

Appendix A: Summary of evidence from surveillance

2018 surveillance of [Diabetes in pregnancy: management from preconception to the postnatal period](#) (2015) NICE guideline NG3

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts. Feedback from topic experts who advised us on the approach to this surveillance review was considered alongside the evidence to reach a final decision on the need to update each section of the guideline.

1.1 Preconception care and planning

Recommendations in this section of the guideline

Information about outcomes and risks for mother and baby

- 1.1.1 Aim to empower women with diabetes to have a positive experience of pregnancy and childbirth by providing information, advice and support that will help to reduce the risks of adverse pregnancy outcomes for mother and baby. [2008]
- 1.1.2 Explain to women with diabetes who are planning to become pregnant that establishing good blood glucose control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. It is important to explain that risks can be reduced but not eliminated. [2008]
- 1.1.3 Give women with diabetes who are planning to become pregnant, and their family members, information about how diabetes affects pregnancy and how pregnancy affects diabetes. The information should cover:
 - the role of diet, body weight and exercise
 - the risks of hypoglycaemia and impaired awareness of hypoglycaemia during pregnancy
 - how nausea and vomiting in pregnancy can affect blood glucose control
 - 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 need for assessment of diabetic retinopathy before and during pregnancy
 - the need for assessment of diabetic nephropathy before pregnancy
 - the importance of maternal blood glucose control during labour and birth and early feeding of the baby, in order to reduce the risk of neonatal hypoglycaemia
 - the possibility of temporary health problems 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. [2008]

The importance of planning pregnancy and the role of contraception

- 1.1.4** Ensure that the importance of avoiding an unplanned pregnancy is an essential component of diabetes education from adolescence for women with diabetes. [2008, amended 2015]
- 1.1.5** Explain to women with diabetes that their choice of contraception should be based on their own preferences and any risk factors (as indicated by UK medical eligibility criteria for contraceptive use [UKMEC] 2009 [revised 2010]. [new 2015]
- 1.1.6** Advise women with diabetes that they can use oral contraceptives (if there are no standard contraindications to their use). [new 2015]
- 1.1.7** Advise women with diabetes who are planning to become pregnant:
- that the risks associated with pregnancy in women with diabetes increase with how long the woman has had diabetes
 - to use contraception until good blood glucose control (assessed by HbA1c level[1] – see recommendation 1.1.18) has been established
 - that blood glucose targets, glucose monitoring, medicines for treating diabetes (including insulin regimens for insulin treated diabetes) and medicines for complications of diabetes will need to be reviewed before and during pregnancy
 - that extra time and effort is needed to manage diabetes during pregnancy and that she will have frequent contact with healthcare professionals. [2015]
- 1.1.8** Give women with diabetes who are planning to become pregnant information about the local arrangements for support during pregnancy, including emergency contact numbers. [2015]

Diet, dietary supplements and body weight

- 1.1.9** Offer women with diabetes who are planning to become pregnant individualised dietary advice. [2008]
- 1.1.10** Offer women with diabetes who are planning to become pregnant and who have a BMI above 27 kg/m² advice on how to lose weight, in line with the NICE guideline on obesity: identification, assessment and management of overweight and obesity in children, young people and adults. [2008]
- 1.1.11** Advise women with diabetes who are planning to become pregnant to take folic acid (5 mg/day) until 12 weeks of gestation to reduce the risk of having a baby with a neural tube defect. [2008]

Monitoring blood glucose and ketones in the preconception period

- 1.1.12** Offer women with diabetes who are planning to become pregnant monthly measurement of their HbA1c level[1]. [2008]
- 1.1.13** Offer women with diabetes who are planning to become pregnant a meter for self-monitoring of blood glucose. [2008]
- 1.1.14** If a woman with diabetes who is planning to become pregnant needs intensification of blood glucose-lowering therapy, advise her to increase the frequency of self-monitoring of blood glucose to include fasting levels and a mixture of pre-meal and post-meal levels. [2008]
- 1.1.15** Offer women with type 1 diabetes who are planning to become pregnant blood ketone testing strips and a meter, and advise them to test for ketonaemia if they become hyperglycaemic or unwell. [new 2015]

Target blood glucose and HbA1c levels in the preconception period

- 1.1.16** Agree individualised targets for self-monitoring of blood glucose with women who have diabetes and are planning to become pregnant, taking into account the risk of hypoglycaemia. [2008]
- 1.1.17** Advise women with diabetes who are planning to become pregnant to aim for the same capillary plasma glucose target ranges as recommended for all people with type 1 diabetes:
- a fasting plasma glucose level of 5–7 mmol/litre on waking and
 - a plasma glucose level of 4–7 mmol/litre before meals at other times of the day.

For more information, see the section on [blood glucose targets](#) in the NICE guideline on type 1 diabetes. [new 2015]

- 1.1.18** Advise women with diabetes who are planning to become pregnant to aim to keep their HbA1c level[1] below 48 mmol/mol (6.5%), if this is achievable without causing problematic hypoglycaemia. [new 2015]
- 1.1.19** Reassure women that any reduction in HbA1c level towards the target of 48 mmol/mol (6.5%) is likely to reduce the risk of congenital malformations in the baby. [new 2015]
- 1.1.20** Strongly advise women with diabetes whose HbA1c level is above 86 mmol/mol (10%) not to get pregnant because of the associated risks (see recommendation 1.1.2). [2015]

Safety of medicines for diabetes before and during pregnancy

- 1.1.21** Women with diabetes may be advised to use metformin[2] as an adjunct or alternative to insulin in the preconception period and during pregnancy, when the likely benefits from improved blood glucose control outweigh the potential for harm. All other oral blood glucose-lowering agents should be discontinued before pregnancy and insulin substituted. [2008]
- 1.1.22** Be aware that data from clinical trials and other sources do not suggest that the rapid-acting insulin analogues (aspart and lispro) adversely affect the pregnancy or the health of the fetus or newborn baby. [2008]
- 1.1.23** Use isophane insulin (also known as NPH insulin) as the first choice for long-acting insulin during pregnancy. Consider continuing treatment with long-acting insulin analogues (insulin detemir or insulin glargine) in women with diabetes who have established good blood glucose control before pregnancy[3]. [2008, amended 2015]

Safety of medicines for complications of diabetes before and during pregnancy

- 1.1.24** Angiotensin-converting enzyme inhibitors and angiotensin-II receptor antagonists should be discontinued before conception or as soon as pregnancy is confirmed. Alternative antihypertensive agents suitable for use during pregnancy should be substituted. [2008]
- 1.1.25** Statins should be discontinued before pregnancy or as soon as pregnancy is confirmed. [2008]

Removing barriers to the uptake of preconception care and when to offer information

- 1.1.26** Explain to women with diabetes about the benefits of preconception blood glucose control at each contact with healthcare professionals, including their diabetes care team, from adolescence. [2008]
- 1.1.27** Document the intentions of women with diabetes regarding pregnancy and contraceptive use at each contact with their diabetes care team from adolescence. [2008]
- 1.1.28** Ensure that preconception care for women with diabetes is given in a supportive environment, and encourage the woman's partner or other family member to attend. [2008, amended 2015]

Education and advice

- 1.1.29** Offer women with diabetes who are planning to become pregnant a structured education programme as soon as possible if they have not already attended one (see the education and information section in the NICE guideline on type 1 diabetes in adults, and the patient education section in the NICE guideline on type 2 diabetes in adults). [2008]
- 1.1.30** Offer women with diabetes who are planning to become pregnant preconception care and advice before discontinuing contraception. [2008]

Retinal assessment in the preconception period

- 1.1.31** Offer retinal assessment (see recommendation 1.1.32) to women with diabetes seeking preconception care at their first appointment (unless they have had an annual retinal assessment in the last 6 months) and then annually if no diabetic retinopathy is found. [2008]
- 1.1.32** Carry out retinal assessment by digital imaging with mydriasis using tropicamide, in line with the UK National Screening Committee's recommendations for annual mydriatic 2-field digital photographic screening as part of a systematic screening programme. [2008]
- 1.1.33** Advise women with diabetes who are planning to become pregnant to defer rapid optimisation of blood glucose control until after retinal assessment and treatment have been completed. [2008]

Renal assessment in the preconception period

- 1.1.34** Offer women with diabetes a renal assessment, including a measure of albuminuria, before discontinuing contraception. If serum creatinine is abnormal (120 micromol/litre or more), the urinary albumin:creatinine ratio is greater than 30 mg/mmol or the estimated glomerular filtration rate (eGFR) is less than 45 ml/minute/1.73 m², referral to a nephrologist should be considered before discontinuing contraception. [2008, amended 2015]

Footnotes

[1] HbA1c values are reported in mmol/mol, using the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) standardised HbA1c test. The equivalent values in %, using the Diabetes Control and Complications Trial (DCCT)-aligned HbA1c test, are reported in parentheses.

