adj3 monitor$)).ti,ab.

#	Searches
28	(CGM or CGMS or CBGM).ti,ab.
29	EXTRACELLULAR FLUID/
30	interstitial.ti,ab.
31	(home glucose adj (test$ or monitor$)).ti,ab.
32	(self adj (test$ or monitor$)).ti,ab.
33	BLOOD GLUCOSE SELF- MONITORING/
34	BGSM.ti,ab.
35	intermittent.ti,ab.
36	IGM.ti,ab.
37	(ICGM or ICBGM).ti,ab.
38	or/26-37
39	and/25,38
40	LETTER/
41	EDITORIAL/
42	NEWS/
43	exp HISTORICAL ARTICLE/
44	ANECDOTES AS TOPIC/
45	COMMENT/
46	CASE REPORT/
47	(letter or comment* or abstracts).ti.
48	or/40-47
49	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50	48 not 49
51	ANIMALS/ not HUMANS/
52	exp ANIMALS, LABORATORY/
53	exp ANIMAL EXPERIMENTATION/
54	exp MODELS, ANIMAL/
55	exp RODENTIA/
56	(rat or rats or mouse or mice).ti.
57	or/50-56
58	39 not 57
59	limit 58 to english language
60	limit 59 to yr="2008 -Current"

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations March 26, 2013
Search Strategy:DiP_update_CGM_mip_270313

#	Searches
1	(gestation$ adj3 diabet$).ti,ab.
2	GDM.ti,ab.
3	(diabet$ adj3 pregnan$).ti,ab.
4	or/1-3
5	(T1DM or T2DM).ti,ab.
6	diabet$.ti,ab.
7	prediabet$.ti,ab.
8	impaired glucose tolerance.ti,ab.

#	Searches
9	IGT.ti,ab.
10	Impaired fasting glucose.ti,ab.
11	IFG.ti,ab.
12	Impaired glucose regulation.ti,ab.
13	IGR.ti,ab.
14	or/5-13
15	(pregnan$ or gestation$).ti,ab.
16	and/14-15
17	or/4,16
18	(continu$ adj2 glucose monitor$).ti,ab.
19	(ambulatory adj3 (glucose adj3 monitor$)).ti,ab.
20	(CGM or CGMS or CBGM).ti,ab.
21	interstitial.ti,ab.
22	(home glucose adj (test$ or monitor$)).ti,ab.
23	(self adj (test$ or monitor$)).ti,ab.
24	("blood glucose" adj self adj monitor$).ti,ab.
25	BGSM.ti,ab.
26	intermittent.ti,ab.
27	IGM.ti,ab.
28	(ICGM or ICBGM).ti,ab.
29	or/18-28
30	and/17,29

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials March 2013
Search Strategy:DiP_update_CGM_cctr_260313

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	GLUCOSE INTOLERANCE/
19	or/6-18

#	Searches
20	PREGNANCY/
21	(pregnan$ or gestation$).ti,ab.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24
26	(continu$ adj2 glucose monitor$).ti,ab.
27	(ambulatory adj3 (glucose adj3 monitor$)).ti,ab.
28	(CGM or CGMS or CBGM).ti,ab.
29	EXTRACELLULAR FLUID/
30	interstitial.ti,ab.
31	(home glucose adj (test$ or monitor$)).ti,ab.
32	(self adj (test$ or monitor$)).ti,ab.
33	BLOOD GLUCOSE SELF- MONITORING/
34	BGSM.ti,ab.
35	intermittent.ti,ab.
36	IGM.ti,ab.
37	(ICGM or ICBGM).ti,ab.
38	or/26-37
39	and/25,38
40	limit 39 to yr="2008 -Current"

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to February 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2013
Search Strategy:DiP_update_CGM_cdsrdare_260313

#	Searches
1	PREGNANCY IN DIABETICS.kw.
2	DIABETES, GESTATIONAL.kw.
3	(gestation$ adj3 diabet$).tw,tx.
4	GDM.tw,tx.
5	or/1-4
6	DIABETES MELLITUS.kw.
7	DIABETES INSIPIDUS.kw.
8	(T1DM or T2DM).tw,tx.
9	diabet$.tw,tx.
10	PREDIABETIC STATE.kw.
11	prediabet$.tw,tx.
12	impaired glucose tolerance.tw,tx.
13	IGT.tw,tx.
14	Impaired fasting glucose.tw,tx.
15	IFG.tw,tx.
16	Impaired glucose regulation.tw,tx.
17	IGR.tw,tx.
18	GLUCOSE INTOLERANCE.kw.
19	or/6-18

#	Searches
20	PREGNANCY.kw.
21	(pregnan$ or gestation$).tw,tx.
22	PREGNANT WOMEN.kw.
23	or/20-22
24	and/19,23
25	or/5,24
26	(continu$ adj2 glucose monitor$).tw,tx.
27	(ambulatory adj3 (glucose adj3 monitor$)).tw,tx.
28	(CGM or CGMS or CBGM).tw,tx.
29	EXTRACELLULAR FLUID.kw.
30	interstitial.tw,tx.
31	(home glucose adj (test$ or monitor$)).tw,tx.
32	(self adj (test$ or monitor$)).tw,tx.
33	BLOOD GLUCOSE SELF- MONITORING.kw.
34	BGSM.tw,tx.
35	intermittent.tw,tx.
36	IGM.tw,tx.
37	(ICGM or ICBGM).tw,tx.
38	or/26-37
39	and/25,38

Database(s): EBM Reviews - Health Technology Assessment 1st Quarter 2013
Search Strategy:DiP_update_CGM_hta_270313

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.tw.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).tw.

#	Searches
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	and/5,24
26	(continu$ adj2 glucose monitor$).tw.
27	(ambulatory adj3 (glucose adj3 monitor$)).tw.
28	(CGM or CGMS or CBGM).tw.
29	EXTRACELLULAR FLUID/
30	interstitial.tw.
31	(home glucose adj (test$ or monitor$)).tw.
32	(self adj (test$ or monitor$)).tw.
33	BLOOD GLUCOSE SELF- MONITORING/
34	BGSM.tw.
35	intermittent.tw.
36	IGM.tw.
37	(ICGM or ICBGM).tw.
38	or/26-37
39	and/25,38

Database(s): Embase 1974 to 2013 April 12
Search Strategy: DiP_update_CGM_embase_150413

#	Searches
1	PREGNANCY DIABETES MELLITUS/ or MATERNAL DIABETES MELLITUS/
2	(gestation$ adj3 diabet$).ti,ab.
3	or/1-2
4	DIABETES MELLITUS/ or IMPAIRED GLUCOSE TOLERANCE/ or INSULIN DEPENDENT DIABETES MELLITUS/ or JUVENILE DIABETES MELLITUS/ or NON INSULIN DEPENDENT DIABETES MELLITUS/
5	(T1DM or T2DM).ti,ab.
6	(IDDM or NIDDM).ti,ab.
7	diabet$.ti.
8	pre?diabet$.ti,ab.
9	impaired fasting glucose.ti,ab.
10	(IGT or IFG).ti,ab.
11	IGR.ti,ab.
12	GLUCOSE INTOLERANCE/
13	or/4-12
14	PREGNANCY/ or PREGNANT WOMAN/
15	(pregnan$ or gestation$).ti,ab.
16	or/14-15
17	and/13,16
18	or/3,17
19	(continu$ adj2 glucose monitor$).ti,ab.
20	(ambulatory adj3 (glucose adj3 monitor$)).ti,ab.
21	(CGM or CGMS or CBGM).ti,ab.
22	INTERSTITIAL FLUID/

#	Searches
23	(interstitial adj2 fluid?).ti,ab.
24	(home glucose adj (test$ or monitor$)).ti,ab.
25	(self adj (test$ or monitor$)).ti,ab.
26	BLOOD GLUCOSE MONITORING/
27	BGSM.ti,ab.
28	(intermittent adj3 monitor$).ti,ab.
29	IGM.ti,ab.
30	(ICGM or ICBGM).ti,ab.
31	or/19-30
32	and/18,31
33	conference abstract.pt.
34	letter.pt. or LETTER/
35	note.pt.
36	editorial.pt.
37	CASE REPORT/ or CASE STUDY/
38	(letter or comment* or abstracts).ti.
39	or/33-38
40	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
41	39 not 40
42	ANIMAL/ not HUMAN/
43	NONHUMAN/
44	exp ANIMAL EXPERIMENT/
45	exp EXPERIMENTAL ANIMAL/
46	ANIMAL MODEL/
47	exp RODENT/
48	(rat or rats or mouse or mice).ti.
49	or/41-48
50	32 not 49
51	limit 50 to english language
52	limit 51 to yr="2008 -Current"

E.8 Search 8: Antenatal specialist teams

Review question 16: What is the effectiveness of specialist teams for pregnant women with diabetes?

Database(s): Ovid MEDLINE(R) 1946 to December Week 4 2012
Search Strategy:DiP_update_specialist_care_medline_070113

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4

#	Searches
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	or/6-17
19	PREGNANCY/
20	(pregnan$ or gestation$).ti,ab.
21	PREGNANT WOMEN/
22	or/19-21
23	and/18,22
24	or/5,23
25	((unified or joint or combined or integrated or specialist or divided or centrali#ed) adj5 (care or clinic$)).ti,ab.
26	(specialist adj3 (team$ or clinic$)).ti,ab.
27	("diabetes-obstetrical" adj clinic$).ti,ab.
28	NURSE MIDWIVES/
29	COMMUNITY HEALTH NURSING/
30	and/28-29
31	(community adj (midwife or midwives or midwifery)).ti,ab.
32	or/25-27,30-31
33	and/24,32
34	LETTER/
35	EDITORIAL/
36	NEWS/
37	exp HISTORICAL ARTICLE/
38	ANECDOTES AS TOPIC/
39	COMMENT/
40	CASE REPORT/
41	(letter or comment* or abstracts).ti.
42	or/34-41
43	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
44	42 not 43
45	ANIMALS/ not HUMANS/
46	exp ANIMALS, LABORATORY/
47	exp ANIMAL EXPERIMENTATION/
48	exp MODELS, ANIMAL/
49	exp RODENTIA/
50	(rat or rats or mouse or mice).ti.

#	Searches
51	or/44-50
52	33 not 51

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations January 04, 2013
Search Strategy: DiP_update_specialist_care_mip_070113

#	Searches
1	(pregnan$ adj3 diabet$).ti,ab.
2	(gestation$ adj3 diabet$).ti,ab.
3	GDM.ti,ab.
4	or/1-3
5	(T1DM or T2DM).ti,ab.
6	diabet$.ti,ab.
7	prediabet$.ti,ab.
8	impaired glucose tolerance.ti,ab.
9	IGT.ti,ab.
10	Impaired fasting glucose.ti,ab.
11	IFG.ti,ab.
12	Impaired glucose regulation.ti,ab.
13	IGR.ti,ab.
14	or/5-13
15	(pregnan$ or gestation$).ti,ab.
16	and/14-15
17	or/4,16
18	((unified or joint or combined or integrated or specialist or divided or centrali#ed) adj5 (care or clinic$)).ti,ab.
19	(specialist adj3 (team$ or clinic$)).ti,ab.
20	("diabetes-obstetrical" adj clinic$).ti,ab.
21	(community adj (midwife or midwives or midwifery)).ti,ab.
22	or/18-21
23	and/17,22

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials December 2012
Search Strategy: DiP_update_specialist_care_cctr_070113

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/

#	Searches
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	or/6-17
19	PREGNANCY/
20	(pregnan$ or gestation$).ti,ab.
21	PREGNANT WOMEN/
22	or/19-21
23	and/18,22
24	or/5,23
25	((unified or joint or combined or integrated or specialist or divided or centrali#ed) adj5 (care or clinic$)).ti,ab.
26	(specialist adj3 (team$ or clinic$)).ti,ab.
27	("diabetes-obstetrical" adj clinic$).ti,ab.
28	NURSE MIDWIVES/
29	COMMUNITY HEALTH NURSING/
30	and/28-29
31	(community adj (midwife or midwives or midwifery)).ti,ab.
32	or/25-27,30-31
33	and/24,32

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to November 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 4th Quarter 2012
Search Strategy: DiP_update_specialist_care_cdsrdare_070113

#	Searches
1	PREGNANCY IN DIABETICS.kw.
2	DIABETES, GESTATIONAL.kw.
3	(gestation$ adj3 diabet$).tw,tx.
4	GDM.ti,ab.
5	or/1-4
6	DIABETES MELLITUS.kw.
7	DIABETES INSIPIDUS.kw.
8	(T1DM or T2DM).tw,tx.
9	diabet$.tw,tx.
10	PREDIABETIC STATE.kw.
11	prediabet$.tw,tx.
12	impaired glucose tolerance.tw,tx.
13	IGT.tw,tx.
14	Impaired fasting glucose.tw,tx.
15	IFG.tw,tx.
16	Impaired glucose regulation.tw,tx.

#	Searches
17	IGR.tw,tx.
18	or/6-17
19	PREGNANCY.kw.
20	(pregnan$ or gestation$).tw,tx.
21	PREGNANT WOMEN.kw.
22	or/19-21
23	and/18,22
24	or/5,23
25	((unified or joint or combined or integrated or specialist or divided or centrali#ed) adj5 (care or clinic$)).tw,tx.
26	(specialist adj3 (team$ or clinic$)).tw,tx.
27	("diabetes-obstetrical" adj clinic$).tw,tx.
28	NURSE MIDWIVES.kw.
29	COMMUNITY HEALTH NURSING.kw.
30	and/28-29
31	(community adj (midwife or midwives or midwifery)).tw,tx.
32	or/25-27,30-31
33	and/24,32

Database(s): EBM Reviews - Health Technology Assessment 4th Quarter 2012
Search Strategy: DiP_update_specialist_care_hta_070113

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	or/6-17
19	PREGNANCY/
20	(pregnan$ or gestation$).tw.
21	PREGNANT WOMEN/
22	or/19-21
23	and/18,22
24	or/5,23

#	Searches
25	((unified or joint or combined or integrated or specialist or divided or centrali#ed) adj5 (care or clinic$)).tw.
26	(specialist adj3 (team$ or clinic$)).tw.
27	("diabetes-obstetrical" adj clinic$).tw.
28	NURSE MIDWIVES/
29	COMMUNITY HEALTH NURSING/
30	and/28-29
31	(community adj (midwife or midwives or midwifery)).tw.
32	or/25-27,30-31
33	and/24,32

Database(s): Embase 1974 to 2013 January 07
Search Strategy: DiP_update_specialist_care_embase_080113

#	Searches
1	PREGNANCY DIABETES MELLITUS/ or MATERNAL DIABETES MELLITUS/
2	(gestation$ adj3 diabet$).ti,ab.
3	or/1-2
4	DIABETES MELLITUS/ or IMPAIRED GLUCOSE TOLERANCE/ or INSULIN DEPENDENT DIABETES MELLITUS/ or JUVENILE DIABETES MELLITUS/ or NON INSULIN DEPENDENT DIABETES MELLITUS/
5	(T1DM or T2DM).ti,ab.
6	(IDDM or NIDDM).ti,ab.
7	diabet$.ti.
8	pre?diabet$.ti,ab.
9	impaired fasting glucose.ti,ab.
10	(IGT or IFG).ti,ab.
11	IGR.ti,ab.
12	GLUCOSE INTOLERANCE/
13	or/4-12
14	PREGNANCY/ or PREGNANT WOMEN/
15	(pregnan$ or gestation$).ti,ab.
16	or/14-15
17	and/13,16
18	or/3,17
19	(specialist adj3 (team$ or clinic$)).ti,ab.
20	((unified or joint or combined or integrated or specialist or divided or centrali#ed) adj5 (care or clinic$)).ti,ab.
21	NURSE MIDWIFE/
22	COMMUNITY HEALTH NURSING/
23	COMMUNITY/
24	or/22-23
25	and/21,24
26	(community adj3 (midwife or midwives or midwifery)).ti,ab.
27	("diabetes-obstetrical" adj clinic$).ti,ab.
28	or/19-20,25-27
29	and/18,28

#	Searches
30	limit 29 to english language

DiP_update_specialist_care_cinahl_090113

#	Query
S47	S27 AND S45
S46	S27 AND S45
S45	S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S42 OR S43 OR S44
S44	AB (community N3 midwi?e*)
S43	TI (community N3 midwi?e*)
S42	S40 AND S41
S41	(MH "COMMUNITY HEALTH NURSING+")
S40	(MH "Nurse Midwifery")
S39	TI (diabetes?obstetrical) or AB (diabetes?obstetrical)
S38	TI (centrali?ed N3 clinic*) or AB (centrali?ed N3 clinic*)
S37	TI (centrali?ed N3 care) or AB (central?ed care)
S36	AB (unified N3 clinic*) or AB (unified N3 clinic*)
S35	TI (unified N3 care) or AB (unified N3 care)
S34	TI (integrated N3 care*) or AB (integrated N3 care*)
S33	TI (integrated N3 clinic*) or AB (integrated N3 clinic*)
S32	TI (joint N3 care) or AB (joint N3 care)
S31	TI (joint N3 clinic*) or AB (joint N3 clinic*)
S30	TI (combined N3 care) or AB (combined N3 care)
S29	TI (specialist N3 clinic*) or AB (specialist N3 clinic*)
S28	TI (specialist N3 team*) or AB (specialist N3 team*)
S27	S5 OR S26
S26	S20 AND S25
S25	S21 OR S22 OR S23 OR S24
S24	(MH "EXPECTANT MOTHERS")
S23	AB (pregnan* or gestation*)
S22	TI (pregnan* or gestation*)
S21	(MH "PREGNANCY")
S20	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19
S19	(MH "GLUCOSE INTOLERANCE")
S18	AB (IGT or IFG or IGR)
S17	TI (IGT or IFG or IGR)
S16	AB ("impaired glucose regulation")
S15	TI ("impaired glucose regulation")
S14	AB ("impaired fasting glucose")
S13	TI ("impaired fasting glucose")
S12	AB ("impaired glucose tolerance")
S11	TI ("impaired glucose tolerance")
S10	TI (prediabet*) or AB (prediabet*)
S9	(MH "PREDIABETIC STATE")

#	Query
S8	TI diabet*
S7	TI (T1DM) or TI (T2DM)
S6	(MH "DIABETES MELLITUS+")
S5	S1 OR S2 OR S3 OR S4
S4	TI (GDM) or AB (GDM)
S3	AB (diabet* N3 pregnan*) or AB (diabet* N3 gestat*) or AB (diabet* N3 gravid*)
S2	TI (diabet* N3 pregnan*) or TI (diabet* N3 gestat*) or TI (diabet* N3 gravid*)
S1	MH DIABETES MELLITUS, GESTATIONAL

E.9 Search 9: Timing of birth

Review question 17: What is the gestational age-specific risk of intrauterine death in pregnancies with type 1, type 2 or gestational diabetes, and the optimal timing of birth?

Database(s): Ovid MEDLINE(R) 1946 to February Week 2 2013
Search Strategy:DiP_update_intrauterine_timing_medline_260213

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).ti,ab.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24
26	FETAL DEATH/
27	((foetal or fetal or fetus$ or foetus$) adj (death or dying or demise)).ti,ab.
28	(intrauterine adj2 death).ti,ab.

#	Searches
29	STILLBIRTH/
30	IUFD.ti,ab.
31	(stillbirth or still?born).ti,ab.
32	INFANT MORTALITY/
33	((peri?natal$ or neo?natal$) adj3 (death? or dying or mortality or demise)).ti,ab.
34	LABOR, INDUCED/
35	((induct$ or induc$) adj3 lab?or).ti,ab.
36	((elective or planned) adj2 (birth? or deliver$ or induct$ or caesar#an$ or cesar#an$)).ti,ab.
37	exp DELIVERY, OBSTETRIC/
38	WATCHFUL WAITING/
39	(expectant adj3 (manag$ or monitor$)).ti,ab.
40	or/26-39
41	GESTATIONAL AGE/
42	(gestation$ adj age?).ti,ab.
43	TIME FACTORS/
44	((time or timing) adj3 (birth or deliver$ or induction or inducted or cesarean? or caesarean or c?section?)).ti,ab.
45	((optimal or optimum) adj3 (time or timing)).ti,ab.
46	or/41-44
47	and/25,40,46
48	LETTER/
49	EDITORIAL/
50	NEWS/
51	exp HISTORICAL ARTICLE/
52	ANECDOTES AS TOPIC/
53	COMMENT/
54	CASE REPORT/
55	(letter or comment* or abstracts).ti.
56	or/48-55
57	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
58	56 not 57
59	ANIMALS/ not HUMANS/
60	exp ANIMALS, LABORATORY/
61	exp ANIMAL EXPERIMENTATION/
62	exp MODELS, ANIMAL/
63	exp RODENTIA/
64	(rat or rats or mouse or mice).ti.
65	or/58-64
66	47 not 65
67	limit 66 to english language
68	limit 67 to yr="2008 -Current"

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations February 25, 2013
Search Strategy:DiP_update_intrauterine_death_timing_mip_260213

#	Searches
1	(gestation$ adj3 diabet$).ti,ab.
2	GDM.ti,ab.
3	(diabet$ adj3 pregnan$).ti,ab.
4	or/1-3
5	(T1DM or T2DM).ti,ab.
6	diabet$.ti,ab.
7	prediabet$.ti,ab.
8	impaired glucose tolerance.ti,ab.
9	IGT.ti,ab.
10	Impaired fasting glucose.ti,ab.
11	IFG.ti,ab.
12	Impaired glucose regulation.ti,ab.
13	IGR.ti,ab.
14	or/5-13
15	(pregnan$ or gestation$).ti,ab.
16	and/14-15
17	or/4,16
18	((foetal or fetal or fetus$ or foetus$) adj (death or dying or demise)).ti,ab.
19	(intrauterine adj2 death).ti,ab.
20	IUFD.ti,ab.
21	(stillbirth or still?born).ti,ab.
22	((peri?natal$ or neo?natal$ or infant?) adj3 (death? or dying or mortality or demise)).ti,ab.
23	((induct$ or induc$) adj3 labo?r).ti,ab.
24	((elective or planned) adj5 (birth? or deliver$ or induct$ or caesar#an$ or cesar#an$)).ti,ab.
25	(obstetric adj3 deliver$).ti,ab.
26	(watchful adj2 waiting).ti,ab.
27	(expectant adj3 (manag$ or monitor$)).ti,ab.
28	or/18-27
29	(gestation$ adj age?).ti,ab.
30	((time or timing) adj3 (birth or deliver$ or induction or inducted or cesarean? or caesarean or c?section?)).ti,ab.
31	((optimal or optimum) adj3 (time or timing)).ti,ab.
32	or/29-31
33	and/17,28,32

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials January 2013
Search Strategy:DiP_update_intrauterine_death_timing_cctr_280213

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).ti,ab.
4	GDM.ti,ab.

#	Searches
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).ti,ab.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.ti,ab.
12	impaired glucose tolerance.ti,ab.
13	IGT.ti,ab.
14	Impaired fasting glucose.ti,ab.
15	IFG.ti,ab.
16	Impaired glucose regulation.ti,ab.
17	IGR.ti,ab.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).ti,ab.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24
26	FETAL DEATH/
27	((foetal or fetal or fetus$ or foetus$) adj (death or dying or demise)).ti,ab.
28	(intrauterine adj2 death).ti,ab.
29	STILLBIRTH/
30	IUFD.ti,ab.
31	(stillbirth or still?born).ti,ab.
32	INFANT MORTALITY/
33	((peri?natal$ or neo?natal$) adj3 (death? or dying or mortality or demise)).ti,ab.
34	LABOR, INDUCED/
35	((induct$ or induc$) adj3 labo?r).ti,ab.
36	((elective or planned) adj2 (birth? or deliver$ or induct$ or caesar#an$ or cesar#an$)).ti,ab.
37	exp DELIVERY, OBSTETRIC/
38	WATCHFUL WAITING/
39	(expectant adj3 (manag$ or monitor$)).ti,ab.
40	or/26-39
41	GESTATIONAL AGE/
42	(gestation$ adj age?).ti,ab.
43	TIME FACTORS/
44	((time or timing) adj3 (birth or deliver$ or induction or inducted or cesarean? or caesarean or c?section?)).ti,ab.
45	((optimal or optimum) adj3 (time or timing)).ti,ab.
46	or/41-44
47	and/25,40,46

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to January 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 1st Quarter 2013
Search Strategy:DiP_update_intrauterine_death_timing_cdsrdare_280213

#	Searches
1	PREGNANCY IN DIABETICS.kw.
2	DIABETES, GESTATIONAL.kw.
3	(gestation$ adj3 diabet$).tw,tx.
4	GDM.tw,tx.
5	or/1-4
6	DIABETES MELLITUS.kw.
7	DIABETES INSIPIDUS.kw.
8	(T1DM or T2DM).tw,tx.
9	diabet$.ti.
10	PREDIABETIC STATE.kw.
11	prediabet$.tw,tx.
12	impaired glucose tolerance.tw,tx.
13	IGT.tw,tx.
14	Impaired fasting glucose.tw,tx.
15	IFG.tw,tx.
16	Impaired glucose regulation.tw,tx.
17	IGR.tw,tx.
18	GLUCOSE INTOLERANCE.kw.
19	or/6-18
20	PREGNANCY.kw.
21	(pregnan$ or gestation$).tw,tx.
22	PREGNANT WOMEN.kw.
23	or/20-22
24	and/19,23
25	or/5,24
26	FETAL DEATH.kw.
27	((foetal or fetal or fetus$ or foetus$) adj (death or dying or demise)).tw,tx.
28	(intrauterine adj2 death).tw,tx.
29	STILLBIRTH.kw.
30	IUFD.tw,tx.
31	(stillbirth or still?born).tw,tx.
32	[INFANT MORTALITY/]
33	((peri?natal$ or neo?natal$) adj3 (death? or dying or mortality or demise)).tw,tx.
34	LABOR, INDUCED.kw.
35	((induct$ or induc$) adj3 labo?r).tw,tx.
36	((elective or planned) adj2 (birth? or deliver$ or induct$ or caesar#an$ or cesar#an$)).tw,tx.
37	DELIVERY, OBSTETRIC.kw.
38	WATCHFUL WAITING.kw.
39	(expectant adj3 (manag$ or monitor$)).tw,tx.
40	or/26-39
41	GESTATIONAL AGE.kw.
42	(gestation$ adj age?).tw,tx.
43	TIME FACTORS.kw.

#	Searches
44	((time or timing) adj3 (birth or deliver$ or induction or inducted or cesarean? or caesarean or c?section?)).tw,tx.
45	((optimal or optimum) adj3 (time or timing)).tw,tx.
46	or/41-44
47	and/25,40,46

Database(s): EBM Reviews - Health Technology Assessment 1st Quarter 2013
Search Strategy:DiP_update_intrauterine_death_timing_hta_280213

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).tw.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24
26	FETAL DEATH/
27	((foetal or fetal or fetus$ or foetus$) adj (death or dying or demise)).tw.
28	(intrauterine adj2 death).tw.
29	STILLBIRTH/
30	IUFD.tw.
31	(stillbirth or still?born).tw.
32	INFANT MORTALITY/
33	((peri?natal$ or neo?natal$) adj3 (death? or dying or mortality or demise)).tw.
34	LABOR, INDUCED/
35	((induct$ or induc$) adj3 labo?r).tw.
36	((elective or planned) adj2 (birth? or deliver$ or induct$ or caesar#an$ or cesar#an$)).tw.

#	Searches
37	exp DELIVERY, OBSTETRIC/
38	WATCHFUL WAITING/
39	(expectant adj3 (manag$ or monitor$)).tw.
40	or/26-39
41	GESTATIONAL AGE/
42	(gestation$ adj age?).tw.
43	TIME FACTORS/
44	((time or timing) adj3 (birth or deliver$ or induction or inducted or cesarean? or caesarean or c?section?)).tw.
45	((optimal or optimum) adj3 (time or timing)).tw.
46	or/41-44
47	and/25,40,46

Database(s): Embase 1974 to 2013 February 27
Search Strategy: DiP_update_intrauterine_death_timing_embase_270213

#	Searches
1	PREGNANCY DIABETES MELLITUS/ or MATERNAL DIABETES MELLITUS/
2	(gestation$ adj3 diabet$).ti,ab.
3	or/1-2
4	DIABETES MELLITUS/ or IMPAIRED GLUCOSE TOLERANCE/ or INSULIN DEPENDENT DIABETES MELLITUS/ or JUVENILE DIABETES MELLITUS/ or NON INSULIN DEPENDENT DIABETES MELLITUS/
5	(T1DM or T2DM).ti,ab.
6	(IDDM or NIDDM).ti,ab.
7	diabet$.ti.
8	pre?diabet$.ti,ab.
9	impaired fasting glucose.ti,ab.
10	(IGT or IFG).ti,ab.
11	IGR.ti,ab.
12	GLUCOSE INTOLERANCE/
13	or/4-12
14	PREGNANCY/ or PREGNANT WOMAN/
15	(pregnan$ or gestation$).ti,ab.
16	or/14-15
17	and/13,16
18	or/3,17
19	FETUS DEATH/ or STILLBIRTH/
20	((foetal or fetal or fetus$ or foetus$) adj (death or dying or demise)).ti,ab.
21	(intrauterine adj2 death).ti,ab.
22	IUFD.ti,ab.
23	(stillbirth or still?born).ti,ab.
24	((peri?natal$ or neo?natal$) adj3 (death? or dying or mortality or demise)).ti,ab.
25	NEWBORN DEATH/
26	LABOR INDUCTION/
27	((induct$ or induc$) adj3 lab?or).ti,ab.

#	Searches
28	((elective or planned) adj2 (birth? or deliver$ or induct$ or caesar#an$ or cesar#an$)).ti,ab.
29	exp DELIVERY/
30	WATCHFUL WAITING/
31	conservative treatment/ or watchful waiting/
32	(expectant adj3 (manag$ or monitor$)).ti,ab.
33	or/19-32
34	GESTATIONAL AGE/
35	(gestation$ adj age?).ti,ab.
36	TIME/
37	((time or timing) adj3 (birth or deliver$ or induction or inducted or cesarean? or caesarean or c?section?)).ti,ab.
38	((optimal or optimum) adj3 (time or timing)).ti,ab.
39	or/34-38
40	and/18,33,39
41	conference abstract.pt.
42	letter.pt. or LETTER/
43	note.pt.
44	editorial.pt.
45	CASE REPORT/ or CASE STUDY/
46	(letter or comment* or abstracts).ti.
47	or/41-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMAL/ not HUMAN/
51	NONHUMAN/
52	exp ANIMAL EXPERIMENT/
53	exp EXPERIMENTAL ANIMAL/
54	ANIMAL MODEL/
55	exp RODENT/
56	(rat or rats or mouse or mice).ti.
57	or/49-56
58	40 not 57
59	limit 58 to english language
60	limit 59 to yr="2008 -Current"

E.10 Search 10: Diagnostic accuracy and timing of postnatal testing

Review question 18: What is the effectiveness of the following tests in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care):

- fasting plasma glucose test
- HbA1c test
- 75 g OGTT?

Review question 19: What is the optimal timing of postnatal testing in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care)?

Database(s): Ovid MEDLINE(R) 1946 to June Week 4 2012
Search Strategy: DiP_update_postnatal_test_medline_090712_2

#	Searches
1	exp DIABETES, GESTATIONAL/
2	exp HYPERGLYCEMIA/
3	exp PREGNANCY/
4	PREGNANT WOMAN/
5	or/2-4
6	and/2,5
7	(glucose adj3 (intoleran$ or dysregulat$)).ti,ab.
8	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).ti,ab.
9	(GDM or HGP).ti,ab.
10	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).ti,ab.
11	(GDM or HGP or IGT or pre?diabet$ or HAPO).ti,ab.
12	or/7-11
13	or/1,6,12
14	POSTPARTUM PERIOD/
15	POSTNATAL CARE/
16	(postnatal$ or post?natal$ or puerper$ or post?partum).ti,ab.
17	((after or following) adj3 (birth$ or deliver$ or parturi$)).ti,ab.
18	AFTERCARE/
19	after?care.ti,ab.
20	or/14-19
21	MASS SCREENING/
22	BLOOD GLUCOSE/
23	GLUCOSE TOLERANCE TEST/
24	HEMOGLOBIN A, GLYCOSYLATED/
25	(FPG or OGTT or HbA1c).ti,ab.
26	((glucose or blood sugar$) adj5 (test$ or assessment$ or monitor$)).ti,ab.
27	((fasting or oral) adj3 glucose).ti,ab.
28	(plasma adj3 glucose).ti,ab.
29	(glucose adj (level$ or read$ or monitor$ or assess$ or check$)).ti,ab.
30	((glycosylated or glycated) adj3 h?emoglobin$).ti,ab.
31	or/21-30
32	and/13,20,31
33	LETTER/
34	EDITORIAL/
35	NEWS/
36	exp HISTORICAL ARTICLE/
37	ANECDOTES AS TOPIC/
38	COMMENT/
39	CASE REPORT/
40	(letter or comment* or abstracts).ti.

#	Searches
41	or/33-40
42	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
43	41 not 42
44	ANIMALS/ not HUMANS/
45	exp ANIMALS, LABORATORY/
46	exp ANIMAL EXPERIMENTATION/
47	exp MODELS, ANIMAL/
48	exp RODENTIA/
49	(rat or rats or mouse or mice).ti.
50	or/43-49
51	32 not 50
52	limit 51 to english language

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations July 06, 2012
Search Strategy: DiP_update_postnatal_test_mip_090712

#	Searches
1	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).ti,ab.
2	(glucose adj3 (impaired or dysregulat$)).ti,ab.
3	(GDM or HGP or IGT or pre?diabet$ or HAPO).ti,ab.
4	or/1-3
5	(postnatal$ or post?natal$ or puerper$ or post?partum).ti,ab.
6	((after or following or post$) adj3 (birth$ or deliver$ or parturi$)).ti,ab.
7	after?care.ti,ab.
8	or/5-7
9	screen$.ti,ab.
10	(FPG or OGTT or HbA1c).ti,ab.
11	((glucose or blood sugar$) adj5 (test$ or assessment$ or monitor$)).ti,ab.
12	((fasting or oral) adj3 glucose).ti,ab.
13	((plasma or blood) adj3 glucose).ti,ab.
14	(glucose adj (level$ or read$ or monitor$ or assess$ or check$)).ti,ab.
15	((glycosylated or glycated) adj3 h?emoglobin$).ti,ab.
16	or/9-15
17	and/4,8,16

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials June 2012
Search Strategy: DiP_update_postnatal_test_cctr_090712

#	Searches
1	exp DIABETES, GESTATIONAL/
2	exp HYPERGLYCEMIA/
3	(glucose adj3 (intoleran$ or dysregulat$)).ti,ab.
4	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).ti,ab.
5	(GDM or HGP).ti,ab.
6	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).ti,ab.
7	(GDM or HGP or IGT or pre?diabet$ or HAPO).ti,ab.

#	Searches
8	or/1-7
9	POSTPARTUM PERIOD/
10	POSTNATAL CARE/
11	(postnatal$ or post?natal$ or puerper$ or post?partum).ti,ab.
12	((after or following) adj3 (birth$ or deliver$ or parturi$)).ti,ab.
13	AFTERCARE/
14	after?care.ti,ab.
15	or/9-14
16	MASS SCREENING/
17	BLOOD GLUCOSE/
18	GLUCOSE TOLERANCE TEST/
19	HEMOGLOBIN A, GLYCOSYLATED/
20	(FPG or OGTT or HbA1c).ti,ab.
21	((glucose or blood sugar$) adj5 (test$ or assessment$ or monitor$)).ti,ab.
22	((fasting or oral) adj3 glucose).ti,ab.
23	(plasma adj3 glucose).ti,ab.
24	(glucose adj (level$ or read$ or monitor$ or assess$ or check$)).ti,ab.
25	((glycosylated or glycated) adj3 h?emoglobin$).ti,ab.
26	or/16-25
27	and/8,15,26

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2012
Search Strategy: DiP_update_postnatal_test_cdsrdare_090712

#	Searches
1	DIABETES, GESTATIONAL.kw.
2	HYPERGLYCEMIA.kw.
3	(glucose adj3 (intoleran$ or dysregulat$)).tw,tx.
4	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).tw,tx.
5	(GDM or HGP).tw,tx.
6	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).tw,tx.
7	(GDM or HGP or IGT or pre?diabet$ or HAPO).tw,tx.
8	or/1-7
9	POSTPARTUM PERIOD.kw.
10	POSTNATAL CARE.kw.
11	(postnatal$ or post?natal$ or puerper$ or post?partum).tw,tx.
12	((after or following) adj3 (birth$ or deliver$ or parturi$)).tw,tx.
13	AFTERCARE.tw.
14	after?care.tw,tx.
15	or/9-14
16	MASS SCREENING.kw.
17	BLOOD GLUCOSE.kw.
18	GLUCOSE TOLERANCE TEST.kw.
19	HEMOGLOBIN A, GLYCOSYLATED.kw.
20	(FPG or OGTT or HbA1c).tw,tx.

#	Searches
21	((glucose or blood sugar$) adj5 (test$ or assessment$ or monitor$)).tw,tx.
22	((fasting or oral) adj3 glucose).tw,tx.
23	(plasma adj3 glucose).tw,tx.
24	(glucose adj (level$ or read$ or monitor$ or assess$ or check$)).tw,tx.
25	((glycosylated or glycated) adj3 h?emoglobin$).tw,tx.
26	or/16-25
27	and/8,15,26

Database(s): EBM Reviews - Health Technology Assessment 1st Quarter 2014
Search Strategy: DiP_update_postnatal_test_RERUN1_hta_270214

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.tw.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	GLUCOSE INTOLERANCE/
19	HYPERGLYCEMIA/
20	hyperglyc?em?.tw.
21	or/6-20
22	PREGNANCY/
23	(pregnan$ or gestation$).tw.
24	PREGNANT WOMEN/
25	PRECONCEPTION CARE/
26	PRENATAL CARE/
27	pre?conception.tw.
28	(pre adj conception).tw.
29	pre?pregnancy.tw.
30	(pre adj pregnancy).tw.
31	(pre?natal$ or pre?conception or ante?natal).tw.
32	(pre adj natal$).tw.
33	(pre adj conception).tw.
34	(ante adj natal$).tw.
35	or/22-34

#	Searches
36	and/21,35
37	or/5,36
38	BLOOD GLUCOSE/
39	(blood adj3 (glucose or sugar?)).tw.
40	BLOOD GLUCOSE SELF-MONITORING/
41	BGSM.tw.
42	(home glucose adj (test$ or monitor$)).tw.
43	(self adj (test$ or monitor$)).tw.
44	GLUCOSE TOLERANCE TEST/
45	OGTT.tw.
46	(glucose adj (toleran$ or test$ or load$)).tw.
47	(fasting adj plasma adj glucose).tw.
48	FPG.tw.
49	HEMOGLOBIN A, GLYCOSYLATED/
50	HbA1c.tw.
51	(h?emoglobin? adj3 glycosylat$).tw.
52	(glycated adj3 h?emoglobin?).tw.
53	or/38-52
54	and/37,53

Database(s): Embase 1974 to 2012 July 06
Search Strategy: DiP_update_postnatal_test_embase_090712

#	Searches
1	PREGNANCY DIABETES MELLITUS/
2	IMPAIRED GLUCOSE TOLERANCE/
3	HYPERGLYCEMIA/
4	((diabet$ or hyperglyc?emi$) adj3 (gestat$ or pregnan$)).ti,ab.
5	(GDM or HGP or IGT or pre?diabet$ or HAPO).ti,ab.
6	or/1-5
7	PUERPERIUM/
8	POSTNATAL CARE/
9	(postnatal$ or post?natal$ or puerper$ or post?partum).ti,ab.
10	((after or follow$) adj3 (birth$ or deliver$ or parturi$)).ti,ab.
11	AFTERCARE/
12	after?care.ti,ab.
13	or/7-12
14	MASS SCREENING/
15	GLUCOSE BLOOD LEVEL/
16	exp GLUCOSE TOLERANCE TEST/
17	GLYCOSYLATED HEMOGLOBIN/
18	(FPG or OGTT or HbA1c).ti,ab.
19	((glucose or blood sugar$) adj5 (test$ or assess$ or monitor$)).ti,ab.
20	((fast$ or oral) adj3 glucose).ti,ab.
21	((glycosylated or glycated) adj3 h?emoglobin).ti,ab.
22	or/14-21

#	Searches
23	and/6,13,22
24	conference abstract.pt.
25	letter.pt. or LETTER/
26	note.pt.
27	editorial.pt.
28	CASE REPORT/ or CASE STUDY/
29	(letter or comment* or abstracts).ti.
30	or/24-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32	30 not 31
33	ANIMAL/ not HUMAN/
34	NONHUMAN/
35	exp ANIMAL EXPERIMENT/
36	exp EXPERIMENTAL ANIMAL/
37	ANIMAL MODEL/
38	exp RODENT/
39	(rat or rats or mouse or mice).ti.
40	or/32-39
41	23 not 40
42	limit 41 to english language

E.11 Search 11: Health economics

A single Health Economics search was conducted across the whole guideline

Database(s): Ovid MEDLINE(R) 1946 to November Week 2 2012
Search Strategy: **DiP_update_population_search_HE_medline_151112**

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.

#	Searches
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp PREGNANCY IN DIABETICS/
23	DIABETES, GESTATIONAL/
24	(gestation$ adj3 diabet$).ti,ab.
25	GDM.ti,ab.
26	or/22-25
27	exp DIABETES MELLITUS/
28	exp DIABETES INSIPIDUS/
29	(T1DM or T2DM).ti,ab.
30	diabet$.ti.
31	PREDIABETIC STATE/
32	prediabet$.ti,ab.
33	impaired glucose tolerance.ti,ab.
34	IGT.ti,ab.
35	Impaired fasting glucose.ti,ab.
36	IFG.ti,ab.
37	Impaired glucose regulation.ti,ab.
38	IGR.ti,ab.
39	GLUCOSE INTOLERANCE/
40	or/27-39
41	PREGNANCY/
42	(pregnan$ or gestation$).ti,ab.
43	PREGNANT WOMEN/
44	or/41-43
45	and/40,44
46	or/26,45
47	and/21,46
48	LETTER/
49	EDITORIAL/
50	NEWS/
51	exp HISTORICAL ARTICLE/
52	ANECDOTES AS TOPIC/
53	COMMENT/
54	CASE REPORT/
55	(letter or comment* or abstracts).ti.
56	or/48-55
57	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
58	56 not 57
59	ANIMALS/ not HUMANS/
60	exp ANIMALS, LABORATORY/
61	exp ANIMAL EXPERIMENTATION/
62	exp MODELS, ANIMAL/
63	exp RODENTIA/

#	Searches
64	(rat or rats or mouse or mice).ti.
65	or/58-64
66	47 not 65
67	limit 66 to english language

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials November 2012
Search Strategy: **DiP_update_population_search_HE_cctr_151112**

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp PREGNANCY IN DIABETICS/
23	DIABETES, GESTATIONAL/
24	(gestation$ adj3 diabet$).ti,ab.
25	GDM.ti,ab.
26	or/22-25
27	exp DIABETES MELLITUS/
28	exp DIABETES INSIPIDUS/
29	(T1DM or T2DM).ti,ab.
30	diabet$.ti.
31	PREDIABETIC STATE/
32	prediabet$.ti,ab.
33	impaired glucose tolerance.ti,ab.
34	IGT.ti,ab.
35	Impaired fasting glucose.ti,ab.
36	IFG.ti,ab.
37	Impaired glucose regulation.ti,ab.
38	IGR.ti,ab.

#	Searches
39	GLUCOSE INTOLERANCE/
40	or/27-39
41	PREGNANCY/
42	(pregnan$ or gestation$).ti,ab.
43	PREGNANT WOMEN/
44	or/41-43
45	and/40,44
46	or/26,45
47	and/21,46

Database(s): EBM Reviews - Health Technology Assessment 4th Quarter 2012
Search Strategy: **EBM Reviews - Health Technology Assessment 4th Quarter 2012**

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).tw.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24

Database(s): EBM Reviews - NHS Economic Evaluation Database 4th Quarter 2012
Search Strategy: **DiP_update_population_search_HE_nhseed_151112**

#	Searches
1	exp PREGNANCY IN DIABETICS/
2	DIABETES, GESTATIONAL/

#	Searches
3	(gestation$ adj3 diabet$).tw.
4	GDM.tw.
5	or/1-4
6	exp DIABETES MELLITUS/
7	exp DIABETES INSIPIDUS/
8	(T1DM or T2DM).tw.
9	diabet$.ti.
10	PREDIABETIC STATE/
11	prediabet$.tw.
12	impaired glucose tolerance.tw.
13	IGT.tw.
14	Impaired fasting glucose.tw.
15	IFG.tw.
16	Impaired glucose regulation.tw.
17	IGR.tw.
18	GLUCOSE INTOLERANCE/
19	or/6-18
20	PREGNANCY/
21	(pregnan$ or gestation$).tw.
22	PREGNANT WOMEN/
23	or/20-22
24	and/19,23
25	or/5,24

Database(s): Embase 1980 to 2012 Week 46
Search Strategy: **DiP_update_population_search_HE_embase_191112**

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	exp PREGNANCY DIABETES MELLITUS/

#	Searches
19	gestational diabet$.ti,ab.
20	GDM.ti,ab.
21	or/18-20
22	exp DIABETES MELLITUS/
23	diabet$.ti.
24	(T?1DM or T?2DM).ti,ab.
25	(IDDM or NIDDM).ti,ab.
26	IMPAIRED GLUCOSE TOLERANCE/
27	IGT.ti,ab.
28	impaired fasting glucose.ti,ab.
29	IFG.ti,ab.
30	impaired glucose regulat$.ti,ab.
31	IGR.ti,ab.
32	GLUCOSE INTOLERANCE/
33	or/22-32
34	PREGNANCY/ or FIRST TRIMESTER PREGNANCY/ or PREGNANT WOMAN/ or SECOND TRIMESTER PREGNANCY/ or THIRD TRIMESTER PREGNANCY/
35	(pregnan$ or gestation$).ti,ab.
36	or/34-35
37	and/33,36
38	or/21,37
39	and/17,38
40	limit 39 to english language

Appendix F: Summary of identified studies

Protocol Question	Total papers identified	Duplicates	Weeded out	Abandoned	Excluded	Included
1. What is the effectiveness of oral oestrogen-containing contraceptives in women with diabetes compared with women without diabetes?	1475	1	1421	3	41	8
2. What is the effectiveness of oral progestogen-containing contraceptives in women with diabetes compared with women without diabetes?	1475	1	1421	3	41	8
3. What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1 or type 2 diabetes who are planning pregnancy?	52	0	52	0	0	0
4. What are the target ranges for blood glucose in women with type 1 or type 2 diabetes who are planning pregnancy?	3297	0	3287	1	9	0
5. What is the target value for HbA1c in women with type 1 or type 2 diabetes who are planning pregnancy?	3295	0	3264	1	22	8
6. What is the effectiveness of the following procedures in detecting glucose intolerance in the first trimester diagnosed using a 75g OGTT	7479	1	7410	1	60	6
7. What is the effectiveness of the following procedures in detecting glucose intolerance in the second trimester diagnosed using a 75g OGTT	7481	3	7333	2	127	11
8. Which criteria should be used to diagnose gestational diabetes using the 75 g OGTT: World Health Organization (WHO) or International Association of Diabetes and Pregnancy Study Groups (IADPSG)?	155	0	121	0	29	5
9. What is the effectiveness of the following interventions (alone or in combination) in women with gestational diabetes: non-pharmacological or pharmacological	1762	0	1593	4	131	34
Q10. What is the effectiveness of blood glucose monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?	3296	0	3253	1	36	6
Q11.What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for women with type 1, type 2 or gestational diabetes during pregnancy?	52	0	52	0	0	0
Q12. What are the target ranges for blood glucose in women with type 1, type 2 or gestational diabetes during pregnancy?	3296	0	3253	1	36	6
Q13. What is the effectiveness of HbA1c monitoring in predicting adverse outcomes in women with type 1, type 2 or gestational diabetes during pregnancy?	3267	0	3226	0	40	0
Q14. What is the target value for HbA1c in women with type 1, type 2 or gestational diabetes during pregnancy?	3296	0	3250	3	42	4

Protocol Question	Total papers identified	Duplicates	Weeded out	Abandoned	Excluded	Included
Q15. To assess whether continuous glucose monitoring during pregnancy is more effective than intermittent capillary blood glucose monitoring for improving: glycaemic control or maternal/fetal outcomes	593	1	555	0	29	5
Q16. What is the effectiveness of specialist teams for pregnant women with diabetes?	337	0	311	0	21	5
Q17. What is the gestational age-specific risk of intrauterine death in pregnancies with type 1, type 2 or gestational diabetes, and the optimal timing of birth?	1023	0	999	5	18	6
Q18. What is the effectiveness of the following tests in the detection of glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care): FPG, OGTT, HbA1c	1317	1	1167	5	93	51
Q19. What is the optimal timing of postnatal testing in detecting glucose intolerance after pregnancy in women who have had gestational diabetes (but are not hyperglycaemic before they are transferred to community care)?	1317	1	1167		93	51

Appendix G: List of excluded studies

G.1 Oral contraception containing oestrogen and/or progestogen

Excluded studies – Review questions 1 and 2	
Study	**Reason for Exclusion**
Use of hormonal contraception in women with coexisting medical conditions, Obstetrics and Gynecology, 107, 1453-1472, 2006	Narrative review with no new data. Individual studies were reviewed where relevant
Aznar,R., Lara,R., Zarco,D., Gonzalez,L., The effect of various contraceptive hormonal therapies in women with normal and diabetic oral glucose tolerance test, Contraception, 13, 299-311, 1976	Does not include relevant outcomes as specified in the protocol
Bacopoulou,F., Greydanus,D.E., Chrousos,G.P., Reproductive and contraceptive issues in chronically ill adolescents, European Journal of Contraception and Reproductive Health Care, 15, 389-404, 2010	Narrative review with no new data. Individual studies considered separately for inclusion where relevant
Charronprochownik,D., FAMILY-PLANNING BEHAVIOR IN YOUNG-WOMEN WITH IDDM, Diabetes, 45, 651-651, 1996	Does not report relevant outcomes
Charron-Prochownik,D., Sereika,S.M., Becker,D., White,N.H., Schmitt,P., Blair Powell III,A., Diaz,A.M., Jones,J., Herman,W.H., Rodgers Fischel ,A.F., McEwan,L., Dinardo,M., Guo,F, Downs,J., Long-Term Effects of the Booster-Enhanced READY-Girls Preconception Counseling Program on Intentions and Behaviors for Family Planning in Teens With Diabetes, Diabetes Care, Published ahead of print, October 15 2013, -, 2013	Intervention is not relevant (pre-conception counselling).
Charron-Prochownik,D., Sereika,S.M., Falsetti,D., Wang,S.L., Becker,D., Jacober,S., Mansfield,J., White,N.H., Knowledge, attitudes and behaviors related to sexuality and family planning in adolescent women with and without diabetes, Pediatric Diabetes, 7, 267-273, 2006	Does not report relevant outcomes
Codner,E., Soto,N., Merino,P.M., Contraception, and pregnancy in adolescents with type 1 diabetes: a review, Pediatric Diabetes, 13, 108-123, 2012	Narrative review. Relevant studies have been considered for inclusion individually
Coster,S., Gulliford,M.C., Seed,P.T., Powrie,J.K., Swaminathan,R., Monitoring blood glucose control in diabetes mellitus: A systematic review, Health Technology Assessment, 4, i-84, 2000	Does not report outcomes of oral contraceptive use in women with or without diabetes
Croft,P., Hannaford,P.C., Risk factors for acute myocardial infarction in women: evidence from the Royal College of General Practitioners' oral contraception study, BMJ, 298, 165-168, 1989	Does not report myocardial infarction in women who take oral contraceptives by whether women have diabetes or not
Damm,P., Mathiesen,E., Clausen,T.D., Petersen,K.R., Contraception for women with diabetes mellitus, Metabolic Syndrome and Related Disorders, 3, 244-249, 2005	Narrative review. Individual studies have been reviewed where relevant
Duffy,T.J., Ray,R., Oral contraceptive use: prospective follow-up of women with suspected glucose intolerance, Contraception, 30, 197-208, 1984	Does not report the relevant outcomes as specified in the protocol
Falsetti,D., Charron-Prochownik,D., Serelka,S., Kitutu,J., Peterson,K., Becker,D., Jacober,S., Mansfield,J., White,N.H., Condom use, pregnancy, and STDs in adolescent females with and without type 1 diabetes, Diabetes Educator, 29, 135-143, 2003	Does not report outcomes separately for women who use contraception and women who do not use contraception
Farley,T.M., Collins,J., Schlesselman,J.J., Hormonal contraception and risk of cardiovascular disease. An international perspective. [47 refs], Contraception, 57, 211-230, 1998	Does not report a comparison of interest
Fontbonne,A., Basdevant,A., Faguer,B., Thomassin,M., Buchsenschutz,D., Contraceptive practice in 209 diabetic women regularly attending a specialized diabetes clinic, Diabete et Metabolisme, 13, 411-416, 1987	Does not report outcomes of interest
Gordon,C.M., Mansfield,M.J., Changing needs of the patient with diabetes mellitus during the teenage years, Current Opinion in Pediatrics, 8, 319-327, 1996	Narrative review with no new data. Individual studies considered separately for inclusion
Heyman,A., Arons,M., Quinn,M., Camplong,L., The role of oral contraceptive agents in cerebral arterial occlusion, Neurology, 19, 519-524, 1969	Does not report a comparison of interest
Jensen,G., Nyboe,J., Appleyard,M., Schnohr,P., Risk factors for acute myocardial infarction in Copenhagen, II: Smoking, alcohol intake, physical activity, obesity, oral contraception, diabetes, lipids, and blood pressure, European Heart Journal, 12, 298-308, 1991	Does not report a comparison of interest
Kirwan,J.F., Tsaloumas,M.D., Vinall,H., Prior,P., Kritzinger,E.E., Dodson,P.M., Sex hormone preparations and retinal vein occlusion, Eye, 11, 53-56, 1997	Did not include any women with diabetes
Kjaer,K., Hagen,C., Sando,S.H., Eshoj,O., Contraception in women with IDDM. An epidemiological study, Diabetes Care, 15, 1585-1590, 1992	Does not report outcomes of interest

Excluded studies – Review questions 1 and 2	
Klein,B.E., Klein,R., Moss,S.E., Mortality and hormone-related exposures in women with diabetes, Diabetes Care, 22, 248-252, 1999	Reports oral contraceptive use as a characteristic rather than comparison group - includes 'ever' and current users of oral contraceptives as one group
Lawrenson,R.A., Leydon,G.M., Williams,T.J., Newson,R.B., Feher,M.D., Patterns of contraception in UK women with Type 1 diabetes mellitus: a GP database study, Diabetic Medicine, 16, 395-399, 1999	Does not report outcomes separately for a comparison of interest
Lidegaard,O., Oral contraceptives, pregnancy and the risk of cerebral thromboembolism: the influence of diabetes, hypertension, migraine and previous thrombotic disease, British Journal of Obstetrics and Gynaecology, 102, 153-159, 1995	Does not report outcomes for women with diabetes who are taking oral contraceptives
Lidegaard,O., Edstrom,B., Kreiner,S., Oral contraceptives and venous thromboembolism: A five-year national case-control study, Contraception, 65, 187-196, 2002	Does not report a comparison of interest
Magill-Lewis,J., Cover story: One-Two Punch, Drug Topics, 148, 30-, 2004	Does not report a comparison of interest
Petersen,K.R., Pharmacodynamic effects of oral contraceptive steroids on biochemical markers for arterial thrombosis: Studies in non-diabetic women and in women with insulin-dependent diabetes mellitus, Danish Medical Bulletin, 49, 43-60, 2002	Narrative review with no new data. Individual studies were reviewed where relevant
Petersen,K.R., Skouby,S.O., Jespersen,J., Contraception guidance in women with pre-existing disturbances in carbohydrate metabolism, The European journal of contraception & reproductive health care : the official journal of the European Society of Contraception, 1, 53-59, 1996	Does not compare the use of oral contraceptives in women with and without diabetes. Data reported for women with diabetes who use oral contraceptives and women with diabetes who do not use oral contraceptives is a summary of the data reported in Skouby et al. (1986). The details from the full paper were included in the current review instead.
Petersen,K.R., Skouby,S.O., Sidelmann,J., Molsted-Pedersen,L., Jespersen,J., Effects of contraceptive steroids on cardiovascular risk factors in women with insulin-dependent diabetes mellitus, American Journal of Obstetrics and Gynecology, 171, 400-405, 1994	The women in this study are included in the Petersen (1995) study, which was included in the review for the guideline (see Petersen et al., 1995).
Radberg,T., Gustafson,A., Skryten,A., Karlsson,K., Oral contraception in diabetic women. Diabetes control, serum and high density lipoprotein lipids during low-dose progestogen, combined oestrogen/progestogen and non-hormonal contraception, ACTA ENDOCRINOL.(COPENHAGEN), 98, 246-251, 1981	Compares two groups of women, one of which was receiving a 50 microgramme dose of ethinyl estradiol, which is excluded from the guideline review as it is not used in current practice
Radberg,T., Gustafson,A., Skryten,A., Karlsson,K., Oral contraception in diabetic women. A cross-over study on serum and high density lipoprotein (HDL) lipids and diabetes control during progestogen and combined estrogen/progestogen contraception, Hormone and Metabolic Research, 14, 61-65, 1982	Compares two groups of women, one of which was receiving a 50 microgramme dose of ethinyl estradiol, which is excluded from the guideline review as it is not used in current practice
Rogovskaya,S., Rivera,R., Grimes,D.A., Chen,P.L., Pierre-Louis,B., Prilepskaya,V., Kulakov,V., Effect of a levonorgestrel intrauterine system on women with type 1 diabetes: a randomized trial, Obstetrics and Gynecology, 105, 811-815, 2005	Comparison of different types of intrauterine contraceptive devices. None of the women received oral contraceptives.
Shawe,J., Lawrenson,R., Hormonal contraception in women with diabetes mellitus: Special considerations, Treatments in Endocrinology, 2, 321-330, 2003	Narrative review with no new data. Individual studies ordered where relevant
Shawe,J., Mulnier,H., Nicholls,P., Lawrenson,R., Use of hormonal contraceptive methods by women with diabetes, Primary care diabetes, 2, 195-199, 2008	Does not report consequences of oral contraceptive use, only the patterns of use in women with and without diabetes
Sidney,S., Siscovick,D.S., Petitti,D.B., Schwartz,S.M., Quesenberry,C.P., Psaty,B.M., Raghunathan,T.E., Kelaghan,J., Koepsell,T.D., Myocardial infarction and use of low-dose oral contraceptives: a pooled analysis of 2 US studies, Circulation, 98, 1058-1063, 1998	Does not report a comparison of interest
Siritho,S., Thrift,A.G., McNeil,J.J., You,R.X., Davis,S.M., Donnan,G.A., Risk of ischemic stroke among users of the oral contraceptive pill: The Melbourne Risk Factor Study (MERFS) Group, Stroke, 34, 1575-1580, 2003	Does not report oral contraceptive use in women with diabetes
Skouby,S.O., Oral contraceptives: effects on glucose and lipid metabolism in insulin-dependent diabetic women and women with previous gestational diabetes. A clinical and biochemical assessment. [112 refs], Danish Medical Bulletin, 35, 157-167, 1988	Does not report a comparison of interest
Snell-Bergeon,Janet K., Dabelea,Dana, Ogden,Lorraine G., Hokanson,John E., Kinney,Gregory L., Ehrlich,James, Rewers,Marian, Reproductive History and Hormonal Birth Control Use Are Associated with Coronary Calcium Progression in Women with Type 1 Diabetes Mellitus, Journal of Clinical Endocrinology & Metabolism, 93, 2142-2148, 2008	Not all women in the 'birth control' group were using birth control at the time of the study and baseline measurements - the group includes women who had used birth control at any point in the past. The study does not report how many women in the birth control group were using birth control at the time of the study. Not all women in the 'birth control' group were using oral contraceptives (around 80% were).

Excluded studies – Review questions 1 and 2	
Spellacy,W.N., Buhi,W.C., Spellacy,C.E., Moses,L.E., Goldzieher,J.W., Glucose, insulin, and growth hormone studies in long-term users of oral contraceptives, American Journal of Obstetrics and Gynecology, 106, 173-182, 1970	Does not report a comparison of interest
Steel,J.M., Prepregnancy counseling and contraception in the insulin-dependent diabetic patient, Clinical Obstetrics and Gynecology, 28, 553-566, 1985	Narrative review with no new data. Individual studies considered separately where relevant
Virkar,K., Barsivala,V., Kulkarni,R.D., Correlation of clinical parameters with glucose tolerance tests in women taking oral contraceptives, Fertility and Sterility, 25, 569-574, 1974	Does not report a comparison of interest
Wiese,J., Osler,M., Contraception in diabetic patients, Acta Endocrinologica, Supplementum. 182, 87-89, 1974	Does not report a comparison of interest
Wingrave,S.J., Kay,C.R., Vessey,M.P., Oral contraceptives and diabetes mellitus, British Medical Journal, 1, 23-, 1979	Does not report a comparison of interest

G.2 Ketone monitoring in the preconception period

There were no excluded studies for review question 3.

