National Institute for Health and Care Excellence

Diabetes in pregnancy (update)
Guideline Consultation Table
11 September 2014 – 23 October 2014

Stakeholder	Order	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
Abbott Diabetes Care	1	Full	General	General	Abbott Diabetes Care supports the update to the NICE diabetes in pregnancy guideline and the response to the comments from the scope noting their incorporation into the draft guideline.	Thank you for your comment.
Abbott Diabetes Care	2	Full	2.2	80	We would support recommendation 15 on blood ketone testing as the evidence supports this as in improved clinical measure. We also support this in recommendation 60 which repeats this advice.	Thank you for your comment.
Abbott Diabetes Care	3	Full	2.2	80	We would reference section 2 regarding the target glucose levels and to ensure that these allow recommendation 18 that HbA1C target of less than 6.5% to be achieved.	Thank you for your comment. The GDG agree that if women achieve the target glucose values in recommendation 17 it is likely that the HbA1c levels recommended in recommendation 18 will be achieved. As there was no direct evidence of this, it was felt better to have two separate adjacent recommendations.
Abbott Diabetes Care	4	Full	2.2	84	Recommendation 57. We support this recommendation on the increased focus on glucose levels during pregnancy to achieve better outcomes.	Thank you for your comment
Aintree University Hospital NHS Foundation Trust	2	Full	4.2 & 4.3	General	Is it possible to clarify acceptable forms of the 75g OGTT? I am aware that some services use point of care testing meters, rather than a laboratory venous blood glucose to diagnose GDM. From looking at most of the references in this section, they also use laboratory venous blood glucose samples however I can find no recommendation about the acceptability of point of care meters. Is it possible for NICE to add	Thank you for your comment. Blood glucose meters have an adjustment built into the design so that the capillary glucose value is converted to the equivalent plasma glucose value. Thus, it does not matter whether the OGTT is undertaken with laboratory assessment of plasma glucose using venous blood or a meter assessment using capillary blood sample.

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					some guidance?	
Aintree University Hospital NHS Foundation Trust	3	Full	4.5.10	General	From the full guidance there is no recommendation with regards to the rapidity at which a woman diagnosed with GDM needs to be seen and educated. This has a great impact on managing GDM and also on the resources a service needs. Is it possible for NICE to consider recommending a timeframe of how soon a patient needs to be seen after a positive OGTT?	Thank you for your comment. There was unanimous agreement in the GDG that once the diagnosis of gestational diabetes had been made, then referral to specialist care and treatment should be prompt. An amendment was made to the full guideline (section 4.4.8.5) and a new recommendation based on current clinical practice timeframes was included stating that women with a diagnosis of gestational diabetes should be offered a review with the joint diabetes and antenatal clinic within 1 week.
Aintree University Hospital NHS Foundation Trust	1	Full	2.2	4 General	Page 79 (also figure 2a P95) Is it possible to consider stating a recommended age to initiate discussions about pregnancy and/or contraception with adolescents who have diabetes. I am worried that 'adolescence' is not specific enough, and trying to ensure that it is done will be hampered.	Thank you for your comments. However, the GDG were aware that puberty and sexual activity start at different ages. Thus, the GDG felt that 'adolescence' was as specific as they could be.
Association of Anaesthetists of Great Britain and Ireland (AAGBI)	1	Full	General	General	No information particularly relevant to anaesthesia , no comments.	Thank you for your comment
BIRMINGHAM WOMEN'S HOSPITAL	1	Full	2.1.2	75	The HAPO thresholds are 5.1 fasting and 8.5 and above at 2 hours.	Thank you for this comment. However, the values you quote are the IADPSG diagnostic criteria. The target values for glucose control recommended in the guideline for fasting, 1 hour and 2 hours are each based on evidence (see Section 5.2 of the Full Guideline).
BIRMINGHA	2	Full	2.1.3	75	What is the evidence for dropping the fasting	Thank you for your comments. The target

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M WOMEN'S HOSPITAL					threshold for blood glucose to a maximum of 5.3 mmol/l? This level is lower than the diagnostic level for the OGTT in the draft guidance but also higher than the HAPO diagnostic threshold for fasting blood glucose.	values for glucose control recommended in the guideline for fasting, 1 hour and 2 hours are each based on evidence (see Section 5.2 of the Full Guideline).
BIRMINGHAM WOMEN'S HOSPITAL	3	Full	2.2.36	82	Need to further define "minority ethnic family origin with a high prevalence of diabetes." for screening as this is unclear which women will be included. Also no mention of cut off for gestation for screening, what evidence is there for doing GTT at 36 weeks gestation or should we be screening women at all gestations and what is the sensitivity for GTT at late gestations?	Thank you for your comment. The text of this recommendation was only amended in the 2015 update of the guideline to broaden the bullet point specifying particular family origins with a high prevalence of diabetes as a risk factor. The phrase 'minority ethnic family origin with high prevalence of diabetes' was agreed given the importance of not overlooking risk factor assessment in women in groups other than those that were listed previously. The phrasing was deliberately not made more explicit because the list would never be comprehensive. Regarding the issue of making different recommendations for different gestation, again this was not possible as this topic was not reviewed for the update.
BIRMINGHAM WOMEN'S HOSPITAL	4	Full	2.2.55	84	Use of Glibenclamide.	Thank you for your comment. Unfortunately we are not clear what change you would like us to make
BIRMINGHAM WOMEN'S HOSPITAL	5	Full	2.2.60 -62	84	Risk of ketoacidosis in ALL women with diabetes in pregnancy, does that really need to include women with GDM, particularly if they have a HbA1c at time of diagnosis to exclude undiagnosed Type 2 diabetes	Thank you for your comment. Amendments to this recommendation and the next recommendation (now recommendations 63 and 64) were made in line with your comment following consultation. Recommendation 63 restricts use of blood ketone testing strips and meters for ketonaemia testing to pregnant women with type 1 diabetes. In recommendation 64,

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						pregnant women with type 2 diabetes or gestational diabetes are advised to seek urgent medical advice if they become hyperglycaemic or unwell, but home testing for ketonaemia is not recommended for these groups of women. The final recommendation (65) is that women with any form of diabetes who is hyperglycaemic or unwell should be tested for ketonaemia. .
BIRMINGHAM WOMEN'S HOSPITAL	6	Full	2.2.67	85	What is the evidence of undiagnosed type 2 DM in all women with gestational diabetes, what are the numbers needed to test with HbA1c to find 1 case of undiagnosed type 2. What are the cost implications at testing all women with gestational diabetes and how will it change their management in the pregnancy? Is that not the role of the postnatal testing in women with GDM?	Thank you for your comment. The use of HbA1c in pregnancy was not prioritised for health economic evaluation. Regarding the benefit of identifying women at increased risk of gestational diabetes, there are several possible interventions that would result if there was a strong suspicion that a woman had previously undiagnosed type 2 diabetes. These include undertaking retinal and renal screening once identified, greater attention to the results of blood glucose monitoring with a high chance of the need for pharmacological treatment and a different monitoring strategy after delivery.
BIRMINGHAM WOMEN'S HOSPITAL	7	Full	2.2.96 -99	87	The data used to change the gestation for birth is retrospective data with no evidence that perinatal mortality will be reduced by earlier birth. The reduction in gestation is likely to lead to increased rates of induction of labour, increased rates of failed induction of labour and increased operative births.	Thank you for your comment. We reconsidered the recommendation about timing of birth in response to stakeholder comments. We felt that the evidence justified making separate recommendations for the timing of birth for women with type 1 or type 2 diabetes and for women with gestational diabetes. For women with gestational diabetes, the

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						data from Rosenstein (2012) demonstrated that there was a significant rise in stillbirth rate after 40+6 days. Whereas the Kjos (1993) study showed that the incidence of babies weight more than 4000g rose after 39+6 days. Given that avoidance of stillbirth was the philosophy underpinning the timing of delivery, the GDG felt that in women with uncomplicated gestational diabetes elective delivery could be delayed until 40+6 days. For women with type 1 or type 2 diabetes the limited data demonstrated that the stillbirth rate rose after 38+6 weeks. Thus such women should be offered elective delivery by 38+6 weeks. We felt that a lower limit should be also included in the recommendation to avoid women with uncomplicated type 1 or type 2 diabetes being advised to have an elective preterm delivery with its associated complications for the woman (such as failed induction of labour and caesarean section) and the baby (such as respiratory distress syndrome and admission to the neonatal unit). The data from Holman (2014) suggested the lower limit of the elective delivery should be 37+0 weeks. Thus we recommended elective delivery for women with uncomplicated type 1 or type 2 diabetes between 37+0 and 38+6 weeks. In making this recommendation, we expect that, in practice, this would result in such women being routinely offered elective delivery nearer 38+6 weeks than 37+0 weeks.

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Central Manchester University Hospitals NHS Foundation Trust	1	Full	2.1.3 42 Table 120	75 82 667	a. One of the reasons for reviewing the guidelines was apparently because WHO 1999 was based on non-pregnant subjects and yet despite the physiological changes of pregnancy it is proposed to retain the figure of 7.8mmol/l? b The diagnostic cutpoints appear to be based totally on the health economic analysis. Women have a right to be informed that there is a continuum of risk associated with hyperglycaemia in pregnancy. While health economic criteria may be appropriate for offering guidance on treatment thresholds it is inappropriate and potentially misleading to apply them to diagnostic criteria. c. Does the cost benefit analysis allow for differing treatment needs across the diagnostic categories e.g. women diagnosed by WHO 2013 (IADPSG) are less likely to need insulin with its associated costs compared with those diagnosed by WHO 1999. d. Recommendation of different criteria by NICE to those in Scotland, Northern Ireland and many other countries globally which have already adopted WHO 2013 will make comparative data impossible and is a totally retrograde step. This fragmented approach will also limit national (across the UK) and international endeavours which aim to improve care and good practice across regions/countries. The WHO criteria have limitations, as was acknowledged in the document, but against the background of decades of controversy and disparate diagnostic cutpoints, for the first time they offer the possibility of a truly international consensus. e. In addition, as it is standard practice in the UK to adopt WHO criteria, deviation from this	Thank you for your detailed comments. We have responded to these in an alphabetised list below. Whilst these responses address the queries regarding the health economics analyses performed, clinical evidence reviews were also considered and recommendations were informed by both health economic and clinical evidence. a) The health economic analysis suggested that using a £30,000 cost per QALY willingness to pay that it may be cost-effective to treat women with a 2 hour OGTT blood glucose value ≥ 7.8mmol/l and <8.5 mmol/l. b) The health economic analysis is based on a logistic regression analysis of HAPO data from UK/Australia which allows for a continuum of risk associated with hyperglycaemia in pregnancy – with OGTT blood glucose values included as regression variables. Some commentators argue that the new IADPSG diagnostic criteria are arbitrary and therefore we do not accept in principle that it is misleading or inappropriate to use the trade-off between costs (which are benefits denied to other NHS patients) and benefits to determine optimal diagnostic thresholds. c) The stakeholder identifies a limitation of the model. The model does not account for differences in the requirement for insulin across different diagnostic categories primarily because we were not aware of

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					practice does not appear to have been justified within the guideline. f. It would appear that only one health economist was involved in the health economic analysis yet the clinical recommendations were considered after protracted deliberation by multiple clinicians. The health economic analysis is complex and has not been subject to external review, beyond the consultation process. It also is not in agreement with other recent studies (e.g. Duran, A., et al. Diabetes Care, 2014. 37(9): p. 2442-50). h. Whilst the statistical significance of the health economic analysis is given, no detail is provided as to the confidence intervals (margin of error) of any of the figures. For example, comparison the recommended figures of fasting 5.6 and 2h 7.8mmol/l with the WHO 2013 figures in Table 120, p 667 it is evident that there is little difference in some adverse outcomes such as shoulder dystocia e.g. WHO 2013 (41 cases) compared with WHO 1999 (40 cases) However some expensive outcomes which are likely to influence cost e.g. NICU admission and pre-eclampsia are different. Can one have absolute confidence in these numbers? i. A fasting value of 5.6mmol/l at the time of diagnosis is inconsistent with recommendation 2.1.3 (64) that women with gestational diabetes should aim for target fasting glucose levels below 5.3mmol/l. It is also inconsistent with what is known about the normal range for fasting glucose in pregnancy.	data linking OGTT blood glucose values at diagnosis to the proportion who subsequently achieve adequate control on diet. Diagnostic strategies which identify women with lower blood glucose values would be expected to have a higher proportion achieving satisfactory blood glucose levels on diet alone. However, where there is a trade-off between a higher two-hour OGTT blood glucose value and lower faster blood glucose value (as is the case when IADPSG diagnostic criteria are compared with WHO 1999 diagnostic criteria for example) then even the direction of the effect is difficult to predict. The model's results are not particularly sensitive to the proportion of women who require insulin as this only constitutes a relatively small part of the treatment cost (approximately 12%). The total cost of treatment in the model including the cost of hypoglycaemia is £1,026 based on 36% of women achieving satisfactory blood glucose levels on diet alone. If the proportion achieving satisfactory blood glucose on diet alone is increased to 50% then the treatment cost would fall by just £35 to £991. In the HAPO dataset 756 were diagnosed with gestational diabetes with 1999 WHO criteria and 1,168 were diagnosed with 3-point IADPSG (or WHO 2013) criteria. If it is assumed that all 756 diagnosed with gestational diabetes with 1999 WHO criteria would be diagnosed with the new WHO 2013 criteria and that this group have 36%

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						success on diet and if it is further assumed that the newly diagnosed or 'extra' 412 patients have 100% success on diet (a best case scenario for IADPSG criteria), even then the overall control on diet would only reach 58.8%. Treatment costs would still be £969, only £57 less than with the baseline assumption. If, for example, we then deduct £57 x 412 from the costs for IADPSG three-point test in Table 117, the ICER for three-point IADPSG relative to 1999 WHO criteria remains at over £44,000 per QALY. When this process is repeated but for the HAPO dataset with NICE risk factors the ICER for three-point IADPSG relative to 1999 WHO criteria is still £39,000 per QALY. Nevertheless, we do accept the point you make is valid and we shall add this point to the discussion of insulin treatment (Section 9.2.4.4 in the full guideline). d) We agree that it would be helpful if an international definition of gestational diabetes was agreed. Whilst the new IADPSG criteria are supported by many they are not universally accepted and remain controversial. Furthermore, it is widely accepted that IADPSG diagnostic criteria for gestational diabetes would increase the woman diagnosed with gestational diabetes and it is important in NICE guidelines that increased use of scarce NHS resources is supported by evidence that this would be cost-effective. We accept that the criteria recommended by this guideline differ from the new WHO

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						criteria. However, the GDG noted that the strength of the WHO recommendation was weak and that the WHO guideline suggests a rapid update of the criteria may be necessary in the light of new health economic evidence. e) The deviation from 2013 WHO criteria results from the health economic analysis presented and discussed in detail in this guideline suggesting that those criteria would not represent a cost effective use of NHS resources. We note that the WHO 2013 criteria have not been universally accepted which is also reflected in the comments we received from stakeholders for this guideline. f) The health economic model developed for this NICE guideline was developed in accordance with NICE methods. You are correct that this model has not been subject to external review (as distinct from consultation) but it was reviewed by NICE's technical team in the Centre for Clinical Practice. We are aware of the recently published Duran paper. This is an interesting paper but we believe it is methodologically flawed in certain respects over and above its limitations as a non-randomised before and after study (see below). To quote from the Cochrane Handbook, 'The results of uncontrolled studies (also called before-and-after studies without a control group) should be treated with caution. The absence of a comparison

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						group makes it impossible to know what would have happened without the intervention.' Below, we identify what we consider some of the important flaws in the Duran paper: It is important in health economic evaluation to include all relevant alternatives. This means comparing a more effective intervention with the next best alternative. If an intervention is compared to an intervention that isn't cost-effective then it may appear cost-effective relative to that when it would not be when compared against something else. Clearly, there are numerous alternative OGTT thresholds that could have been used but this paper considers only one as part of a one-step diagnostic process. It confuses a decision with respect to screening strategy with that of diagnostic threshold. So, for example, a better assessment of IADPSG criteria would involve a one-step screening strategy with IADPSG diagnostic thresholds against a one-step screening strategy with different diagnostic thresholds. Sequential screening strategies will generally miss more cases and this would also be the case also if two OGTT IADPSG positives were required for a diagnosis of gestational diabetes as against a single OGTT IADPSG positive for a diagnosis of gestational diabetes. It has been suggested that 40% of pregnant women who had a second OGTT shortly after an abnormal result had a normal result the second time (Neiger & Coustan, 1991).The paper does not quantify any inherent uncertainty around their estimates