[2] Although metformin is commonly used in UK clinical practice in the management of diabetes in pregnancy and lactation, and there is strong evidence for its effectiveness and safety (presented in the full version of the guideline), at the time of publication (February 2015) metformin did not have a UK marketing authorisation for this indication. The summary of product characteristics advises that when a patient plans to become pregnant and during pregnancy, diabetes should not be treated with metformin but insulin should be used to maintain blood glucose levels. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[3] At the time of publication (February 2015), long-acting insulin analogues did not have UK marketing authorisation for use during pregnancy in women with diabetes. However, the summaries of product characteristics (SPCs) for insulin detemir and insulin glargine state that their use may be considered during pregnancy; see the SPCs of the individual products for details. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Surveillance decision

These recommendations should be updated. An editorial amendment is also needed to add a footnote at the end of 1.1.10 to clarify BMI cut-offs for different ethnicities. Suggested wording: The BMI cut-off should consider the variation in risk for different ethnic groups, see the [NICE guideline on BMI \(PH46\)](#).

Preconception care and planning

Previous surveillance

This guideline has never had a surveillance review undertaken as it is an update of a previous guideline (CG63). However, CG63, was the subject of a surveillance review in 2011 which resulted in the guideline being updated to form NG3. This section of the guideline had 13/34 recommendations updated or amended 2015.

The 2011 surveillance identified 2 trials focussing on risks of gestational diabetes (1),(2) which found that women with gestational diabetes or borderline gestational diabetes are at increased risk of maternal and infant adverse pregnancy events. This is in line with current recommendations.

2018 surveillance summary

One Cochrane review (3) (n=7 studies including 707 women; results based on n=3 studies including 241 women) studied the effectiveness of metformin versus insulin in the preconception period and during pregnancy (also see section 1.2 below). The evidence base was deemed low quality but results suggest possible reductions in caesarean section, pregnancy-induced hypertension, and neonatal hypoglycaemia with metformin used during the preconception period and pregnancy compared with insulin for women with type 2 diabetes diagnosed before or during their pregnancy. There was no clear effects on pre-eclampsia, induction of labour and babies that are large-for-gestational age.

One Cochrane review (4) (n=3 studies including 254 adolescent girls) assessed the effects of preconception care in adolescent girls with type 1 or 2 diabetes and their infants. The

authors reported that there was insufficient data available to assess the effects of preconception care for diabetic women on health outcomes for mothers and their infants.

The recently published CONCEPTT trial (5) (n=325 women; 215 pregnant and 110 planning pregnancy with type 1 diabetes) found improvements in a range of neonatal outcomes with CGM plus standard care, compared with standard care alone, including neonatal intensive care admission, large for gestational age and neonatal hypoglycaemia for pregnant women. There were no clear benefits for women planning pregnancy, possibly due to the small sample size, but the authors noted that many women may be uncomfortable changing monitoring modality during early pregnancy, thus initiating CGM pre-pregnancy may be of benefit.

Topic expert feedback and additional information

One expert questioned whether monthly HbA1c tests during pregnancy (recommendation 1.1.12) were likely to be cost effective but did not provide any evidence.

One expert suggested that the safety of glibenclamide is established and should be mentioned as a treatment option in the preconception period (recommendation 1.1.21). However, another expert felt the safety of glibenclamide was uncertain – see surveillance summary for section 1.2 below. However, we did not identify any MHRA safety warnings for glibenclamide in pregnancy (see section 1.2).

One expert queried the choice of beta-blockers and suggested switching to labetalol from atenolol and bisoprolol (recommendation 1.1.24). However, no evidence was provided to

support this and the recommendation does not currently specify individual drugs.

Impact statement

Through the 2018 surveillance review, two Cochrane reviews evaluating preconception care were identified. One review found insufficient evidence to assess preconception protocols. One review found that metformin may be associated with reductions in caesarean section, pregnancy-induced hypertension, and neonatal hypoglycaemia, compared with insulin for women with type 2 diabetes. This new evidence is unlikely to change recommendations as recommendation 1.1.21 already advises that metformin may be an adjunct or alternative to insulin.

There is new evidence on continuous glucose monitoring in antenatal women with type 1 diabetes. The recent CONCEPTT trial indicates improved neonatal outcomes with continuous glucose monitoring and advocates routine usage in pregnant women with type 1 diabetes. The benefits were not seen in the planning pregnancy stage, possibly due to the small sample size, but the authors noted that women may be uncomfortable changing monitoring modality during early pregnancy, thus initiating CGM pre-pregnancy may be of benefit. This could potentially create a new recommendation on continuous glucose monitoring during preconception planning and care.

Evidence identified in previous surveillance which indicated women with gestational diabetes or borderline gestational diabetes are at increased risk of maternal and infant adverse pregnancy events is in line with current recommendations.

An editorial amendment is needed to add a footnote at the end of 1.1.10 to clarify BMI cut-offs for different ethnicities.

New evidence was identified that may change guideline recommendations.

1.2 Gestational diabetes

Risk assessment, testing and diagnosis

Recommendations in this section of the guideline

Risk assessment

- 1.2.1** So that women can make an informed decision about risk assessment and testing for gestational diabetes, explain that:
- in some women, gestational diabetes will respond to changes in diet and exercise
 - the majority of women will need oral blood glucose-lowering agents or insulin therapy if changes in diet and exercise do not control gestational diabetes effectively
 - if gestational diabetes is not detected and controlled, there is a small increased risk of serious adverse birth complications such as shoulder dystocia
 - a diagnosis of gestational diabetes will lead to increased monitoring, and may lead to increased interventions, during both pregnancy and labour. [new 2015]
- 1.2.2** Assess risk of gestational diabetes using risk factors in a healthy population. At the booking appointment, determine the following risk factors for gestational diabetes:
- 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)
 - minority ethnic family origin with a high prevalence of diabetes.
 - Offer women with any one of these risk factors testing for gestational diabetes (see recommendations 1.2.5–1.2.7). [2008, amended 2015]
- 1.2.3** Do not use fasting plasma glucose, random blood glucose, HbA1c, glucose challenge test or urinalysis for glucose to assess risk of developing gestational diabetes. [2015]

Glycosuria detected by routine antenatal testing

- 1.2.4** Be aware that glycosuria of 2+ or above on 1 occasion or of 1+ or above on 2 or more occasions detected by reagent strip testing during routine antenatal care may indicate undiagnosed gestational diabetes. If this is observed, consider further testing to exclude gestational diabetes. [new 2015]

Testing

- 1.2.5** Use the 2-hour 75 g oral glucose tolerance test (OGTT) to test for gestational diabetes in women with risk factors (see recommendation 1.2.2). [2015]
- 1.2.6** Offer women who have had gestational diabetes in a previous pregnancy:
- early self-monitoring of blood glucose or
 - a 75 g 2-hour OGTT as soon as possible after booking (whether in the first or second trimester), and a further 75 g 2-hour OGTT at 24–28 weeks if the results of the first OGTT are normal. [new 2015]

1.2.7 Offer women with any of the other risk factors for gestational diabetes (see recommendation 1.2.2) a 75 g 2-hour OGTT at 24–28 weeks. [2015]

Diagnosis

1.2.8 Diagnose gestational diabetes if the woman has either:

- a fasting plasma glucose level of 5.6 mmol/litre or above or
- a 2-hour plasma glucose level of 7.8 mmol/litre or above. [new 2015]

1.2.9 Offer women with a diagnosis of gestational diabetes a review with the joint diabetes and antenatal clinic within 1 week. [new 2015]

1.2.10 Inform the primary healthcare team when a woman is diagnosed with gestational diabetes (see also the NICE guideline on patient experience in adult NHS services in relation to continuity of care). [new 2015]

Interventions

1.2.11 Explain to women with gestational diabetes::

- about the implications (both short and long term) of the diagnosis for her and her baby
- that good blood glucose control throughout pregnancy will reduce the risk of fetal macrosomia, trauma during birth (for her and her baby), induction of labour and/or caesarean section, neonatal hypoglycaemia and perinatal death
- that treatment includes changes in diet and exercise, and could involve medicines. [new 2015]

1.2.12 Teach women with gestational diabetes about self-monitoring of blood glucose. [2015]

1.2.13 Use the same capillary plasma glucose target levels for women with gestational diabetes as for women with pre-existing diabetes (see recommendations 1.3.5 and 1.3.6). [2015]

1.2.14 Tailor blood glucose-lowering therapy to the blood glucose profile and personal preferences of the woman with gestational diabetes. [new 2015]

1.2.15 Offer women advice about changes in diet and exercise at the time of diagnosis of gestational diabetes. [new 2015]

1.2.16 Advise women with gestational diabetes to eat a healthy diet during pregnancy, and emphasise that foods with a low glycaemic index should replace those with a high glycaemic index. [new 2015]

1.2.17 Refer all women with gestational diabetes to a dietitian. [new 2015]

1.2.18 Advise women with gestational diabetes to take regular exercise (such as walking for 30 minutes after a meal) to improve blood glucose control. [new 2015]

1.2.19 Offer a trial of changes in diet and exercise to women with gestational diabetes who have a fasting plasma glucose level below 7 mmol/litre at diagnosis. [new 2015]

1.2.20 Offer metformin[2] to women with gestational diabetes if blood glucose targets are not met using changes in diet and exercise within 1–2 weeks. [new 2015]

1.2.21 Offer insulin instead of metformin to women with gestational diabetes if metformin is contraindicated or unacceptable to the woman. [new 2015]