G.3 Blood glucose target values in the preconception period

Excluded studies – Review question 4	
Study	**Reason for Exclusion**
Dong,L., Liu,E., Guo,J., Pan,L., Li,B., Leng,J., Zhang,C., Zhang,Y., Li,N., Hu,G., Relationship between maternal fasting glucose levels at 4-12 gestational weeks and offspring growth and development in early infancy, Diabetes Research and Clinical Practice, 102, 210-217, 2013	Only report mean SD for birth weight
Kitzmiller,J.L., Gavin,L.A., Gin,G.D., Jovanovic-Peterson,L., Main,E.K., Zigrang,W.D., Preconception care of diabetes. Glycemic control prevents congenital anomalies, JAMA, 265, 731-736, 1991	Data compared in pre-conception care women versus post-conception care. Data not analysed with respect to blood glucose values or targets.
Mills,J.L., Simpson,J.L., Driscoll,S.G., Jovanovic-Peterson,L., Van,Allen M., Aarons,J.H., Metzger,B., Bieber,F.R., Knopp,R.H., Holmes,L.B., Incidence of spontaneous abortion among normal women and insulin-dependent diabetic women whose pregnancies were identified within 21 days of conception, New England Journal of Medicine N.Engl.J.Med., 319, 1617-1623, 1988	No targets or thresholds given. Dichotomous data are not compared according to blood glucose values for mortality and miscarriages (diabetic versus non-diabetic women). Only mean blood glucose values are presented for comparative data for miscarriages.
The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus New England Journal of Medicine 1993	The study population is all adults, not pregnant women
The Diabetes Control and Complications Trial Research Group. Pregnancy outcomes in the Diabetes Control and Complications Trial. American Journal of Obstetrics and Gynecology 1996;174(4):1343–53.	This study specifies the blood glucose targets that were given for the intensive therapy group, but no target value details were specified for the conventional group
DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. British Medical Journal 2002;325:746–8.	The study population is adults with Type 1 diabetes, not pregnant women
Tieu,Joanna, Middleton,Philippa, Crowther,Caroline A., Preconception care for diabetic women for improving maternal and infant health, Cochrane Database of Systematic Reviews, -, 2011	Wrong intervention and no results reported
Wahabi,H.A., Alzeidan,R.A., Esmaeil,S.A., Pre-pregnancy care for women with pre-gestational diabetes mellitus: A systematic review and meta-analysis, BMC Public Health, 12, 2012	Systematic review of RCTs: intervention is care not HbA1c target

G.4 HbA1c target values in the preconception period

Excluded studies – Review question 5	
Study	**Reason for Exclusion**
Akhlaghi,F., Rajabian,R., Talebi,F., Correlation of HbA1c and outcome of pregnancy in insulin dependent diabetic women, Iranian Journal of Obstetrics, Gynecology and Infertility, 15, 1-6, 2012	Abstract in English but main article not in English.
Cyganek,K., Hebda-Szydlo,A., Skupien,J., Katra,B., Janas,I., Borodako,A., Kaim,I., Klupa,T., Reron,A., Malecki,M.T., Glycemic control and pregnancy outcomes in women with type 2 diabetes from Poland. The impact of pregnancy planning and a comparison with type 1 diabetes subjects, Endocrine, 40, 243-249, 2011	Compares outcomes in type 1 diabetes versus type 2 diabetes and not according to HbA1c values.

Excluded studies – Review question 5	
Glinianaia,S.V., Tennant,P.W.G., Bilous,R.W., Rankin,J., Bell,R., HbA1c and birthweight in women with pre-conception type 1 and type 2 diabetes: A population-based cohort study, Diabetologia, 55, 3193-3203, 2012	No targets given. Threshold analysis is based on regression with only coefficients presented. Odds ratios for above/below an HbA1c of 7% are presented for LGA risk but in relation to the interaction between peri-conception HbA1c and during the third trimester. Shows an increased risk of LGA for HbA1c increasing during pregnancy.
Gold,A.E., Reilly,R., Little,J., Walker,J.D., The effect of glycemic control in the pre-conception period and early pregnancy on birth weight in women with IDDM, Diabetes Care, 21, 535-538, 1998	No specified HbA1c targets; no threshold analysis. Mean HbA1c only.
Goldman,J.A., Dicker,D., Feldberg,D., Yeshaya,A., Samuel,N., Karp,M., Pregnancy outcome in patients with insulin-dependent diabetes mellitus with preconceptional diabetic control: a comparative study, American Journal of Obstetrics and Gynecology, 155, 293-297, 1986	No specified HbA1c targets; no threshold analysis. Mean HbA1c only. Neonatal hypoglycaemia, pre-eclampsia and Caesarean section are not relevant to the protocol.
Gutaj,P., Zawiejska,A., Wender-Ozegowska,E., Brazert,J., Maternal factors predictive of firsttrimester pregnancy loss in women with pregestational diabetes, Polskie Archiwum Medycyny Wewnetrznej, 123, 21-28, 2013	No specified HbA1c targets; no threshold analysis. Mean HbA1c only in miscarriage versus no miscarriage.
Holmes,V.A., Young,I.S., Patterson,C.C., Pearson,D.W., Walker,J.D., Maresh,M.J., McCance,D.R., Diabetes and Pre-eclampsia Intervention Trial Study Group., Optimal glycemic control, pre-eclampsia, and gestational hypertension in women with type 1 diabetes in the diabetes and pre-eclampsia intervention trial, Diabetes Care, 34, 1683-1688, 2011	No suitable outcomes reported according to the protocol
Jensen,D.M., Damm,P., Moelsted-Pedersen,L., Ovesen,P., Westergaard,J.G., Moeller,M., Beck-Nielsen,H., Outcomes in type 1 diabetic pregnancies: a nationwide, population-based study, Diabetes Care, 27, 2819-2823, 2004	No specified HbA1c targets; no threshold analysis. Mean HbA1c for serious outcome versus no serious outcome.
Klinke,J., Toth,E.L., Preconception care for women with type 1 diabetes, Canadian Family PhysicianCan.Fam.Physician, 49, 769-773, 2003	Systematic review with no data provided
Lisowski,L.A., Verheijen,P.M., Copel,J.A., Kleinman,C.S., Wassink,S., Visser,G.H., Meijboom,E.J., Congenital heart disease in pregnancies complicated by maternal diabetes mellitus. An international clinical collaboration, literature review, and meta-analysis. [64 refs], Herz, 35, 19-26, 2010	No targets/threshold analysis. Comparison is for congenital malformations in the offspring of diabetic versus non-diabetic women.
Miodovnik,M., Mimouni,F., Tsang,R.C., Ammar,E., Kaplan,L., Siddiqi,T.A., Glycemic control and spontaneous abortion in insulin-dependent diabetic women, Obstetrics and GynecologyObstet.Gynecol., 68, 366-369, 1986	No specified HbA1c targets. Mean HbA1c only was reported for abortion versus no abortion.
Rosenn,B., Miodovnik,M., Combs,C.A., Khoury,J., Siddiqi,T.A., Pre-conception management of insulin-dependent diabetes: improvement of pregnancy outcome, Obstetrics and GynecologyObstet.Gynecol., 77, 846-849, 1991	No specified HbA1c targets; no threshold analysis. Mean HbA1c in abortion versus no abortion.
Steel,J.M., Johnstone,F.D., Hepburn,D.A., Smith,A.F., Can prepregnancy care of diabetic women reduce the risk of abnormal babies?, BMJ, 301, 1070-1074, 1990	Outcomes not analysed in relation to HbA1c levels
Tieu,Joanna, Middleton,Philippa, Crowther,Caroline A., Preconception care for diabetic women for improving maternal and infant health, Cochrane Database of Systematic Reviews, -, 2011	Wrong intervention and no results reported
Valuk,J., Factors influencing birth weight in infants of diabetic mothers., Diabetes, 35, 96A-, 1986	Abstract only.
Veres,M., Babes,A., Lacziko,S., Correlations between the values of maternal glycemia from the last trimester of pregnancy and fetal birth weight, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 20, 259-265, 2013	Report associations using ROC analysis - not a threshold
Wahabi,H.A., Alzeidan,R.A., Bawazeer,G.A., Alansari,L.A., Esmaeil,S.A., Preconception care for diabetic women for improving maternal and fetal outcomes: A systematic review and meta-analysis, BMC Pregnancy and Childbirth, 10 , 2010. Article Number, -, 2010	Systematic review of RCTs: intervention is care not HbA1c target
Wahabi,H.A., Alzeidan,R.A., Esmaeil,S.A., Pre-pregnancy care for women with pre-gestational diabetes mellitus: a systematic review and meta-analysis, BMC Public Health, 12, 792-, 2012	Systematic review of RCTs: intervention is care not HbA1c target
Wong,V.W., Suwandarathne,H., Russell,H., Women with pre-existing diabetes under the care of diabetes specialist prior to pregnancy: are their outcomes better?, Australian and New Zealand Journal of Obstetrics and Gynaecology, 53, 207-210, 2013	Compares mean HbA1c only in women who saw a specialist pre-conception vs. those who did not. No targets or thresholds used.

G.5 Screening for gestational diabetes in the first trimester

Excluded studies – Review question 6	
Study	**Reason for Exclusion**
Agarwal,M.M., Dhatt,G.S., Fasting plasma glucose as a screening test for gestational diabetes mellitus. [43 refs], Archives of Gynecology and Obstetrics, 275, 81-87, 2007	Systematic review: individual studies checked for inclusion
Agarwal,M.M., Dhatt,G.S., Punnose,J., Koster,G., Gestational diabetes in a high-risk population: using the fasting plasma glucose to simplify the diagnostic algorithm, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 120, 39-44, 2005	The majority of screening tests were performed in the second trimester (median 25 weeks, range 7-40 weeks)
Agarwal,M.M., Dhatt,G.S., Shah,S.M., Gestational diabetes mellitus: simplifying the international association of diabetes and pregnancy diagnostic algorithm using fasting plasma glucose, Diabetes Care, 33, 2018-2020, 2010	Excluded from this review because no screening test is performed in the first trimester
Alto,W.A., No need for routine glycosuria/proteinuria screen in pregnant women, Journal of Family Practice, 54, 978-983, 2005	Systematic review: individual studies checked for inclusion
Balaji,V., Balaji,M., Anjalakshi,C., Cynthia,A., Arthi,T., Seshiah,V., Inadequacy of fasting plasma glucose to diagnose gestational diabetes mellitus in Asian Indian women, Diabetes Research and Clinical Practice, 94, e21-e23, 2011	Excluded from this review because no screening test is performed in the first trimester
Balaji,V., Madhuri,B.S., Ashalatha,S., Sheela,S., Suresh,S., Seshiah,V., A1C in gestational diabetes mellitus in Asian Indian women, Diabetes Care, 30, 1865-1867, 2007	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75g oral glucose tolerance test (WHO 1999) were used to diagnose gestational diabetes
Bartha,J.L., Martinez-Del-Fresno,P., Comino-Delgado,R., Early diagnosis of gestational diabetes mellitus and prevention of diabetes-related complications, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 109, 41-44, 2003	100g oral glucose tolerance test used as diagnostic test
Bartha,J.L., Martinez-Del-Fresno,P., Comino-Delgado,R., Gestational diabetes mellitus diagnosed during early pregnancy, American Journal of Obstetrics and Gynecology, 182, 346-350, 2000	100g oral glucose tolerance test used as diagnostic test
Berg,M., Adlerberth,A., Sultan,B., Wennergren,M., Wallin,G., Early random capillary glucose level screening and multidisciplinary antenatal teamwork to improve outcome in gestational diabetes mellitus, Acta Obstetricia et Gynecologica Scandinavica, 86, 283-290, 2007	Results are not analysed by trimester because 5 or 6 screening tests were performed throughout pregnancy from gestational week 8 onwards
Berger,H., Crane,J., Farine,D., Armson,A., De La,Ronde S., Keenan-Lindsay,L., Leduc,L., Reid,G., Van,Aerde J., Maternal-Fetal Medicine Committee, Executive and Coundil fo the Society of Obstetricians and Gynaecologists of Canada., Screening for gestational diabetes mellitus, Journal of Obstetrics and Gynaecology Canada: JOGC, 24, 894-912, 2002	Systematic review: individual studies checked for inclusion
Brody,S.C., Harris,R., Lohr,K., Screening for gestational diabetes: a summary of the evidence for the U.S. Preventive Services Task Force. [104 refs], Obstetrics and Gynecology, 101, 380-392, 2003	Systematic review: individual studies checked for inclusion
Buhling,K.J., Elze,L., Henrich,W., Starr,E., Stein,U., Siebert,G., Dudenhausen,J.W., The usefulness of glycosuria and the influence of maternal blood pressure in screening for gestational diabetes, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 113, 145-148, 2004	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Centre for Reviews and Dissemination., Screening for gestational diabetes: a systematic review and economic evaluation (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2012	Abstract only: systematic review identified
Chamberlain,C., Yore,D., Li,H., Williams,E., Oldenburg,B., Oats,J., McNamara,B., Eades,S., Diabetes in pregnancy among indigenous women in Australia, Canada, New Zealand, and the United States: a method for systematic review of studies with different designs, BMC Pregnancy and Childbirth, 11, 104-, 2011	Protocol for systematic review only
Cheng,Y.W., Esakoff,T.F., Block-Kurbisch,I., Ustinov,A., Shafer,S., Caughey,A.B., Screening or diagnostic: markedly elevated glucose loading test and perinatal outcomes, Journal of Maternal-Fetal and Neonatal Medicine, 19, 729-734, 2006	Excluded from the guideline update because an oral glucose tolerance test was not used as diagnostic test
Farah,N., McGoldrick,A., Fattah,C., O'Connor,N., Kennelly,M.M., Turner,M.J., Body Mass Index (BMI) and glucose intolerance during pregnancy in white European women, Journal of Reproduction and Infertility, 13, 95-99, 2012	100g oral glucose tolerance test used as diagnostic test
Farrar,Diane, Duley,Lelia, Lawlor,Debbie A., Different strategies for diagnosing gestational diabetes to improve maternal and infant health, Cochrane Database of Systematic Reviews, -, 2012	Systematic review of methods of performing an oral glucose tolerance test: individual trials checked for inclusion
Fedele,D., Lapolla,A., A protocol of screening of gestational diabetes mellitus, Annali Dell'Istituto Superiore di Sanita, 33, 383-387, 1997	100g oral glucose tolerance test used as diagnostic test

Excluded studies – Review question 6	
Guedj,A.M., When should screening be performed for gestational diabetes?, Diabetes and Metabolism, 36, 652-657, 2010	Systematic review: individual studies checked for inclusion
Health,Technology Assessment, A clinical and economic evaluation of screening and diagnostic tests to identify and treat women with gestational diabetes: association between maternal risk factors, glucose levels, and adverse outcomes (Project record), Health Technology Assessment Database, -, 2014	Abstract of a protocol
Hieronimus,S., Le Meaux,J.P., Relevance of gestational diabetes mellitus screening and comparison of selective with universal strategies, Diabetes and Metabolism, 36, 575-586, 2010	Systematic review: individual studies checked for inclusion
Hillier,T.A., Vesco,K.K., Pedula,K.L., Beil,T.L., Whitlock,E.P., Pettitt,D.J., Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. [21 refs][Summary for patients in Ann Intern Med. 2008 May 20;148(10):I60; PMID: 18490671], Annals of Internal Medicine, 148, 766-775, 2008	Systematic review: individual studies checked for inclusion
Hooper,D.E., Detecting GD and preeclampsia. Effectiveness of routine urine screening for glucose and protein, Journal of Reproductive Medicine, 41, 885-888, 1996	100g oral glucose tolerance test used as diagnostic test
Jensen,D.M., Damm,P., Sorensen,B., Molsted-Pedersen,L., Westergaard,J.G., Korsholm,L., Ovesen,P., Beck-Nielsen,H., Proposed diagnostic thresholds for gestational diabetes mellitus according to a 75-g oral glucose tolerance test. Maternal and perinatal outcomes in 3260 Danish women, Diabetic Medicine, #20, 51-57, 2003	Excluded from this review in the guideline update because no screening test is performed in the first trimester
Jorgensen,L.G., Schytte,T., Brandslund,I., Stahl,M., Petersen,P.H., Andersen,B., Fasting and post-glucose load--reference limits for peripheral venous plasma glucose concentration in pregnant women, Clinical Chemistry and Laboratory Medicine, 41, 187-199, 2003	Excluded from this review because the screening test was performed during the second and third trimesters
Langer,O., Brustman,L., Anyaegbunam,A., Mazze,R., The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy, American Journal of Obstetrics and Gynecology, 157, 758-763, 1987	Excluded from the guideline update because the 100g oral glucose tolerance test is used as the diagnostic test
Maegawa,Y., Sugiyama,T., Kusaka,H., Mitao,M., Toyoda,N., Screening tests for gestational diabetes in Japan in the 1st and 2nd trimester of pregnancy, Diabetes Research and Clinical Practice, 62, 47-53, 2003	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Mello,G., Parretti,E., Cioni,R., Lucchetti,R., Carignani,L., Martini,E., Mecacci,F., Lagazio,C., Pratesi,M., The 75-gram glucose load in pregnancy: relation between glucose levels and anthropometric characteristics of infants born to women with normal glucose metabolism, Diabetes Care, 26, 1206-1210, 2003	Excluded from the guideline update because the diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Minsart,A.F., Lescrainier,J.P., Vokaer,A., Selective versus universal screening for gestational diabetes mellitus: an evaluation of Naylor's model, Gynecologic and Obstetric Investigation, 68, 154-159, 2009	100g oral glucose tolerance test used as diagnostic test
Mortensen,H.B., Molsted-Pedersen,L., Kuhl,C., Backer,P., A screening procedure for diabetes in pregnancy, Diabete et Metabolisme, 11, 249-253, 1985	50g oral glucose tolerance test used as diagnostic test
Most,O.L., Kim,J.H., Arslan,A.A., Klauser,C., Maternal and neonatal outcomes in early glucose tolerance testing in an obstetric population in New York city, Journal of Perinatal Medicine, 37, 114-117, 2009	100g oral glucose tolerance test used as diagnostic test
Omori,Y., Minei,S., Uchigata,Y., Shimizu,M., Sanaka,M., Honda,M., Hirata,Y., Comparison of diagnostic criteria of IGT, borderline, and GDM. Blood glucose curve and IRI response, Diabetes, 40 Suppl 2, 30-34, 1991	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Ostlund,I., Hanson,U., Bjorklund,A., Hjertberg,R., Eva,N., Nordlander,E., Swahn,M.L., Wager,J., Maternal and fetal outcomes if gestational impaired glucose tolerance is not treated, Diabetes Care, 26, 2107-2111, 2003	Excluded from the guideline update because the diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Pugh,S.K., Poole,A.T., Hill,J.B., Magann,E.F., Chauhan,S.P., Morrison,J.C., Abnormal 1 hour glucose challenge test followed by a normal 3 hour glucose tolerance test: does it identify adverse pregnancy outcome?, Journal of the Mississippi State Medical Association, 51, 3-6, 2010	100g oral glucose tolerance test used as diagnostic test
Rehder,P.M., Pereira,B.G., E,SilvaJ.L.P., The prognostic value of a normal oral glucose tolerance test in pregnant women who tested positive at screening: A validation study, Diabetology and Metabolic Syndrome, 4, -, 2012	100g oral glucose tolerance test used as diagnostic test
Riskin-Mashiah,S., Damti,A., Younes,G., Auslender,R., First trimester fasting hyperglycemia as a predictor for the development of gestational diabetes mellitus, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 152, 163-167, 2010	100g oral glucose tolerance test used as diagnostic test
Riskin-Mashiah,S., Younes,G., Damti,A., Auslender,R., First-trimester fasting hyperglycemia and adverse pregnancy outcomes, Diabetes Care, 32, 1639-1643, 2009	100g oral glucose tolerance test used as diagnostic test
Sacks,D.A., Chen,W., Wolde-Tsadik,G., Buchanan,T.A., Fasting plasma glucose test at the first prenatal visit as a screen for gestational diabetes, Obstetrics and Gynecology, 101, 1197-1203, 2003	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol

Excluded studies – Review question 6	
Sacks,D.A., Greenspoon,J.S., bu-Fadil,S., Henry,H.M., Wolde-Tsadik,G., Yao,J.F., Toward universal criteria for gestational diabetes: the 75-gram glucose tolerance test in pregnancy, American Journal of Obstetrics and Gynecology, 172, 607-614, 1995	Excluded from this review in the guideline update because no screening test is performed in the first trimester
Saldana,T.M., Siega-Riz,A.M., Adair,L.S., Savitz,D.A., Thorp,J.M.,Jr., The association between impaired glucose tolerance and birth weight among black and white women in central North Carolina, Diabetes Care, 26, 656-661, 2003	Excluded from the guideline update because 100g oral glucose tolerance test used as diagnostic test
Scott,D.A., Loveman,E., McIntyre,L., Waugh,N., Screening for gestational diabetes: a systematic review and economic evaluation. [256 refs], Health Technology Assessment (Winchester, England), 6, 1-161, 2002	Systematic review: individual studies checked for inclusion
Sermer,M., Naylor,C.D., Farine,D., Kenshole,A.B., Ritchie,J.W., Gare,D.J., Cohen,H.R., McArthur,K., Holzapfel,S., Biringer,A., The Toronto Tri-Hospital Gestational Diabetes Project. A preliminary review, Diabetes Care, 21 Suppl 2, B33-B42, 1998	Excluded from the guideline update because the 100g oral glucose tolerance test is used as the diagnostic test
Seshiah,V., Balaji,V., Balaji,M.S., Panneerselvam,A., Thamizharasi,M., Arthi,T., Glycemic level at the first visit and prediction of GDM, Journal of the Association of Physicians of India, 55, 630-632, 2007	Excluded from this review because the screening test was performed at the first antenatal appointment which was in the second trimester
Seshiah,V., Cynthia,A., Balaji,V., Balaji,M.S., Ashalata,S., Sheela,R., Thamizharasi,M., Arthi,T., Detection and care of women with gestational diabetes mellitus from early weeks of pregnancy results in birth weight of newborn babies appropriate for gestational age, Diabetes Research and Clinical Practice, 80, 199-202, 2008	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75g oral glucose tolerance test (WHO 1994) were used to diagnose gestational diabetes
Shirazian,N., Emdadi,R., Mahboubi,M., Motevallian,A., Fazel-Sarjuei,Z., Sedighpour,N., Fadaki,S.F., Shahmoradi,N., Screening for gestational diabetes: usefulness of clinical risk factors, Archives of Gynecology and Obstetrics, 280, 933-937, 2009	Excluded because the diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Simmons,D., McElduff,A., McIntyre,H.D., Elrishi,M., Gestational diabetes mellitus: NICE for the U.S.? A comparison of the American Diabetes Association and the American College of Obstetricians and Gynecologists guidelines with the U.K. National Institute for Health and Clinical Excellence guidelines, Diabetes Care, 33, 34-37, 2010	Narrative review
Sutherland,H.W., Stowers,J.M., McKenzie,C., Simplifying the clinical problem of glycosuria in pregnancy, Lancet, 1, 1069-1071, 1970	The diagnostic test performed is an intravenous, and not an oral, glucose tolerance test
Syed,M., Javed,H., Yakoob,M.Y., Bhutta,Z.A., Effect of screening and management of diabetes during pregnancy on stillbirths, BMC Public Health, 11 Suppl 3, S2-, 2011	Systematic review: individual studies checked for inclusion
Tallarigo,L., Giampietro,O., Penno,G., Miccoli,R., Gregori,G., Navalesi,R., Relation of glucose tolerance to complications of pregnancy in nondiabetic women, New England Journal of Medicine, 315, 989-992, 1986	Excluded from the guideline update because the 100g oral glucose tolerance test is used as the diagnostic test
Teede,H.J., Harrison,C.L., Teh,W.T., Paul,E., Allan,C.A., Gestational diabetes: development of an early risk prediction tool to facilitate opportunities for prevention, Australian and New Zealand Journal of Obstetrics and Gynaecology, 51, 499-504, 2011	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Tieu,Joanna, Middleton,Philippa, McPhee,Andrew J., Crowther,Caroline A., Screening and subsequent management for gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, -, 2011	Systematic review: individual trials checked for inclusion
U.S, Preventive Services, Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement.[Summary for patients in Ann Intern Med. 2008 May 20;148(10):I60; PMID: 18490671], Annals of Internal Medicine, 148, 759-765, 2008	Recommendation statement : no relevant studies included
van,Leeuwen M., Louwerse,M.D., Opmeer,B.C., Limpens,J., Serlie,M.J., Reitsma,J.B., Mol,B.W., Glucose challenge test for detecting gestational diabetes mellitus: a systematic review, BJOG: An International Journal of Obstetrics and Gynaecology, 119, 393-401, 2012	Systematic review : individual studies checked for inclusion
van,Leeuwen M., Opmeer,B.C., Yilmaz,Y., Limpens,J., Serlie,M.J., Mol,B.W., Accuracy of the random glucose test as screening test for gestational diabetes mellitus: a systematic review, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 154, 130-135, 2011	Systematic review : individual studies checked for inclusion
van,Leeuwen M., Opmeer,B.C., Zweers,E.J., van,Ballegooie E., ter Brugge,H.G., de Valk,H.W., Visser,G.H., Mol,B.W., External validation of a clinical scoring system for the risk of gestational diabetes mellitus, Diabetes Research and Clinical Practice, 85, 96-101, 2009	Excluded from this review because no relevant first trimester data are provided. An unknown number of women with gestational diabetes diagnosed in the first trimester are excluded from the study.
Virally,M., Laloi-Michelin,M., Methods for the screening and diagnosis of gestational diabetes mellitus between 24 and 28 weeks of pregnancy, Diabetes and Metabolism, 36, 549-565, 2010	Systematic review : individual studies checked for inclusion
Waugh,N., Royle,P., Clar,C., Henderson,R., Cummins,E., Hadden,D., Lindsay,R., Pearson,D., Screening for hyperglycaemia in pregnancy: A rapid update for the National Screening Committee, Health Technology Assessment, 14, 1-202, 2010	Systematic review : individual studies checked for inclusion

Excluded studies – Review question 6	
Weiss,P.A., Haeusler,M., Tamussino,K., Haas,J., Can glucose tolerance test predict fetal hyperinsulinism?, BJOG: An International Journal of Obstetrics and Gynaecology, 107, 1480-1485, 2000	Excluded from the guideline update because the 75g oral glucose tolerance test is not consistently used as diagnostic test for all subjects
Wijeyaratne,C.N., Ginige,S., Arasalingam,A., Egodage,C., Wijewardhena,K., Screening for gestational diabetes mellitus: the Sri Lankan experience, Ceylon Medical Journal, 51, 53-58, 2006	Excluded from this review because no screening test is performed in the first trimester
Wong,V.W., Garden,F., Jalaludin,B., Hyperglycaemia following glucose challenge test during pregnancy: when can a screening test become diagnostic?, Diabetes Research and Clinical Practice, 83, 394-396, 2009	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol

G.6 Screening for gestational diabetes in the second trimester

Excluded studies – Review question 7	
Study	**Reason for Exclusion**
Agarwal,M.M., Dhatt,G.S., Fasting plasma glucose as a screening test for gestational diabetes mellitus. [43 refs], Archives of Gynecology and Obstetrics, 275, 81-87, 2007	Systematic review: individual studies checked for inclusion
Agarwal,M.M., Dhatt,G.S., Othman,Y., Gupta,R., Gestational diabetes: fasting capillary glucose as a screening test in a multi-ethnic, high-risk population, Diabetic Medicine, 26, 760-765, 2009	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Agarwal,M.M., Dhatt,G.S., Safraou,M.F., Gestational diabetes: using a portable glucometer to simplify the approach to screening, Gynecologic and Obstetric Investigation, 66, 178-183, 2008	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Agarwal,M.M., Hughes,P.F., Ezimokhai,M., Screening for gestational diabetes in a high-risk population using fasting plasma glucose, International Journal of Gynaecology and Obstetrics, 68, 147-148, 2000	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Agarwal,M.M., Punnose,J., Screening for gestational diabetes in high-risk populations: The United Arab Emirates experience, Annals of Saudi Medicine, 21, 117-119, 2001	100g oral glucose tolerance test used as diagnostic test
Agarwal,M.M., Weigl,B., Hod,M., Gestational diabetes screening: the low-cost algorithm, International Journal of Gynaecology and Obstetrics, 115 Suppl 1, S30-S33, 2011	Narrative review
Al,Mahroos S., Nagalla,D.S., Yousif,W., Sanad,H., A population-based screening for gestational diabetes mellitus in non-diabetic women in Bahrain.[Erratum appears in Ann Saudi Med. 2005 Jul-Aug;25(4):352], Annals of Saudi Medicine, 25, 129-133, 2005	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Alberico,S., Strazzanti,C., De,Santo D., De,Seta F., Lenardon,P., Bernardon,M., Zicari,S., Guaschino,S., Gestational diabetes: universal or selective screening?, Journal of Maternal-Fetal and Neonatal Medicine, 16, 331-337, 2004	100g oral glucose tolerance test used as diagnostic test
Aldasouqi,S.A., Gossain,V.V., A proposal for a role of HbA in screening for gestational diabetes, Diabetic Medicine, 26, 833-834, 2009	No relevant data as it refers to a study where women are tested in the third trimester
Al-Saweer,A., Al-Sairfi,S., The use of glucose screen test alone in diagnosing gestational diabetes mellitus in Bahrain-preliminary report, Bahrain Medical Bulletin, 30, 49-51, 2008	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Alto,W.A., No need for routine glycosuria/proteinuria screen in pregnant women, Journal of Family Practice, 54, 978-983, 2005	Systematic review: individual studies checked for inclusion
Atia,H.C., Koren,Y., Weintraub,A.Y., Novack,L., Sheiner,E., Is a value of over 200mg/dL in the oral glucose tolerance test, a marker of severity in patients with gestational diabetes mellitus?, Journal of Maternal-Fetal and Neonatal Medicine, 26, 1259-1262, 2013	The study did not examine any screening tests prior to performing a diagnostic OGTT
Avalos,G.E., Owens,L.A., Dunne,F., Applying current screening tools for gestational diabetes mellitus to a european population: Is it time for change?, Diabetes Care, 36, 3040-3044, 2013	Insufficient data are presented to to derive relevant diagnostic data
Bakiner,O., Bozkirli,E., Ozsahin,K., Sariturk,C., Ertorer,E., Risk Factors That can Predict Antenatal Insulin Need in Gestational Diabetes, Journal of Clinical Medicine Research, 5, 381-388, 2013	Does not examine the diagnostic accuracy of screening tests to a diagnostic OGTT
Balaji,V., Balaji,M., Anjalakshi,C., Cynthia,A., Arthi,T., Seshiah,V., Inadequacy of fasting plasma glucose to diagnose gestational diabetes mellitus in Asian Indian women, Diabetes Research and Clinical Practice, 94, e21-e23, 2011	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75 gram oral glucose tolerance test were used to diagnose gestational diabetes
Balaji,V., Madhuri,B.S., Ashalatha,S., Sheela,S., Suresh,S., Seshiah,V., A1C in gestational diabetes mellitus in Asian Indian women, Diabetes Care, 30, 1865-1867, 2007	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75 gram oral glucose tolerance test were used to diagnose gestational diabetes

Excluded studies – Review question 7	
Bartha,J.L., Martinez-Del-Fresno,P., Comino-Delgado,R., Early diagnosis of gestational diabetes mellitus and prevention of diabetes-related complications, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 109, 41-44, 2003	100 gram oral glucose tolerance test used as diagnostic test
Bartha,J.L., Martinez-Del-Fresno,P., Comino-Delgado,R., Gestational diabetes mellitus diagnosed during early pregnancy, American Journal of Obstetrics and Gynecology, 182, 346-350, 2000	100 gram oral glucose tolerance test used as diagnostic test
Bassaw,B., Mohammed,N., Ramsewak,S., Bassawh,L., Khan,A., Bhola,M., Chekuri,A., Pregnancy outcome among women universally screened for gestational diabetes mellitus with a lime-flavoured drink, Journal of Obstetrics and Gynaecology, 32, 422-425, 2012	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Benhalima,K., Van,Crombrugge P., Hanssens,M., Devlieger,R., Verhaeghe,J., Mathieu,C., Gestational diabetes: overview of the new consensus screening strategy and diagnostic criteria, Acta Clinica Belgica, 67, 255-261, 2012	Narrative review
Benjamin,F., Wilson,S.J., Deutsch,S., Seltzer,V.L., Droesch,K., Droesch,J., Effect of advancing pregnancy on the glucose tolerance test and on the 50-g oral glucose load screening test for gestational diabetes, Obstetrics and Gynecology, 68, 362-365, 1986	100g oral glucose tolerance test used as diagnostic test
Berg,M., Adlerberth,A., Sultan,B., Wennergren,M., Wallin,G., Early random capillary glucose level screening and multidisciplinary antenatal teamwork to improve outcome in gestational diabetes mellitus, Acta Obstetricia et Gynecologica Scandinavica, 86, 283-290, 2007	Results are not analysed by trimester because 5 or 6 screening tests were performed throughout pregnancy from gestational week 8 onwards
Berger,H., Crane,J., Farine,D., Armson,A., De La,Ronde S., Keenan-Lindsay,L., Leduc,L., Reid,G., Van,Aerde J., Maternal-Fetal Medicine Committee, Executive and Coundil fo the Society of Obstetricians and Gynaecologists of Canada., Screening for gestational diabetes mellitus, Journal of Obstetrics and Gynaecology Canada: JOGC, 24, 894-912, 2002	Systematic review: individual studies checked for inclusion
Brody,S.C., Harris,R., Lohr,K., Screening for gestational diabetes: a summary of the evidence for the U.S. Preventive Services Task Force. [104 refs], Obstetrics and Gynecology, 101, 380-392, 2003	Systematic review: individual studies checked for inclusion
Buhling,K.J., Elze,L., Henrich,W., Starr,E., Stein,U., Siebert,G., Dudenhausen,J.W., The usefulness of glycosuria and the influence of maternal blood pressure in screening for gestational diabetes, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 113, 145-148, 2004	The diagnostic test applied to the oral glucose tolerance test are not relevant according to the protocol
Capula,C., Chiefari,E., Vero,A., Arcidiacono,B., Iiritano,S., Puccio,L., Pullano,V., Foti,D.P., Brunetti,A., Vero,R., Gestational diabetes mellitus: screening and outcomes in southern italian pregnant women, Isrn Endocrinology Print, 2013, 387495-, 2013	The study did not examine the diagnostic accuracy of screening techniques but examined outcomes in selected and unselected populations
Catalano,P.M., McIntyre,H.D., Cruickshank,J.K., McCance,D.R., Dyer,A.R., Metzger,B.E., Lowe,L.P., Trimble,E.R., Coustan,D.R., Hadden,D.R., Persson,B., Hod,M., Oats,J.J., HAPO Study Cooperative Research Group., The hyperglycemia and adverse pregnancy outcome study: associations of GDM and obesity with pregnancy outcomes, Diabetes Care, 35, 780-786, 2012	Duplicate
Centre for Reviews and Dissemination., Screening for gestational diabetes: a systematic review and economic evaluation (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2012	Abstract only: systematic review identified
Chamberlain,C., Yore,D., Li,H., Williams,E., Oldenburg,B., Oats,J., McNamara,B., Eades,S., Diabetes in pregnancy among indigenous women in Australia, Canada, New Zealand, and the United States: a method for systematic review of studies with different designs, BMC Pregnancy and Childbirth, 11, 104-, 2011	Protocol for systematic review only
Cheng,Y.W., Esakoff,T.F., Block-Kurbisch,I., Ustinov,A., Shafer,S., Caughey,A.B., Screening or diagnostic: markedly elevated glucose loading test and perinatal outcomes, Journal of Maternal-Fetal and Neonatal Medicine, 19, 729-734, 2006	Excluded from the guideline update because an oral glucose tolerance test was not used as diagnostic test
Cosson,E., Cussac-Pillegand,C., Benbara,A., Pharisien,I., Jaber,Y., Banu,I., Nguyen,M.T., Valensi,P., Carbillon,L., The diagnostic and prognostic performance of a selective screening strategy for gestational diabetes mellitus according to ethnicity in Europe, Journal of Clinical Endocrinology and Metabolism, 99, 996-1005, 2014	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Cosson,E., Benchimol,M., Carbillon,L., Pharisien,I., Paries,J., Valensi,P., Lormeau,B., Bolie,S., Uzan,M., Attali,J.R., Universal rather than selective screening for gestational diabetes mellitus may improve fetal outcomes, Diabetes and Metabolism, 32, 140-146, 2006	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Coustan,D.R., Widness,J.A., Carpenter,M.W., Rotondo,L., Pratt,D.C., The "breakfast tolerance test": screening for gestational diabetes with a standardized mixed nutrient meal, American Journal of Obstetrics and Gynecology, 157, 1113-1117, 1987	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Crete,J.E., Anasti,J.N., Diagnosis of gestational diabetes mellitus: can we avoid the glucose challenge test?, Journal of the American Association of Nurse Practitioners, 25, 329-333, 2013	100g oral glucose tolerance test used as diagnostic test

Excluded studies – Review question 7	
Davey,R.X., Hamblin,P.S., Selective versus universal screening for gestational diabetes mellitus: an evaluation of predictive risk factors, Medical Journal of Australia, 174, 118-121, 2001	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Dennedy,M.C., Avalos,G., O'Reilly,M.W., O'Sullivan,E.P., Dunne,F.P., The impact of maternal obesity on gestational outcomes, Irish Medical Journal, 105, 23-25, 2012	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Donovan,L., Hartling,L., Muise,M., Guthrie,A., Vandermeer,B., Dryden,D.M., Screening tests for gestational diabetes: a systematic review for the U.S. Preventive Services Task Force, Annals of Internal Medicine, 159, 115-122, 2013	Systematic review: individual studies checked for inclusion
Ezimokhai,M., Joseph,A., Bradley-Watson,P., Audit of pregnancies complicated by diabetes from one center five years apart with selective versus universal screening, Annals of the New York Academy of Sciences, 1084, 132-140, 2006	100 gram oral glucose tolerance test used as diagnostic test
Fadl,H., Ostlund,I., Nilsson,K., Hanson,U., Fasting capillary glucose as a screening test for gestational diabetes mellitus, BJOG: An International Journal of Obstetrics and Gynaecology, 113, 1067-1071, 2006	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Farah,N., McGoldrick,A., Fattah,C., O'Connor,N., Kennelly,M.M., Turner,M.J., Body Mass Index (BMI) and glucose intolerance during pregnancy in white European women, Journal of Reproduction and Infertility, 13, 95-99, 2012	100 gram oral glucose tolerance test used as diagnostic test
Farrar,Diane, Duley,Lelia, Lawlor,Debbie A., Different strategies for diagnosing gestational diabetes to improve maternal and infant health, Cochrane Database of Systematic Reviews, -, 2012	Systematic review of methods of performing an oral glucose tolerance test: individual trials checked for inclusion
Fedele,D., Lapolla,A., A protocol of screening of gestational diabetes mellitus, Annali Dell'Istituto Superiore di Sanita, 33, 383-387, 1997	100 gram oral glucose tolerance test used as diagnostic test
Gandhi,P., Farrell,T., Gestational diabetes mellitus (GDM) screening in morbidly obese pregnant women, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 159, 329-332, 2011	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Guedj,A.M., When should screening be performed for gestational diabetes?, Diabetes and Metabolism, 36, 652-657, 2010	Systematic review: individual studies checked for inclusion
Gobl,C.S., Bozkurt,L., Rivic,P., Schernthaner,G., Weitgasser,R., Pacini,G., Mittlbock,M., Bancher-Todesca,D., Lechleitner,M., Kautzky-Willer,A., A two-step screening algorithm including fasting plasma glucose measurement and a risk estimation model is an accurate strategy for detecting gestational diabetes mellitus, Diabetologia, 55, 3173-3181, 2012	Insufficient data presented to construct 2x2 contingency table
HAPO Study Cooperative Research Group, Metzger,B.E., Lowe,L.P., Dyer,A.R., Trimble,E.R., Chaovarindr,U., Coustan,D.R., Hadden,D.R., McCance,D.R., Hod,M., McIntyre,H.D., Oats,J.J., Persson,B., Rogers,M.S., Sacks,D.A., Hyperglycemia and adverse pregnancy outcomes, New England Journal of Medicine, 358, 1991-2002, 2008	OGTT results are interpreted categorically in the analyses presented rather than dichotomously using diagnostic criteria
Hartling,L., Dryden,D.M., Guthrie,A., Muise,M., Vandermeer,B., Aktary,W.M., Pasichnyk,D., Seida,J.C., Donovan,L., Screening and diagnosing gestational diabetes mellitus, Evidence Report/Technology Assessment, 1-327, 2012	Systematic review: individual studies checked for inclusion
Hayes,L., Bilous,R., Bilous,M., Brandon,H., Crowder,D., Emmerson,C., Lewis-Barned,N., Bell,R., Universal screening to identify gestational diabetes: A multi-centre study in the North of England, Diabetes Research and Clinical Practice, 100, e74-e77, 2013	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Health,Technology Assessment, A clinical and economic evaluation of screening and diagnostic tests to identify and treat women with gestational diabetes: association between maternal risk factors, glucose levels, and adverse outcomes (Project record), Health Technology Assessment Database, -, 2014	Abstract of a protocol
Hieronimus,S., Le Meaux,J.P., Relevance of gestational diabetes mellitus screening and comparison of selective with universal strategies, Diabetes and Metabolism, 36, 575-586, 2010	Systematic review: individual studies checked for inclusion
Hillier,T.A., Vesco,K.K., Pedula,K.L., Beil,T.L., Whitlock,E.P., Pettitt,D.J., Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. [21 refs][Summary for patients in Ann Intern Med. 2008 May 20;148(10):I60; PMID: 18490671], Annals of Internal Medicine, 148, 766-775, 2008	Systematic review: individual studies checked for inclusion
Hooper,D.E., Detecting GD and preeclampsia. Effectiveness of routine urine screening for glucose and protein, Journal of Reproductive Medicine, 41, 885-888, 1996	100 gram oral glucose tolerance test used as diagnostic test
Jensen,D.M., Damm,P., Sorensen,B., Molsted-Pedersen,L., Westergaard,J.G., Korsholm,L., Ovesen,P., Beck-Nielsen,H., Proposed diagnostic thresholds for gestational diabetes mellitus according to a 75-g oral glucose tolerance test. Maternal and perinatal outcomes in 3260 Danish women, Diabetic Medicine, #20, 51-57, 2003	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75 gram oral glucose tolerance test were used to diagnose gestational diabetes
Jensen,D.M., Molsted-Pedersen,L., Beck-Nielsen,H., Westergaard,J.G., Ovesen,P., Damm,P., Screening for gestational diabetes mellitus by a model based on risk indicators: A prospective study, American Journal of Obstetrics and Gynecology, 189, 1383-1388, 2003	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol

Excluded studies – Review question 7	
Jenum,A.K., Mrokrid,K., Sletner,L., Vange,S., Torper,J.L., Nakstad,B., Voldner,N., Rognerud-Jensen,O.H., Berntsen,S., Mosdlo,A., Skrivarhaug,T., Vardal,M.H., Holme,I., Yajnik,C.S., Birkeland,K.I., Impact of ethnicity on gestational diabetes identified with the WHO and the modified International Association of Diabetes and Pregnancy Study Groups criteria: A population-based cohort study, European Journal of Endocrinology, 166, 317-324, 2012	Study examines the prevalence of different risk factors and ethnicities in women with gestational diabetes diagnosed using different criteria
Jorgensen,L.G., Schytte,T., Brandslund,I., Stahl,M., Petersen,P.H., Andersen,B., Fasting and post-glucose load--reference limits for peripheral venous plasma glucose concentration in pregnant women, Clinical Chemistry and Laboratory Medicine, 41, 187-199, 2003	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Jovanovic,L., Definition, size of the problem, screening and diagnostic criteria: who should be screened, cost-effectiveness, and feasibility of screening, International Journal of Gynaecology and Obstetrics, 104 Suppl 1, S17-S19, 2009	Narrative review
Jowett,N.I., Samanta,A.K., Burden,A.C., Screening for diabetes in pregnancy: is a random blood glucose enough?, Diabetic Medicine, 4, 160-163, 1987	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Juutinen,J., Hartikainen,A.L., Bloigu,R., Tapanainen,J.S., A retrospective study on 435 women with gestational diabetes: fasting plasma glucose is not sensitive enough for screening but predicts a need for insulin treatment, Diabetes Care, 23, 1858-1859, 2000	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Kalamegham,R., Nuwayhid,B.S., Mulla,Z.D., Prevalence of gestational fasting and postload single dysglycemia in Mexican-American women and their relative significance in identifying carbohydrate intolerance, American Journal of Perinatology, 27, 697-704, 2010	100 gram oral glucose tolerance test used as diagnostic test
Kalter-Leibovici,O., Freedman,L.S., Olmer,L., Liebermann,N., Heymann,A., Tal,O., Lerner-Geva,L., Melamed,N., Hod,M., Screening and diagnosis of gestational diabetes mellitus: critical appraisal of the new International Association of Diabetes in Pregnancy Study Group recommendations on a national level.[Erratum appears in Diabetes Care. 2012 Dec;35(12):2718], Diabetes Care, 35, 1894-1896, 2012	The study does not report any relevant outcomes
Kumar,M.M., Sharma,R., Gestational diabetes mellitus - Screening and diagnosis by one step procedure, Biosciences Biotechnology Research Asia, 9, 853-856, 2012	The study did not examine the diagnostic accuracy of screening techniques but examined outcomes in selected and unselected populations
Landon,M.B., Mele,L., Spong,C.Y., Carpenter,M.W., Ramin,S.M., Casey,B., Wapner,R.J., Varner,M.W., Rouse,D.J., Thorp,J.M., Sciscione,A., Catalano,P., Harper,M., Saade,G., Caritis,S.N., Sorokin,Y., Peaceman,A.M., Tolosa,J.E., Anderson,G.D., The relationship between maternal glycemia and perinatal outcome, Obstetrics and Gynecology, 117, 218-224, 2011	100 gram oral glucose tolerance test used as diagnostic test
Langer,O., Brustman,L., Anyaegbunam,A., Mazze,R., The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy, American Journal of Obstetrics and Gynecology, 157, 758-763, 1987	Excluded from the guideline update because the 100 gram oral glucose tolerance test is used as the diagnostic test
Lind,T., Anderson,J., Does random blood glucose sampling outdate testing for glycosuria in the detection of diabetes during pregnancy?, British Medical Journal Clinical Research Ed., 289, 1569-1571, 1984	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Loke,D.F., Chua,S., Kek,L.P., Thai,A.C., Ratnam,S.S., Glycosylated hemoglobins in pregnant women with normal and abnormal glucose tolerance, Gynecologic and Obstetric Investigation, 37, 25-29, 1994	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Lowe,L.P., Coustan,D.R., Metzger,B.E., Hadden,D.R., Dyer,A.R., Hod,M., Lowe,J., Oats,J.J.N., McCance,D.R., Persson,B., Lappin,T.R.J., Trimble,E.R., Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: Associations of maternal A1C and glucose with pregnancy outcomes, Diabetes Care, 35, 574-580, 2012	OGTT results are not interpreted using any diagnostic criteria in the analyses presented
Maegawa,Y., Sugiyama,T., Kusaka,H., Mitao,M., Toyoda,N., Screening tests for gestational diabetes in Japan in the 1st and 2nd trimester of pregnancy, Diabetes Research and Clinical Practice, 62, 47-53, 2003	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Mello,G., Parretti,E., Cioni,R., Lucchetti,R., Carignani,L., Martini,E., Mecacci,F., Lagazio,C., Pratesi,M., The 75-gram glucose load in pregnancy: relation between glucose levels and anthropometric characteristics of infants born to women with normal glucose metabolism, Diabetes Care, 26, 1206-1210, 2003	Excluded from the guideline update because the diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol.
Minsart,A.F., Lescrainier,J.P., Vokaer,A., Selective versus universal screening for gestational diabetes mellitus: an evaluation of Naylor's model, Gynecologic and Obstetric Investigation, 68, 154-159, 2009	100 gram oral glucose tolerance test used as diagnostic test
Mortensen,H.B., Molsted-Pedersen,L., Kuhl,C., Backer,P., A screening procedure for diabetes in pregnancy, Diabete et Metabolisme, 11, 249-253, 1985	50 gram oral glucose tolerance test used as diagnostic test
Moses,R.G., Moses,J., Davis,W.S., Gestational diabetes: do lean young caucasian women need to be tested?, Diabetes Care, 21, 1803-1806, 1998	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol

Excluded studies – Review question 7	
Most,O.L., Kim,J.H., Arslan,A.A., Klauser,C., Maternal and neonatal outcomes in early glucose tolerance testing in an obstetric population in New York city, Journal of Perinatal Medicine, 37, 114-117, 2009	100 gram oral glucose tolerance test used as diagnostic test
Nasrat,A.A., Johnstone,F.D., Hasan,S.A., Is random plasma glucose an efficient screening test for abnormal glucose tolerance in pregnancy?, British Journal of Obstetrics and Gynaecology, 95, 855-860, 1988	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Nucci,L.B., Schmidt,M.I., Duncan,B.B., Fuchs,S.C., Fleck,E.T., Santos Britto,M.M., Nutritional status of pregnant women: prevalence and associated pregnancy outcomes, Rev Saude Publica, 35, 502-507, 2001	No relevant data
Omori,Y., Minei,S., Uchigata,Y., Shimizu,M., Sanaka,M., Honda,M., Hirata,Y., Comparison of diagnostic criteria of IGT, borderline, and GDM. Blood glucose curve and IRI response, Diabetes, 40 Suppl 2, 30-34, 1991	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Ostlund,I., Hanson,U., Bjorklund,A., Hjertberg,R., Eva,N., Nordlander,E., Swahn,M.L., Wager,J., Maternal and fetal outcomes if gestational impaired glucose tolerance is not treated, Diabetes Care, 26, 2107-2111, 2003	Excluded from the guideline update because the diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Pintaudi,B., Di,Vieste G., Corrado,F., Lucisano,G., Pellegrini,F., Giunta,L., Nicolucci,A., D'Anna,R., Di,Benedetto A., Improvement of selective screening strategy for gestational diabetes through a more accurate definition of high-risk groups, European Journal of Endocrinology, 170, 87-93, 2014	Study does not report results for risk factors that are relevant to the protocol
Poomalar,G.K., Rangaswamy,V., A comparison of fasting plasma glucose and glucose challenge test for screening of gestational diabetes mellitus, Journal of Obstetrics and Gynaecology, 33, 447-450, 2013	Includes women in the second and third trimester but does not report results separately for these groups
Pugh,S.K., Poole,A.T., Hill,J.B., Magann,E.F., Chauhan,S.P., Morrison,J.C., Abnormal 1 hour glucose challenge test followed by a normal 3 hour glucose tolerance test: does it identify adverse pregnancy outcome?, Journal of the Mississippi State Medical Association, 51, 3-6, 2010	100 gram oral glucose tolerance test used as diagnostic test
Rehder,P.M., Pereira,B.G., E,SilvaJ.L.P., The prognostic value of a normal oral glucose tolerance test in pregnant women who tested positive at screening: A validation study, Diabetology and Metabolic Syndrome, 4, -, 2012	100 gram oral glucose tolerance test used as diagnostic test
Reichelt,A.J., Spichler,E.R., Branchtein,L., Nucci,L.B., Franco,L.J., Schmidt,M.I., Fasting plasma glucose is a useful test for the detection of gestational diabetes. Brazilian Study of Gestational Diabetes (EBDG) Working Group, Diabetes Care, 21, 1246-1249, 1998	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Rey,E., Hudon,L., Michon,N., Boucher,P., Ethier,J., Saint-Louis,P., Fasting plasma glucose versus glucose challenge test: screening for gestational diabetes and cost effectiveness, Clinical Biochemistry, 37, 780-784, 2004	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Riskin-Mashiah,S., Younes,G., Damti,A., Auslender,R., First-trimester fasting hyperglycemia and adverse pregnancy outcomes, Diabetes Care, 32, 1639-1643, 2009	100 gram oral glucose tolerance test used as diagnostic test
Roberts,R.N., McManus,J., Dobbs,S., Hadden,D.R., A standardised breakfast tolerance test in pregnancy: comparison with the 75 g oral glucose tolerance test in unselected mothers and in those with impaired glucose tolerance, Ulster Medical Journal, 66, 18-23, 1997	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Sacks,D.A., Chen,W., Wolde-Tsadik,G., Buchanan,T.A., Fasting plasma glucose test at the first prenatal visit as a screen for gestational diabetes, Obstetrics and Gynecology, 101, 1197-1203, 2003	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Sacks,D.A., Greenspoon,J.S., bu-Fadil,S., Henry,H.M., Wolde-Tsadik,G., Yao,J.F., Toward universal criteria for gestational diabetes: the 75-gram glucose tolerance test in pregnancy, American Journal of Obstetrics and Gynecology, 172, 607-614, 1995	No relevant outcomes
Saldana,T.M., Siega-Riz,A.M., Adair,L.S., Savitz,D.A., Thorp,J.M.,Jr., The association between impaired glucose tolerance and birth weight among black and white women in central North Carolina, Diabetes Care, 26, 656-661, 2003	Excluded from the guideline update because 100 gram oral glucose tolerance test used as diagnostic test
Savona-Ventura,C., Vassallo,J., Marre,M., Karamanos,B.G., Erratum: A composite risk assessment model to screen for gestational diabetes mellitus among Mediterranean women (International Journal of Gynecology and Obstetrics (2013) 120 (240-244)), International Journal of Gynecology and Obstetrics, 122, 88-, 2013	No relevant data presented
Savona-Ventura,C., Vassallo,J., Marre,M., Karamanos,B.G., A composite risk assessment model to screen for gestational diabetes mellitus among Mediterranean women, International Journal of Gynecology and Obstetrics, 120, 240-244, 2013	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Schaas,C.M., Titianu,M., Stamatian,M., Onofriescu,M., Relations between perinatal outcomes and gestational diabetes, Gineco.eu, 9, 167-169, 2013	The diagnostic criteria applied to the oral glucose tolerance test are not reported
Scott,D.A., Loveman,E., McIntyre,L., Waugh,N., Screening for gestational diabetes: a systematic review and economic evaluation. [256 refs], Health Technology Assessment (Winchester, England), 6, 1-161, 2002	Systematic review: individual studies checked for inclusion
Scott,D.A., Loveman,E., McIntyre,L., Waugh,N., Screening for gestational diabetes: a systematic review and economic evaluation (Structured abstract), Health Technology Assessment Database, -, 2012	Systematic review: individual studies checked for inclusion

Excluded studies – Review question 7	
Sermer,M., Naylor,C.D., Farine,D., Kenshole,A.B., Ritchie,J.W., Gare,D.J., Cohen,H.R., McArthur,K., Holzapfel,S., Biringer,A., The Toronto Tri-Hospital Gestational Diabetes Project. A preliminary review, Diabetes Care, 21 Suppl 2, B33-B42, 1998	Excluded from the guideline update because the 100 gram oral glucose tolerance test is used as the diagnostic test
Seshiah,V., Balaji,V., Balaji,M.S., Panneerselvam,A., Thamizharasi,M., Arthi,T., Glycemic level at the first visit and prediction of GDM, Journal of the Association of Physicians of India, 55, 630-632, 2007	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75 gram oral glucose tolerance test were used to diagnose gestational diabetes
Seshiah,V., Cynthia,A., Balaji,V., Balaji,M.S., Ashalata,S., Sheela,R., Thamizharasi,M., Arthi,T., Detection and care of women with gestational diabetes mellitus from early weeks of pregnancy results in birth weight of newborn babies appropriate for gestational age, Diabetes Research and Clinical Practice, 80, 199-202, 2008	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75 gram oral glucose tolerance test (WHO 1994) were used to diagnose gestational diabetes
Sevket,O., Ates,S., Uysal,O., Molla,T., Dansuk,R., Kelekci,S., To evaluate the prevalence and clinical outcomes using a one-step method versus a two-step method to screen gestational diabetes mellitus, Journal of Maternal-Fetal and Neonatal Medicine, 27, 36-41, 2014	The comparison made in this study is not relevant according to the protocol
Sharma,K., Wahi,P., Gupta,A., Jandial,K., Bhagat,R., Gupta,R., Gupta,S., Singh,J., Single glucose challenge test procedure for diagnosis of gestational diabetes mellitus: a Jammu cohort study, Journal of the Association of Physicians of India, 61, 558-559, 2013	This study considers the use of the Glucose Challenge Test as a diagnostic test, rather than an OGTT
Shirazian,N., Emdadi,R., Mahboubi,M., Motevallian,A., Fazel-Sarjuei,Z., Sedighpour,N., Fadaki,S.F., Shahmoradi,N., Screening for gestational diabetes: usefulness of clinical risk factors, Archives of Gynecology and Obstetrics, 280, 933-937, 2009	Excluded because the diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol.
Simmons,D., McElduff,A., McIntyre,H.D., Elrishi,M., Gestational diabetes mellitus: NICE for the U.S.? A comparison of the American Diabetes Association and the American College of Obstetricians and Gynecologists guidelines with the U.K. National Institute for Health and Clinical Excellence guidelines, Diabetes Care, 33, 34-37, 2010	Narrative review
Siribaddana,S.H., Deshabandu,R., Rajapakse,D., Silva,K., Fernando,D.J., The prevalence of gestational diabetes in a Sri Lankan antenatal clinic, The Ceylon medical journal, 43, 88-91, 1998	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Sutherland,H.W., Stowers,J.M., McKenzie,C., Simplifying the clinical problem of glycosuria in pregnancy, Lancet, 1, 1069-1071, 1970	The diagnostic test performed is an intravenous, and not an oral, glucose tolerance test
Syed,M., Javed,H., Yakoob,M.Y., Bhutta,Z.A., Effect of screening and management of diabetes during pregnancy on stillbirths, BMC Public Health, 11 Suppl 3, S2-, 2011	Systematic review: individual studies checked for inclusion
Tallarigo,L., Giampietro,O., Penno,G., Miccoli,R., Gregori,G., Navalesi,R., Relation of glucose tolerance to complications of pregnancy in nondiabetic women, New England Journal of Medicine, 315, 989-992, 1986	Excluded from the guideline update because the 100 gram oral glucose tolerance test is used as the diagnostic test
Tam,W.H., Rogers,M.S., Yip,S.K., Lau,T.K., Leung,T.Y., Which screening test is the best for gestational impaired glucose tolerance and gestational diabetes mellitus?, Diabetes Care, 23, 1432-, 2000	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Tan,P.C., Ling,L.P., Omar,S.Z., The 50-g glucose challenge test and pregnancy outcome in a multiethnic Asian population at high risk for gestational diabetes, International Journal of Gynaecology and Obstetrics, 105, 50-55, 2009	Approximately half of all screening was performed after gestational week 28 and many of these tests were undertaken well into the third trimester
Teede,H.J., Harrison,C.L., Teh,W.T., Paul,E., Allan,C.A., Gestational diabetes: development of an early risk prediction tool to facilitate opportunities for prevention, Australian and New Zealand Journal of Obstetrics and Gynaecology, 51, 499-504, 2011	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Teh,W.T., Teede,H.J., Paul,E., Harrison,C.L., Wallace,E.M., Allan,C., Risk factors for gestational diabetes mellitus: implications for the application of screening guidelines, Australian and New Zealand Journal of Obstetrics and Gynaecology, 51, 26-30, 2011	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Tieu,Joanna, McPhee,Andrew J., Crowther,Caroline A., Middleton,Philippa, Screening and subsequent management for gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, -, 2014	Cochrane systematic review inclide studies checked for reevance here. 1 quasi RCT used 100g OGTT and 3 RCTs examined different loading doses of glucose in screening tests
Tieu,Joanna, Middleton,Philippa, McPhee,Andrew J., Crowther,Caroline A., Screening and subsequent management for gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, -, 2011	Systematic review: individual trials checked for inclusion
Torloni,M.R., Betran,A.P., Horta,B.L., Nakamura,M.U., Atallah,A.N., Moron,A.F., Valente,O., Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. [102 refs], Obesity Reviews, 10, 194-203, 2009	Systematic review: individual studies checked for inclusion
Tran,T.S., Hirst,J.E., Do,M.A., Morris,J.M., Jeffery,H.E., Early prediction of gestational diabetes mellitus in Vietnam: clinical impact of currently recommended diagnostic criteria, Diabetes Care, 36, 618-624, 2013	No relevant diagnostic accuracy data are reported

Excluded studies – Review question 7	
Tripathi,R., Tolia,N., Gupta,V.K., Mala,Y.M., Ramji,S., Tyagi,S., Screening for gestational diabetes mellitus: a prospective study in a tertiary care institution of North India, Journal of Obstetrics and Gynaecology Research, 38, 351-357, 2012	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
U.S, Preventive Services, Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement.[Summary for patients in Ann Intern Med. 2008 May 20;148(10):I60; PMID: 18490671], Annals of Internal Medicine, 148, 759-765, 2008	Recommendation statement: no relevant studies included
van,Leeuwen M., Louwerse,M.D., Opmeer,B.C., Limpens,J., Serlie,M.J., Reitsma,J.B., Mol,B.W., Glucose challenge test for detecting gestational diabetes mellitus: a systematic review, BJOG: An International Journal of Obstetrics and Gynaecology, 119, 393-401, 2012	Systematic review: individual studies checked for inclusion
van,Leeuwen M., Opmeer,B.C., Yilmaz,Y., Limpens,J., Serlie,M.J., Mol,B.W., Accuracy of the random glucose test as screening test for gestational diabetes mellitus: a systematic review, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 154, 130-135, 2011	Systematic review: individual studies checked for inclusion
van,Leeuwen M., Opmeer,B.C., Zweers,E.J., van,Ballegooie E., ter Brugge,H.G., de Valk,H.W., Visser,G.H., Mol,B.W., Estimating the risk of gestational diabetes mellitus: a clinical prediction model based on patient characteristics and medical history, BJOG: An International Journal of Obstetrics and Gynaecology, 117, 69-75, 2010	The clinical prediction model developed would not be of use in clinical practice
van,Leeuwen M., Zweers,E.J., Opmeer,B.C., van,Ballegooie E., ter Brugge,H.G., de Valk,H.W., Mol,B.W., Visser,G.H., Comparison of accuracy measures of two screening tests for gestational diabetes mellitus, Diabetes Care, 30, 2779-2784, 2007	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Van,LeeuwenM, Vijgen,S., Opmeer,B.C., Evers,I., Mol,B.W., Cost-effectiveness analysis of screening for GDM, American Journal of Obstetrics and Gynecology, 201, S109-, 2009	Abstract only
Virally,M., Laloi-Michelin,M., Methods for the screening and diagnosis of gestational diabetes mellitus between 24 and 28 weeks of pregnancy, Diabetes and Metabolism, 36, 549-565, 2010	Systematic review: individual studies checked for inclusion
Wagaarachchi,P.T., Fernando,L., Premachadra,P., Fernando,D.J., Screening based on risk factors for gestational diabetes in an Asian population, Journal of Obstetrics & GynaecologyJ Obstet Gynaecol, 21, 32-34, 2001	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Waugh,N., Royle,P., Clar,C., Henderson,R., Cummins,E., Hadden,D., Lindsay,R., Pearson,D., Screening for hyperglycaemia in pregnancy: A rapid update for the National Screening Committee, Health Technology Assessment, 14, 1-202, 2010	Systematic review: individual studies checked for inclusion
Weiss,P.A., Haeusler,M., Tamussino,K., Haas,J., Can glucose tolerance test predict fetal hyperinsulinism?, BJOG: An International Journal of Obstetrics and Gynaecology, 107, 1480-1485, 2000	Excluded from the guideline update because the 75 gram oral glucose tolerance test is not consistently used as diagnostic test for all subjects
Wijeyaratne,C.N., Ginige,S., Arasalingam,A., Egodage,C., Wijewardhena,K., Screening for gestational diabetes mellitus: the Sri Lankan experience, Ceylon Medical Journal, 51, 53-58, 2006	Only the 2 hour plasma glucose values and not the fasting plasma glucose values derived from a 75g oral glucose tolerance test (WHO 1999) were used to diagnose gestational diabetes
Wong,T., Ross,G.P., Jalaludin,B.B., Flack,J.R., The clinical significance of overt diabetes in pregnancy, Diabetic Medicine, 30, 468-474, 2013	The diagnostic criteria and tests applied are not relevant according to the protocol
Wong,V.W., Garden,F., Jalaludin,B., Hyperglycaemia following glucose challenge test during pregnancy: when can a screening test become diagnostic?, Diabetes Research and Clinical Practice, 83, 394-396, 2009	The diagnostic criteria applied to the oral glucose tolerance test are not relevant according to the protocol
Zhu,W.W., Fan,L., Yang,H.X., Kong,L.Y., Su,S.P., Wang,Z.L., Hu,Y.L., Zhang,M.H., Sun,L.Z., Mi,Y., Du,X.P., Zhang,H., Wang,Y.H., Huang,Y.P., Zhong,L.R., Wu,H.R., Li,N., Wang,Y.F., Kapur,A., Fasting plasma glucose at 24-28 weeks to screen for gestational diabetes mellitus: new evidence from China, Diabetes Care, 36, 2038-2040, 2013	No relevant data are reported. Letter that compares testing fasting plasma glucose and fasting capillary glucose