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						of cost-effectiveness/costs. Most quality checklists for appraising cost-effectiveness analysis say that such uncertainty should be addressed. The differences in CS rates reported are very large and the saving from this reduction is greater than the total saving and hence can be considered to be a key driver of their finding/conclusion that IADPSG criteria saves costs (is cost-effective). The reduction in CS rates is far greater than that observed in the relevant trials and we doubt that the change in diagnostic criteria alone can explain the reduction. Our reasoning is as follows: The population can be split into three - assuming IADPSG picks up all those 'missed' by C-C (probably not 100% true but a reasonable approximation)Those picked up by C-C criteria (10.6%) Those not picked up by C-C or IADPSG (64.5%) Those only picked up by IADPSG (24.9%) – this plus those picked up by C-C criteria gives the 35.5% gestational diabetes rate the paper cites. The change to using IADPSG criteria can only explain changes in CS rates in Group 3 as Group 1 are treated anyway and Group 2 are never treated. If it changes in Groups 1 & 2 then there is something occurring that is unrelated to gestational diabetes .The CS rate in Group 1 we 'know' is 27.6% (51 cases of CS, 185 gestational diabetes; Table 2 Duran paper); The CS rate in Group 2 we 'know' is 18.5% (182 cases of CS, 984 NGT; Table 2 Duran paper) We know in time period 1 the overall CS rate is

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						25.9% (Table 2 Duran paper) Therefore the CS rate in Group 3 in period 1 has to be 55.1% - as the overall CS rate is a weighted average of the CS rate in all 3 groups We know in time period 2 the overall CS rate is 19.7% (Table 2 Duran paper) Therefore the CS rate in Group 3 in period 2 has to fall to 27.9% to give the overall CS rate, holding the CS rate in Group 1 and Group 2 constant Is 55% in Group 3 without treatment before baseline plausible? They have 'disease' by IADPSG criteria but presumably milder than those identified with C_C criteria. Is a 50% reduction in CS rates from treatment realistic? It's much greater than was observed in ACHOIS/Landon. If the answer to one or both these questions is 'no' then almost certainly there are other factors influencing the CS rate. h) Confidence intervals are underpinned by a probability distribution around a point estimate. However, the model output is a function of numerous inputs which have sampling uncertainty. The standard way to take into account uncertainty in economic evaluation across multiple input parameters is to perform probabilistic sensitivity analysis, as was done for the model produced for this guideline. This involves repeated simulation of the model, sampling parameter values from a probability distribution in order to take account sampling uncertainty in model inputs (and therefore output). This involves repeated simulation of the model, sampling

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						parameter values from a probability distribution in order to take account sampling uncertainty in model inputs (and therefore output). So, for example, treatment effectiveness is sampled in the PSA and the relative risks sampled will be drawn from the same probability distribution as would be used to derive a 95% confidence interval for the relative risk. However, not only are relative risks sampled in the PSA but also costs and the coefficients in the regression model. The deterministic output or point estimate for a number of outcomes in the model are presented and the distribution around these point estimates is taken into account in the probabilistic sensitivity analysis. i) The diagnostic and target fasting values are determined by the evidence. The diagnostic criteria were determined on the basis of the Health Economic analysis using over 6000 women from the HAPO dataset. The target values were taken from the studies reporting on the relationship between blood glucose values and adverse outcomes.
Central Manchester University Hospitals NHS Foundation Trust	2	Full	2.1.3 Table 73 98 5.11.9 Table	75 76 87 511 512	"Advise women with uncomplicated gestational diabetes to give birth no later than 39 weeks + 6 days" To our knowledge, there is no good evidence to support this recommendation particularly if the women has normal blood sugars, a normally grown baby and no other obstetric risk factors. Delivery by 39+6 requires induction planning at 39+3 onwards. Would it not be more appropriate	Thank you for your comment. We reconsidered the recommendation about timing of birth in response to stakeholder comments. We felt that the evidence justified making separate recommendations for the timing of birth for women with type 1 or type 2 diabetes and for women with gestational

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					to suggest delivery by 40+6?	diabetes. For women with gestational diabetes, the data from Rosenstein (2012) demonstrated that there was a significant rise in stillbirth rate after 40+6 days. Whereas the Kjos (1993) study showed that the incidence of babies weight more than 4000g rose after 39+6 days. Given that avoidance of stillbirth was the philosophy underpinning the timing of delivery, the GDG felt that in women with uncomplicated gestational diabetes elective delivery could be delayed until 40+6 days. For women with type 1 or type 2 diabetes the limited data demonstrated that the stillbirth rate rose after 38+6 weeks. Thus such women should be offered elective delivery by 38+6 weeks. We felt that a lower limit should be also included in the recommendation to avoid women with uncomplicated type 1 or type 2 diabetes being advised to have an elective preterm delivery with its associated complications for the woman (such as failed induction of labour and caesarean section) and the baby (such as respiratory distress syndrome and admission to the neonatal unit). The data from Holman (2014) suggested the lower limit of the elective delivery should be 37+0 weeks. Thus we recommended elective delivery for women with uncomplicated type 1 or type 2 diabetes between 37+0 and 38+6 weeks. In making this recommendation, we expect

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						that, in practice, this would result in such women being routinely offered elective delivery nearer 38+6 weeks than 37+0 weeks.
Central Manchester University Hospitals NHS Foundation Trust	3	Full	34	81	"the urinary albumin:creatinine ratio is greater than 30 mg/mmol" The threshold for an abnormal ACR is > 3 and for protein:creatinine ratio (PCR) > 20mg/mmol in most hospitals in non pregnant subjects. These values are considerable lower than that cited in the guideline and should be revised.	Thank you for your comment. However, this topic was not prioritised in the scope for update. Thus the recommendations not reviewed and unchanged from the 2008 version of the guideline.
Central Manchester University Hospitals NHS Foundation Trust	4	Full	35	81	"most women (about 70%) will need oral blood glucose lowering agents or insulin" Putting a figure seems unwise. This value is dependent on the diagnostic criteria and will depend on the ethnicity and the diagnostic criteria used. It seems unwise to give such a specific figure and an alternative such as 'the majority of women ' would seem more appropriate.	Thank you for your comment. As described in the 'Evidence to recommendations' section of the chapter, the figure of 70% was the average of the proportion women with gestational diabetes in the clinical practice of GDG who needed pharmacological intervention. They acknowledged that the figure was affected by a number of factors. They concluded that it would be correct to say that the majority of women with gestational diabetes in their practice needed pharmacological intervention. They changed the recommendation accordingly.
Central Manchester University Hospitals NHS Foundation Trust	5	Full	36	82	"minority ethnic family origin with a high prevalence of diabetes" Are these listed?	Thank you for your comment. The text of this recommendation was only amended in the 2015 update of the guideline to broaden the bullet point specifying particular family origins with a high prevalence of diabetes as a risk factor. The phrase 'minority ethnic family origin with high prevalence of diabetes' was agreed given the importance of not overlooking risk factor assessment in women in groups other than those that were listed previously. The phrasing was

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						deliberately not made more explicit because the list would never be comprehensive.
Central Manchester University Hospitals NHS Foundation Trust	6	Full	37	82	"Do not screen for GDM using….urine analysis for glucose" This needs clarification as it could be interpreted as meaning that the urine should not be checked for glucose at routine antenatal visits. However, (38) "If glycosuria is detected by routine urine analysis.." implies that routine urine analysis is advisable. Accordingly suggest omit urinalysis from recommendation 37.	Thank you for your comment. In summary, the evidence relating to glycosuria as a predictor of glucose intolerance in pregnancy is that there is no evidence of its value as a population screening test, but, there is observational data that glycosuria increases the likelihood of gestational diabetes. Because of the screening evidence (or lack of it) the original guideline and the ANC guideline do not recommend it for population screening in pregnancy. However, we recognise that urinalysis is undertaken routinely in pregnancy using reagent strips that not only record the presence of protein but other substances including glucose. Thus we have made a recommendation based on the observational data presented in the original guideline. The text of the guideline and the recommendations have been amended to make these points clearer.
Central Manchester University Hospitals NHS Foundation Trust	7	Full	39	82	Should include gestation at which testing should be performed rather than this being in a separate recommendation	Thank you for your comment. However, it was felt that it addressing the timing of the testing/screening in separate recommendations (40 and 41) was clearer.
Central Manchester University Hospitals NHS	8	Full	44	82	There is no evidence of any quality reporting that women with gestational diabetes and normal blood sugar levels (as opposed to type 2 diabetes) have an increased risk of perinatal death. In addition, this is likely to add to the	Thank you for your comment. We disagree with the stakeholder's position and believe that women should be informed of the risks associated with unmanaged gestational diabetes with appropriate management

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Foundation Trust					anxiety of these women following diagnosis and seems totally inappropriate.	these risks can be diminished.
Central Manchester University Hospitals NHS Foundation Trust	9	Full	51	83	Newly diagnosed GDM. Offering trial of diet/exercise insulin if fasting <7mmol/l. Where is the evidence to support 7.0mmol/l? It may be appropriate to check another fasting/preprandial glucose value to ensure the woman had actually fasted Clearly, the higher the glucose level, the more likely that additional treatment will be needed in addition to diet, however, it seems unlikely that women with a fasting glucose of 7 mmol/l will achieve euglycaemia (fasting glucose < 5.3 mmol/l) with lifestyle modification alone. Diet and exercise may reduce fasting blood glucose by about 0.5mmol/l. The figure of <7.0 should be lowered and <6.5mmol/l would appear a more appropriate cut off and the text should be qualified to indicate that these women need early review to assess the need for additional treatment. .	Thank you for your comment. Whilst the GDG were of the general view that in principle the treatment offered to women with the diagnosis of gestational diabetes should be to start with the simplest and cheapest option (diet and exercise) before proceed to the pharmacological agents. However, they acknowledged that some women would have such severe glucose intolerance that lifestyle change (diet and exercise) would be extremely unlikely to reduce the blood glucose values to the target range. For such women the GDG felt that good blood glucose control would be achieved by starting treatment with insulin (in addition to diet and exercise) with or without metformin. There was no evidence to inform the threshold for starting with pharmacological treatment but the GDG felt that it was reasonable to use a fasting blood glucose value of 7.0 mmol/litre as this the threshold for the diagnosis of diabetes
Central Manchester University Hospitals NHS Foundation Trust	10	Full	54	83	If GDM fasting ≥7mmol/l "offer immediate treatment with insulin and/or metformin". Should this not be "insulin with or without metformin"? Extrapolating from the MIG trial the possibility that metformin/ exercise/diet can bring fasting values from ≥7 to ≤5.3 (recommended upper target) is remote.	Thank you for your comment. The GDG agreed with you and have amended the recommendation accordingly.
Central Manchester University Hospitals NHS	11	Full	55	84	Use of glibenclamide. The promotion of glibenclamide as appropriate medication was heavily based on the claims (subsequently refuted) that it did not cross the placenta. Many women suffer GI side effects	Thank you for your comment. We agree that the claims that glibenclamide does not cross the placenta have been discredited, but RCT data for glibenclamide were available for review by the GDG when

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Foundation Trust					from metformin, but these usually settle. If the clause "who cannot tolerate metformin" is placed as the first bullet point, this may lead to many women being prescribed glibenclamide which seems illadvised as its safety and efficacy has not been adequately assessed. We suggest that that these 2 bullet points be reversed. There is an ongoing (HTA funded) trial to determine the safety and efficacy of glibenclamide in pregnancy – to pre-empt these results is premature and unjustifiable. Indeed the implication that glibenclamide is safe outside a randomised trial setting might hamper recruitment to the above trial and seriously jeopardise the ability to establish evidence-based recommendations.	developing the recommendation. The recommendation for the limited situations when glibenclamide could be considered is supplemented by further advice for the prescriber to follow relevant professional guidance, to take full responsibility for the decision to use and to seek informed consent from the woman. Hence we do not agree that this recommendation would affect recruitment to ongoing studies. However, we agree that many women tolerate metformin with time, and have amended the order of the bullet points in the recommendation to reflect this, as suggested.
Central Manchester University Hospitals NHS Foundation Trust	12	Full	60	84	Blood ketone testing strips and meter and hyperglycaemia. This has significant cost implications particular if it is also intended to apply to women with GDM. How is hyperglycaemia defined? If these are guidelines with significant cost implications then hyperglycaemia must be more rigorously defined. One definition of hyperglycaemia might be 'blood glucose more than 15.0mmol/l on 2 occasions an hour apart and/or more than 90 minutes after eating?' In addition, ketone testing does not appear to have been included in the cost benefit analysis and will change across the diagnostic categories dependent on the degree of glycaemia.	Thank you for your comment. Amendments to this recommendation and the next recommendation (now recommendations 63 and 64) were made in line with your comment following consultation. Recommendation 63 restricts use of blood ketone testing strips and meters for ketonaemia testing to pregnant women with type 1 diabetes. In recommendation 64, pregnant women with type 2 diabetes or gestational diabetes are advised to seek urgent medical advice if they become hyperglycaemic or unwell, but home testing for ketonaemia is not recommended for these groups of women. The final recommendation (65) is that women with any form of diabetes who is hyperglycaemic or unwell should be tested for ketonaemia
Central Manchester	13	Full	64	84	Targets "Advise pregnant women with diabetes who are on metformin, insulin or glibenclamide	Thank you for your comments. In making recommendations about target values for

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University Hospitals NHS Foundation Trust					to maintain glucose levels above 4mmol/l" It would be more appropriate to include "..on insulin or oral therapy"? The order of these agents as described seems to give undue preference to the use of glibenclamide in pregnancy which seems unwise for the reasons stated above. As there is no evidence base for "above 4" (presumably it should read 4.0) and therefore is a consensus view. Alternatively, if may be preferable to encourage avoidance of glucose values "below 4.0mmol/l". as this would be more easily understood by women and their care givers. . "fasting below 5.3mmol/l" – This value seems appropriate, but is inconsistent with the 5.6mmol/l being advised as a diagnostic threshold as highlighted above	women with diabetes in pregnancy, we were inclined to use those values for which the evidence showed some benefit. Accordingly, from the evidence they suggested that the following would be reasonable targets: Fasting level = less than 5.3 or 5.6 mmol/litre (Rowan et al reported a lower incidence of pre-eclampsia and LGA with a target threshold of 5.3 mmol/litre. However, Farrag, reported a higher incidence of maternal hypoglycaemic episodes with a target threshold of 5.6 mmol/litre) 1 hour value = or less than 7.8 mmol/litre (Combs et al in a study of women who largely measured the 1 hour values reported a lower incidence of LGA with a target threshold of 7.8 mmol/litre.) 2 hour value = less than 6.4 mmol/litre (Rowan et al reported a lower incidence of pre-eclampsia and LGA with a target threshold of 6.4 mmol/litre.) Regarding setting a lower level blood glucose level, ideally, women should strive for blood glucose levels as near to normal as is safely achievable. For women taking insulin and glibenclamide inevitably this be associated with a risk of hypoglycaemia and we felt that it would be sensible to provide a limit for the lower level of blood glucose for women on these treatments. However, there was no evidence identified in the review. Thus 4.0 mmol/litre was chosen because this was the 'safe' lower target value recommended by Diabetes UK. For women on diet and exercise or

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						metformin the risk of hypoglycaemia was very low and we did not feel that it was necessary to set a lower limit for women on these treatments. The recommendations about the lower glucose target was amended in view of these comments.
Central Manchester University Hospitals NHS Foundation Trust	14	Full	65	84	This statement seems out of place/obsolete given the recommendation in 68.	Thank you for your comment. Both recommendations are required because recommendation 65 makes that statement that HbA1c levels should not be routinely used to assess a woman's blood glucose control whereas recommendation 68 stipulated the non-routine situations when HBA1c levels should be considered to assess a woman's blood glucose control in the second and third trimesters of pregnancy
Central Manchester University Hospitals NHS Foundation Trust	15	Full	67	85	67 "Measure HbA1c in all women with a diagnosis of GDM.." a. It should be stated that a significantly elevated HbA1c at diagnosis of GDM may point to previously undiagnosed diabetes (this may be either type 1 or type 2 diabetes and not just type 2) b. It should be made clear that HbA1C measurement is indicated when GDM is first identified, i.e. 1st, 2nd or 3rd trimester. As noted above, this is purely to offer insight into the possibility of previously undiagnosed diabetes. c. Screening for undiagnosed hyperglycaemia at booking seems wise and was recommended by the IADPSG criteria. Possible measures might include an HbA1c or fasting glucose. However, with the exception of HbA1c measurement at booking, which can be used for diagnosis of diabetes (if > 6.5%), HbA1c measurement in	Thank you for your comment. Several stakeholders raised similar concerns so we re-discussed the evidence in the draft guidance. We acknowledge that it is difficult to conduct a study that would determine target values for HbA1c. However, the GDG were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was nonetheless a marker of risk of adverse outcome and could be of value in practice

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					later pregnancy does not offer any insight into minor degrees of glucose intolerance.	for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome. In the light of these considerations the GDG decided to amend their recommendations to reflect their conclusions that HbA1c should not be used in a diabetic pregnancy to assess glucose control, however, it should be used in specific circumstances to assess the risk in those pregnancies with 48mmol/mol (6.5%) as a threshold.
Central Manchester University Hospitals NHS Foundation Trust	16	Full	68	85	"Consider measuring HbA1c in the 2nd & 3rd trimester if…" There is a wealth of national and international evidence that increasing HbA1c is associated with multiple adverse perinatal outcomes, including stillbirth, large for gestational age, pre-term delivery and neonatal death. Most recent evidence comes from the National Pregnancy in Diabetes audit and a detailed review of the DAPIT cohort (In press Diabetes Care). These data would strongly support the clinical utility of regular HbA1c measurement throughout the whole of pregnancy. In view of this it is inappropriate not to measure HbA1c in all women, at least once in the second trimester and once in the third trimester and possibly even on a monthly basis. If significantly elevated, women should be considered at particular high	Thank you for your comment. Several stakeholders raised similar concerns so we re-discussed the evidence in the draft guidance. We acknowledge that it is difficult to conduct a study that would determine target values for HbA1c. However, we were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was nonetheless a marker of risk of adverse

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					risk and merit more intensive supervision. The evidence would suggest that these risks increase if the HbA1c is ≥6.5% in early pregnancy and from ≥6.0% in later pregnancy. Mindful of the physiological fall of HbA1c in diabetic pregnancy and the fact that HbA1c levels in normal pregnancy remain ≤ 5.7%, it would seem prudent to aim for near euglycaemia and an HbA1c <6.0% in late pregnancy. In addition the cost of the test is trivial compared with the other costs incurred. The suggestion that HbA1c is only of interest at booking is also inconsistent with the advice to measure it monthly before pregnancy. It is inappropriate to suggest that HbA1c measurement should be considered if confirmation that the woman is reaching target glucose levels is required. CGM data confirm that very few women spend even 20 hours per day within target; indeed women with type 1 diabetes spend on average 8-10 hours per day with glucose levels outside the target range (Murphy HR Diab Care 2007). Furthermore while the need for simplicity is acknowledged, it may be inappropriate to recommend the same BG targets for type 1 and type 2 diabetes. There is ample evidence that type 2 diabetes is a less severe glycaemic disturbance and that tighter HbA1c targets and CGM glucose levels can be achieved more easily. The NPID audit showed that twice as many women with type 2 diabetes achieved HbA1c levels < 6.1% and or <7.0% at booking compared to type 1 diabetes. Likewise women with type 2 diabetes have lower second and third trimester HbA1c values than women with	outcome and could be of value in practice for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome. In the light of these considerations we decided to amend their recommendations to reflect their conclusions that HbA1c should not be used in a diabetic pregnancy to assess glucose control, however, it should be used in specific circumstances to assess the risk in those pregnancies with 48mmol/mol (6.5%) as a threshold.