1.2.22 Offer addition of insulin to the treatments of changes in diet, exercise and metformin[2] for women with gestational diabetes if blood glucose targets are not met. [new 2015]

- 1.2.23** Offer immediate treatment with insulin, with or without metformin[2], as well as changes in diet and exercise, to women with gestational diabetes who have a fasting plasma glucose level of 7.0 mmol/litre or above at diagnosis. [new 2015]
- 1.2.24** Consider immediate treatment with insulin, with or without metformin[2], as well as changes in diet and exercise, for women with gestational diabetes who have a fasting plasma glucose level of between 6.0 and 6.9 mmol/litre if there are complications such as macrosomia or hydramnios. [new 2015].
- 1.2.25** Consider glibenclamide[4] for women with gestational diabetes:
- in whom blood glucose targets are not achieved with metformin but who decline insulin therapy or
 - who cannot tolerate metformin. [new 2015]

Footnotes

[2] Although metformin is commonly used in UK clinical practice in the management of diabetes in pregnancy and lactation, and there is strong evidence for its effectiveness and safety (presented in the full version of the guideline), at the time of publication (February 2015) metformin did not have a UK marketing authorisation for this indication. The summary of product characteristics advises that when a patient plans to become pregnant and during pregnancy, diabetes should not be treated with metformin but insulin should be used to maintain blood glucose levels. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4] At the time of publication (February 2015) glibenclamide was contraindicated for use up to gestational week 11 and did not have UK marketing authorisation for use during the second and third trimesters of pregnancy in women with gestational diabetes. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Surveillance decision

These recommendations should not be updated.

An editorial amendment is needed for bullet point 1 of recommendation 1.2.11 to provide a footnote with a link to the DVLA guidance on diabetes and driving.

Suggested footnote: Advice for women on driving with diabetes is available from the DVLA website: <https://www.gov.uk/diabetes-driving>

An editorial amendment to footnote 4 is needed to update the information on glibenclamide.

Suggested footnote: At the time of surveillance review (April 2018) the UK marketing authorisation for glibenclamide varied between different brands with regards to use in pregnancy. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Gestational diabetes

Previous surveillance

This guideline has never had a surveillance review undertaken as it is an update of a previous guideline (CG63). However, CG63, was the subject of a surveillance review in 2011 which resulted in the guideline being updated to form NG3. This section of the guideline had all 25 recommendations updated or amended in 2015.

2018 surveillance summary

Diagnosis of gestational diabetes

A total of 11 studies were identified that focussed on the criteria for diagnosing gestational diabetes; 5 studies focussed on NICE criteria compared with the International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria, and 6 studies focussed on IADPSG and other non-NICE criteria.

NICE criteria (n=5)

One prospective cohort study (n=554 women who had an OGTT) (6) found that universal screening with IADPSG resulted in a prevalence of gestational diabetes mellitus (GDM) of 25.8% compared with 17% with NICE criteria in South Africa. Selective risk factor screening with IADPSG resulted in a prevalence of 15.2% compared with 3.6% with NICE criteria, although risk factors were found to be a poor screening test.

One retrospective observational study (n=4,646 women who had an OGTT) (7) found that 23.1% would be diagnosed with IADPSG criteria compared with 17.8% with NICE criteria in Croatia. Women who would not have been diagnosed with the NICE criteria (fasting plasma glucose levels of 5.1-5.5 mmol/L) had an increased risk of adverse maternal and perinatal outcome.

One analysis of a case control and cohort (n=523 women in case control and 6,930

women in the cohort study) (8) found that the incident cohort of GDM prevalence was 3.7% with WHO 1999 criteria, 11.4% with NICE criteria, and 13.7% with WHO 2013 criteria. The additional cases found by the WHO 2013 and NICE criteria were deemed 'moderate' dysglycaemia. There were also cases identified by WHO 1999, that were not found by WHO 2013 and NICE criteria that were deemed intermediate cases.

One cost-effectiveness analysis (n=25,284 women from 4 HAPO centres) (9) found that the NICE criteria for GDM were cost-effective compared to the WHO 2013 alternative at a threshold of £30,000 per QALY.

One retrospective observational study (n=25,543 women) (10) found that the prevalence of GDM was 4.62% with IADPSG criteria and 4.13% with NICE criteria. Women who tested positive for IADPSG but negative for NICE (n=387) had a higher risk of having a large-for-gestational-age infant, Caesarean delivery and polyhydramnios compared with women with negative screening results and no OGTT.

IADPSG criteria or other non-NICE criteria (n=6)

One review (n=8 cohort studies including 29,983 women) (11) found that women meeting criteria for GDM by IADPSG criteria have an increased risk of adverse pregnancy outcomes, such as preeclampsia, gestational hypertension, and large for gestational age, compared with GDM-negative controls.

One Cochrane review (n=7 RCTs including 1,420 women) (12) found that there is insufficient evidence to determine which strategy is best for diagnosing GDM.

One review and economic analysis using individual patient data (n=58 studies; number of women not reported) (12) found that glucose thresholds to identify infants at high risk of being born large for gestational age or with high adiposity for South Asian women were fasting and post-load glucose levels of

5.2 mmol/l and 7.2 mmol/l, respectively and for white British (WB) women they were 5.4 and 7.5 mmol/l. Cost-effectiveness analysis indicated that it was cost-effective to routinely identify and treat GDM, although there was uncertainty around long-term benefits to mothers and infants.

One systematic review (13) (n=38 studies; number of women not reported) found that higher glucose thresholds was not consistently associated with a greater risk of adverse pregnancy outcomes.

One prospective RCT (14) (n=1,000 women) found that the incidence of GDM was 19.2% with one-step IADPSG compared with 11.8% with two-step ACOG. Maternal and fetal outcomes were comparable between both groups apart from a higher risk of preterm delivery and neonatal hypoglycaemia with the two-step ACOG.

One randomised study (15) (n=786 women) found that the prevalence of GDM was 14.5% with the one-step IADPSG compared with 6% with a two-step method. Women who were defined as having normal glucose tolerance by IADPSG had better perinatal outcomes than women who were GCT-positive with a negative OGTT and women who were defined as having normal glucose tolerance by GCT.

Interventions for GDM

There were 6 Cochrane reviews that focussed on interventions for GDM. There was 1 review (16) of myo-inositol for treating GDM (2 studies including 142 women and babies) which found that there was insufficient data to assess the effects.

There was 1 review of oral diabetic agents in women with GDM (17) (n=14 studies including 1,487 women and babies) which found that there was insufficient evidence to be able to inform clinical practice.

There were 4 reviews of lifestyle, diet or exercise programmes for GDM. One review (18) (n=15 trials including 4,501 women) found

that lifestyle interventions are associated with a decreased risk of the baby being born large, but long-term maternal and child outcomes were poorly reported.

One review (19) (n=19 trials including 1,398 women) focussed on different diet interventions for women with GDM. The review found little difference between diet interventions, apart from a potential decrease in caesarean sections with the DASH diet.

There were 2 reviews of exercise interventions; 1 in women with GDM (20) (n=11 trials including 638 women) and 1 in women with pre-existing diabetes (21) (0 trials). The reviews found that there was insufficient evidence to be able to determine the effects of different exercise programmes in women with GDM or pre-existing diabetes.

Topic expert feedback and additional information

Topic experts highlighted a study on the use of glibenclamide during pregnancy (22) that indicates it crosses the placenta in approximately 70% of maternal quantities, which may be a cause for caution in the 3rd trimester of pregnancy (recommendation 1.2.25).

To address this issue a range of sources were checked, including the BNF, MHRA, EMA, UKTIS, and Toxbase. There were no safety warnings found on the use of glibenclamide in pregnancy. The UKTIS currently state (dated 2016) that 'Data on the use of glibenclamide in pregnancy consist of >9,500 exposures.' And that: 'Glibenclamide may be considered in the treatment of gestational diabetes where metformin is ineffective or not tolerated, and where treatment with insulin is declined.' The MHRA confirmed that they are currently not planning to review the safety of glibenclamide in pregnancy.

One expert indicated that OGTT is not appropriate for post-bypass patients and that

there are generally capacity issues with OGTT as demand is high (recommendation 1.2.7).

Several experts indicated that there are capacity issues caused by the diagnostic criteria for gestational diabetes (recommendation 1.2.8) and variation across the country.

One expert highlighted that there are capacity issues with dieticians and another expert indicated that referral to a dietician applies to all diabetes patients so is not specific to gestational diabetes (recommendation 1.2.17).

One expert indicated that the guideline should link to DVLA guidance on driving with gestational diabetes. This seems to fit best with recommendation 1.2.11.

Impact statement

All recommendations in this section were updated or amended 2015.

The 2018 surveillance process identified new evidence on the diagnostic criteria for identifying women with GDM; however, this evidence is contradictory and does not show a clear advantage of one diagnostic criteria over another. Five studies specifically focussed on NICE criteria, of which all studies found NICE criteria to give a lower prevalence of GDM compared with WHO 2013 or IADPSG criteria. However, 2 studies found that NICE criteria missed some women with an increased risk for

adverse pregnancy outcomes, such as large for gestational age and caesarean section.