G.7 Diagnostic criteria for gestational diabetes

Excluded studies – Review question 8	
Study	**Reason for Exclusion**
Agarwal,M.M., Weigl,B., Hod,M., Gestational diabetes screening: the low-cost algorithm, International Journal of Gynaecology and Obstetrics, 115 Suppl 1, S30-S33, 2011	No comparison between World Health Organization (WHO) and International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria reported

Excluded studies – Review question 8	
Balaji,V., Balaji,M., Anjalakshi,C., Cynthia,A., Arthi,T., Seshiah,V., Inadequacy of fasting plasma glucose to diagnose gestational diabetes mellitus in Asian Indian women, Diabetes Research and Clinical Practice, 94, e21-e23, 2011	The WHO diagnosis of gestational diabetes used in this study is based solely on 2 hour plasma glucose results from the oral glucose tolerance test (OGTT) and does not incorporate fasting plasma glucose (FPG) test results
Black,M.H., Sacks,D.A., Xiang,A.H., Lawrence,J.M., Clinical outcomes of pregnancies complicated by mild gestational diabetes mellitus differ by combinations of abnormal oral glucose tolerance test values, Diabetes Care, 33, 2524-2530, 2010	No comparison between WHO and IADPSG criteria reported
Blatt,A.J., Nakamoto,J.M., Kaufman,H.W., Gaps in diabetes screening during pregnancy and postpartum, Obstetrics and Gynecology, 117, 61-68, 2011	No comparison between WHO and IADPSG criteria reported
Catalano,P.M., McIntyre,H.D., Cruickshank,J.K., McCance,D.R., Dyer,A.R., Metzger,B.E., Lowe,L.P., Trimble,E.R., Coustan,D.R., Hadden,D.R., Persson,B., Hod,M., Oats,J.J., HAPO Study Cooperative Research Group., The hyperglycemia and adverse pregnancy outcome study: associations of GDM and obesity with pregnancy outcomes, Diabetes Care, 35, 780-786, 2012	No comparison between WHO and IADPSG criteria reported
Disse,E., Graeppi-Dulac,J., Joncour-Mills,G., Dupuis,O., Thivolet,C., Heterogeneity of pregnancy outcomes and risk of LGA neonates in Caucasian females according to IADPSG criteria for gestational diabetes mellitus, Diabetes and Metabolism, 39, 132-138, 2013	Relevant diagnostic accuracy or outcome data comparing WHO and IADPSG diagnostic criteria are not available
Falavigna,M., Prestes,I., Schmidt,M.I., Duncan,B.B., Colagiuri,S., Roglic,G., Impact of gestational diabetes mellitus screening strategies on perinatal outcomes: a simulation study, Diabetes Research and Clinical Practice, 99, 358-365, 2013	Relevant diagnostic accuracy or outcome data comparing WHO and IADPSG diagnostic criteria are not available
Flack,J.R., Ross,G.P., Ho,S., McElduff,A., Recommended changes to diagnostic criteria for gestational diabetes: impact on workload, Australian and New Zealand Journal of Obstetrics and Gynaecology, 50, 439-443, 2010	No comparison between WHO and IADPSG criteria reported
Harrison,C.L., Lombard,C.B., Teede,H.J., Understanding health behaviours in a cohort of pregnant women at risk of gestational diabetes mellitus: an observational study, BJOG: An International Journal of Obstetrics and Gynaecology, 119, 731-738, 2012	No comparison between WHO and IADPSG criteria reported
Hartling,L., Dryden,D.M., Guthrie,A., Muise,M., Vandermeer,B., Aktary,W.M., Pasichnyk,D., Seida,J.C., Donovan,L., Screening and diagnosing gestational diabetes mellitus, Evidence Report/Technology Assessment, 1-327, 2012	Systematic review: individual studies checked for inclusion
Huynh,J., Ratnaike,S., Bartalotta,C., Permezel,M., Houlihan,C., Challenging the glucose challenge test, Australian and New Zealand Journal of Obstetrics and Gynaecology, 51, 22-25, 2011	No comparison between WHO and IADPSG criteria reported
International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger,B.E., Gabbe,S.G., Persson,B., Buchanan,T.A., Catalano,P.A., Damm,P., Dyer,A.R., Leiva,A., Hod,M., Kitzmiler,J.L., Lowe,L.P., McIntyre,H.D., Oats,J.J., Omori,Y., Schmidt,M.I., International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. [57 refs], Diabetes Care, 33, 676-682, 2010	No comparison between WHO and IADPSG criteria reported
Jenum,A.K., Morkrid,K., Sletner,L., Vangen,S., Torper,J.L., Nakstad,B., Voldner,N., Rognerud-Jensen,O.H., Berntsen,S., Mosdol,A., Skrivarhaug,T., Vardal,M.H., Holme,I., Yajnik,C.S., Birkeland,K.I., Impact of ethnicity on gestational diabetes identified with the WHO and the modified International Association of Diabetes and Pregnancy Study Groups criteria: a population-based cohort study.[Erratum appears in Eur J Endocrinol. 2012 Mar;166(3):561 Note: Vange, Siri [corrected to Vangen, Siri]], European Journal of Endocrinology, 166, 317-324, 2012	Duplicate
Jenum,A.K., Morkrid,K., Sletner,L., Vange,S., Torper,J.L., Nakstad,B., Voldner,N., Rognerud-Jensen,O.H., Berntsen,S., Mosdol,A., Skrivarhaug,T., Vardal,M.H., Holme,I., Yajnik,C.S., Birkeland,K.I., Impact of ethnicity on gestational diabetes identified with the WHO and the modified International Association of Diabetes and Pregnancy Study Groups criteria: A population-based cohort study (European Journal of Endocrinology (2012) 166, (317-324)), European Journal of Endocrinology, 166, 561-, 2012	The correction made in this erratum statement is not relevant to this review question
Kalter-Leibovici,O., Freedman,L.S., Olmer,L., Liebermann,N., Heymann,A., Tal,O., Lerner-Geva,L., Melamed,N., Hod,M., Screening and diagnosis of gestational diabetes mellitus: Critical appraisal of the new International Association of Diabetes in Pregnancy Study Group recommendations on a national level (Diabetes Care (2012) 35, (1894-1896), Diabetes Care, 35, 2718-, 2012	Erratum statement for an excluded study
Kalter-Leibovici,O., Freedman,L.S., Olmer,L., Liebermann,N., Heymann,A., Tal,O., Lerner-Geva,L., Melamed,N., Hod,M., Screening and diagnosis of gestational diabetes mellitus: critical appraisal of the new International Association of Diabetes in Pregnancy Study Group recommendations on a national level.[Erratum appears in Diabetes Care. 2012 Dec;35(12):2718], Diabetes Care, 35, 1894-1896, 2012	No comparison between WHO and IADPSG criteria reported(IADPSG criteria only are used)

Excluded studies – Review question 8	
Kendrick,J.M., Screening and diagnosing gestational diabetes mellitus revisited: implications from HAPO, Journal of Perinatal and Neonatal Nursing, 25, 226-232, 2011	Narrative review
Lieberman,N., Kalter-Leibovici,O., Hod,M., Global adaptation of IADPSG recommendations: a national approach, International Journal of Gynaecology and Obstetrics, 115 Suppl 1, S45-S47, 2011	Narrative review
Morikawa,M., Yamada,T., Yamada,T., Akaishi,R., Nishida,R., Cho,K., Minakami,H., Change in the number of patients after the adoption of IADPSG criteria for hyperglycemia during pregnancy in Japanese women, Diabetes Research and Clinical Practice, 90, 339-342, 2010	No comparison between WHO and IADPSG criteria reported
Moses,R.G., Gestational diabetes mellitus: implications of an increased frequency with IADPSG criteria, Diabetes Care, 35, 461-462, 2012	Narrative review
Moses,R.G., Morris,G.J., Petocz,P., San,Gil F., Garg,D., The impact of potential new diagnostic criteria on the prevalence of gestational diabetes mellitus in Australia, Medical Journal of Australia, 194, 338-340, 2011	No comparison between WHO and IADPSG criteria reported
O'Sullivan,E.P., Avalos,G., O'Reilly,M., Dennedy,M.C., Gaffney,G., Dunne,F., Atlantic,D.I.P., Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria, Diabetologia, 54, 1670-1675, 2011	The FPG threshold used to diagnose gestational diabetes according to the WHO criteria is lower in this study than in the WHO definition used in the review question
Reyes-Munoz,E., Parra,A., Castillo-Mora,A., Ortega-Gonzalez,C., Effect of the diagnostic criteria of the international association of diabetes and pregnancy study groups on the prevalence of gestational diabetes mellitus in urban mexican women: A cross-sectional study, Endocrine Practice, 18, 146-151, 2012	No comparison between WHO and IADPSG criteria reported
Sacks,D.A., Hadden,D.R., Maresh,M., Deerochanawong,C., Dyer,A.R., Metzger,B.E., Lowe,L.P., Coustan,D.R., Hod,M., Oats,J.J., Persson,B., Trimble,E.R., HAPO Study Cooperative Research Group., Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, Diabetes Care, 35, 526-528, 2012	No comparison between WHO and IADPSG criteria reported
Savona-Ventura,C., Vassallo,J., Marre,M., Karamanos,B.G., MGSD:GDM Study Group., Hyperglycaemia in pregnancy in Mediterranean women, Acta Diabetologica, 49, 473-480, 2012	No comparison between WHO and IADPSG criteria reported
Seshiah,V., Balaji,V., Shah,S.N., Joshi,S., Das,A.K., Sahay,B.K., Banerjee,S., Zargar,A.H., Balaji,M., Diagnosis of gestational diabetes mellitus in the community, Journal of the Association of Physicians of India, 60, 15-17, 2012	The WHO diagnosis of gestational diabetes used in this study is based solely on 2 hour plasma glucose results from the oral glucose tolerance test (OGTT) and does not incorporate fasting plasma glucose (FPG) test results
Tran,T.S., Hirst,J.E., Do,M.A., Morris,J.M., Jeffery,H.E., Early prediction of gestational diabetes mellitus in Vietnam: clinical impact of currently recommended diagnostic criteria, Diabetes Care, 36, 618-624, 2013	Relevant diagnostic accuracy or outcome data comparing WHO and IADPSG diagnostic criteria are not available
Wendland,E.M., Torloni,M.R., Falavigna,M., Trujillo,J., Dode,M.A., Campos,M.A., Duncan,B.B., Schmidt,M.I., Gestational diabetes and pregnancy outcomes--a systematic review of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria, BMC Pregnancy and Childbirth, 12, 23-, 2012	Duplicate
Wendland,E.M., Duncan,B.B., Mengue,S.S., Schmidt,M.I., Lesser than diabetes hyperglycemia in pregnancy is related to perinatal mortality: a cohort study in Brazil, BMC Pregnancy and Childbirth, 11, 92-, 2011	Population and perinatal mortality outcomes in this study reported in Wendland 2012

G.8 Interventions for gestational diabetes

Excluded studies – Review question 9	
Study	**Reason for Exclusion**
Afaghi,A., Ghanei,L., Ziaee,A., Effect of low glycemic load diet with and without wheat bran on glucose control in gestational diabetes mellitus: A randomized trial, Indian Journal of Endocrinology and Metabolism, 17, 689-692, 2013	The only outcome reported is maternal blood glucose therefore not relevant to review protocol.
Algert,S., Shragg,P., Hollingsworth,D.R., Moderate caloric restriction in obese women with gestational diabetes, Obstetrics and Gynecology, 65, 487-491, 1985	Cohort study.
Alwan,Nisreen, Tuffnell,Derek J., West,Jane, Treatments for gestational diabetes, Cochrane Database of Systematic Reviews, -, 2011	Systematic review - checked for relevant trials
Anjalakshi,C., Balaji,V., Balaji,M.S., Seshiah,V., A prospective study comparing insulin and glibenclamide in gestational diabetes mellitus in Asian Indian women, Diabetes Research and Clinical Practice, 76, 474-475, 2007	No relevant outcomes

Excluded studies – Review question 9	
Bahado-Singh,R.O., Mele,L., Landon,M.B., Ramin,S.M., Carpenter,M.W., Casey,B., Wapner,R.J., Varner,M.W., Rouse,D.J., Thorp,Jr, Sciscione,A., Catalano,P., Harper,M., Saade,G., Caritis,S.N., Peaceman,A.M., Tolosa,J.E., Fetal male gender and the benefits of treatment of mild gestational diabetes mellitus, American Journal of Obstetrics and Gynecology, 206, 422-422, 2012	No relevant results
Balaji,V., Balaji,M.S., Alexander,C., Ashalata,S., Sheela,Suganthi R., Suresh,S., Seshiah,V., Premixed insulin aspart 30 (Biasp 30) vs. premixed human insulin 30 (BHI 30) in gestational diabetes mellitus--a pilot study, Journal of the Association of Physicians of India, 58, 99-101, 2010	Comparison not relevant (insulin vs insulin)
Balaji,V., Balaji,M.S., Alexander,C., Ashalata,S., Suganthi,R.S., Suresh,S., Seshiah,V., Premixed insulin aspart 30 (biasp 30) vs premixed human insulin 30 (bhi 30) in gestational diabetes mellitus a[Euro sign]" a pilot study, Journal of the Associations of the Physicians of India, 58, 96-97, 2010	Comparison not relevant (insulin vs insulin)
Barbour,L.A., Van Pelt,R.E., Brumbaugh,D.E., Hernandez,T.L., Friedman,J.E., Comment on: Rowan et al. Metformin in Gestational diabetes: The Offspring Follow-Up (MiG TOFU): body composition at 2 years of age. Diabetes Care 2011;34:2279-2284, Diabetes Care, 35, e28-, 2012	Not a randomised controlled trial
Blachier,A., Alberti,C., Korb,D., Schmitz,T., Patrick,V., Christine,B., Oury,J.F., Sibony,O., Diet or medically treated gestational diabetes: is there any difference for obstetrical and neonatal complications? A French cohort study, Journal of Perinatal Medicine, 42, 315-319, 2014	Not a randomised controlled trial (prospective cohort)
Bochner,C.J., Medearis,A.L., Williams,J.,III, Castro,L., Hobel,C.J., Wade,M.E., Early third-trimester ultrasound screening in gestational diabetes to determine the risk of macrosomia and labor dystocia at term, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 157, 703-708, 1987	Cohort study.
Bonomo,M., Cetin,I., Pisoni,M.P., Faden,D., Mion,E., Taricco,E., Nobile de,Santis M., Radaelli,T., Motta,G., Costa,M., Solerte,L., Morabito,A., Flexible treatment of gestational diabetes modulated on ultrasound evaluation of intrauterine growth: a controlled randomized clinical trial, Diabetes and MetabolismDiabetes Metab., 30, 237-244, 2004	Not relevant to protocol (ultrasound).
Botta,R.M., Di Giovanni,B.M., Cammilleri,F., Taravella,V., Predictive factors for insulin treatment in women with diagnosis of gestational diabetes, Annali Dell'Istituto Superiore di Sanita, 33, 403-406, 1997	Cohort study.
Buchanan,T.A., Kjos,S.L., Montoro,M.N., Wu,P.Y., Madrilejo,N.G., Gonzalez,M., Nunez,V., Pantoja,P.M., Xiang,A., Use of fetal ultrasound to select metabolic therapy for pregnancies complicated by mild gestational diabetes, Diabetes Care, 17, 275-283, 1994	Not relevant to protocol (ultrasound).
Buchanan,T.A., Kjos,S.L., Montoro,M.N., Wu,P.Y., Madrilejo,N.G., Gonzalez,M., Nunez,V., Pantoja,P.M., Xiang,A., Use of fetal ultrasound to select metabolic therapy for pregnancies complicated by mild gestational diabetes, Diabetes Care, 17, 275-283, 1994	The population (Hispanic women) is not relevant to the United Kingdom population of women with gestational diabetes.
Buchbinder,A., Miodovnik,M., Khoury,J., Sibai,B.M., Is the use of insulin lispro safe in pregnancy?, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 11, 232-237, 2002	Narrative review
Bung,P., Artal,R., Khodiguian,N., [Regular exercise therapy in disorders of carbohydrate metabolism in pregnancy--results of a prospective, randomized longitudinal study], Geburtshilfe und Frauenheilkunde, 53, 188-193, 1993	In German
Bung,P., Artal,R., Khodiguian,N., Kjos,S., Exercise in gestational diabetes. An optional therapeutic approach?, Diabetes, 40 Suppl 2, 182-185, 1991	Comparison not relevant to protocol.
Casson,I.F., Outcomes of pregnancy in insulin dependent diabetic women: results of a five year population cohort study, British Medical JournalBMJ, 315, 275-278, 1997	Not relevant to protocol (insulin comparison).
Caughey,A.B., Management of diabetes in pregnancy, Advanced Studies in Medicine, 6, 309-318, 2006	Narrative review
Centre for Reviews and Dissemination., Oral hypoglycemic agents vs insulin in management of gestational diabetes: a systematic review and metaanalysis (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2012	Original study identified
Ceysens,Gilles, Rouiller,Dominique, Boulvain,Michel, Exercise for diabetic pregnant women, Cochrane Database of Systematic Reviews, -, 2009	Systematic review - checked for relevant studies - exercise
Chasan-Taber,L., Marcus,B.H., Stanek,E.,III, Ciccolo,J.T., Marquez,D.X., Solomon,C.G., Markenson,G., A randomized controlled trial of prenatal physical activity to prevent gestational diabetes: design and methods, Journal of Women's Health, 18, 851-859, 2009	Protocol only.

Excluded studies – Review question 9	
Cheung,N.W., Smith,B.J., van der Ploeg,H.P., Cinnadaio,N., Bauman,A., A pilot structured behavioural intervention trial to increase physical activity among women with recent gestational diabetes, Diabetes Research and Clinical Practice, 92, e27-e29, 2011	Intervention not relevant (intervention delivered postpartum)
Clapp III,J.E., Effect of dietary carbohydrate on the glucose and insulin response to mixed caloric intake and exercise in both nonpregnant and pregnant women, Diabetes Care, 21, B107-B112, 1998	No relevant outcomes - glucose
Clapp,J.F.,III, Maternal carbohydrate intake and pregnancy outcome, Proceedings of the Nutrition SocietyProc.Nutr.Soc., 61, 45-50, 2002	Literature review.
Conway,D.L., Gonzales,O., Skiver,D., Use of glyburide for the treatment of gestational diabetes: the San Antonio experience, Journal of Maternal-Fetal and Neonatal MedicineJ Matern Fetal Neonatal Med, 15, 51-55, 2004	Cohort study.
Cummins,E., Royle,P., Snaith,A., Greene,A., Robertson,L., McIntyre,L., Waugh,N., Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: systematic review and economic evaluation (Structured abstract), Health Technology Assessment Database, -, 2012	No comparison to insulin
Deveer,R., Deveer,M., Akbaba,E., Engin-Ustun,Y., Aydogan,P., Celikkaya,H., Danisman,N., Mollamahmutoglu,L., The effect of diet on pregnancy outcomes among pregnant with abnormal glucose challenge test, European Review for Medical and Pharmacological Sciences, 17, 1258-1261, 2013	Randomisation was performed using days of the week therefore this is a quasi-randomised trial and does not match the review protocol.
Dornan,T., Hollis,S., Critical appraisal of published research evidence: treatment of gestational diabetes. [19 refs], Diabetic Medicine, Suppl 3, 1-5, 2001	No relevant results reported
Dornhorst,A., Frost,G., The principles of dietary management of gestational diabetes: reflection on current evidence., Journal of Human Nutrition and DieteticsJ Hum Nutr Diet, 15, 145-156, 2002	Narrative review.
Dornhorst,A., Nicholls,J.S., Probst,F., Paterson,C.M., Hollier,K.L., Elkeles,R.S., Beard,R.W., Calorie restriction for treatment of gestational diabetes, Diabetes, 40 Suppl 2, 161-164, 1991	Observational study.
Dornhorst,A., Frost,G., The principles of dietary management of gestational diabetes: reflection on current evidence. [94 refs], Journal of Human Nutrition and Dietetics, 15, 145-156, 2002	Narrative review
Edson,E.J., Bracco,O.L., Vambergue,A., Koivisto,V., Managing diabetes during pregnancy with insulin lispro: a safe alternative to human insulin, Endocrine Practice, 16, 1020-1027, 2010	Comparison not relevant (insulin vs insulin)
Elnour,A.A., El,Mugammar,I, Jaber,T., Revel,T., McElnay,J.C., Pharmaceutical care of patients with gestational diabetes mellitus, Journal of Evaluation in Clinical Practice, 14, 131-140, 2008	Comparison not relevant
Falavigna,M., Schmidt,M., Trujillo,J., Alves,L., Wendland,E., Torloni,M., Colagiuri,S., Duncan,B., Effectiveness of gestational diabetes treatment: a systematic review with quality of evidence assessment, Diabetes Research and Clinical Practice, 98, 396-405, 2012	Systematic review - checked for relevant studies. Three already included in NCC review, one previously excluded. Four were requested, of these two were included and two excluded (O'Sullivan 1966 and 1974).
Ferrara,A., Hedderson,M.M., Albright,C.L., Ehrlich,S.F., Quesenberry,C.P.,Jr., Peng,T., Feng,J., Ching,J., Crites,Y., A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial, Diabetes Care, 34, 1519-1525, 2011	No relevant outcomes
Fraser,R.B., The effect of pregnancy on the normal range of the oral glucose tolerance in Africans, East African Medical Journal, 58, 90-94, 1981	Response to oral glucose tolerance test in pregnant versus non-pregnant women.
Fraser,R.B., Ford,F.A., Lawrence,G.F., Insulin sensitivity in third trimester pregnancy. A randomized study of dietary effects, British Journal of Obstetrics and GynaecologyBr.J.Obstet.Gynaecol., 95, 223-229, 1988	Mixed population of pregnant and non-pregnant women - data not presented separately and no relevant outcomes.
Gillen,L., Tapsell,L.C., Martin,G.S., Daniells,S., Knights,S., Moses,R.G., The type and frequency of consumption of carbohydrate-rich foods may play a role in the clinical expression of insulin resistance during pregnancy, Nutrition and Dietetics: Journal of the Dietitians Association of Australia, 59, 135-143, 2002	Case control study.
Gillmer,M.D.G., Maresh,M., Beard,R.W., Low energy diets in the treatment of gestational diabetes, Acta Endocrinologica, Supplement, 112, 44-49, 1986	Only reports mean values for neonatal glucose and birth weight.
Giuffrida,F, Castro,A.,Atallah,A., Dib,S., Diet plus insulin compared to diet alone in the treatment of gestational diabetes mellitus: a systematic review, Brazilian Journal of Medical and Biological Research, 36, 1297-1300, 2003	Systematic review. 5 studies already included in the NCC review. One other study was previously excluded.
Giuffrida,F.M.A., Castro,A.A., Atallah,A.N., Dib,S.A., Diet plus insulin compared to diet alone in the treatment of gestational diabetes mellitus: A systematic review, Brazilian Journal of Medical and Biological Research, 36, 1297-1300, 2003	Systematic review - checked for relevant studies

Excluded studies – Review question 9	
Gojnic,M., Perovic,M., Pervulov,M., Ljubic,A., The effects of adjuvant insulin therapy among pregnant women with IGT who failed to achieve the desired glycemia levels by diet and moderate physical activity, Journal of Maternal-Fetal and Neonatal Medicine, 25, 2028-2034, 2012	Comparison not relevant and no detail provided about the content of the diet therefore not helpful in informing recommendations.
Gui,J., Liu,Q., Feng,L., Metformin vs insulin in the management of gestational diabetes: a meta-analysis, PLoS ONE [Electronic Resource], 8, e64585-, 2013	Meta-analysis: 3 studies already included in NCC review, 2 identified separately in reruns search and included as individual studies.
Han,S., Crowther,C.A., Middleton,P., Heatley,E., Different types of dietary advice for women with gestational diabetes mellitus, Cochrane Database of Systematic Reviews, 3, CD009275-, 2013	Of the included studies: 4 were already included in the original NCC review, 2 had previously been weeded out, 2 had previously been excluded. One further study by Grant (2011) was requested (same study as for the review by Mohd Yusof).
Han,Shanshan, Crowther,Caroline A., Middleton,Philippa, Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria, Cochrane Database of Systematic Reviews, -, 2012	Cochrane review. All four studies included separately in NCC review.
Hartling,L., Dryden,D.M., Guthrie,A., Muise,M., Vandermeer,B., Donovan,L., Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research, Annals of Internal Medicine, 159, 123-129, 2013	Systematic review. Includes cohort studies which are not relevant to the NCC protocol. All RCTs included are already included in the NCC review.
Hassan,J.A., Karim,N., Sheikh,Z., Metformin prevents macrosomia and neonatal morbidity in gestational diabetes, Pakistan Journal of Medical Sciences, 28, 384-389, 2012	Allocation is alternate therefore is not random. Quasi-randomised trial.
Heller,S., McCance,D.R., Moghissi,E., Nazeri,A., Kordonouri,O., Diversity in diabetes: the role of insulin aspart, Diabetes/Metabolism Research Reviews, 28, 50-61, 2012	Comparison not relevant (insulin vs insulin)
Hernandez,T.L., Van Pelt,R.E., Anderson,M.A., Daniels,L.J., West,N.A., Donahoo,W.T., Friedman,J.E., Barbour,L.A., A higher-complex carbohydrate diet in gestational diabetes mellitus achieves glucose targets and lowers postprandial lipids: a randomized crossover study, Diabetes Care, 37, 1254-1262, 2014	No relevant outcomes. Mean maternal glucose and AUC only.
Ho,F.L.W., Liew,C.F., Cunanan,E.C., Lee,K.O., Oral hypoglycaemic agents for diabetes in pregnancy - An appraisal of the current evidence for oral anti-diabetic drug use in pregnancy, Annals of the Academy of Medicine Singapore, 36, 672-678, 2007	Systematic review - checked for relevant studies within class drugs
Horvath,K., Koch,K., Jeitler,K., Matyas,E., Bender,R., Bastian,H., Lange,S., Siebenhofer,A., Effects of treatment in women with gestational diabetes mellitus: Systematic review and meta-analysis, BMJ, 340, 796-, 2010	Systematic review - checked for relevant studies
Hutchinson,A., Haugabrook,C., Long,L., Mason,L., Kipikasa,J., Adair,D., A comparison of glyburide/metformin and insulin for gestational diabetes, American Journal of Obstetrics and Gynecology, 199, S200, 2008-, 2008	Conference proceedings.
Ilic,S., Jovanovic,L., Pettitt,D.J., Comparison of the effect of saturated and monounsaturated fat on postprandial plasma glucose and insulin concentration in women with gestational diabetes mellitus, American Journal of Perinatology, 16, 489-495, 1999	No relevant outcomes.
Jacobson,G.F., Ramos,G.A., Ching,J.Y., Kirby,R.S., Ferrara,A., Field,D.R., Comparison of glyburide and insulin for the management of gestational diabetes in a large managed care organization, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 193, 118-124, 2005	Cohort study.
Jacqueminet,S., Jannot-Lamotte,M.F., Therapeutic management of gestational diabetes, Diabetes and Metabolism, 36, 658-671, 2010	No relevant outcomes
Jovanovic,L., Howard,C., Pettitt,D., Zisser,H., Ospina,P., Insulin aspart vs. regular human insulin in basal/bolus therapy for patients with gestational diabetes mellitus: safety and efficacy, Diabetologia, 48, A 317-, 2005	Conference proceedings.
Jovanovic,L., Ilic,S., Pettitt,D.J., Hugo,K., Gutierrez,M., Bowsher,R.R., Bastyr,E.J.,III, Metabolic and immunologic effects of insulin lispro in gestational diabetes, Diabetes Care, 22, 1422-1427, 1999	Not relevant to protocol (insulin comparison).
Jovanovic,L., Howard,C., Pettitt,D., Zisser,H., Ospina,P., Insulin aspart vs. regular human insulin in basal/bolus therapy for patients with gestational diabetes mellitus: safety and efficacy, Diabetologia, 48, A317, 2005-, 2005	Conference procnot relevanteedings
Jovanovic,L., Ilic,S., Pettitt,D.J., Hugo,K., Gutierrez,M., Bowsher,R.R., Bastyr,E.J.,III, Metabolic and immunologic effects of insulin lispro in gestational diabetes, Diabetes Care, 22, 1422-1427, 1999	Comparison not relevant (insulin vs insulin)
Kaveh,M., Kiani,A., Salehi,M., Amouei,S., Impact of education on nutrition and exercise on the level of knowledge and metabolic control indicators (FBS & PPBS) of gestational diabetes mellitus (GDM) patients, Iranian Journal of Endocrinology and Metabolism, 13, 442-449, 2012	In Persian

Excluded studies – Review question 9	
Kitzmiller,J.L., Elixhauser,A., Carr,S., Major,C.A., de,Veciana M., ng-Kilduff,L., Weschler,J.M., Assessment of costs and benefits of management of gestational diabetes mellitus, Diabetes Care, 21 Suppl 2, B123-B130, 1998	Not a randomised contolled trial not relevant
Kjos,S.L., Schaefer-Graf,U., Sardesi,S., Peters,R.K., Buley,A., Xiang,A.H., Bryne,J.D., Sutherland,C., Montoro,M.N., Buchanan,T.A., A randomized controlled trial using glycemic plus fetal ultrasound parameters versus glycemic parameters to determine insulin therapy in gestational diabetes with fasting hyperglycemia.[see comment], Diabetes Care, 24, 1904-1910, 2001	Not relevant to protocol (ultrasound).
Kjos,S.L., Schaefer-Graf,U., Sardesi,S., Peters,R.K., Buley,A., Xiang,A.H., Bryne,J.D., Sutherland,C., Montoro,M.N., Buchanan,T.A., A randomized controlled trial using glycemic plus fetal ultrasound parameters versus glycemic parameters to determine insulin therapy in gestational diabetes with fasting hyperglycemia, Diabetes Care, 24, 1904-1910, 2001	Comparison not relevant
Knopp,R.H., Magee,M.S., Raisys,V., Benedetti,T., Bonet,B., Hypocaloric diets and ketogenesis in the management of obese gestational diabetic women. [63 refs], Journal of the American College of Nutrition, 10, 649-667, 1991	Outcomes not relevant
Korpi-Hyovalti,E.A., Laaksonen,D.E., Schwab,U.S., Vanhapiha,T.H., Vihla,K.R., Heinonen,S.T., Niskanen,L.K., Feasibility of a lifestyle intervention in early pregnancy to prevent deterioration of glucose tolerance, BMC Public Health, Vol.11, pp.179, 2011., -, -32676	Comparison not relevant
Kremer,C.J., Duff,P., Glyburide for the treatment of gestational diabetes, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 190, 1438-1439, 2004	Cohort study.
Landon,M.B., Is there a benefit to the treatment of mild gestational diabetes mellitus?. [20 refs], American Journal of Obstetrics and Gynecology, 202, 649-653, 2010	Narrative review
Lauszus,F.F., Rasmussen,O.W., Henriksen,J.E., Klebe,J.G., Jensen,L., Lauszus,K.S., Hermansen,K., Effect of a high monounsaturated fatty acid diet on blood pressure and glucose metabolism in women with gestational diabetes mellitus, European Journal of Clinical Nutrition, 55, 436-443, 2001	No relevant outcomes.
Lepercq,J., Lin,J., Hall,G.C., Wang,E., Dain,M.P., Riddle,M.C., Home,P.D., Meta-Analysis of Maternal and Neonatal Outcomes Associated with the Use of Insulin Glargine versus NPH Insulin during Pregnancy, Obstetrics and Gynecology International, 2012, 649070-, 2012	Comparison not relevant (insulin vs insulin)
Lesser,K.B., Gruppuso,P.A., Terry,R.B., Carpenter,M.W., Exercise fails to improve postprandial glycemic excursion in women with gestational diabetes, Journal of Maternal-Fetal MedicineJ.Matern.Fetal Med., 5, 211-217, 1996	One-off acute exercise period with 14 hour follow-up.
Lewis,B.A., Martinson,B.C., Sherwood,N.E., Avery,M.D., A pilot study evaluating a telephone-based exercise intervention for pregnant and postpartum women, Journal of Midwifery and Women's Health, 56, 127-131, 2011	Population not relevant
Li,D.F., Wong,V.C., O'Hoy,K.M., Yeung,C.Y., Ma,H.K., Is treatment needed for mild impairment of glucose tolerance in pregnancy? A randomized controlled trial, British Journal of Obstetrics and Gynaecology, 94, 851-854, 1987	Women were assigned to treatment groups using alternate allocation (quasi-randomised trial).
Lim,J.M.H., Tayob,Y., O'Brien,P.M.S., Shaw,R.W., A comparison between the pregnancy outcome of women with Gestation Diabetes treated with Glibenclamide and those treated with insulin, Medical Journal of Malaysia, 52, 377-381, 1997	Not a randomised controlled trial
Lin,J., Lepercq,J., Hall,G., Dain,M.P., Riddle,M.C., Home,P.D., A meta-analysis of maternal outcomes in pregnant women using insulin glargine compared with NPH insulin, Diabetologia, 54, S487-S488, 2011	Comparison not relevant (insulin vs insulin)
Lombard,C., Harrison,C., Teede,H., A randomized controlled trial investigating self-weighing and the prevention of excess weight gain in early pregnancy, Endocrine Reviews, 32, -, 2011	Population not relevant
Louie,J.C., Brand-Miller,J.C., Markovic,T.P., Ross,G.P., Moses,R.G., Glycemic index and pregnancy: a systematic literature review, Journal of Nutrition and Metabolism, 2010, 282464-, 2010	Systematic review of the literature but not of the published data i.e. no data analysis.
Madden,S.G., Loeb,S.J., Smith,C.A., An integrative literature review of lifestyle interventions for the prevention of type II diabetes mellitus. [38 refs], Journal of Clinical Nursing, 17, 2243-2256, 2008	Systematic review - checked for relevant studies.
Maresh,M., Gillmer,M.D.G., Beard,R.W., The effect of diet and insulin on metabolic profiles of women with gestational diabetes mellitus, Diabetes, 34, 88-93, 1985	Quasi-randomised trial which uses alternate allocation to assign treatment groups.
McFarland,M.B., Langer,O., Conway,D.L., Berkus,M.D., Dietary therapy for gestational diabetes: how long is long enough?, Obstetrics and Gynecology, 93, 978-982, 1999	Not a randomised controlled trial.

Excluded studies – Review question 9	
Mecacci,F., Carignani,L., Cioni,R., Bartoli,E., Parretti,E., La,Torre P., Scarselli,G., Mello,G., Maternal metabolic control and perinatal outcome in women with gestational diabetes treated with regular or lispro insulin: comparison with non-diabetic pregnant women, European Journal of Obstetrics, Gynecology and Reproductive BiologyEur J Obstet Gynecol Reprod Biol, 111, 19-24, 2003	Not relevant to protocol (insulin comparison).
Mecacci,F., Carignani,L., Cioni,R., Bartoli,E., Parretti,E., La,Torre P., Scarselli,G., Mello,G., Maternal metabolic control and perinatal outcome in women with gestational diabetes treated with regular or lispro insulin: comparison with non-diabetic pregnant women, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 111, 19-24, 2003	Comparison not relevant (insulin vs insulin)
Mohd Yusof,B.N., Firouzi,S., Mohd,Shariff Z., Mustafa,N., Mohamed Ismail,N.A., Kamaruddin,N.A., Weighing the evidence of low glycemic index dietary intervention for the management of gestational diabetes mellitus: an Asian perspective, International Journal of Food Sciences and Nutrition, 65, 144-150, 2014	Systematic review. Two of the included studies were already included in the original NCC review. One further study by Grant (2011) was requested.
Moore,L,Briery,C., Martin,R., Hood,E., Bofill,J, Morrison,J., Metformin (M) vs. Insulin (I) in A2 Diabetics. A Randomized Clinical Trial, American Journal of Obstetrics and GynecologyAm J Obstet Gynecol, 191, S8-, 2004	Abstract only and population included in Moore 2007.
Moore,L., Clokey,D., Curet,L., A randomized controlled trial of metformin and glyburide in gestational diabetes, American Journal of Obstetrics and Gynecology, 199, S34, 2008-, 2008	Conference proceedings.
Moore,L., Clokey,D., Robinson,A., A randomized trial of metformin compared to glyburide in the treatment of gestational diabetes [abstract], American Journal of Obstetrics and Gynecology, 193, S92, 2005-, 2005	Conference abstract only.
Moretti,M.E., Rezvani,M., Koren,G., Safety of glyburide for gestational diabetes: A meta-analysis of pregnancy outcomes, Annals of Pharmacotherapy, 42, 483-490, 2008	Systematic review - checked for relevant studies.
Moss,J.R., Crowther,C.A., Hiller,J.E., Willson,K.J., Robinson,J.S., Australian Carbohydrate Intolerance Study in Pregnant Women Group, Costs and consequences of treatment for mild gestational diabetes mellitus - evaluation from the ACHOIS randomised trial, BMC Pregnancy and Childbirth, Vol.7, pp.27, 2007., -, -32676	No relevant outcomes.
Nachum,Z., Ben-Shlomo,I., Weiner,E., Shalev,E., Twice daily versus four times daily insulin dose regimens for diabetes in pregnancy: randomised controlled trial, BMJ, 319, 1223-1227, 1999	Comparison not relevant (insulin vs insulin)
Nicholson,W., Bolen,S., Witkop,C.T., Neale,D., Wilson,L., Bass,E., Benefits and risks of oral diabetes agents compared with insulin in women with gestational diabetes: A systematic review, Obstetrics and Gynecology, 113, 193-205, 2009	Systematic review - checked for relevant studies.
Nicholson,W.K., Wilson,L.M., Witkop,C.T., Baptiste-Roberts,K., Bennett,W.L., Bolen,S., Barone,B.B., Golden,S.H., Gary,T.L., Neale,D.M., Bass,E.B., Therapeutic management, delivery, and postpartum risk assessment and screening in gestational diabetes. [107 refs], Evidence Report/Technology Assessment, 1-96, 2008	Systematic review - checked for relevant studies.
Nolan,C.J., Improved glucose tolerance in gestational diabetic women on a low fat, high unrefined carbohydrate diet, Australian and New Zealand Journal of Obstetrics and Gynaecology, 24, 174-177, 1984	No relevant outcomes.
Ostman,E.M., Frid,A.H., Groop,L.C., Bjorck,I.M.E., A dietary exchange of common bread for tailored bread of low glycaemic index and rich in dietary fibre improved insulin economy in young women with impaired glucose tolerance, European Journal of Clinical NutritionEur.J.Clin.Nutr., 60, 334-341, 2006	Women were not pregnant: history of gestational diabetes and at risk for type 2 diabetes.
O'Sullivan,J.B., Gellis,S.S., Dandrow,R.V., Tenney,B.O., The potential diabetic and her treatment in pregnancy, Obstetrics and gynecologyObstet Gynecol, 27, 683-689, 1966	Incorrect comparison according to review protocol - diet plus insulin versus standard care.
O'Sullivan,J.B., Mahan,C.M., Insulin treatment and high risk groups, Diabetes Care, 3, 482-485, 1980	Not a randomised controlled trial.
O'Sullivan,J.B., Mahan,C.M., Charles,D., Dandrow,R.V., Medical treatment of the gestational diabetic, Obstetrics and Gynecology, 43, 817-821, 1974	Incorrect comparison according to review protocol - diet plus insulin versus standard care.
Pantalone,K.M., Faiman,C., Olansky,L., Insulin glargine use during pregnancy, Endocrine Practice, 17, 448-455, 2011	Comparison not relevant (insulin vs insulin)
Perez-Ferre,N., Galindo,M., Fernandez,M.D., Velasco,V., de la Cruz,M.J., Martin,P., del,Valle L., Calle-Pascual,A.L., A Telemedicine system based on Internet and short message service as a new approach in the follow-up of patients with gestational diabetes, Diabetes Research and Clinical Practice, 87, e15-e17, 2010	No relevant outcomes

Excluded studies – Review question 9	
Perichart-Perera,O., Balas-Nakash,M., Rodriguez-Cano,A., Legorreta-Legorreta,J., Parra-Covarrubias,A., Vadillo-Ortega,F., Low glycemic index carbohydrates versus all types of carbohydrates for treating diabetes in pregnancy: A randomized clinical trial to evaluate the effect of glycemic control, International Journal of Endocrinology, 2012 , 2012. Article Number, -, 2012	Most outcomes are nutrient-based. The need for insulin is reported as mean dosages not the number of women who received insulin. Type 2 diabetes and GDM data are not reported separately.
Peterson,C.M., Jovanovic-Peterson,L., Randomized crossover study of 40% vs. 55% carbohydrate weight loss strategies in women with previous gestational diabetes mellitus and non-diabetic women of 130-200% ideal body weight, Journal of the American College of NutritionJ.Am.Coll.Nutr., 14, 369-375, 1995	Women not pregnant: history of gestational diabetes.
Pettitt,D.J., Ospina,P., Kolaczynski,J.W., Jovanovic,L., Comparison of an insulin analog, insulin aspart, and regular human insulin with no insulin in gestational diabetes mellitus, Diabetes Care, 26, 183-186, 2003	Not relevant to protocol (insulin comparison).
Pettitt,D.J., Ospina,P., Howard,C., Zisser,H., Jovanovic,L., Efficacy, safety and lack of immunogenicity of insulin aspart compared with regular human insulin for women with gestational diabetes mellitus, Diabetic Medicine, 24, 1129-1135, 2007	Comparison not relevant (insulin vs insulin)
Pollex,E., Moretti,M.E., Koren,G., Feig,D.S., Safety of insulin glargine use in pregnancy: a systematic review and meta-analysis, Annals of Pharmacotherapy, 45, 9-16, 2011	Comparison not relevant (insulin vs insulin)
Poolsup,N., Suksomboon,N., Amin,M., Effect of treatment of gestational diabetes mellitus: A systematic review and meta-analysis, PloS one, 9, -, 2014	Systematic review. Studies checked for eligibility: 6 already included in NCC review, 4 excluded.
Poyhonen-Alho,M., Teramo,K., Kaaja,R., Treatment of gestational diabetes with short- or long-acting insulin and neonatal outcome: a pilot study, Acta Obstetricia et Gynecologica ScandinavicaActa Obstet.Gynecol.Scand., 81, 258-259, 2002	Not relevant to protocol (insulin comparison).
Reece,E.A., Hagay,Z., Gay,L.J., O'Connor,T., DeGennaro,N., Homko,C.J., Wiznitzer,A., A randomized clinical trial of a fiber-enriched diabetic diet vs. the standard American Diabetes Association-recommended diet in the management of diabetes mellitus in pregnancy, Journal of Maternal-Fetal Investigation, 5, 8-12, 1995	No relevant outcomes.
Rosenberg,V.A., Eglinton,G.S., Rauch,E.R., Skupski,D.W., Intrapartum maternal glycemic control in women with insulin requiring diabetes: a randomized clinical trial of rotating fluids versus insulin drip, American Journal of Obstetrics and Gynecology, 195, 1095-1099, 2006	Comparison not relevant
Rossi,G., Somigliana,E., Moschetta,M., Bottani,B., Barbieri,M., Vignali,M., Adequate timing of fetal ultrasound to guide metabolic therapy in mild gestational diabetes mellitus. Results from a randomized study, Acta Obstetricia et Gynecologica ScandinavicaActa Obstet.Gynecol.Scand., 79, 649-654, 2000	Not relevant to protocol (ultrasound).
Rowan,J.A., MiG,Investigators, A trial in progress: gestational diabetes. Treatment with metformin compared with insulin (the Metformin in Gestational Diabetes [MiG] trial).[Erratum appears in Diabetes Care. 2007 Dec;30(12):3154], Diabetes Care, 30 Suppl 2, S214-S219, 2007	no relevant results
Sacks,D.A., Chen,W., Wolde-Tsadik,G., Buchanan,T.A., When is fasting really fasting? The influence of time of day, interval after a meal, and maternal body mass on maternal glycemia in gestational diabetes, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 181, 904-911, 1999	Cohort study.
Sameshima,H., Kamitomo,M., Kajiya,S., Kai,M., Ikenoue,T., Insulin-meal interval and short-term glucose fluctuation in tightly controlled gestational diabetes mellitus, The Journal of maternal-fetal medicine, 10, 241-245, 2001	Not relevant to protocol (insulin comparison).
Schaefer-Graf,U.M., Kjos,S.L., Fauzan,O.H., Buhling,K.J., Siebert,G., Buhrer,C., Ladendorf,B., Dudenhausen,J.W., Vetter,K., A randomized trial evaluating a predominantly fetal growth-based strategy to guide management of gestational diabetes in Caucasian women., Diabetes Care, 27, 297-302, 2004	Not relevant to protocol (ultrasound).
Schuster,M.W., Chauhan,S.P., McLaughlin,B.N., Perry,Jr, Morrison,J.C., Comparison of insulin regimens and administration modalities in pregnancy complicated by diabetes, Journal of the Mississippi State Medical Association, 39, 208-212, 1998	Comparison not relevant.
Silva,J.C., Bertini,A.M., Taborda,W., Becker,F., Bebber,F.R., Aquim,G.M., Viesi,J.M., [Glibenclamide in the treatment for gestational diabetes mellitus in a compared study to insulin], Arquivos brasileiros de endocrinologia e metabologia, 51, 541-546, 2007	In Portuguese
Silva,J.C., Pacheco,C., Bizato,J., de Souza,B.V., Ribeiro,T.E., Bertini,A.M., Metformin compared with glyburide for the management of gestational diabetes, International Journal of Gynaecology and Obstetrics, 111, 37-40, 2010	Comparison not relevant (oral drugs vs oral drugs) within class diet
Smits,M.W., Paulk,T.H., Kee,C.C., Assessing the impact of an outpatient education program for patients with gestational diabetes, Diabetes EducatorDiabetes Educ., 21, 129-134, 1995	Descriptive study.

Excluded studies – Review question 9	
Symons,Downs D., Ulbrecht,J.S., Understanding exercise beliefs and behaviors in women with gestational diabetes mellitus, Diabetes Care, 29, 236-240, 2006	Retrospective study.
Tempe,A., Mayanglambam,R.D., Glyburide as treatment option for gestational diabetes mellitus, Journal of Obstetrics and Gynaecology Research, 39, 1147-1152, 2013	Alternate allocation used therefore not truly random (quasi-randomised trial).
Thomas,J., Metformin safe treatment for gestational diabetes, Australian Journal of Pharmacy, 90, 73-, 2009	Narrative review
Thomaz de,Lima H., Lopes,Rosado E., Ribeiro Neves,P.A., Correa Monteiro,Machado R., Mello de,Oliveira L., Saunders,C., Systematic review; Nutritional therapy in gestational diabetes mellitus, Nutricion Hospitalaria, 28, 1806-1814, 2013	Systematic review. All included were checked for eligibility: 4 were already included in the original NCC review, 1 was weeded out (trial of guidelines not specific diets).
Tieu,J., Crowther,C.A., Middleton,P., Dietary advice in pregnancy for preventing gestational diabetes mellitus. [47 refs], Cochrane Database of Systematic Reviews, CD006674-, 2008	Population not relevant (i.e. not women after GDM diagnosed).
Tieu,Joanna, Crowther,Caroline A., Middleton,Philippa, Dietary advice in pregnancy for preventing gestational diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2011	Population not relevant (i.e. not women after GDM diagnosed).
Todorova,K., Palaveev,O., Petkova,V.B., Stefanova,M., Dimitrova,Z., A pharmacoeconomical model for choice of a treatment for pregnant women with gestational diabetes, Acta Diabetologica, 44, 144-148, 2007	Not a randomised controlled trial
Vanky,E., Salvesen,K.A., Heimstad,R., Fougner,K.J., Romundstad,P., Carlsen,S.M., Metformin reduces pregnancy complications without affecting androgen levels in pregnant polycystic ovary syndrome women: results of a randomized study, Human Reproduction, 19, 1734-1740, 2004	Population not relevant
Waheed,S., Malik,F.P., Mazhar,S.B., Efficacy of metformin versus insulin in the management of pregnancy with diabetes, Jcpsp, Journal of the College of Physicians and Surgeons - Pakistan, 23, 866-869, 2013	No relevant outcomes reported. The study addresses efficacy only of glucose and HbA1c control.
Walkinshaw,Stephen A., Dietary regulation for 'gestational diabetes', Cochrane Database of Systematic Reviews, -, 2010	Withdrawn Cochrane review
Wechter,D.J., Kaufmann,R.C., Amankwah,K.S., Rightmire,D.A., Eardley,S.P., Verhulst,S., Zinzilieta,M., Young,J., Teich,J., Singleton,J.A., Prevention of neonatal macrosomia in gestational diabetes by the use of intensive dietary therapy and home glucose monitoring, American Journal of Perinatology, 8, 131-134, 1991	Cohort study.
Wein,P., Beischer,N., Harris,C., Permezel,M., A trial of simple versus intensified dietary modification for prevention of progression to diabetes mellitus in women with impaired glucose tolerance, Australian and New Zealand Journal of Obstetrics and Gynaecology, 39, 162-166, 1999	Long-term follow-up only. Women included were not pregnant.
Wensel,T.M., Role of metformin in the treatment of gestational diabetes, Annals of Pharmacotherapy, 43, 939-943, 2009	Systematic review - checked for relevant studies
Yogev,Y., Ben-Haroush,A., Chen,R., Rosenn,B., Hod,M., Langer,O., Undiagnosed asymptomatic hypoglycemia: diet, insulin, and glyburide for gestational diabetic pregnancy, Obstetrics and GynecologyObstet.Gynecol., 104, 88-93, 2004	Cohort study.
Zeng,Y.C., Li,M.J., Chen,Y., Jiang,L., Wang,S.M., Mo,X.L., Li,B.Y., The use of glyburide in the management of gestational diabetes mellitus: A meta-analysis, Advances in Medical Sciences, 59, 95-101, 2014	Systematic review. Studies checked for eligibility: 3 already included in NCC review, 2 excluded

G.9 Antenatal blood glucose monitoring

Excluded studies – Review question 10	
Study	**Reason for Exclusion**
Carmody,D., Doyle,A., Firth,R.G., Byrne,M.M., Daly,S., Mc,Auliffe F., Foley,M., Coulter-Smith,S., Kinsley,B.T., Teenage pregnancy in type 1 diabetes mellitus, Pediatric Diabetes, 11, 111-115, 2010	Comparison of teenagers and older women. Does not compare monitoring strategies
Coster,S., Gulliford,M.C., Seed,P.T., Powrie,J.K., Swaminathan,R., Monitoring blood glucose control in diabetes mellitus: a systematic review, Health Technology Assessment Database, 4, -, 2000	Included studies were checked for relevance. Four had already been excluded by the NCC in original searches, three had been included. Three other studies were requested and of these one was included (Varner) and two excluded (Goldstein, Stubbs).
Crowther,C.A., Hague,W.M., Middleton,P.F., Baghurst,P.A., McPhee,A.J., Tran,T.S., Yelland,L.N., Ashwood,P., Han,S., Dodd,J.M., Robinson,J.S., IDEAL Study Group., The IDEAL study: investigation of dietary advice and lifestyle for women with borderline gestational diabetes: a randomised controlled trial - study protocol, BMC Pregnancy and Childbirth, 12, 106-, 2012	Protocol only

Excluded studies – Review question 10	
Crowther,C.A., Hiller,J.E., Moss,J.R., McPhee,A.J., Jeffries,W.S., Robinson,J.S., Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group., Effect of treatment of gestational diabetes mellitus on pregnancy outcomes, New England Journal of Medicine, 352, 2477-2486, 2005	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Dalfra,M.G., Chilelli,N.C., Di,CianniG, Mello,G., Lencioni,C., Biagioni,S., Scalese,M., Sartore,G., Lapolla,A., Glucose fluctuations during gestation: An additional tool for monitoring pregnancy complicated by diabetes, International Journal of Endocrinology, 2013 , 2013. Article Number, -, 2013	Continuous glucose monitoring only.
di Biase,N., Napoli,A., Sabbatini,A., Borrello,E., Buongiorno,A.M., Fallucca,F., Telemedicine in the treatment of diabetic pregnancy, Annali Dell'Istituto Superiore di Sanita, 33, 347-351, 1997	Women in both groups used the same monitoring strategy
Durnwald,C.P., Mele,L., Spong,C.Y., Ramin,S.M., Varner,M.W., Rouse,D.J., Sciscione,A., Catalano,P., Saade,G., Sorokin,Y., Tolosa,J.E., Casey,B., Anderson,G.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (MFMU), Glycemic characteristics and neonatal outcomes of women treated for mild gestational diabetes, Obstetrics and Gynecology, 117, 819-827, 2011	Does not compare monitoring strategies
Feig,D.S., Cleave,B., Tomlinson,G., Long-term effects of a diabetes and pregnancy program: does the education last?, Diabetes Care, 29, 526-530, 2006	Does not compare monitoring strategies
Garner,P., Okun,N., Keely,E., Wells,G., Perkins,S., Sylvain,J., Belcher,J., A randomized controlled trial of strict glycemic control and tertiary level obstetric care versus routine obstetric care in the management of gestational diabetes: a pilot study, American Journal of Obstetrics and GynecologyAm J Obstet Gynecol, 177, 190-195, 1997	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Gill,Madeleine G., Nguyen,ThuyMy N., Bain,Emily, Crowther,Caroline A., Middleton,Philippa, Home versus hospital glucose monitoring for gestational diabetes during pregnancy, Cochrane Database of Systematic Reviews, -, 2014	Protocol only.
Glinianaia,S.V., Tennant,P.W.G., Bilous,R.W., Rankin,J., Bell,R., HbA1c and birthweight in women with pre-conception type 1 and type 2 diabetes: A population-based cohort study, Diabetologia, 55, 3193-3203, 2012	Non-comparative study
Goldstein,A., Elliott,J., Lederman,S., Worcester,B., Russell,P., Linzey,E.M., Economic effects of self-monitoring of blood glucose concentrations by women with insulin-dependent diabetes during pregnancy, Journal of Reproductive Medicine, 27, 449-450, 1982	Economic data on hospital stay only.
Gutaj,P., Zawiejska,A., Wender-Ozegowska,E., Brazert,J., Maternal factors predictive of firsttrimester pregnancy loss in women with pregestational diabetes, Polskie Archiwum Medycyny Wewnetrznej, 123, 21-28, 2013	Does not compare monitoring strategies
Hanson,U., Persson,B., Enochsson,E., Lennerhagen,P., Lindgren,F., Lundstrom,V., Lunell,N.O., Nilsson,B.A., Nilsson,L., Stangenberg,M., Self-monitoring of blood glucose by diabetic women during the third trimester of pregnancy, American Journal of Obstetrics and GynecologyAm J Obstet Gynecol, 150, 817-821, 1984	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Hiramatsu,Y., Shimizu,I., Omori,Y., Nakabayashi,M., JGA (Japan Glycated Albumin) Study Group., Determination of reference intervals of glycated albumin and hemoglobin A1c in healthy pregnant Japanese women and analysis of their time courses and influencing factors during pregnancy, Endocrine Journal, 59, 145-151, 2012	Does not compare monitoring strategies
Inkster,M.E., Fahey,T.P., Donnan,P.T., Leese,G.P., Mires,G.J., Murphy,D.J., Poor glycated haemoglobin control and adverse pregnancy outcomes in type 1 and type 2 diabetes mellitus: systematic review of observational studies, BMC Pregnancy and Childbirth, 6, 30-, 2006	Does not compare monitoring strategies
Jovanovic,L., The role of continuous glucose monitoring in gestational diabetes mellitus, Diabetes Technology and Therapeutics, 2 Suppl 1, S67-S71, 2000	Not relevant to this question - considered for inclusion in the continuous blood glucose monitoring review
Jovanovic,L., Peterson,C.M., Saxena,B.B., Dawood,M.Y., Saudek,C.D., Feasibility of maintaining normal glucose profiles in insulin-dependent pregnant diabetic women, American Journal of Medicine, 68, 105-112, 1980	Non-comparative study
Jovanovic,L., Savas,H., Mehta,M., Trujillo,A., Pettitt,D.J., Frequent monitoring of A1C during pregnancy as a treatment tool to guide therapy, Diabetes Care, 34, 53-54, 2011	Non-comparative study
Jovanovic,L., Druzin,M., Peterson,C.M., Effect of euglycemia on the outcome of pregnancy in insulin-dependent diabetic women as compared with normal control subjects, American Journal of Medicine, 71, 921-927, 1981	Initially a trial of blood glucose vs. urine monitoring which was stopped early. All women were switched to blood glucose monitoring. Comparison group is non-diabetic women.
Jovanovic,L.G., Using meal-based self-monitoring of blood glucose as a tool to improve outcomes in pregnancy complicated by diabetes. [25 refs], Endocrine Practice, 14, 239-247, 2008	Narrative review with no new data

Excluded studies – Review question 10	
Kerssen,A., De Valk,H.W., Visser,G.H., Do HbA(1)c levels and the self-monitoring of blood glucose levels adequately reflect glycaemic control during pregnancy in women with type 1 diabetes mellitus?, Diabetologia, 49, 25-28, 2006	Not relevant to this question - comparison of continuous glucose monitoring and intermittent monitoring
Kong,G.W., Tam,W.H., Chan,M.H., So,W.Y., Lam,C.W., Yiu,I.P., Loo,K.M., Li,C.Y., Comparison in the performance of glucose meters in blood glucose monitoring during pregnancy, Gynecologic and Obstetric Investigation, 69, 264-269, 2010	Compares different types of meters. Does not compare monitoring strategies
Laird,J., McFarland,K.F., Fasting blood glucose levels and initiation of insulin therapy in gestational diabetes, Endocrine Practice, 2, 330-332, 1996	Does not compare monitoring strategies
Landon,M.B., Spong,C.Y., Thom,E., Carpenter,M.W., Ramin,S.M., Casey,B., Wapner,R.J., Varner,M.W., Rouse,D.J., Thorp,J.M.,Jr., Sciscione,A., Catalano,P., Harper,M., Saade,G., Lain,K.Y., Sorokin,Y., Peaceman,A.M., Tolosa,J.E., Anderson,G.B., Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-fetal Medicine Units Network., A multicenter, randomized trial of treatment for mild gestational diabetes, New England Journal of Medicine, 361, 1339-1348, 2009	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Mendez-Figueroa,H., Daley,J., Lopes,V.V., Coustan,D.R., Comparing daily versus less frequent blood glucose monitoring in patients with mild gestational diabetes, Journal of Maternal-Fetal and Neonatal Medicine, 26, 1268-1272, 2013	Outcome not relevant to protocol (time until initiation of pharmacological therapy).
Middleton,Philippa, Crowther,Caroline A., Simmonds,Lucy, Different intensities of glycaemic control for pregnant women with pre-existing diabetes, Cochrane Database of Systematic Reviews, -, 2012	Does not compare monitoring strategies
Moy,Ming Foong, Ray,Amita, Buckley,Brian S., Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes, Cochrane Database of Systematic Reviews, -, 2012	Protocol only
Moy,F.M., Ray,A., Buckley,B.S., Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes, Cochrane Database of Systematic Reviews, 4, CD009613-, 2014	Systematic review. Studies checked for eligibility: 2 already included in NCC review, 2 weeded out, 4 excluded, 1 requested to check (Wojcicki, 2001).
Peacock,I., Hunter,J.C., Walford,S., Allison,S.P., Davison,J., Clarke,P., Symonds,E.M., Tattersall,R.B., Self-monitoring of blood glucose in diabetic pregnancy, British Medical Journal, 2, 1333-1336, 1979	Does not compare monitoring strategies
Pelaez-Crisologo,Ma, Castillo-Torralba,M.G.A.G., Festin,M.R., Different techniques of blood glucose monitoring in women with gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, 2009. Article Number, -, 2009	Protocol only
Rackham,O., Paize,F., Weindling,A.M., Cause of death in infants of women with pregestational diabetes mellitus and the relationship with glycemic control, Postgraduate Medicine, 121, 26-32, 2009	Does not compare monitoring strategies
Secher,A.L., Ringholm,L., Andersen,H.U., Damm,P., Mathiesen,E.R., The effect of real-time continuous glucose monitoring in pregnant women with diabetes: a randomized controlled trial, Diabetes Care, 36, 1877-1883, 2013	Monitoring performed is not intermittent
Stubbs,S.M., Brudenell,J.M., Pyke,D.A., Watkins,P.J., Stubbs,W.A., Alberti,K.G., Management of the pregnant diabetic: home or hospital, with or without glucose meters?, Lancet, 1, 1122-1124, 1980	Comparison is blood glucose monitoring vs. urine monitoring therefore is not relevant to the protocol.
Sturrock,N.D., Fay,T.N., Pound,N., Kirk,B.A., Danks,L.E., Analysis of 44,279 blood glucose estimations in relation to outcomes in 80 pregnant diabetic women, Journal of Obstetrics and Gynaecology, 21, 253-257, 2001	Does not compare monitoring strategies
Syed,M., Javed,H., Yakoob,M.Y., Bhutta,Z.A., Effect of screening and management of diabetes during pregnancy on stillbirths, BMC Public Health, 11 Suppl 3, S2-, 2011	Does not provide enough detail regarding the included studies. Included studies considered separately for inclusion in the NCC review.
Wechter,D.J., Kaufmann,R.C., Amankwah,K.S., Rightmire,D.A., Eardley,S.P., Verhulst,S., Zinzilieta,M., Young,J., Teich,J., Singleton,J.A., Prevention of neonatal macrosomia in gestational diabetes by the use of intensive dietary therapy and home glucose monitoring, American Journal of Perinatology, 8, 131-134, 1991	Does not compare monitoring strategies
Wilson,N., Ashawesh,K., Kulambil Padinjakara,R.N., Anwar,A., The multidisciplinary diabetes-endocrinology clinic and postprandial blood glucose monitoring in the management of gestational diabetes: impact on maternal and neonatal outcomes, Experimental and Clinical Endocrinology and Diabetes, 117, 486-489, 2009	Not clear which monitoring strategy/ies the 1 hour postprandial measurement is compared to
Wong,M.L., Butson,S., Gatling,W., Masding,M.G., The management of women with gestational diabetes can be stratified according to diagnostic oral glucose tolerance test results, Practical Diabetes International, 25, 61-63, 2008	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Yogev,Y., Chen,R., Ben-Haroush,A., Phillip,M., Jovanovic,L., Hod,M., Continuous glucose monitoring for the evaluation of gravid women with type 1 diabetes mellitus, Obstetrics and Gynecology, 101, 633-638, 2003	Not relevant to this question. Comparison of continuous glucose monitoring and intermittent monitoring

Excluded studies – Review question 10	
Young,B.C., Ecker,J.L., Fetal macrosomia and shoulder dystocia in women with gestational diabetes: Risks amenable to treatment?, Current Diabetes Reports, 13, 12-18, 2013	Narrative review. No new data.