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					type 1 diabetes and this is associated with fewer LGA babies and fewer NICU admissions. Any relaxation of glycaemic control targets in type 2 diabetes could jeopardise the recent progress that has been achieved since CEMACH. This should be qualified in the guideline.	
Central Manchester University Hospitals NHS Foundation Trust	17	Full	77	85	While it is reasonable to suggest that CGM should not be routinely offered to women with diabetes the suggestion that it may be offered to "women with unstable blood glucose levels" is applicable to **all** women with type 1 diabetes! It would be more appropriate to advise that CGM may be helpful in carefully selected women in whom glucose control is particularly problematic. .	Thank you for your comment. However, we feel that the wording is clear and supports the approach you advocate.
Central Manchester University Hospitals NHS Foundation Trust	18	Full	78	86	Continuous glucose monitoring "..including 24-hour contact with a member of the diabetes care team who is expert in its use" It is inappropriate to say that 24 advice is needed for CGM. Rather, 24 hour advice should be available for all pregnant women with diabetes, and particularly if they use CSII. If the CGM appears not to be working in a satisfactory manner then the woman reverts to normal testing and if her glycaemic control is poor then she will seek advice as normal. In addition technical support is available 24/7 from the CGM manufacturer. This recommendation does not appear either to be necessary or evidence based.	Thank you for your comment. The recommendation was discussed following stakeholder consultation. It was agreed that 24 hour advice should be available for all pregnant women with diabetes. However, whilst the provision of support was essential for women using CGM from someone who was expert in its use, it was not necessary to stipulate that this had to be 24h support from a diabetologist. The recommendation was amended to reflect this
Central Manchester University Hospitals NHS Foundation	19	Full	98	87	"Advise women with GDM to give birth no later than 39weeks + 6 days." In practice this means that there will be fewer inductions and probably as a result fewer failed inductions and caesarean sections. Does the Health Economic Analysis allow for this?	Thank you for your comment. We reconsidered the recommendation about timing of birth in response to your comment. We felt that the evidence justified making separate recommendations for the timing of

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Trust					As mentioned above, there is no evidence of any quality suggesting that women with GDM have an increased risk of perinatal mortality. Accordingly provided that maternal and fetal monitoring is satisfactory, fetal growth normal and maternal glucose monitoring in target, then there is no logical reason to advise induction and such an intervention may increase adverse outcomes.	birth for women with type 1 or type 2 diabetes and for women with gestational diabetes. For women with gestational diabetes, the data from Rosenstein (2012) demonstrated that there was a significant rise in stillbirth rate after 40+6 days. Whereas the Kjos (1993) study showed that the incidence of babies weight more than 4000g rose after 39+6 days. Given that avoidance of stillbirth was the philosophy underpinning the timing of delivery, the GDG felt that in women with uncomplicated gestational diabetes the recommendation for elective delivery could be extended from 39weeks + 6 days until 40 weeks +6 days. No health economic literature was found that considered the cost-effectiveness of timing of birth for women with gestational diabetes and de novo analysis was not undertaken. The health economic analysis reported in Chapter 9 does not model the impact of timing of birth on induction of labour and caesarean section. The model on cost-effective diagnostic thresholds for gestational diabetes uses a logistic regression to predict the baseline risk of induction of labour, caesarean section and other outcomes for a woman with gestational diabetes based on their blood glucose values and other covariates, which do not include gestational age at birth. This logistic regression analysis is based on a UK/Australian subset of the HAPO dataset. For women identified with gestational diabetes and treated, the model adjusted

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						the risk of various outcomes (including induction of labour and caesarean section) based on the treatment effect sizes reported in the Crowther 2005 and Landon 2009 studies. Our view is that it would be very difficult to model the impact of advice on a maximum gestational age before birth on both the baseline risk of induction of labour and caesarean section and on the treatment effect size with existing data. However, we accept that increasing the time allowed for spontaneous labour is likely to impact on the number of inductions although this would be the case for all strategies.
Central Manchester University Hospitals NHS Foundation Trust	20	Full	128	89	128 Post natal testing after GDM Practically and logistically, it may be attractive to omit the postnatal OGTT. Unfortunately annual testing in the community is not occurring universally and until such time as general practice follow up is secure, to advise against a postnatal OGTT seems ill advised. It should also be noted that failure to do an OGTT will miss around 7-10% of women with type 2 diabetes and a fasting value alone will miss 10-20% of women with IGT. Diagnosis by HbA1c at this stage is limited by altered red blood cell turn over following delivery. In addition the postnatal visit offers a unique opportunity to screen for other CV risk factors and encourage lifestyle change where necessary. There is no evidence to suggest that attendance rates for a fasting plasma glucose sample are better than for an OGTT. This paragraph needs rewording to better reflect this by saying that one does not need to offer a GTT if a robust system of 1 year	Thank you for your comment. It is acknowledged that the woman who had gestational diabetes is at risk of developing type 2 diabetes. The evidence reviewed demonstrated that a significant proportion of women would develop the condition in the first year after the pregnancy and some in the first three months. Hence it was important to include recommendation about testing in the first three months as well as annually. We agreed with you about the need to try and improve compliance and uptake of postnatal testing by being flexible presenting them with the options of either a fasting blood glucose at 6-13 weeks or an HbA1c at 13 weeks . Finally, we have acknowledged that women who had gestational diabetes and their postnatal test result (fasting glucose or HbA1c) shows them to be 'at risk' for Type 2 diabetes, then they should be managed in

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					follow up is in place.	accordance with the NICE guideline 'Preventing type 2 diabetes: risk identification and interventions for individuals at high risk' (PH 38).
Central Manchester University Hospitals NHS Foundation Trust	21	Full	129	90	Post Fasting result. If ≥7.0mmol/l offer a repeat fasting, an HbA1c or a GTT. Is ≥7.0 not diagnostic of diabetes or is the repetition for confirmation purposes? Is an OGTT really indicated in this scenario?	Thank you for your comments. In the light of them and similar comments from other stakeholders the GDG have reviewed this section and rewritten it significantly. Specifically they have made more detailed recommendation about women whose postnatal test results (fasting glucose or HbA1c) suggest they are at 'high risk of type 2 diabetes'. These include cross referral to the NICE guideline 'Preventing type 2 diabetes: risk identification and interventions for individuals at high risk' (PH 38).
Central Manchester University Hospitals NHS Foundation Trust	22	Full	130	90	Post natal HbA1c Where does the figure of 39 (5.7%) come from? Is this making reference to the ADA criteria for diagnosis of impaired glucose metabolism? As noted above HbA1c may be inaccurate for diagnosis in the early postnatal period.	Thank you for your comment. We were aware that in 2011 the WHO recommended an HbA1c diagnostic threshold for type 2 diabetes should be 48 mmol/mol (is 6.5%). However, the WHO did not provide specific guidance on HbA1c criteria for people at increased risk of Type 2 diabetes. We noted that a report from a UK expert advisory group on the implementation of WHO guidance recommended using HbA1c values between 42-47 mmol/mol (6.0-6.4%) to indicate that a person was at high risk of type 2 diabetes. Importantly, that expert group did recognise that there is a continuum of risk across a range of subdiabetic HbA1c levels and that people with an HbA1c below 42 mmol/mol (6.0%) may also be at risk (John 2012). Given this acknowledgement that lower values than 42

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						mmol/mol (6.0%) were indicative of risk and the finding in the review undertaken for this question that 39 mmol/mol (5.7%) was associated with a positive likelihood ratio of 11.23 for the diagnosis of diabetes ('a very useful test') we felt that in the first three months postpartum a lower value of 39 mmol/mol (5.7%) would represent a more useful threshold for screening and was based on evidence.
Diabetes UK	1	NICE	General	General	There is nothing explicitly about the management of gestational weight gain especially in the obese/overweight. This is a major omission. 4Women should be advised of the influence of haemoglobin turnover on HbA1c result. Where HbA1c has been recommended, there should be explicit recommendation for women with anaemia or haemoglobin turnover issues. There is nothing on the emotional impact of gestational diabetes diagnosis and how this is manage	Thank you for your comments. However, a) this topic was not in the scope for the Guideline update, b) there are already two NICE Guidelines about the management of people with obesity which are cross-referenced in the Guideline (Obesity: working with local communities. NICE public health guidance 42 (2012); Weight management before, during and after pregnancy. NICE public health guidance 27 (2010); Obesity. NICE clinical guideline 43 (2006)). The latter has been partially updated by NICE clinical guidance 189; Obesity: identification, assessment and management of overweight and obesity in children, young people and adults. Finally, the Antenatal Care Guideline (Antenatal care. NICE clinical guideline 62 (2008)) recommends that, in general, pregnant women should not diet. The GDG acknowledged the difficulty created by anaemia and red cell turnover in pregnancy which makes it difficult to specify the normal range for pregnancy. As a consequence they noted that HbA1c

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						monitoring in pregnancy was not recommended in the previous guideline and agreed that there is no evidence to recommend its routine use in pregnancy as a measure of glucose control. At the present time it is not possible to advocate an alternative measure of average glycaemic control. However, the GDG believed several observational studies support the view that HbA1c was an indicator of risk of adverse outcome in a diabetic pregnancy with that risk increasing progressively above 48 mmol/mol (6.5%). They thus amended the recommendations to reflect this. The emotional impact of a diagnosis of gestational diabetes was not proposed by stakeholders at the scoping stage of this guideline update as a topic that should be reviewed.
Diabetes UK	2	NICE	1.1.3	15	Information to women to cover: • Point two should read: the risks of hypoglycaemia and impaired awareness of hypoglycaemia during pregnancy if receiving insulin therapy especially in the first trimester • Point five should read: the need for assessment of diabetic retinopathy before and during pregnancy and the risks of development and/or progression of retinopathy during pregnancy Women also need to know about the increased risk of pre-eclampsia and associated premature	Thank you for your comments. However, this topic was not prioritised for review in this guideline update.

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					delivery which can be associated with offspring with cognitive impairment	
Diabetes UK	3	NICE	1.1.5	16	Reliability of contraception should also be discussed, particularly the increased risks of failure with barrier methods and oral contraception	Thank you for your comment. The use of barrier methods of contraception was not within the parameters of the review protocol. The associated protocol and review of oral contraceptives (see full guideline) specified pregnancy rate as an outcome. However, there was no evidence available for this outcome and no recommendation was made.
Diabetes UK	4	NICE	1.1.11	17	Diabetes team members have wider responsibilities and the opportunity should be taken to review rubella status, smoking, alcohol and non-diabetes medications	Thank you for your comment. Whilst we agree that there are wider clinical and lifestyle considerations for all pregnant women, this guideline pertains to diabetes in pregnancy. These topics are covered in the Antenatal Care Guideline (CG62).
Diabetes UK	5	NICE	1.1.12	17	Do we have evidence for this and is it cost effective? This should say at least every 3 months and up to monthly during the stabilisation period and where needed for maintenance	Thank you for your comment. However, these are 2008 recommendations and they have not been updated.
Diabetes UK	6	NICE	1.1.17	18	Since the Type 1 diabetes guidelines is not due until August, women should strive for targets during pregnancy where it is safe to do so and with the understanding that these are difficult to achieve both before and during pregnancy	Thank you for your comment. The new recommended targets in the consultation draft of the updated NICE clinical guidance 15 'Type 1 diabetes: the diagnosis and management of type 1 diabetes in include 'a fasting plasma glucose level of 5-7 mmol/litre on waking and a plasma plasma glucose level of 4-7 mmol/litre before meals at other times of the day.' In addition, the Type 1 diabetes guidance recommends aiming for a target HbA1c level of 48 mmol/mol (6.5%) or lower. We felt these

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						targets were sufficiently stringent for women planning to become pregnant. The consultation draft of the updated NICE CG 15 is available from the NICE website http://www.nice.org.uk/guidance/indevelopment/gid-cgwaver122/consultation Consultation closes at 5pm on 4 March 2015
Diabetes UK	7	NICE	1.1.21	18	Women should be advised that metformin crosses the placenta, that there is no evidence of teratogenesis or adverse pregnancy outcomes but that long term safety data are limited	We are currently awaiting further information in order to respond to this comment.
Diabetes UK	8	NICE	1.1.23	19	There is now substantial data for Levemir. Many people are very concerned about the increased risk of hypoglycaemia with the use of Isophane insulin in insulin sensitive women during pre-pregnancy and antenatal. Therefore, there should be a differentiation between Type 1 and Type 2 diabetes here.	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to the recommendation that states '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

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						information'. No amendment was made to differentiate between women with type 1 or type 2 diabetes.
Diabetes UK	9	NICE	1.2.1	21	This is inadequate to allow women to make an informed choice, for example, it does not include the risk of macrosomia and pre-eclampsia, which women need to know based on their own family history, prior experience and concerns and which we have good evidence can be reduced with treatment. The risk of eg stillbirth and other complications may be important to individual women. A standard information sheet should be produced that lists the risks including those that we have RCT evidence can be reduced (e.g. stillbirth, fractures, nerve palsies)	Thank you for your comment. We feel that all the potential complications cannot realistically be listed. Thus the decision was taken to use the phrase 'serious birth complications' and to allow the health professional to expand on these in their discussions with the woman.
Diabetes UK	10	NICE	1.2.2	22	It is worth considering lowering previous macrosomia to less than 4kg (from 4.5kg) or defining this as above 90th centile given the wide disparity of normal fetal birth weight distribution across different ethnic groups and increased risk of long term complications to the offspring if birth weight is >90th centile? As nearly all non-white populations are at high risk e.g. all Asians, Africans, south Americans- the point on 'minority ethnic family origin with high prevalence of diabetes' should be more explicit and say 'all non-European ethnic groups' or 'all non-Caucasian ethnic groups' Also, women with PCOS or who have undergone fertility treatment should be tested as they are high risk of undiagnosed Type 2 diabetes Screening at 24-28 weeks should be offered to	Thank you for your comments. A review of the risk factors for gestational diabetes was not prioritised in the scope for the guideline update although the amendment was made to broaden the original guideline's recommendation bullet point specifying particular family origins with a high prevalence of diabetes as a risk factor. The phrase 'minority ethnic family origin with high prevalence of diabetes' was agreed given the importance of not overlooking risk factor assessment in women in groups other than those that were listed previously. The phrasing was not made more explicit (eg 'all non-European ethnic groups' or 'all non-Caucasian ethnic groups' as suggested) because this would not be an accurate description of the ethnicities with a higher risk. The health economic analysis undertaken

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					all women and they can decline if they wish. Women need to be informed of risk factors including grand multiparity, age, PCOS. As risk factor screening applies only to white women, it is inappropriate not to offer women screening; they will know their family history and background and can decide. A standard information leaflet should be used. There are many studies showing risk factor screening is a failed population based strategy because of its implementation issues and this is particularly the case here where the risk factors are not comprehensive enough.	for the subject of screening for gestational diabetes in fact does demonstrate that screening using risk factors is both clinically and economically effective.
Diabetes UK	11	NICE	1.2.3	22	There no comment on HbA1c? There is as much data for random glucose and HbA1c; these might be better if an OGTT is not possible-or go straight to self-glucose monitoring.	Thank you for your comment. The value of the HbA1c as a screening test in both the first and second trimester was reviewed. There were no studies of HbA1c in the first trimester. There was only one study of HbA1c in the second trimester. However, we did not consider this evidence was sufficiently strong to support a recommendation to use the test. We have now amended the recommendation to make that clearer. The value of a random plasma glucose as a screening test was also reviewed. Only one retrospective cohort study was identified that fulfilled the criteria set out in the protocol for the question. The study was conducted in the UK and provided very low quality evidence from an analysis to maximise estimations of diagnostic accuracy (using WHO diagnostic criteria) that, using likelihood ratios, a random blood glucose test in the second trimester is moderately useful for ruling in