Contrary to this, 1 study found that NICE criteria was cost-effective compared with WHO 2013 / IADPSG criteria. The reasons for these differences are not clear but could be due to the different populations studied, different timings of the tests, and different ways of capturing adverse pregnancy outcomes.

Topic experts also highlighted that NICE diagnostic criteria are not implemented across all of England as there are capacity issues with the criteria. However, the IADPSG/WHO 2013 criteria lead to a higher incidence of GDM diagnosis, compared with NICE criteria, so reverting to these criteria would exacerbate the capacity issues with uncertain benefits.

Given the contradictory evidence on which diagnostic criteria is best, but the potential that NICE criteria may be cost-effective compared with IADPSG/WHO 2013 criteria, it does not appear warranted to update recommendation 1.2.8 at this time point.

An editorial amendment is suggested to link to the DVLA guidelines on driving with gestational diabetes. This seems to fit best with recommendation 1.2.11.

New evidence is unlikely to change guideline recommendations

1.3 Antenatal care for women with diabetes

Recommendations in this section of the guideline

Monitoring blood glucose

- 1.3.1** Advise pregnant women with type 1 diabetes to test their fasting, pre-meal, 1-hour post-meal and bedtime blood glucose levels daily during pregnancy. [new 2015]
- 1.3.2** Advise pregnant women with type 2 diabetes or gestational diabetes who are on a multiple daily insulin injection regimen to test their fasting, pre-meal, 1-hour post-meal and bedtime blood glucose levels daily during pregnancy. [new 2015]
- 1.3.3** Advise pregnant women with type 2 diabetes or gestational diabetes to test their fasting and 1-hour post-meal blood glucose levels daily during pregnancy if they are:
- on diet and exercise therapy, or
 - taking oral therapy (with or without diet and exercise therapy) or single-dose intermediate-acting or long-acting insulin. [new 2015]

Target blood glucose levels

- 1.3.4** Agree individualised targets for self monitoring of blood glucose with women with diabetes in pregnancy, taking into account the risk of hypoglycaemia. [2008]
- 1.3.5** Advise pregnant women with any form of diabetes to maintain their capillary plasma glucose below the following target levels, if these are achievable without causing problematic hypoglycaemia:
- fasting: 5.3 mmol/litre
 - and
 - 1 hour after meals: 7.8 mmol/litre or
 - 2 hours after meals: 6.4 mmol/litre. [new 2015]
- 1.3.6** Advise pregnant women with diabetes who are on insulin or glibenclamide to maintain their capillary plasma glucose level above 4 mmol/litre. [new 2015]

Monitoring HbA1c

- 1.3.7** Measure HbA1c levels in all pregnant women with pre-existing diabetes at the booking appointment to determine the level of risk for the pregnancy. [new 2015]
- 1.3.8** Consider measuring HbA1c levels in the second and third trimesters of pregnancy for women with pre-existing diabetes to assess the level of risk for the pregnancy. [new 2015]
- 1.3.9** Be aware that level of risk for the pregnancy for women with pre-existing diabetes increases with an HbA1c level above 48 mmol/mol (6.5%). [new 2015]
- 1.3.10** Measure HbA1c levels in all women with gestational diabetes at the time of diagnosis to identify those who may have pre-existing type 2 diabetes. [new 2015]
- 1.3.11** Do not use HbA1c levels routinely to assess a woman's blood glucose control in the second and third trimesters of pregnancy. [2008]

Managing diabetes during pregnancy

Insulin treatment and risks of hypoglycaemia

- 1.3.12** Be aware that the rapid-acting insulin analogues (aspart and lispro) have advantages over soluble human insulin during pregnancy and consider their use. [2008]
- 1.3.13** Advise women with insulin-treated diabetes of the risks of hypoglycaemia and impaired awareness of hypoglycaemia in pregnancy, particularly in the first trimester. [2008]
- 1.3.14** Advise pregnant women with insulin-treated diabetes to always have available a fast-acting form of glucose (for example, dextrose tablets or glucose-containing drinks). [2008, amended 2015]
- 1.3.15** Provide glucagon to pregnant women with type 1 diabetes for use if needed. Instruct the woman and her partner or other family members in its use. [2008, amended 2015]
- 1.3.16** Offer women with insulin-treated diabetes continuous subcutaneous insulin infusion (CSII; also known as insulin pump therapy) during pregnancy if adequate blood glucose control is not obtained by multiple daily injections of insulin without significant disabling hypoglycaemia[5]. [2008]

Continuous glucose monitoring

- 1.3.17** Do not offer continuous glucose monitoring routinely to pregnant women with diabetes. [new 2015]
- 1.3.18** Consider continuous glucose monitoring for pregnant women on insulin therapy:
- who have problematic severe hypoglycaemia (with or without impaired awareness of hypoglycaemia) or
 - who have unstable blood glucose levels (to minimise variability) or
 - to gain information about variability in blood glucose levels. [new 2015]
- 1.3.19** Ensure that support is available for pregnant women who are using continuous glucose monitoring from a member of the joint diabetes and antenatal care team with expertise in its use. [new 2015]

Ketone testing and diabetic ketoacidosis

- 1.3.20** Offer pregnant women with type 1 diabetes blood ketone testing strips and a meter, and advise them to test for ketonaemia and to seek urgent medical advice if they become hyperglycaemic or unwell. [new 2015]
- 1.3.21** Advise pregnant women with type 2 diabetes or gestational diabetes to seek urgent medical advice if they become hyperglycaemic or unwell. [new 2015]
- 1.3.22** Test urgently for ketonaemia if a pregnant woman with any form of diabetes presents with hyperglycaemia or is unwell, to exclude diabetic ketoacidosis. [new 2015]
- 1.3.23** During pregnancy, admit immediately women who are suspected of having diabetic ketoacidosis for level 2 critical care[6], where they can receive both medical and obstetric care. [2008]

Retinal assessment during pregnancy

- 1.3.24 Offer pregnant women with pre-existing diabetes retinal assessment by digital imaging with mydriasis using tropicamide following their first antenatal clinic appointment (unless they have had a retinal assessment in the last 3 months), and again at 28 weeks. If any diabetic retinopathy is present at booking, perform an additional retinal assessment at 16–20 weeks. [2008, amended 2015]
- 1.3.25 Diabetic retinopathy should not be considered a contraindication to rapid optimisation of blood glucose control in women who present with a high HbA1c in early pregnancy. [2008]
- 1.3.26 Ensure that women who have preproliferative diabetic retinopathy or any form of referable retinopathy diagnosed during pregnancy have ophthalmological follow-up for at least 6 months after the birth of the baby. [2008, amended 2015]
- 1.3.27 Diabetic retinopathy should not be considered a contraindication to vaginal birth. [2008]

Renal assessment during pregnancy

- 1.3.28 If renal assessment has not been undertaken in the preceding 3 months in women with pre-existing diabetes, arrange it at the first contact in pregnancy. If the serum creatinine is abnormal (120 micromol/litre or more), the urinary albumin:creatinine ratio is greater than 30 mg/mmol or total protein excretion exceeds 0.5 g/day, referral to a nephrologist should be considered (eGFR should not be used during pregnancy). Thromboprophylaxis should be considered for women with nephrotic range proteinuria above 5 g/day (albumin:creatinine ratio greater than 220 mg/mmol). [2008, amended 2015]

Preventing pre-eclampsia

- 1.3.29 For guidance on using antiplatelet agents to reduce the risk of pre-eclampsia in pregnant women with diabetes, see recommendation 1.1.2.1 in the NICE guideline on hypertension in pregnancy. [new 2015]

Detecting congenital malformations

- 1.3.30 Offer women with diabetes an ultrasound scan for detecting fetal structural abnormalities, including examination of the fetal heart (4 chambers, outflow tracts and 3 vessels), at 20 weeks. [2008, amended 2015]

Monitoring fetal growth and wellbeing

- 1.3.31 Offer pregnant women with diabetes ultrasound monitoring of fetal growth and amniotic fluid volume every 4 weeks from 28 to 36 weeks. [2008]
- 1.3.32 Routine monitoring of fetal wellbeing (using methods such as fetal umbilical artery Doppler recording, fetal heart rate recording and biophysical profile testing) before 38 weeks is not recommended in pregnant women with diabetes, unless there is a risk of fetal growth restriction. [2008, amended 2015]
- 1.3.33 Provide an individualised approach to monitoring fetal growth and wellbeing for women with diabetes and a risk of fetal growth restriction (macrovascular disease and/or nephropathy). [2008, amended 2015]

Organisation of antenatal care

- 1.3.34** Offer immediate contact with a joint diabetes and antenatal clinic to women with diabetes who are pregnant. [2008]
- 1.3.35** Ensure that women with diabetes have contact with the joint diabetes and antenatal clinic for assessment of blood glucose control every 1–2 weeks throughout pregnancy. [2008, amended 2015]
- 1.3.36** At antenatal appointments, provide care specifically for women with diabetes, in addition to the care provided routinely for healthy pregnant women (see the NICE guideline on antenatal care). Table 1 describes how care for women with diabetes differs from routine antenatal care. At each appointment, offer the woman ongoing opportunities for information and education. [2008, amended 2015]