G.10 Antenatal ketone monitoring

There were no excluded studies for review question 11

G.11 Antenatal blood glucose targets

Excluded studies – Review question 12	
Study	**Reason for Exclusion**
Anderberg,E., Kallen,K., Berntorp,K., The impact of gestational diabetes mellitus on pregnancy outcome comparing different cut-off criteria for abnormal glucose tolerance, Acta Obstetricia et Gynecologica Scandinavica, 89, 1532-1537, 2010	Compares different levels of glucose tolerance in relation to GDM diagnosis. Analysis based on an OGTT (one off test). No targets given.
Aschwald,C.L., Catanzaro,R.B., Weiss,E.P., Gavard,J.A., Steitz,K.A., Mostello,D.J., Large-for-gestational-age infants of type 1 diabetic mothers: an effect of preprandial hyperglycemia?, Gynecological Endocrinology, 25, 653-660, 2009	Outcome (macrosomia) not reported with respect to target values.
Cohen,O., Keidar,N., Simchen,M., Weisz,B., Dolitsky,M., Sivan,E., Macrosomia in well controlled CSII treated Type I diabetic pregnancy, Gynecological Endocrinology, 24, 611-613, 2008	States glycaemic control within guidelines but does not state explicitly these ref. values
Dalfra,M.G., Sartore,G., Di,Cianni G., Mello,G., Lencioni,C., Ottanelli,S., Sposato,J., Valgimigli,F., Scuffi,C., Scalese,M., Lapolla,A., Glucose variability in diabetic pregnancy, Diabetes Technology and Therapeutics, 13, 853-859, 2011	No threshold analysis; mean values. Most comparisons are for type 1 versus gestational diabetes versus controls.
Damm,P., Mersebach,H., Rastam,J., Kaaja,R., Hod,M., McCance,D.R., Mathiesen,E.R., Poor pregnancy outcome in women with type 1 diabetes is predicted by elevated HbA1c and spikes of high glucose values in the third trimester, Journal of Maternal-Fetal and Neonatal Medicine, 27, 149-154, 2014	The association between glucose and outcomes was determined using regression to obtain a risk threshold. Plasma glucose values upon which regression results were based were any value > 11mmol/l rather than being specific to meal times.
Dicker,D., Feldberg,D., Samuel,N., Yeshaya,A., Karp,M., Goldman,J.A., Spontaneous abortion in patients with insulin-dependent diabetes mellitus: the effect of preconceptional diabetic control, American Journal of Obstetrics and Gynecology, 158, 1161-1164, 1988	No target levels or thresholds given. Mean blood glucose for abortion versus pregnancy > 22 weeksâ€ ™ gestation
Durnwald,C., Glycemic characteristics of women treated for mild gestational diabetes and perinatal outcomes, American Journal of Obstetrics and Gynecology, 201, S107-, 2009	Conference abstract
Durnwald,C.P., Mele,L., Spong,C.Y., Ramin,S.M., Varner,M.W., Rouse,D.J., Sciscione,A., Catalano,P., Saade,G., Sorokin,Y., Tolosa,J.E., Casey,B., Anderson,G.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (MFMU), Glycemic characteristics and neonatal outcomes of women treated for mild gestational diabetes, Obstetrics and Gynecology, 117, 819-827, 2011	Outcomes are related to median blood glucose values and change over time only, not to a threshold. No targets given.
Figueroa,D., Landon,M.B., Mele,L., Spong,C.Y., Ramin,S.M., Casey,B., Wapner,R.J., Varner,M.W., Thorp,J.M.,Jr., Sciscione,A., Catalano,P., Harper,M., Saade,G., Caritis,S.N., Sorokin,Y., Peaceman,A.M., Tolosa,J.E., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network., Relationship between 1-hour glucose challenge test results and perinatal outcomes, Obstetrics and Gynecology, 121, 1241-1247, 2013	Analysis based on glucose screening results only. Comparison group is women with negative screening test results.
Fotinos,C., Dodson,S., French,L., Does tight control of blood glucose in pregnant women with diabetes improve neonatal outcomes?., Journal of Family PracticeJ.Fam.Pract., 53, 838-841, 2004	Narrative review which combines dietary interventions, pre-conception care and pregnancy care. Studies checked for inclusion. None relevant. One relevant Cochrane review was checked - studies have already been included (Farrag
Fuhrmann,K., Treatment of pregnant insulin-dependent diabetic women, Acta Endocrinologica, Supplementum. 277, 74-76, 1986	Does not examine outcomes by target values or by threshold. The per cent of women who achieved targets is not given by target level but by whether targets were assigned before or during pregnancy.

Excluded studies – Review question 12	
Fuhrmann,K., Reiher,H., Semmler,K., Glockner,E., The effect of intensified conventional insulin therapy before and during pregnancy on the malformation rate in offspring of diabetic mothers, Experimental and Clinical Endocrinology, 83, 173-177, 1984	Does not examine outcomes by target values or by threshold. The per cent of women who achieved targets is not given by target level but by whether targets were assigned before or during pregnancy.
HAPO Study Cooperative Research Group, Metzger,B.E., Lowe,L.P., Dyer,A.R., Trimble,E.R., Chaovarindr,U., Coustan,D.R., Hadden,D.R., McCance,D.R., Hod,M., McIntyre,H.D., Oats,J.J., Persson,B., Rogers,M.S., Sacks,D.A., Hyperglycemia and adverse pregnancy outcomes, New England Journal of Medicine, 358, 1991-2002, 2008	The study examined the relationship of 75g OGTT glucose values (a one off test) and outcomes in a population of pregnant women. Women who had values diagnostic (at the time of the study) of GDM and diabetes were excluded. The study was used in order to redefine GDM diagnostic criteria and as such includes women with what was then considered to be normal blood glucose values. The women were not being treated to control their blood glucose values.
Jensen,D.M., Damm,P., Moelsted-Pedersen,L., Ovesen,P., Westergaard,J.G., Moeller,M., Beck-Nielsen,H., Outcomes in type 1 diabetic pregnancies: a nationwide, population-based study, Diabetes Care, 27, 2819-2823, 2004	No specified targets. Compares outcomes in women who self-monitored daily or at any time during pregnancy versus those who did not.
Jensen,D.M., Korsholm,L., Ovesen,P., Beck-Nielsen,H., Molsted-Pedersen,L., Damm,P., Adverse pregnancy outcome in women with mild glucose intolerance: is there a clinically meaningful threshold value for glucose?, Acta Obstetricia et Gynecologica Scandinavica, 87, 59-62, 2008	DiagnosticTreatment threshold levels not self-monitoring thresholds.
Jovanovic,L., Druzin,M., Peterson,C.M., Effect of euglycemia on the outcome of pregnancy in insulin-dependent diabetic women as compared with normal control subjects, American Journal of Medicine, 71, 921-927, 1981	No thresholds suggested. Comparator group is non-diabetic women. Initially this study was a trial of urine versus blood glucose monitoring which was stopped early due to ethics.
Jovanovic-Peterson,L., Peterson,C.M., Reed,G.F., Metzger,B.E., Mills,J.L., Knopp,R.H., Aarons,J.H., Maternal postprandial glucose levels and infant birth weight: the Diabetes in Early Pregnancy Study. The National Institute of Child Health and Human Development--Diabetes in Early Pregnancy Study, American Journal of Obstetrics and Gynecology, 164, 103-111, 1991	No target levels given â€“ mean blood glucose values only per trimester. Comparator group is non-diabetic women.
Karlsson,K., Kjellmer,I., The outcome of diabetic pregnancies in relation to the mother's blood sugar level, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 112, 213-220, 1972	A minority of the women (12.5%) were diagnosed with GDM during pregnancy with an intravenous glucose test. The remainder had pre-existing diabetes (Whiteâ€ ™s classification). For calculation of mean blood glucose, all women were tested three times daily in hospital between 30-32 weeks using a laboratory method. These values were used to calculate mean blood glucose in all women with available data. The paper does not specify the times when the 3 samples were taken or relate these to meal times. Target values were not given to women.
Kerenyi,Z., Tamas,G., Kivimaki,M., Peterfalvi,A., Madarasz,E., Bosnyak,Z., Tabak,A.G., Maternal glycemia and risk of large-for-gestational-age babies in a population-based screening, Diabetes Care, 32, 2200-2205, 2009	The study reported the relationship between fasting blood glucose values obtained during a diagnostic 75g OGTT between 22 and 30 weeksâ€ ™ to determine whether the woman had GDM (a one off test). None of the women were being treated at the time of the study to control their blood glucose values. Women had blood glucose levels below those diagnostic of GDM.
Kitzmiller,J.L., Gavin,L.A., Gin,G.D., Jovanovic-Peterson,L., Main,E.K., Zigrang,W.D., Preconception care of diabetes. Glycemic control prevents congenital anomalies, JAMA, 265, 731-736, 1991	Comparison is pre-pregnancy vs. pregnancy education. Outcome (neonatal mortality) not analysed with respect to target values.
Langer,O., Rodriguez,D.A., Xenakis,E.M., McFarland,M.B., Berkus,M.D., Arrendondo,F., Intensified versus conventional management of gestational diabetes., American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 170, 1036-1046, 1994	Comparison is of management strategies to attain metabolic goals and is not a comparison of different thresholds
Middleton,Philippa, Crowther,Caroline A., Simmonds,Lucy, Different intensities of glycaemic control for pregnant women with pre-existing diabetes, Cochrane Database of Systematic Reviews, -, 2012	Cochrane review. Individual studies were checked for inclusion or exclusion and are reported separately.
Miodovnik,M., High spontaneous premature labour rate in insulin-dependent diabetic women: An association with poor glycaemic control., Scientific abstracts of the seventh Annual Meeting of the Society for Perinatal Obstretrics, Lake Buena Vista, Florida, February 5-7, -, 1987	Mean HbA1 values for preterm labour.
Most,O., Langer,O., Gestational diabetes: Maternal weight gain in relation to fetal growth, treatment modality, BMI and glycemic control, Journal of Maternal-Fetal and Neonatal Medicine, 25, 2458-2463, 2012	Does not examine the effects of blood glucose levels on outcomes (maternal weight gain). Large for gestational age is reported with respect to weight gain not blood glucose.

Excluded studies – Review question 12	
Parretti,E., Mecacci,F., Papini,M., Cioni,R., Carignani,L., Mignosa,M., La Torre,P., Mello,G., Third-trimester maternal glucose levels from diurnal profiles in nondiabetic pregnancies: correlation with sonographic parameters of fetal growth, Diabetes Care, 24, 1319-1323, 2001	The population is in pregnant women who do not have diabetes.
Prutsky,G.J., Domecq,J.P., Wang,Z., Carranza Leon,B.G., Elraiyah,T., Nabhan,M., Sundaresh,V., Vella,A., Montori,V.M., Murad,M.H., Glucose targets in pregnant women with diabetes: a systematic review and meta-analysis, Journal of Clinical Endocrinology and Metabolism, 98, 4319-4324, 2013	Included studies are all GDM intervention papers and not related to targets achieved/recorded. Women in each arm therefore received differing treatments in each study.
Riskin-Mashiah,S., Younes,G., Damti,A., Auslender,R., First-trimester fasting hyperglycemia and adverse pregnancy outcomes, Diabetes Care, 32, 1639-1643, 2009	Women with pre-existing diabetes or a high fasting blood glucose were excluded. GDM was reported as an outcome in women with normal fasting blood glucose values. LGA was also reported as an outcome in women with normal fasting blood glucose. LGA is not only reported in women who developed GDM but also those who were not diabetic. It is not possible to separate out the GDM patients.
Rosenn,B., Minor congenital malformations in infants of insulin-diabetic women: association with poor glycaemic control., Obstetrics and GynecologyObstet.Gynecol., 76, 745-749, 1990	Thresholds are not examined in the data analysis. Mean blood glucose only for congenital malformation versus no malformation.
Rosenn,B., Miodovnik,M., Combs,C.A., Khoury,J., Siddiqi,T.A., Glycemic thresholds for spontaneous abortion and congenital malformations in insulin-dependent diabetes mellitus, Obstetrics and GynecologyObstet.Gynecol., 84, 515-520, 1994	Outcomes not relevant to protocol
Rosenn,B.M., Miodovnik,M., Holcberg,G., Khoury,J.C., Siddiqi,T.A., Hypoglycemia: the price of intensive insulin therapy for pregnant women with insulin-dependent diabetes mellitus, Obstetrics and Gynecology, 85, 417-422, 1995	Does not examine outcomes by target values or threshold â€“ abortions, hypoglycaemic episodes and malformations are reported with respect to gestational age. Does not quantify no. of women not achieving glycaemic control target. Targets were the same for all women.
Savona-Ventura,C., Craus,J., Vella,K., Grima,S., Lowest threshold values for the 75g oral glucose tolerance test in pregnancy, Malta Medical Journal, 22, 18-20, 2010	Data were analysed based on the results of a 75g OGTT during the third trimester for diagnosis of GDM (a one off test). None of the women were being treated at the time of the study to control their blood glucose values.
Sturrock,N.D., Fay,T.N., Pound,N., Kirk,B.A., Danks,L.E., Analysis of 44,279 blood glucose estimations in relation to outcomes in 80 pregnant diabetic women, Journal of Obstetrics and Gynaecology, 21, 253-257, 2001	Does not quantify numbero. of women not achieving glycaemic control target. No comparative data â€“ mean blood glucose values only and correlational data only for blood glucose with respect to birth weight. Targets were the same for all women.
Valuk,J., Factors influencing birth weight in infants of diabetic mothers., Diabetes, 35, 96A-, 1986	Abstract only.
Veres,M., Babes,A., Lacziko,S., Correlations between the values of maternal glycemia from the last trimester of pregnancy and fetal birth weight, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 20, 259-265, 2013	Report associations using ROC analysis - not a threshold.
Wendland,E.M., Duncan,B.B., Mengue,S.S., Schmidt,M.I., Lesser than diabetes hyperglycemia in pregnancy is related to perinatal mortality: a cohort study in Brazil, BMC Pregnancy and Childbirth, 11, 92-, 2011	Data were analysed based on the results of a 75g OGTT during the third trimester for diagnosis of GDM (a one off test). None of the women were being treated at the time of the study to control their blood glucose values. The study reports the correlation of both mean fasting glucose levels and mean 2h glucose levels to neonatal mortality rather than looking at specific thresholds. Wrong population.
Wendland,E.M., Torloni,M.R., Falavigna,M., Trujillo,J., Dode,M.A., Campos,M.A., Duncan,B.B., Schmidt,M.I., Gestational diabetes and pregnancy outcomes--a systematic review of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria, BMC Pregnancy and Childbirth, 12, 23-, 2012	Comparison is outcomes in women with GDM versus those without GDM based on different diagnostic criteria. Study populations are non-diabetic women or mixed with no subgroup analyses by glucose threshold. No targets.

G.12 Antenatal HbA1c monitoring

Excluded studies – Review question 13	
Study	**Reason for Exclusion**
Bancroft,K., Tuffnell,D.J., Mason,G.C., Rogerson,L.J., Mansfield,M., A randomised controlled pilot study of the management of gestational impaired glucose tolerance, BJOG: An International Journal of Obstetrics and Gynaecology, 107, 959-963, 2000	Does not compare HbA1c monitoring strategies
Carmody,D., Doyle,A., Firth,R.G., Byrne,M.M., Daly,S., Mc,Auliffe F., Foley,M., Coulter-Smith,S., Kinsley,B.T., Teenage pregnancy in type 1 diabetes mellitus, Pediatric Diabetes, 11, 111-115, 2010	Comparison of teenagers and older women. Does not compare monitoring strategies
Crowther,C.A., Hague,W.M., Middleton,P.F., Baghurst,P.A., McPhee,A.J., Tran,T.S., Yelland,L.N., Ashwood,P., Han,S., Dodd,J.M., Robinson,J.S., IDEAL Study Group., The IDEAL study: investigation of dietary advice and lifestyle for women with borderline gestational diabetes: a randomised controlled trial - study protocol, BMC Pregnancy and Childbirth, 12, 106-, 2012	Protocol only
Crowther,C.A., Hiller,J.E., Moss,J.R., McPhee,A.J., Jeffries,W.S., Robinson,J.S., Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group., Effect of treatment of gestational diabetes mellitus on pregnancy outcomes, New England Journal of Medicine, 352, 2477-2486, 2005	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
de Veciana,M., Major,C.A., Morgan,M.A., Asrat,T., Toohey,J.S., Lien,J.M., Evans,A.T., Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy, New England Journal of MedicineN.Engl.J.Med., 333, 1237-1241, 1995	Does not compare HbA1c monitoring strategies
di Biase,N., Napoli,A., Sabbatini,A., Borrello,E., Buongiorno,A.M., Fallucca,F., Telemedicine in the treatment of diabetic pregnancy, Annali Dell'Istituto Superiore di Sanita, 33, 347-351, 1997	Women in both groups used the same monitoring strategy
Durnwald,C.P., Mele,L., Spong,C.Y., Ramin,S.M., Varner,M.W., Rouse,D.J., Sciscione,A., Catalano,P., Saade,G., Sorokin,Y., Tolosa,J.E., Casey,B., Anderson,G.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (MFMU), Glycemic characteristics and neonatal outcomes of women treated for mild gestational diabetes, Obstetrics and Gynecology, 117, 819-827, 2011	Does not compare monitoring strategies
Espersen,T., Klebe,J.G., Self-monitoring of blood glucose in pregnant diabetics. A comparative study of the blood glucose level and course of pregnancy in pregnant diabetics on an out-patient regime before and after the introduction of methods for home analysis of blood glucose, Acta Obstetricia et Gynecologica Scandinavica, 64, 11-14, 1985	Does not compare HbA1c monitoring strategies
Feig,D.S., Cleave,B., Tomlinson,G., Long-term effects of a diabetes and pregnancy program: does the education last?, Diabetes Care, 29, 526-530, 2006	Does not compare monitoring strategies
Garner,P., Okun,N., Keely,E., Wells,G., Perkins,S., Sylvain,J., Belcher,J., A randomized controlled trial of strict glycemic control and tertiary level obstetric care versus routine obstetric care in the management of gestational diabetes: a pilot study, American Journal of Obstetrics and GynecologyAm J Obstet Gynecol, 177, 190-195, 1997	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Glinianaia,S.V., Tennant,P.W.G., Bilous,R.W., Rankin,J., Bell,R., HbA1c and birthweight in women with pre-conception type 1 and type 2 diabetes: A population-based cohort study, Diabetologia, 55, 3193-3203, 2012	Non-comparative study
Goldberg,J.D., Franklin,B., Lasser,D., Jornsay,D.L., Hausknecht,R.U., Ginsberg-Fellner,F., Berkowitz,R.L., Gestational diabetes: impact of home glucose monitoring on neonatal birth weight, American Journal of Obstetrics and Gynecology, 154, 546-550, 1986	Does not compare HbA1c monitoring strategies
Gutaj,P., Zawiejska,A., Wender-Ozegowska,E., Brazert,J., Maternal factors predictive of firsttrimester pregnancy loss in women with pregestational diabetes, Polskie Archiwum Medycyny Wewnetrznej, 123, 21-28, 2013	Does not compare monitoring strategies
Hanson,U., Persson,B., Enochsson,E., Lennerhagen,P., Lindgren,F., Lundstrom,V., Lunell,N.O., Nilsson,B.A., Nilsson,L., Stangenberg,M., Self-monitoring of blood glucose by diabetic women during the third trimester of pregnancy, American Journal of Obstetrics and GynecologyAm J Obstet Gynecol, 150, 817-821, 1984	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Hawkins,J.S., Casey,B.M., Lo,J.Y., Moss,K., McIntire,D.D., Leveno,K.J., Weekly compared with daily blood glucose monitoring in women with diet-treated gestational diabetes, Obstetrics and Gynecology, 113, 1307-1312, 2009	Does not compare HbA1c monitoring strategies

Excluded studies – Review question 13	
Hiramatsu,Y., Shimizu,I., Omori,Y., Nakabayashi,M., JGA (Japan Glycated Albumin) Study Group., Determination of reference intervals of glycated albumin and hemoglobin A1c in healthy pregnant Japanese women and analysis of their time courses and influencing factors during pregnancy, Endocrine Journal, 59, 145-151, 2012	Does not compare monitoring strategies
Inkster,M.E., Fahey,T.P., Donnan,P.T., Leese,G.P., Mires,G.J., Murphy,D.J., Poor glycated haemoglobin control and adverse pregnancy outcomes in type 1 and type 2 diabetes mellitus: systematic review of observational studies, BMC Pregnancy and Childbirth, 6, 30-, 2006	Does not compare monitoring strategies
Jovanovic,L., The role of continuous glucose monitoring in gestational diabetes mellitus, Diabetes Technology and Therapeutics, 2 Suppl 1, S67-S71, 2000	Not relevant to this question - considered for inclusion in the continuous blood glucose monitoring review
Jovanovic,L., Peterson,C.M., Saxena,B.B., Dawood,M.Y., Saudek,C.D., Feasibility of maintaining normal glucose profiles in insulin-dependent pregnant diabetic women, American Journal of Medicine, 68, 105-112, 1980	Non-comparative study
Jovanovic,L., Savas,H., Mehta,M., Trujillo,A., Pettitt,D.J., Frequent monitoring of A1C during pregnancy as a treatment tool to guide therapy, Diabetes Care, 34, 53-54, 2011	Non-comparative study
Jovanovic,L.G., Using meal-based self-monitoring of blood glucose as a tool to improve outcomes in pregnancy complicated by diabetes. [25 refs], Endocrine Practice, 14, 239-247, 2008	Narrative review with no new data
Kerssen,A., De Valk,H.W., Visser,G.H., Do HbA(1)c levels and the self-monitoring of blood glucose levels adequately reflect glycaemic control during pregnancy in women with type 1 diabetes mellitus?, Diabetologia, 49, 25-28, 2006	Not relevant to this question - comparison of continuous glucose monitoring and intermittent monitoring
Kong,G.W., Tam,W.H., Chan,M.H., So,W.Y., Lam,C.W., Yiu,I.P., Loo,K.M., Li,C.Y., Comparison in the performance of glucose meters in blood glucose monitoring during pregnancy, Gynecologic and Obstetric Investigation, 69, 264-269, 2010	Compares different types of meters. Does not compare monitoring strategies
Laird,J., McFarland,K.F., Fasting blood glucose levels and initiation of insulin therapy in gestational diabetes, Endocrine Practice, 2, 330-332, 1996	Does not compare monitoring strategies
Landon,M.B., Spong,C.Y., Thom,E., Carpenter,M.W., Ramin,S.M., Casey,B., Wapner,R.J., Varner,M.W., Rouse,D.J., Thorp,J.M.,Jr., Sciscione,A., Catalano,P., Harper,M., Saade,G., Lain,K.Y., Sorokin,Y., Peaceman,A.M., Tolosa,J.E., Anderson,G.B., Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-fetal Medicine Units Network., A multicenter, randomized trial of treatment for mild gestational diabetes, New England Journal of Medicine, 361, 1339-1348, 2009	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Langer,O., Rodriguez,D.A., Xenakis,E.M., McFarland,M.B., Berkus,M.D., Arrendondo,F., Intensified versus conventional management of gestational diabetes, American Journal of Obstetrics and Gynecology, 170, 1036-1046, 1994	Does not compare HbA1c monitoring strategies
Manderson,J.G., Patterson,C.C., Hadden,D.R., Traub,A.I., Ennis,C., McCance,D.R., Preprandial versus postprandial blood glucose monitoring in type 1 diabetic pregnancy: a randomized controlled clinical trial, American Journal of Obstetrics and Gynecology, 189, 507-512, 2003	Does not compare HbA1c monitoring strategies
Middleton,Philippa, Crowther,Caroline A., Simmonds,Lucy, Different intensities of glycaemic control for pregnant women with pre-existing diabetes, Cochrane Database of Systematic Reviews, -, 2012	Does not compare monitoring strategies
Moy,Ming Foong, Ray,Amita, Buckley,Brian S., Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes, Cochrane Database of Systematic Reviews, -, 2012	Protocol only
Peacock,I., Hunter,J.C., Walford,S., Allison,S.P., Davison,J., Clarke,P., Symonds,E.M., Tattersall,R.B., Self-monitoring of blood glucose in diabetic pregnancy, British Medical Journal, 2, 1333-1336, 1979	Does not compare monitoring strategies
Pelaez-Crisologo,Ma, Castillo-Torralba,M.G.A.G., Festin,M.R., Different techniques of blood glucose monitoring in women with gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, 2009. Article Number, -, 2009	Protocol only
Rackham,O., Paize,F., Weindling,A.M., Cause of death in infants of women with pregestational diabetes mellitus and the relationship with glycemic control, Postgraduate Medicine, 121, 26-32, 2009	Does not compare monitoring strategies
Sturrock,N.D., Fay,T.N., Pound,N., Kirk,B.A., Danks,L.E., Analysis of 44,279 blood glucose estimations in relation to outcomes in 80 pregnant diabetic women, Journal of Obstetrics and Gynaecology, 21, 253-257, 2001	Does not compare monitoring strategies

Excluded studies – Review question 13	
Syed,M., Javed,H., Yakoob,M.Y., Bhutta,Z.A., Effect of screening and management of diabetes during pregnancy on stillbirths, BMC Public Health, 11 Suppl 3, S2-, 2011	Does not provide enough detail regarding the included studies. Included studies considered separately for inclusion in the NCC review.
Wechter,D.J., Kaufmann,R.C., Amankwah,K.S., Rightmire,D.A., Eardley,S.P., Verhulst,S., Zinzilieta,M., Young,J., Teich,J., Singleton,J.A., Prevention of neonatal macrosomia in gestational diabetes by the use of intensive dietary therapy and home glucose monitoring, American Journal of Perinatology, 8, 131-134, 1991	Does not compare monitoring strategies
Weisz,B., Shrim,A., Homko,C.J., Schiff,E., Epstein,G.S., Sivan,E., One hour versus two hours postprandial glucose measurement in gestational diabetes: a prospective study, Journal of Perinatology, 25, 241-244, 2005	Does not compare HbA1c monitoring strategies
Wilson,N., Ashawesh,K., Kulambil Padinjakara,R.N., Anwar,A., The multidisciplinary diabetes-endocrinology clinic and postprandial blood glucose monitoring in the management of gestational diabetes: impact on maternal and neonatal outcomes, Experimental and Clinical Endocrinology and Diabetes, 117, 486-489, 2009	Not clear which monitoring strategy/ies the 1 hour postprandial measurement is compared to
Wong,M.L., Butson,S., Gatling,W., Masding,M.G., The management of women with gestational diabetes can be stratified according to diagnostic oral glucose tolerance test results, Practical Diabetes International, 25, 61-63, 2008	Monitoring is compared as part of a larger package of care - it is not possible to determine the effects of monitoring alone
Yogev,Y., Chen,R., Ben-Haroush,A., Phillip,M., Jovanovic,L., Hod,M., Continuous glucose monitoring for the evaluation of gravid women with type 1 diabetes mellitus, Obstetrics and Gynecology, 101, 633-638, 2003	Not relevant to this question. Comparison of continuous glucose monitoring and intermittent monitoring
Young,B.C., Ecker,J.L., Fetal macrosomia and shoulder dystocia in women with gestational diabetes: Risks amenable to treatment?, Current Diabetes Reports, 13, 12-18, 2013	Narrative review. No new data.

G.13 Antenatal HbA1c targets

Excluded studies – Review question 14	
Study	**Reason for Exclusion**
Anderberg,E., Kallen,K., Berntorp,K., The impact of gestational diabetes mellitus on pregnancy outcome comparing different cut-off criteria for abnormal glucose tolerance, Acta Obstetricia et Gynecologica Scandinavica, 89, 1532-1537, 2010	Blood glucose data only
Arumugam,K., Abdul,Majeed N., Glycated haemoglobin is a good predictor of neonatal hypoglycaemia in pregnancies complicated by diabetes, Malaysian Journal of Pathology, 33, 21-24, 2011	Women were not given pre-specified targets for HbA1c - ROC analysis was used to determine risk for different HbA1c values. No effect size was calculable – only sensitivity and specificity were presented for each HbA1c value.
Aschwald,C.L., Catanzaro,R.B., Weiss,E.P., Gavard,J.A., Steitz,K.A., Mostello,D.J., Large-for-gestational-age infants of type 1 diabetic mothers: an effect of preprandial hyperglycemia?, Gynecological Endocrinology, 25, 653-660, 2009	Outcome not reported in relation to targets set for HbA1c. Results are presented according to the percentage of women with blood glucose above the target which accurately predicts the outcome (macrosomia).
Balsells,M., Garcia-Patterson,A., Gich,I., Corcoy,R., Maternal and fetal outcome in women with type 2 versus type 1 diabetes mellitus: a systematic review and metaanalysis. [53 refs], Journal of Clinical Endocrinology and Metabolism, 94, 4284-4291, 2009	Compares outcomes in type 1 diabetes versus type 2 diabetes and not according to HbA1c target values.
Carmody,D., Doyle,A., Firth,R.G., Byrne,M.M., Daly,S., Mc,Auliffe F., Foley,M., Coulter-Smith,S., Kinsley,B.T., Teenage pregnancy in type 1 diabetes mellitus, Pediatric Diabetes, 11, 111-115, 2010	No threshold analysis; outcomes not assessed in relation to HbA1c levels. Mean HbA1c only. Comparison is between teenagers and adults.
Cohen,O., Keidar,N., Simchen,M., Weisz,B., Dolitsky,M., Sivan,E., Macrosomia in well controlled CSII treated Type I diabetic pregnancy, Gynecological Endocrinology, 24, 611-613, 2008	No targets; outcomes not analysed by HbA1c level/threshold - mean HbA1c values only. Study is correlational.
Combs,C.A., Gunderson,E., Kitzmiller,J.L., Gavin,L.A., Main,E.K., Relationship of fetal macrosomia to maternal postprandial glucose control during pregnancy., Diabetes Care, 15, 1251-1257, 1992	No specified HbA1c targets - mean HbA1c values only.
Cyganek,K., Hebda-Szydlo,A., Katra,B., Skupien,J., Klupa,T., Janas,I., Kaim,I., Sieradzki,J., Reron,A., Malecki,M.T., Glycemic control and selected pregnancy outcomes in type 1 diabetes women on continuous subcutaneous insulin infusion and multiple daily injections: the significance of pregnancy planning, Diabetes Technology and Therapeutics, 12, 41-47, 2010	No specified HbA1c targets; no threshold analysis mean HbA1c values only in planned vs. unplanned pregnancies.
Dalfra,M.G., Sartore,G., Di,Cianni G., Mello,G., Lencioni,C., Ottanelli,S., Sposato,J., Valgimigli,F., Scuffi,C., Scalese,M., Lapolla,A., Glucose variability in diabetic pregnancy, Diabetes Technology and Therapeutics, 13, 853-859, 2011	No threshold analysis; mostly blood glucose data. Mean HbA1c only. Most comparisons are for type 1 versus gestational diabetes versus controls.

Excluded studies – Review question 14	
Damm,P., Mersebach,H., Rastam,J., Kaaja,R., Hod,M., McCance,D.R., Mathiesen,E.R., Poor pregnancy outcome in women with type 1 diabetes is predicted by elevated HbA1c and spikes of high glucose values in the third trimester, Journal of Maternal-Fetal and Neonatal Medicine, 27, 149-154, 2014	Data for the % of LGA births by HbA1c category is presented. The total number of LGA births (n = 88) is reported however it is not possible to calculate how many non-LGA births occurred in each HbA1c category therefore RRs are not calculable.
de Veciana,M., Major,C.A., Morgan,M.A., Asrat,T., Toohey,J.S., Lien,J.M., Evans,A.T., Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy, New England Journal of MedicineN.Engl.J.Med., 333, 1237-1241, 1995	No specified HbA1c targets; outcomes not analysed according to HbA1c levels. Comparison is pre- versus post-prandial monitoring.
Diabetes and Pregnancy Group,France, French multicentric survey of outcome of pregnancy in women with pregestational diabetes, Diabetes Care, 26, 2990-2993, 2003	HbA1c represents pre-pregnancy glycaemic control.
Dicker,D., Feldberg,D., Samuel,N., Yeshaya,A., Karp,M., Goldman,J.A., Spontaneous abortion in patients with insulin-dependent diabetes mellitus: the effect of preconceptional diabetic control, American Journal of Obstetrics and Gynecology, 158, 1161-1164, 1988	No specified HbA1c targets or thresholds - mean HbA1c values per trimester only for abortion versus pregnancy > 22 weeks' gestation.
Evers,I.M., De Valk,H.W., Mol,B.W.J., Ter Braak,E.W.M.T., Visser,G.H.A., Macrosomia despite good glycaemic control in Type I diabetic pregnancy; results of a nationwide study in The Netherlands, Diabetologia, 45, 1484-1489, 2002	No specific targets given; outcome reported as mean HbA1c levels in macrosomia vs. no macrosomia
Glinianaia,S.V., Tennant,P.W.G., Bilous,R.W., Rankin,J., Bell,R., HbA1c and birthweight in women with pre-conception type 1 and type 2 diabetes: A population-based cohort study, Diabetologia, 55, 3193-3203, 2012	No targets given. Threshold analysis is based on regression with only coefficients presented. Odds ratios for above/below an HbA1c of 7% are presented for LGA risk but in relation to the interaction between peri-conception HbA1c and during the third trimester. Shows an increased risk of LGA for HbA1c increasing during pregnancy.
Greene,M.F., Hare,J.W., Cloherty,J.P., Benacerraf,B.R., Soeldner,J.S., First-trimester hemoglobin A1 and risk for major malformation and spontaneous abortion in diabetic pregnancy.[see comment], Teratology, 39, 225-231, 1989	No relevant outcomes reported
Gutaj,P., Zawiejska,A., Wender-Ozegowska,E., Brazert,J., Maternal factors predictive of firsttrimester pregnancy loss in women with pregestational diabetes, Polskie Archiwum Medycyny Wewnetrznej, 123, 21-28, 2013	No specified HbA1c targets; no threshold analysis. Mean HbA1c only in miscarriage versus no miscarriage. Outcome not relevant to protocol.
Holmes,V.A., Young,I.S., Patterson,C.C., Pearson,D.W., Walker,J.D., Maresh,M.J., McCance,D.R., Diabetes and Pre-eclampsia Intervention Trial Study Group., Optimal glycemic control, pre-eclampsia, and gestational hypertension in women with type 1 diabetes in the diabetes and pre-eclampsia intervention trial, Diabetes Care, 34, 1683-1688, 2011	Results were presented in four categories as ORs for each group vs. the reference group of optimal control (OR = 1). No single threshold for HbA1c was presented and dichotomisation could not be applied. Numbers of events were not reported for each category.
Inkster,M.E., Fahey,T.P., Donnan,P.T., Leese,G.P., Mires,G.J., Murphy,D.J., Poor glycated haemoglobin control and adverse pregnancy outcomes in type 1 and type 2 diabetes mellitus: systematic review of observational studies, BMC Pregnancy and Childbirth, 6, 30-, 2006	Systematic review-; one relevant study (Vaarasmaki) obtained for further analysis. Other studies did not report relevant outcomes relevant to the protocol.
Jensen,D.M., Damm,P., Moelsted-Pedersen,L., Ovesen,P., Westergaard,J.G., Moeller,M., Beck-Nielsen,H., Outcomes in type 1 diabetic pregnancies: a nationwide, population-based study, Diabetes Care, 27, 2819-2823, 2004	No specified HbA1c targets; no threshold analysis. Mean HbA1c for serious outcome versus no serious outcome.
Jovanovic,L., Druzin,M., Peterson,C.M., Effect of euglycemia on the outcome of pregnancy in insulin-dependent diabetic women as compared with normal control subjects, American Journal of Medicine, 71, 921-927, 1981	No specified HbA1c targets or thresholds given. Comparator group is non-diabetic women. Initially this study was a trial of urine versus blood glucose monitoring which was stopped early due to ethics.
Jovanovic,L., Savas,H., Mehta,M., Trujillo,A., Pettitt,D.J., Frequent monitoring of A1C during pregnancy as a treatment tool to guide therapy, Diabetes Care, 34, 53-54, 2011	Monitoring data only
Jovanovic-Peterson,L., Peterson,C.M., Reed,G.F., Metzger,B.E., Mills,J.L., Knopp,R.H., Aarons,J.H., Maternal postprandial glucose levels and infant birth weight: the Diabetes in Early Pregnancy Study. The National Institute of Child Health and Human Development--Diabetes in Early Pregnancy Study, American Journal of Obstetrics and Gynecology, 164, 103-111, 1991	No specified HbA1c targets – mean HbA1c values only per trimester. Comparator group is non-diabetic women.
Klinke,J., Toth,E.L., Preconception care for women with type 1 diabetes, Canadian Family PhysicianCan.Fam.Physician, 49, 769-773, 2003	Systematic review with no data provided.
Lisowski,L.A., Verheijen,P.M., Copel,J.A., Kleinman,C.S., Wassink,S., Visser,G.H., Meijboom,E.J., Congenital heart disease in pregnancies complicated by maternal diabetes mellitus. An international clinical collaboration, literature review, and meta-analysis. [64 refs], Herz, 35, 19-26, 2010	No targets/threshold analysis; no relevant outcomes reported (congenital malformations only).

Excluded studies – Review question 14	
Lucas,M.J., Leveno,K.J., Williams,M.L., Raskin,P., Whalley,P.J., Early pregnancy glycosylated hemoglobin, severity of diabetes, and fetal malformations, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 161, 426-431, 1989	No relevant outcomes reported
Manderson,J.G., Patterson,C.C., Hadden,D.R., Traub,A.I., Ennis,C., McCance,D.R., Preprandial versus postprandial blood glucose monitoring in type 1 diabetic pregnancy: a randomized controlled clinical trial, American Journal of Obstetrics and Gynecology, 189, 507-512, 2003	No specified HbA1c targets; randomisation to monitoring not targets
Miller,E., Hare,J.W., Cloherty,J.P., Dunn,P.J., Gleason,R.E., Soeldner,J.S., Kitzmiller,J.L., Elevated maternal hemoglobin A1c in early pregnancy and major congenital anomalies in infants of diabetic mothers, New England Journal of MedicineN.Engl.J.Med., 304, 1331-1334, 1981	No relevant outcomes reported
Mills,J.L., Simpson,J.L., Driscoll,S.G., Jovanovic-Peterson,L., Van,Allen M., Aarons,J.H., Metzger,B., Bieber,F.R., Knopp,R.H., Holmes,L.B., Incidence of spontaneous abortion among normal women and insulin-dependent diabetic women whose pregnancies were identified within 21 days of conception, New England Journal of MedicineN.Engl.J.Med., 319, 1617-1623, 1988	Not HbA1c - HbA1a1; also no targets specified. Mean HbA1a1 in diabetic versus non-diabetic women.
Miodovnik,M., Mimouni,F., Tsang,R.C., Ammar,E., Kaplan,L., Siddiqi,T.A., Glycemic control and spontaneous abortion in insulin-dependent diabetic women, Obstetrics and GynecologyObstet.Gynecol., 68, 366-369, 1986	Mean HbA1 values for preterm labour - outcome not relevant to protocol.
Miodovnik,M., Skillman,C., Holroyde,J.C., Butler,J.B., Wendel,J.S., Siddiqi,T.A., Elevated maternal glycohemoglobin in early pregnancy and spontaneous abortion among insulin-dependent diabetic women, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 153, 439-442, 1985	No relevant outcomes reported; no targets set; threshold analysis uses clinically irrelevant value of 12%
Miodovnik,M., Mimouni,F., Siddiqi,T.A., Berk,M.A., Wittekind,C., High spontaneous premature labour rate in insulin-dependent diabetic women: An association with poor glycaemic control, Obstet Gynecol., 72:175, 1988	Mean HbA1 values for preterm labour - outcome not relevant to protocol.
Nielsen,G.L., Moller,M., Sorensen,H.T., HbA1c in early diabetic pregnancy and pregnancy outcomes: A Danish population-based cohort study of 573 pregnancies in women with type 1 diabetes, Diabetes Care, 29, 2612-2616, 2006	All outcomes are grouped together as good or adverse in comparative analyses.
Rackham,O., Paize,F., Weindling,A.M., Cause of death in infants of women with pregestational diabetes mellitus and the relationship with glycemic control, Postgraduate Medicine, 121, 26-32, 2009	No threshold analysis; polynomial regressions only for infant death. Comparison for most outcomes is type 1 versus type 2 diabetes.
Rosenn,B., Minor congenital malformations in infants of insulin-diabetic women: association with poor glycaemic control., Obstetrics and GynecologyObstet.Gynecol., 76, 745-749, 1990	Blood glucose targets only; mean HbA1c only for congenital malformation versus no malformation.
Rosenn,B., Miodovnik,M., Combs,C.A., Khoury,J., Siddiqi,T.A., Glycemic thresholds for spontaneous abortion and congenital malformations in insulin-dependent diabetes mellitus, Obstetrics and GynecologyObstet.Gynecol., 84, 515-520, 1994	No specified HbA1c targets - ROC analysis of mean HbA1c values to obtain thresholds for increased risk of malformations. Outcome not relevant to protocol.
Rowan,J.A., Gao,W., Hague,W.M., McIntyre,H.D., Glycemia and its relationship to outcomes in the metformin in gestational diabetes trial, Diabetes Care, 33, 9-16, 2010	No specified HbA1c targets; HbA1c at baseline only
Starikov,R.S., Inman,K., Chien,E.K., Anderson,B.L., Rouse,D.J., Lopes,V., Coustan,D.R., Can hemoglobin A1c in early pregnancy predict adverse pregnancy outcomes in diabetic patients?, Journal of Diabetes and its Complications, 28, 203-207, 2014	Women were not given pre-specified targets for HbA1c
Sturrock,N.D., Fay,T.N., Pound,N., Kirk,B.A., Danks,L.E., Analysis of 44,279 blood glucose estimations in relation to outcomes in 80 pregnant diabetic women, Journal of Obstetrics and Gynaecology, 21, 253-257, 2001	No specified HbA1c targets or thresholds. No comparative data - correlational for HbA1c with respect to birth weight.
Suhonen,L., Hiilesmaa,V., Teramo,K., Glycaemic control during early pregnancy and fetal malformations in women with type I diabetes mellitus, Diabetologia, 43, 79-82, 2000	No relevant outcomes reported
Wyse,L.J., Jones,M., Mandel,F., Relationship of glycosylated hemoglobin, fetal macrosomia, and birthweight macrosomia, American Journal of Perinatology, 11, 260-262, 1994	No specified HbA1c targets used in analysis. HbA1c value of 6.3% is reported with respect to ultrasound markers only not the per cent of large for gestational age babies.
Ylinen,K., Aula,P., Stenman,U.H., Kesaniemi-Kuokkanen,T., Teramo,K., Risk of minor and major fetal malformations in diabetics with high haemoglobin A1c values in early pregnancy, British Medical JournalBMJ, 289, 345-346, 1984	No relevant outcomes reported

G.14 Antenatal continuous glucose monitoring

Excluded studies – Review question 15	
Study	**Reason for Exclusion**
Cao,X., Wang,Z., Yang,C., Mo,X., Xiu,L., Li,Y., Xiao,H., Comprehensive intensive therapy for Chinese gestational diabetes benefits both newborns and mothers, Diabetes Technology and Therapeutics, 14, 1002-1007, 2012	Does not compare continuous glucose monitoring with intermittent capillary blood glucose monitoring
Centre for Reviews and Dissemination., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HbA1c) levels in type 1 diabetic patients: a systematic review (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2013	Structured abstract. Full paper not ordered as women who were pregnant were excluded by the authors.
Centre for Reviews and Dissemination., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2013	Structured abstract. Full paper ordered separately for consideration.
Centre for Reviews and Dissemination., Monitoring blood glucose control in diabetes mellitus: a systematic review (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2013	Structured abstract. Full paper ordered separately for consideration.
Centre for Reviews and Dissemination., Self-monitoring of blood glucose as part of a multi-component therapy among non-insulin requiring type 2 diabetes patients: a meta-analysis (1966 - 2004) (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2013	Structured abstract. Full paper not ordered as the authors excluded women who were pregnant.
Chen,R., Yogev,Y., Ben-Haroush,A., Jovanovic,L., Hod,M., Phillip,M., Continuous glucose monitoring for the evaluation and improved control of gestational diabetes mellitus, Journal of Maternal-Fetal and Neonatal Medicine, 14, 256-260, 2003	Data for hypoglycaemia are reported with respect to treatment with insulin not us of CGM. No other relevant outcomes are reported.
Coster,S., Gulliford,M.C., Seed,P.T., Powrie,J.K., Swaminathan,R., Monitoring blood glucose control in diabetes mellitus: A systematic review, Health Technology Assessment, 4, i-84, 2000	Published prior to the 2008 guideline
Coster,S., Gulliford,M.C., Seed,P.T., Powrie,J.K., Swaminathan,R., Monitoring blood glucose control in diabetes mellitus: a systematic review (Structured abstract), Health Technology Assessment Database, -, 2013	Structured abstract. Full paper ordered for consideration.
De,Block C., Keenoy,B., Van,Gaal L., A review of current evidence with continuous glucose monitoring in patients with diabetes, Journal of Diabetes Science and Technology, 2, 718-727, 2008	Narrative review with no new data. Cited studies were considered separately for inclusion.
Ghio,A., Lencioni,C., Romero,F., A real-time continuous glucose monitoring for diabetic women during the delivery, Diabetologia, 52, S462-, 2009	Abstract only.
Greven,Wendela L., Hoeks,Lette B., de Valk,Harold, Continuous glucose monitoring systems for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2010	Cochrane review protocol. Full review not searched for as studies of pregnant women were excluded by the authors.
Hewapathirana,N.M., O'Sullivan,E., Murphy,H.R., Role of continuous glucose monitoring in the management of diabetic pregnancy, Current Diabetes Reports, 13, 34-42, 2013	Narrative review with no new data. Cited studies considered for inclusion.
Jovanovic,L., The role of continuous glucose monitoring in gestational diabetes mellitus, Diabetes Technology and Therapeutics, 2 Suppl 1, S67-S71, 2000	Does not compare intermittent and continuous glucose monitoring
Kerssen,Anneloes, de Valk,Harold W., Visser,Gerard H.A., Day-to-day glucose variability during pregnancy in women with Type 1 diabetes mellitus: glucose profiles measured with the Continuous Glucose Monitoring System, BJOG : an international journal of obstetrics and gynaecologyBJOG, 111, 919-924, 2004	No relevant outcomes.
Kitzmiller,J.L., Block,J.M., Brown,F.M., Catalano,P.M., Conway,D.L., Coustan,D.R., Gunderson,E.P., Herman,W.H., Hoffman,L.D., Inturrisi,M., Jovanovic,L.B., Kjos,S.I., Knopp,R.H., Montoro,M.N., Ogata,E.S., Paramsothy,P., Reader,D.M., Rosenn,B.M., Thomas,A.M., Kirkman,M.S., Managing preexisting diabetes for pregnancy: summary of evidence and consensus recommendations for care, Diabetes Care, 31, 1060-1079, 2008	Consensus paper with no new data
Langendam,M., Luijf,Y.M., Hooft,L., Devries,J.H., Mudde,A.H., Scholten,R.J., Continuous glucose monitoring systems for type 1 diabetes mellitus, Cochrane Database of Systematic Reviews, 1, CD008101-, 2012	None of the included studies reported on women who were pregnant
Lee-Parritz,A., New technologies for the management of pregestational diabetes mellitus, Obstetrical and Gynecological Survey, 67, 167-175, 2012	Narrative review. Cited studies considered for inclusion separately.
McLachlan,Kylie, Jenkins,Alicia, O'Neal,David, The role of continuous glucose monitoring in clinical decision-making in diabetes in pregnancy, Australian and New Zealand Journal of Obstetrics and Gynaecology, , 186-190, 2007	Does not compare continuous glucose monitoring with intermittent capillary blood glucose monitoring

Excluded studies – Review question 15	
Moy,Ming Foong, Ray,Amita, Buckley,Brian S., Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes, Cochrane Database of Systematic Reviews, -, 2012	Protocol rather than a full review. Cochrane Pregnancy and Childbirth group report this review is progressing slowly. Publication date of the full review is unknown.
Moy,F.M., Ray,A., Buckley,B.S., Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes, Cochrane Database of Systematic Reviews, 4, CD009613-, 2014	Systematic review. Studies checked for eligibility for this review
Murphy,H.R., Raynian,G., Lewis,K., Kelly,S., Johal,B., Duffield,K., Fowler,D., Campbell,P.J., Temple,R.C., Effectiveness of continuous glucose monitoring in pregnant women with diabetes: Randomized clinical trial, Obstetrical and Gynecological Survey, 64, 216-218, 2009	Abstract. Full paper ordered for consideration.
PelaezCrisologo,Cristina Ma, CastilloTorralba,Geraldine Maria, Festin,Mario R., Different techniques of blood glucose monitoring in women with gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, -, 2009	Protocol rather than a full review. Cochrane Pregnancy and Childbirth group report this review has stalled and likely to be withdrawn from the Cochrane library.
Pickup,J.C., Freeman,S.C., Sutton,A.J., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, BMJ, 343, d3805-, 2011	Excluded studies of pregnant women
Purins,A., Hiller,J.E., Continuous glucose monitoring in pregnant women with diabetes, Adelaide Health Technology Assessment (AHTA) on behalf of National Horizon Scanning Unit (HealthPACT and MSAC), -, 2009	Review with no new data. Individual study references considered separately for inclusion.
Purins,A., Hiller,J.E., Continuous glucose monitoring in pregnant women with diabetes (Structured abstract), Health Technology Assessment Database, -, 2013	Structured abstract. Full paper ordered for consideration.
Secher,A.L., Ringholm,L., Andersen,H.U., Damm,P., Mathiesen,E.R., The effect of real-time continuous glucose monitoring in pregnant women with diabetes: a randomized controlled trial, Diabetes Care, 36, 1877-1883, 2013	Duplicate of Secher study already included in this review.
Secher,A.L., Stage,E., Ringholm,L., Barfred,C., Damm,P., Mathiesen,E.R., Real-time continuous glucose monitoring as a tool to prevent severe hypoglycaemia in selected pregnant women with Type 1 diabetes - an observational study, Diabetic Medicine, 31, 352-356, 2014	Study design is observational not an RCT. The protocol specifies that non-randomised studies will only be included if RCTs are not available. All other studies included in the review are RCTs therefore this study is not eligible for inclusion.
Voormolen,D.N., DeVries,J.H., Evers,I.M., Mol,B.W., Franx,A., The efficacy and effectiveness of continuous glucose monitoring during pregnancy: a systematic review, Obstetrical and Gynecological Survey, 68, 753-763, 2013	Systematic review. Studies checked for inclusion: 4 previously included, 2 previously weeded out, one previously excluded, 3 new papers were requested and subsequently excluded (Chen, Kerssen, Ghio).
Voormolen,D.N., Devries,J.H., Franx,A., Mol,B.W., Evers,I.M., Effectiveness of continuous glucose monitoring during diabetic pregnancy (GlucoMOMS trial); a randomised controlled trial, BMC Pregnancy and Childbirth, 12, 164-, 2012	Protocol for a future trial - no data reported

G.15 Antenatal specialist teams

Excluded studies – Review question 16	
Study	**Reason for Exclusion**
Anderberg,E., Berntorp,K., Crang-Svalenius,E., Diabetes and pregnancy: women's opinions about the care provided during the childbearing year, Scandinavian Journal of Caring Sciences, 23, 161-170, 2009	Does not compare opinions for different types/models of care
Carvalheiro,M., Diabetes in pregnancy: state of the art in the Mediterranean countries, Portugal, Annali Dell'Istituto Superiore di Sanita, 33, 303-306, 1997	Does not compare different types/models of care
Dunne,F.P., Audit of the recommendations of care for pregnant women with diabetes mellitus in the West Midlands, UK, Practical Diabetes International, 15, 230-232, 1998	Does not compare outcomes from different types/models of care
Dunne,F.P., Avalos,G., Durkan,M., Mitchell,Y., Gallacher,T., Keenan,M., Hogan,M., Carmody,L.A., Gaffney,G., TLANTIC,D.I.P., ATLANTIC DIP: pregnancy outcomes for women with type 1 and type 2 diabetes, Irish Medical Journal, 105, 6-9, 2012	Study compares pregnant women with diabetes to the background pregnant population. Some data and information from this study is relevant to an included study, and has been extracted and flagged where used.
Finlay,A., Heddle,M., Hundley,V., Mowat,L., Lang,G., Pearson,D., Research. Continuity of carer during pregnancy for diabetic women, British Journal of Midwifery, 8, 207-214, 2000	Does not compare types of specialist care in pregnant women with diabetes
Fox,R., Watson,J., Close,C., Evans,K., Moran,S., Integrated care pathway for diabetes in pregnancy, Journal of Integrated Care Pathways, 8, 27-40, 2004	Does not compare types of care

Excluded studies – Review question 16	
Gayle,C., Germain,S., Marsh,M.S., Rajasingham,D., Brackenridge,A., Carroll,P., Amiel,S.A., Thomas,S., Comparing pregnancy outcomes for intensive versus routine antenatal treatment of gestational diabetes based on a 75gram oral glucose tolerance test 2-hour blood glucose 7.8 - 8.9mmol/l, Diabetologia, 53, S435-, 2010	Abstract - full paper not available
Gayle,C., Germain,S., Marsh,M.S., Rajasingham,D., Carroll,P., Brackenridge,A., Amiel,S.A., Thomas,S., Management of gestational diabetes using the World Health Organisation (WHO) criteria in a diabetes antenatal clinic benefit women compared to routine care based on European Association for the Study of Diabetes (EASD) criteria. A comparison of treatment based on an oral glucose tolerance test 2-hour blood glucose 7.8 - 8.9 mmol/l, Diabetic Medicine, 27, 35-, 2010	Abstract - full paper not available
Harris,G.D., White,R.D., Diabetes management and exercise in pregnant patients with diabetes, Clinical Diabetes, 23, 165-168, 2005	Narrative review. Does not compare types of care.
Hjelm,K., Berntorp,K., Frid,A., Aberg,A., Apelqvist,J., Beliefs about health and illness in women managed for gestational diabetes in two organisations, Midwifery, 24, 168-182, 2008	Does not report outcomes of interest to the GDG - qualitative study of women's beliefs about health and illness
Kavvoura,F.K., Graham,D., Crowley,R., Simpson,H., Street,P., Elsheikh,M., Diabetes antenatal care at a large district general hospital: An audit from 1997 to 2010, Diabetic Medicine, 29, 153-, 2012	Abstract - full paper not available
Mills,L.S., Naylor,G., Developing diabetes in pregnancy, the clinical demands increase: Working in new and novel ways, Diabetic Medicine, 27, 168-, 2010	Abstract - full paper not available
Owens,L., Avalos,G., Dunne,F., Atlantic dip-closing the loop: A change in clinical practice can improve outcomes in pregestational diabetes mellitus, Irish Journal of Medical Science, 181, S356-, 2012	Conference abstract. Full paper (Owens, 2012) considered separately for inclusion.
Owens,L.A., Avalos,G., Carmody,L., Dunne,F., Dip,A., Atlantic dip-closing the loop: A change in clinical practice can improve outcomes for women with pre-gestational diabetes mellitus, Diabetes, 61, A338-, 2012	Conference abstract. Full paper considered separately for inclusion (Owens, 2012).
Owens,Lisa A., Avalos,Gloria, Kirwan,Breda, Carmody,Louise, Dunne,Fidelma, ATLANTIC DIP: Closing the Loop: A change in clinical practice can improve outcomes for women with pregestational diabetes, Diabetes Care, 35, 1669-1671, 2012	Same study reported in Owens (2012) with more detail, which is included in the guideline review
Ridout,J., Roberts,C., Cox,K., Gable,D., Triage of referrals in the first six months of a fully integrated community intermediate care service for Type 2 diabetes: The westminster diabetes partnership, Diabetic Medicine, 26, 198-, 2009	Does not report outcomes when comparing types of care. Abstract.
Steel,J.M., Johnstone,F.D., Hepburn,D.A., Smith,A.F., Can prepregnancy care of diabetic women reduce the risk of abnormal babies?, BMJ, 301, 1070-1074, 1990	Comparison of pre-pregnancy advice, not care during pregnancy
Stenhouse,E., Letherby,G., Stephen,N., Being a pregnant woman with diabetes: Managing the process, Diabetic Medicine, 27, 171-, 2010	Abstract - full paper not available
Stenhouse,E., Millward,A., Wylie,J., An exploration of infant feeding choices for qwomen whose pregnancy is complicated by gestational diabetes, Diabetic Medicine, 28, 175-, 2011	Abstract - full paper not available
Wylie,J., Millward,A., Stenhouse,E., Pregnant women's understanding and knowledge of gestational diabetes and the impact of diagnosis on their pregnancy experience, Diabetic Medicine, 28, 175-, 2011	Abstract - full paper not available
York,R., Brown,L.P., Samuels,P., Finkler,S.A., Jacobsen,B., Persely,C.A., Swank,A., Robbins,D., A randomized trial of early discharge and nurse specialist transitional follow-up care of high-risk childbearing women, Nursing Research, 46, 254-261, 1997	Comparison of different types of care after hospitalisation.