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						'overt diabetes in pregnancy' and not useful as a test for ruling out 'overt diabetes in pregnancy' at a threshold category of 7.51 to 7.59 mmol/L. However, the original WHO diagnostic thresholds used in the study were not recommended as suitable for diagnosis of gestational diabetes. Thus, overall, we considered that the evidence was not strong enough to make a recommendation to use a random glucose as a screening tool.
Diabetes UK	12	NICE	1.2.6	22	Is the purpose of this recommendation to ensure that women with undiagnosed established diabetes are recognised? • Is there a purpose in home monitoring for this group? Could unnecessary monitoring be avoided by diagnostic laboratory test e.g. the 75g OGTT? • Should the criteria for 75g OGTT be specified here? Presumably the cut-offs for this will be those used for established diabetes given how close they test is to booking	Thank you for your comment. We believe that given the high risk of recurrence of gestational diabetes in a subsequent pregnancy, the use of regular self-monitoring of blood glucose values would be something with which the woman would be familiar/practised from her previous pregnancy, and, is likely to identify a recurrence of gestational diabetes more quickly than intermittent OGTTs. Recommendation 1.2.8 in the NICE guideline describes the diagnostic thresholds of the OGTT.
Diabetes UK	13	NICE	1.2.8	23	These criteria are strange. It would be interesting to know where this fasting cut-off originates from as this is not in keeping with the new WHO criteria. If we go ahead with these cut offs, we will be increasingly out of alignment with the WHO and rest of the world. This undermines a key need to ensure that all criteria for gestational diabetes are aligned to allow comparisons and more data to inform the collation of evidence. Studies using these criteria risk being rejected from higher ranking journals for these reasons.	Thank you for your comments. The rationale for these cut-offs is given in Section 4.4 of the consultation version of the full guideline. Health economic analysis was undertaken to assist in making a recommendation and this work, referenced in Section 4.4, is described in more detail in Chapter 9 of the Full Guideline. The health economic analysis is underpinned by HAPO data, using data from over 6,000 patients in UK and Australian centres. Logistic regression analysis was used to develop a

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					These thresholds are comparable to legacy thresholds which have no relationship to the risks to the offspring as shown by HAPO. The approach should be about the woman and her baby. This is achieved by aligning with HAPO fasting, 1 hour and 2 hour relationships and then rationing decided based upon the risks. • By choosing 5.6 mmol/l, the GDG has failed to align with the ACHOIS criteria of 7.8/7.8 and hence no argument regarding what was in the RCT's is valid • Thresholds should be based upon odds ratios either overall eg 5.1/10/8.5 vs 5.3/10.6/9 or an individual mix eg 5.3/10/8.5. • If these thresholds are adopted, women should be informed that other parts of the world are using 5.1/10/8.5 and that NICE has decided to ration based upon health economic modelling.	prediction model based on OGTT values amongst other variables. This model was then used to predict the baseline risk for a number of outcomes (neonatal/maternal) for all women in the dataset. The exponential of the regression coefficients for blood glucose values represent the odds ratios. Some commentators (e.g. Cundy 2014) have criticised IADPSG (new WHO) diagnostic criteria for gestational diabetes on the basis that the fasting threshold is less than the inclusion criteria for intervention studies such as ACHOIS and argue there is no evidence that treatment would offer a benefit in these patients with 'milder' disease. Whilst this criticism is perhaps not unreasonable, the model takes a pragmatic view given the state of the debate and the absence of trial based evidence to support proposed diagnostic thresholds. It assumes that treatment is effective in all women diagnosed regardless of blood glucose level and that the relative treatment effect is the same across all treated women. The absolute treatment effect depends on the baseline risk and therefore women with lower blood glucose values will therefore derive less benefit. Diagnostic strategies with lower thresholds will derive more benefit overall but the issue is whether that additional benefit is achieved at an acceptable cost. The odds of adverse events at given blood glucose levels and with/without treatment are key components of the health economic model.

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						We accept that the criteria recommended by this guideline differ from the new WHO criteria. However, we noted the strength of the WHO recommendation was weak and that the WHO guideline suggests a rapid update of the criteria may be necessary in the light of new health economic evidence.
Diabetes UK	14	NICE	1.2.15	24	There should also be a discussion about the amount of carbohydrate and the need to reduce amounts to achieve good blood glucose control.	Thank you for your comments. However, the 16 included studies did not provide the detail required to develop a recommendation.
Diabetes UK		NICE	1.2.17	24	1.2.17 On what basis are we setting a target of 7mmol/l? Most would commence an agent if >6mmol/l depending on current diet	Thank you for your comment. We were of the general view that, in principle, the treatment offered to women with the diagnosis of gestational diabetes should begin with the simplest and cheapest option that is diet and exercise, before proceeding to the pharmacological agents. However, we acknowledge that some women would have such severe glucose intolerance that lifestyle change (diet and exercise) would be extremely unlikely to reduce the blood glucose values to the target range. For such women we felt that good blood glucose control would be achieved by starting treatment with insulin (in addition to diet and exercise) with or without metformin. There was no evidence to inform the threshold for starting with pharmacological treatment but we felt that it was reasonable to use a fasting blood glucose value of 7.0 mmol/litre as this is the threshold for the diagnosis of diabetes.
Diabetes UK	15	NICE	1.2.18	24	Women should be given the choice of Metformin vs insulin as many women are concerned about Metformin crossing the placenta. For many	Thank you for your comment. However, overall, on the basis of the evidence, showing the comparability of clinical

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					women, it is more appropriate to go directly onto insulin e.g. if they present later in the pregnancy	effectiveness of metformin compared to insulin, its greater acceptability and ease of administration, we felt metformin should be offered first, followed by insulin if metformin were contraindicated or unacceptable.
Diabetes UK	16	NICE	1.2.20	24	7mmol/l is too high in third trimester-possibly fine earlier if not too early	Thank you for your comments. Whilst we were of the general view that, in principle, the treatment offered to women with the diagnosis of gestational diabetes should be to start with the simplest and cheapest option, that is, diet and exercise, before proceeding to treatment with pharmacological agents. However, we acknowledge that some women would have such severe glucose intolerance that lifestyle change (diet and exercise) would be extremely unlikely to reduce the blood glucose values to the target range. For such women we felt that good blood glucose control would be achieved by starting treatment with insulin (in addition to diet and exercise) with or without metformin. There was no evidence to inform the threshold for starting with pharmacological treatment but we felt that it was reasonable to use a fasting blood glucose value of 7.0 mmol/litre as this the threshold for the diagnosis of diabetes.
Diabetes UK	17	NICE	1.3.4	25	Why does home ketone testing apply to women with gestational diabetes and Type 2 diabetes? Given cost implications and education resources, is this required for all women with diabetes? Should we limit home ketone testing to women with Type 1 diabetes, and then do hospital testing for all women when they present with hyperglycaemia and unwell as in 1.3.6?	Thank you for your comment. Amendments to this recommendation and the next recommendation (now recommendations 1.3.20 and 1.3.21) were made in line with your comment following consultation. Recommendation 1.3.20 restricts use of blood ketone testing strips and meters for ketonaemia testing to pregnant women with

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						type 1 diabetes. In recommendation 1.3.21, pregnant women with type 2 diabetes or gestational diabetes are advised to seek urgent medical advice if they become hyperglycaemic or unwell, but home testing for ketonaemia is not recommended for these groups of women. The final recommendation (1.3.22) is that women with any form of diabetes who is hyperglycaemic or unwell should be tested for ketonaemia.
Diabetes UK	18	NICE	1.3.8	26	For practicalities, should we align treatment targets for fasting blood glucose levels to the cut-off for diagnosing gestational diabetes? That way, there is one less fasting target to remember?	Thank you for your comment. However, the glucose targets recommended for a) the diagnosis of gestational diabetes and b) the management of women with any form of diabetes were based on very clear evidence for each, which we used as the basis of our recommendations.
Diabetes UK	19	NICE	1.3.9	26	HbA1c is an important test to detect adherence issues even when unexpected in those with pre-gestational diabetes; it also helps audit and service development. We would recommend HbA1c each trimester in women with pre-existing diabetes	Several stakeholders raised similar concerns so we re-discussed the evidence in the draft guidance. CEMACH data were sought for inclusion in the guideline early in development but were not available in the public domain. The GDG were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was nonetheless a marker of risk of adverse outcome and

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						could be of value in practice for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome. In the light of these considerations the GDG decided to amend their recommendations (1.3.7 to 1.3.11) to reflect their conclusions that HbA1c should not be used in a diabetic pregnancy to assess glucose control, however, it should be used in specific circumstances to assess the risk in those pregnancies with 48mmol/mol (6.5%) as a threshold.
Diabetes UK	20	NICE	1.3.11	26	There is some benefit to do this as it encourages people to consider the risk of undiagnosed Type 2 diabetes. Given that, there is very little longitudinal data on HbA1c changes during pregnancy how would 'abnormal' HbA1c result affect follow-up of such women? Does abnormal result preclude the need for post-partum confirmation of the diagnosis?	Thank you for your comment. However, whilst we felt that women with a high HbA1c at the time of diagnosis of presumed gestational diabetes in pregnancy may actually have type 2 diabetes previously unrecognised, the evidence relating to the postnatal testing of women with gestational diabetes did not distinguish this subgroup thus we did not feel that they could make a separate recommendation. However, we recommend that women with gestational diabetes continue with pre- and post-prandial glucose monitoring immediately after delivery to identify those who in fact did not have 'true' gestational diabetes but actually had pre-existing type 2 diabetes. The former would become euglycaemic

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						after birth and the latter would not. Those who persisted with glucose intolerance after birth would be referred for ongoing care by the diabetes team.
Diabetes UK	21	NICE	1.3.17	27	Should the statement read 'without the risk of significant disabling hypoglycaemia'? Also, should this be considered as a recommendation for preconception care planning?	Thank you for your comments. However, this is a recommendation from the 2008 version of the guideline and this section was not updated. Therefore we are unable to change the recommendation.
Diabetes UK	22	NICE	1.3.24	29	Why is there emphasis on last 12 months? Should screening be offered as soon as possible for every women or may be say those who have not had screening for the last 3months. By using 12month, we risk women who may have had their last screening 11month prior to booking having to go beyond 12 months without screening.	Thank you for your comment. This was discussed following consultation and amendments have been made to Table 1 and to the corresponding recommendation 1.3.24 to address your concern.
Diabetes UK	23	NICE	1.4.5	33	Given the lower fasting glucose cut-off for gestational diabetes diagnosis, the incidence of gestational diabetes is likely to increase significantly. This could have big implications for C-section rates given the approximately 25% failure of induction of labour. Does this recommendation apply to all gestational diabetes cases i.e. even those who are diet controlled? Is there evidence base for this?	Thank you for your comment. In the light of this the GDG have reconsidered the recommendation about timing of birth. The GDG felt that the evidence justified making separate guidance regarding timing of birth for women with type 1 or type 2 diabetes and for women with gestational diabetes.
Diabetes UK	24	NICE	1.4.11	34	Should the consideration for intravenous dextrose and insulin infusion during labour be extended to women with Type 2 diabetes on insulin and women with gestational diabetes on >40iu /24 hours?	Thank you for your comment. Recommendation 1.4.12 addresses the circumstance when an IV dextrose and insulin should be used in women with type 2 or gestational diabetes.
Diabetes UK	25	NICE	1.6.6	37	We should highlight the exception where women may not be suitable for	Thanks you for your comment. However, this section of the guideline was not

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					routine diabetes care arrangement e.g. • If planning further pregnancies within 12 months or • if there are problems with insulin management during breastfeeding; this may require close liaison with midwifery services	prioritised for review in this guideline update during scoping.
Diabetes UK	26	NICE	1.6.11	37	Does waiting for 13 weeks represent enough time to check the HbA1c if this is to be used as diagnostic criteria? Given that, most pregnancy induced hypervolaemia is eliminated in first two weeks with full return to normal circulatory volume by 6 weeks, should this cut-off be longer than 13 weeks? The recommendation regarding not routinely using OGTT sounds very reasonable for women who are not going to have future pregnancies (eg those with tubal ligation or who are adamant they will have no more and will use long acting contraception). However, for women who are likely to have further pregnancies potentially with undiagnosed diabetes, this may pose an unacceptable risk. There should be a section here that says OGTT for women who are planning, or are likely to have, future pregnancies. Any health economic modelling over this decision making should include the risk of malformations and their management. In the meantime, OGTT should be offered. If women decide not to attend for OGTT, then this is their choice and other opportunistic testing can be used. Studies showing reduced attendance for OGTT should not be a reason to withdraw this option to	Thank you for your comment. The recommendation was discussed and amended following consultation. The GDG noted that the evidence demonstrated that a fasting blood glucose was a better test for identifying women at risk of diabetes postnatally and recommended that this test be performed at any time between 6-13 weeks. In order to pragmatic and give women options, an HbA1c test was also recommended if the women had opted not to undergo a fasting test within 13 week post-pregnancy period. The evidence demonstrated that an HbA1c taken between 6-13 weeks after birth did identify some women with type 2 diabetes (as you suggest), but delaying the test until 13 weeks avoided the theoretical possibility that an earlier test may actually reflect hyperglycaemia present in the gestational diabetes pregnancy. The recommendation for a FPG test rather than 75g OGTT was made on a careful review of the data comparing their diagnostic accuracy for the detection of type 2 diabetes postpartum and was not based not on the uptake rates of the test.

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					women who might get pregnant again.	Recommendation 1.6.14 confirms that all women with gestational diabetes who have a negative postnatal test for diabetes, should have an annual HbA1c test and recommendation 1.6.15 confirms that women who have been diagnosed with gestational diabetes, should be offered early self-monitoring of blood glucose or an early OGTT in future pregnancies. Further, recommendations 1.1.2, 1.1.7, 1.1.12, 1.1.18 – 1.1.20 address the risk of congenital malformations during pregnancy, prior to conception. Hence, although no health economic modelling incorporating the risk of malformations and their management was performed, the GDG felt that these recommendations would cover women having subsequent pregnancies without the need for an OGTT to be performed.
Diabetes UK	27	NICE	1.6.13	38	The use of 39 – 47 mmo/ mol is not consistent with other guideline (e.g. Type 2 diabetes prevention guidelines) which uses 42 – 47mmol/mol to indicate high risk.	Thank you for your comment. We were aware that in 2011 the WHO recommended an HbA1c diagnostic threshold for type 2 diabetes should be 48 mmol/mol (is 6.5%). However, the WHO did not provide specific guidance on HbA1c criteria for people at increased risk of Type 2 diabetes. We noted that a report from a UK expert advisory group on the implementation of WHO guidance recommended using HbA1c values between 42-47 mmol/mol (6.0-6.4%) to indicate that a person was at high risk of type 2 diabetes. Importantly, that expert group did recognise that there is a continuum of risk across a range of

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						subdiabetic HbA1c levels and that people with an HbA1c below 42 mmol/mol (6.0%) may also be at risk (John 2012). Given this acknowledgement that lower values than 42 mmol/mol (6.0%) were indicative of risk and the finding in the review undertaken for this question that 39 mmol/mol (5.7%) was associated with a positive likelihood ratio of 11.23 for the diagnosis of diabetes ('a very useful test') we felt that in the first three months postpartum a lower value of 39 mmol/mol (5.7%) would represent a more useful threshold for screening and was based on evidence.
Eli Lilly and Company	1	NICE	General	General	Thank you for the opportunity to comment on the draft guideline. We have no specific comments regarding your provisional recommendations at this time.	Thank you for your comment.
Gloucestershire Hospitals NHS Foundation Trust	2	Full	General	General	Need to provide guidance re location and pre-conceptual care. ? Primary care or something we really have to set up in secondary care. If so how do we access. Advice on this would be helpful	Thank you for your comment. However, this section of the guideline was not prioritised for review during scoping.
Gloucestershire Hospitals NHS Foundation Trust	3	Full	General	General	Increasing workload ++	Thank you for your comment. We assume you are referring to the likely increase in workload associated with the greater number of women diagnosed as having gestational diabetes using the new criteria. However, the very detailed health economic analysis undertaken for that question takes on board workload in setting the criteria for gestational diabetes and concluded that it is cost effective (see below). Apart from the probable increase in gestational diabetes numbers the number of other diabetics and

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						associated workload should be unchanged. NICE's explicit remit is to consider cost-effectiveness and it is acceptable for the GDG to make recommendations which will generate extra workload on the basis that this would represent a cost-effective use of scarce NHS resources. However, notwithstanding this we are sympathetic to your concern and we accept that a lower fasting cut-off than in the 2008 guideline will lead to more cases being diagnosed. However, we are not sure that this lower threshold will lead to a huge extra workload. The issue is explored in Section 9.2.3.1 of the consultation version of the guideline and in Figure 6 in particular. Although, there was considerable variation across the patient datasets the increase in women diagnosed with 5.6/7.8 compared with 7.0/7.8 across all datasets was 15%. This may overstate any increase in workload in practice also as the GDG were of the strong opinion that many centres use a lower fasting threshold than that recommended in the 2008 guideline. Furthermore, the increase in workload is not as marked as if the even lower IADPSG fasting criteria were adopted.
Gloucestershire Hospitals NHS Foundation Trust	1	Full	2.1.3	75	Spelling of Glibenclamide is incorrect	Thank you for your comment. This has been corrected.
King's College	1	NICE	Post natal care of	13	The post-pregnancy check in women with GDM: a. In women from the black	Thank you for your comments.