Table 1 Timetable of antenatal appointments

Appointment	Care for women with diabetes during pregnancy*
Booking appointment (joint diabetes and antenatal care) – ideally by 10 weeks	<p>Discuss information, education and advice about how diabetes will affect the pregnancy, birth and early parenting (such as breastfeeding and initial care of the baby).</p> <p>If the woman has been attending for preconception care and advice, continue to provide information, education and advice in relation to achieving optimal blood glucose control (including dietary advice).</p> <p>If the woman has not attended for preconception care and advice, give information, education and advice for the first time, take a clinical history to establish the extent of diabetes-related complications (including neuropathy and vascular disease), and review medicines for diabetes and its complications.</p> <p>Offer retinal assessment for women with pre-existing diabetes unless the woman has been assessed in the last 3 months.</p> <p>Offer renal assessment for women with pre-existing diabetes if this has not been performed in the last 3 months.</p> <p>Arrange contact with the joint diabetes and antenatal clinic every 1–2 weeks throughout pregnancy for all women with diabetes.</p> <p>Measure HbA1c levels for women with pre-existing diabetes to determine the level of risk for the pregnancy.</p> <p>Offer self-monitoring of blood glucose or a 75 g 2-hour OGTT as soon as possible for women with a history of gestational diabetes who book in the first trimester.</p> <p>Confirm viability of pregnancy and gestational age at 7–9 weeks.</p>
16 weeks	<p>Offer retinal assessment at 16–20 weeks to women with pre-existing diabetes if diabetic retinopathy was present at their first antenatal clinic visit.</p> <p>Offer self-monitoring of blood glucose or a 75 g 2-hour OGTT as soon as possible for women with a history of gestational diabetes who book in the second trimester.</p>
20 weeks	<p>Offer an ultrasound scan for detecting fetal structural abnormalities, including examination of the fetal heart (4 chambers, outflow tracts and 3 vessels).</p>
28 weeks	<p>Offer ultrasound monitoring of fetal growth and amniotic fluid volume.</p> <p>Offer retinal assessment to all women with pre-existing diabetes.</p> <p>Women diagnosed with gestational diabetes as a result of routine antenatal testing at 24–28 weeks enter the care pathway.</p>
32 weeks	<p>Offer ultrasound monitoring of fetal growth and amniotic fluid volume.</p>

	Offer nulliparous women all routine investigations normally scheduled for 31 weeks in routine antenatal care.
34 weeks	No additional or different care for women with diabetes.
36 weeks	Offer ultrasound monitoring of fetal growth and amniotic fluid volume. Provide information and advice about: <ul style="list-style-type: none"> • timing, mode and management of birth • analgesia and anaesthesia • changes to blood glucose-lowering therapy during and after birth • care of the baby after birth • initiation of breastfeeding and the effect of breastfeeding on blood glucose control • contraception and follow-up.
37 ⁺⁰ weeks to 38 ⁺⁶ weeks	Offer induction of labour, or caesarean section if indicated, to women with type 1 or type 2 diabetes; otherwise await spontaneous labour.
38 weeks	Offer tests of fetal wellbeing.
39 weeks	Offer tests of fetal wellbeing. Advise women with uncomplicated gestational diabetes to give birth no later than 40 ⁺⁶ weeks.
<p>* Women with diabetes should also receive routine care according to the schedule of appointments in the NICE guideline on antenatal care, including appointments at 25 weeks (for nulliparous women) and 34 weeks, but with the exception of the appointment for nulliparous women at 31 weeks.</p> <p>OGTT = oral glucose tolerance test.</p>	

Preterm labour in women with diabetes

- 1.3.37** Diabetes should not be considered a contraindication to antenatal steroids for fetal lung maturation or to tocolysis. [2008]
- 1.3.38** In women with insulin-treated diabetes who are receiving steroids for fetal lung maturation, give additional insulin according to an agreed protocol and monitor them closely. [2008, amended 2015]
- 1.3.39** Do not use betamimetic medicines for tocolysis in women with diabetes. [2008]

Footnotes

[5] For the purpose of this guidance, 'disabling hypoglycaemia' means the repeated and unpredicted occurrence of hypoglycaemia requiring third-party assistance that results in continuing anxiety about recurrence and is associated with significant adverse effect on quality of life.

[6] Level 2 critical care is defined as care for patients requiring detailed observation or intervention, including support for a single failing organ system or postoperative care and those 'stepping down' from higher levels of care.

Surveillance decision

These recommendations should be updated. An amendment is also needed to add a caveat to reduce unnecessary retinal screening.

Antenatal care for women with diabetes

Previous surveillance

This guideline has never had a surveillance review undertaken as it is an update of a previous guideline (CG63). However, CG63, was the subject of a surveillance review in 2011 which resulted in the guideline being updated to form NG3. This section of the guideline had 26/39 recommendations updated or amended 2015.

The 2011 surveillance review identified a number of studies related to this section of the guideline but these have been superseded by the 2018 review.

2018 surveillance

Target blood glucose levels

There were 2 Cochrane reviews that focussed on target blood glucose levels (recommendation 1.3.5): one review (23) included 3 trials comprising 223 women with type 1 diabetes; and 1 review (24) included 1 trial comprising 180 women with gestational diabetes). The 2 reviews found that there was limited evidence in women with gestational diabetes, and little difference in outcomes between tight-moderate and tight glucose control in women with type 1 diabetes, but that loose control (fasting plasma glucose above 7mmol/L) was associated with greater adverse pregnancy outcomes, such as caesarean section, pre-eclampsia, and large birth weight in women with type 1 diabetes.

HbA1c testing in 2nd or 3rd trimester

Six studies focussed on the utility of HbA1c testing during the 2nd and 3rd trimester of pregnancy on adverse pregnancy outcomes.

Four studies (a post-hoc analysis of an RCT (25) in 91 women; a cohort study (26) in 301 women; a cohort study (27) in 1,989 women; and a cohort study (28) in 272 women) found that elevated HbA1c levels in the 3rd trimester is a significant predictor of poor late pregnancy outcomes.

One prospective trial (29) (n=725 women) found that elevated 2nd and 3rd trimester HbA1c levels were significantly associated with increased risks of large for gestational age, preterm delivery, pre-eclampsia, and need for neonatal glucose infusion.

One cohort study (30) (n=1,959 women) found that elevated 2nd trimester HbA1c levels were significantly associated with increased risks of preterm delivery, neonatal hyperbilirubinemia, and neonatal asphyxia.

Effective and safe forms of insulin

There were 14 publications relating to 10 studies: 4 studies which focussed on the effectiveness and safety of different types of insulin, and 6 studies which focussed on insulin pumps for diabetes in pregnancy.

Insulin pumps (n=6)

One Cochrane review (n=5 RCTs including 153 women) (31) focussed on insulin pumps versus multiple daily insulin injections. There was insufficient evidence from the studies to determine the effectiveness and safety of insulin pumps.

Two systematic reviews focussed on the effectiveness and safety of insulin pumps versus multiple daily injections. One review (32) (n=7 cohort studies; number of women not reported) found no difference between subcutaneous insulin pumps and multiple daily injections in pregnant women with type 1

diabetes, although the evidence base was deemed insufficient. One review (33) (n=38 studies including 4,499 pregnancies) found an increase in large for gestational age, macrosomia births and spontaneous abortions (deemed possibly due to reporting bias) in women with type 1 diabetes on insulin pumps compared with multiple daily injections. There was no increase in other fetal complications.

Two studies reporting on 1 RCT focussed on the use of closed loop automated insulin delivery versus sensor augmented insulin pumps (n=16 pregnant women with type 1 diabetes). One report of the RCT (34) found that overnight closed-loop therapy resulted in significantly better glucose control than sensor-augmented pump therapy. One report of the RCT (35) focussed on the qualitative experience of women receiving closed loop automated insulin and found that women slightly overestimated their glycaemic response.

One RCT (36) (n=90 women) found insulin pumps provided more precise control of glucose in pregnant women with gestational diabetes, compared with multiple daily injections, though no neonatal outcomes were presented.

Types of insulin (n=5)

One Cochrane review (n=53 studies including 7,381 women) (37) focussed on insulin versus other forms of insulin, oral diabetic agents and non-pharmacological treatments for the treatment of women with diabetes. There was insufficient evidence to determine the relative effectiveness and safety of different forms of insulin.

One review (38) (n=5 trials including 554 women) found no evidence of adverse pregnancy outcomes in pregnant women with type 1 or 2 diabetes with any insulin analogues, although the evidence base was limited.

Two systematic reviews focussed on the effectiveness and safety of different insulin types. One review (39) (n=29 studies; number

of women not reported) found no evidence of increased congenital anomalies in pregnant women with diabetes with insulin analogues (lispro, aspart, glargine, detemir) compared with human insulin, although the included studies were insufficiently powered to detect differences. One review (40) (n=24 studies including 3,734 women) found no evidence of adverse pregnancy outcomes in pregnant women with diabetes treated with aspart, glargine, or detemir compared with regular insulin, although lispro was associated with increased birth weight.