G.16 Timing of birth

Excluded studies: Review question 17	
Study	**Reason for Exclusion**
Boulvain,Michel, Stan,Catalin M., Irion,Olivier, Elective delivery in diabetic pregnant women, Cochrane Database of Systematic Reviews, -, 2009	Systematic review: checked for relevant studies
Catalano,P.M., Sacks,D.A., Timing of indicated late preterm and early-term birth in chronic medical complications: diabetes, Seminars in Perinatology, 35, 297-301, 2011	Narrative review. No novel data is presented
Coleman,T.L., Randall,H., Graves,W., Lindsay,M., Vaginal birth after cesarean among women with gestational diabetes, American Journal of Obstetrics and GynecologyAm.J.Obstet.Gynecol., 184, 1104-1107, 2001	The outcomes examined for the comparison (of women with and without gestational diabetes) are not relevant to the protocol
Conway,D.L., Langer,O., Elective delivery of infants with macrosomia in diabetic women: reduced shoulder dystocia versus increased cesarean deliveries, American Journal of Obstetrics and GynecologyAm J Obstet Gynecol, 178, 922-925, 1998	The comparison of caesarean section with induction of labour during elective delivery is not relevant to the protocol
Garabedian,C., Deruelle,P., Delivery (timing, route, peripartum glycemic control) in women with gestational diabetes mellitus, Diabetes and Metabolism, 36, 515-521, 2010	A review performed to inform guideline recommendations: checked for relevant references

Excluded studies: Review question 17	
Hod,M., Bar,J., Peled,Y., Fried,S., Katz,I., Itzhak,M., Ashkenazi,S., Schindel,B., Ben Rafael,Z., Antepartum management protocol. Timing and mode of delivery in gestational diabetes, Diabetes Care, 21, B113-B117, 1998	A comparison of obstetric management protocols during different time periods is presented and is not relevant to the comparison specified in the protocol(elective delivery versus expectant management)
Hod,Moshe, Merlob,Paul, Friedman,Shmuel, Schoenfeld,Alex, Ovadia,Jardena, Gestational Diabetes Mellitus: A Survey of Perinatal Complications in the 1980s, Diabetes, 40, 74-78, 1991	The outcomes examined for the comparison (of women with and without pre-gestational or gestational diabetes) are not relevant to the protocol
Hod,Moshe, Rabinerson,David, Kaplan,Bari, Peled,Yoav, Bar,Jacob, Shindel,Bella, Merlob,Paul, Ovadia,Jardena, Neri,Alexander, Perinatal complications following gestational diabetes mellitus how âsweetâ is ill?, Acta Obstetricia et Gynecologica ScandinavicaActa Obstet Gynecol Scand, 75, 809-815, 1996	The outcomes examined for the comparison (of women with and without pre-gestational or gestational diabetes) are not relevant to the protocol
Kock,K., Kock,F., Klein,K., Bancher-Todesca,D., Helmer,H., Diabetes mellitus and the risk of preterm birth with regard to the risk of spontaneous preterm birth, Journal of Maternal-Fetal and Neonatal Medicine, 23, 1004-1008, 2010	The outcomes examined for the comparison (of women with and without pre-gestational or gestational diabetes) are not relevant to the protocol
Lopez-de-Andres,A., Carrasco-Garrido,P., Gil-de-Miguel,A., Hernandez-Barrera,V., Jimenez-Garcia,R., Trends in deliveries in women with gestational diabetes in Spain, 2001-2008, Diabetes Research and Clinical Practice, 91, e27-e29, 2011	No comparative data that is relevant to the protocol is presented
Lurie,S., Matzkel,A., Weissman,A., Gotlibe,Z., Friedman,A., Outcome of pregnancy in class A1 and A2 gestational diabetic patients delivered beyond 40 weeks' gestation, American Journal of Perinatology, 9, 484-488, 1992	The comparisons examined (deliveries at <40weeks in women with gestational diabetes and at >40weeks in women with and without gestational diabetes) were not relevant to the protocol
Naylor,C.D., Sermer,M., Chen,E., Sykora,K., Cesarean delivery in relation to birth weight and gestational glucose tolerance. Pathophysiology or practice style?, JAMA: the journal of the American Medical AssociationJAMA, 275, 1165-1170, 1996	The outcomes examined for the comparison (of women with and without gestational diabetes) are not relevant to the protocol
Nicholson,W.K., Wilson,L.M., Witkop,C.T., Baptiste-Roberts,K., Bennett,W.L., Bolen,S., Barone,B.B., Golden,S.H., Gary,T.L., Neale,D.M., Bass,E.B., Therapeutic management, delivery, and postpartum risk assessment and screening in gestational diabetes. [107 refs], Evidence Report/Technology Assessment, 1-96, 2008	Systematic review: checked for relevant studies
Nordlander,E., Hanson,U., Persson,B., Factors influencing neonatal morbidity in gestational diabetic pregnancy, British journal of obstetrics and gynaecology, 96, 671-678, 1989	The outcomes examined for the comparison (of women with and without gestational diabetes) are not relevant to the protocol
Peled,Y., Perri,T., Chen,R., Pardo,J., Bar,J., Hod,M., Gestational diabetes mellitus--implications of different treatment protocols, Journal of Pediatric Endocrinology, 17, 847-852, 2004	The comparison examined is of obstetric management protocols during different time periods and is not relevant to the protocol(comparison of expectant management versus elective delivery)
Rayburn,W.F., Sokkary,N., Clokey,D.E., Moore,L.E., Curet,L.B., Consequences of routine delivery at 38 weeks for A-2 gestational diabetes, Journal of Maternal-Fetal and Neonatal Medicine, 18, 333-337, 2005	The comparison examined (women with A1 vs A2 gestational diabetes) is not relevant to the protocol
Witkop,C.T., Neale,D., Wilson,L.M., Bass,E.B., Nicholson,W.K., Active compared with expectant delivery management in women with gestational diabetes: a systematic review. [15 refs][Erratum appears in Obstet Gynecol. 2020 Feb;115(2 Pt 1):387], Obstetrics and Gynecology, 113, 206-217, 2009	Systematic review: checked for any relevant studies

G.17 Diagnostic accuracy and timing of postnatal testing

Excluded studies – Review questions 18 and 19	
Study	**Reason for Exclusion**
Albareda,M., Caballero,A., Badell,G., Rodriguez-Espinosa,J., Ordonez-Llanos,J., de,Leiva A., Corcoy,R., Metabolic syndrome at follow-up in women with and without gestational diabetes mellitus in index pregnancy, Metabolism: Clinical and Experimental, 54, 1115-1121, 2005	National Cholesterol Education Program (NCEP) 2001 criteria - study evaluates the prevalence of fasting glucose >=6.1mmol/l and other metabolic syndrome components in women with gestational diabetes compared to women without gestational diabetes
Ali,Z., Alexis,S.D., Occurrence of diabetes mellitus after gestational diabetes mellitus in Trinidad, Diabetes Care, 13, 527-529, 1990	Pospartum OGTT results assessed by WHO 1980 criteria
Baker,A.M., Brody,S.C., Salisbury,K., Schectman,R., Hartmann,K.E., Postpartum glucose tolerance screening in women with gestational diabetes in the state of North Carolina, North Carolina Medical Journal, 70, 14-19, 2009	No relevant data

Excluded studies – Review questions 18 and 19	
Beischer,N.A., Wein,P., Sheedy,M.T., Dargaville,R., Studies of postnatal diabetes mellitus in women who had gestational diabetes. Part 1. Estimation of the prevalence of unrecognized prepregnancy diabetes mellitus, Australian and New Zealand Journal of Obstetrics and Gynaecology, 37, 412-419, 1997	WHO 1985 criteria used to define postnatal diabetes
Benjamin,E., Winters,D., Mayfield,J., Gohdes,D., Diabetes in pregnancy in Zuni Indian women. Prevalence and subsequent development of clinical diabetes after gestational diabetes, Diabetes Care, 16, 1231-1235, 1993	Postnatal diabetes defined by the NDDG criteria
Bennett,W.L., Bolen,S., Wilson,L.M., Bass,E.B., Nicholson,W.K., Performance characteristics of postpartum screening tests for type 2 diabetes mellitus in women with a history of gestational diabetes mellitus: a systematic review. [38 refs], Journal of Women's Health, 18, 979-987, 2009	Review paper - individual studies have been checked for inclusion
Bian,X., Gao,P., Xiong,X., Xu,H., Qian,M., Liu,S., Risk factors for development of diabetes mellitus in women with a history of gestational diabetes mellitus, Chinese Medical Journal, 113, 759-762, 2000	WHO 1985 criteria used to define diabetes
Buchanan,T.A., Xiang,A.H., Kjos,S.L., Trigo,E., Lee,W.P., Peters,R.K., Antepartum predictors of the development of type 2 diabetes in Latino women 11-26 months after pregnancies complicated by gestational diabetes, Diabetes, 48, 2430-2436, 1999	WHO 1985 criteria used to define postnatal diabetes
Bukulmez,O., Durukan,T., Postpartum oral glucose tolerance tests in mothers of macarosomic infants: inadequacy of current antenatal test criteria in detecting prediabetic state, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 86, 29-34, 1999	Article not of relevance for review question
Burt,R.L., Leake,N.H., Oral glucose tolerance test during pregnancy and the early puerperium, Obstetrics and Gynecology, 33, 48-53, 1969	No relevant data
Catalano,P.M., Vargo,K.M., Bernstein,I.M., Amini,S.B., Incidence and risk factors associated with abnormal postpartum glucose tolerance in women with gestational diabetes, American Journal of Obstetrics and Gynecology, 165, 914-919, 1991	Postpartum OGTT results were assessed according to the NDDG criteria (not the same cut-offs as the WHO 1999 criteria)
Cho,N.H., Jang,H.C., Park,H.K., Cho,Y.W., Waist circumference is the key risk factor for diabetes in Korean women with history of gestational diabetes, Diabetes Research and Clinical Practice, 71, 177-183, 2006	Postpartum OGTT results were assessed according to the NDDG criteria
Chodick,G., Elchalal,U., Sella,T., Heymann,A.D., Porath,A., Kokia,E., Shalev,V., The risk of overt diabetes mellitus among women with gestational diabetes: a population-based study, Diabetic Medicine, 27, 779-785, 2010	Subjects underwent 50g glucose challenge tests not OGTT by the WHO criteria
Cocilovo,G., Tomasi,F., Guerra,S., Zampini,A., Cocurullo,A., Risk factors associated with persistence of glucose intolerance one year after gestational diabetes, Diabete et Metabolisme, 16, 187-191, 1990	Postpartum OGTT values were assessed by NDDG criteria
Committee on Obstetric Practice., ACOG Committee Opinion No. 435: postpartum screening for abnormal glucose tolerance in women who had gestational diabetes mellitus, Obstetrics and Gynecology, 113, 1419-1421, 2009	Opinion piece - no relevant data
Coustan,D.R., Carpenter,M.W., O'Sullivan,P.S., Carr,S.R., Gestational diabetes: predictors of subsequent disordered glucose metabolism, American Journal of Obstetrics and Gynecology, 168, 1139-1144, 1993	Criteria used to define postnatal diabetes and IGT similar to the NDDG criteria
Cypryk,K., Czupryniak,L., Wilczynski,J., Lewinski,A., Diabetes screening after gestational diabetes mellitus: poor performance of fasting plasma glucose, Acta Diabetologica, 41, 5-8, 2004	WHO 1985 criteria used to diagnose gestational diabetes
Dacus,J.V., Meyer,N.L., Muram,D., Stilson,R., Phipps,P., Sibai,B.M., Gestational diabetes: postpartum glucose tolerance testing, American Journal of Obstetrics and Gynecology, 171, 927-931, 1994	Postpartum OGTT results were assessed according to the NDDG criteria (not the same cut-offs as the WHO 1999 criteria)
Dalfra,M.G., Lapolla,A., Masin,M., Giglia,G., Dalla,Barba B., Toniato,R., Fedele,D., Antepartum and early postpartum predictors of type 2 diabetes development in women with gestational diabetes mellitus, Diabetes and Metabolism, 27, 675-680, 2001	WHO 1980 criteria used to define postnatal diabetes
Damm,P., Gestational diabetes mellitus and subsequent development of overt diabetes mellitus. [176 refs], Danish Medical Bulletin, 45, 495-509, 1998	Review paper - individual studies checked for inclusion
Damm,P., Kuhl,C., Bertelsen,A., Molsted-Pedersen,L., Predictive factors for the development of diabetes in women with previous gestational diabetes mellitus, American Journal of Obstetrics and Gynecology, 167, 607-616, 1992	WHO 1985 criteria used to define postnatal diabetes
Dornhorst,A., Bailey,P.C., Anyaoku,V., Elkeles,R.S., Johnston,D.G., Beard,R.W., Abnormalities of glucose tolerance following gestational diabetes, Quarterly Journal of Medicine, 77, 1219-1228, 1990	WHO 1985 criteria used to define postnatal diabetes
Efendic,S., Hanson,U., Persson,B., Wajngot,A., Luft,R., Glucose tolerance, insulin release, and insulin sensitivity in normal-weight women with previous gestational diabetes mellitus, Diabetes, 36, 413-419, 1987	Criteria for postpartum OGTT unclear - study defines results in terms of normal, borderline and decreased OGTT. Cut-offs for these categories do not match the WHO 1999 criteria

Excluded studies – Review questions 18 and 19	
Farrell,J., Forrest,J.M., Storey,G.N., Yue,D.K., Shearman,R.P., Turtle,J.R., Gestational diabetes--infant malformations and subsequent maternal glucose tolerance, Australian and New Zealand Journal of Obstetrics and Gynaecology, 26, 11-16, 1986	WHO 1980 criteria used to define postnatal diabetes
Feig,D.S., Zinman,B., Wang,X., Hux,J.E., Risk of development of diabetes mellitus after diagnosis of gestational diabetes.[Erratum appears in CMAJ. 2008 Aug 12;179(4):344], CMAJ Canadian Medical Association Journal, 179, 229-234, 2008	It is unclear whether diabetes was diagnosed on the basis of FPG, OGTT or another method. Also, study does not distinguish between type 1 and 2 diabetes.
Flack,J.R., Payne,T.J., Ross,G.P., Post-partum glucose tolerance assessment in women diagnosed with gestational diabetes: Evidence supporting the need to undertake an oral glucose tolerance test, Diabetic Medicine, 27, 243-244, 2010	Criteria used to assess postpartum OGTT not reported
Fuchtenbusch,M., Ferber,K., Standl,E., Ziegler,A.G., Prediction of type 1 diabetes postpartum in patients with gestational diabetes mellitus by combined islet cell autoantibody screening: a prospective multicenter study, Diabetes, 46, 1459-1467, 1997	Postnatal test results interpreted according to the WHO 1985 criteria
Fuhrmann,K., Targets in oral glucose tolerance testing, Carbohydrate Metabolism in Pregnancy and the Newborn IV, 227-238, 1989	No relevant data: study examines the reproducibility of the 75g OGTT during pregnancy not postnatally
Grant,P.T., Oats,J.N., Beischer,N.A., The long-term follow-up of women with gestational diabetes, Australian and New Zealand Journal of Obstetrics and Gynaecology, 26, 17-22, 1986	WHO 1980 criteria used to define postnatal diabetes
Greenberg,L.R., Moore,T.R., Murphy,H., Gestational diabetes mellitus: antenatal variables as predictors of postpartum glucose intolerance, Obstetrics and Gynecology, 86, 97-101, 1995	Postpartum OGTT results were assessed according to the NDDG criteria (not the same cut-offs as the WHO 1999 criteria)
Gunderson,E.P., Matias,S.L., Hurston,S.R., Dewey,K.G., Ferrara,A., Quesenberry,C.P.,Jr., Lo,J.C., Sternfeld,B., Selby,J.V., Study of Women, Infant Feeding, and Type 2 diabetes mellitus after GDM pregnancy (SWIFT), a prospective cohort study: methodology and design, BMC Public Health, 11, 952-, 2011	No relevant data
Hadden,D., The development of diabetes and its relation to pregnancy: the long term and short term historical viewpoint, Carbohydrate Metabolism in Pregnancy and the Newborn IV, 1-8, 1989	No relevant data
Hale,N.L., Probst,J.C., Liu,J., Martin,A.B., Bennett,K.J., Glover,S., Postpartum Screening for Diabetes among Medicaid-Eligible South Carolina Women with Gestational Diabetes, Womens Health Issues, 22, e163-e169, 2012	No relevant data - article focuses on rates of postpartum screening
Henry, O.A; Beischer, N.A,, Long-term implications of gestational diabetes for the mother, Baillereâ€ ™s Clinical Obstetrics and Gynecology, 461-483, 1991	Criteria used to define postnatal diabetes not reported but unlikely to be the WHO 1999 criteria as article was published in 1991
Hunger-Dathe,W., Mosebach,N., Samann,A., Wolf,G., Muller,U.A., Prevalence of impaired glucose tolerance 6 years after gestational diabetes, Experimental and Clinical Endocrinology and Diabetes, 114, 11-17, 2006	Postpartum OGTT results assessed according to German guidelines (not the WHO criteria)
Hunt,K.J., Logan,S.L., Conway,D.L., Korte,J.E., Postpartum screening following GDM: how well are we doing?. [41 refs], Current Diabetes Reports, 10, 235-241, 2010	No relevant data
Jang,H.C., Gestational diabetes in Korea: incidence and risk factors of diabetes in women with previous gestational diabetes, Diabetes and Metabolism Journal, 35, 1-7, 2011	Review article - individual studies have been checked for inclusion
Jarvela,I.Y., Juutinen,J., Koskela,P., Hartikainen,A.L., Kulmala,P., Knip,M., Tapanainen,J.S., Gestational diabetes identifies women at risk for permanent type 1 and type 2 diabetes in fertile age: predictive role of autoantibodies, Diabetes Care, 29, 607-612, 2006	No OGTT data during follow-up. Diagnosis of diabetes was based on questionnaire information and on the use of oral antihyperglycaemic medication
Kakad,R., Anwar,A., Dyer,P., Webber,J., Dale,J., Fasting plasma glucose is not sufficient to detect ongoing glucose intolerance after pregnancy complicated by gestational diabetes, Experimental and Clinical Endocrinology and Diabetes, 118, 234-236, 2010	Although the article states the WHO criteria were used, the cut-offs reported do not match the WHO criteria exactly (normal: FPG<6.0, 2-hour glucose <7.8, IFG: FPG 6.0-7.0, 2-hour glucose <7.8, IGT: FPG<7.0, 2-hour glucose 7.8-11.0, Diabetes: FPG>/=7.1 or 2-hour glucose >/=11.0mmol/l)
Kaufmann,R.C., Schleyhahn,F.T., Huffman,D.G., Amankwah,K.S., Gestational diabetes diagnostic criteria: long-term maternal follow-up, American Journal of Obstetrics and Gynecology, 172, 621-625, 1995	A modified form of the NDDG criteria used to define participants as normal, glucose intolerant or diabetic
Kaufmann,R.C., Smith,T., Bochantin,T., Khardori,R., Evans,M.S., Steahly,L., Failure to obtain follow-up testing for gestational diabetic patients in a rural population, Obstetrics and Gynecology, 93, 734-737, 1999	NDDG criteria used to define glucose intolerance
Kim,C., Newton,K.M., Knopp,R.H., Gestational diabetes and the incidence of type 2 diabetes: a systematic review. [55 refs], Diabetes Care, 25, 1862-1868, 2002	Review paper - individual studies checked for inclusion

Excluded studies – Review questions 18 and 19	
Kjos,S.L., Buchanan,T.A., Greenspoon,J.S., Montoro,M., Bernstein,G.S., Mestman,J.H., Gestational diabetes mellitus: the prevalence of glucose intolerance and diabetes mellitus in the first two months post partum, American Journal of Obstetrics and Gynecology, 163, 93-98, 1990	Postpartum OGTT results were assessed according to the NDDG criteria (not the same cut-offs as the WHO 1999 criteria)
Kjos,S.L., Peters,R.K., Xiang,A., Henry,O.A., Montoro,M., Buchanan,T.A., Predicting future diabetes in Latino women with gestational diabetes. Utility of early postpartum glucose tolerance testing, Diabetes, 44, 586-591, 1995	NDDG criteria used to define diabetes
Ko,G.T., Chan,J.C., Tsang,L.W., Li,C.Y., Cockram,C.S., Glucose intolerance and other cardiovascular risk factors in chinese women with a history of gestational diabetes mellitus, Australian and New Zealand Journal of Obstetrics and Gynaecology, 39, 478-483, 1999	WHO 1985 criteria used to define postnatal diabetes
Kwak,S.H., Kim,H.S., Choi,S.H., Lim,S., Cho,Y.M., Park,K.S., Jang,H.C., Kim,M.Y., Cho,N.H., Metzger,B.E., Subsequent pregnancy after gestational diabetes mellitus: frequency and risk factors for recurrence in Korean women, Diabetes Care, 31, 1867-1871, 2008	No relevant data - study aims to determine the frequency of recurrent gestational diabetes and to find risk factors that can predict the recurrence of gestational diabetes in women with previous gestational diabetes
Lam,K.S., Li,D.F., Lauder,I.J., Lee,C.P., Kung,A.W., Ma,J.T., Prediction of persistent carbohydrate intolerance in patients with gestational diabetes, Diabetes Research and Clinical Practice, 12, 181-186, 1991	WHO 1980 criteria used to define postnatal diabetes
Lee,C.P., Wong,H.S., Chan,F.Y., Pun,T.C., To,W.K., Lam,Y.H., Baldwin,S., Wong,V.C.W., Long-term prognosis of women with abnormal glucose tolerance in pregnancy, Australian and New Zealand Journal of Obstetrics and Gynaecology, 34, 507-510, 1994	Postpartum OGTT results assessed by modified WHO criteria. Normal (fasting <6.0mmol/l, 2 hour <8mmol/l), IGT (fasting <8mmol/l, 2 hour >/=8 and <11.0mmol/l), Diabetes (>/=8.0, 2 hour any level or any level >/=11.0)
Lee,K.F., Mak,M.W., Lau,K.O., Chung,H.H., Risk of development of diabetes mellitus in Chinese women with persistently impaired glucose tolerance after gestational diabetes, Hong Kong Medical Journal, 17, 195-201, 2011	Study aims to find out after gestational diabetes, how many women with postpartum IGT progress to diabetes (women who have not returned to normoglycaemia after pregnancy)
Linne,Y., Barkeling,B., Rossner,S., Natural course of gestational diabetes mellitus: long term follow up of women in the SPAWN study, BJOG: An International Journal of Obstetrics and Gynaecology, 109, 1227-1231, 2002	Postnatal diabetes defined by 2-hour blood glucose value >10mmol/l (not the WHO criteria)
LOVE,E.J., STEVENSON,J.A., KINCH,R.A., EVALUATION OF ORAL AND INTRAVENOUS GLUCOSE TOLERANCE TESTS FOR THE DIAGNOSIS OF "PREDIABETES" IN THE PUERPERIUM, American Journal of Obstetrics and Gynecology, 88, 283-290, 1964	Article not of relevance
Mazze,R.S., Langer,O., Primary, secondary, and tertiary prevention. Program for diabetes in pregnancy, Diabetes Care, 11, 263-268, 1988	Criteria used to define postnatal diabetes not reported
McGrath,N.M., Coats,A., Barach,O., Improved post-partum follow-up of patients with gestational diabetes mellitus using HbA1c, Diabetic Medicine, 30, 1264-1265, 2013	Criteria used to assess the postpartum OGTT results are not reported
Mehmet,S., Fincher,S., Ibrahim,S., NICE challenge on postnatal reclassification of glucose tolerance in women previously diagnosed with gestational diabetes mellitus, Practical Diabetes International, 27, 346-348, 2010	Name of the criteria used to assess postpartum OGTTs was not explicitly stated. Cut-offs given were similar but not exactly the same as WHO 1999: FPG <6.0, FPG 6.0-6.9, FPG>/=7.0, 2-hour PG <7.8, 2-hour PG 7.8-11.0, 2-hour PG >/=11.1. Corresponding categories (IFG, IGT, Diabetes)for these cut-offs were not reported in the article
Mestman,J.H., Anderson,G.V., Guadalupe,V., Follow-up study of 360 subjects with abnormal carbohydrate metabolism during pregnancy, Obstetrics and Gynecology, 39, 421-425, 1972	Criteria for interpreting postpartum OGTT were those proposed by Fajans (non-WHO)
Metzger,B.E., Bybee,D.E., Freinkel,N., Phelps,R.L., Radvany,R.M., Vaisrub,N., Gestational diabetes mellitus. Correlations between the phenotypic and genotypic characteristics of the mother and abnormal glucose tolerance during the first year postpartum, Diabetes, 34 Suppl 2, 111-115, 1985	100g postpartum OGTTs were interpreted by criteria similar to those recommended by the NDDG
Metzger,B.E., Cho,N.H., Roston,S.M., Radvany,R., Prepregnancy weight and antepartum insulin secretion predict glucose tolerance five years after gestational diabetes mellitus, Diabetes Care, 16, 1598-1605, 1993	Postpartum OGTT results were assessed by the NDDG criteria
Mohamed,N., Dooley,J., Gestational diabetes and subsequent development of NIDDM in aboriginal women of northwestern Ontario, International Journal of Circumpolar Health, 57 Suppl 1, 355-358, 1998	Diabetes was defined according to WHO standards by either an abnormal 75g glucose tolerance test, fasting and 2 hour postprandial or a random blood glucose. Article does not state whether the 1985 or 1999 criteria were used but unlikely to be 1999 criteria because the article was published in 1998
Morrison,M.K., Collins,C.E., Lowe,J.M., Postnatal testing for diabetes in Australian women following gestational diabetes mellitus, Australian and New Zealand Journal of Obstetrics and Gynaecology, 49, 494-498, 2009	No relevant data
Mukerji,G., Chiu,M., Shah,B.R., Impact of gestational diabetes on the risk of diabetes following pregnancy among Chinese and South Asian women, Diabetologia, 55, 2148-2153, 2012	Diagnostic criteria used to assess the postpartum OGTT results are not reported

Excluded studies – Review questions 18 and 19	
Nicholson,W.K., Wilson,L.M., Witkop,C.T., Baptiste-Roberts,K., Bennett,W.L., Bolen,S., Barone,B.B., Golden,S.H., Gary,T.L., Neale,D.M., Bass,E.B., Therapeutic management, delivery, and postpartum risk assessment and screening in gestational diabetes. [107 refs], Evidence Report/Technology Assessment, 1-96, 2008	Individual studies have been checked for inclusion
Oats,J.N., Beischer,N.A., The persistence of abnormal glucose tolerance after delivery, Obstetrics and Gynecology, 75, 397-401, 1990	WHO 1985 criteria used to classify postnatal diabetes
O'Sullivan,J.B., Diabetes mellitus after GDM, Diabetes, 40 Suppl 2, 131-135, 1991	All studies in this review were published before 1990 and so they could not have used the WHO 1999 criteria
O'Sullivan,J.B., The Boston gestational diabetes studies: review and perspectives, Carbohydrate metabolism in pregnancy and the newborn, 287-294, 1989	WHO 1985 criteria used to define postnatal diabetes
Persson,B., Hanson,U., Hartling,S.G., Binder,C., Follow-up of women with previous GDM. Insulin, C-peptide, and proinsulin responses to oral glucose load, Diabetes, 40 Suppl 2, 136-141, 1991	WHO 1985 criteria used to define postnatal diabetes
Peters,R.K., Kjos,S.L., Xiang,A., Buchanan,T.A., Long-term diabetogenic effect of single pregnancy in women with previous gestational diabetes mellitus, Lancet, 347, 227-230, 1996	Postpartum OGTT values were assessed according to the NDDG criteria
Pettitt,D.J., Knowler,W.C., Baird,H.R., Bennett,P.H., Gestational diabetes: infant and maternal complications of pregnancy in relation to third-trimester glucose tolerance in the Pima Indians, Diabetes Care, 3, 458-464, 1980	OGTT was performed during the third trimester of pregnancy, not postnatally
Pettitt,D.J., Narayan,K.M., Hanson,R.L., Knowler,W.C., Incidence of diabetes mellitus in women following impaired glucose tolerance in pregnancy is lower than following impaired glucose tolerance in the non-pregnant state, Diabetologia, 39, 1334-1337, 1996	WHO 1985 criteria used to define postnatal diabetes
Picon,M.J., Murri,M., Munoz,A., Fernandez-Garcia,J.C., Gomez-Huelgas,R., Tinahones,F.J., Hemoglobin A1c versus oral glucose tolerance test in postpartum diabetes screening, Diabetes Care, 35, 1648-1653, 2012	Criteria used to assess the postpartum OGTT results are not similar to WHO 1999 criteria
Pierce,M.B., Modder,J., Mortagy,I., Hughes,H., Springett,A., Baldeweg,S., Follow-up of women with gestational diabetes in England, Archives of Disease in Childhood: Fetal and Neonatal Edition, 95, Fa38-Fa39, 2010	Conference abstract
Reidy,J., Chalupka,S., Gestational diabetes-what comes next?, AAOHN Journal, 58, 80-, 2010	No relevant data
Retnakaran,R., Qi,Y., Connelly,P.W., Sermer,M., Hanley,A.J., Zinman,B., Risk of early progression to prediabetes or diabetes in women with recent gestational dysglycaemia but normal glucose tolerance at 3-month postpartum, Clinical Endocrinology, 73, 476-483, 2010	Incidence data is presented in terms of prediabetes/diabetes. Though cut-off in article for diabetes matches the WHO criteria, the prediabetes (IGT) cut-off does not match WHO.
Retnakaran,R., Qi,Y., Sermer,M., Connelly,P.W., Hanley,A.J., Zinman,B., Glucose intolerance in pregnancy and future risk of pre-diabetes or diabetes, Diabetes Care, 31, 2026-2031, 2008	Study focuses on how antenatal factors predict dysglycaemia at 3 months' postpartum
Retnakaran,R., Qi,Y., Sermer,M., Connelly,P.W., Zinman,B., Hanley,A.J., Isolated hyperglycemia at 1 hour on oral glucose tolerance test in pregnancy resembles gestational diabetes mellitus in predicting postpartum metabolic dysfunction, Diabetes Care, 31, 1275-1281, 2008	Study focuses on how isolated hyperglycaemia at 1 hour on OGTT during pregnancy resembles gestational diabetes in predicting postpartum metabolic dysfunction
Russell,M.A., Phipps,M.G., Olson,C.L., Welch,H.G., Carpenter,M.W., Rates of postpartum glucose testing after gestational diabetes mellitus, Obstetrics and Gynecology, 108, 1456-1462, 2006	Cut-off for postpartum diabetes does not exactly match the WHO criteria (>7 or >11.1 instead of >=).
Saleh,A.K., Moussa,M.A., Hathout,H., Postpartum glycated hemoglobin A1c and glucose tolerance test in mothers of large babies, International Journal of Gynaecology and Obstetrics, 26, 5-9, 1988	Population not of interest - focus is on women with large babies not women with gestational diabetes
Salzberger,M., Sharon,A., Liban,E., Significance of the oral glucose tolerance test performed on the third day after delivery for the diagnosis of diabetes in pregnancy, Israel Journal of Medical Sciences, 11, 629-631, 1975	Article examines the significance of the OGTT in diagnosing diabetes in pregnancy not postnatal diabetes
Sameshima,H., Higo,T., Ikenoue,T., Longitudinal changes in plasma glucose values of the 75-g glucose tolerance test in triplet pregnancies, American Journal of Perinatology, 21, 49-55, 2004	No relevant data
Seghieri,G., Tesi,F., De,Bellis A., Anichini,R., Fabbri,G., Seghieri,M., Franconi,F., Long term predictors of post-partum glucose metabolism in women with gestational diabetes mellitus, Experimental and Clinical Endocrinology and Diabetes, 118, 485-489, 2010	IGT or type 2 diabetes was diagnosed on the basis of a 2-hour plasma glucose at OGTT of >=7.8mmol/l
Shah,B., Lowe,J., Inadequate screening for type 2 diabetes following pregnancy complicated by gestational diabetes, Canadian Journal of Diabetes, 33, 192-, 2009	Conference abstract
Shah,B.R., Lipscombe,L.L., Feig,D.S., Lowe,J.M., Missed opportunities for type 2 diabetes testing following gestational diabetes: a population-based cohort study, BJOG: An International Journal of Obstetrics and Gynaecology, 118, 1484-1490, 2011	No relevant data

Excluded studies – Review questions 18 and 19	
Sinha,B., Brydon,P., Taylor,R.S., Hollins,A., Munro,A., Jenkins,D., Dunne,F., Maternal ante-natal parameters as predictors of persistent postnatal glucose intolerance: a comparative study between Afro-Caribbeans, Asians and Caucasians, Diabetic Medicine, 20, 382-386, 2003	Criteria used to define postpartum OGTT results not reported
Smirnakis,K.V., Chasan-Taber,L., Wolf,M., Markenson,G., Ecker,J.L., Thadhani,R., Postpartum diabetes screening in women with a history of gestational diabetes, Obstetrics and Gynecology, 106, 1297-1303, 2005	No relevant data
Stage,E., Ronneby,H., Damm,P., Lifestyle change after gestational diabetes, Diabetes Research and Clinical Practice, 63, 67-72, 2004	Postnatal criteria used to define diabetes and IGT not reported
Stangenberg,M., Agarwal,N., Rahman,F., Sheth,K., al,Sedeiry S., De,Vol E., Frequency of HLA genes and islet cell antibodies (ICA) and result of postpartum oral glucose tolerance tests (OGTT) in Saudi Arabian women with abnormal OGTT during pregnancy, Diabetes Research, 14, 9-13, 1990	Postnatal OGTT evaluated according to the WHO criteria. Assuming this refers to the WHO 1985/1980 criteria because the article was published in 1990 (i.e. before publication of the WHO 1999 criteria)
Steinhart,J.R., Sugarman,J.R., Connell,F.A., Gestational diabetes is a herald of NIDDM in Navajo women. High rate of abnormal glucose tolerance after GDM, Diabetes Care, 20, 943-947, 1997	WHO 1985 criteria used to define postnatal diabetes
Tan,Y.Y., Yeo,S.H., Liauw,P.C., Is postnatal oral glucose tolerance testing necessary in all women with gestational diabetes, Singapore Medical Journal, 37, 384-388, 1996	WHO 1985 criteria used to define postnatal diabetes
tley-Lewis,R., Levkoff,S., Stuebe,A., Seely,E.W., Gestational diabetes mellitus: Postpartum opportunities for the diagnosis and prevention of type 2 diabetes mellitus, Nature Clinical Practice Endocrinology and Metabolism, 4, 552-558, 2008	Review paper discussing current guidelines for postpartum screening, how they might be implemented, and who should take responsibility for screening women at risk of type 2 diabetes (no relevant data)
Vitoratos,N., Salamalekis,E., Loghis,S., Kassanos,D., Giannaris,D., Creatsas,G., Changes of glucose tolerance after delivery in women with gestational diabetes, Clinical and Experimental Obstetrics and Gynecology, 27, 212-214, 2000	WHO 1985 criteria used to define postnatal diabetes
Wein,P., Beischer,N.A., Sheedy,M.T., Studies of postnatal diabetes mellitus in women who had gestational diabetes. Part 2. Prevalence and predictors of diabetes mellitus after delivery, Australian and New Zealand Journal of Obstetrics and Gynaecology, 37, 420-423, 1997	WHO 1985 criteria used to define postnatal diabetes
Weinert,L.S., Mastella,L.S., Oppermann,M.L., Silveiro,S.P., Guimaraes,L.S., Reichelt,A.J., Postpartum glucose tolerance status 6 to 12 weeks after gestational diabetes mellitus: a Brazilian cohort, Arquivos Brasileiros de Endocrinologia e Metabologia, 58, 197-204, 2014	Criteria used to assess the postpartum OGTT results are not similar to WHO 1999 criteria
Werner,E.F., Tarabulsi,G., Han,C., Satin,A., Early postpartum diabetes screening for women with gestational diabetes mellitus, Obstetrics and Gynecology, 123 Suppl 1, 82S-, 2014	Abstract
Zonenberg,A., Telejko,B., Topolska,J., Szelachowska,M., Zarzycka,B., Modzelewska,A., Nikolajuk,A., Kinalska,I., Gorska,M., Factors predisposing to disturbed carbohydrate tolerance in patients with previous gestational diabetes mellitus, Diabetologia Doswiadczalna i Kliniczna, 6, 143-150, 2006	Timing of postnatal test not reported. Also, postpartum OGTT values were assessed according to Polish Diabetes Association guidelines

Appendix H: Evidence tables

Evidence tables are in a separate Appendices file – Appendix H.

Appendix I: Minimally important differences

I.1 Preconception care

Table 5: MIDs for continuous outcomes for the review of oral contraception in women with diabetes compared to those without diabetes

Outcome	MID
Filtration fraction	0.01
Glomerular filtration rate	0.51
Plasma renin activity	0.005
RPF	9.685
Urine NA	0.51
Urine protein	22.68
Fasting glucose (mg/dl)	18.09
Fasting glucose (mmol/l)	1
Mean arterial pressure	1.02

Table 6: MIDs for mean change from baseline for outcomes to 3 months in women with diabetes using or not using oral contraceptives

Outcome	Group	Author	MID
HbA1c (%)	Combi low estrogen OC TYPE 1	Grigoryan	0.204
HbA1c (%)	Combi low estrogen OC TYPE 2	Grigoryan	0.272
HbA1c (%)	Combi standard OC TYPE 1	Grigoryan	0.127
HbA1c (%)	Combi standard OC TYPE 2	Grigoryan	0.222
HbA1c (%)	Combi low progestogen OC TYPE 1	Grigoryan	0.127
HbA1c (%)	Combi low progestogen OC TYPE 2	Grigoryan	0.249
HbA1c (%)	IUD group TYPE 1	Grigoryan	0.296
HbA1c (%)	IUD group TYPE 2	Grigoryan	0.06
HbA1c (%)	No contraceptives	Grigoryan	0.241
Total cholesterol (mmol/l)	OC	Diab	0.416
Total cholesterol (mmol/l)	IUD	Diab	0.105
Total cholesterol (mmol/l)	OC	Petersen	NC
Total cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol/total cholesterol (mmol/l)	OC	Petersen	NC
HDL cholesterol/total cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol (mmol/l)	OC	Diab	0.19
HDL cholesterol (mmol/l)	IUD	Diab	0.14
HDL cholesterol (mmol/l)	OC	Petersen	NC
HDL cholesterol (mmol/l)	No OC	Petersen	NC
HDL2 cholesterol (mmol/l)	OC	Petersen	NC
HDL2 cholesterol (mmol/l)	No OC	Petersen	NC
HDL3 cholesterol (mmol/l)	OC	Petersen	NC
HDL3 cholesterol (mmol/l)	No OC	Petersen	NC

Outcome	Group	Author	MID
Triglycerides (mmol/l)	OC	Diab	0.388
Triglycerides (mmol/l)	IUD	Diab	0.288
Triglycerides (mmol/l)	OC	Petersen	NC
Triglycerides (mmol/l)	No OC	Petersen	NC
Triglycerides (mmol/l)	Monophasic combined LD OC	Skouby	NC
Triglycerides (mmol/l)	Progestogen only OC	Skouby	NC
Systolic blood pressure (mmHg)	OC	Diab	0.083
Systolic blood pressure (mmHg)	IUD	Diab	0.111
Diastolic blood pressure (mmHg)	OC	Diab	NC
Diastolic blood pressure (mmHg)	IUD	Diab	NC

Table 7: MIDs for mean change from baseline for outcomes to 6 months in women with diabetes using or not using oral contraceptives

Outcome	Group	Author	MID
HbA1c (%)	Monophasic combined LD OC	Skouby	0.356
HbA1c (%)	Progestogen only OC	Skouby	0.385
HbA1c (%)	Triphasic combined OC	Skouby	0.243
HbA1c (%)	Monophasic HD combined OC	Skouby	0.282
HbA1c (%)	Combi low estrogen OC TYPE 1	Grigoryan	0.175
HbA1c (%)	Combi low estrogen OC TYPE 2	Grigoryan	0.204
HbA1c (%)	Combi standard OC TYPE 1	Grigoryan	0.127
HbA1c (%)	Combi standard OC TYPE 2	Grigoryan	0.279
HbA1c (%)	Combi low progestogen OC TYPE 1	Grigoryan	0.175
HbA1c (%)	Combi low progestogen OC TYPE 2	Grigoryan	0.226
HbA1c (%)	IUD group TYPE 1	Grigoryan	0.127
HbA1c (%)	IUD group TYPE 2	Grigoryan	0.342
HbA1c (%)	No contraceptives	Grigoryan	0.274
Total cholesterol (mmol/l)	OC	Diab	0.378
Total cholesterol (mmol/l)	IUD	Diab	0.241
Total cholesterol (mmol/l)	OC	Petersen	NC
Total cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol/total cholesterol (mmol/l)	Monophasic combined LD OC	Skouby	0.049
HDL cholesterol/total cholesterol (mmol/l)	Progestogen only OC	Skouby	0.049
HDL cholesterol/total cholesterol (mmol/l)	Triphasic combined OC	Skouby	0.049
HDL cholesterol/total cholesterol (mmol/l)	Monophasic combined HD OC	Skouby	0.049
HDL cholesterol/total cholesterol (mmol/l)	OC	Petersen	NC

Outcome	Group	Author	MID
HDL cholesterol/total cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol (mmol/l)	OC	Diab	0.175
HDL cholesterol (mmol/l)	IUD	Diab	0.143
HDL cholesterol (mmol/l)	OC	Petersen	NC
HDL cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol (mmol/l)	Monophasic combined LD OC	Skouby	0.055
HDL cholesterol (mmol/l)	Progestogen only OC	Skouby	0.052
HDL cholesterol (mmol/l)	Triphasic combined OC	Skouby	0.049
HDL cholesterol (mmol/l)	Monophasic combined HD OC	Skouby	0.073
HDL2 cholesterol (mmol/l)	OC	Petersen	NC
HDL2 cholesterol (mmol/l)	No OC	Petersen	NC
HDL3 cholesterol (mmol/l)	OC	Petersen	NC
HDL3 cholesterol (mmol/l)	No OC	Petersen	NC
LDL cholesterol (mmol/l)	Monophasic combined LD OC	Skouby	0.194
LDL cholesterol (mmol/l)	Progestogen only OC	Skouby	0.101
LDL cholesterol (mmol/l)	Triphasic combined OC	Skouby	0.127
LDL cholesterol (mmol/l)	Monophasic combined HD OC	Skouby	0.195
LDL cholesterol (mmol/l)	OC	Diab	0.448
LDL cholesterol (mmol/l)	IUD	Diab	0.32
LDL cholesterol (mmol/l)	OC	Petersen	NC
LDL cholesterol (mmol/l)	No OC	Petersen	NC
VLDL cholesterol (mmol/l)	OC	Petersen	NC
VLDL cholesterol (mmol/l)	No OC	Petersen	NC
VLDL cholesterol (mmol/l)	Monophasic combined LD OC	Skouby	0.091
VLDL cholesterol (mmol/l)	Progestogen only OC	Skouby	0.05
VLDL cholesterol (mmol/l)	Triphasic combined OC	Skouby	0.05
VLDL cholesterol (mmol/l)	Monophasic combined HD OC	Skouby	0.053
Triglycerides (mmol/l)	OC	Diab	0.084
Triglycerides (mmol/l)	IUD	Diab	0.082
Triglycerides (mmol/l)	OC	Petersen	NC
Triglycerides (mmol/l)	No OC	Petersen	NC
Triglycerides (mmol/l)	Monophasic combined LD OC	Skouby	0.208
Triglycerides (mmol/l)	Progestogen only OC	Skouby	0.053
Triglycerides (mmol/l)	Triphasic combined OC	Skouby	0.128
Triglycerides (mmol/l)	Monophasic HD combined OC	Skouby	0.083
Free fatty acids (mmol/l)	Monophasic combined LD OC	Skouby	58.663
Free fatty acids (mmol/l)	Progestogen only OC	Skouby	79.434
Free fatty acids (mmol/l)	Triphasic combined OC	Skouby	59.837
Free fatty acids (mmol/l)	Monophasic HD combined OC	Skouby	73.043
Systolic blood pressure (mmHg)	OC	Diab	1.765
Systolic blood pressure (mmHg)	IUD	Diab	1.801
Diastolic blood pressure (mmHg)	OC	Diab	1.92
Diastolic blood pressure (mmHg)	IUD	Diab	2.391

Table 8: MIDs for mean change from baseline for outcomes to 9 months in women with diabetes using or not using oral contraceptives

Outcome	Group	Author	MID
HbA1c (%)	Combi low estrogen OC TYPE 1	Grigoryan	0.149
HbA1c (%)	Combi low estrogen OC TYPE 2	Grigoryan	0.251
HbA1c (%)	Combi standard OC TYPE 1	Grigoryan	0.232
HbA1c (%)	Combi standard OC TYPE 2	Grigoryan	0.201
HbA1c (%)	Combi low progestogen OC TYPE 1	Grigoryan	0.233
HbA1c (%)	Combi low progestogen OC TYPE 2	Grigoryan	0.188
HbA1c (%)	IUD group TYPE 1	Grigoryan	0.244
HbA1c (%)	IUD group TYPE 2	Grigoryan	0.279
HbA1c (%)	No contraceptives	Grigoryan	0.325
Total cholesterol (mmol/l)	OC	Diab	0.385
Total cholesterol (mmol/l)	IUD	Diab	0.206
HDL cholesterol (mmol/l)	OC	Diab	0.181
HDL cholesterol (mmol/l)	IUD	Diab	0.101

Table 9: MIDs for mean change from baseline for outcomes to 3 months in women with diabetes using or not using oral contraceptives

Outcome	Group	Author	MID
HbA1c (%)	OC	Petersen	NC
HbA1c (%)	No OC	Petersen	NC
HbA1c (%)	Combi low estrogen OC TYPE 1	Grigoryan	0.233
HbA1c (%)	Combi low estrogen OC TYPE 2	Grigoryan	0.3
HbA1c (%)	Combi standard OC TYPE 1	Grigoryan	0.172
HbA1c (%)	Combi standard OC TYPE 2	Grigoryan	0.174
HbA1c (%)	Combi low progestogen OC TYPE 1	Grigoryan	0.173
HbA1c (%)	Combi low progestogen OC TYPE 2	Grigoryan	0.278
HbA1c (%)	IUD group TYPE 1	Grigoryan	0.263
HbA1c (%)	IUD group TYPE 2	Grigoryan	0.264
HbA1c (%)	No contraceptives	Grigoryan	0.228
Total cholesterol (mmol/l)	OC	Petersen	NC
Total cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol/total cholesterol (mmol/l)	OC	Petersen	NC
HDL cholesterol/total cholesterol (mmol/l)	No OC	Petersen	NC
HDL cholesterol (mmol/l)	OC	Petersen	NC
HDL cholesterol (mmol/l)	No OC	Petersen	NC
HDL2 cholesterol (mmol/l)	OC	Petersen	NC
HDL2 cholesterol (mmol/l)	No OC	Petersen	NC
HDL3 cholesterol (mmol/l)	OC	Petersen	NC
HDL3 cholesterol (mmol/l)	No OC	Petersen	NC
LDL cholesterol (mmol/l)	OC	Petersen	NC

Outcome	Group	Author	MID
LDL cholesterol (mmol/l)	No OC	Petersen	NC
VLDL cholesterol (mmol/l)	OC	Petersen	NC
VLDL cholesterol (mmol/l)	No OC	Petersen	NC
Triglycerides (mmol/l)	OC	Petersen	NC
Triglycerides (mmol/l)	No OC	Petersen	NC
Free fatty acids (mmol/l)	OC	Petersen	NC
Free fatty acids (mmol/l)	No OC	Petersen	NC
Arterial blood pressure (mmHg)	OC	Petersen	NC
Arterial blood pressure (mmHg)	No OC	Petersen	NC

I.2 Continuous glucose monitoring

Table 10: MIDs for continuous outcomes for the review of continuous glucose monitoring

Outcome	MID
Gestational age at birth	0.65
HbA1c (28 to 32 weeks)	0.36
HbA1c (32 to 36 weeks)	0.36
Mean glucose level	0.45
Days in NICU per treated neonate	0.86

I.3 Antenatal specialist teams

Table 11: MIDs for continuous outcomes for the review of antenatal specialist teams

	MID
HbA1c in the first trimester in women with Type 1 or 2 diabetes	0.415
HbA1c in the second trimester in women with Type 1 or 2 diabetes	0.465

Appendix J: Compiled forest plots

J.1 Interventions for gestational diabetes

J.1.1 Comparison: Diet versus standard care

Figure 1: Caesarean section

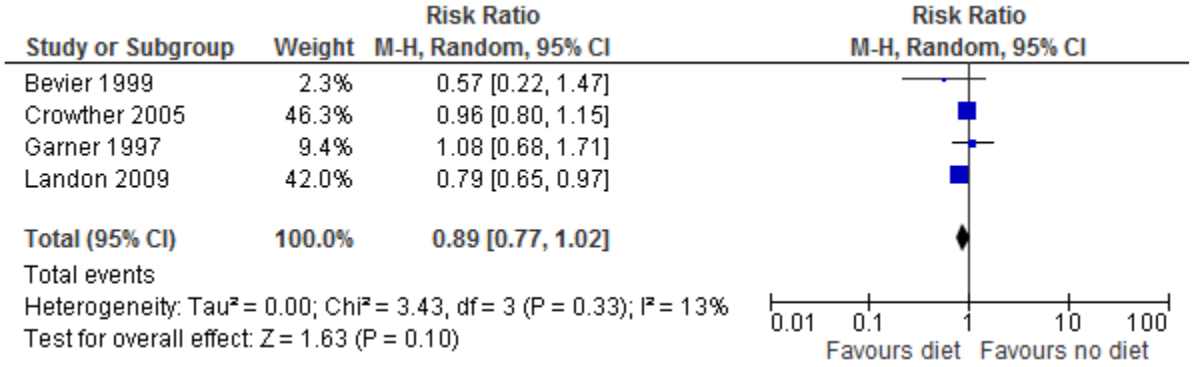


Figure 2: Induction of labour

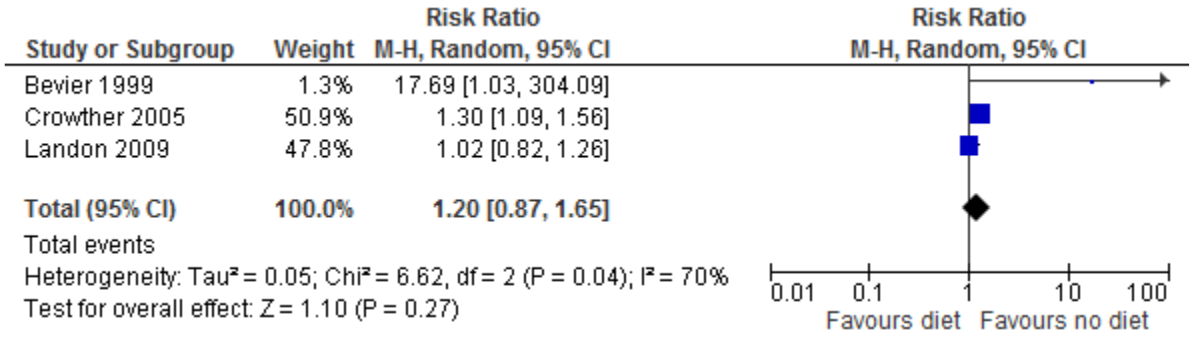


Figure 3: Large for gestational age births

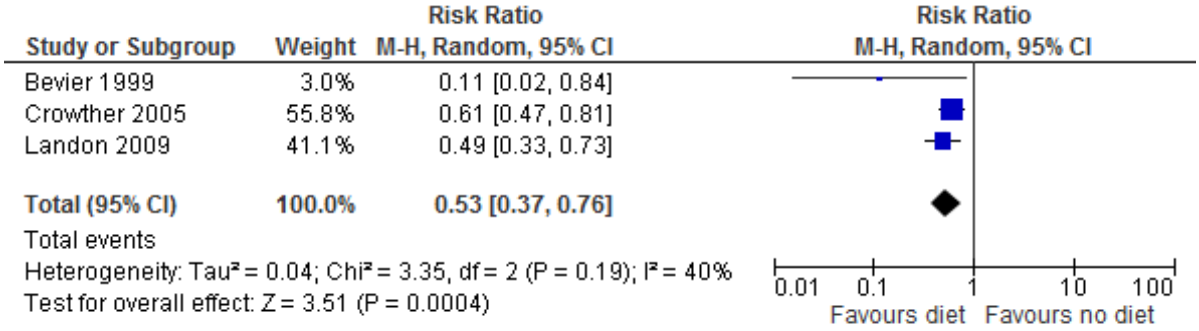
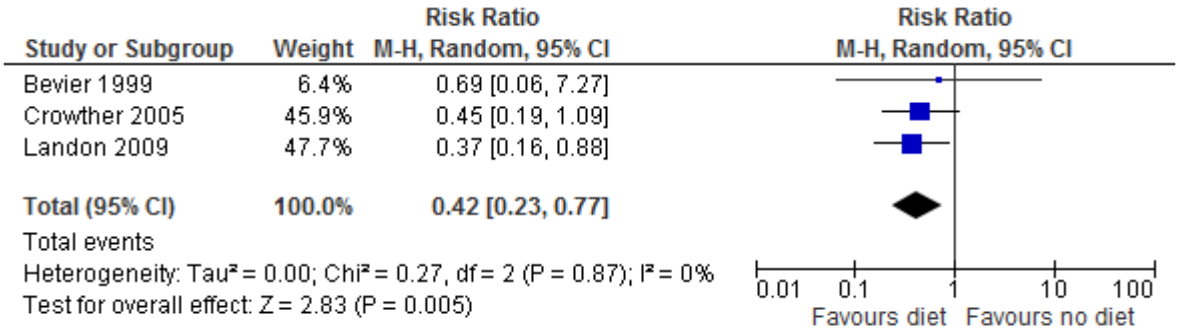


Figure 4: Shoulder dystocia



J.1.2 Comparison: Metformin versus insulin

Figure 5: Spontaneous vaginal birth

Figure 6: Induction of labour

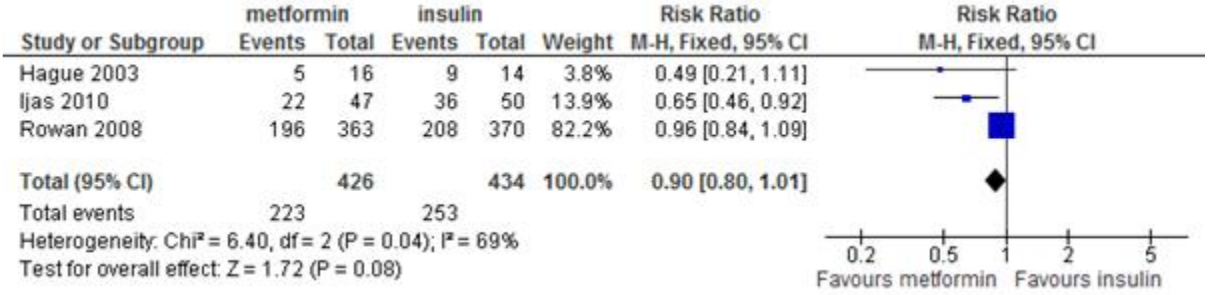
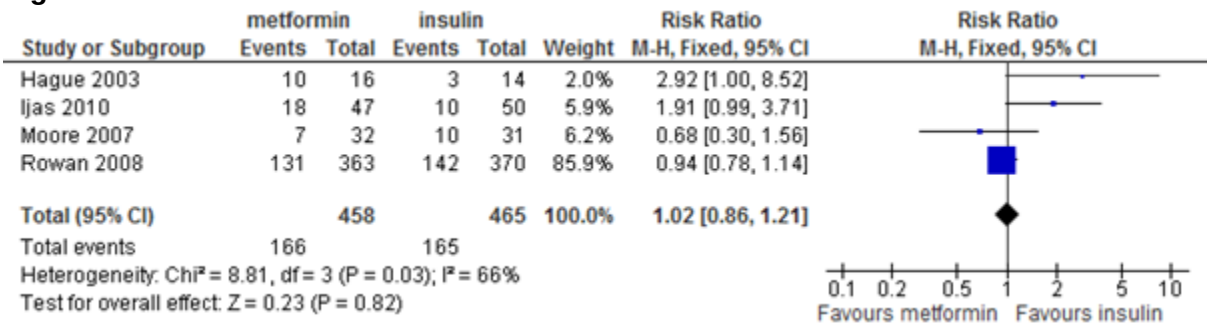


Figure 7: Caesarean section



J.2 Continuous glucose monitoring

J.2.1 Comparison: Continuous versus intermittent monitoring

Figure 8: Vaginal (unassisted/non-instrumental) birth

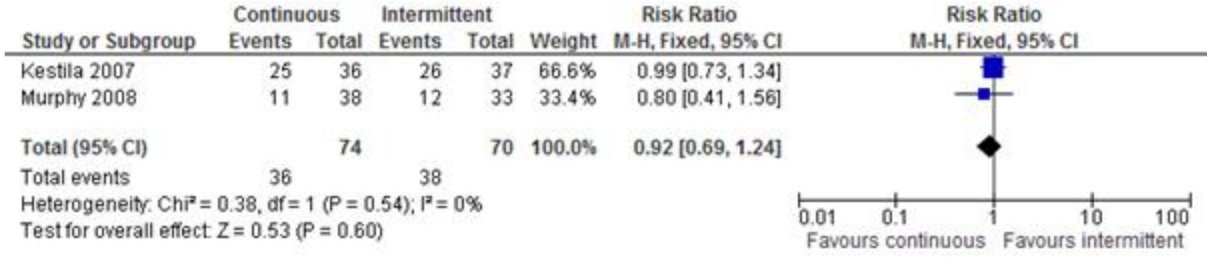


Figure 9: Caesarean section

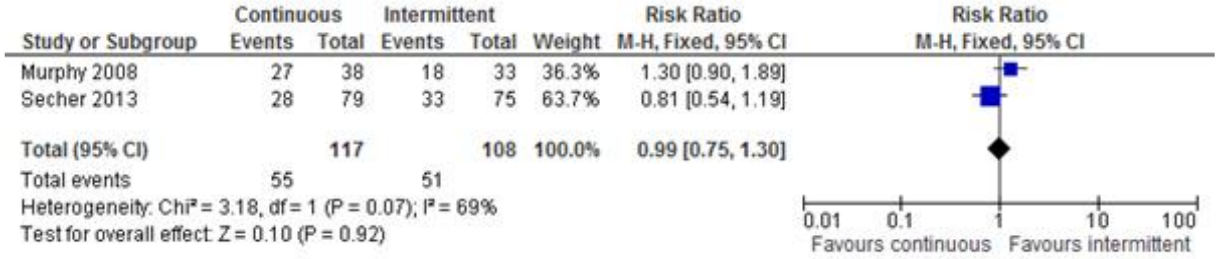


Figure 10: Caesarean section

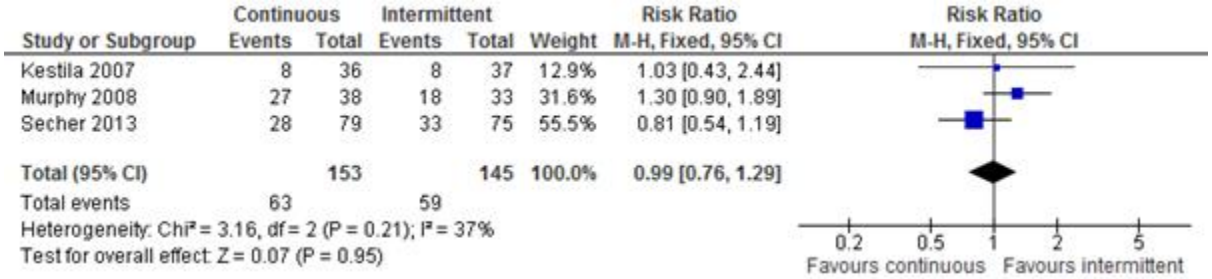


Figure 11: Preterm birth (<37 weeks)

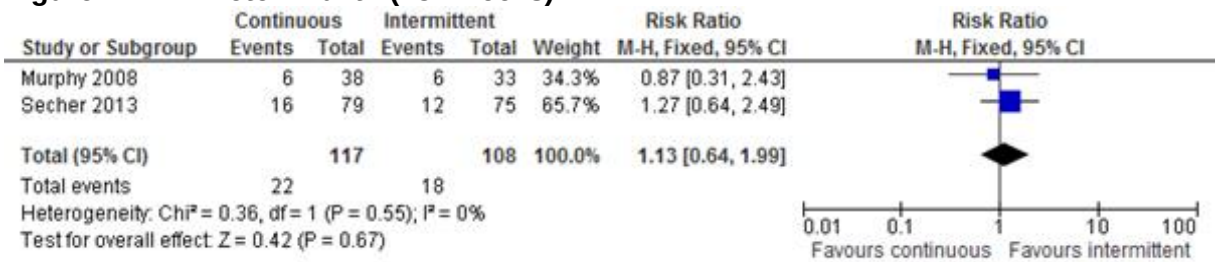


Figure 12: Preterm birth (<37 weeks)

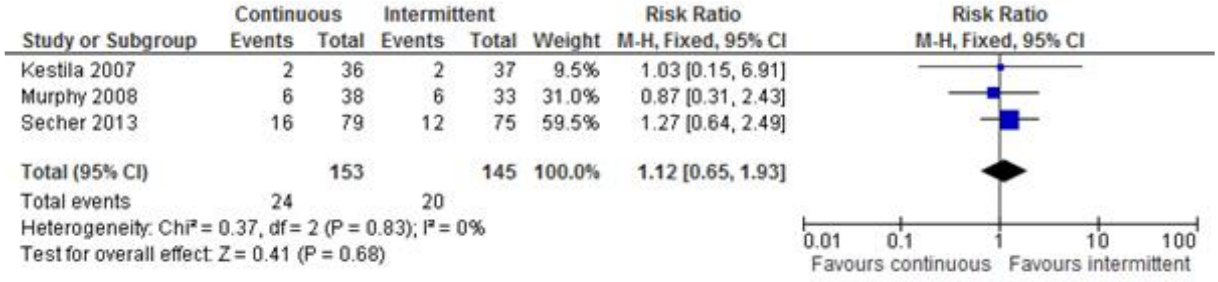


Figure 13: Large for gestational age (≥ 90th Centile)

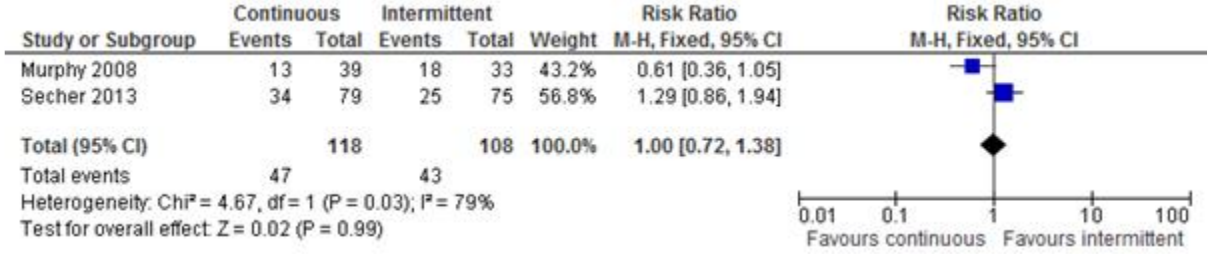


Figure 14: Large for gestational age (≥ 90th Centile)

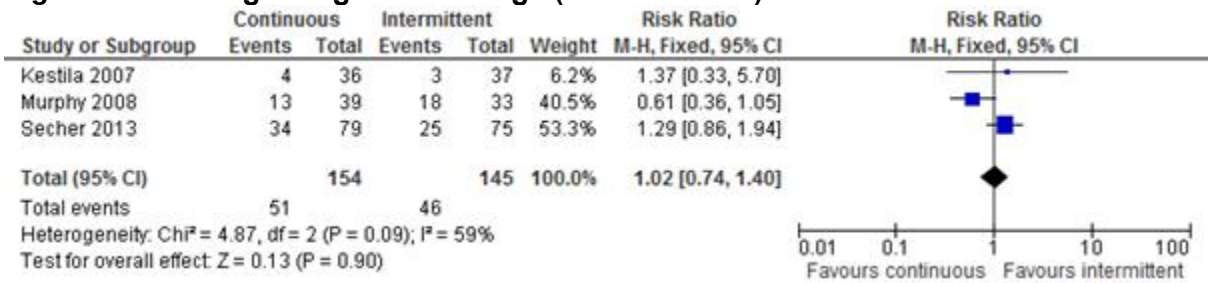
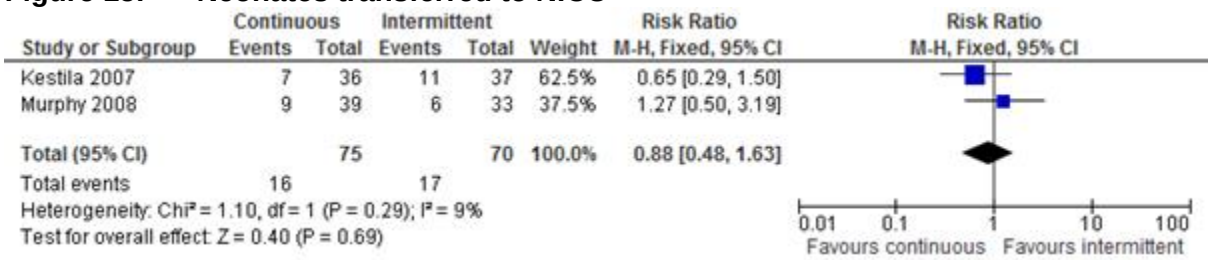