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Hospital			GDM	of 58	community, GDM is commonly diagnosed on the post-glucose load glucose and their need for therapy in pregnancy is entirely related to controlling post-prandial glucose, with normal fasting glucose control. For women whose problem is unequivocally post-partum, we should be checking post pregnancy with a challenge, not a fasting, test b. At six weeks, women are still close to the tight metabolic control of pregnancy and in many cases actively breast feeding, both features which will provide relatively short-duration improvement in glucose control. The six-week scheduling of the test dates from the days of a 6 week post natal baby check in hospital and there seems no reason not to delay to 3 months now that these checks are not done. The 13 week time slot seems much more likely to avoid false negatives, or positive, results c. The annual HbA1c check in women with a history of GDM is very welcome but would it not also be sensible to include an HbA1c at the start of planning the next pregnancy and at first reporting of a new	a) Post-glucose load testing: No evidence was submitted to support your statement about the need for this to be the approach used in certain ethnic minority communities. There was no evidence of the value of this test in the guideline review. The only evidence that was identified related to fasting blood glucose or HbA1c. Hence the recommendations advocate one or other of these two tests to identify the women at risk of diabetes. b) Timing of the test: the evidence presented clearly demonstrated that some women develop type 2 diabetes within the first three months after birth. Thus, testing at some point in that period is prudent. In the majority of the studies, the number of women receiving a postnatal test was much lower than the number of women who were eligible to participate. Hence we recognise that the compliance of women with postnatal testing is not great but we felt that uptake might be improved by offering the choice of tests (fasting blood glucose or HbA1c) and some flexibility regarding the timing of the fasting glucose test (6-13 weeks). c) HbA1c testing when planning a pregnancy and at the start of a pregnancy: we feel that provided the woman with a history of gestational diabetes has her HbA1c tested every year, there is little benefit in rechecking if she starts to plan for another pregnancy. This conclusion if

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					pregnancy?	supported by the fact that if she were to get pregnant, the guideline recommends that she either commences self-monitoring or has a 75g OGTT to rule out a recurrence when she presents in the next pregnancy.
King's College Hospital	3	NICE	1.1.23	19	Is there not evidence showing lack of increase in adverse events with insulin detemir? If the GDG wish to caution against detemir, a statement suggesting women who cannot achieve stable background insulin replacement with NPH insulins should be offered insulin pump therapy (CSII) by a centre that has experience in CSII support.	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to the recommendation that states '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'.
King's College Hospital	2	NICE	1.1.3	20	Should not this advice also include risk of congenital abnormality related to high HbA1c at conception?	Thank you for your comment. Whilst this 2008 recommendation has not been updated, recommendation 1.1.2 in the NICE guideline addresses this point.
King's College Hospital	4	NICE	1.2.17 and 1.2.20	24	Advice on fasting plasma glucose concentrations alone should be supplemented by advice for 2 hr and post-prandial glucose concentrations as many women from the British Black community have solely post-prandial	Thank you for your comments. However, we did not feel we could make any change to the recommendations for three reasons: a) no evidence was submitted to support your statement about the pattern of

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					hyperglycaemia.	hyperglycaemia in the black diabetic population; b) we did not find any evidence of determining the best starting therapeutic interventions in this subpopulation on the basis of the 2 hour post-prandial values, and, c) we felt that post-prandial values were more amenable to dietary intervention (which all women should be following) rather than pharmacological intervention.
King's College Hospital	5	NICE	1.3.8	26	It is essential to offer women lower limits to a desirable glucose concentration range. We would suggest a lower limit plasma glucose of 3.6 mmol/l for pre-prandial and 4 mmol/l for post-meal. We have had very good results using the Jovanovic targets of 3.6 – 5.5vmmol/l pre meal and 4 – 7 mmol/l one hour post meal but we are aware that there are no RCT data to support these values over the ones you have chosen. It is however important to remember that targets and achieved glucose concentrations are not the same and the latter tend to be higher than the former.	Thank you for your comments. In making recommendations about target values for women with diabetes in pregnancy, the GDG were inclined to use those values for which the evidence showed some benefit. Accordingly, from the evidence they suggested that the following would be reasonable targets: Fasting level = less than 5.3 or 5.6 mmol/litre (Rowan et al reported a lower incidence of pre-eclampsia and LGA with a target threshold of 5.3 mmol/litre. However, Farrag, reported a higher incidence of maternal hypoglycaemic episodes with a target threshold of 5.6 mmol/litre) 1 hour value = or less than 7.8 mmol/litre (Combs et al in a study of women who largely measured the 1 hour values reported a lower incidence of LGA with a target threshold of 7.8 mmol/litre.) 2 hour value = less than 6.4 mmol/litre (Rowan et al reported a lower incidence of pre-eclampsia and LGA with a target threshold of 6.4 mmol/litre.) Regarding setting a lower level blood glucose level, ideally, women should strive for blood glucose levels as near to normal

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						as is safely achievable. For women taking insulin and glibenclamide inevitably this be associated with a risk of hypoglycaemia and the GDG felt that it would be sensible to provide a limit for the lower level of blood glucose for women on these treatments. However, there was no evidence identified in the review that could inform the GDG. Thus, they chose 4.0 mmol/litre because this was the 'safe' lower target value recommended by Diabetes UK. For women on diet and exercise or metformin the risk of hypoglycaemia was very low and the GDG did not feel that it was necessary to set a lower limit for women on these treatments. The GDG amended their recommendations about the lower glucose target in view of these comments.
King's College Hospital	6	NICE	1.3.12	27	We would like to see inclusion of HbA1c as an audit tool and also as a check on home blood glucose measurements, acknowledging that (a) some women do not achieve accurate reporting of sufficient test results and (b) glycation rate may be important and varies among individuals. We recommend once a trimester.	Thank you for your comment. Several stakeholders raised similar concerns so we re-discussed the evidence in the draft guidance. We acknowledge that it is difficult to conduct a study that would determine target values for HbA1c. However, the GDG were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was nonetheless a marker of risk of adverse

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						outcome and could be of value in practice for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome. In the light of these considerations the GDG decided to amend their recommendations to reflect their conclusions that HbA1c should not be used in a diabetic pregnancy to assess glucose control, however, it should be used in specific circumstances to assess the risk in those pregnancies with 48mmol/mol (6.5%) as a threshold.
King's College Hospital	7	NICE	1.4 intrapartum care	32	Again we are aware of a dearth of RCT data for this, but it is our practice to intensify fetal monitoring (usually with an admission) in women using insulin when there is an unexplained progressive reduction in insulin requirements below 10%, especially if accompanied by hypoglycaemia not responsive to insulin dose reduction on the basis that placental function has driven increased insulin requirement and if there is a premature excessive reduction in insulin requirement this is therefore compatible with a decline in placental function. Our monitoring comprises clinical assessment, repeat u/s with Doppler measurements and 3 daily CTG recordings with regular review by the MDT	Thank you for your comment. However, as you acknowledge, there is dearth of good quality evidence in connection with intrapartum management of women with diabetes. Thus the GDG were reluctant to make recommendations that were not based on some evidence. They found no evidence of the link between falling insulin and adverse pregnancy outcome.

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King's College Hospital	8	NICE	1.4.10	33	We welcome this but would appreciate guidance on action to be taken if the limits set are exceeded. Our policy is to use variable rate insulin infusion in addition to pre-meal subcutaneous insulin if the woman is still eating, or a glucose and intravenous insulin infusion if she is in established labour and/or we have advised her not to eat.	Thank you for your comment. This point is addressed in recommendation 1.4.12.
King's College Hospital	9	NICE	1.6 Postnatal Care	36	Would the GDG recommend a schedule of monitoring of plasma glucose in GDM women post-partum?	Thank you for your comment. However, this topic was not prioritised for review in this guideline update during scoping.
King's College Hospital	10	NICE	1.6.11	38	Please may we refer to our request above that for women whose hyperglycaemia in pregnancy was exclusively or predominantly post-prandial, an OGTT is offered at 3 months?	Thank your for your comment. No evidence was submitted to support your view that an OGTT should be offered to women with largely postprandial hyperglycaemia in pregnancy. In the evidence review for postnatal testing there was no subanalysis for this group. The evidence that was identified related to fasting blood glucose or HbA1c, thus the GDG felt they could only make recommendations using these tests.
MacDonald Obstetric Medicine Society	5	NICE	Table 1	12	The guidance about retinal screening is not clear. It states that retinal screening should be arranged at booking if this has not been undertaken in the previous 12 months and then at 16–20 weeks to women with pre-existing diabetes if diabetic retinopathy was present at their first antenatal clinic visit. It is not clear when women who have recently been screened in the previous year prior to pregnancy should	Thank you for your comment. This was discussed following consultation and amendments have been made to Table 1 and to the corresponding recommendation 1.3.24 to address your concern.

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					be first screened in pregnancy. Similarly the guidance reads as though women who were found to have retinopathy during the first and second trimester should not be offered screening in the 3rd trimester. · In the last guidance, we recommended screening in the 1st and 3rd trimester with an additional screen in the 2ndtrimester if retinopathy was present in the 1st trimester. This still seems appropriate and appears to be the intention of the GDG (recommendation 1.3.23 and 24) but the wording in the table does not seem to reflect this.	
MacDonald Obstetric Medicine Society	6	NICE	Ultrasound scanning	12	While it is common practice to offer growth scans at 28, 32 and 36 weeks, the value of the 32 week scan has not been justified as it is unclear how this changes clinical practice. This requires careful balance especially with ultrasound capacity related issues.	Thank you for your comment. However, this topic was not prioritised for review in this guideline update during scoping.
MacDonald Obstetric Medicine Society	7	NICE	Table 1	13	Should tests of well-being be offered to all women irrespective of type of diabetes and treatment required -- again statements to this effect should be balanced unless there is clear evidence to support.	Thank you for your comment. However, whilst this topic was not prioritised for review in this guideline update, the section addressing this in the original version of the guideline found that there was not sufficient evidence to make separate recommendations about type of diabetes and/or treatment required.
MacDonald Obstetric Medicine Society	8	NICE	Timing of delivery:	13	again we are not convinced that there is sufficient data to make clear statement about delivery at 40 weeks for all women with GDM . This has significant implications for practical	Thank you for your comment. We reconsidered the recommendation about timing of birth in response to stakeholder comments.

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					management and without clear evidence of benefit we would suggest a different statement here. As glucose is a continuous variable, this seems a bit excessive for a woman who has, for example, an isolated elevated glucose during the OGTT who maintains normoglycaemia and fetal growth through lifestyle alone, especially with the reducing threshold for diagnosis. Surely some clinical judgement is needed here, particularly given the poor quality of the evidence	We felt that the evidence justified making separate recommendations for the timing of birth for women with type 1 or type 2 diabetes and for women with gestational diabetes. For women with gestational diabetes, the data from Rosenstein (2012) demonstrated that there was a significant rise in stillbirth rate after 40+6 days. Whereas the Kjos (1993) study showed that the incidence of babies weight more than 4000g rose after 39+6 days. Given that avoidance of stillbirth was the philosophy underpinning the timing of delivery, the GDG felt that in women with uncomplicated gestational diabetes elective delivery could be delayed until 40+6 days. For women with type 1 or type 2 diabetes the limited data demonstrated that the stillbirth rate rose after 38+6 weeks. Thus such women should be offered elective delivery by 38+6 weeks. We felt that a lower limit should be also included in the recommendation to avoid women with uncomplicated type 1 or type 2 diabetes being advised to have an elective preterm delivery with its associated complications for the woman (such as failed induction of labour and caesarean section) and the baby (such as respiratory distress syndrome and admission to the neonatal unit). The data from Holman (2014) suggested the lower limit of the elective delivery should be 37+0 weeks. Thus we

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						recommended elective delivery for women with uncomplicated type 1 or type 2 diabetes between 37+0 and 38+6 weeks. In making this recommendation, we expect that, in practice, this would result in such women being routinely offered elective delivery nearer 38+6 weeks than 37+0 weeks.
MacDonald Obstetric Medicine Society	1	NICE	Pre-conception glucose targets:	17	The 2008 guidelines were criticised for its stringent glucose targets and the latest values are more pragmatic. Nevertheless, where women (particularly those with T2DM) can achieve lower HbA1c, this could still be of benefit.	Thank you for your comments. The glucose targets are based on the best available evidence. Nevertheless, we believe they are less stringent than those in the original guideline. The targets apply to women with any type of diabetes. Finally, though the recommended HbA1c target is 48mmol/mol there is a separate recommendation which states that reducing HbA1c values towards that target is beneficial.
MacDonald Obstetric Medicine Society	2	NICE	Diagnosis of GDM	21	This is a particularly thorny issue and we think that the proposed guidelines provide a welcome compromise between the current guidance and the IADPSG.	Thank you for your comment.
MacDonald Obstetric Medicine Society	4	NICE	Diabetic ketoacidosis	25	We accept that occasionally women with other types of diabetes may develop DKA and so this seems a reasonable change.	Thank you for your comment.
MacDonald Obstetric Medicine Society	3	NICE	Antenatal glucose targets	26	These seem appropriate but will increase need for pharmacological treatment. Increasing the lower range of FBG to 4 mmol/L will fit better with targets outside pregnancy and will reduce hypoglycaemia	Thank you for your comment
MacDonald Obstetric Medicine Society	9	NICE	1.3.10 and 1.3.11:	26	Note typo for HbA1c	Thank you for your comment. This has been corrected.

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MacDonald Obstetric Medicine Society	10	NICE	1.3.26	29	Should this guidance also include the terms used by the national screening programme, e.g. R2, R3, M1?	Thank you for your comment. This recommendation was not prioritised for review or amendment (using the national screening programme terms suggested) in the guideline update. We do not believe that the wording contradicts the national screening programme.
MacDonald Obstetric Medicine Society	11	NICE	1.6.12	38	In the last bullet point, HbA1c should only be used if the woman is more than 13 weeks postnatal.	Thank you for your comment. However, this recommendation was revised following consultation and no longer makes reference to HbA1c testing in the final bullet point.
MacDonald Obstetric Medicine Society	12	NICE	1.6.13	38	The HBA1c values used in this section seem to be out of keeping with NICE guidance PH38 (Preventing type 2 diabetes: risk identification and interventions for individuals at high risk). Based on the studies cited in the guidance, this does not seem justified and might lead to confusion. Suggest harmonising the values.	Thank you for your comment. We were aware that in 2011 the WHO recommended an HbA1c diagnostic threshold for type 2 diabetes should be 48 mmol/mol (is 6.5%). However, the WHO did not provide specific guidance on HbA1c criteria for people at increased risk of Type 2 diabetes. We noted that a report from a UK expert advisory group on the implementation of WHO guidance recommended using HbA1c values between 42-47 mmol/mol (6.0-6.4%) to indicate that a person was at high risk of type 2 diabetes. Importantly, that expert group did recognise that there is a continuum of risk across a range of subdiabetic HbA1c levels and that people with an HbA1c below 42 mmol/mol (6.0%) may also be at risk (John 2012). Given this acknowledgement that lower values than 42 mmol/mol (6.0%) were indicative of risk and the finding in the review undertaken for this question that 39 mmol/mol (5.7%) was associated with a positive likelihood ratio of 11.23 for the diagnosis of diabetes ('a very useful test') we felt that in the first three

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						months postpartum a lower value of 39 mmol/mol (5.7%) would represent a more useful threshold for screening and was based on evidence.
Medtronic	1	Full	5.5.11	31	Nocturnal Hypoglycemia can affect glucose variability throughout the day. This has been shown in a study by Scott where he has used functional data analysis to show that circadian variation in glucose is associated with the development of macrosomia in diabetic pregnancy. The functional regression model showed that glucose levels are associated with macrosomia with 95%CI. The author concludes that these results confirm established evidence that postprandial hyperglycaemia during the day is associated with macrosomia, but gives novel information about the contribution of nocturnal glucose control and suggests that relative hypo-glycemia has an important role to play. (Scott 2014) IQWIG has confirmed this year in a meta-analysis that CGM allows more patients with T1DM to reach target levels below 7%, thus that hyperglycaemia can be reduced more efficiently compared to SMBG. There is no reason to believe that this does not pertain also to women from preconception and throughout pregnancy with DMT1 (Geelhood Oct 2013, The Netherland Journal of Medicine, Vol 72 No7).	Thank you for your comment. The contribution of circadian variation in the development of adverse outcomes (such as macrosomia) was not prioritised for review in this guideline and hence the Scott 2014 paper suggested would not be eligible for inclusion. We were unable to source the Dutch paper by Geelhood 2013 paper to assess its eligibility for inclusion to the guideline. Whilst we all agree that hypoglycaemia (at any time of day) carries risk but on the basis of the currently available evidence, CGM is not the answer. However, that research was limited and thus the further research was recommended.
Medtronic	2	Full	5.5.11	32	The most important aspect of care during pregnancy is the establishment and maintenance of tight glucose control. In pregnancy, the achievement of this goal, entails	Thank you for your comment. The review from which this research recommendation comes, addressed the value of CGM vs IGM and found no benefit. We all agree that

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					risk for severe maternal hypoglycaemia. More than 80% of the severe 2-hour events <60mg/dl occur at night. (Ly 2012). These prolonged nocturnal hypoglycemic events are dangerous for the pregnant women and her baby. Severe Hypoglycemia occurs in up to 40% of women with type 1 diabetes. Hypoglycemic coma occurs in about 20% of women with type 1diabetes, with maternal death in about 1 in 500. Women with hypoglycemic events before pregnancy and those with the lowest HbA1C values are at highest risk. Case reports on the effect of maternal hypoglycemia on the condition of the fetus are conflicting. On one hand hypoglycemia does not impose significant teratogenic effects in a human fetus but severe and prolonged hypoglycemia leading to coma has been described to effect the fetus with initial fetal tachycardia and later on fetal bradycardia and reduced fetal movements. (Rosenn B, 2000, Kimmerle R1992, Rayburn W, 1986, Rosenn BM 1995, Evers IM 2002, Ter Braak EW 2002) Klonoff confirmed in a posthoc analysis of the Aspire data published by Bergenstal, that the Low Glucose Insulin Suspend (LGS) feature was associated with a lower risk of nocturnal hypoglycemic events in patients with type 1 diabetes and pre-bedtime sensor glucose values <200 mg/dL,. Bergenstal also showed that LGS can reduce	hypoglycaemia (at any time of day) carries risk but on the basis of the currently available evidence, CGM is not the answer. However, that research was limited and thus the further research was recommended.