Four studies reporting on 1 RCT (41–44) (n=87 women) found that insulin detemir is non-inferior to insulin Neutral Protamine Hagedorn (NPH) for women with gestational diabetes and type 2 diabetes.

Continuous glucose monitoring

Ten studies were identified which focussed on the effectiveness of continuous glucose monitoring (CGM): 2 Cochrane reviews (1 focussing on gestational diabetes and 1 of pre-existing diabetes), 1 systematic review and 7 RCTs.

The recently published CONCEPTT trial (5) (n=325 women; 215 pregnant and 110 planning pregnancy with type 1 diabetes) found improvements in a range of neonatal outcomes with CGM plus standard care, compared with standard care alone, including neonatal intensive care admission, large for gestational age and neonatal hypoglycaemia for pregnant women. There were no clear benefits for women planning pregnancy but the authors noted that many women may be uncomfortable changing monitoring modality during early pregnancy, thus starting pre-pregnancy may be of benefit.

The most recent systematic review (45), included 3 RCTs in women with type 1 diabetes. Of the 3 included RCTs(46)(47)(5), 1 found no effects of CGM and 2 RCTs found CGM was associated with improved glycaemic control and neonatal outcomes, compared with

standard care. This review included the CONCEPTT trial. (5)

Both of the Cochrane reviews (48,49)) looked at the broader question of setting for glucose monitoring, and each of the reviews included only 2 studies of CGM. The Cochrane reviews did not find any evidence of a benefit of CGM, but both were limited by data and neither review included the recent CONCEPTT trial. (5)

One RCT (50) of a retrospective CGM (6-day sensor) at 28, 32 or 36 weeks' gestation, compared with standard care (n=50 women), found improvements in HbA1c levels without increasing hypoglycaemia.

One trial (51) of a single application of real time continuous glucose monitoring as an educational tool in pregnant women shortly after diagnosis of gestational diabetes (n=130 women) was not associated with improvements in glycaemic control or pregnancy outcomes.

One trial (52) of intermittent use of continuous glucose monitoring for 5-7 days every 6 weeks in pregnant women with type 1 or type 2 diabetes requiring insulin (n=304 women) did not decrease the risk of large for gestational age or glycaemic control.

One trial (53) of continuous glucose monitoring in women with gestational diabetes who required insulin (n=24 women) was associated with significantly improved glycaemic control, compared to finger stick glucose alone. However, CGM was also associated with a significant increase in insulin usage and an increase in hypoglycaemic events.

Organisation of antenatal care

One Cochrane review (54) (n=0 studies) found that there was no published trial evidence to address the issue of whether women should be encouraged to express breast milk in the antenatal period.

Topic expert feedback and additional information

A topic expert indicated that HbA1c might have clinical utility in the second and third trimester of pregnancy (recommendation 1.3.11) and provided evidence, which has been incorporated into the surveillance summary of new evidence above.

Several topic experts suggested that there might be new evidence on different forms of insulin and insulin pumps and provided evidence (recommendation 1.3.12 and 1.3.16), which has been incorporated into the surveillance summary of new evidence above.

One expert stated that there is a need to check for ketones if the pump is blocked or detached as there is a risk high of ketosis if the insulin supply is interrupted (recommendation 1.3.20).

Several topic experts suggested that there might be new evidence on continuous glucose monitoring and provided evidence (recommendation 1.3.17), which has been incorporated into the surveillance summary of new evidence above.

One expert stated that aspirin is advised for preventing pre-eclampsia in pre-existing diabetes. NG3 recommendation 1.3.29 cross-refers to NICE guideline CG107 Hypertension in pregnancy, which advises women at risk of pre-eclampsia to take aspirin daily.

One expert queried the frequency of ultrasound monitoring for fetal growth (recommendation 1.3.31). However, no evidence was identified to indicate the recommendation should be changed.

One expert indicated that the Joint British Diabetes Societies guideline recommends that all patients be admitted for intravenous insulin support (VBII) rather than subcutaneous insulin with increased dose. However the guideline indicated that management of labour in diabetes varies across hospitals. This is unlikely to change recommendation 1.3.38 as this recommendation only states to 'monitor closely' and does not specify the setting.

A NICE medical innovation briefing was also identified as being of relevance: [Health app: GDm-Health for people with gestational diabetes](#) (November 2017) MIB131. This briefing found that the app may be cost saving (reduced clinic visits) and improve patient satisfaction (more convenient) in women with gestational diabetes although the evidence base was limited.

Impact statement

The 2018 surveillance process identified new evidence that relates to several recommendations.

There was new evidence from 2 Cochrane reviews for target blood glucose levels (recommendation 1.3.5), which indicated that fasting blood glucose levels above 7mmol/L may be associated with increased pregnancy risks in women with gestational diabetes (no evidence for pre-existing diabetes). This is in line with the guideline recommendation to aim for fasting blood glucose of 5.3 mmol/L. As such, it is not recommended to update recommendation 1.3.5 at this time point.

There was new evidence that HbA1c testing could be of clinical value in the 2nd and 3rd trimester of pregnancy for identifying increased infant morbidity, pre-term delivery and macrosomia. This supports recommendation 1.3.8 which suggests to consider measuring HbA1c in the 2nd and 3rd trimester of pregnancy to assess risk.

There was new evidence that different forms of insulin (aspart, lispro, detemir, glargine) are not associated with adverse pregnancy outcomes, compared with standard insulin, although lispro may be associated with increased birth weight. This does not contradict recommendation 1.3.12, which suggests that rapid acting insulin analogues may be of use in pregnancy.

There was new evidence on insulin pumps, which showed mixed effects. Some studies

indicated it provided better glucose control but some studies found that pumps do not offer any advantages over multiple daily injections. One expert also highlighted that there is a need to check for ketones if the pump is blocked or detached. This evidence is potentially immature, and is not specifically from women who cannot manage their glucose levels with multiple daily injections without disabling hypoglycaemia. As such, it is unlikely to alter the current recommendation 1.3.16 to offer women with insulin-treated diabetes continuous subcutaneous insulin infusion during pregnancy if adequate blood glucose control is not obtained by multiple daily injections of insulin without significant disabling hypoglycaemia.

There was new evidence on continuous glucose monitoring in pregnant women with type 1 diabetes. The recent CONCEPTT trial indicates improved neonatal outcomes with continuous glucose monitoring and advocates routine usage in pregnant women with type 1 diabetes. This could potentially alter recommendation 1.3.17, which currently advises do not offer continuous glucose monitoring routinely to pregnant women with diabetes.

There was stakeholder feedback which indicated that there is a problem with the interpretation of recommendations around retinal assessment during pregnancy, which causes unnecessary retinal screening. An amendment to the guideline is needed to clarify that if a women with pre-existing diabetes presents for retinal assessment at 13-16 weeks without a screen in the last 3 months and background retinopathy is present (R1), the 16-20 week screen is not required and the woman can be screened again at 28 weeks.

New evidence was identified that may change guideline recommendations.

1.4 Intrapartum care

Timing and mode of birth

- 1.4.1 Discuss the timing and mode of birth with pregnant women with diabetes during antenatal appointments, especially during the third trimester. [new 2015]
- 1.4.2 Advise pregnant women with type 1 or type 2 diabetes and no other complications to have an elective birth by induction of labour, or by elective caesarean section if indicated, between 37+0 weeks and 38+6 weeks of pregnancy. [new 2015]
- 1.4.3 Consider elective birth before 37+0 weeks for women with type 1 or type 2 diabetes if there are metabolic or any other maternal or fetal complications. [new 2015]
- 1.4.4 Advise women with gestational diabetes to give birth no later than 40+6 weeks, and offer elective birth (by induction of labour, or by caesarean section if indicated) to women who have not given birth by this time. [new 2015]
- 1.4.5 Consider elective birth before 40+6 weeks for women with gestational diabetes if there are maternal or fetal complications. [new 2015]
- 1.4.6 Diabetes should not in itself be considered a contraindication to attempting vaginal birth after a previous caesarean section. [2008]
- 1.4.7 Explain to pregnant women with diabetes who have an ultrasound-diagnosed macrosomic foetus about the risks and benefits of vaginal birth, induction of labour and caesarean section. [2008]

Anaesthesia

- 1.4.8 Offer women with diabetes and comorbidities such as obesity or autonomic neuropathy an anaesthetic assessment in the third trimester of pregnancy. [2008]
- 1.4.9 If general anaesthesia is used for the birth in women with diabetes, monitor blood glucose every 30 minutes from induction of general anaesthesia until after the baby is born and the woman is fully conscious. [2008]

Blood glucose control during labour and birth

- 1.4.10 Monitor capillary plasma glucose every hour during labour and birth in women with diabetes, and ensure that it is maintained between 4 and 7 mmol/litre. [2008, amended 2015]
- 1.4.11 Intravenous dextrose and insulin infusion should be considered for women with type 1 diabetes from the onset of established labour. [2008]
- 1.4.12 Use intravenous dextrose and insulin infusion during labour and birth for women with diabetes whose capillary plasma glucose is not maintained between 4 and 7 mmol/litre. [2008, amended 2015]

Surveillance decision

No new information was identified at any surveillance review. These recommendations should not be updated.