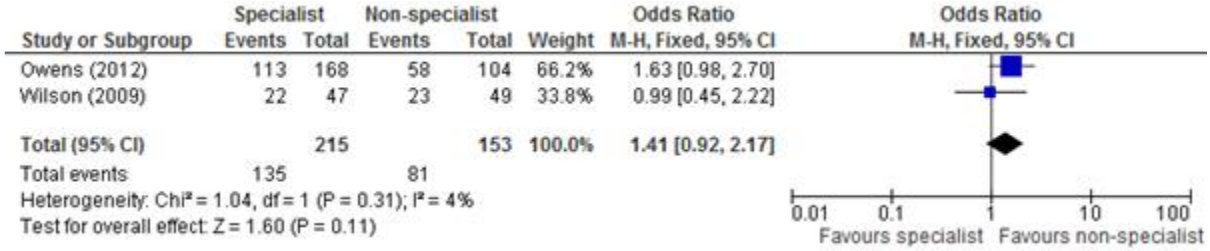
Figure 15: Neonates transferred to NICU



J.3 Specialist Teams

J.3.1 Comparison: Specialist team versus non-specialist team

Figure 16: Vaginal (unassisted/non-instrumental) birth



J.3.2 Comparison: Centralised versus peripheral care

Figure 17: Neonatal deaths

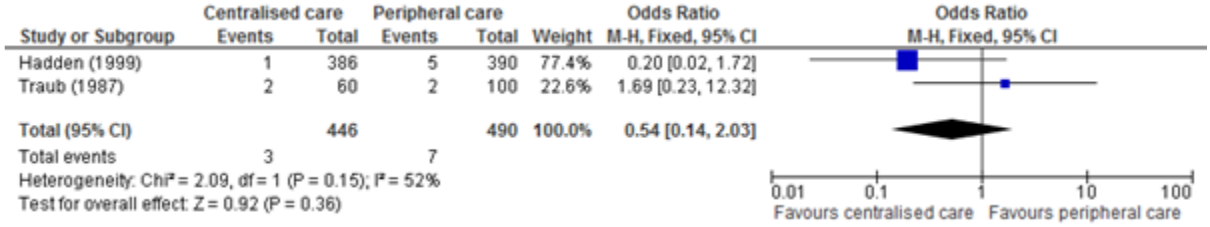


Figure 18: Total fetal loss

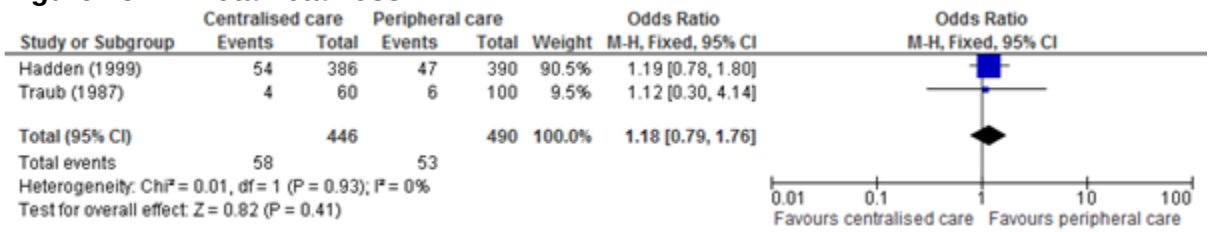


Figure 19: Stillbirth

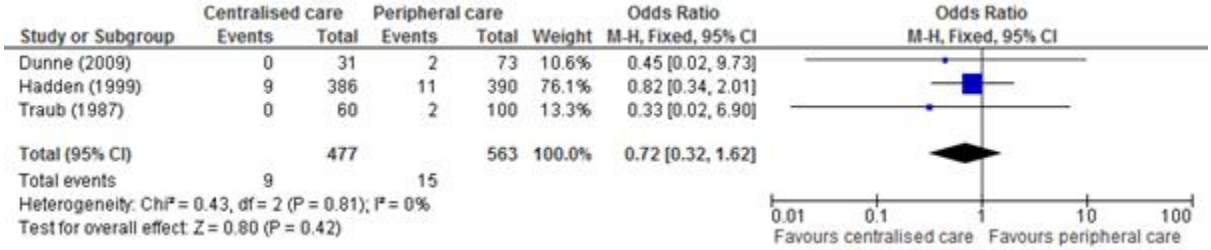


Figure 20: Miscarriage

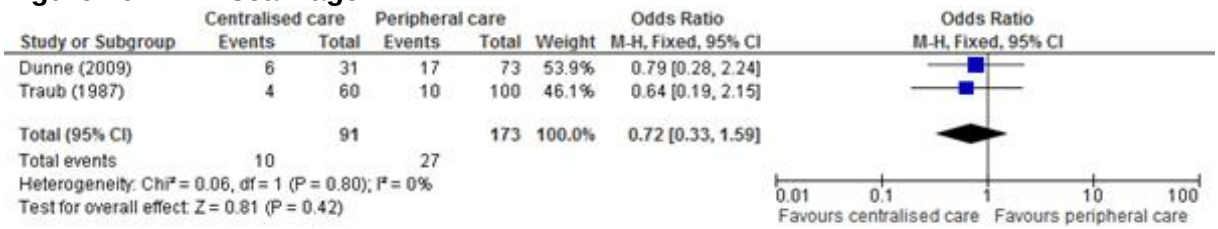
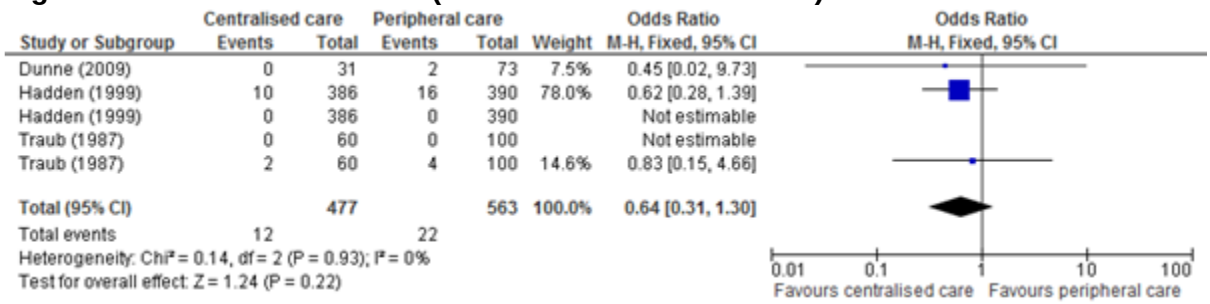


Figure 21: Perinatal deaths (stillbirth and neonatal data)



Appendix K: Heath economics – list of studies excluded from the review of the literature

Excluded studies - 0. HEALTH ECONOMIC POPULATION (ONLY) SEARCH	
Study	**Reason for Exclusion**
Ali,F.M., Farah,N., O'Dwyer,V., O'Connor,C., Kennelly,M.M., Turner,M.J., The impact of new national guidelines on screening for gestational diabetes mellitus, Irish Medical Journal, 106, 57-59, 2013	Short-term resource impact on new screening guidelines for gestational diabetes mellitus in Ireland. No econ evaluation undertaken.
Banerjee,S., Tran,K., Li,H., Cimon,K., Daneman,D., Simpson,S., Campbell,K., Short-acting insulin analogues for diabetes mellitus: meta-analysis of clinical outcomes and assessment of cost-effectiveness (Structured abstract), Health Technology Assessment Database, -, 2014	Two CBAs and two cost comparisons identified, but not for gestational diabetes patients. No CUA identified in review.
Coster,S., Gulliford,M.C., Seed,P.T., Powrie,J.K., Swaminathan,R., Monitoring blood glucose control in diabetes mellitus: A systematic review, Health Technology Assessment, 4, i-84, 2000	No CEA/CUA
Cummins,E., Royle,P., Snaith,A., Greene,A., Robertson,L., McIntyre,L., Waugh,N., Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: systematic review and economic evaluation (Structured abstract), Health Technology Assessment Database, -, 2014	Not population of interest
Franklin,B.E., Farland,M.Z., Thomas,J., McFarland,M.S., Ray,S.M., Byrd,D.C., Pharmacoeconomic Analysis of the Diabetes Initiative Program: A Pharmacist-Physician Collaborative Care Model, Annals of Pharmacotherapy, 47, 1627-1634, 2013	Pregnant patients excluded from study
Fryer,A.A., Shelley-Hitchin,A., Duff,C., Hodgson,E., Stirling,K., Hanna,F.W.F., Does HbA1c have a role as a diagnostic tool in gestational diabetes mellitus (GDM)?, Practical Diabetes, 29, 124a-, 2012	No economic evaluation
Gillespie,P., O'Neill,C., Cullinan,J., Dunne,F., The effect of Gestational Diabetes Mellitus (GDM) on maternity care and costs in Ireland, Diabetologia, 55, S449-, 2012	Effect of GDM on mode of delivery
Gobl,C.S., Bozkurt,L., Rivic,P., Schernthaner,G., Weitgasser,R., Pacini,G., Mittlbock,M., Bancher-Todesca,D., Lechleitner,M., Kautzky-Willer,A., A two-step screening algorithm including fasting plasma glucose measurement and a risk estimation model is an accurate strategy for detecting gestational diabetes mellitus, Diabetologia, 55, 3173-3181, 2012	Clinical study, efficacy of screening; no cost analysis.
Health,Technology Assessment, A clinical and economic evaluation of screening and diagnostic tests to identify and treat women with gestational diabetes: association between maternal risk factors, glucose levels, and adverse outcomes (Project record), Health Technology Assessment Database, -, 2014	Work in progress. Due for publication December 2015
Lenoir-Wijnkoop,I., Nuijten,M., Uauy,R., Health economic model for assessing the impact of high birth weight on public health, Annals of Nutrition and Metabolism, 63, 399-, 2013	Conference abstract
Luoto,R., Kolu,P., Raitanen,J., Rissanen,P., Cost-effectiveness of lifestyle counselling in primary prevention of gestational diabetes, European Journal of Epidemiology, 28, S186-S187, 2013	Conference abstract
May,C.J., Nayak,U.A., Dawidziak,M., Churchill,D., Baskar,V., Viswanath,A.K., Additional utility of HbA1c in postnatal glycaemic assessment in women with gestational diabetes, Diabetic Medicine, 28, 172-, 2011	Clinical study, screening for GDM; no cost analysis.
McIntyre,H.D., Diagnosing gestational diabetes mellitus: Rationed or rationally related to risk?, Diabetes Care, 36, 2879-2880, 2013	No economic evaluation undertaken
Murphy,A., Guilar,A., Donat,D., Nutrition education for women with newly diagnosed gestational diabetes mellitus: Small-group vs. individual counselling, Canadian Journal of Diabetes, 28, 147-151, 2004	No costs/cost effectiveness model
Myagerimath,R., Albert,S., Nwosu,E.C., Outcome of glucose tolerance test in a district general hospital, BJOG: An International Journal of Obstetrics and Gynaecology, 120, 134-, 2013	Conference presentation. No costs data presented
Noctor,E., Crowe,C., Avalos,G., Carmody,L., Wickham,B., O'Shea,P., Gaffney,G., Dunne,F., Comparison of fasting plasma glucose and HbA1c for follow-up of women with previous gestational diabetes, Irish Journal of Medical Science, 181, S350-, 2012	No costs
Noctor,E., Crowe,C., Carmody,L.A., Wickham,B., Avalos,G., Gaffney,G., O'Shea,P., Dunne,F., ATLANTIC DIP: The prevalence of pre-diabetes/diabetes up to 5 years post partum in women with previous gestational diabetes along the Atlantic coast, Diabetologia, 55, S442-, 2012	No costs/economic analysis
Oostdam,N., Bosmans,J., Wouters,M.G.A.J., Eekhoff,E.M.W., van,MechelenW, van,PoppelM, Cost-effectiveness of an exercise program during pregnancy to prevent gestational diabetes: Results of an	Wrong PICO.

Excluded studies - 0. HEALTH ECONOMIC POPULATION (ONLY) SEARCH	
economic evaluation alongside a randomised controlled trial, BMC Pregnancy and Childbirth, 12 , 2012. Article Number, -, 2012	
Pelaez-Crisologo,Ma, Castillo-Torralba,M.G.A.G., Festin,M.R., Different techniques of blood glucose monitoring in women with gestational diabetes for improving maternal and infant health, Cochrane Database of Systematic Reviews, 2009. Article Number, -, 2009	Protocol; no CEA/CUA
Pereira Gray,D.J., Evans,P.H., Wright,C., Langley,P., The cost of diagnosing Type 2 diabetes mellitus by clinical opportunistic screening in general practice, Diabetic Medicine, 29, 863-868, 2012	Pregnant women excluded from study
Phaloprakarn,C., Tangjitgamol,S., Diagnosis of gestational diabetes mellitus using a modified 100 g oral glucose tolerance test, Journal of Perinatology, 28, 7-11, 2008	No analysis of costs
Racusin,D., Andrabi,S., Crawford,N., Sangi-Haghpeykar,H., Showalter,L., Sharma,S., Haymond,M., Aagaard,K., Twizzlers as a cost effective and a equivalent alternative to the glucola beverage in screening for gestational diabetes (GDM), Reproductive Sciences, 19, 307A-, 2012	Conference abstract and not an economic evaluation
Racusin,D., Antony,K., Showalter,L., Sharma,S., Haymond,M., Aagaard,K., Twizzlers as a cost effective and equivalent alternative to the glucola beverage in diabetes screening, American Journal of Obstetrics and Gynecology, 210, S131-, 2014	Conference abstract and not an economic evaluation
Racusin,D.A., Crawford,N.S., Andrabi,S., Suter,M.A., Sangi-Haghpeykar,H., Showalter,L., Sharma,S., Haymond,M., Aagaard,K.M., Twizzlers as a cost-effective and equivalent alternative to the glucola beverage in diabetes screening, Diabetes Care, 36, e169-e170, 2013	Not a full economic evaluation
Reel,M., Werner,E., Pettker,C., Funai,E., Thung,S., Screening for gestational diabetes with a 1 hour glucose challenge test: Is a 130mg/dL threshold more cost-effective than a 140mg/dL threshold?, American Journal of Obstetrics and Gynecology, 204, S117-S118, 2011	Cost-effectiveness for different thresholds of blood glucose levels, but thresholds not comparator of interest/relevant to question.
Salemi,J.L., Comins,M.M., Chandler,K., Mogos,M.F., Salihu,H.M., A practical approach for calculating reliable cost estimates from observational data: application to cost analyses in maternal and child health, Applied Health Economics and Health Policy, 11, 343-357, 2013	Costing of US healthcare for maternal and child health
Scott,D.A., Loveman,E., McIntyre,L., Waugh,N., Screening for gestational diabetes: a systematic review and economic evaluation. [256 refs], Health Technology Assessment (Winchester, England), 6, 1-161, 2002	Already included in previous guideline (2008).
Shivanath,M., Nayar,R., Emmerson,C., Loughney,A., Purvis,A., Fairs,A., Smart,J., Forbister,R., Will 'simple telehealth' help in the management of women with gestational diabetes?, BJOG: An International Journal of Obstetrics and Gynaecology, 120, 111-, 2013	Conference abstract
Todorova,K., Palaveev,O., Petkova,V.B., Stefanova,M., Dimitrova,Z., A pharmacoeconomical model for choice of a treatment for pregnant women with gestational diabetes, Acta Diabetologica, 44, 144-148, 2007	Cost analysis (Bulgaria) only
Uy,J., Fogelfeld,L., Guerra,Y., Cumulative clinical experience with use of insulin lispro: Critical appraisal, role in therapy, and patient considerations, Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 5, 1-10, 2012	Reviews previous cost-effectiveness studies
Waugh,N., Royle,P., Clar,C., Henderson,R., Cummins,E., Hadden,D., Lindsay,R., Pearson,D., Screening for hyperglycaemia in pregnancy: a rapid update for the National Screening Committee, Health Technology Assessment (Winchester, England), 14, 1-183, 2010	No economic evaluation; none of the identified studies were published after 2008, should have been/were included in previous guideline.
Zacharieva,S.Z., Todorova-Ananieva,K.N., Konova,E.I., Petkova,V.B., Guerguiev,S.R., Dimitrova,Z.D., Pharmacoeconomic analysis for the future treatment of diabetes mellitus after gestational diabetes, Diabetologia, 52, S409-, 2009	"prophylactic method/preventive programme": no details on test used

Appendix L:Health economics – list of studies included in the review of the literature

Avalos GE, Owens LA, Dunne F for the ATLANTIC DIP Collaborators. Applying current screening tools for gestational diabetes mellitus to a European population: is it time for change? Diabetes Care 2013;36: 3040–3044

Berger, H and Sermer, M. Counterpoint: selective screening for gestational diabetes mellitus. Diabetes Care 2009; 32: 1352-1354

Cavassini,A.C., Lima,S.A., Calderon,I.M., Rudge,M.V. Cost-benefit of hospitalization compared with outpatient care for pregnant women with pregestational and gestational diabetes or with mild hyperglycemia, in Brazi.l Sao Paulo Medical Journal; Revista Paulista de Medicina 2012 130:17-26

Culligan, PJ, Myers, JA, Goldberg, RP, Blackwell, L, Gohmann, SF and Abell TD. Elective cesarean section to prevent anal incontinence and brachial plexus injuries associated with macrosomia – a decision analysis. Int Urogynecol J Pelvic Floor Dysfunc 2005; 16: 19–28

Cundy, T, Ackermann, E and Ryan, EA. Gestational diabetes: new criteria may triple the prevalence but effect on outcome is unclear. BMJ 2014; 348: g1567

Gillespie, P, Cullinan, J, O'Neill, C, and Dunne, F for ATLANTIC DIP Collaborators. Modeling the independent effects of gestational diabetes mellitus on maternity care and costs. Diabetes Care 2013; 36: 1111-1116

Gillespie, P, O'Neill, C, Avalos,G, and Dunne, FP for ATLANTIC DIP Collaborators. New estimates of the costs of universal screening for gestational diabetes mellitus in Ireland. Irish Medical Journal 2012; 105: 15-18

Holt, RI, Coleman, MA and McCance, DR. The implications of the new International Association of Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria for gestational diabetes. Diabet. Med. 2011: 28, 382–385

Kim,C, Herman,WH and Vijan,S. Efficacy and cost of postpartum screening strategies for diabetes among women with histories of gestational diabetes mellitus. Diabetes Care 2007; 30: 1102-1106

Kolu, P, Raitanen, J, Rissanen, P and Luoto, R. Cost-Effectiveness of lifestyle counselling as primary revention of gestational diabetes mellitus: findings from a cluster-randomised trial PLoS ONE 2013; 10:1371/journal.pone.0056392

Kolu,P, Raitanen, J, Rissanen, P and Luoto, R. Health care costs associated with gestational diabetes mellitus among high-risk women--results from a randomised trial. BMC Pregnancy and Childbirth 2012, 12:71

Marseille, E, Lohse, N, Jiwani, A, et al. The cost-effectiveness of gestational diabetes screening including prevention of type 2 diabetes: Application of a new model in India and Israel. Journal of Maternal-Fetal and Neonatal Medicine 2013; 26: 802-810

Metzger BE, Gabbe SG, Persson B, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010; 33: 676-82.

Mission, J, Ohno, M, Cheng, Y and Caughey, A. Treating patients in HAPO glucose category 4 to improve maternal and neonatal outcomes: a cost effectiveness analysis. American Journal of Obstetrics and Gynecology 2013; 208: p.S122

Mission, J, Ohno, M, Yanit, K, Cheng, Y and Caughey, A. Gestational diabetes screening with the new IADPSG 2 hour glucose tolerance test vs the 1 hour glucose challenge test: a cost-effectiveness analysis. American Journal of Obstetrics and Gynecology 2012; 206: p.S126

Mission, J, Ohno, M, Yanit, K, Pilliod, R, Cheng, Y, and Caughey, AB. Treating patients in HAPO glucose category 5 to improve maternal and neonatal outcomes: a cost effectiveness analysis. American Journal of Obstetrics and Gynecology 2012; 206: p.S126

Mission, JF, Ohno, MS, Cheng, YW and Caughey, AB. Gestational diabetes screening with the new IADPSG guidelines: a cost-effectiveness analysis American Journal of Obstetrics and Gynecology 2012; 207: 326-326

Moses, RG and Cheung, NW. Point: Universal screening for gestational diabetes mellitus. Diabetes Care 2009; 32: 1349-1351

Moses, RG. New consensus criteria for GDM: problem solved or Pandora's box. Diabetes Care 2010; 33: 690-691

Moss, JR, Crowther, CA, Hiller, JE, Willson, KJ and Robinson, JS, the Australian Carbohydrate Intolerance Study in Pregnant Women Group. Costs and consequences of treatment for mild gestational diabetes mellitus - evaluation from the ACHOIS randomised trial. BMC Pregnancy and Childbirth 2007, 7:27

Munigoti, SP, Davies, R and Peters,J. Impact of adopting the IADPSG criteria for diagnosing gestationa;l diabetes. Diabetic Medicine 2011; 28:170-

Nayeri, U, Tabbah, S, Werner, E. et al. Labor induction at 38 weeks versus expectant management of insulin-requiring diabetics in pregnancy: a cost effective analysis. American Journal of Obstetrics and Gynecology 2014; 210: p.S230

Neuhauser D and Lewicki AM. What do we gain from the sixth stool guaiac? N Engl J Med. 1975; 293: 226-8.

Nguyen, N, Allen, A, Gorman, M. et al. Group prenatal care for women with pre-gestational type II diabetes mellitus: a cost-effectiveness analysis. American Journal of Obstetrics and Gynecology 2014; 210: p.S190

Ohno, MS, Sparks, TN, Cheng, YW and Caughey, AB. Treating mild gestational diabetes mellitus: a cost-effectiveness analysis. American Journal of Obstetrics and Gynecology 2011; 205: 282-287

Oostdam, N, Bosmans, J, Wouters, MG, et al. Cost-effectiveness of an exercise program during pregnancy to prevent gestational diabetes: results of an economic evaluation alongside a randomised controlled trial. BMC Pregnancy and Childbirth 2012, 12:64

O'Sullivan JB snd Mahan C. Criteria for oral glucose tolerance test in pregnancy. Diabetes 1964;13: 278-85.

Ratner RE. Prevention of Type 2 diabetes in women with previous gestational diabetes. Diabetes Care 2007; 30: S242-S245.

Round,JA, Jacklin, P, Fraser, RB, et al. Screening for gestational diabetes mellitus: cost-utility of different screening strategies based on a woman's individual risk of disease. Diabetologia 2011; 54: p.256-263

van Leeuwen, M, Vijgen, S, Opmeer, BC et al. Cost-effectiveness analysis of screening for GDM. American Journal of Obstetrics and Gynecology 2009; 201: p.S109

van Leeuwen, M, Louwerse, M, Opmeer, B et al. Glucose challenge test for detecting gestational diabetes: a systematic review. BJOG 2012; 119: 393–401.

Waugh, N, Pearson, D and Royle, P. Screening for hyperglycaemia in pregnancy: consensus and controversy. Best Practice & Research Clinical Endocrinology & Metabolism 2010; 24: 553–571

Werner, EF, Pettker, CM, Zuckerwise, L et al. Screening for gestational diabetes mellitus: are the criteria proposed by the international association of the Diabetes and Pregnancy Study Groups cost-effective? Diabetes Care 2012; 35: 529-535

Appendix M: Deleted text from previous guideline

M.1 Text deleted from preconception care

Calcium-channel blockers

A cohort study examined the potential teratogenicity of calcium-channel blockers.[110] Six teratogen information services prospectively collected and followed up 78 women with first-trimester exposure to calcium-channel blockers. Pregnancy outcome was compared with that of a control group matched for maternal age and smoking habits. There was no increase in major malformation rates (calcium-channel blockers 3.0% (2/66); nonteratogenic controls 0%; P = 0.27). The defects reported were attributable to maternal diabetes or co-ingestion of teratogens. The increase in preterm birth (calcium-channel blockers 28%, nonteratogenic controls 9%, P = 0.003), attributed to maternal disease by stepwise regression, was the most important factor responsible for the observed decrease in birthweight (mean −334 g versus nonteratogenic controls, P = 0.08). This study suggests that calcium-channel blockers do not represent a major teratogenic risk. [EL = 2++]

Another cohort study investigated the effect of verapamil infused intravenously after plasma volume expansion with dextran-70 in nine women with severe gestational proteinuric hypertension.[111] The haemodynamic response in the women and adverse fetal effects were monitored. Verapamil produced a statistically significant reduction in mean arterial pressure and systemic vascular resistance without adversely affecting cardiac output. The decrease in blood pressure was smooth and controlled and was associated with an insignificant increase in heart rate. There were no adverse fetal effects, as evidenced by cardiotocographic monitoring. The apparent effectiveness of verapamil in this study justifies further investigation. [EL = 2+]

A reference guide to medicines in pregnancy and lactation reported that there were limited data for the use of diltiazem in pregnant women, and suggested that it presents a high risk to the fetus. There were no studies investigating the use of amlodipine or nisoldipine in pregnant women, and the reference guide suggested that these present a moderate risk to the fetus. There were limited data for the use of felodipine, nicardipine or nimodipine in pregnant women, and the reference guide suggested that they present a risk to the fetus. There were limited data for the use of isradipine in pregnant women and the reference guide suggested that it presents a low risk to the fetus. There were limited data for the use of nifedipine in pregnant women, and the reference guide suggested that it presents a low risk to the fetus. The reference guide suggested that verapamil is compatible with pregnancy. There was no review of lacidipine or lercanidipine.[77] [EL = 3]

The British National Formulary suggests that the calcium-channel blocker verapamil may reduce uterine blood flow leading to fetal hypoxia and that it may inhibit labour; the manufacturer advises women to avoid it in the first trimester of pregnancy unless absolutely necessary.[78] Amlodipine and nimodipine have no information available about possible harms; the manufacturers advise pregnant women to avoid them, but the risk to the fetus should be balanced against the risk of uncontrolled maternal hypertension. Isradipine, nifedipine and nicardipine may inhibit labour; the manufacturers advise pregnant women to avoid them, but the risk to the fetus should be balanced against the risk of uncontrolled maternal hypertension. Felodipine may inhibitlabour and pregnant women are advised to avoid it. Nisoldipine should be avoided by pregnant women. Lacidipine may inhibit labour; the manufacturer advises pregnant women to avoid it. Lercanidipine and diltiazem have no information available; the manufacturer advises pregnant women to avoid them.

There is information on the use of calcium-channel blockers during breastfeeding in Section 8.1.

Evidence statement

Two small cohort studies suggest that calcium-channel blockers do not have a teratogenic effect, but no large-scale trials of their effectiveness and safety in pregnancy were identified. The British National Formulary recommends that they should be avoided in pregnancy.

From evidence to recommendations

Calcium-channel blockers should be avoided throughout pregnancy because of the risk of disruption to labour and fetal hypoxia. However, the risk to the fetus should be balanced against the risk of uncontrolled maternal hypertension in deciding whether to discontinue nifedipene.

M.2 Text deleted from antenatal care

5.3 Monitoring blood glucose and ketones during pregnancy

Description of the evidence

Two RCTs were identified that investigated preprandial versus postprandial monitoring of blood glucose during pregnancy.

The first study consisted of 61 women with type 1 diabetes who were randomly assigned at 16 weeks of gestation to either preprandial or postprandial blood glucose monitoring.[202] All women were on a four-times-daily basal bolus insulin regimen. The preprandial group was asked to monitor before breakfast and preprandially. The postprandial group was asked to monitor before breakfast and 1 hour after meals. CBG readings were measured by using a memory-based glucose reflectance meter. Insulin doses and glucose readings were also recorded by diary and brought to the clinic. The postprandial monitoring group had a significantly reduced incidence of pre-eclampsia (3% versus 21%, $P < 0.05$), greater success in achieving glycaemic control targets (55% versus 30%, $P < 0.001$) and smaller neonatal triceps skinfold thickness (4.5 ± 0.9 versus

5.1 ± 1.3, $P = 0.05$). [EL = 1++]

The second study consisted of 66 women with gestational diabetes who required insulin therapy.[155] The ethnic background of the sample was 85% Hispanic, 11% white and 4% black or Asian. Women were randomly assigned to monitor either preprandial or 1 hour postprandial blood glucose levels. The preprandial monitoring protocol required daily monitoring of fasting, preprandial and bedtime CBG concentrations. The postprandial protocol required daily monitoring of blood glucose concentrations before breakfast (fasting) and 1 hour after each meal. The women measured their blood glucose concentration using memory-based reflectance glucometers. All blood glucose values as well as insulin doses and dietary intake were recorded. There were 3/33 (9%) macrosomic babies in the postprandial monitoring group compared with 12/33 (36%) in the preprandial monitoring group ($P = 0.01$). Women in the postprandial group were significantly less likely to have a caesarean section for cephalopelvic disproportion (12% versus 36%, $P = 0.04$) or a baby with neonatal hypoglycaemia (3% versus 21%, $P = 0.05$). There were also fewer instances of shoulder dystocia (3% versus 18%) and third- or fourth-degree perineal laceration (9% versus 24%). [EL = 1++]

The ACHOIS trial randomly assigned 1000 women with gestational diabetes to either an intervention group or routine care.[153] The intervention was a package of care that included instructions on self-monitoring of blood glucose four times daily until blood glucose levels had been in the recommended range for 2 weeks (fasting glucose levels more than 3.5 mmol/litre and 5.5 mmol/litre or less, preprandial levels 5.5 mmol/litre or less and 2 hour postprandial levels

7.0 mmol/litre or less) followed by daily monitoring at rotating times. The package of care also included insulin therapy with the dose adjusted on the basis of glucose levels and individualised dietary advice from a qualified dietitian. The rate of serious perinatal outcomes among babieswas significantly lower in the intervention group (1% versus 4%, P = 0.01). The number needed to treat to prevent a serious outcome in a baby was 34. There was no significant difference between groups in maternal quality of life. [EL = 1++]

Three studies were identified that reported on the use of continuous blood glucose monitoring in women with diabetes. Two cohort studies were in women with type 1 diabetes[209,210] [EL = 2+] and one case series was in women with gestational diabetes.[211] [EL = 3] All three studies reported hyperglycaemic episodes undetected by self-monitoring of blood glucose. These episodes were usually due to the consumption of high carbohydrate food between meals and were undetected by self-monitoring protocols that required testing only after main meals. The three studies showed that examining 72 hour glucose profiles can help to identify patterns of glucose control, better target insulin treatment, assist in patient education and improve dietary adherence.

A retrospective study[120] examined the effect of an intensive diabetes management programme during pregnancy on women's long-term self-management behaviours and glycaemic control. There was a significant improvement in all diabetes self-management behaviours, including frequency of self-monitoring of blood glucose, frequency of insulin injections, and frequency and complexity of insulin dose adjustment from entry to the programme to the baby's birth. There was also a significant improvement in HbA_{1c} from entry to the baby's birth. [EL = 2−]

An RCT[212] investigated whether glycaemic control achieved by women using telephone modems for the transmission of self-monitored blood glucose data was better than that achieved by women managed in a similar fashion without modem connection. The study showed that telemedicine is a practical way of providing specialist care to pregnant women. [EL = 1+]

A systematic review of observational studies[213] investigated the risk of adverse pregnancy outcomes in pregnant women with diabetes in relation to glycaemic control. The review showed that an increase in adverse pregnancy outcomes in women with diabetes who had poor glycaemic control (congenital malformations, pooled OR 3.44, 95% CI 2.30 to 5.15; risk reduction of congenital malformation 0.39–0.59 for each 1% decrease in HbA_{1c}; miscarriage, pooled OR 3.23, 95% CI 1.64 to 6.36; perinatal mortality, pooled OR 3.03, 95% CI 1.87 to 4.92). [EL = 3]

No studies were identified that assessed how ketones should be monitored during pregnancy.

Existing guidance

The NSF for diabetes[20] recommends that 'women should be supported and encouraged to monitor their blood glucose regularly'.

Evidence statement

Two high quality RCTs have found better pregnancy outcomes for women with diabetes when blood glucose is monitored 1 hour after meals than when it is monitored before meals. One RCT found that a treatment package that included self-monitoring of blood glucose improved outcomes in women with gestational diabetes compared with routine obstetric care. Two cohort studies and a case series showed that self-monitoring of blood glucose undertaken only after main meals may not detect hyperglycaemia following the consumption of food between meals.

No studies were found on monitoring for ketones during pregnancy.

From evidence to recommendations

The evidence regarding the effectiveness of self-monitoring of blood glucose 1 hour after meals for improving pregnancy outcomes suggests that postprandial monitoring should not be restricted to main meals. The effectiveness of monitoring using meters supports the provision of such meters (see Section 3.5).

The GDG's view is that women with insulin-treated diabetes are vulnerable to nocturnal hypoglycaemia during pregnancy and that it is good clinical practice to undertake an additional test before going to bed at night.

M.3 Text deleted from intrapartum care

Timing and mode of birth

Optimal timing of birth

An RCT (n = 200) from the USA compared the outcomes of birth after 38 weeks of gestation in women with insulin-requiring diabetes.[323] Those enrolled had gestational diabetes (n = 187) or pre-existing diabetes (n = 13). In women with pre-existing diabetes, the expectant management of pregnancy after 38 weeks of gestation did not reduce the incidence of caesarean section, but rather led to an increased prevalence of LGA babies (23% versus 10%) and shoulder dystocia (3% versus 0%). Given the risk associated with birth after 38 weeks of gestation, the study suggested that active induction of labour at 38 weeks of gestation should be considered in women with insulin-requiring diabetes, but if this is not pursued careful monitoring of fetal growth should be performed. [EL = 1+]

A case–control study (n = 260) from Israel compared inducing labour at 38–39 weeks of gestation with allowing pregnancy to continue naturally in women with type 1 diabetes.[331] There were no differences between the two groups at baseline. The rate of shoulder dystocia was 1.4% in the induction of labour group compared with 10.2% in the non-induced group who gave birth beyond 40 weeks of gestation (P < 0.05). No differences in caesarean section rates or birthweights of babies were found. The rate of shoulder dystocia was lower in the babies of women who had induction of labour at 38–39 weeks of gestation than in those without induction (1.4% versus 10.2%, P < 0.05). The study recommended elective induction of labour for women with insulin- requiring diabetes in order to reduce the rate of shoulder dystocia. [EL = 2−]

A case–control study (n = 3778) from Canada examined the relationship between gestational glucose intolerance (3 hour 100 g OGGT) and fetal outcomes.[318] The study identified four groups: negative gestational diabetes (n = 2940), false-positive gestational diabetes (n = 580), untreated borderline gestational diabetes (n = 115) and known

treated gestational diabetes (n = 143). There were no significant differences in gestational age at birth (39.8 ± 1.8 weeks for women without diabetes, 39.8 ± 1.8 for women with borderline diabetes and 39.3 ± 1.6, P > 0.20 for women with gestational diabetes). There were no differences among the groups in the rates of fetal distress or shoulder dystocia. [EL = 2+]

A cohort study (n = 317) from Israel conducted between 1993 and 1995 examined the effect of intensive management of gestational diabetes with diet in relation to birth timing and outcomes and compared the effect with that for women without diabetes.[324] The gestational age at birth for women with gestational diabetes was 39 ± 2.5 weeks and that of women without diabetes was 39 ± 1.5 weeks. [EL = 2+]

A case–control study (n = 428) from the USA examined the mean gestational ages at birth of babies of women with gestational diabetes and those in a control group without maternal diabetes.[332] The study found no significant difference between women with diabetes and the controls in gestational age at birth (38. 4 ± 2.8 weeks versus 39 ± 2.9 weeks), shoulder dystocia, Apgar scores, neonatal death or prolonged hospital stay after birth. The study suggests that if pregnancy is not interrupted then the gestational age at birth is similar between women with diabetes and those without diabetes, and neonatal outcomes do not differ between the two groups. [EL = 2−]

Current practice

The CEMACH enquiry reported that women with pre-existing diabetes had high rates of obstetric intervention with a 39% induction of labour rate compared with 21% in the general maternity population. The reasons given for induction of labour were that it was routine for women with diabetes (48.4%), general obstetric complications (13.9%), presumed fetal compromise (9.4%), large baby or polyhydramnios (8.5%) and diabetes complications (2.1%), and the remainder were other clinical reasons, preterm rupture of membranes, maternal request, or unknown or inadequately described.[2] [EL = 3–4]

The caesarean section rate was 67%, which is three times higher than the general maternity population (24%). The indications for elective and emergency caesarean section were presumed fetal compromise (28.3%), previous caesarean section (24.9%), general obstetric complication (14.2%), failure to progress in labour (13.9%), large baby (3.7%), diabetes complications (2.5%) and routine for diabetes (1.9%), and the remainder were due to other clinical reasons, maternal request, reason unknown or inadequately described. [EL = 3–4]

The preterm birth rate was 35.8% compared with 7.4% in the general maternity population. Of the total births 26.4% were iatrogenic and 9.4% were spontaneous preterm births (including preterm rupture of the membranes requiring induction) which is higher than in the general maternity population. The majority of iatrogenic preterm births were due to preterm caesarean sections, 21.9% of which were for previous caesarean section, large baby, maternal request or routine for maternal diabetes. [EL = 3–4]

The enquiry case–control study found that 8% (15/178) of women with poor pregnancy outcomes and 2% (4/202) of women with good pregnancy outcome had no details of discussion about timing and mode of birth in their medical records.[33] A lack of discussion was associated with poor pregnancy outcome (OR 4.0, 95% CI 1.2 to 12.7, adjusted for maternal age and deprivation). Additional case–control analysis showed an association with fetal or neonatal death, but not with fetal congenital anomaly, although it is important to note that women who did not have a discussion also gave birth at an earlier gestational age. The majority of women (65% of 382 women) were assessed as having optimal care during labour and birth and there was no association of sub-optimal care and pregnancy outcome. The most frequent issues

noted were poor management of maternal risks, inappropriate decisions relating to birth and inadequate fetal surveillance during labour or delay in acting on signs of fetal compromise. [EL = 3–4]

The condition of the baby at birth was reported by the CEMACH enquiry: 2.6% of live births had an Apgar score of less than 7 at 5 minutes. The corresponding figure for the general maternity population is 0.76%. [EL = 3–4]

The enquiry found that 6.9% (261/3808) of pregnancies led to *in utero* losses (there were also two early neonatal deaths, twins born live at 20 weeks of gestation who both died within 1 hour of birth). This is thought to be an underestimate of the actual number of pregnancies that ended.

Evidence statements

Five studies were considered in relation to optimal timing of birth in women with diabetes. An RCT involving women with insulin-requiring diabetes and a case–control study involving women with type 1 diabetes compared elective induction of labour at 38–39 weeks of gestation with expectant management. There were more LGA babies and cases of shoulder dystocia in the expectant management groups. Routine induction of labour at 38–39 weeks of gestation did not increase the rate of caesarean section. The remaining studies allowed comparison of gestational ages at birth between babies of women with diabetes and those of women without diabetes, but these none of these studies was specifically designed to address the optimal timing of birth in women with diabetes.

From evidence to recommendations

Routine induction of labour for women with diabetes at 38–39 weeks of gestation reduces the risk of stillbirth and shoulder dystocia without increasing the risk of caesarean section. However, there was insufficient evidence to determine the precise gestational age at which elective induction of labour should be offered. The GDG's discussions highlighted the need to balance the risk of fetal lung immaturity which may be associated with induction at 36–37 weeks of gestation against the risk of stillbirth associated with later induction. In the absence of evidence to determine whether elective birth through induction of labour, or elective caesarean section if indicated, should be offered before 38 weeks of gestation, the GDG's view was that elective birth should be offered after 38 completed weeks of gestation. No evidence was identified to suggest that the indications for elective caesarean section in preference to induction of labour in women with diabetes would be any different to those in women without diabetes.

Evidence shows that diabetes should not be considered a contraindication to attempting VBAC.

M.4 Text deleted from postnatal care

Information and follow-up after birth

Follow up screening

A retrospective diagnostic study (n = 152) from the UK examined whether an FPG test at 6 weeks postpartum could be used to determine which women needed an OGTT.[408] The study compared FPG with OGTT (as the gold standard). A total of 122 women had results available for analysis. Using a cut-off for FPG of 6.0 mmol/litre, the sensitivity was 100% and the specificity was 94% for identifying those who had diabetes

compared to OGTT. The study concluded that FPG could be used to determine who should undergo an OGTT. [EL = 2]

A retrospective diagnostic study (n = 298) from Singapore examined whether the results of an antenatal OGTT could be used to predict which of those women who had been diagnosed with gestational diabetes would go on to develop diabetes, the aim being to avoid the need for a 6 week follow-up OGTT.[409] The study compared the antenatal OGTT results with the postnatal OGTT results. At a cut-off of 4.5 mmol/litre the sensitivity was 73.9% and specificity was 70.3%. For a 2 hour OGTT the cut-off was 10.5 mmol/litre with a sensitivity of 55.1% and a specificity of 84.7%. The authors concluded that antenatal OGTT results could not be used reliably to predict postnatal OGTT results. [EL = 3]

Existing guidance

The NSF for diabetes[20] recommends that services should be in place for women with pre-existing diabetes and those who have been diagnosed with gestational diabetes.

'Pregestational diabetes: Following delivery, all women should be offered the opportunity to be reviewed by the multidisciplinary team and to discuss the future self-management of their diabetes and the implications of breastfeeding. They should all be offered contraceptive advice and should all receive a six-week postpartum check.

Gestational diabetes: Six weeks after delivery, a 75 g oral glucose tolerance test should be undertaken to determine whether the woman:

- still has diabetes; or
- now has impaired glucose tolerance; or
- has returned to normal.

Women who are found still to have diabetes should be managed accordingly.

Those who are found still to have impaired glucose regulation and those who have returned to normal should be advised that they have an increased risk of developing:

- gestational diabetes in subsequent pregnancies; and
- type 2 diabetes later in life, a risk that can be reduced by eating a balanced diet, maintaining a healthy weight and increasing their physical activity levels. They should also be given advice about the symptoms and signs of diabetes.

Those who are found still to have impaired glucose regulation should also be offered a full assessment of their cardiovascular risk and appropriate follow-up.'

Evidence statement

Two diagnostic studies showed that follow-up of women with gestational diabetes was required to accurately identify ongoing disruption of glucose metabolism, suggesting a clinical need for postnatal testing of women who have been diagnosed with gestational diabetes.

There is evidence from a diagnostic study that FPG measurements have high sensitivity and specificity compared with OGTTs (the gold standard). They are also less costly than OGTTs and it is the GDG's view that using OGTTs instead of FPG measurements would not affect outcomes. Women who have been diagnosed with gestational diabetes should, therefore, be offered blood glucose testing using FPG, rather than an OGTT. This represents a change in clinical practice that will bring a cost saving to the NHS.

Research recommendations for information and follow-up after birth

Are there suitable long-term pharmacological interventions to be recommended postnatally for women who have been diagnosed with gestational diabetes to prevent the onset of type 2 diabetes?

Why this is important

Oral hypoglycaemic agents such rosiglitazone and metformin offer the possibility of pharmacological treatment for prevention of progression to type 2 diabetes in women who have been diagnosed with gestational diabetes. As yet there have been no clinical studies to investigate the effectiveness of oral hypoglycaemic agents in this context. Randomised controlled trials are needed to determine the clinical and cost-effectiveness of such treatments compared to diet and exercise.

Appendix N: Health economics from the 2008 guideline

N.1 Cost-effectiveness of self-management programmes for women with diabetes who are planning a pregnancy

N.1.1 Introduction

A review of the health economics literature identified a single study from the USA addressing the cost-effectiveness of preconception care and advice for women with pre-existing diabetes.[410] Although not explicitly described as such, the study used a decision-analytic approach to determine whether, as a result of averted complications, the additional costs of preconception care and advice yielded net savings compared with no preconception care and advice. The study reported that a mixture of literature review, expert opinion and surveys of medical care were used to estimate the costs and clinical consequences of preconception care and advice compared with 'doing nothing'. Doing nothing in this case meant no preconception care and advice, although antenatal care would, of course, be provided in the event of a pregnancy. The study concluded that preconception care and advice would yield cost savings, with each $1 spent on preconception care and advice realising a saving of $1.86 as a result of fewer births, lower antenatal care costs arising from better glycaemic control, and fewer adverse maternal and neonatal outcomes. The authors reported a number of sensitivity analyses, none of which fundamentally altered the results. Furthermore, the study reported that conservative estimates had been used when there was uncertainty with regard to parameter values and that their assumptions were, therefore, generally biased against preconception care and advice. However, the study also noted that the assumption of full adherence to the preconception care and advice programme may have been a limitation of the analysis.

The study is quite dated and therefore the usual caveats about the generalisability of costs from one healthcare setting to another are even more important than normal. Furthermore, changes to parameter values undertaken as part of the sensitivity analysis may not have been quite as conservative as suggested by the authors of the study. Finally, additional clinical studies and a meta-analysis which included more recent data[121] have been published since the cost-effectiveness study. Therefore, a de novo health economic model was developed for this guideline.

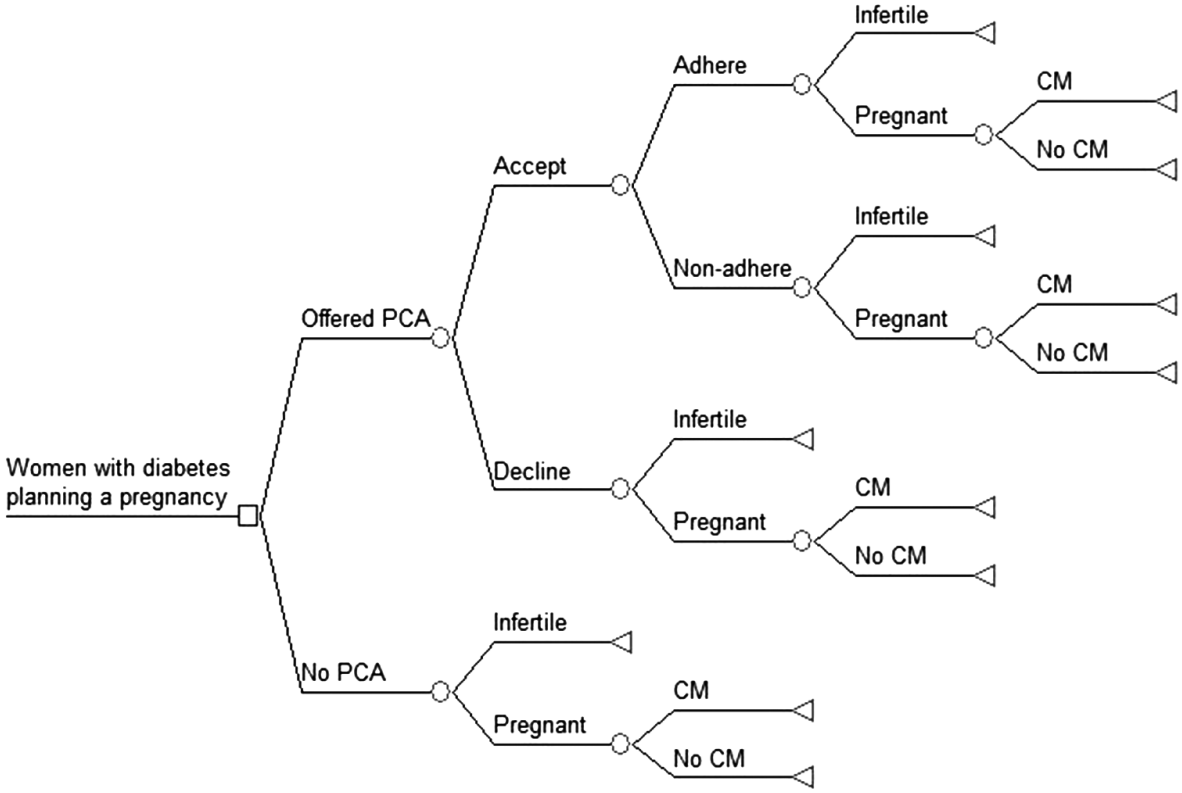
An economic evaluation has suggested that structured education programmes for people with pre-existing diabetes are cost-effective in the UK setting.[411] This is consistent with existing NICE guidance on self-management of diabetes.[18] Examples of structured education programmes available in the UK are DAFNE[69] for people with type 1 diabetes and DESMOND and X-PERT for people with type 2 diabetes. The evidence suggests that such programmes lead to improved glycaemic control. For women with diabetes who are planning a pregnancy and those who are already pregnant, good glycaemic control has benefits over and above those associated with good glycaemic control outside pregnancy because of the adverse maternal and neonatal outcomes associated with poor glycaemic control in the periconceptional period and pregnancy (see Sections 3.6 and 5.2).

Improvement in glycaemic control is also an important putative benefit of preconception care and advice. However, it is unlikely that studies of preconception care and advice have disentangled whether there are any additional improvements in relation to glycaemic control over and above those which would be achieved with a structured education programme alone. To the extent that there is further improvement in glycaemic control with preconception care and advice, it cannot be assumed that the effect size would be the same as preconception care and advice in the absence of a structured education programme. Indeed, it seems likely that there would be diminishing returns, with further improvement possible, but at a lower rate.

However, there are other benefits of preconception care and advice which are specific to diabetes in pregnancy which by themselves may make its provision clinically effective and possibly cost-effective. For example, advice on preconception folic acid is particularly important given the elevated risk of neural tube defects in babies of women with diabetes (see Sections 3.4 and 5.4). Furthermore, advice on contraception may also improve outcomes by increasing the number of pregnancies in women with diabetes that are associated with good glycaemic control.

A decision tree was developed for the guideline in Microsoft Excel® and also, for validation purposes, in TreeAge Pro 2006® (see Figure 22).

Figure 22: Preconception care and advice (PCA) versus no preconception care and advice decision tree showing major congenital malformation (CM) rates resulting from pregnancies in women with diabetes



As shown in the decision tree, it is assumed that a proportion of women are infertile and therefore do not benefit from preconception care and advice even if they accept an offer of such advice and adhere to it. It is assumed that women who are offered and adhere to preconception care and advice have a lower major congenital malformation rate than pregnant women in the no preconception care and advice arm. It is additionally assumed that those women in the preconception care and advice arm who either decline preconception care and advice or do not adhere to advice will have a congenital malformation rate equivalent to women with diabetes in the no preconception care and advice arm. The effectiveness of preconception care and advice is measured in terms of the number of major congenital malformations averted. In addition to the costs of the advice itself, the model also takes into account 'downstream savings' from averted congenital malformations. Considerable uncertainty surrounds the inputs of this model (see below for details) and therefore the results and sensitivity analysis are both undertaken to address the 'what if' in terms of thresholds for cost-effectiveness.

N.1.2 Model parameters

The parameter values used in the baseline model are shown in Tables 12, 13 and 14. The model assumes that there are administration costs in just offering a preconception care and advice service to women with diabetes who are planning a pregnancy and therefore this is included as a cost parameter. However, it is assumed that this cost can be limited to the population of concern (women with diabetes who are planning a pregnancy). It does not assume that the offer is made to all women with diabetes who are of childbearing age regardless of whether they are actively planning a pregnancy. However, this could be addressed in sensitivity analysis by assuming higher offer costs. The published cost-

effectiveness study described above[410] suggested that preconception care and advice would result in lower antenatal costs due to improved glycaemic control during pregnancy. The model structure allows this consideration to be factored in, but at baseline it conservatively assumes that preconception care and advice does not yield any cost saving in this respect compared with the no preconception care and advice alternative. In a similar conservative vein, no QALY gain is attached to averted major congenital malformations at baseline although the results are presented to show a minimum number of QALYs per congenital malformation averted that would be needed for cost-effectiveness given a particular incremental cost of preconception care and advice.

Table 12: Costs (using 2006 prices)

Resource item	Value	Source	Notes
Offer preconception care and advice	£10	GDG estimate	Administration cost in offering a preconception care and advice service
Preconception care and advice	£615	NICE Technology Appraisal 60, Diabetes (types 1 and 2) – patient education models (2003)[18]	2003 cost of £545 but updated for inflation using the Hospital and Community Health Services (HCHS)[a] Index
Additional costs of antenatal care with poor glycaemic control	£0		At baseline it is conservatively assumed that preconception care and advice does not result in lower antenatal costs
Cost of a major congenital malformationb	£81,000	Elixhauser et al. (1993)[410]	Weighted cost of major congenital malformations using an exchange rate of £1 to $2 and the HCHS index to update for inflation[c]

[a] *A price inflation index based on changes to the price of goods and services supplied to the healthcare sector.*
b Anencephaly, spina bifida, hydrocephalus, transposition of the great arteries, tetralogy of Fallot, coarctation of aorta, renal agenesis, anal/rectal atresia, caudal regression.
c Clearly there are limitations using these dated US data. As far as we are aware, equivalent UK costings do not exist. The costing of such a wide range of congenital malformations is methodologically complex and time consuming. Therefore, with the resources available for this guideline it was not possible to generate our own cost estimates based on UK NHS data. The known limitations of these data are addressed by sensitivity analysis.

Table 13: Probabilities

Variable	Value	Source
Decline preconception care and advice	0.5	GDG estimate
Adhere to preconception care and advice	0.8	GDG estimate
Fertile	0.9	Elixhauser et al. (1993)410
Major congenital malformation rate (preconception care and advice)	0.021	Ray et al. (2001)[121]
Major congenital malformation rate (no preconception care and advice)	0.065	Ray et al. (2001)[121]

Table 14: Quality-adjusted life years

Resource item	Value	Source	Notes
Willingness to pay for a QALY	£20,000	NICE guidelines manual (2007)23	
QALY gain from averted major congenital malformation	0		A conservative baseline assumption

N.1.3 Results

The baseline results suggest that preconception care and advice is cost-effective (see Table 15). In a population of 1000 women with diabetes who are planning pregnancy, the model shows a cost saving of almost £1 million and 16 averted major congenital malformations. There is no necessity to estimate a QALY gain to establish cost-effectiveness as preconception care and advice dominates, being cheaper and more effective than no preconception care and advice.

Table 15: Baseline results in a population of 1000 women with diabetes who are planning pregnancy

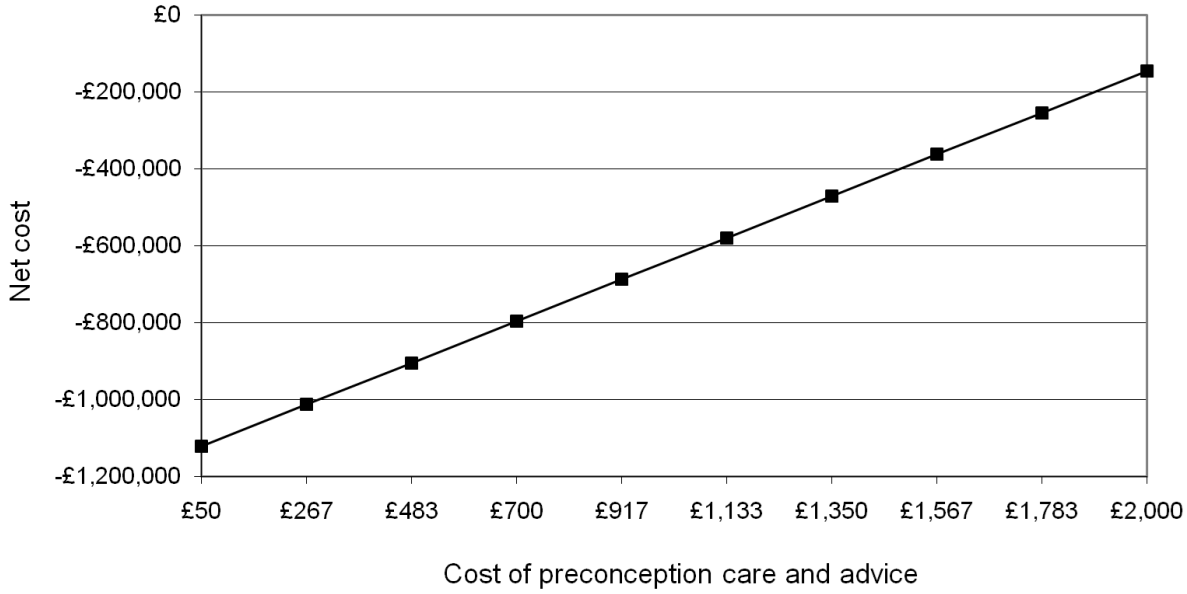
Item	Value
Net costs of preconception care and advice	−£965,540
Major congenital malformations averted	15.84
QALY gain needed per major congenital malformation averted	N/A
Incremental cost-effectiveness ratio (ICER)	Preconception care and advice dominates

N.1.4 Sensitivity analysis

Considerable uncertainty surrounds the data inputs of the model and therefore sensitivity analysis was used to assess how robust the baseline conclusions would be given different assumptions. This sensitivity analysis was primarily undertaken on a one-way basis, where one parameter value was varied while holding all other parameter values constant. This gives an indication as to whether uncertainty surrounding the exact value of the parameter is likely to have an important bearing on the model's conclusions. Additionally, thresholds for cost-effectiveness were calculated for scenarios where sensitivity analysis indicated that preconception care and advice may not be the dominant strategy. This involved calculating the QALY gain which would be needed to satisfy a cost-effectiveness threshold of £20,000 per QALY where preconception care and advice involved incremental costs relative to no preconception care and advice.

There are potentially many different models of preconception care and advice. At one end of the spectrum there could be a group session with a diabetes specialist nurse, but a more resource-intensive model might involve a one-to-one consultation with a multidisciplinary team. Figure 23 shows the effect of varying the cost of preconception care and advice between £50 and £2,000. The results suggest that preconception care and advice would be cost saving and hence dominant even at a cost of £2,000 per woman.

Figure 23: Net cost of preconception care and advice, varying costs of preconception care and advice

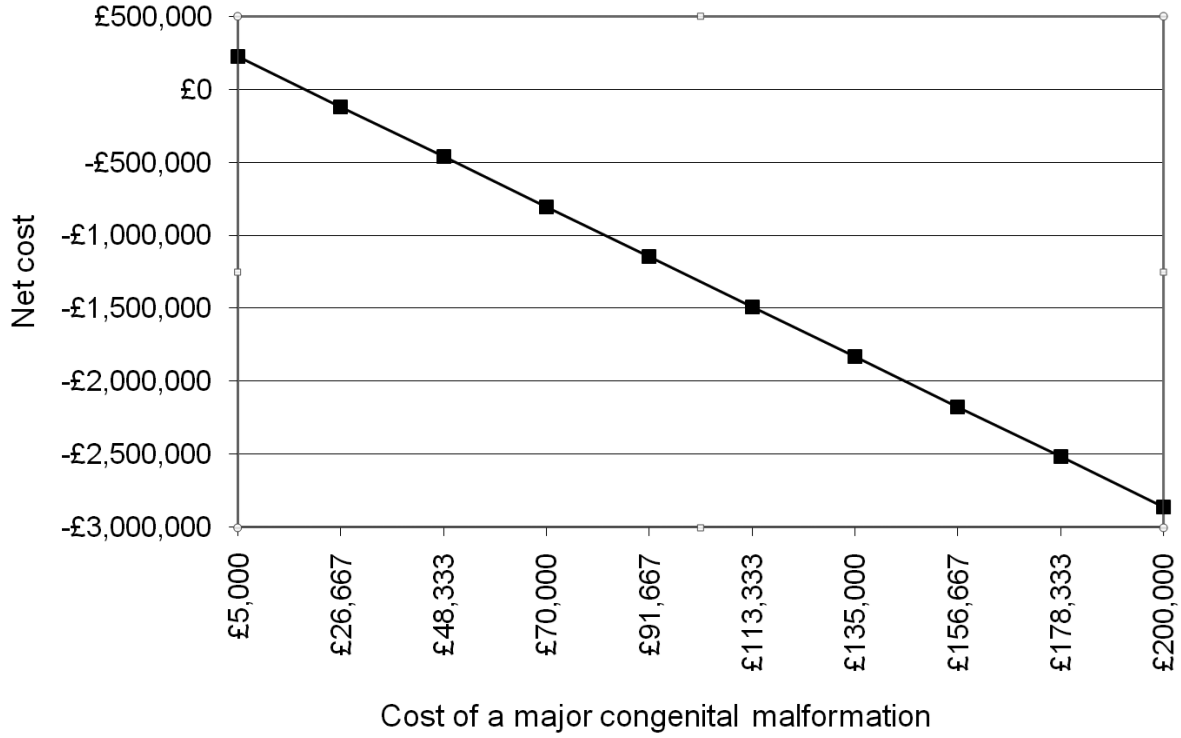


Another important source of uncertainty concerns the cost of a major congenital malformation. The baseline estimate was derived from a study conducted in the healthcare setting in the USA. There are a number of reasons why this may not accurately reflect costs to the NHS:

- the healthcare system in the USA differs markedly from that in the UK
- even in the context of the USA, the figures are presented as fairly 'broad brush' estimates
- the original study is quite dated and treatments may have changed.

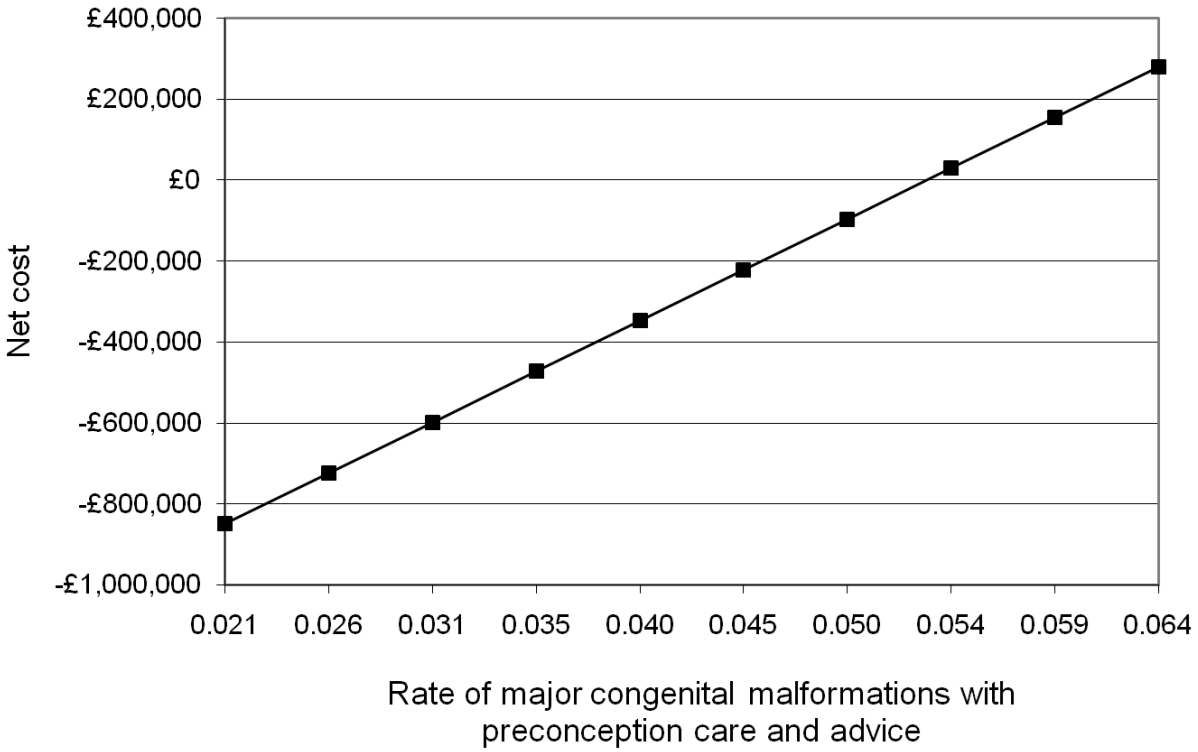
Figure 24 shows the impact of varying the cost of a major congenital malformation between £5,000 and £200,000 as part of a one-way sensitivity analysis. This shows that preconception care and advice would be cost saving as long as a major congenital malformation cost more than £20,044. If a major congenital malformation cost £5,000, then a QALY gain of 0.75 per major congenital malformation averted would be required for cost-effectiveness. Given the usually large impact of a major congenital malformation on lifetime health, it can be reasonably assumed that the QALY gain would be sufficient for cost-effectiveness in such a scenario.