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					the duration patients spend in nocturnal hypoglycemia < 70mg/dl by 37.5% compared to the control group (P<0.001); the duration of blood glucose levels <50mg/dl was reduced by 57% (Bergenstal N Engl J Med. 2013) And the rate of events with glucose levels <50mg/dl and lasting more than 120 min has been reduced by 74% using LGS (Weinstock ADA 2014 form ASPIRE) vs no LGS. Therefore it may be unethical to authorise further studies in such a delicate population who are at high risk of hypos in a randomised setting. Pregnancy outcomes achieved with CGM could be captured in the next national audit.	
Medtronic	3	Full	5.5.10	78 77	Currently 24 hours technical support is provided by law for patients using CGM technology by the manufacturer. This is a mandatory service and reduces the burden on the NHS. 24h availability of a Diabetologist should be provided for all pregnant women with type 1 regardless of the technology they use for insulin delivery. CGM with LGS feature improves safety for pregnant women with type 1 diabetes as it reduces HbA1c without increasing the risk of hypos, We therefore feel that 24h support from a diabetologist should not be indicated as a mandatory requirement for women that are using CGM only.	Thank you for your comment. We discussed the recommendation and agreed that whilst the provision of support was essential for women using CGM from someone who was expert in its use, it was not necessary to stipulate that this had to be 24h support from a diabetologist. The recommendation has been amended accordingly.
Merck Sharp & Dohme UK Ltd	1	NICE	General	General	MSD appreciates the opportunity to comment on the draft guideline diabetes in pregnancy. I can confirm that we have no comments.	Thank you for your comment.
National Diabetes	2	NICE	General	General	Why are HbA1c results in % still being included in guidance when laboratory HbA1c results are	Thank you for your comment. Both units are specified in accordance with agreed

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Nurse Consultant Group				and P18	only reported in mmol/mol and have been since October 2011. And all HCP should be using and discussing HbA1c results in mmol/mol	presentational styles used in all NICE diabetes guidelines currently in development.
National Diabetes Nurse Consultant Group	1	NICE	1.3.8	26	There is no mention of advice for insulin treated women re. driving. This could be included along with the some information on the risk of losing hypo warning signs as the blood glucose post 2 hour targets have been lowered in the new guidance	Thanks you for your comment. This is addressed in section 6.4 of the Full Guideline. Though this section has not been formally updated there are links there to the relevant government websites where the appropriate guidance for women with diabetes can be found. The following website has been added: https://www.gov.uk/diabetes-driving
Newcastle upon Tyne NHS Hospitals Trust	4	NICE Full	General	General	The text throughout and the Table recommend that eyes and renal status are checked at booking if not done within the preceding 12 months. Yet at 16 weeks, there is a recommendation to rescreen eyes if abnormal at booking. This is all very confusing, and at times the guidance seems contradictory. It also risks some women having had retinal screening 11 months pre booking not having their eyes checked until 28 weeks. It would be much clearer and simpler to be pragmatic and advise that all women should be offered retinal screening at booking, unless done within say the previous 3 months. The same comments apply to measurements of renal function (urine albumin excretion and serum creatinine).	Thank you for your comment. The suggested amendment has been made to the retinal assessment recommendation 1.3.24. However, no amendment has been made to the renal assessment recommendation 1.3.28.
Newcastle upon Tyne NHS Hospitals Trust	5	NICE	Table 1	13	Reading this in isolation implies that women should be delivered at 37 weeks. It is only later in the guidance that it becomes clear that this is not what is being advised. The statement needs to be re-worded to something such as : "discuss/arrange IOL/C/S at 37 – 38+6 weeks".	Thank you for your comment. We agree and have amended the recommendation as you suggest for greater clarity.
Newcastle	1	NICE	1.1.17	18	Until we know what the new Type 1 guideline	Thank you for your comment. The new

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upon Tyne NHS Hospitals Trust					recommends this is not helpful. We very much doubt that the type 1 guideline will recommend an HbA1c target of <48 mmol/mol as suggested here, so that capillary glucose targets pre-pregnancy should be correspondingly lower.	recommended targets in the consultation draft of the updated NICE clinical guidance 15 'Type 1 diabetes: the diagnosis and management of type 1 diabetes in include 'a fasting plasma glucose level of 5-7 mmol/litre on waking and a plasma plasma glucose level of 4-7 mmol/litre before meals at other times of the day.' In addition, the Type 1 diabetes guidance recommends aiming for a target HbA1c level of 48 mmol/mol (6.5%) or lower. We felt these targets were sufficiently stringent for women planning to become pregnant. The consultation draft of the updated NICE CG 15 is available from the NICE website http://www.nice.org.uk/guidance/indevelopment/gid-cgwaver122/consultation Consultation closes at 5pm on 4 March 2015
Newcastle upon Tyne NHS Hospitals Trust	7	NICE	1.1.23	19	We are extremely surprised that this recommendation has not been updated, and does not contain any discussion of the risks and benefits of continuing long-acting analogues. The evidence for the safety of short-acting analogues (which are recommended) is in our opinion no stronger than for long-acting analogue insulins. Many women with type 1 diabetes will be taking long-acting analogues pre-conception, a substantial number because of problematic nocturnal hypoglycaemia on isophane insulin. Whilst they could switch to isophane pre-pregnancy, on the theoretical risk that analogues are harmful, they would then loose the benefits of lower rates of nocturnal hypoglycaemia, at a time when they are aiming	Thank you for your comment, Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to the recommendation that states '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

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					for tight glucose control with its associated increased risk of hypoglycaemia. For most women planning pregnancy, the risks of hypoglycaemia are very real and a barrier to tight glucose control, and outweigh a theoretical risk of unknown problems with long-acting analogues. For those women who have not had pre-pregnancy care, we would need to discuss switching insulin at first contact, probably during very early pregnancy. This would run the risk of an acute deterioration in glucose control during the change-over period, at a time when tight control is absolutely critical. We would strongly suggest that the guideline is modified to include a risk-benefit discussion and that long-acting analogues are not prohibited for women with type 1 diabetes. We accept that for type 2 diabetes and for gestational diabetes the place of long acting analogues is very limited.	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'.
Newcastle upon Tyne NHS Hospitals Trust	2	NICE	1.2.8	23	Whilst we accept the scientific rationale for this, it must be recognised that lowering the fasting cut-off will generate a huge extra workload for an already very stressed system. Extra resources will be required to meet.	Thank you for this comment. NICE's remit is to consider the clinical and cost-effectiveness of its recommendations and it is acceptable for the GDG to make recommendations which could generate extra workload provided that this would represent a cost-effective use of scarce NHS resources. Notwithstanding this, we are sympathetic to your concern and accept that a lower fasting cut-off than was in the 2008 guideline will lead to more cases being diagnosed. The issue is explored in Section 9.2.3.1 and figure 6 of the full guideline. Although, there was considerable variation across the patient datasets, the increase in women diagnosed

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						with 5.6/7.8 compared with 7.0/7.8 across all datasets was 15%. This may overstate any increase in workload for the NHS in practice also as we are aware of many centres that use a lower fasting threshold than that recommended in the 2008 guideline. Furthermore, the increase in workload is not as marked as if the even lower IADPSG fasting criteria were adopted.
Newcastle upon Tyne NHS Hospitals Trust	8	NICE	1.3.4	25	We would strongly support this recommendation for all women with type 1 diabetes and possibly for women with type 2 diabetes on insulin. However, we do not believe that it is cost-effective to provide all pregnant women with diabetes a blood ketone meter. It risks generating needless worry and confusion in the women. The advice to check blood ketones in all women during intercurrent illness is very appropriate.	Thank you for your comment. Amendments to this recommendation and the next recommendation (now recommendations 1.3.20 and 1.3.21) were made in line with your comment following consultation. Recommendation 1.3.20 restricts use of blood ketone testing strips and meters for ketonaemia testing to pregnant women with type 1 diabetes. In recommendation 1.3.21, pregnant women with type 2 diabetes or gestational diabetes are advised to seek urgent medical advice if they become hyperglycaemic or unwell, but home testing for ketonaemia is not recommended for these groups of women. The final recommendation (1.3.22) is that women with any form of diabetes who is hyperglycaemic or unwell should be tested for ketonaemia.
Newcastle upon Tyne NHS Hospitals Trust	3	NICE	1.3.8	26	Why set the fasting glucose target at <5.3 mmol/l, rather than at the diagnostic cut off of 5.6 mmol/l? This will simply confuse women and health care professionals. It would be much better to have the same level for diagnosis and treatment target Why give a 2 h target here? All the other	Thank you for your comments. However, these values are determined by the evidence. The diagnostic criteria were determined on the basis of the Health Economic analysis using over 6000 women from the HAPO dataset. The target values were taken from the studies reporting on

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					recommendations in the guideline stick with a one hour glucose target. It is unrealistic to ask women to do both 1h and 2 h glucose measurements.	the relationship between blood glucose values and adverse outcomes. We agree that it would be unrealistic to expect women to test their postprandial glucose twice. The 1 h and 2h targets are presented to provide flexibility as to when women can measure postprandial blood glucose. In response to your comment, we have amended the presentation of the recommendation for clarity.
Newcastle upon Tyne NHS Hospitals Trust	6	NICE	1.6.11	38	The draft guideline acknowledges that attendance for post-natal OGTT is <50 %. We suspect that attendance for a fasting glucose sample, with or without an OGTT thereafter, will also be low. National recommendations are to move away from glucose measurements to using HbA1c as the screening test of choice for Type 2 diabetes in all other screening situations. Thus is seems appropriate to recommend HbA1c post-natally too. Offering an HbA1c test, which can be done non-fasting and at any time of day, will likely be accepted by far more women than fasting glucose. Other guidelines also suggest that we can use HbA1c to stratify risk – low risk of current diabetes, intermediate risk and high risk – and there is no reason why we cannot do the same post-natally. However, the cut-offs suggested in the draft guidance are the US cut-offs, and not those recommended by the UK expert committee: <42 mmol/mol – low current risk; 42-47 mmol/mol – intermediate risk; ≥48 mmol/mol – probable diabetes (Diabetic Medicine 2012,29:1350-1357). We strongly suggest using these cut-offs, to avoid wholesale confusion.	Thank you for your comment. We were aware that in 2011 the WHO recommended an HbA1c diagnostic threshold for type 2 diabetes should be 48 mmol/mol (is 6.5%). However, the WHO did not provide specific guidance on HbA1c criteria for people at increased risk of Type 2 diabetes. We noted that a report from a UK expert advisory group on the implementation of WHO guidance recommended using HbA1c values between 42-47 mmol/mol (6.0-6.4%) to indicate that a person was at high risk of type 2 diabetes. Importantly, that expert group did recognise that there is a continuum of risk across a range of subdiabetic HbA1c levels and that people with an HbA1c below 42 mmol/mol (6.0%) may also be at risk (John 2012). Given this acknowledgement that lower values than 42 mmol/mol (6.0%) were indicative of risk and the finding in the review undertaken for this question that 39 mmol/mol (5.7%) was associated with a positive likelihood ratio of 11.23 for the diagnosis of diabetes ('a very useful test') we felt that in the first three

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						months postpartum a lower value of 39 mmol/mol (5.7%) would represent a more useful threshold for screening and was based on evidence.
NHS Choices	1	Full	General	General	Digital Assessment Service welcome the guidance and have no comments on its content as part of the consultation.	Thank you for your comment.
NHS England	1	NICE	General	General	Thank you for the opportunity to comment on the above draft guideline. I wish to confirm that NHS England has no substantive comments to make regarding this consultation.	Thank you for your comment.
NORDISK LTD	12	Full	General	General	The recent National Pregnancy in Diabetes (NPID) audit report for 2013 shows that only 5% of women with Type 1 diabetes achieved the target blood glucose readings for early pregnancy set out in national guidelines. In addition, almost half (46%) of women with type 1 diabetes had a baby that was large for the length of pregnancy. It is therefore important that women are given the choice of medicines that can help can them achieve glycaemic control and without disabling hypoglycaemia, i.e. long-acting insulins such as insulin detemir.	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to recommendation 23 that states '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'.
NORDISK LTD	13	Full	General	General	Novo Nordisk appreciates the extensive work and efforts involved in the NICE clinical guidelines review process are thankful for this	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping and

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					opportunity and request that the above information is kindly considered to help in updating the NICE diabetes clinical guidelines as it is important that they accurately reflect the licensed status of existing medicines. **References:** Mathiesen et al. Maternal Efficacy and Safety Outcomes in a Randomized, Controlled Trial Comparing Insulin DetemirWith NPH Insulin in 310 Pregnant Women With Type 1 Diabetes. Diabetic Medicine 2012; DOI: 10.2337/dc11-2264 Hode et al. A randomized trial comparing perinatal outcomes using insulin detemir or neutral protamine Hagedorn in type 1 diabetes. Matern Fetal Neonatal Med, 2014; 27(1): 7–13 Mello et al. Continuous subcutaneous insulin infusion (CSII) versus multiple daily injections (MDI) of rapid-acting insulin analogues and detemir in type 1 diabetic (T1D) pregnant women. J Matern Fetal Neonatal Med, Early Online: 1–6; 2014 Informa UK Ltd. DOI: 10.3109/14767058.2014.914922 Tredici et al. Perinatal Outcomes in Obese, Over- and Normal- Weight Pregnant Women with GDM (Gestational Diabetes Mellitus) Treated with Detemir and Aspart. Diabetes. 2011;60(suppl1):2419-PO Todorova et al. Pregnancy Outcomes in Women with Type 1 Diabetes Treated With Long	hence the study references suggested would not be eligible for inclusion in the guideline. However, a footnote has been added to recommendation 23 that states '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'. Although the National Pregnancy in Diabetes Audit 2013 reference is not included because no relevant data is presented, some studies using data collected through the audit are included (eg Holman 2014 in Timing of Birth review).

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					Acting Insulin Analogs. A Case Control Study. Case Study. Acta Med Bulg. 2010:37(2):21-31 Lapolla et al. Use of insulin detemir in pregnancy: a report on 10 Type 1 diabetic women. Diabetic Medicine 2009; 26, 1179–1183 Callesen et al. Treatment with the long-acting insulin analogues detemir or glargine during pregnancy in women with type 1 diabetes: comparison of glycaemic control and pregnancy outcome. The Journal of Maternal-Fetal and Neonatal Medicine, 2013; 26(6): 588–592 Suffecool et al. Does insulin detemir improve pregnancy outcome in pregnant women with diabetes? Am J Obstet Gynecol. 2012;1(Suppl S):S128 [abstract 261] Insulin detemir (Levemir®) SUMMARY OF PRODUCT CHARACTERISTICS (SPC) Available at: http://www.medicines.org.uk/emc/medicine/14584 National Pregnancy in Diabetes Audit – 2013. HSCIC. October 2014 http://www.hscic.gov.uk/catalogue/PUB15491 (Please do not hesitate to contact us if you may need us to provide any of these references).	
NORDISK LTD	8	Full	5.4.1.4	445	Novo Nordisk requests that this section is updated to include insulin detemir as an option for treatment in type 1 diabetes and also	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping and

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					highlight that there is clinical data on the use of insulin detemir in pregnancy to justify considering its use in pregnancy	hence no amendments have been made to the corresponding evidence summary in the full guideline. However, a footnote has been added to recommendation 23 that states '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'
NORDISK LTD	9	Full	5.4.3	446	With reference to the second paragraph under 'Evidence statement', 'Rapid-acting insulin analogues (insulin aspart and insulin lispro) are associated with fewer episodes of hypoglycaemia compared with regular human insulin. When compared with regular human insulin the use of rapid-acting insulin analogues during pregnancy has also been associated with a reduction in postprandial glucose excursions, an improvement in overall glycaemic control and an improvement in patient satisfaction.'. Novo Nordisk suggest updating this statement to include that insulin detemir is also associated with fewer episodes of hypoglycaemia compared with regular human insulin, and now there is	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping and hence no amendments have been made to the corresponding evidence summary in the full guideline. However, a footnote has been added to recommendation 23 that states '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

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					RCT data in pregnancy that merits consideration of use of insulin detemir in pregnancy.	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'
NORDISK LTD	10	Full	5.4.4	447	With reference to third paragraph under the section 'From evidence to recommendations', 'The evidence supports the use of the rapid-acting insulin analogues insulin aspart and insulin lispro in women with diabetes in pregnancy, and also insulin pump therapy (CSII) in women who have difficulty achieving glycaemic control without disabling hypoglycaemia.' Novo Nordisk requests that this section should now be updated to include insulin detemir as there is now data to show that insulin detemir can be considered in pregnancy i.e. 'The evidence supports the use of the rapid-acting insulin analogues insulin aspart and insulin lispro, and the long-acting insulin analogue, insulin detemir, in women with diabetes in pregnancy, and also insulin pump therapy (CSII) in women who have difficulty achieving glycaemic control without disabling hypoglycaemia.'	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping and hence no amendments have been made to the corresponding evidence summary in the full guideline. However, a footnote has been added to recommendation 23 that states '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'.
NORDISK LTD	11	Full	5.4.5	447	Novo Nordisk would like to highlight that point 69, under 'Recommendations', i.e. 'Be aware that the rapid-acting insulin analogues (insulin	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping.