1.5 Neonatal care

Initial assessment and criteria for admission to intensive or special care

- 1.5.1** Advise women with diabetes to give birth in hospitals where advanced neonatal resuscitation skills are available 24 hours a day. [2008]
- 1.5.2** Babies of women with diabetes should stay with their mothers unless there is a clinical complication or there are abnormal clinical signs that warrant admission for intensive or special care. [2008]
- 1.5.3** Carry out blood glucose testing routinely in babies of women with diabetes at 2–4 hours after birth. Carry out blood tests for polycythaemia, hyperbilirubinaemia, hypocalcaemia and hypomagnesaemia for babies with clinical signs. [2008]
- 1.5.4** Perform an echocardiogram for babies of women with diabetes if they show clinical signs associated with congenital heart disease or cardiomyopathy, including heart murmur. The timing of the examination will depend on the clinical circumstances. [2008]
- 1.5.5** Admit babies of women with diabetes to the neonatal unit if they have:
- hypoglycaemia associated with abnormal clinical signs
 - respiratory distress
 - signs of cardiac decompensation from congenital heart disease or cardiomyopathy
 - signs of neonatal encephalopathy
 - signs of polycythaemia and are likely to need partial exchange transfusion
 - need for intravenous fluids
 - need for tube feeding (unless adequate support is available on the postnatal ward)
 - jaundice requiring intense phototherapy and frequent monitoring of bilirubinaemia
 - been born before 34 weeks (or between 34 and 36 weeks if dictated clinically by the initial assessment of the baby and feeding on the labour ward). [2008]
- 1.5.6** Do not transfer babies of women with diabetes to community care until they are at least 24 hours old, and not before you are satisfied that the baby is maintaining blood glucose levels and is feeding well. [2008]

Preventing and assessing neonatal hypoglycaemia

- 1.5.7** All maternity units should have a written policy for the prevention, detection and management of hypoglycaemia in babies of women with diabetes. [2008]
- 1.5.8** Test the blood glucose of babies of women with diabetes using a quality-assured method validated for neonatal use (ward-based glucose electrode or laboratory analysis). [2008]
- 1.5.9** Women with diabetes should feed their babies as soon as possible after birth (within 30 minutes) and then at frequent intervals (every 2–3 hours) until feeding maintains pre-feed capillary plasma glucose levels at a minimum of 2.0 mmol/litre. [2008, amended 2015]
- 1.5.10** If capillary plasma glucose values are below 2.0 mmol/litre on 2 consecutive readings despite maximal support for feeding, if there are abnormal clinical signs or if the baby will not feed orally effectively, use additional measures such as tube feeding or intravenous dextrose. Only implement additional measures if one or more of these criteria are met. [2008, amended 2015]

1.5.11 Test blood glucose levels in babies of women with diabetes who present with clinical signs of hypoglycaemia, and treat those who are hypoglycaemic with intravenous dextrose as soon as possible. [2008, amended 2015]

Surveillance decision

No new information was identified at any surveillance review. These recommendations should not be updated.

1.6 Postnatal care

Blood glucose control, medicines and breastfeeding

- 1.6.1 Women with insulin-treated pre-existing diabetes should reduce their insulin immediately after birth and monitor their blood glucose levels carefully to establish the appropriate dose. [2008]
- 1.6.2 Explain to women with insulin-treated pre-existing diabetes that they are at increased risk of hypoglycaemia in the postnatal period, especially when breastfeeding, and advise them to have a meal or snack available before or during feeds. [2008]
- 1.6.3 Women who have been diagnosed with gestational diabetes should discontinue blood glucose-lowering therapy immediately after birth. [2008]
- 1.6.4 Women with pre-existing type 2 diabetes who are breastfeeding can resume or continue to take metformin[2] and glibenclamide[4] immediately after birth, but should avoid other oral blood glucose-lowering agents while breastfeeding. [2008]
- 1.6.5 Women with diabetes who are breastfeeding should continue to avoid any medicines for the treatment of diabetes complications that were discontinued for safety reasons in the preconception period. [2008]

Information and follow-up after birth

Women with pre-existing diabetes

- 1.6.6 Refer women with pre-existing diabetes back to their routine diabetes care arrangements. [2008]
- 1.6.7 Remind women with diabetes of the importance of contraception and the need for preconception care when planning future pregnancies. [2008]

Women diagnosed with gestational diabetes

- 1.6.8 Test blood glucose in women who were diagnosed with gestational diabetes to exclude persisting hyperglycaemia before they are transferred to community care. [2008]
- 1.6.9 Remind women who were diagnosed with gestational diabetes of the symptoms of hyperglycaemia. [2008]
- 1.6.10 Explain to women who were diagnosed with gestational diabetes about the risks of gestational diabetes in future pregnancies, and offer them testing for diabetes[7] when planning future pregnancies. [2008, amended 2015]
- 1.6.11 For women who were diagnosed with gestational diabetes and whose blood glucose levels returned to normal after the birth:
 - Offer lifestyle advice (including weight control, diet and exercise).
 - Offer a fasting plasma glucose test 6–13 weeks after the birth to exclude diabetes (for practical reasons this might take place at the 6-week postnatal check).
 - If a fasting plasma glucose test has not been performed by 13 weeks, offer a fasting plasma glucose test, or an HbA1c test if a fasting plasma glucose test is not possible, after 13 weeks.
 - Do not routinely offer a 75 g 2-hour OGTT. [new 2015]
- 1.6.12 For women having a fasting plasma glucose test as the postnatal test:

- Advise women with a fasting plasma glucose level below 6.0 mmol/litre that:
 - they have a low probability of having diabetes at present
 - they should continue to follow the lifestyle advice (including weight control, diet and exercise) given after the birth
 - they will need an annual test to check that their blood glucose levels are normal
 - they have a moderate risk of developing type 2 diabetes, and offer them advice and guidance in line with the NICE guideline on preventing type 2 diabetes[8].
- Advise women with a fasting plasma glucose level between 6.0 and 6.9 mmol/litre that they are at high risk of developing type 2 diabetes, and offer them advice, guidance and interventions in line with the NICE guideline on preventing type 2 diabetes[8]
- Advise women with a fasting plasma glucose level of 7.0 mmol/litre or above that they are likely to have type 2 diabetes, and offer them a diagnostic test to confirm diabetes. [new 2015]

1.6.13 For women having an HbA1c test as the postnatal test:

- Advise women with an HbA1c level below 39 mmol/mol (5.7%) that:
 - they have a low probability of having diabetes at present
 - they should continue to follow the lifestyle advice (including weight control, diet and exercise) given after the birth
 - they will need an annual test to check that their blood glucose levels are normal
 - they have a moderate risk of developing type 2 diabetes, and offer them advice and guidance in line with the NICE guideline on preventing type 2 diabetes[8].
- Advise women with an HbA1c level between 39 and 47 mmol/mol (5.7% and 6.4%) that they are at high risk of developing type 2 diabetes, and offer them advice, guidance and interventions in line with the NICE guideline on preventing type 2 diabetes[8].
- Advise women with an HbA1c level of 48 mmol/mol (6.5%) or above that they have type 2 diabetes and refer them for further care. [new 2015]

1.6.14 Offer an annual HbA1c test to women who were diagnosed with gestational diabetes who have a negative postnatal test for diabetes. [new 2015]

1.6.15 Offer women who were diagnosed with gestational diabetes early self-monitoring of blood glucose or an OGTT in future pregnancies. Offer a subsequent OGTT if the first OGTT results in early pregnancy are normal (see [recommendation 1.2.6](#)). [2008, amended 2015]

Footnotes

[2] Although metformin is commonly used in UK clinical practice in the management of diabetes in pregnancy and lactation, and there is strong evidence for its effectiveness and safety (presented in the full version of the guideline), at the time of publication (February 2015) metformin did not have a UK

marketing authorisation for this indication. The summary of product characteristics advises that when a patient plans to become pregnant and during pregnancy, diabetes should not be treated with metformin but insulin should be used to maintain blood glucose levels. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4] At the time of publication (February 2015) glibenclamide was contraindicated for use up to gestational week 11 and did not have UK marketing authorisation for use during the second and third trimesters of pregnancy in women with gestational diabetes. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[7] See Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation (2011).

[8] Note that the threshold for defining a moderate risk of developing type 2 diabetes postnatally for women who have had gestational diabetes is different from that given in NICE guideline on preventing type 2 diabetes, because of the different populations.

Surveillance decision

These recommendations should not be updated. An amendment to footnote 8 is needed for clarification of risk. Suggested footnote: [8] Note that the threshold for defining a moderate and high risk of developing type 2 diabetes postnatally for women who have had gestational diabetes is different from that given in the NICE guideline on [preventing type 2 diabetes](#), because of the different populations

Postnatal care

Previous surveillance

This guideline has never had a surveillance review undertaken as it is an update of a previous guideline (CG63). However, CG63, was the subject of a surveillance review in 2011 which resulted in the guideline being updated to form NG3. This section of the guideline had 6/15 recommendations updated or amended 2015.