Figure 24: Net cost of preconception care and advice, varying costs of a major congenital malformation



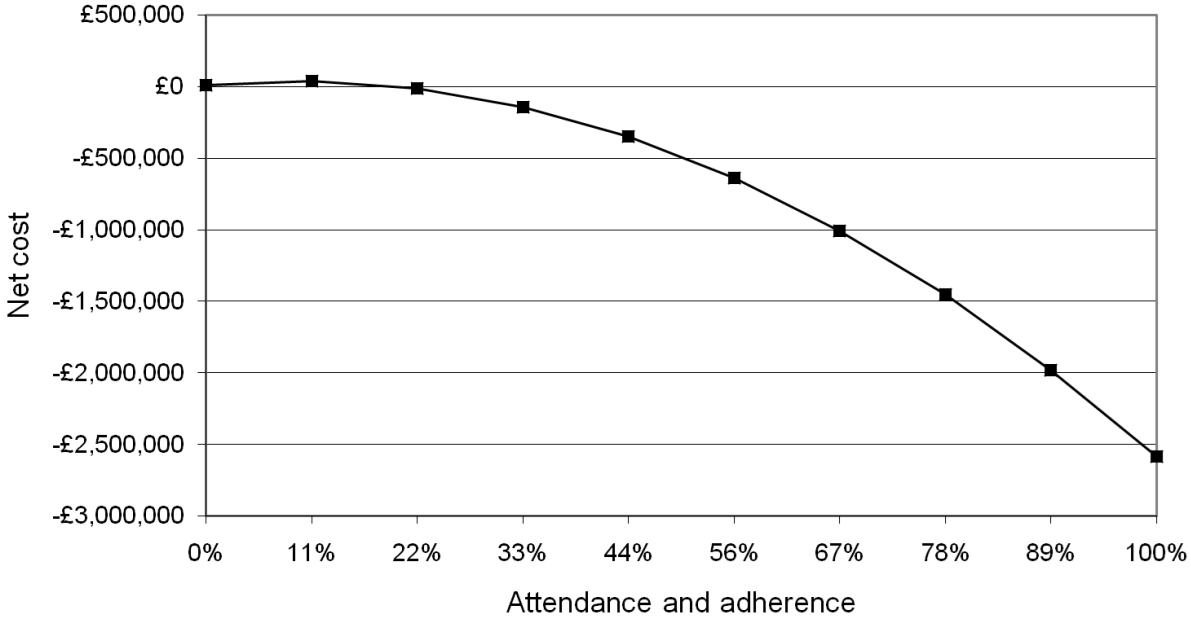
The effect of varying the assumption about the effectiveness of preconception care and advice is shown in Figure 25 The clinical effectiveness of the intervention is given by the absolute difference in the major congenital malformation rate between preconception care and advice and the no preconception care and advice alternative. Figure 25 shows the situation where the major congenital malformation rate for no preconception care and advice is held constant at 0.065 whilst the major congenital malformation rate for preconception care and advice is varied between the baseline 0.021 (absolute difference 0.044) and 0.064 (absolute difference 0.001). Preconception care and advice is dominant as long as the major congenital malformation rate with preconception care and advice is no more than 0.054 (absolute difference of at least 0.011), which is considerably less than that estimated by a recent meta-analysis.[121] As long as the absolute difference is at least 0.005 then it seems likely that preconception care and advice will be cost-effective. If the absolute difference is less than 0.005 then at least five more QALYs would be needed per averted major congenital malformation and it cannot necessarily be assumed a priori that this would be the case.

Figure 25: Net cost of preconception care and advice, varying rates of major congenital malformations with preconception care and advice



Finally, the impact of changing the assumptions about attendance and adherence was assessed by comparing the worst-case scenario (no attendance with zero adherence) with the best-case scenario (full attendance and adherence with the programme). Figure 26 shows the impact of increasing attendance and adherence in equal proportions between the worst-case and best-case scenarios. Initially, as attendance and adherence increase the net cost of preconception care and advice increases slightly. This is because the costs of providing preconception care and advice are not fully offset by reduced costs of congenital malformations at low adherence rates. However, when attendance and adherence reach a level of 21%, then preconception care and advice is dominant, producing a net cost saving in addition to the reduction in major congenital malformations.

Figure 26: Net cost of preconception care and advice, varying rates of attendance and adherence with preconception care and advice



N.1.5 Discussion

The baseline effectiveness of preconception care and advice in terms of major congenital malformations averted was based on results presented in a recent meta-analysis.[121] The results of the meta-analysis need to be treated with a degree of caution because of the heterogeneous nature of the individual studies included and because of systematic differences reported between women with diabetes who attended preconception care and advice and those who did not. For example, smokers were more prevalent in the no preconception care and advice group (30.2% versus 19.6%) and confounding could plausibly be responsible for at least some of the observed effect. It has been suggested that the availability of a preconception clinic separates women with diabetes into two groups, one containing highly motivated women with well-controlled diabetes who attend and have a low rate of congenital abnormalities and the other containing women who, for various reasons, book late, have worse glycaemic control, and have a congenital abnormality rate of 7.5–10.9%.[412] Furthermore, the effectiveness of preconception care and advice may be diluted when it is offered additionally to structured education programmes rather than as a stand-alone intervention. If a woman's glycaemic control has improved as a result of structured education then the scope for preconception care and advice to achieve further improvement may be limited.

The threshold sensitivity analysis undertaken using the model suggests that only a relatively small reduction in the major congenital malformation rate (as little as 0.005) is necessary for preconception care and advice to be considered cost-effective. This threshold for cost-effectiveness is much less than the absolute difference of 0.044 suggested in the published meta-analysis, and also less than 0.13 (the absolute difference between the upper 95% confidence limit reported in the meta-analysis for the major congenital malformation rate with preconception care and advice (worst case) and the lower 95% confidence limit for the major congenital malformation rate with no preconception care and advice (best case).[121] Preconception care and advice of some sort does, therefore, seem to be justified on economic grounds. The published meta-analysis suggested that the preconception care and advice interventions included were heterogeneous and this raises important questions from

an economic perspective in terms of what is the 'best' or most cost-effective form of preconception care and advice. This is particularly important as there is likely to be considerable variation in cost between different models of preconception care and advice and it is important to know what incremental benefits are achieved by more resource-intensive forms of the intervention. If less resource-intensive preconception care and advice is almost as effective then the incremental cost-effectiveness ratio for some preconception care and advice interventions is likely to be unacceptably high.

N.2 Cost-effectiveness of screening, diagnosis and treatment for gestational diabetes

N.2.1 Systematic review of screening

A systematic search of the literature identified [337] studies potentially related to the clinical question. After reviewing the abstracts, [33] articles were retrieved for further appraisal and eight have been included in this section of the review. Six papers were identified that examined the cost-effectiveness of screening for gestational diabetes. Two additional papers were identified that considered the cost-effectiveness of screening for and treatment of gestational diabetes.

N.2.1.1 Screening and treatment of gestational diabetes

A study conducted in France[441] examined three strategies for screening for gestational diabetes using a decision analysis model. Under strategy one, women deemed to be at higher risk of gestational diabetes based on a series of risk factors (family history of diabetes in a first-degree relative, age over 35 years, BMI greater than 27 kg/m², previous history of gestational diabetes, pre-eclampsia, fetal death after 3 months of gestation or previous macrosomia) were given a non-fasting 50 g OGTT. In strategy two all women were given the 50 g OGTT and in strategy three all women were given a 75 g OGTT. Data on costs were collected through a prospective study of 120 pregnancies and clinical data were taken from a review of published literature. Incremental analysis was reported in terms of cost per additional case prevented of macrosomia, prematurity, perinatal mortality or hypertensive disorder. All strategies were compared with a baseline of no screening for each outcome. The authors recommended strategy one, screening the population of high-risk pregnant women using the 50 g OGTT, based on its favourable ICER for preventing perinatal mortality (€7870[a], compared with €8660 and €29,400 for strategies two and three, respectively).

A retrospective study conducted in Italy[442] examined the costs and outcomes for two groups of women. The first group had universal screening using a 50 g GCT while the second were screened based on the presence of given risk factors (history of gestational diabetes, previous macrosomia, family history of diabetes mellitus, age over 30 years and body mass). All women that tested positive in either screening group underwent a 100 g OGTT. Universal screening was found to be more costly than the selective screening approach per case of gestational diabetes diagnosed (€424 and €406, respectively) and that treatment cost €366. No incremental analysis was reported. The authors concluded that, based on the savings from downstream interventions associated with untreated gestational diabetes, such as caesarean section, screening in some form was justified.

N.2.1.2 Screening for gestational diabetes

A cost–utility analysis[443] examined four screening strategies for gestational diabetes. The strategies were no screening, a 75 g OGTT, a 100 g OGTT and a sequential test (50 g GCT followed by a 100 g OGTT). The authors concluded that the sequential testing strategy was

a Exchange rate of £1 = €1.31, from markets.ft.com/ft/markets/currencies.asp on 28 February 2008

cost-effective, although in a high-prevalence population the 100 g OGTT may be an alternative cost-effective screening strategy. The study was conducted from a societal perspective, which could limit its applicability for decision making in an NHS setting, as this may overestimate costs. References were given for clinical and cost parameters but no specific details of these were reported. No detail was provided on what components comprised the total cost of each strategy and no unit costs were reported. Incremental analysis was undertaken and outcomes reported in QALYs, with maternal and infant outcomes reported separately. Sources for utility estimates were not provided. Given these drawbacks, the results of this study cannot be generalised to an NHS setting.

One study from the UK[124] examined the cost per case of gestational diabetes detected. Six screening strategies were considered: universal FPG, universal GCT with 7.8 mmol/litre cut-off, universal GCT with 8.2 mmol/litre cut-off, GCT with 8.2 mmol/litre cut-off in women aged over 25 years, GCT with 8.2 mmol/litre cut-off in women aged over 25 years and risk factors, and universal OGTT. The authors recommended the use of a universal FPG or giving a GCT to those over age 25 years and with risk factors. The FPG detected an additional 6009 cases at a cost of £489 per additional case detected when compared with GCT. A strategy of universal OGTT was predicted to detect an additional 1493 cases compared with the universal FPG, at a cost per additional case detected of £4,665.

Four studies reported in US dollars estimated the cost per case detected of gestational diabetes.[444–447] One study[44]4 examined the cost per case diagnosed of six different strategies. Incremental analysis was not reported. The authors recommended screening women aged over 25 years using a 50 g 1 hour glucose screening test. In a second study445 the authors examined the cost per case diagnosed using different thresholds for the diagnosis of gestational diabetes in a high-risk population. The cost per case of gestational diabetes identified by a 50 g oral glucose screening test was $114 at a cut-off of 7.2 mmol/litre and $106 at a cut-off of 8.3 mmol/litre. The authors made no conclusion on the cost-effectiveness of either approach. A third study446 examined the cost per case diagnosed of gestational diabetes in two groups of women. Group 1 had historical or clinical risk factors for gestational diabetes and group 2 were offered routine screening. Screening was with a 50 g GCT followed by a OGTT for women with greater than 150 mg/100 ml. The number of cases of gestational diabetes diagnosed did not differ between groups. The cost per case diagnosed of the testing programme was $329. A fourth study[447] was conducted in Iran and reported in US dollars. Women were stratified into high-, intermediate- and low-risk groups based on American Diabetes Association (ADA) criteria. The authors recommended universal screening in a high-prevalence population such as theirs, with a cost per case diagnosed of $80.56. No incremental analysis was reported.

N.2.2 Introduction to the model

The recently published ACHOIS trial demonstrated potential benefit of treatment for mild gestational diabetes.[153] However, while clinical effectiveness is a necessary condition for cost-effectiveness it is not sufficient. Resources have competing uses and showing that resources yield a benefit does not demonstrate that an even greater benefit could not be produced if those resources were deployed in an alternative use. Furthermore, treatment requires identification of those affected by gestational diabetes using some screening/diagnostic strategy which further reduces scarce resources available to other NHS patients. Therefore, the cost-effectiveness of treatment will partly be determined by the ability to identify patients for treatment via screening in a cost-effective fashion. Similarly, the cost-effectiveness of screening is predicated on an efficacious treatment which gives an acceptable cost per effect given the finite resources available.

Therefore, the cost-effectiveness of screening, diagnosis and treatment for gestational diabetes are highly interdependent. As a result, a single cost-effectiveness model addressing screening, diagnosis and treatment for gestational diabetes was developed jointly by the

diabetes in pregnancy and antenatal care GDGs to enable them to make recommendations on this area of care for pregnant women.

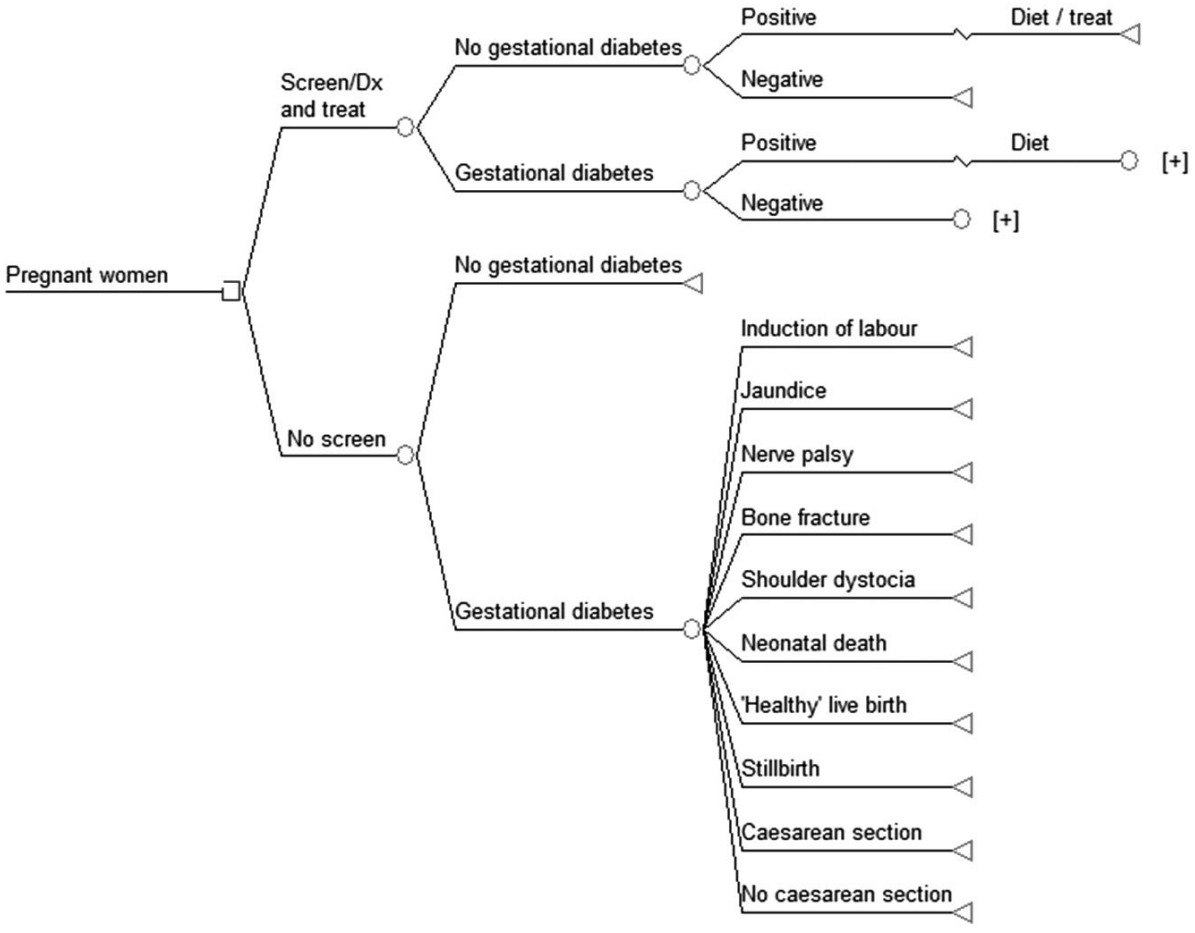
However, in addition to this single model incorporating both screening and treatment, a separate cost-minimisation analysis of the various treatment options is also presented. This better illustrates the cost-effectiveness of different treatment alternatives, under the assumption of equivalent effectiveness, where the decision to screen for cases and treat has been accepted on economic grounds.

N.2.2.1 The decision tree

The model utilises a decision-analytic approach. In this approach, competing alternatives represent the decisions. Then, by considering the probabilities of different scenarios under each decision, drawing on best available evidence, the expected costs and effects of each decision can be computed and compared.

At its most basic, this cost-effectiveness model can be represented as the decision to screen and treat patients identified with gestational diabetes versus no screening, which was the recommendation of the previous antenatal care guideline (Figure 27).

Figure 27: The basic decision tree structure;



[+] denotes that the tree is truncated – see Figure 29 for the treatment sub-tree; the sub-tree for those with gestational diabetes who are undetected on screening is the same as the sub-tree for women with gestational diabetes who are not screened; Dx = diagnose

Data from the ACHOIS intervention group were used to estimate the outcomes and associated costs of treating true positives. As ACHOIS was limited to those with 'mild' gestational diabetes, the costs and effects may be an underestimate of the true costs and

effects in the population under consideration. The outcomes and associated costs of false negatives were estimated from the routine care group in ACHOIS. It is also necessary to consider the cost of providing treatment to women falsely diagnosed with gestational diabetes (false positives). The outcomes for women without gestational diabetes (true negatives and false positives) in the screening arms were not considered as the perinatal outcomes for these pregnancies do not differ from those in the population of otherwise healthy pregnant women.

In Figure 27 the decision, for diagrammatic simplicity, is depicted as screen versus no screen. However, given an initial decision to screen there is then the decision of how to screen. The various screening options that have been considered in this model are described in the next section.

The key outputs of each screening strategy are the costs of screening and treating women and the number of women accurately diagnosed with gestational diabetes. There are four possible outcomes when applying a diagnostic test:

- true positive – the patient is diagnosed as positive and has the condition/disease
- false positive – the patient is diagnosed as positive but does not have the condition/disease
- true negative – the patient is not diagnosed with the condition/disease and does not have it
- false negative – the patient is not diagnosed with the condition/disease but does in fact have it.

The number of individuals diagnosed correctly is determined by the accuracy of the diagnostic test applied (sensitivity and specificity) and by the prevalence of the condition in the population being tested. The treatment and outcome sub-trees are identical for each screening strategy in this model but the costs and effects will vary according to the numbers diagnosed as having gestational diabetes or not.

N.2.3 Screening strategies

Table 16 contains a list of the various strategies that have been considered as screening strategies for gestational diabetes. All screening methods, including risk factor screening, screening blood tests and universal diagnostic tests, have been considered in isolation. Combinations of these tests have then been considered.

Not all possible strategies have been considered – particularly where they are clinically inappropriate, for example treating patients based on the presence of a risk factor alone. Some strategies have been excluded from further analysis after preliminary analysis showed them to be dominated by alternative strategies. Limitations in the data are discussed in greater detail later in this appendix.

Risk factors that have been considered:

- age ≥ 30 years
- age ≥ 25 years
- high-risk ethnic background (ethnicity; see Table 20)
- BMI ≥ 27 kg/m² (high BMI)
- family history of diabetes.

Screening blood tests considered:

- FPG
- random blood glucose (RBG)
- 1 hour 50 g GCT.

Diagnostic blood test considered:

- 2 hour 75 g oral glucose tolerance test (OGTT).

Table 16: List of screening strategies

Strategy number	Risk factor	Screening blood test	Screening diagnostic test
1	–	–	OGTT
2	ADA criteria[a]	FPG	OGTT
3	ADA criteria	RBG	OGTT
4	ADA criteria	GCT	OGTT
5	ADA criteria	FPG	–
6	ADA criteria	–	OGTT
7	ADA criteria	GCT	–
8	–	FPG	–
9	–	RBG	–
10	–	GCT	–
11	–	FPG	OGTT
12	–	GCT	OGTT
13	Age ≥ 30 years	FPG	OGTT
14	Age ≥ 30 years	GCT	OGTT
15	Age ≥ 25 years	FPG	OGTT
16	Age ≥ 25 years	GCT	OGTT
17	Age ≥ 30 years	–	OGTT
18	Age ≥ 25 years	–	OGTT
19	High-risk ethnicity	FPG	OGTT
20	High-risk ethnicity	GCT	OGTT
21	High-risk ethnicity	–	OGTT

(a) Having one or more of the following risk factors: age > 25 years; BMI> 27 kg/m²; family history of diabetes; high-risk ethnic group.

N.2.3.1 Screening strategy assumptions

Decision analysis is used to help us make decisions about the best treatment or intervention to use, based on grounds of cost and clinical effectiveness. When developing a decision analysis model it is necessary to make simplifying assumptions to highlight what the important elements of the model might be and to reduce the complexity of the model. It is not possible to consider every possible potential outcome in a model and it is important to focus on those with the greatest relevance in answering the question at hand. The assumptions used in the model of screening strategies are given below:

- A 2 hour 75 g OGTT is used as the gold standard diagnostic test (refer to Section 4.4 for details) and is assumed to be 100% sensitive and specific.
- It has not been possible to establish an accurate fertility rate in some population subgroups. It is therefore assumed that the fertility rate among women with a high BMI is the same as the rate among women with a BMI in the normal range. This may overestimate the number of pregnancies in this group, as high BMI is associated with fertility problems.[448]
- The available data on BMI are not consistent. Population level data on BMI from the Office of National Statistics or the Health Survey for England is presented as overweight and obese with a BMI greater than or equal to 25 kg/m², whereas the data presented in the

literature[129] used a BMI greater than or equal to 27 kg/m² to define some at risk of gestational diabetes based on BMI. It was assumed initially that the risk of those with a BMI greater than 25 kg/m² is equal to that of those with a BMI greater than 27 kg/m², though this assumption could be relaxed in sensitivity analysis. If there is a genuine difference in the subpopulation (BMI 25–27 kg/m²), this assumption may overestimate the number of cases of gestational diabetes in the at-risk population and lead to a greater number of false positive diagnoses of gestational diabetes.

N.2.3.2 Screening strategy input parameters

The parameters used to populate the model have been chosen based on the best available evidence, and those relating to screening are listed in Tables 17 to 20.

Table 17: Accuracy of screening and diagnostic blood tests

Test	Sensitivity	Specificity	Source
FPG	0.88	0.78	Reichelt et al. (1998)449
RBG	0.48	0.97	Ostlund and Hanson (2004)450
1 hour 50 g GCT	0.80	0.43	Seshiah et al. (2004)451
2 hour 75 g OGTT	1.0	1.0	Gold standard

Table 18: Cost of screening and diagnostic blood tests

Variable	Cost	Source
Risk factor screening	£2	GDG estimate
FPG	£5.39	Updated from Scott et al. (2002)124
RBG	£5.39	Updated from Scott et al. (2002)124
1 hour 50 g GCT	£10.61	Updated from Scott et al. (2002)124
2 hour 75 g OGTT	£28.58	Updated from Scott et al. (2002)124

Table 19: Risk factors for gestational diabetes – age

Risk factor	% of population (Source)	% of women with gestational diabetes (source)	PPV (%)
Age ≥ 30 years	48.7 (ONS, 2005)	0.65 (Coustan, 1993)452	4.7
Age ≥ 25 years	74.2 (ONS, 2005)	0.85 (Coustan, 1993)452	4.0

Table 20: Risk factors for gestational diabetes other than age

Risk factor	% of population (Source)	% of women with gestational diabetes (source)	PPV (%)
Gestational diabetes in a previous pregnancy	3.5 (HES, 2005)	30 (Weeks et al., 1994)453	10.5
Family history of diabetes	10.0 (Davey and Hamblin, 2001)129	39.9 (Davey and Hamblin, 2001)129	14.0
High-risk ethnic group	8.5 (ONS, 2001)	68.7 (Davey and Hamblin, 2001)129	28.1
BMI ≥ 27 kg/m²	35.8 (ONS, 2001)	36.2 (Davey and Hamblin, 2001)129	3.5

After some initial modelling, the GDG expressed concern that test acceptability might be an additional important consideration. Some women may find the tests inconvenient and

unpleasant, especially where they are required to fast for a period beforehand. Table 21 lists the input parameters relating to test acceptability.

Table 21: Test acceptance

Test	Initial test acceptance	Test acceptance if identified as 'at risk'	Source
FPG	0.50	0.90	GDG estimate
RBG	0.90	1.00	GDG estimate
1 hour 50 g GCT	0.70	1.00	GDG estimate
2 hour 75 g OGTT	0.40	0.90	GDG estimate

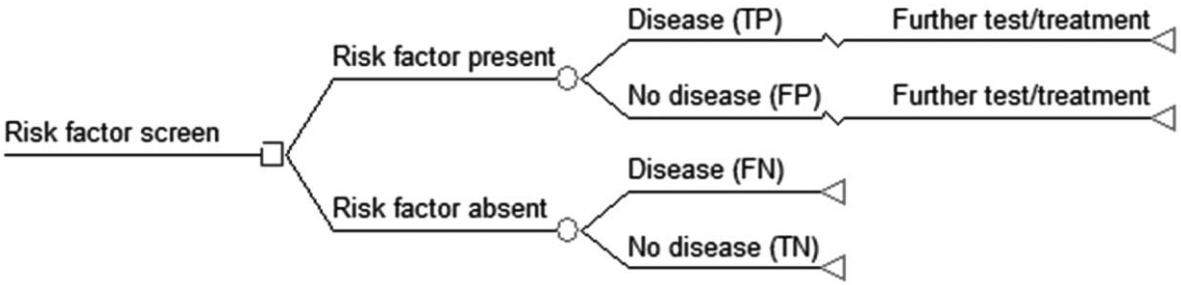
The model assumes that women are more likely to accept a test if they have already been identified as being at higher risk, either by risk factor or a previous screening test. The baseline values reflected the views of the GDG, but clearly considerable uncertainty surrounds the actual test acceptance, and thus sensitivity analysis was undertaken to determine to what extent test acceptance determines the cost-effectiveness conclusions of the model.

N.2.3.3 Incorporating risk factors within the model

General overview

In terms of the decision tree for the gestational diabetes screening/treatment model, risk factors can be thought of analogously to diagnostic tests (Figure 28).

Figure 28: Decision tree for risk factors



TP = true positive; FP = false positive; FN = false negative; TN = true negative

Positives from a risk factor screen or screen/diagnostic test progress to the next stage of testing or treatment. Negatives do not progress.

The detection rate of a risk factor screen is given by the true positive rate[b]. This detection rate is an important component of the model, as treatment costs and effects are predicated on it. Its flip-side (false negatives) is also important because there may be 'downstream' costs associated with missed cases.

b In our gestational diabetes model, this is complicated by assumptions made about test acceptance

In the economic model of screening we are also concerned with the unnecessary costs of screening which are caused by false negatives. The screening does not lead to improved outcomes in women with gestational diabetes and the scarce resources used in screening have an opportunity cost in terms of the benefit they could have achieved if used elsewhere in the healthcare system[c].

Therefore, the screening strategy with the highest detection rate is not necessarily the most cost-effective. There may be some desirable trade-off between detection and unnecessary testing and treatment.

The methodological problem

The data requirements for the model for any risk factor screening strategy are conceptually straightforward:

- what is the disease prevalence?
- what proportion of the population meets the risk criteria[d]?
- what proportion of cases is detected in the population who meet the criteria?

With answers to these questions the true positive, false positive, true negative and false negative branches of the decision tree can be completed.

The literature tends to focus on the detection rates of a particular risk factor (or more rarely combination of risk factors). Using Office for National Statistics (ONS) data in combination with the literature it is possible to estimate the true positive, false positive, true negative and false negative rates for a single risk factor screen at baseline prevalence. However, given data limitations, it is much more difficult to derive these estimates for screening strategies based on combinations of risk factors.

Prevalence varies across the country and this is potentially important in the cost-effectiveness of screening as it influences the trade-off between detection and false positives. Therefore, the model has been developed to explore how the conclusion may vary at different disease prevalence. To do this required that we model a relationship between changes in disease prevalence and the proportion classed at 'high risk'. This poses further methodological difficulties because of the complex and interdependent relationship between risk factors.

With sufficient individual level data, it is possible to envisage a multiple regression equation which would predict the change in prevalence arising from a change in the proportions with different risk factor (RF) combinations.

$$\text{Prevalence} = a + b_1RF_1 + b_2RF_2 + b_3RF_3 + \ldots + b_nRF_n$$

Such a model could be used to predict individual risk of disease.

However, in this model, risk factor proportion would be the dependent variable. As a result any model change in gestational diabetes prevalence would lead to a change in risk factor proportion. However, in reality, it is likely that different combinations of risk factors are consistent with the same overall disease prevalence. So, for example, a relatively young pregnant population may have the same gestational diabetes prevalence as an older pregnant population, if the younger population has a higher proportion in high-risk ethnic groups. This means that the most cost-effective screening strategy may be determined by the demographic characteristics of a particular population rather than prevalence per se (although the latter is a function of the former).

c It is not explicitly addressed in the model, but an undesirable consequence of screening may be the unnecessary inconvenience and worry associated with false positives.

d This information obviously also gives the proportion who do not meet the criteria.

Our approach to modelling risk factor screening

Owing to data limitations and methodological complexity, our approach involved certain simplifying assumptions and the accuracy of the model may ultimately depend on whether these give a sufficiently good approximation to the real world.

Each risk factor screening strategy involves dividing the population in two – those at 'high' risk and those at 'low' risk[e]. Logically, the disease prevalence is the weighted average of the respective prevalence in these two groups. The weights are the proportions in each of the groups.

Prevalence = (proportion high risk × high-risk prevalence) + (proportion low risk × low-risk prevalence)

The first step is to estimate a PPV for each risk factor screen, i.e. what proportion of the high-risk group had gestational diabetes? This gives the prevalence of gestational diabetes for the high-risk group. Next, an NPV is calculated, i.e. what proportion of the low-risk group did not have gestational diabetes. The prevalence in the low-risk group is given by 1 − NPV. These estimates use a combination of the literature and ONS data and they are probably reasonably good at baseline because they are not based on a simplified model extrapolation[f].

We then assume that the PPV and NPV are independent of prevalence. In a hypothetical scenario where there was just one risk factor for a disease, this would be correct. However, this linear relationship between risk factor proportion and prevalence is clearly a simplifying assumption in this case.

The model does not capture the impact and interdependence of multiple risk factors. As the proportion with a risk factor (e.g. age) increases, there would be concomitant increases in the proportion with multiple risk factors, which would change the PPV in those of 'at risk' age. This would exert an upward pressure on prevalence over and above that arising from the change in a single risk factor. In practice, changes in gestational diabetes prevalence are likely to lead to a smaller change in risk factor proportion than that implied by the model. This is even true for the ADA strategy, as clearly there is no reason why the proportion with multiple risk factors should be constant with respect to prevalence. Similarly, if the low-risk group have some risk factors then their disease prevalence (1 − NPV) is also likely to change with the demographic differences associated with changing disease prevalence.

Recognising these simplifying assumptions as a limitation, it should also be noted that the software developed for modelling included an option to override the model relationship between prevalence and risk factors. If this option were chosen, the user of the software would themselves select the 'at risk' proportion and the proportion of cases that would exist in this population. This can be used to reflect better local data, if known, or to conduct sensitivity analysis. Such sensitivity analysis may indicate to what extent the simplifying assumptions drive the cost-effectiveness conclusions.

Below we outline in more detail the assumptions that were made for each risk factor screening strategy used in the model.

ADA criteria:

ADA selective screening criteria exclude women who are:

- age < 25 years

e 'High' and 'low' risk should be interpreted as a comparison of two groups, where one has a higher level of risk than the other.

f ADA may be a slight exception because the paper used to derive PPV and NPV values was based on a US population with a lower prevalence than our baseline model.

- BMI < 27 kg/m²
- low-prevalence ethnic group
- no first-degree relative with history of diabetes.

The PPV and NPV for the ADA criteria were calculated as follows, using a retrospective study by Danilenko-Dixon et al.454 which compared selective screening (using ADA criteria) with universal screening. The authors estimated that only 10% would be exempt from screening in their population (of which 17.8% were under 25 years), i.e. having none of the ADA risk factors. They found that 3% (17/564) of gestational diabetes cases were missed using ADA criteria[g]. The prevalence of gestational diabetes in their population was 3% (564/18 504) (see Table 22).

Table 22: Calculating PPV and NPV using ADA criteria as a risk factor screen

Parameter	Value
n	18 504
Prevalence = 564 / 18 504	3.05%
High risk = 0.9 × 18 504	16 654
Gestational diabetes cases in high risk = 564 − 17	547
PPV = 547/ 16 654	3.28%
Low risk = 0.1 × 18 504	1,850
Gestational diabetes cases in low risk	17
NPV = 1833/1850	99.1%

In this case, we needed to model the relationship between ADA parameters and prevalence even for our baseline analysis, because the calculations are taken from a population having different disease prevalence.

The key assumption in modelling this was to assume that the PPV and NPV were independent of disease prevalence. The PPV is essentially the disease prevalence in the high-risk group. The gestational diabetes prevalence in the low-risk group is given by 1 − NPV (0.92%).

The overall prevalence can then be seen as a weighted average of the high-risk and low-risk groups. For a given population gestational diabetes prevalence, it is therefore possible to estimate the proportions in the high-risk and low-risk categories. The PPV in conjunction with the high-risk proportion gives the detection rate.

What this modelled relationship implies is that for prevalence of 3.28% or more, all the population would be high risk as defined by ADA and therefore this is what our model assumes for the baseline prevalence (3.5%). This would not be the case in reality for reasons outlined in the preceding section[h].

Ethnicity:

Here ‘high risk’ is defined as women in a ‘high’ prevalence ethnic group and ‘low risk’ is defined as women in a ‘low’ prevalence ethnic group.

The approach we used was similar to that used for the ADA criteria and is described in Table 23.

g Another study by Williams et al.[462] suggested 4% of gestational diabetes cases would be missed by ADA criteria.

h However, given the study on which our calculations were based, > 90% proportion ‘high risk’ and > 97% gestational diabetes detection might be considered ‘realistic’

Table 23: Calculating PPV and NPV in using high-risk ethnicity as a risk factor screen

Parameter	Value	Source
Proportion of high risk	8.5%	ONS[a]
Proportion of gestational diabetes high-risk ethnic group	68.7%	Weeks et al. (1994)453
Births	645 835	ONS
Births high-risk ethnic groups	54 896	Calculated
Gestational diabetes prevalence	3.5%	GDG estimate
Gestational diabetes births	22 604	Calculated
Gestational diabetes births high-risk ethnic groups	15 529	Calculated
PPV (15 529/54 896)	28.1%	Calculated

Again it was assumed that PPV and NPV were independent of disease prevalence. As with the ADA criteria, these provide prevalence in the high-risk and low-risk group with the overall population prevalence being a weighted average of the two[i]. Therefore, it is possible to estimate the high-risk ethnic group proportion from any given population gestational diabetes prevalence.

The model suggests that at a population prevalence of 2%, the high-risk ethnic proportion would be 2.98%. At a gestational diabetes prevalence of 10% it predicts 32.6%. On the face of it, these seem fairly plausible estimates but with the caveat that they are derived from a high-risk prevalence which is much higher than the literature would suggest.

BMI of 27 kg/m² or more:

This strategy identifies high-risk women as having a BMI of 27 kg/m² or more and low-risk women has having a BMI of less than 27 kg/m². The proportion of high-risk women in this strategy at baseline was calculated as shown in Table 24.

Table 24: Calculating PPV and NPV using a BMI of 27 kg/m² or more as a risk factor screen

Parameter	Value	Source
High-risk BMI proportion	0.358	ONS[a]
Proportion of gestational diabetes high-risk BMI	0.362	Davey and Hamblin (2001)[129]
Births	645 835	ONS
High-risk BMI births	231 209	Calculated
Low-risk BMI births	414 624	Calculated
Gestational diabetes prevalence	0.035	GDG estimate
Gestational diabetes births	22 604	Calculated
High-risk BMI gestational diabetes births	8 183	Calculated
Low-risk BMI gestational diabetes births	14 421	Calculated
PPV (8183/231 209)	3.5%	Calculated
NPV (400 203/414 624)	96.5%	Calculated

Family history of diabetes:

This strategy identifies high-risk women as having a first-degree relative with a history of diabetes and low-risk women has having no first-degree relative with a history of diabetes.

i A prevalence of 28.1% for 'high-risk' ethnic groups seems considerably higher than values quoted in the literature.

The proportion of high-risk women in this strategy at baseline was calculated as shown in Table 25.

Table 25: Calculating PPV and NPV using a first-degree relative with a history of diabetes as a risk factor screen

Parameter	Value	Source
High-risk family history proportion	0.10	Davey and Hamblin (2001)[129]
Proportion of gestational diabetes high-risk history	0.399	Davey and Hamblin (2001)[129]
Births	645 8[35]	ONS
Low-risk family history births	581 [252]	Calculated
High-risk family history births	64 [584]	Calculated
Gestational diabetes prevalence	0.035	GDG estimate
Gestational diabetes births	22 [604].	Calculated
High-risk family history gestational diabetes births	9,018	Calculated
Low-risk family history gestational diabetes births	13 [586]	Calculated
PPV (9018/64 584)	14.0%	Calculated
NPV (567 666/581 252)	97.6%	Calculated

Age ≥ 25 years:

This strategy identifies high-risk women as 25 years of age or older and low-risk women being 24 years of age or less. At baseline this gives a high-risk proportion of 74.2% and low-risk proportion of 25.8% (source: ONS).

The detection rate is then derived using a PPV, which is again assumed not to change with disease prevalence. The proportion of high-risk women in this strategy at baseline was calculated as shown in Table 26.

Table 26: Calculating PPV and NPV using age 25 years or older as a risk factor screen

Parameter	Value	Source
Total births	645 [835]	ONS
Total births ≥ 25 years	478 [860]	ONS
Gestational diabetes prevalence	3.5%	GDG estimate
Gestational diabetes births (0.035 × 645 835)	22 [604]	Calculated
Proportion detected ≥ 25 years	85%	Coustan (1993)452
Gestational diabetes detected (0.85 × 22 604)	19 [214]	Calculated
PPV (19 214/478 860)	4.01%	Calculated
NPV (163 585/166 975)	98.0%	Calculated

It should be noted that the model assumes that all the population is in the high-risk category for prevalence values of 4.01% and above.

Age ≥ 30 years:

The method is the same as for age ≥ 25 years, but using an older age threshold to define the high-risk and low-risk proportion. At baseline this gives a high-risk proportion of 48.7% and low-risk proportion of 51.3% (source: ONS).

The detection rate is then derived using a PPV, which is again assumed not to change with disease prevalence (Table 27).

Table 27: Calculating PPV and NPV using aged 30 years or older as a risk factor screen

Parameter	Value	Source
Total births	645 835	ONS
Total births ≥ 30 years	314 512	ONS
Gestational diabetes prevalence	3.5%	GDG estimate
Gestational diabetes births (0.035 × 645 [835])	22 604	Calculated
Proportion detected ≥ 30 years	65%	Coustan (1993)[452]
Gestational diabetes detected (0.65 × 22 [604])	14 693	Calculated
PPV (14 693/314 [512])	4.7%	Calculated
NPV (323 412/331 [323])	97.6%	Calculated

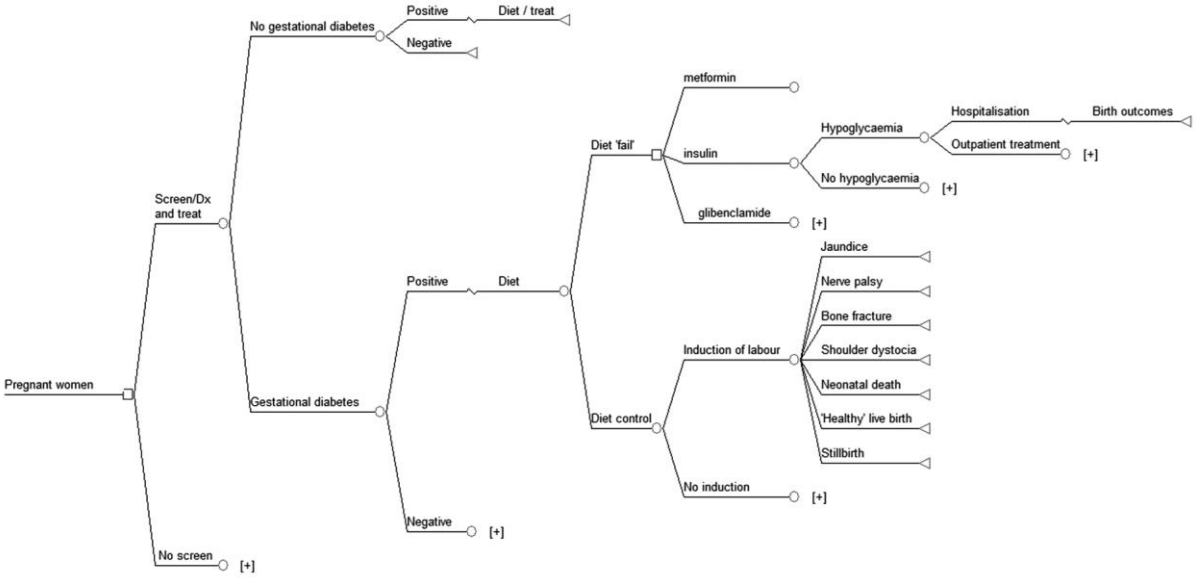
It should be noted that the model assumes that all the population is in the high-risk category for prevalence values of 4.7% and above.

N.2.4 Treatment

N.2.4.1 Treatment decision tree

The basic decision tree for treatment is depicted in Figure 29.

Figure 29: The basic treatment sub-tree



The screening part of the model produces an output of true positives, false negatives, false positives and true negatives and these numbers then inform the probabilities attached to given patient treatment pathways following a positive or negative diagnosis of gestational diabetes.

As far as possible, treatment was modelled according to the ACHOIS protocol, as this is what the effectiveness data were based upon. It is assumed that women with gestational diabetes would start treatment at a gestational age of 27 weeks and that this would continue for 90 days.

The treatment protocol used in the model is outlined below.

Diet

Initial treatment aims to control blood glucose using diet. This part of treatment consists of:

- 30 minutes of individualised dietary advice from a qualified dietitian
- 30 minutes of instruction on self-monitoring of blood glucose provided by a specialist nurse (band 5/6)
- self-monitoring of blood glucose, four times daily (costing of self-monitoring of blood glucose includes one monitor, and assumes one lancet and one test strip per reading)
- 5 minutes of assessment of control after 10 days on diet by a specialist nurse.

At this 10 day assessment, women with gestational diabetes are judged to have achieved adequate control with diet or not. If they have achieved adequate control, they remain on dietary control until the end of their pregnancy, with self-monitoring of blood glucose reduced to twice daily.

If women are deemed not to have achieved adequate control with diet, medical treatment (insulin analogue, glibenclamide, metformin) is then initiated.

Insulin analogue

- 45 minutes of instruction from a diabetes specialist nurse
- daily insulin dose: 20 units
- pre-filled disposable injection device
- twice-daily injections (two needles per day of treatment)
- a proportion of women will experience hypoglycaemia and a small proportion of these will be severe cases requiring an inpatient admission
- self-monitoring of blood glucose, two times daily.

Glibenclamide and metformin, two alternative oral hypoglycaemic treatments to analogue insulin, were also included in the model. An RCT of glyburide (glibenclamide) versus insulin for gestational diabetes showed no statistically significant differences in outcomes. The effectiveness of metformin is currently being investigated as part of the ongoing MIG trial and is therefore a potential treatment option. The basic tree structure for an oral hypoglycaemic treatment, such as glibenclamide, would be as illustrated in Figure 30.

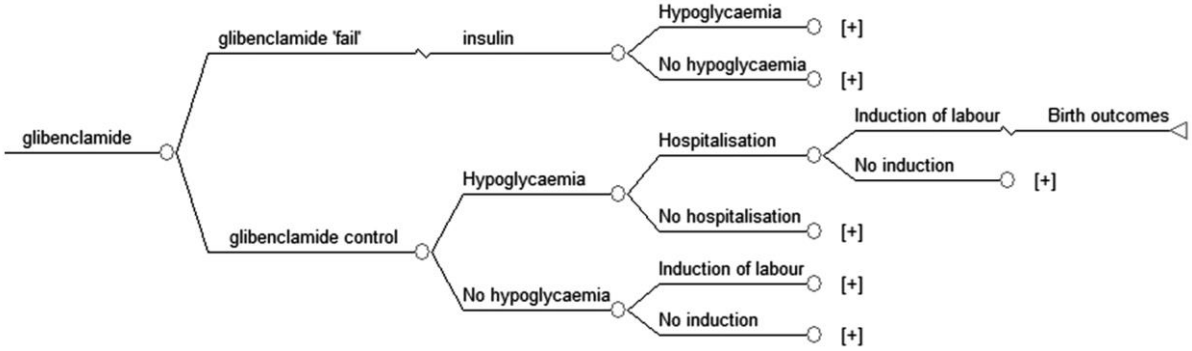
Glibenclamide

- daily dose: 15 mg.

Metformin

- daily dose: 1.5 g.

Figure 30: Glibenclamide treatment sub-tree



N.2.4.2 Outcomes and downstream costs

The model uses the following outcomes presented in the ACHOIS study to estimate the incremental QALY gain associated with screening, diagnosis and treatment of gestational diabetes:

- stillbirth
- neonatal death
- maternal health state utility.

Furthermore, the following outcomes from ACHOIS are assumed to have downstream cost implications. Costs are assigned to these outcomes and included in the evaluation of incremental costs:

- neonatal death
- shoulder dystocia
- bone fracture
- admission to neonatal unit
- jaundice requiring phototherapy
- induction of labour
- caesarean section.

We used the outcome data of ACHOIS for 'serious perinatal complications' as the measure of the effectiveness in the model. The trial data allow this to be easily done for deterministic sensitivity analysis, with the different event rates giving well-defined relative risks. In order to reflect the individual components of the composite measure, a weighted cost and QALY was calculated for a serious perinatal complication based on the QALY and costs associated with each of the individual components. In order to calculate the weights, it was assumed, based on the lack of statistical significance for any difference, that the proportion of serious perinatal complications accounted for by individual components did not differ according to whether they were treated for gestational diabetes or not. Therefore, the data on individual events were pooled across both arms of the trial in order to estimate the weighting for individual components (Table 28).

Table 28: ACHOIS trial outcome data for serious perinatal complications combined across control and intervention groups

Outcome	Total	Weight
All serious perinatal complications	32	1.00
Stillbirth	3	0.09
Neonatal death	2	0.06
Shoulder dystocia	23	0.72
Bone fracture	1	0.03
Nerve palsy	3	0.09

N.2.4.3 Treatment model parameters

The baseline parameter values for all model treatment inputs are shown in Tables 29 to 35.

Table 29: Treatment timeframe

Variable	Value (days)	Source	Notes
Treatment	90	Diabetes in	The diabetes in pregnancy GDG consensus was that

Variable	Value (days)	Source	Notes
duration		pregnancy GDG	treatment would usually commence between 26 and 28 weeks of gestation1. Taking the midpoint of 27 weeks, 90 days is a reasonable approximation of the typical time to term.
Exclusive diet	10	Diabetes in pregnancy GDG	The diabetes in pregnancy GDG suggested that diet alone would be given 7–14 days to achieve adequate control.
4 × daily SMBG	10	ACHOIS[153]	The ACHOIS protocol suggested that SMBG be done 4 × daily until glucose levels had been in the recommended range for 2 weeks.

SMBG = self-monitoring of blood glucose.

Table 30: Cost of healthcare professionals' time

Variable	Time (minutes)	Cost per hour	Source	Notes
Dietary advice	30	£28	Curtis and Netten (2006)[456]	Unit costs of a dietitian for an hour of client contact
SMBG instruction	30	£63	Curtis and Netten (2006)[456] GDG estimate	Unit cost of a nurse specialist (community) for an hour of client contact
Control with diet; assessment/review	5	£63	Curtis and Netten (2006)[456] GDG estimate	Unit cost of a nurse specialist (community) for an hour of client contact
Insulin instruction	45	£63	Curtis and Netten (2006)[456] GDG estimate	Unit cost of a nurse specialist (community) for an hour of client contact
Risk factor screening questions	2	£63	Curtis and Netten (2006)[456] GDG estimate	Unit cost of a nurse specialist (community) for an hour of client contact

SMBG = self-monitoring of blood glucose.

Table 31: Self-monitoring of blood glucose and treatment costs

Variable	Cost	Source	Notes
Blood glucose monitor	£7.79	BNF 52 (2006)[457]	
Test strips	£0.31 each	BNF 52 (2006)[457]	Many makes, all similarly priced. £15.55 for a pack of 50 was the cheapest found from a small sample.
Lancets	£0.03 each	BNF 52 (2006)[457]	
Needles	£0.09 each	BNF 52 (2006)[457]	£8.57 for a pack of 100 needles
Insulin analogue (Humalog®)	£0.39 per day	BNF 52 (2006)[457]	This is based on a dose of 20 units per day. A pre-filled disposable pen has 1500 units and costs £29.46.
Glibenclamide	£0.16	BNF 52 (2006)[457]	Based on 15 mg daily. A 5 mg 28 tablet pack costs £1.50.
Metformin	£0.10	BNF 52 (2006)[457]	Based on 1.5 g daily. A 500 mg 84 tablet pack costs £2.85.
Treatment of severe hypoglycaemia	£403	Curtis and Netten	Average cost per patient journey for paramedic ambulance: £323.

Variable	Cost	Source	Notes
		(2006)456 NHS Reference Costs 2005–06	A&ccident and emergncy admission with low-cost investigation: £80.

Table 32: 'Downstream' outcome costs

Variable	Cost	Source	Notes
Admission to neonatal unit	£1,676	NHS Reference Costs 2004	Assume 2 days of neonatal intensive care at £838 per day.
Induction of labour	£20	Davies and Drummond (1991)458 and (1993)459	Updated to 2006 prices using Retail Price Index published by ONS.
Neonatal death	£2,568	NHS Tariff 2006 NHS Reference Costs 2004	From NHS Reference Costs 2004 finished consultant episode (FCE) data assume that 25% of neonatal deaths are < 2 days (n = 974). NHS Reference Costs for this is £527. For remaining 75% assume 2 days of neonatal intensive care (£838 × 2) and neonate with one major diagnosis which has an NHS Tariff of £1,572. £1,676 + £1,572 = £3,248
Shoulder dystocia	£629	NHS Tariff 2006	Cost for neonate with one minor diagnosis (HRG N03)
Bone fracture	£629	NHS Tariff 2006	Cost for neonate with one minor diagnosis (HRG N03)
Nerve palsy	£629	NHS Tariff 2006	Cost for neonate with one minor diagnosis (HRG N03)
Phototherapy	£629	NHS Tariff 2006	Cost for neonate with one minor diagnosis (HRG N03)
Emergency caesarean section	£1,205	NHS Reference Costs 2004	Incremental cost over and above that of a normal vaginal birth
Elective caesarean section	£822	NHS Reference costs 2004	Incremental cost over and above that of a normal vaginal birth

HRG = Health Resource Group.

Table 33: Treatment pathway probabilities

Variable	Value	Source	Notes
Control with diet	0.86	Persson et al. (1985)[172]	–
Control with glibenclamide	0.96	Langer et al. (2000)[74]	GDG member suggested that data from Southampton (their local practice) indicate a higher failure rate (23%).
Control with metformin	0.96	–	Assumed the same as for glibenclamide.
Hypoglycaemia on insulin therapy	0.20	Langer et al. (2000)[74]	–
Hypoglycaemia on insulin analogue	0.20	–	Assumed the same as for insulin.
Hypoglycaemia on glibenclamide	0.02	Langer et al. (2000)74	–
Hypoglycaemia on	0.02	–	Assumed the same as for glibenclamide.

Variable	Value	Source	Notes
metformin			
Severe hypoglycaemia requiring hospitalisation	0.05	GDG estimate	–

Table 34: ACHOIS outcome probabilities

Variable	Treatment value	No treatment value	Source
Serious perinatal complications	0.014	0.044	ACHOIS[153]
Admission to neonatal unit	0.706	0.613	ACHOIS[153]
Induction of labour	0.374	0.286	ACHOIS[153]
Elective caesarean section	0.142	0.116	ACHOIS[153]
Emergency caesarean section	0.158	0.197	ACHOIS[153]
Jaundice (phototherapy)	0.087	0.092	ACHOIS[153]

Table 35: QALYs

Variable	QALY	Source	Notes
Averted death (stillbirth/neonatal)	25		This is the approximate lifetime QALYs from 75 years lived in perfect health with QALYS discounted at 3.5% per annum.
Maternal QALY – treatment (during pregnancy)	0.72	ACHOIS[153]	It is assumed that this QALY gain persists throughout treatment.
Maternal QALY – no treatment (during pregnancy)	0.70	ACHOIS[153]	It is assumed that this QALY gain persists throughout treatment.
Maternal QALY – treatment (3 months postpartum)	0.79	ACHOIS[153]	It is assumed that this QALY gain covers the entire 3 months postpartum period.
Maternal QALY – no treatment (3 months postpartum)	0.78	ACHOIS[153]	It is assumed that this QALY gain covers the entire 3 months postpartum period.

N.2.5 Baseline results

The baseline results from the modelling exercise are given based on a population of 10 000 pregnant women and assume a baseline prevalence of gestational diabetes of 3.5%. The total cost and QALYs generated for each strategy under the baseline assumptions are presented in Table 36 and are plotted on a cost-effectiveness plane in Figure 31. The origin represents the no screening/no treatment option and all costs and QALYs are measured relative to this.

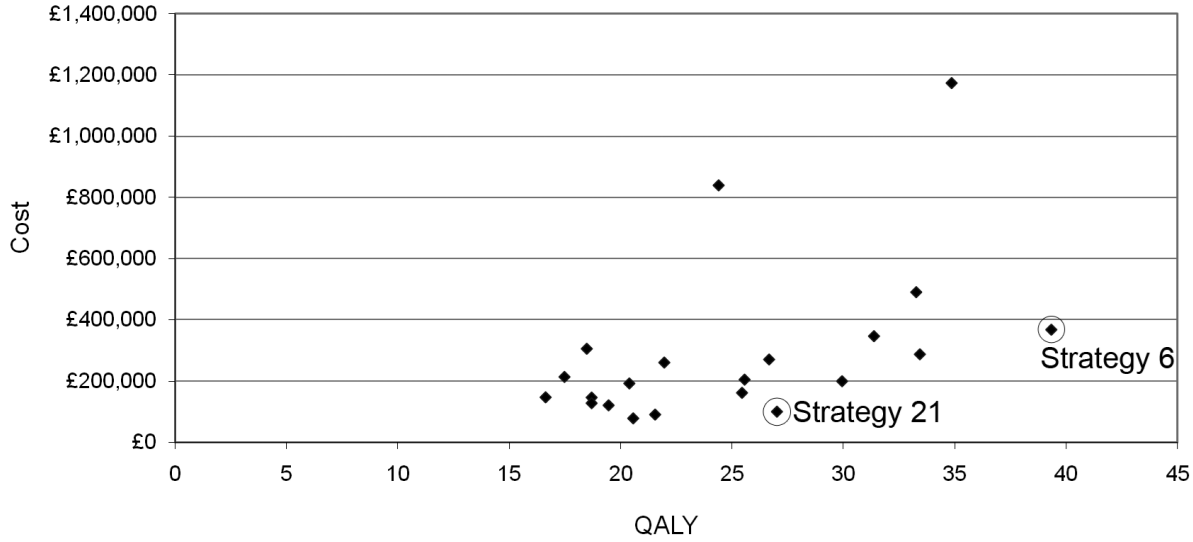
Table 36: Total QALYs and cost for each screening strategy

Screening strategy[a]	QALYs	Cost
11	16.63	£146,188
1	17.48	£212,816
8	18.48	£304,753
9	18.70	£145,419
3	18.70	£126,929
13	19.46	£119,940
14	20.39	£191,529

Screening strategy[a]	QALYs	Cost
19	20.56	£77,465
20	21.55	£89,758
12	21.96	£259,791
10	24.40	£838,561
15	25.45	£160,670
17	25.56	£203,902
16	26.66	£269,731
21	27.01	£99,341
2	29.94	£198,769
4	31.37	£345,932
5	33.26	£489,580
18	33.43	£286,763
7	34.85	£1,172,747
6	39.33	£367,009

(a) Ranked in order of effectiveness (from fewest to most QALYs).

Figure 31: The cost-effectiveness plane for the baseline analysis



As can be seen from Figure 31, a number of strategies are more expensive than the two circled and yet offer a lower QALY gain. Such strategies can unambiguously be excluded (they are said to be (strictly) dominated). Once these strategies are excluded the remainder are again ranked in order of effectiveness. Moving down the list, it is possible to calculate the incremental costs and incremental QALYs of selecting a given strategy relative to the next best strategy. From this, the ICER is derived which effectively shows the cost of 'buying' QALYs. It is then possible to exclude certain further strategies on the grounds of 'extended dominance'. Extended dominance occurs when a strategy has a higher ICER than a more effective strategy. If the decision maker was willing to buy QALYs at the cost implied by the ICER of the less effective strategy, they would logically be willing to buy (and prefer) strategies where additional QALYs could be obtained at a lower cost.

In Table 37 all but two of the strategies are excluded on these dominance grounds. The ICER for strategy 21 is calculated relative to no screening/treatment and the ICER for

strategy 6 is calculated relative to strategy [21]. The cost-effective option is the most effective strategy which falls within the willingness to pay threshold set by the decision maker.

Table 37: ICER for non-dominated strategies

Strategy	QALYs	Cost	Incremental QALYs	Incremental cost	ICER
21	27.01	£99,341	27.01	£99,341	£3,677
6	39.33	£367,009	12.31	£267,668	£21,738

The baseline analysis suggests that a strategy of offering women from a high-risk ethnic background a diagnostic test (strategy 21) would be cost-effective when compared with not offering a screening, with an ICER of £3,677. The strategy of offering a diagnostic test to those women who are deemed to be at increased risk according to the ADA criteria (strategy 6) has an ICER of £21,738 when compared with strategy [21]. Although it is higher than the £20,000 per QALY threshold suggested by NICE, it is comfortably under the maximum willingness to pay per QALY of £30,000 and may be considered cost-effective under certain circumstances, for example if it is believed some salient piece of information falls outside the model such as the identification of women at higher risk of developing type 2 diabetes in the future. Thus it is possible that strategy 6 could reasonably be argued to be cost-effective.

N.2.6 Sensitivity analysis

All decision analysis models are subject to uncertainty460 and there are two common approaches to dealing with this uncertainty – making use of a reference case (that is, a standard of good practice) and sensitivity analysis. This model takes as its reference case the standards for conducting economic evaluations included in the 2007 version of the NICE guidelines manual.[23] The methods and assumptions used in the model are highlighted above in detail and were tested using a second method of examining uncertainty, sensitivity analysis. In the analyses presented below we primarily used a series of one-way and multi-way sensitivity analyses to explore what happened when the value of one or more parameters is changed. This allows us to see what happens to the model results when these values are changed, and thus the implications for our baseline results. The analyses that follow explore the uncertainty in a number of key areas, including:

- the reliability of the trial data on which the likelihood of an event occurring was based
- the prevalence of gestational diabetes in the population
- the proportion of women that would undergo a screening or diagnostic blood test if it were offered as a first-line test or based on identification of a potentially high-risk population
- treatment options
- the efficacy of using risk factors to define high- and low-risk populations, based on the presence of one or more of the risk factors highlighted in the ADA criteria (age over 25 years, BMI greater than 27 kg/m², family history of diabetes or from a high-risk ethnic background).

Tables 38 to 42 give the sensitivity analysis ICER for strategies which have not been excluded on the grounds of strict or extended dominance.

N.2.6.1 Outcomes

The outcome that had the greatest influence on the model results was the number of perinatal deaths (stillbirths and neonatal deaths). This is because of the non-negligible weight given to this outcome as a proportion of all serious perinatal complications and the significant gain in QALYs to be made by preventing a perinatal death. In the ACHOIS trial there were five perinatal deaths recorded in those who received no treatment (n = 524) while

in the treatment arm there were none (n = 506). This difference was not statistically significant. The number of deaths in the control group was similar to the number of perinatal deaths that would be expected in the general population according to ONS data on perinatal mortality (in 2005 there were 5.4 stillbirths, 2.6 early neonatal deaths and 3.4 late neonatal deaths per 1000 total births in England and Wales). The authors of the ACHOIS study highlight that at least one death in the control group was unrelated to gestational diabetes.

Table 38 shows the results of the models when the number of perinatal deaths in each group was assumed to be different to that reported in the ACHOIS trial. As the number of perinatal deaths decreases, the cost-effectiveness of the various strategies changes. When only four deaths in the trial group are attributed to gestational diabetes, the ICERs of both strategies 21 and 6 become less favourable and this continues until only one perinatal death is attributed to gestational diabetes. Even when there is only a single death assumed, there is still a screening, diagnosis and treatment strategy that would be considered cost-effective – in this case strategy [21]. However, if no perinatal deaths are attributed to gestational diabetes, then there is no strategy for screening, diagnosis and treatment that could be considered cost-effective.

This result demonstrates that the model is highly sensitive to the potential QALYs gained by preventing even a single perinatal death. The model also potentially underestimates the QALYs to be gained by preventing other adverse outcomes, such as shoulder dystocia or nerve palsy, and may therefore underestimate the cost-effectiveness of screening. However, the ICERs when no deaths are assumed are sufficiently large to suggest that the potential QALY gain from preventing some of these events would not be adequate for these strategies to be cost-effective.

What is clear from this analysis is that the potential benefits to the NHS with respect to QALYs gained from intervention are likely to be felt in the form of preventing perinatal deaths, and the cost-effectiveness of screening, diagnosis and treatment strategies are highly influenced in the model by this particular adverse outcome.

Table 38: Effect on ICER of varying the number of perinatal deaths attributable to gestational diabetes

Strategy	QALYs	Cost	Incremental QALYs	Incremental cost	ICER
Four deaths					
21	21.26	£99,490	21.26	£99,490	£4,680
6	30.95	£367,227	9.69	£267,737	£27,633
Three deaths					
21	15.80	£100,136	15.80	£100,136	£6,336
6	23.01	£368,167	7.20	£268,031	£37,209
Two deaths					
21	10.69	£100,287	10.69	£100,287	£9,385
6	15.56	£368,386	4.87	£268,100	£55,042
One death					
21	5.94	£100,473	5.94	£100,473	£16,913
6	8.65	£368,657	2.71	£268,184	£99,045
No deaths					
21	1.61	£101,069	1.61	£101,069	£62,854
6	2.34	£369,525	0.73	£268,456	£366,272

N.2.6.2 Gestational diabetes prevalence

The prevalence of a disease can often be a very important determinant of the cost-effectiveness of screening. Tables 39 and 40 show how the results of the model varied for different prevalences of gestational diabetes. The results suggest that varying the prevalence over a range of 3 percentage points has little impact on the cost-effectiveness conclusions of the model, but it should be remembered that the simplified model relationship between risk factor proportions and gestational diabetes prevalence has a bearing on these results.