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					aspart and insulin lispro) have advantages over soluble human insulin during pregnancy and consider their use. [2008]' is updated include 'Be aware that the rapid-acting insulin analogues (insulin aspart and insulin lispro) and the long-acting analogue, insulin detemir, have advantages over soluble human insulin during pregnancy and consider their use.' This is because there is now clinical data on the use of insulin detemir in pregnancy available. The Levemir® SPC now states 'Treatment with Levemir® can be considered during pregnancy, but any potential benefit must be weighed against a possibly increased risk of an adverse pregnancy outcome.'	However, a footnote has been added to recommendation 23 that states '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'
NOVO NORDISK LTD	1	Full	2.2	79	Point 7 - 'Advise women with diabetes who are planning to become pregnant'. Novo Nordisk recommends adding to this point: 'Medication will need to be reviewed in terms of considering using medications that have an evidence base in pregnancy.' It is important to differentiate medications that have a strong evidence base such as randomised controlled trials that give confidence for use in pregnancy.	Thank you for your comment. As described in the NICE Guidelines Manual 2012, the strength of the evidence base underlying NICE recommendations is conveyed in their wording. Sections 9.1 (Interpreting the evidence to make recommendations) and 9.3.3 (Reflect the strength of the recommendation) of the manual describe how this methodology was used in this guideline update to formulate the wording of the recommendations.
NOVO NORDISK LTD	2	Full	2.2	80	Point 23 - 'Explain to women with insulin-treated diabetes who are planning to become pregnant that there is insufficient evidence about the use of long-acting insulin analogues during	Thank you for your comment. . Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to

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				-81	pregnancy. Therefore isophane insulin (also known as NPH insulin) remains the first choice for long-acting insulin during pregnancy. [2008]' We note that this statement has not been updated from the previous guidance. Novo Nordisk requests that this statement is amended as there is randomised controlled trial (RCT) data now available on the use of insulin detemir in pregnancy and that treatment with insulin detemir can be considered in pregnancy after a benefit risk assessment.	recommendation 23 that states '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'.
NOVO NORDISK LTD	3	Full	2.2	97	Fig 2c, third bullet – 'Explain to women with insulin-treated diabetes who are planning to become pregnant that there is insufficient evidence about the use of long-acting insulin analogues during pregnancy. Therefore isophane insulin (also known as NPH insulin) remains the first choice for long-acting insulin during pregnancy. [2008]' Novo Nordisk would like to request updating of this statement to reflect that there is RCT data on the use of insulin detemir in pregnancy available.	Thank you for your comment. . Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to recommendation 23 that states '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

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						documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information'.
NOVO NORDISK LTD	4	Full	3.8.1.1	230	Novo Nordisk requests that the section 'Insulin analogues' needs updating as follows: '**Insulin analogues**. Insulin analogues are synthetic insulins created by modifying the chemical structure of insulin to produce either faster acting pre-prandial insulin or longer acting basal insulin. The insulin analogues currently licensed for use in the UK are the rapid-acting analogues insulin lispro, insulin aspart and insulin glulisine and the long-acting analogues insulin degludec, insulin detemir and insulin glargine. Of these only insulin aspart and insulin detemir have been studied specifically in prospective, double blind RCTs in pregnancy and have licence considerations for their use during pregnancy. No double blind, prospective RCTs were identified in relation to the effectiveness and safety of insulin degludec, insulin glargine, human insulin, insulin lispro or insulin glulisine in pregnancy, although some research is in progress.'	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping and hence no amendments have been made to the corresponding evidence summary in the full guideline. However, a footnote has been added to recommendation 23 that states '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'
NOVO NORDISK LTD	4	Full	3.8.1.1	230	Novo Nordisk recommends that a separate sub-section on insulin detemir is included to reflect the available clinical data in pregnancy, particularly the RCT data which is high grade clinical evidence that is not available with all insulin analogues. This is reflected in the licensing of insulin detemir as the Levemir® SPC (Section 4.6. Fertility, pregnancy and lactation)	Thank you for your comments. Insulin analogues were not prioritised for review in this guideline update during scoping and hence the study references suggested would not be eligible for inclusion in the guideline. However, a footnote has been added to recommendation 23 that states 'At the time of publication (February 2015),

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					states: 'Treatment with Levemir® can be considered during pregnancy, but any potential benefit must be weighed against a possibly increased risk of an adverse pregnancy outcome.' This section should include an overview of clinical evidence now available: • In an open-label RCT, pregnant women with type 1 diabetes (n=310) were treated in a basal-bolus treatment regimen with insulin detemir (n=152) or NPH (Neutral Protamine Hagedorn) insulin (n=158) as basal insulin, both in combination with insulin aspart. Primary objective of this study was to assess the effect of insulin detemir on blood glucose regulation in pregnant women with diabetes. Insulin detemir was non-inferior to NPH insulin in HbA_{1c}. Fasting plasma glucose was significantly lower with insulin detemir versus NPH insulin at both 24 and 36 gestational weeks. Major and minor hypoglycaemia rates during pregnancy were similar between groups (Mathiesen et al.). • Also insulin detemir was as well tolerated as NPH insulin as regards perinatal outcomes in pregnant women with Type 1 diabetes and no safety issues were identified (Hod et al.). • The overall rates of maternal adverse events were similar for insulin detemir and NPH insulin treatment groups. There was no difference in the incidence of adverse events	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'.

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					in the offspring between the treatment groups or in the number of adverse events per child. A numerically higher frequency of serious adverse events in the mothers (61 (40%) vs. 49 (31%)) and in the newborn children (36 (24%) vs. 32 (20%)) was seen for detemir compared to NPH. The number of live born children of women becoming pregnant after randomisation were 50 (83%) for detemir and 55 (89%) for NPH. The frequency of congenital malformations was 4 (5%) for detemir and 11 (7%) for NPH with 3 (4%) major malformations for detemir and 3 (2%) for NPH. • Post-marketing data from an additional 250 outcomes from pregnant women exposed to detemir indicate no adverse effects of insulin detemir on pregnancy and no malformative or foetal/neonatal toxicity of insulin detemir. • A comparison of two treatment regimens, multiple daily injections (MDI) of insulin detemir and insulin aspart and continuous subcutaneous insulin infusion (CSII) with insulin aspart was assessed in pregnant women (n=53) with type 1 diabetes. Overall, there were no significant differences between CSII and MDI groups in terms of HbA_{1C}, total fasting plasma glucose and postprandial glucose, rate of foetal fat mass growth and maternal foetal outcomes (Mello et al.). • A study comparing women with gestational	

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					diabetes mellitus (GDM) (n=81) treated with insulin detemir and insulin aspart by body mass index (BMI) found that there were no significant differences in total and weekly mean glycaemic levels or foetal outcomes between normal-weight, overweight or obese women (Tredici et al.). • Similar HbA_{1C} levels were observed in a 2 year prospective case control study in pregnant women with type 1 diabetes (n=90) taking insulin detemir, NPH insulin or insulin glargine in combination with insulin aspart. Severe hypoglycemia was observed in the NPH insulin group at a rate of 16%. No severe hypoglycemia was observed in patients treated with insulin detemir or insulin glargine, and the frequency of mild hypoglycemic episodes was similar between the two basal insulin analogues. There was no statistically significant difference between the three groups for the frequency of pre-eclampsia. The newborn's body weight in the insulin glargine group was statistically higher than the insulin detemir or NPH insulin groups. Two stillbirths and 9 miscarriages were observed in 11 women. Most women delivered with a caesarean section and there were no cases of newborn malformation or postnatal death (Todorova et al.). • There are also some retrospective studies using insulin detemir in relevant populations in pregnancy, as follows:	

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					➢ Lapolla et al. conducted a retrospective assessment of 10 women with type 1 diabetes who were on detemir at least 3 months before conception and throughout their pregnancy. Throughout the pregnancies, HbA_{1C} progressively decreased from a mean of 8.1% to 5.9%, with one event of severe hypoglycemia reported. No infants had major or minor malformations; two infants were admitted to the neonatal intensive care unit, one for severe hypoglycemia and one with seizures. ➢ Callesen et al conducted a retrospective study of pregnancies in women with type 1 diabetes and a living fetus at 22 gestational weeks using detemir (n=67) or insulin glargine (n=46) from conception. Glycaemic control at 33 weeks and pregnancy outcomes were comparable in women using insulin detemir or insulin glargine except for a lower percentage of infants large for their gestational age in women using insulin glargine. ➢ In a retrospective cohort study in pregnant women with type 2 diabetes or gestational diabetes mellitus treated with insulin detemir and insulin aspart compared to NPH insulin and insulin aspart, similar glycemic control and maternal hypoglycemia rates were observed. Mean PPG and FPG values were 111.11 mg/dL and 98.4 mg/dL for	

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					insulin detemir treated patients and 104.5 and 92.6 for NPH insulin treated patients. Higher birth weight and macrosomia was seen in newborns of mothers treated with detemir. (Suffecool et al.). (Please see below the full references for the studies mentioned above).	
NOVO NORDISK LTD	5	Full	3.8.3	233	Novo Nordisk would like to highlight that the last paragraph under the heading 'Evidence statement' needs updating to accurately reflect that there is RCT data in pregnancy available. Our suggestion would be to amend the statement to: 'RCTs and observational studies have shown that insulin aspart and insulin detemir is effective for managing diabetes in pregnancy without increasing the risk of hypoglycaemia. A large number of studies have shown no indication that insulin lispro is teratogenic. There have been no clinical trials of insulin degludec, insulin glulisine, insulin glargine or human insulin in pregnancy'.	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping and hence no amendments have been made to the corresponding evidence summary in the full guideline. However, a footnote has been added to recommendation 23 that states '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'
NOVO NORDISK	6	Full	3.8.4	234	Based on the comments and evidence noted in this proforma, Novo Nordisk requests that the	Thank you for your comment. Insulin analogues were not prioritised for review in

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LTD					last paragraph in this section is amended such that 'detemir' is removed from the list of products with no data in pregnancy. Hence this paragraph becomes: 'The use of insulin glulisine and insulin glargine during pregnancy should be avoided until more data are available on their safety'. Please note that despite earlier reference to insulin aspart in the document i.e. section 3.8.1 on p230, in referring to the RCT evidence that is available, it has been disregarded in this section 3.8.4. We strongly recommend that a statement is included in section 3.8.4 explaining the randomised controlled trial evidence for insulin aspart.	this guideline update during scoping and hence no amendments have been made to the corresponding evidence summaries in the full guideline. However, a footnote has been added to recommendation 23 that states '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'
NOVO NORDISK LTD	7	Full	3.8.5	234	Novo Nordisk recommends updating the point 23 – 'Explain to women with insulin-treated diabetes who are planning to become pregnant that there is insufficient evidence about the use of long-acting insulin analogues during pregnancy. Therefore isophane insulin (also known as NPH insulin) remains the first choice for long-acting insulin during pregnancy. [2008]' as this statement is untrue. This needs updating to reflect that there is RCT data in pregnancy available for insulin detemir and that it is licensed for use in pregnancy. Not all insulins have RCT data in pregnancy.	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to recommendation 23 that states '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.

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					Hence we suggest the following amendment: 'Explain to women with insulin-treated diabetes who are planning to become pregnant that there is now sufficient safety evidence available for the use of insulin detemir in pregnancy. Therefore insulin detemir should be the preferred option for long-acting insulin during 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'
Obstetricians and Gynaecologists	25	Full	5.8.1	478	Table 68 - Spelling of hydrocephalus and microcephaly Caudal regression syndrome- should this be grouped in with the CNS disorders? Uretal duplication- do the authors mean urethral duplication or ureteric duplication?	Thank you for your comment. The incorrect spelling has been corrected in the table to specify ureteral rather than uretal.
Obstetricians and Gynaecologists	26	Full	5.10.2.10	494	Table 71 - Formatting of bullet points under 16 week heading.	Thank you for your comment. This formatting issue has been addressed
Obstetricians and Gynaecologists	27	Full	5.10.2.10	496	Table 71 - This is a little confusing – there are recommendations to offer delivery should not go beyond 39+6 in women but on page 496 there is a table going up to 41 weeks with the comment "no extra care for women with diabetes at 41 weeks. Surely this appointment should not be there as the recommendation is to deliver by 40 weeks.	Thank you for your comment. Whilst the guideline recommends that women with diabetes in pregnancy are offered delivery (at 40+6 weeks for uncomplicated gestational diabetes, 37-38+ weeks for uncomplicated type 1 or 2 diabetes) we recognise that women may decline this offer and continue with the pregnancy. Providing ongoing care to such women is mandatory - hence the mention of 41 weeks.
Roche	1	Full	1 Introduction	57	Roche Diabetes Care's comments are as follows: The landmark HAPO study demonstrated a continuous relationship between glycaemia and adverse pregnancy outcome in a global	Thank you for your comments. However, we disagree with your suggestion that no cost-benefit analysis has been undertaken in setting the diagnostic criteria for gestational diabetes. Much of Chapter 9 relates to an economic evaluation of

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					population of women without gestational diabetes. However no cost benefit analysis of the new guidance has been undertaken and this was thought to be a priority for the guideline update. The role of HbA1c in the diagnosis and management of diabetic pregnancy remains controversial.	diagnostic criteria for gestational diabetes, including the IADPSG criteria. Following HAPO, the health economic model uses logistic regression analysis to predict the risk of adverse pregnancy outcomes based on blood glucose values. The prediction model is based on individual patient data (n>6,000) from UK and Australian HAPO study centres. RCT data is then used to derive a relative treatment effect to the predicted baseline risk depending on whether a particular diagnostic threshold would identify a woman as having gestational diabetes or not. This model was used to inform guideline recommendations on diagnostic thresholds for gestational diabetes.
Roche	2	Full	1.1.2 Aim of guideline	58	We strongly support the guideline's efforts and would like to see greater emphasis on delivering : • glycaemic control in the preconception, antenatal and intrapartum periods • changes to medications for diabetes and its complications before or during pregnancy • management of diabetic emergencies (for example, hypoglycaemia and ketoacidosis) and diabetic complications (such as retinopathy) during pregnancy	Thank you for your comment. The GDG feel that these comments are covered sufficiently in the guideline.
Roche	3	Full	1.1 For whom is the	58	We welcome the guideline's focus on those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales	Thank you for your comment.