2018 surveillance summary

Two Cochrane reviews were identified that focussed on the post-natal period. One review (55) (n=1 trial including 256 women) assessed

whether reminder systems increase the uptake of testing for type 2 diabetes or impaired glucose tolerance in women with a history of gestational diabetes. The review found a significant increase in uptake of testing following postal reminders, but was limited by the lack of evidence for other reminder systems.

One review aimed to assess the effects of interconception care (care provided to women between pregnancies) in women with a history of gestational diabetes (56) (n=1 trial including 256 women) but found no published RCTs that addressed this issue.

Topic expert feedback and additional information

One topic expert indicated that the oral glucose tolerance test (OGTT) may have value in the post-natal period; however, there was no published data provided to support this.

Impact statement

New evidence for the 2018 surveillance review was identified from 2 new Cochrane reviews, however both reviews were limited by a lack of good quality studies. Feedback from topic experts indicated that OGTT may be of value in the post-natal period but there was no published data provided to support this. Given this lack of new evidence, it is not recommended to update this section of the guideline at this time point.

New evidence is unlikely to change recommendations.

Research recommendations

Research recommendations considered in surveillance

Preconception care

1. What is the efficacy (measured by pregnancy rate) of oral oestrogen-containing contraceptives in women with diabetes compared with women without diabetes
2. What is the efficacy (measured by pregnancy rate) of oral progestogen-containing contraceptives in women with diabetes compared with women without diabetes?
3. What are the long term effects of oral contraceptives in women with diabetes on glycaemic control and hypoglycaemic therapy (e.g. insulin dose? (epidemiological study)
4. What is the difference in pregnancy outcome in women who have attended pre-conception care and those that have not?
5. What is the relationship between pre-pregnancy glucose control and ketonaemia and the risk of miscarriage?
6. Achieving glycaemic targets pre-pregnancy – what can be done to help women achieve the best possible glycaemic control?
7. Achieving glycaemic targets pre-pregnancy – what are the barriers?
8. Achieving glycaemic targets pre-pregnancy – what is the role of the health care professional?
9. Achieving glycaemic targets pre-pregnancy – what is the role of telemedicine?
10. What are the roles of insulin pump therapy (continuous subcutaneous insulin infusion) and continuous glucose monitoring in helping women achieve glucose targets pre pregnancy?
11. What is the long term impact for children born to women with different degrees of preconception glycaemic control?
12. What is the experience for women with type 1 and type 2 diabetes going through preconception and pregnancy?
13. What is the most clinically and cost-effective form of preconception care and advice for women with diabetes? [2008]

Summary of findings

No new evidence relevant to these research recommendations was found and no ongoing studies were identified.

Surveillance decision

These research recommendations will be considered again at the next surveillance point.

Gestational diabetes

14. What is the incidence in both unselected and high risk populations of previously undetected type 2 diabetes and gestational diabetes in the first trimester of pregnancy and the relationship to adverse pregnancy outcomes?
15. When should testing for gestational diabetes take place – in the first or second trimester?
16. What is the optimum dietary and exercise strategy for the initial management of women diagnosed with gestational diabetes?
17. What is the positive predictive value of one or more positive urine tests for glucose in the first trimester for a diagnosis of gestational diabetes?
18. Do women with gestational diabetes achieving good glucose control with diet, exercise and metformin need to have blood glucose tested as frequently as women taking insulin?

Summary of findings

There were 4 reviews of lifestyle, diet or exercise programmes for gestational diabetes, which found insufficient evidence to be able to determine the optimal dietary and exercise interventions for women diagnosed with gestational diabetes (see the surveillance summary for section 1.2 above for more details).

Surveillance decision

These research recommendations will be considered again at the next surveillance point.

Antenatal care

19. Post-meal blood glucose testing in women with diabetes in pregnancy: is the 1 hour test more acceptable than the 2 hour test?
20. What is the optimum frequency of blood glucose testing in pregnancy in women with pre-existing diabetes who are not taking insulin?
21. What is the value of ketone testing in pregnancy in women with type 2 diabetes or GDM?
22. What is the role of CGM in helping women achieve blood glucose targets in pregnancy?
23. What is the role of telemedicine in helping women achieve blood glucose targets in pregnancy?
24. What sequence and/or combinations of therapies best enable women to achieve blood glucose targets?
25. What are the barriers that women experience to achieving blood glucose targets?
26. What are the normal ranges for HbA1c in non-diabetic pregnancy?
27. Which is the optimum timing of the post-prandial blood glucose test in pregnancy – 1, 1.5 or 2 hours?
28. What are the barriers to testing blood glucose frequently in pregnancy?
29. Are other glycosylated molecules better than HbA1c at summarising blood glucose control in pregnancy?

30. Do new-generation CSII pumps offer an advantage over traditional intermittent insulin injections in terms of pregnancy outcomes in women with type 1 diabetes? [2008]
31. What is the role of continuous glucose monitoring in women with type 1 and 2 diabetes in preparation for pregnancy?
32. How should continuous glucose monitoring be used in women during pregnancy with type 1 and 2 diabetes who have recurrent severe hypoglycaemia or hypoglycaemia unawareness?
33. Is continuous glucose monitoring acceptable to women to manage diabetes in pregnancy compared to conventional care?
34. Should retinal assessment during pregnancy be offered to women diagnosed with gestational diabetes who are suspected of having pre-existing diabetes?
35. Does identification of microalbuminuria during pregnancy offer the opportunity for appropriate pharmacological treatment to prevent progression to pre-eclampsia in women with pre-existing diabetes?
36. How reliable is first-trimester screening for Down's syndrome incorporating levels of pregnancy-associated plasma protein (PAPP-A) in women with pre-existing diabetes?
37. How effective is transvaginal ultrasound for the detection of congenital malformations in women with diabetes and coexisting obesity?
38. How can the fetus at risk of intrauterine death be identified in women with diabetes?

Summary of findings

There is new evidence that different forms of insulin (aspart, lispro, detemir, glargine) are not associated with adverse pregnancy outcomes, compared with standard insulin. There is new evidence that insulin pumps do not offer any advantages over multiple daily injections and may be associated with increased fetal complications, such as large for gestational age, although the evidence base is limited and potentially still immature. There is also new evidence on continuous glucose monitoring in pregnant women with type 1 diabetes, although the evidence is mixed with some studies showing improved neonatal outcomes compared with standard care, and some studies showing no benefits. None of the evidence is likely to change current recommendations.

Surveillance decision

These research recommendations will be considered again at the next surveillance point.

Intrapartum care

39. What is the relationship between timing of elective delivery in women with diabetes and the outcome in the baby?
40. What is the optimum gestation for delivering women with uncomplicated gestational diabetes?
41. What are the risks and benefits associated with analgesia and anaesthesia in women with diabetes?
42. What is the optimal method for controlling glycaemia during labour and birth?

Summary of findings

No new evidence relevant to these research recommendations was found and no ongoing studies were identified.

Surveillance decision

These research recommendations will be considered again at the next surveillance point.

Neonatal care

43. Is systematic banking of colostrum antenatally of any benefit in pregnancies complicated by diabetes?

Summary of findings

One Cochrane review (54) found that there was no published trial evidence to address the issue of whether women should be encouraged to express breast milk antenatally.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

Postnatal care

44. What is the efficacy of HbA1c as a diagnostic test for detecting impaired glucose tolerance in the postnatal period?

45. What is the optimal timing of an HbA1c test for detecting diabetes and/or glucose intolerance in the postnatal period?

46. What is the best test for detecting impaired glucose intolerance in the immediate postpartum period?

47. Why women do not engage with postnatal glucose tolerance testing? Surveillance of uptake in the postnatal test for diabetes

48. Does the diagnosis of IGT influence the uptake of life style changes after birth in a woman with previous GDM?

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

Summary of findings

No new evidence relevant to these research recommendations was found and no ongoing studies were identified.

Surveillance decision

These research recommendations will be considered again at the next surveillance point.

Editorial and factual corrections identified during surveillance

During the surveillance process the following editorial or factual corrections were identified:

An editorial amendment to add a footnote at the end of 1.1.10 to clarify BMI in different ethnic groups. Suggested wording: The BMI cut-off should consider the variation in risk for different ethnic groups, see the [NICE guideline on BMI \(PH46\)](#).

An amendment to recommendation 1.1.11 to clarify that a prescription is needed for 5mg folic acid, to reduce the risks of women inadvertently using a lower dose over-the-counter formulation.

An editorial amendment to add a footnote to the end of bullet point 1 of recommendation 1.2.11 is needed to provide a link to the DVLA guidance on diabetes and driving. Suggested footnote: Advice for women on driving with diabetes is available from the [DVLA website](#).

An editorial amendment to footnote 4. The amended footnote will be: [4] At the time of surveillance review (April 2018) the UK marketing authorisation for glibenclamide varied between different brands with regards to use in pregnancy. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

An amendment to the recommendations on retinal screening, section 1.3, to add a caveat to reduce unnecessary retinal screening.

An amendment to footnote 8. The amended footnote will be: [8] Note that the threshold for defining a moderate and high risk of developing type 2 diabetes postnatally for women who have had gestational diabetes is different from that given in the NICE guideline on preventing type 2 diabetes, because of the different populations.

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