Table 39: Gestational diabetes prevalence of 2%

Strategy	QALYs	Cost	Incremental QALYs	Incremental cost	ICER
21	9.41	£48,856	9.41	£48,856	£5,192
2	12.84	£100,583	3.43	£51,727	£15,085
6	16.87	£177,118	4.03	£76,536	£19,005

Table 40: Gestational diabetes prevalence of 5%

Strategy	QALYs	Cost	Incremental QALYs	Incremental cost	ICER
19	33.97	£113,694	33.97	£113,694	£3,347
21	44.62	£149,825	10.65	£36,131	£3,392
6	56.18	£401,205	11.56	£251,379	£21,738
18	56.18	£401,205	11.56	£251,379	£21,738

N.2.6.3 Test acceptance

As noted earlier, test acceptance rates are potentially an important source of uncertainty within the model, especially as with default assumptions there is an inverse relationship between test accuracy and test acceptance. Tables 41 and 42 show how the results varied when it was assumed that all women were tested in populations with a relatively low and relatively high disease prevalence, respectively.

Table 41: Gestational diabetes prevalence of 2% and 100% test acceptance

Strategy	QALY	Cost	Incremental QALY	Incremental cost	ICER
21	10.46	£51,385	10.46	£51,385	£4,915
11	21.12	£163,434	10.66	£112,049	£10,507
1	24.97	£336,113	3.85	£172,679	£44,852

Table 42: Gestational diabetes prevalence of 5% and 100% test acceptance

Strategy	QALY	Cost	Incremental QALY	Incremental cost	ICER
19	41.93	£130,634	41.93	£130,634	£3,115
21	49.58	£161,816	7.64	£31,183	£4,079
1	62.43	£411,583	12.85	£249,766	£19,439

The results show that a universal screening strategy using the gold standard diagnostic test becomes more cost-effective as disease prevalence increases. This is because of its advantages over other test options in terms of its detection rate. However, its advantages in terms of detection rate are negated if it is assumed that the test has a low level of acceptance.

A threshold analysis, with all other model parameters at their baseline values, showed that, even if test acceptance for FPG/OGTT in women identified as 'at risk' fell from 90% at baseline to 52%, strategy 6 would remain the preferred option up to a willingness to pay threshold of £20,000 per QALY.

N.2.6.4 Treatment option

The model also allowed the ICERs for different strategies to be calculated for different treatment options (analogue insulin, glibenclamide and metformin). Table 43 shows that the choice of treatment option in the model made little difference to the ICERs for the screening strategies. This is because treatment represents a relatively small proportion of the total costs, and because all the incremental analysis is undertaken with treatment cost as a given. For example, a lower treatment cost will reduce the cost of each strategy but may have relatively little impact on the incremental costs.

Table 43: ICER for strategy 6 for different treatment options in the baseline model

Treatment	ICER
Analogue insulin	£21,738
Glibenclamide	£21,647
Metformin	£21,642

N.2.6.5 Single risk factors

The baseline analysis suggested that strategy 6 was a borderline cost-effective strategy using a willingness to pay threshold of £20,000 per QALY. However, the GDG expressed concerns over the number of women that would have to undergo a OGTT if strategy 6 were adopted. A large proportion of women tested would be tested based on age criteria alone – under the baseline assumptions as many as 90% might be offered the diagnostic test. This would be a considerable inconvenience to a large number of women, only a small minority of whom would ultimately benefit from the testing process, as well as putting a strain on local services. As a result it was decided that the use of screening based on risk factors other than age should be considered.

The PPVs and NPVs of different risk factor combinations are not accurately known which means that the relative cost-effectiveness of different combinations of any of the single risk factors could not be calculated. However, it may be the case that where single risk factors are cost-effective on their own, then any combination of these is also likely to be cost-effective. Therefore an analysis of the cost-effectiveness of each single risk factor, followed by an OGTT, has been performed, with each risk factor plus OGTT combination compared with a strategy of no screening or treatment. The results are presented in Table 44.

Table 44: ICER for single risk factor strategies followed by a diagnostic test when compared with a strategy of no screening or treatment

Strategy	QALY	Cost	ICER
Ethnicity	9.55	£66,226	£6,935
BMI	6.29	£80,109	£12,736
Family history	15.73	£81,915	£5,208

Any strategy where a single risk factor from the ADA criteria other than age is applied alone, followed by a diagnostic test, has an ICER that is below the threshold of £20,000 and could in each case be considered cost-effective on its own.

The above analysis established that screening, diagnosis and treatment of gestational diabetes is generally cost-effective in some populations. Below we consider the cost-effectiveness of the various treatment options for gestational diabetes.

N.2.7 Cost analysis of different treatment options for gestational diabetes

A systematic review of the literature, targeted at the guideline question on what is cost-effective treatment for gestational diabetes, identified a single paper for inclusion.461 This paper described a cost model to compare the costs of an oral hypoglycaemic, glyburide (glibenclamide), with those of insulin for the treatment of gestational diabetes. The paper justifies what is essentially a cost minimisation approach on the basis that glyburide and insulin confer similar glycaemic control.[74] Their model, based in a US setting, excluded resource items that were identical in both treatments. Included in the costs for insulin were drug costs, costs of the consumables needed to administer the insulin and the cost of instructing women with gestational diabetes on how to draw up the insulin and inject themselves. The cost of glyburide was based on the average wholesale cost of a milligram of drug multiplied by the weekly dose expected to be necessary for glycaemic control. In addition, it was assumed that 4% of patients would not achieve control with glyburide and would have to switch to insulin. Therefore, the model also incorporated a cost for glyburide treatment failure. Women switching to insulin also incurred the educational costs associated with insulin treatment. Finally, the model also included the downstream costs of hypoglycaemia, which was assumed to be more common in insulin-treated gestational diabetes. In the baseline analysis, glyburide produced an average cost saving of $166 per woman. The authors reported that most sensitivity analyses did not alter the direction of this finding. A threshold analysis suggested that insulin was only less costly than glyburide at the highest wholesale cost of $18.24 per week in conjunction with a daily dose of 18.9 g, which is considerably higher than what is believed to be necessary to achieve good glycaemic control. A similar cost model was developed to compare the cost of insulin analogue (lispro) with that of two oral hypoglycaemics (glibenclamide and metformin) in a UK context.

N.2.7.1 Introduction

A cost minimisation analysis can be considered to be a special case of cost-effectiveness analysis when the interventions being compared are equally efficacious. In such a scenario, the cheapest option is unambiguously cost-effective as it dominates the alternatives, being cheaper and equally effective. A randomised study[74] failed to find significant differences in outcomes (maternal and neonatal) between glyburide and insulin treatment in women with gestational diabetes. It is on this basis, and in the absence of any conflicting evidence, that such a cost minimisation analysis might be justifiable to determine the cost-effectiveness of various gestational diabetes treatments. Of course, no evidence of a difference is not the same as evidence of no difference, but the P values in this study were particularly large and the inference of no difference does not arise as a result of some outcomes being just the wrong side of an arbitrary 5% cut-off point for statistical significance.

Insulin analogue was used in this cost comparison rather than insulin, as this is what would be offered to women with gestational diabetes in the UK. Implicit in this is an assumption that outcomes with an insulin analogue would be equivalent to those with insulin. Metformin was additionally added into this analysis as the ongoing MIG study is assessing its use in women with gestational diabetes and it could potentially be an important treatment option in the UK.

N.2.7.2 Method

The basic structure of the cost analysis is shown in Figure 32. It is assumed that a diagnosis of gestational diabetes would be made at a gestational age of 27 weeks. As described in the screening, diagnosis and treatment model, women with gestational diabetes would start with dietary treatment. In women who do not achieve adequate glycaemic control after 10 days, pharmocological therapy would be commenced and this is the starting point for the cost comparison.

Costs which are common to all treatments, such as those associated with self-monitoring of blood glucose, are not included in the analysis. The costs for a woman taking insulin

analogue include the time of a diabetes specialist nurse in providing instruction on how to administer the drug. Women with gestational diabetes are assumed to use a pre-filled disposable injection pen (e.g. Humalog® Mix50) and to be on a daily dose of 20 units administered in twice-daily injections. Therefore, they require two needles per day for their injection pen. The cost of glibenclamide is the drug cost based on a daily dose of 15 mg. Similarly, the cost of metformin is based on a daily dose of 1.5 g.

In addition to the cost of treatment it is important also to consider downstream costs. Overall outcomes are assumed not to differ, but following the Langer study74 the model addresses a possible differential in the hypoglycaemia risk between the different treatments. It is additionally assumed at baseline that 5% of hypoglycaemic events will be 'severe' and it is these for which there will typically be an NHS resource implication. The cost of a 'severe' hypoglycaemic event is assumed to be the cost of a paramedic ambulance journey and an admission to an accident and emergency department.

The complete list of model parameters is given in Tables 45 to 47.

Figure 32: Gestational diabetes treatment cost model

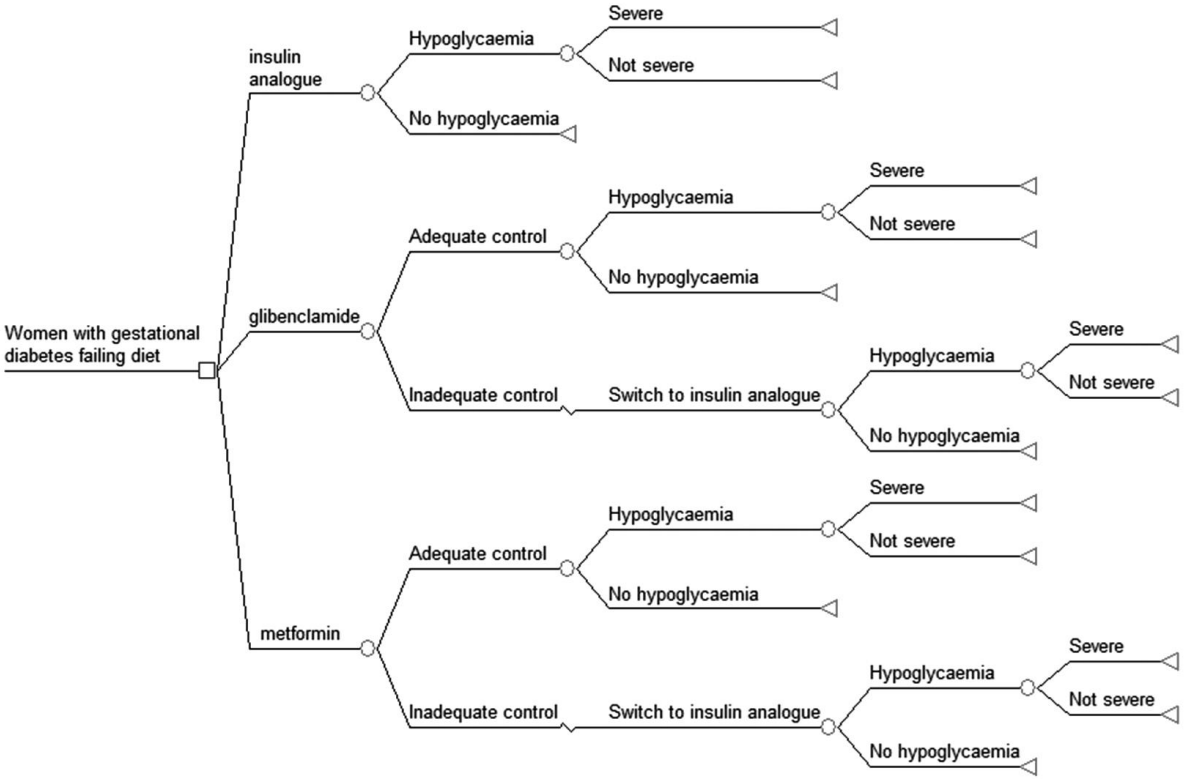


Table 45: Treatment timeframe (days)

Variable	Value (days)	Source	Notes
Treatment duration	80	Diabetes in pregnancy GDG	It is assumed a gestational diabetes diagnosis would be made at 27 weeks of gestation. Women with gestational diabetes would be given approximately 10 days to achieve control with diet and 80 days is a reasonable approximation of the typical time to term at the commencement of pharmacological treatment.
Oral hypoglycaemic trial period	14	ACHOIS[153]	

Table 46: Costs

Variable	Cost	Source	Notes
Insulin instruction	£47.25	Curtis and Netten (2006)456 GDG estimate	This is based on an instruction time of 45 minutes with instruction provided by a specialist nurse.
Insulin analogue	£0.57 per day	BNF 52 (2006)457	This is based on a dose of 20 units per day. A pre-filled disposable pen has 1500 units and costs £29.46. It is further assumed that injections are twice daily, requiring two needles at £0.09 each.
Glibenclamide	£0.16	BNF 52 (2006)457	Based on 15 mg daily. A 5 mg 28 tablet pack costs £1.50.
Metformin	£0.10	BNF 52 (2006)457	Based on 1.5 g daily. A 500 mg 84 tablet pack costs £2.85.
Switching cost of oral hypoglycaemia failure	£0.00	GDG estimate	It is assumed there is no additional cost over and above those incurred by all women with gestational diabetes starting insulin analogue treatment.
Treatment of severe hypoglycaemia	£403	Curtis and Netten (2006)456 NHS Reference Costs 2005–06	Average cost per patient journey for paramedic ambulance: £323. Admission to an accident and emergency department with low-cost investigation: £80.

Table 47: Probabilities

Variable	Probability	Source	Notes
Control with glibenclamide	0.96	Langer et al. (2000)[74] GDG estimate	A GDG member reported 0.77 for this parameter in his clinical practice.
Control with metformin	0.96	Langer et al. (2000)[74]	Assumed identical to glibenclamide.
Hypoglycaemia on insulin analogue	0.20	Langer et al. (2000)[74]	Assumed to be the same as Langer found for insulin.
Hypoglycaemia on glibenclamide	0.02	Langer et al. (2000)[74]	–
Hypoglycaemia on metformin	0.02	Langer et al. (2000)[74]	Assumed identical to glibenclamide.
Proportion of hypoglycaemia that is 'severe'	0.05	GDG estimate	–

N.2.7.3 Results

Table 48 lists the cost per patient of each of the three treatment options. These show the oral hypoglycaemics to be considerably cheaper than analogue insulin. Of the oral hypoglycamics, metformin is the cheapest and, with the assumption of equal clinical effectiveness, the most cost-effective treatment.

Table 48: Cost per woman with gestational diabetes

Treatment	Average cost per woman with gestational diabetes

Treatment	Average cost per woman with gestational diabetes
Insulin analogue	£96.92
Glibenclamide	£16.32
Metformin	£11.68

N.2.7.4 Sensitivity analysis

A number of sensitivity analyses were undertaken to determine how robust the conclusion of the baseline result was to changes in model parameters where some uncertainty exists as to their 'true' value. For ease of exposition, most sensitivity analyses focus on a comparison of glibenclamide and insulin analogue on the basis that, apart from a small difference in costs, these are assumed to be identical treatments in terms of both outcomes and downstream costs.

However, threshold analyses were also undertaken which showed that, holding all other factors constant, metformin remained cheapest as long as control on metformin was at least 90.3% (with control on glibenclamide 96%) or control on metformin was at least 72.3% (with control on glibenclamide 77%).

Figure 33 shows how the incremental cost of insulin analogue varied with different assumptions about the proportion of women with gestational diabetes who achieve adequate glycaemic control with glibenclamide. Although the differential in cost declines with reduced glibenclamide clinical effectiveness, insulin analogue continues to be the more costly option even if only 40% of women achieve adequate glycaemic control with glibenclamide. Figure 34 shows that the cost analysis is not sensitive to the risk of hypoglycaemia in women taking glibenclamide. Similarly, Figure 35 shows that the costs of treating hypoglycaemia are not an important determinant of the additional costs of insulin analogue.

Figure 33: Incremental cost of insulin analogue as control on glibenclamide varies

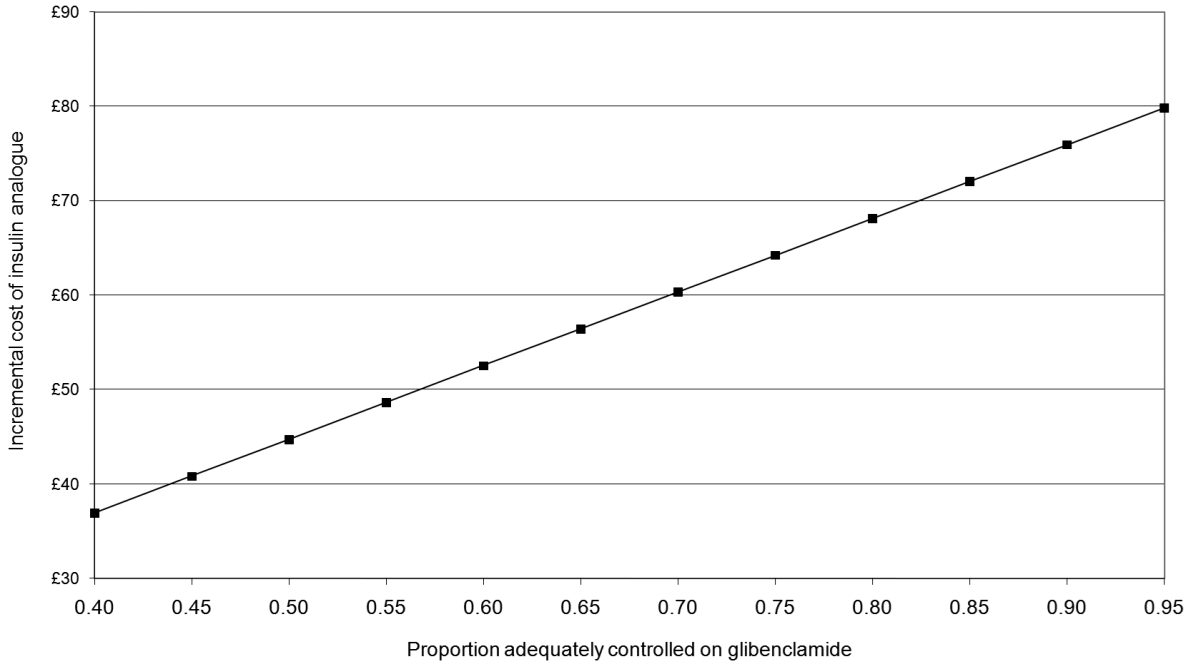


Figure 34: Incremental cost of insulin analogue as hypoglycaemia risk of insulin analogue varies

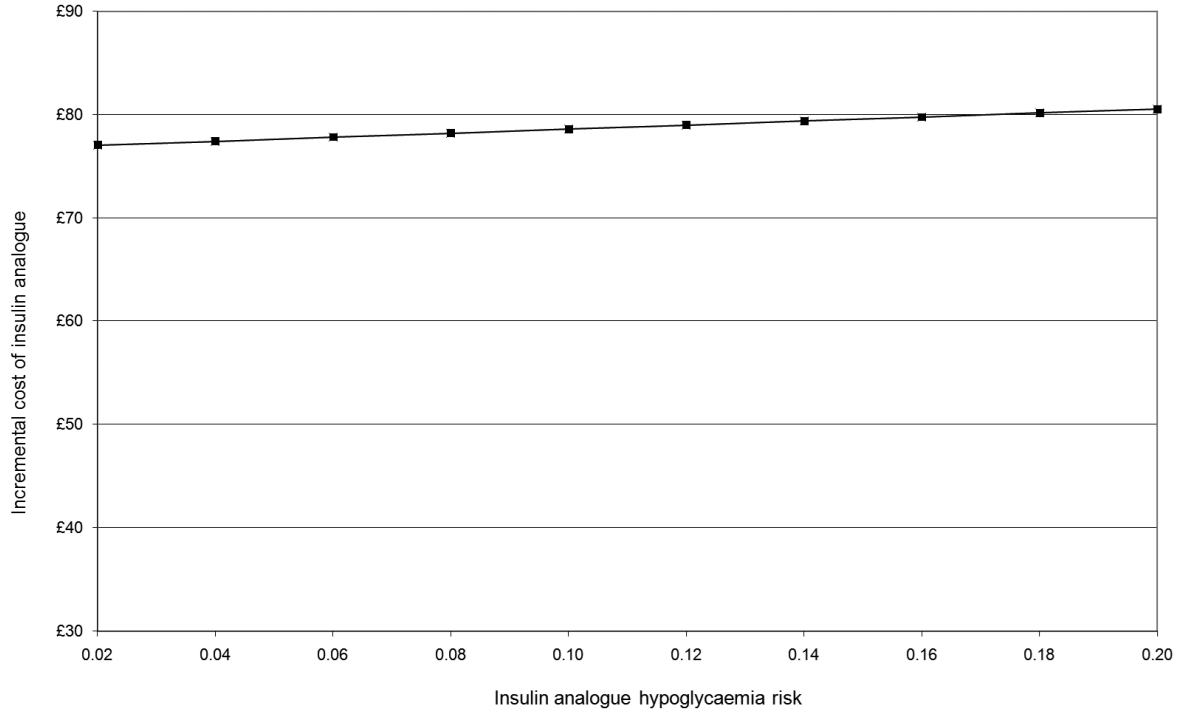
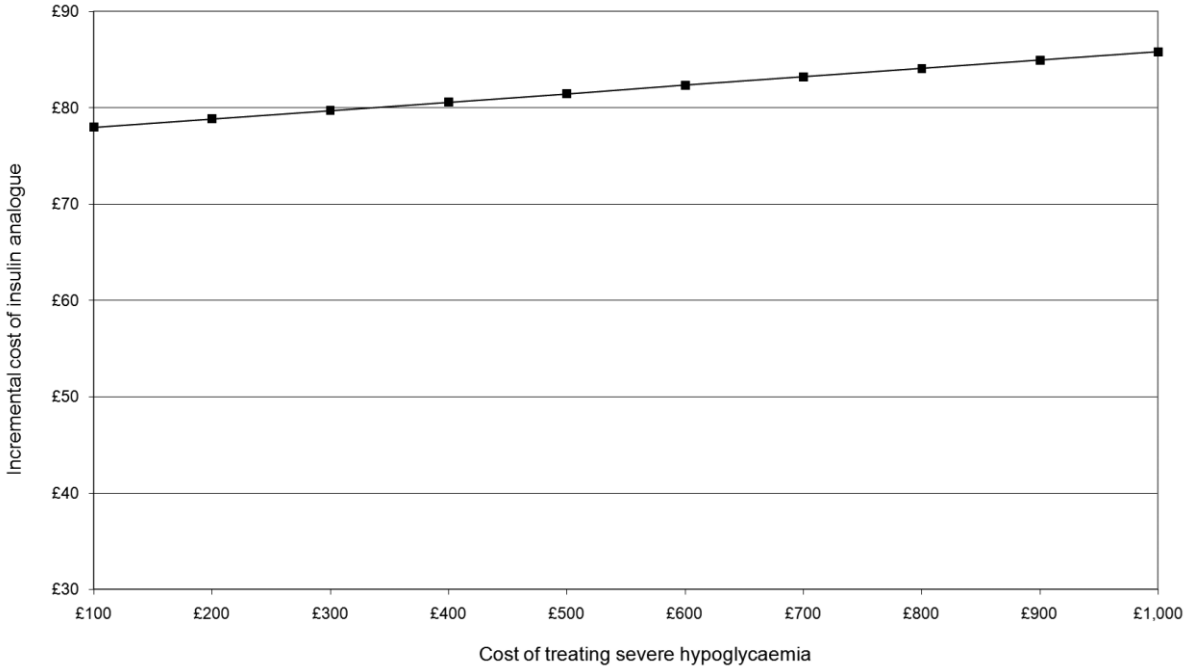


Figure 35: Incremental cost of insulin analogue as cost of treating severe hypoglycaemia varies



N.2.7.5 Discussion

Using the data from ACHOIS, this guideline has demonstrated that screening, diagnosis and treatment for gestational diabetes is cost-effective and that this finding is not contingent on the type of pharmacological treatment used (insulin analogue or oral hypoglycaemic agents). However, given that the treatments have different resource implications for the NHS, it does not follow that all treatments are equally cost-effective. One study[74] suggested that 'among women with gestational diabetes, the degree of glycaemic control and the perinatal outcomes were essentially the same for those treated with glyburide (glibenclamide) and those treated with insulin. The lack of differences between the infants born to mothers in the two treatment groups corroborated the results in the mothers'. Therefore, if it is argued on the basis of this study that glibenclamide is equally effective as insulin analogue and would have achieved similar outcomes to those observed with diet and insulin treatment in ACHOIS, then we can say that the results presented here suggest that glibenclamide is a more cost-effective treatment for gestational diabetes than insulin analogue. Sensitivity analysis suggested that this conclusion was robust when model parameters were changed in a one-way fashion. The diabetes in pregnancy GDG has suggested that the proportion of women with gestational diabetes achieving control with glibenclamide may be lower in clinical practice than that observed by Langer et al.[74] However, as the sensitivity analysis shows, glibenclamide continues to be cost-saving compared with insulin analogue even with a much smaller proportion achieving adequate control.

As yet, there is no evidence to justify a cost minimisation approach with metformin. However, if it too was shown to be as effective as insulin analogue then it would be the most cost-effective treatment of all.

One caveat to these findings is the assumption that there is no cost to the NHS in switching from an oral hypoglycaemic agent to insulin analogue, other than those ordinarily incurred for women with gestational diabetes taking insulin analogue. If there were a 'switching cost', then the cost-effectiveness of the oral hypoglycaemic agents would be less than that implied here.

N.3 Cost-effectiveness of screening for congenital cardiac malformations

N.3.1 Introduction

A review of the health economics literature identified a single study addressing the cost-effectiveness of screening for congenital cardiac malformations in pregnant women with diabetes.[413] In the study, a decision-analytic model was used to compare the cost-effectiveness of four screening strategies for congenital cardiac malformations in a healthcare setting in the USA. The strategies were: no screening; selective fetal echocardiography after abnormal detailed anatomical survey (a four chamber view of the heart plus outflow tracts was included as part of the detailed anatomical survey); fetal echocardiography for high HbA1c only; and universal fetal echocardiography. Costs and outcomes were modelled for a hypothetical cohort of 40 000 pregnant women with diabetes and with a 2.1% prevalence of major cardiac malformations. The sensitivities and specificities for each strategy were derived from a literature search and costs included tests, terminations of pregnancy, and the healthcare costs of a major cardiac malformation over and above those needed for a healthy child. Effectiveness was measured using QALYs derived by assigning different utilities to different outcomes (major cardiac defect 0.5, fetal death 0.07, and healthy neonate 1.0) and then multiplying by the life expectancy with each outcome. The utility weights were discounted at a rate of 3% per year. The study reported that selective fetal echocardiogram after abnormal detailed anatomical survey dominated all

other strategies with baseline assumptions. However, the study also noted that universal fetal echocardiogram yielded the highest detection rate of cardiac anomalies. As a result of a probabilistic sensitivity analysis, the study reported that the model results were robust when considering parameter uncertainty. However, the scenarios presented did not reflect current UK practice or viable alternatives. In addition, there are concerns about the generalisability of cost-effectiveness results from healthcare settings outside the UK and it was, therefore, decided to develop a model for this guideline to compare the cost-effectiveness of two screening strategies in the UK context.

A decision tree model was developed for the guideline in Microsoft Excel® to assess the cost-effectiveness of second-trimester screening for congenital cardiac malformations in pregnant women with diabetes. Current UK practice is to screen pregnant women using a four chamber ultrasound scan at 20 weeks of gestation, but using a four chamber plus outflow tracts view may allow the detection of some abnormalities, such as TGA and tetralogy of Fallot, which are not usually visible with a four chamber view. Screening for these malformations in pregnant women with diabetes is likely to be relatively more cost-effective than in pregnant women without diabetes because the prevalence of these anomalies is much higher in women with diabetes.[414]

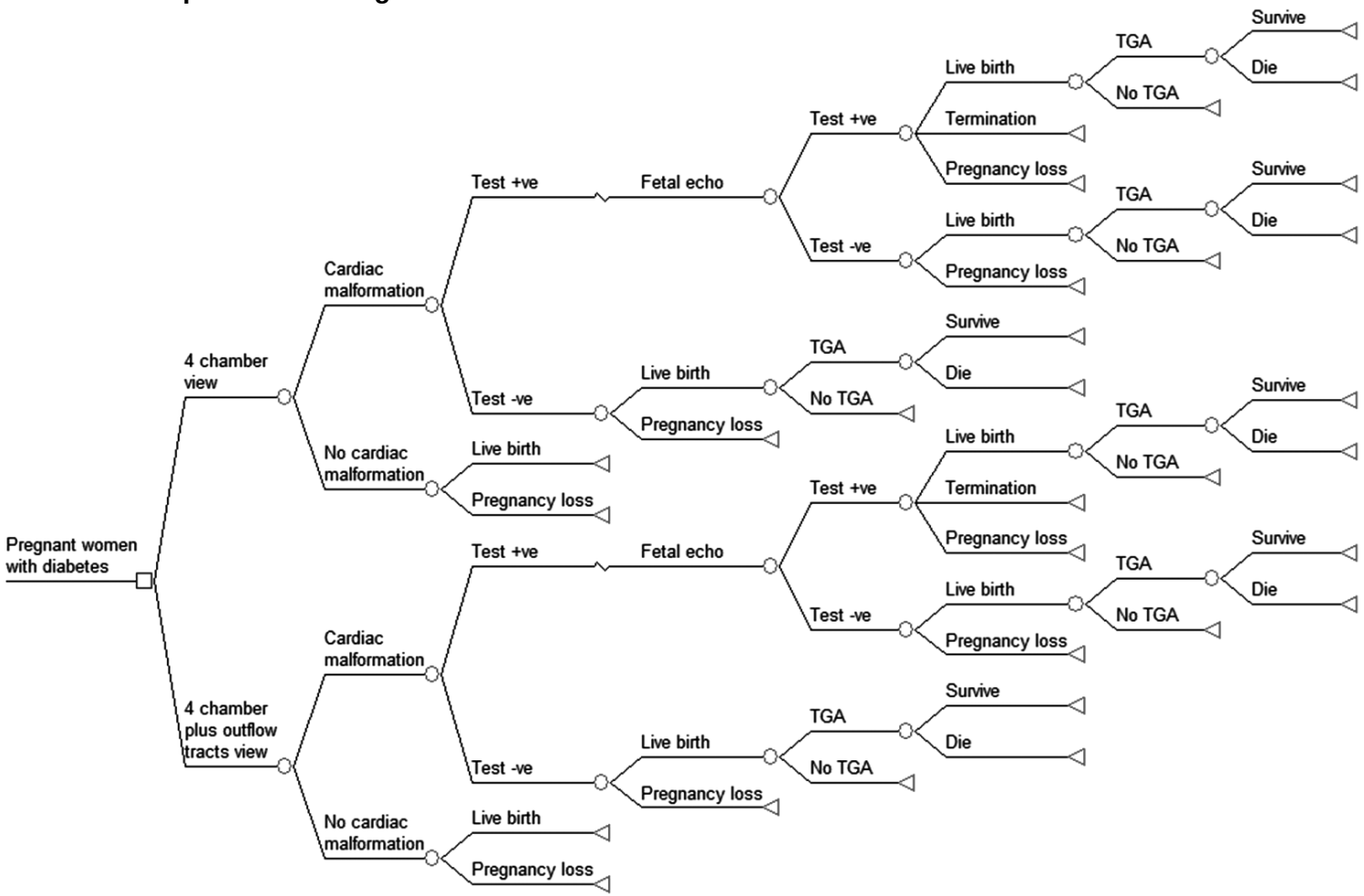
There are two principal reasons why it may be beneficial to screen for congenital cardiac malformations:

- it allows women to consider termination of pregnancy
- improved outcomes for women and/or babies.

There are difficulties in considering the cost-effectiveness of screening using termination as a positive outcome and the evidence that screening produces a survival advantage is limited.[415] Nevertheless, there is some evidence suggesting that an antenatal diagnosis of TGA may reduce mortality. This is important for the health economic analysis because TGA is an anomaly that would not normally be identifiable with a four chamber view, but it would be with the addition of a view of the outflow tracts and, therefore, the model particularly focuses on the cost-effectiveness of antenatal diagnosis of TGA.

The basic decision tree structure is illustrated in Figure 36. At 20 weeks of gestation women receive either a four chamber view ultrasound scan or four chamber plus outflow tracts view ultrasound scan. Women with a positive result on either scan will then be referred for fetal echocardiography to confirm diagnosis and guide subsequent treatment. If the diagnosis is confirmed then the woman has the option to terminate or continue the pregnancy. If the woman chooses to continue the pregnancy then she will either give birth to a live baby or suffer a pregnancy loss. A proportion of babies born with cardiac malformations will have TGA and they may survive or die.

Figure 36: Four chamber plus outflow tracts view versus four chamber view decision tree for women with diabetes; TGA = transposition of the great arteries



N.3.2 Model parameters

The parameter values used in the baseline model are shown in Tables 49 to 52.

Table 49: Population characteristics

Characteristic	Value	Source	Notes
Population	1000		Prevalence data are often given as rates per 1000 head of population and the ICER from the model is not affected by population size.
Prevalence of cardiac malformations at 20 weeks of gestation	0.0032	Wren et al. (2003)[414]	Wren's value of 3.2% is for prevalence at birth.[a]
Proportion of cardiac malformations that are TGA in women with diabetes	0.144	Wren et al. (2003)[414]	
Pregnancy loss after 20 weeks of gestation (no cardiac malformations present)	0.0115	Ritchie et al. (2004)[416]	Derived from survival probability from second trimester to birth.
Pregnancy loss after 20 weeks of gestation (cardiac malformations present)	0.0405	Ritchie et al. (2004)[416]	Derived from survival probability from second trimester to birth.

ICER = incremental cost-effectiveness ratio; TGA = transposition of the great arteries.
a The prevalence of cardiac malformations at 20 weeks of gestation may be slightly higher than at birth if terminations and fetal death are higher in affected than non-affected pregnancies. This is likely to represent a small bias in the model against the four chamber plus outflow tracts view, but this is not important if the four chamber plus outflow tracts view is shown to be cost-effective.

Table 50: Costs

Characteristic	Cost	Source	Notes
Four chamber view ultrasound scan	£34	NHS Reference Costs 2005–06	Mean value for a maternity ultrasound
Four chamber plus outflow tracts view ultrasound scan	£46	GDG estimate	Based on estimate that appointment slots would be 20 minutes compared with 15 minutes for a four chamber view.[a]
Fetal echocardiography	£62	NHS Reference Costs 2005–06	Mean value for an echocardiogram
Termination of pregnancy	£492	NHS Tariff 2006/07	Cost of a surgical termination
Birth	£3,000	NHS Reference Costs 2003; NHS General Medical Services Revised Fees and Allowances	A weighted average including birth, GP fees, other maternity events, outpatient visits, neonatal care, tests

Characteristic	Cost	Source	Notes
		2003–04	

a The cost of the four chamber plus outflow tracts view does not take into account the fact that the number of equivocal scans is likely to increase.

Table 51: Test characteristics

Characteristic	Value	Source	Notes
Four chamber view sensitivity	0.73	Smith et al. (1997)[275] (see www.d4pro.com/IDM/site/idm4cr.pdf)	
Four chamber view specificity	1.00	Smith et al. (1997)[275]	
Four chamber plus outflow tracts view sensitivity	0.82	Smith et al. (1997)[275]	
Four chamber plus outflow tracts view specificity	1.00	Smith et al. (1997)[275]	
TGA proportion of malformations only detectable on four chamber plus outflow tracts view	0.36	Ogge et al. (2006)[417]	In 58 cases of congenital cardiac defects, 14 were only usually diagnosable with outflow-tract view. Of these, five were TGA.[a]
Fetal echocardiography sensitivity	0.92	Pan et al.[440]	
Fetal echocardiography specificity	0.95	Pan et al.[440]	
Termination of pregnancy rate for diagnosis of cardiac malformation	0.25	Ritchie et al. (2004)[416]	

TGA = transposition of the great arteries.
a Only one TGA was actually detected, giving the four chamber plus outflow tracts view a sensitivity for detecting TGA of only 20%.

Table 52: Outcomes and quality-adjusted life years

Characteristic	Value	Source	Notes
Life expectancy if TGA treated successfully (years)	76	ONS (2006)	UK life expectancy at birth (2003–05) is 76.6 years for males and 81.0 years for females.
TGA mortality detected antenatally	0.018	Wessex UK (1994–2005), EUROCAT, Bonnet 1988–97,418 Bonnet 1998–2002,419 Kumar 1988–964[20]	Results reported in presentation by Wellesley et al. (4/226).
TGA mortality detected postnatally	0.166	Wessex UK (1994–2005), EUROCAT, Bonnet 1998–974[18]	Results reported in presentation by Wellesley et al. (70/422).
QALY weight successful TGA treatment	1.0		Assumes no long-term morbidity associated with successful TGA treatment.
Annual discount rate	3.5%		Discount rate stipulated by NICE guidelines manual 2007.[23]

QALY = quality-adjusted life year; TGA = transposition of the great arteries.

N.3.3 Results

With baseline results, the four chamber view is the cheapest strategy for screening for cardiac malformations. As shown in Table 53, the difference is almost entirely explained by the higher cost of the four chamber plus outflow tracts view ultrasound scan. However, the higher sensitivity of the four chamber plus outflow tracts view results in 1.91 more live births per 1000 pregnancies having detected cardiac malformations antenatally (Table 54). A proportion of these (36% at baseline) would be TGA and given the baseline assumption about lower mortality for TGA with an antenatal diagnosis this leads to a concomitant 6.86 neonatal deaths averted per 10 000 pregnancies (Table 55). Following on from these cost and effects the estimated ICER for the four chamber plus outflow tracts view is £3,806 per QALY.

Table 53: Costs of four chamber and four chamber plus outflow tracts view strategies

Costs	Four chamber view	Four chamber plus outflow tracts view
Cardiac scan	£34,000	£46,000
Fetal echocardiogram	£1,448	£1,627
Termination of pregnancy	£2,643	£2,969
Birth	£2,947,250	£2,945,344
Total cost	£2,985,342	£2,995,940
Cost per woman	£2,985	£2,996

Table 54: Outcomes of four chamber and four chamber plus outflow tracts view strategies

Outcomes	Four chamber view	Four chamber plus outflow tracts view
Pregnancy loss	12.21	12.18
Termination of pregnancy	5.37	6.04
Healthy live birth	956.87	956.87
Live birth, cardiac malformation detected	15.47	17.37
Live birth, cardiac malformation not detected	10.08	7.54

Table 55: Incremental cost-effectiveness of four chamber plus outflow tracts view

Incremental values	Four chamber plus outflow tracts view
Costs	£10,598
Antenatal diagnosis of cardiac malformations	1.91
Antenatal diagnosis of TGA	0.686
Neonatal deaths averted	0.102
QALYs	2.784
ICER	£3,806 per QALY

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; TGA = transposition of the great arteries.

N.3.4 Sensitivity analysis

A number of one-way sensitivity analyses were undertaken to assess to what extent uncertainty over certain parameter values was likely to be important in interpreting the baseline results. The results of the sensitivity analyses are presented in Figures 37 to 42. A £30,000 cost per QALY threshold is indicated in each of the figures.

Figure 37: Incremental cost per QALY, varying sensitivity of the four chamber view

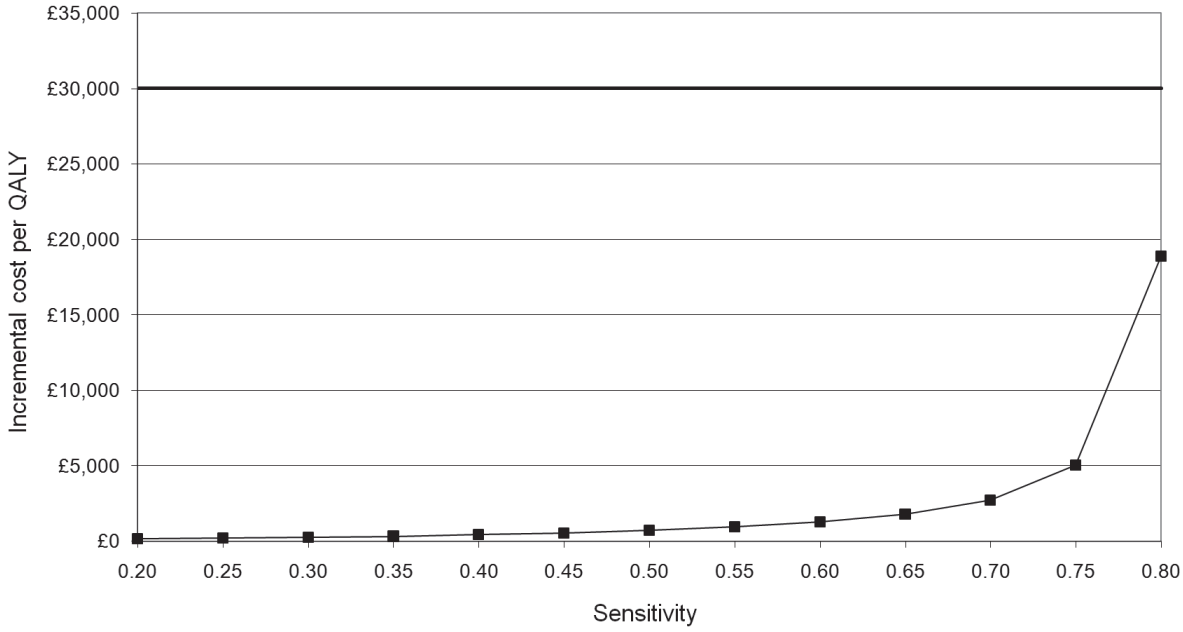


Figure 38: Incremental cost per QALY, varying cost of the four chamber plus outflow tracts view

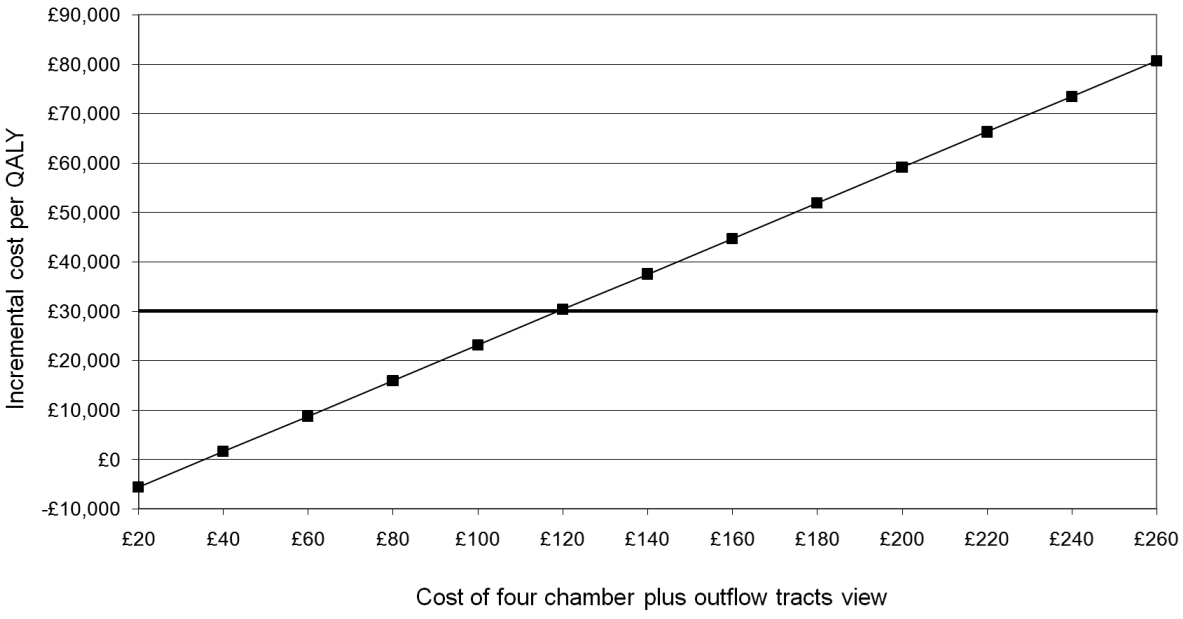
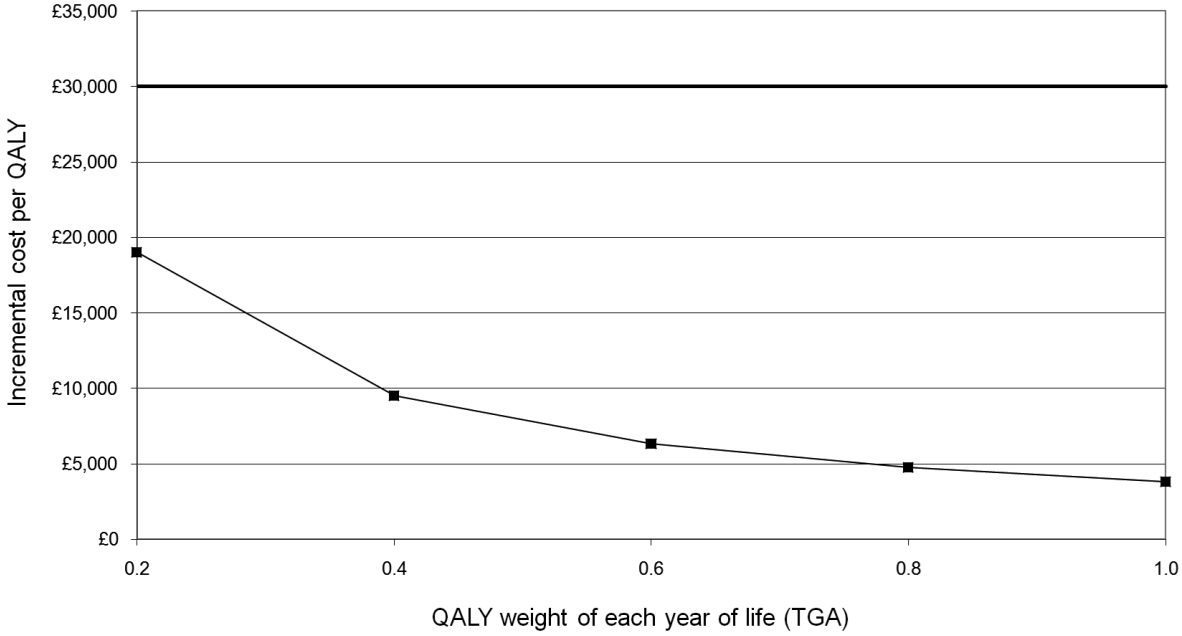


Figure 39: Incremental cost per QALY, varying QALY weight of each baby treated for transposition of the great arteries (TGA)



The model assumes that TGA is the only cardiac malformation where an antenatal diagnosis confers a benefit in terms of improved health outcomes for the woman and/or the baby. The baseline parameter values give a TGA prevalence of approximately 4.6 per 1000 pregnancies in women with diabetes. With the baseline assumptions for perinatal mortality in relation to TGA detected antenatally or not, one neonatal death would be averted for every seven TGA malformations detected. If a screening strategy involving a four chamber plus outflow tracts viewb detected all TGA malformations then the number of pregnant women with diabetes needed to screen with the four chamber plus outflow tracts view rather than the four chamber view to avert one neonatal death would be 1466.

The literature does not generally provide test sensitivity and specificity for individual cardiac malformations; instead it gives a value for detecting any cardiac malformation. Hence, the improved sensitivity of the four chamber plus outflow tracts view compared with the four chamber view occurs because the four chamber plus outflow tracts view detects additional malformations that cannot usually be observed with the four chamber view (the sensitivity of detecting TGA with the four chamber view is 0%). The model follows the literature in using overall sensitivities and specificities and it is this which generates the additional 1.91 antenatal diagnoses of cardiac malformations using the four chamber plus outflow tracts view. The model assumption is that these additional diagnoses are for malformations that would not normally be detectable with a four chamber view, but would be detectable with a view of the outflow tracts. However, as TGA is not the only malformation falling into this category, the model does not assume that all additional antenatal diagnoses are TGA. It uses published data[417] to estimate that 36% of the additional diagnoses would be TGA, which leads to the model result that a four chamber plus outflow tracts view would identify 0.686 TGA per 1000 pregnant women with diabetes. It should be noted that, although this is only 15% of the total TGA malformations present in the population, the four chamber plus

outflow tracts view still appears cost-effective with such a low detection rate. However, it may be appropriate to assume a relatively low detection rate as published data reported that only one out of five TGA malformations was detected with a four chamber plus outflow tracts view.[417] With the baseline detection rate used in the model it would be necessary to screen approximately 9800 pregnant women with diabetes using a four chamber plus outflow tracts view to avert one neonatal death.

The baseline results suggest that the detection rate threshold for TGA for the four chamber plus outflow tracts view to achieve cost-effectiveness is quite low. The one-way sensitivity analyses indicate thresholds for cost-effectiveness for other parameter values. Figure 37 suggests that the four chamber plus outflow tracts view would be cost-effective even if the test sensitivity for the four chamber view was within two percentage points of the sensitivity of the four chamber plus outflow tracts view. As the four chamber view sensitivity approaches that of the four chamber plus outflow tracts view there comes a point where there is only very limited added value in terms of detecting cardiac malformations using the four chamber plus outflow tracts view. The key issue here is the difference in test sensitivity between the four chamber view and the four chamber plus outflow tracts view, rather than the absolute values. The one-way sensitivity analysis of the sensitivity of the four chamber view is undertaken holding the sensitivity of the four chamber plus outflow tracts view constant at 82%. The sensitivity analysis suggests that the four chamber plus outflow tracts view requires a sensitivity that is at least four percentage points higher than the sensitivity for the four chamber view in order to achieve cost-effectiveness.

Figure 38 shows that the cost-effectiveness of the four chamber plus outflow tracts view compared with the four chamber view is quite sensitive to the costs of screening. Again it is the difference between screening costs using the four chamber view and the four chamber plus outflow tracts view that is important, rather than the absolute costs of the screening tests. However, the cost of the four chamber plus outflow tracts view would have to be £120 (for an incremental screening cost of £86) and well above the baseline estimate before the four chamber view would be preferred on cost-effectiveness grounds.

Figures 39 and 40 show that the cost-effectiveness of the four chamber plus outflow tracts view is not sensitive to assumptions about QALYs or life expectancy within plausible ranges. Baseline values suggest that the incremental costs of the four chamber plus outflow tracts view are £3,806 in a population of 1000 pregnant women with diabetes. Therefore, only 0.13 incremental QALYs are needed to generate a cost per QALY of £30,000. With baseline values this is approximately 1.3 QALYs per neonatal death averted.

Figure 40:Incremental cost per QALY, varying mortality with diagnosis of transposition of the great arteries (TGA)

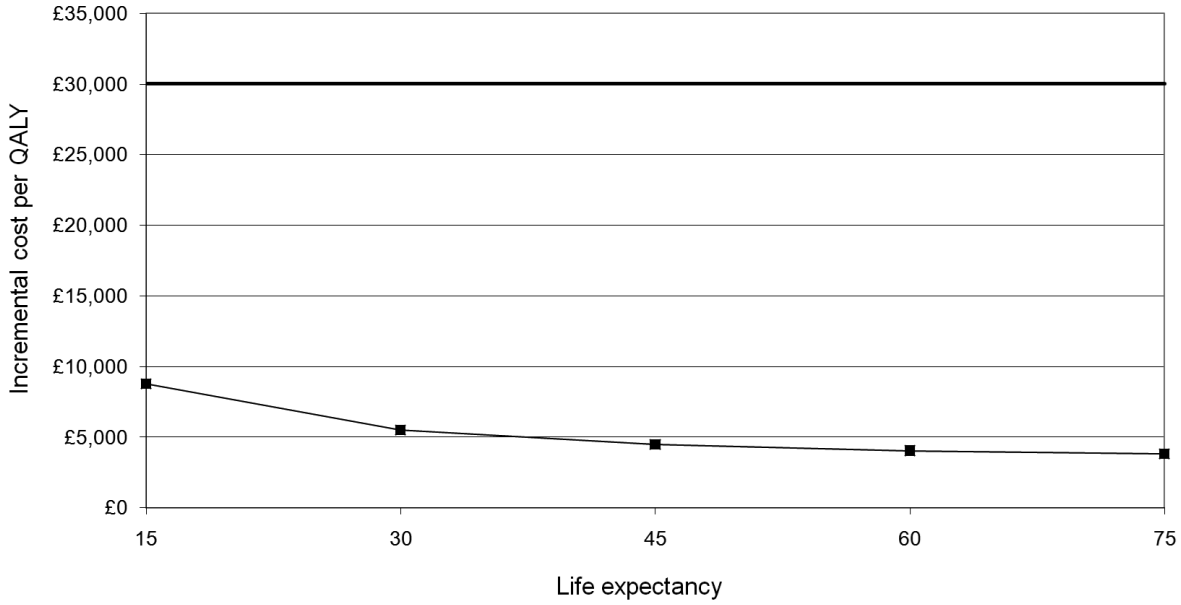


Figure 41: Incremental cost per QALY, varying mortality with diagnosis of transposition of the great arteries (TGA)

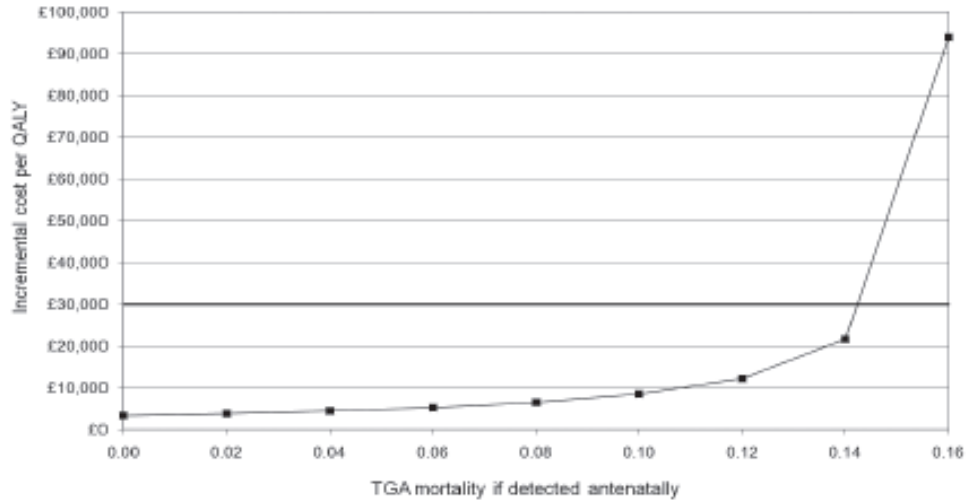
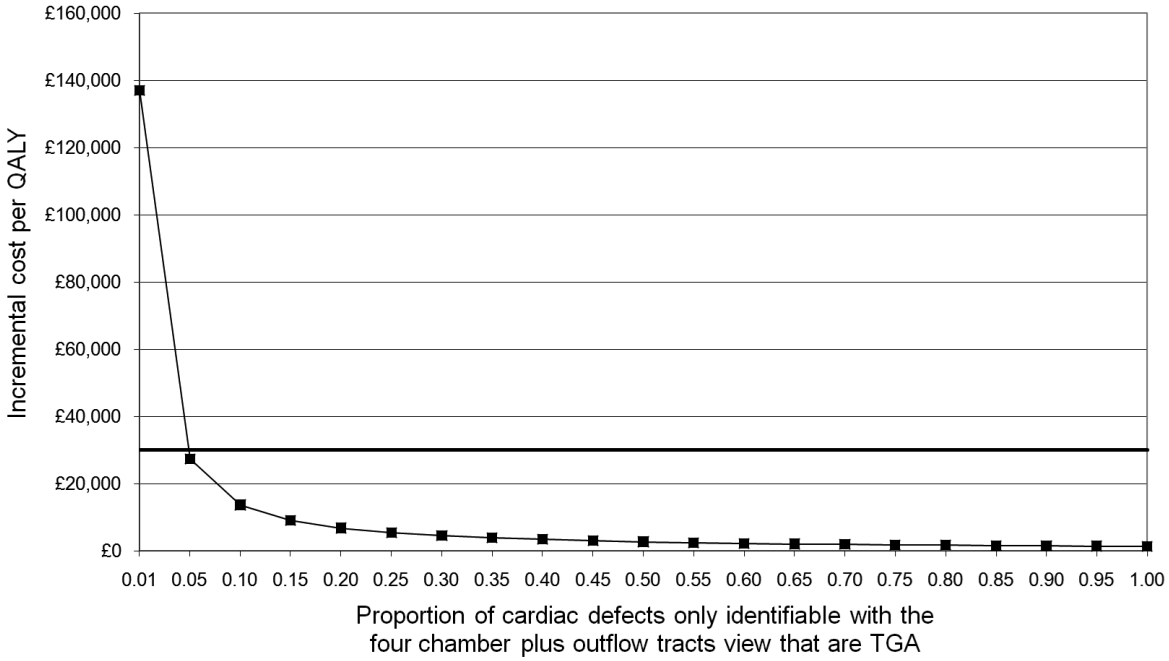


Figure 42:Incremental cost per QALY, varying the proportion of cardiac malformations only identifiable with four chamber plus outflow tracts view that are transposition of the great arteries (TGA)



N.3.5 Discussion

With baseline values the model suggests that the four chamber plus outflow tracts view is cost-effective for screening for cardiac malformations in pregnant women with diabetes compared with the four chamber view. Although the higher costs of the four chamber plus outflow tracts view make it more expensive than the four chamber view the ICER of £3,806 is substantially below the £20,000 per QALY threshold used by NICE as a willingness to pay for cost-effectiveness. NICE states that interventions with a cost per QALY of less than £20,000 should be considered cost-effective, but there must be 'strong reasons' for considering any intervention to be cost-effective if the cost per QALY is greater than £30,000.[23].

The model assumes that TGA is the only cardiac malformation where an antenatal diagnosis confers a benefit in terms of improved health outcomes for the woman and/or the baby. The baseline parameter values give a TGA prevalence of approximately 4.6 per 1000 pregnancies in women with diabetes. With the baseline assumptions for perinatal mortality in relation to TGA detected antenatally or not, one neonatal death would be averted for every seven TGA malformations detected. If a screening strategy involving a four chamber plus outflow tracts view detected all TGA malformations then the number of pregnant women with diabetes needed to screen with the four chamber plus outflow tracts view rather than the four chamber view to avert one neonatal death would be 1466.

The literature does not generally provide test sensitivity and specificity for individual cardiac malformations; instead it gives a value for detecting any cardiac malformation. Hence, the improved sensitivity of the four chamber plus outflow tracts view compared with the four chamber view occurs because the four chamber plus outflow tracts view detects additional malformations that cannot usually be observed with the four chamber view (the sensitivity of detecting TGA with the four chamber view is 0%). The model follows the literature in using overall sensitivities and specificities and it is this which generates the additional 1.91 antenatal diagnoses of cardiac malformations using the four chamber plus outflow tracts

view. The model assumption is that these additional diagnoses are for malformations that would not normally be detectable with a four chamber view, but would be detectable with a view of the outflow tracts. However, as TGA is not the only malformation falling into this category, the model does not assume that all additional antenatal diagnoses are TGA. It uses published data[417] to estimate that 36% of the additional diagnoses would be TGA, which leads to the model result that a four chamber plus outflow tracts view would identify 0.686 TGA per 1000 pregnant women with diabetes. It should be noted that, although this is only 15% of the total TGA malformations present in the population, the four chamber plus outflow tracts view still appears cost-effective with such a low detection rate. However, it may be appropriate to assume a relatively low detection rate as published data reported that only one out of five TGA malformations was detected with a four chamber plus outflow tracts view.[417] With the baseline detection rate used in the model it would be necessary to screen approximately 9800 pregnant women with diabetes using a four chamber plus outflow tracts view to avert one neonatal death.

The baseline results suggest that the detection rate threshold for TGA for the four chamber plus outflow tracts view to achieve cost-effectiveness is quite low. The one-way sensitivity analyses indicate thresholds for cost-effectiveness for other parameter values. Figure 37 suggests that the four chamber plus outflow tracts view would be cost-effective even if the test sensitivity for the four chamber view was within two percentage points of the sensitivity of the four chamber plus outflow tracts view. As the four chamber view sensitivity approaches that of the four chamber plus outflow tracts view there comes a point where there is only very limited added value in terms of detecting cardiac malformations using the four chamber plus outflow tracts view. The key issue here is the difference in test sensitivity between the four chamber view and the four chamber plus outflow tracts view, rather than the absolute values. The one-way sensitivity analysis of the sensitivity of the four chamber view is undertaken holding the sensitivity of the four chamber plus outflow tracts view constant at 82%. The sensitivity analysis suggests that the four chamber plus outflow tracts view requires a sensitivity that is at least four percentage points higher than the sensitivity for the four chamber view in order to achieve cost-effectiveness.

Figure 38 shows that the cost-effectiveness of the four chamber plus outflow tracts view compared with the four chamber view is quite sensitive to the costs of screening. Again it is the difference between screening costs using the four chamber view and the four chamber plus outflow tracts view that is important, rather than the absolute costs of the screening tests. However, the cost of the four chamber plus outflow tracts view would have to be £120 (for an incremental screening cost of £86) and well above the baseline estimate before the four chamber view would be preferred on cost-effectiveness grounds.

Figures 39 and 40 show that the cost-effectiveness of the four chamber plus outflow tracts view is not sensitive to assumptions about QALYs or life expectancy within plausible ranges. Baseline values suggest that the incremental costs of the four chamber plus outflow tracts view are £3,806 in a population of 1000 pregnant women with diabetes. Therefore, only 0.13 incremental QALYs are needed to generate a cost per QALY of £30,000. With baseline values this is approximately 1.3 QALYs per neonatal death averted.

Figure 41 shows that the results of the model are sensitive to the assumptions made in relation to the positive impact that an antenatal diagnosis of TGA has on mortality. However, the ‘best’ estimate used for baseline mortality for antenatally detected TGA mortality (1.8%) is comfortably below the threshold (14%) needed to yield a cost per QALY of £30,000.

Finally, Figure 42 shows that cost-effectiveness is sensitive to the proportion of additional cardiac malformations detected with the four chamber plus outflow tracts view that are assumed to be TGA. However, this relates to the earlier discussion about the overall detection rate of TGA. Given the way the model is constructed, a lower proportion of TGA malformations implies a lower detection rate. Here, TGA would have to account for less than

5% of the additional cardiac malformations detected for the ICER for four chamber plus outflow tracts view to exceed £30,000 per QALY.

The results of the sensitivity analyses suggest that the cost-effectiveness of screening for cardiac malformations based on the four chamber plus outflow tracts view is robust and is unaffected by one-way variation of model parameters within plausible ranges.

The model only addresses cost-effectiveness of screening for cardiac malformations in terms of the impact that antenatal diagnosis has on improved health outcomes. It does not address the 'value' or cost-effectiveness of such screening in providing information to inform a decision about termination of pregnancy. Clearly, the cost-effectiveness of termination of pregnancy is problematic ethically and it does not readily fit into a QALY paradigm.