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			guideline intended?		commissioners, and public health, trust and care-home managers	
Roche	4	Full	1.1.7 Guideline methodol ogy	60	While we recognise the highest available level of evidence was selected for each clinical question, we are aware that the highest level of evidence may not be available for all outcomes of interest. For diagnostic tests, in addition to test evaluation studies, using linked evidence approaches could be considered as well patient-relevant outcomes. Reference: Merlin, T; Lehman, S: "The "linked evidence approach" to assess medical tests: A critical analysis"; International Journal of Technology Assessment in Health Care, 29 (3), 343-350, 2013	Thank you for your comment and for submitting this paper. This guideline was developed in accordance with the methodology described in the NICE Guidelines Manual 2012 which ensures a consistent and transparent approach across NICE's guideline development program. Section 9.1 provides the rationale for how the evidence is narratively interpreted to make recommendations in NICE guidelines.
Roche	5	Full	3.5 Monitorin g blood glucose and ketones in the preconce ption period 3.5.2.7 Recomme ndations	213	13. Women with diabetes who are planning to become pregnant, should be offered a blood glucose meter to encourage self-monitoring, and an adequate supply of test strips, based on her individual health & lifestyle needs. 14. Pregnant women with diabetes should have access to adequate blood glucose and ketone testing strips and a meter, and advise them to test for ketonaemia if they become hyperglycaemic or unwell.	Thank for you for your comment, however, we are unable to respond as it is unclear what amendment is requested
Roche	6	Full	5 Antenatal	386	During pregnancy, women with diabetes were to be advised to test fasting blood glucose levels	Thank you for your comment. Table 46 in the full guideline is the GRADE profile that examines the evidence for monitoring of

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			care 5.1 Monitoring blood glucose and ketones during pregnancy		and blood glucose levels 1 hour after every meal and women with insulin-treated diabetes were to be advised to additionally test blood glucose levels before going to bed at night. The review question in this update does not examine the evidence available for the performance of self-monitoring at all, but specifically focuses on the frequency of monitoring blood glucose and timing relative to meals,besides deciding on any adjustment including insulin dose adjustment."	blood glucose compared to no monitoring. The subsequent GRADE profiles then go on to examine the timing and frequency of monitoring.
Roche	7	Full	5.1.4 Evidence profile	390	Thee are inconsistencies labeling in tables and text regarding tables 48-52.	Thank you for your comment. This has now been amended
Roche	8	Full	5.1.5.2.1 Daily monitoring vs. weekly monitoring (Table 47)	404	As type 2 diabetes could also include non-insulin-dependent pregnant women, the text could describe the population clearer in this respect.	Thank you for your comment. We disagree and do not believe that there is a need for an amendment.
Roche	9	Full	5.1.7 Evidence to recommendations (and	405	Testing weekly or less frequently may not be the cause of an instrumental birth, but rather be related to a selection e.g. more severe cases testing at a higher frequency.	Thank you for your comment. We agree that the more frequent testing is not a direct cause of the increase risk of instrumental birth, but merely an association. However, we do not say that it is a cause.

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			5.1.7.1)			
Roche	10	Full	5.1.7.4.2 Daily monitoring vs weekly monitoring	407	Such testing regimes are questionable for insulin-dependent and for non-insulin-dependent patients.	Thank you for your comment. We agree that the frequency of testing in some of the studies would not now be considered to be acceptable. But it is from this evidence that we have recommended a far more intensive approach to monitoring.
Roche	11	Full	5.1.9 Recommendations	408	57. Advise pregnant women with type 1 diabetes to test their fasting, preprandial, 1- hour postprandial and bedtime blood glucose levels daily during pregnancy, besides deciding on any adjustment including insulin dose adjustment. 58. Advise pregnant women with type 2 diabetes or gestational diabetes who are on a multiple daily insulin injection regimen to test their fasting, preprandial, 1-hour postprandial and bedtime blood glucose levels daily during pregnancy. [new 2015] This statement could also be related to women who use insulin pumps.	Thank you for your comment. We did not believe amendment to the recommendations as suggested was necessary
Roche	12	Full	5.1.10 Research recommendations (and 20. What is the	409	Where a lack of clinical evidence exists, decisions on frequency of testing should be led by the patient, in partnership with her healthcare professional. A joined up approach would include having access to a blood glucose meter and adequate testing strips, based on her health and lifestyle	Thank you for your comment. However, we felt that the evidence for the frequency of testing in such patients was not strong and that further research was required. Such more robust data would then more usefully inform the discussion between healthcare professional and patient.

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			optimum frequency of blood glucose testing in pregnancy in women with pre-existing diabetes who are not taking insulin?		requirements.	
Roche	13	Full	5.3 HbA1c values for women with type 1, type 2 or gestational diabetes during pregnancy - monitoring and target values (5.3.18) Research recomme	443	28. What are the barriers to testing blood glucose frequently in pregnancy? In addition to the barriers listed in the consultation document, access to appropriate blood glucose testing meters and adequate supply of testing strips is an ongoing for people with diabetes should also be explored.	Thank you for your comment. The GDG were satisfied with the wording of the research recommendation and did not make an amendment.

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			ndations			
Roche	14	Appendices	General	General	Additional appendices which should be included: 1. Belicar P, Jeandidier N, Renard E, Boivin S, Gross P, Pinget M, et al. Implanted insulin pump may represent a chance for young women with unstable type 1 diabetes to give birth. Diabetes Care. 1999;22(6):1001-2. 2. Fonseca V, Menon R, O'Brien PM, Fernando ON, Stephen R, Dandona P. Diabetic Pregnancy Managed with Intraperitoneal Insulin. Diabet Med. 1987;4(1):74-6. 3. Hofmann HM, Weiss PA, Haas JG. Continuous insulin delivery systems for the pregnant diabetic patient. Acta Diabetologica Latina. 1986;23(3):201-14. 4. Jeandidier N, Boivin S, Treisser A, Pinget M. Intraperitoneal insulin pump therapy during pregnancy: Two cases. Pract Diab Int. 1995;12(6):280. 5. Schnell O, Gerlach E, Hillebrand B, Walter H, Standl E. A case of diabetic pregnancy controlled with a percutaneous access device for intraperitoneal insulin infusion. Diabetes Care. 1994;17(11):1354-5.	Thank you for your comment. We have considered the papers suggested however, none would be eligible for inclusion in the guideline because they are case reports (Fonseca 1987 – one case, Jeandidier 1995 – two cases and Schnell 1994 – one case) or case series (Belicar 1999 – eight cases and Hofman 1986 – six cases) that do not provide comparative data and as they all investigate insulin pump therapy, were not relevant to any of the reviews that were performed in this guideline update.
Royal College of General Practitioners	1	Full	General	General	In 2010 the King's Fund published its report: **The role of GPs in maternity care – what does the future hold?** It highlighted several issues and principles,	Thank you for your comment. The GDG membership included a GP and their role was discussed. It was decided that recommendation 44 was sufficient in that the primary health care team should be

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					which are relevant to updated Diabetes in pregnancy guidelines. These include: • The implications for a woman's general health care, both physical and psychological, if GPs are not involved in maternity care. • The role of general practice in meeting the stated preferences of pregnant women for continuity of care and post-natal support. • The potential for GPs to provide co-ordination and advocacy for women who have complicated medical histories in addition to being pregnant. In the updated guidelines there is no reference to this report, continuity of care or the role of the GP or generalist in the care of women with diabetes in pregnancy. There are 4 references to primary care:	informed when a woman has a diagnosis of gestational diabetes.
Royal College of General Practitioners	6	Full	General	General	The guidelines should address the role of GP in diabetes in pregnancy and the lifetime follow up of women with gestational diabetes which I believe is poorly addressed. Smith A Shakespeare J Dixon A **The role of GPs in maternity care – what does the future hold?** 2010 The Kings Fund (MH)	Thank you for your comment. The GDG membership included a GP and their role was discussed. It was decided that recommendation 44 was sufficient in that the primary health care team should be informed when a woman has a diagnosis of gestational diabetes.

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Royal College of General Practitioners	7	Full	General	General	Women with a history of GDM are seven times more likely to develop type 2 diabetes than women who have had a normal pregnancy. In light of this fact I would recommend that the guideline promotes the maintaining of a register, by GPs, of women discharged with a diagnosis of GDM. There should be an accompanying recommendation that women on this register undergo annual testing for the development of diabetes. (SL)	Thank you for your comment. The recommendations addressing postnatal testing of women who had (and recovered from) gestational diabetes are clear in terms of when these women should be screened. It includes an annual test for the rest of their lives. However, whilst it is not explicitly stated who should conduct these tests (because it would be dependent upon and vary with local factors) we assumed that the annual test would be undertaken in primary care. This need not necessarily be undertaken personally by the GP, but perhaps by a practice nurse in the first instance and only involve the GP if the result is abnormal. In addition, we recommended that women with a history of gestational diabetes and a 'high risk' post natal test should be managed in accordance with the recommendations in the NICE Clinical Guideline 'Preventing type 2 diabetes - risk identification and interventions for individuals at high risk' (PH 38).
Royal College of General Practitioners	8	Full	General	General	There should be an acknowledgment that children born to mothers who had gestational diabetes during pregnancy are at a greater risk of developing obesity and type 2 diabetes later in life. Again, given that overweight/obese children grow into similar adult phenotypes, GPs should be reminded to watch for excessive childhood weight gain so that appropriate parental advice may be issued. (SL)	Thank you for your comment. However, this was not prioritised for review in this guideline update during scoping.
Royal College of	2	Full	General	216	"lack of provision of blood glucose strips from primary care". What evidence is there of this? It	Thank you for your comment. We agree with them and have removed any reference

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General Practitioners					is unclear if general practice is not involved why it should have responsibility for provision. I think that the GP should meet any pregnant woman at least once during her pregnancy and postnatal to help develop an ongoing relationship of trust and not just used as a cost center to provide medication or testing equipment they are not involved in but are expected to take responsibility for. (MH)	to the availability of glucose strips in primary care.
Royal College of General Practitioners	3	Full	general	217	Telehealth in primary care is costly and as yet unproven so its use in pregnancy needs evaluation. (MH)	Thank you for your comment. We have added the need for health economic evaluation to the research recommendation.
Royal College of General Practitioners	4	Full	General	312	"And would not need to see their GP and their care could be entirely midwifery led." GPs need to see pregnant women during pregnancy and postpartum to help in their relationships with women and their families. (MH)	Thank you for your comment. We have changed the text in the 'Evidence to recommendations secton to reflect those in the Antenatal Care guideline (CG 62) which recommends involvement of the general practitioner. This reflects the fact that we felt this was especially important when women were diagnosed with gestational diabetes.
Royal College of General Practitioners	5	Full	General	313	"Why are hospitals asking GPs to prescribe medications or testing kits that they are initiating?" in the GMC guidance 2013 in prescribing and managing medicines and devices states "You are responsible for the prescriptions you sign and your decisions and actions when you supply and administer medicines and devices or authorise or instruct others to do so. You must be prepared to explain and justify your decisions and actions when prescribing, administering and managing medicines." If the woman is attending hospital and medication is initiated there then the first scripts should be issued by the hospital rather	Thank you for your comment. We have amended the text to endorse the points you make.

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					putting primary in the difficult position of being forced to issue them mainly to reduce hospital costs rather than for the patient's convenience. (MH)	
Royal College of Nursing	3	NICE	General	General	The RCN feels It would assist perinatal wellbeing and maternity outcomes if NICE incorporated a Patient Information Leaflet with the standard advice in the updated guideline summarised for women with gestational and type1 diabetes. This would also help GPs and Midwives without experience of combined outpatient appointments (maternity and diabetes) to support key messages directed at women, when care is also provided in a primary care or community setting.	Thank you for your comment. NICE are producing an 'Information for the Public' version which will address this.
Royal College of Nursing	1	NICE	1.4.2	32	The RCN believes It would be helpful to review the criteria for membrane sweep alongside any advice regarding induction of labour between 37 and 40 weeks. The routine advice in NICE induction of labour draft guideline does not appear to take into account women with diabetes who may have indications for an earlier membrane sweep.	Thank you for your comment. We did not consider that induction of labour should be undertaken in any different way in women with diabetes in pregnancy and therefore the indications for a membrane sweep in women with diabetes in pregnancy was not prioritised for review.
Royal College of Nursing	2	NICE	1.4.4	33	For services aiming to reduce Caesarean Section (CS) rates as part of the commissioners CQUIN targets; this section appears to be offering women a choice between CS and Induction of labour. Greater detail in this area of the standard would assist service providers to maintain the expected levels of CS in light of probable increased numbers of pregnant women with gestational diabetes.	Thank you for your comment. The GDG felt that elective birth should be offered to women with diabetes who fail to go into labour spontaneously because of the increasing risk of stillbirth with advancing gestation. There are only two methods of elective birth - a) induction of labour with the hope of a vaginal birth, and b) caesarean section. So the recommendation 1.4.4 mentions both. A number of factors will influence which method is chosen.
Royal	1	Full	General	General	Given the long list of	Thank you for your comment. NICE are

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College of Obstetricians and Gynaecologists					information/advice/reminders to impart to women with diabetes in pregnancy it would be helpful to have a succinct Patient Information Document that states clearly everything that the woman needs to understand and know? It would be good if a reference to such a document could be included here as I am sure it would help the doctor as much as the woman.	producing an Information for the Public version which will address this and there is a link to this in the full guideline.
Royal College of Obstetricians and Gynaecologists	2	Full	General	General	Could the term fetal growth restriction (FGR) be used throughout rather than IUGR? This is consistent with RCOG terminology – thank you.	Thank you for your comment. Intrauterine growth restriction has been updated to fetal growth restriction throughout the guideline.
Royal College of Obstetricians and Gynaecologists	3	Full	General	General	One comment: as this document is looking at the overall care provided to Diabetic mothers, consideration should be given to referring to: "NICE Guideline on Hypertension in Pregnancy" – specifically the administration of antiplatelet drugs – aspirin 75 mg. This would be another area to highlight use of aspirin.	Thank you for your comment. We have now acknowledged and made a link to the Hypertension in pregnancy clinical guidance (CG107) regarding offering LDA (75mgs daily) to all women with diabetes. We have retained the recommendation about increased LDA dose in women with proteinuria.
Royal College of Obstetricians and Gynaecologists	4	Full	2.1.3	75	Point 116 – suggest swap the 2 sentences around so that it starts: 'only implement additional measures if one or more of these criteria are met'	Thank you for your comment. However, this was not in the scope of review for this Guideline update
Royal College of Obstetricians and Gynaecologists	5	Full	2	75 - 90	It might be helpful to separate the recommendations in to women with pre-existing diabetes and women who develop gestational diabetes. This would make table 73 (pages 76 - 77 much clearer)	Thank you for your comment. Chapter headings have been inserted in the list of recommendations which we believe addresses this issue.
Royal College of	6	Full	2.1.2	75	I noted with interest the diagnostic criteria for GDM. I understand the rationale for this on the	Thank you for your comment. We agree that it would be helpful if an international

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Obstetricians and Gynaecologists					basis of economic evaluation but surely it would be helpful if we could agree on an international level what the diagnostic criteria are for the purpose of comparison of outcomes to guide best practice. I'm not quite clear therefore why the IADPSG criteria haven't been adopted in line with other groups	definition of gestational diabetes was agreed. Whilst the new IADPSG criteria are supported by many, they are not universally accepted and continue to be debated and remain controversial. Furthermore, it is widely accepted that IADPSG diagnostic criteria would increase the woman diagnosed with gestational diabetes and it is important in NICE guidelines that increased use of scarce NHS resources is supported by evidence that this would be cost-effective. Some commentators have criticised the arbitrary nature of IADPSG diagnostic thresholds and those thresholds were certainly not developed using any formal consideration of whether any additional benefits of diagnosing more women would justify the additional costs. We accept that the criteria recommended by this guideline differ from the new WHO criteria. However, the GDG noted that the strength of the WHO recommendation was weak and that the WHO guideline suggests a rapid update of the criteria may be necessary in the light of new health economic evidence.
Royal College of Obstetricians and Gynaecologists	7	Full	2.1.3	75	Spelling of insulin.	Thank you for your comment. This has been corrected.
Royal College of Obstetrician	8	Full	2.1.4	78	Advise pregnant women with …between 37+0 weeks and 38+6 weeks gestation. I think this should be 'Offer pregnant women	Thank you for your comment. We reconsidered the recommendation about timing of birth in response to stakeholder

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s and Gynaecologists					with type 1 or 2….'. The evidence for this statement is of low or very low quality. There are no RCTs comparing expectant with elective delivery at 37+0 to 38+6 weeks gestation. The argument for this is to offset the increased risk of stillbirth at this gestation. However the guideline authors state that while the risk of stillbirth in type 1 and type and type 2 diabetics is lowest in the 37th and 38th week of pregnancy in the UK study, there was no significant difference in stillbirth rates when compared to non diabetics at any gestational age except at 39 weeks. The other retrospective study in type 1 diabetics shows a nadir at 38 weeks. I am not clear what the evidence is that supports delivery before 38 weeks. The authors of the guideline have commented on the increased neonatal morbidity at 37-38 weeks gestation. This is higher as a result of TTN at 37 weeks compared to 38 weeks. This is not insignificant and would have to be offset against the small risk of stillbirth between 37+0 and 38 +0 weeks gestation. There are no RCTs that demonstrate a reduction in stillbirth in type 1 or 2 diabetes with a policy of elective delivery at these gestational ages. We do not know that any potential reduction might be balanced by an increase in neonatal mortality by doing so. I therefore feel that if we are to advocate delivery from 37 weeks onwards this must be offered following discussion with the woman about the potential risks involved.	comments. We felt that the evidence justified making separate recommendations for the timing of birth for women with type 1 or type 2 diabetes and for women with gestational diabetes. For women with gestational diabetes, the data from Rosenstein (2012) demonstrated that there was a significant rise in stillbirth rate after 40+6 days. Whereas the Kjos (1993) study showed that the incidence of babies weight more than 4000g rose after 39+6 days. Given that avoidance of stillbirth was the philosophy underpinning the timing of delivery, the GDG felt that in women with uncomplicated gestational diabetes elective delivery could be delayed until 40+6 days. For women with type 1 or type 2 diabetes the limited data demonstrated that the stillbirth rate rose after 38+6 weeks. Thus such women should be offered elective delivery by 38+6 weeks. We felt that a lower limit should be also included in the recommendation to avoid women with uncomplicated type 1 or type 2 diabetes being advised to have an elective preterm delivery with its associated complications for the woman (such as failed induction of labour and caesarean section) and the baby (such as respiratory distress syndrome and admission to the neonatal unit). The data from Holman (2014) suggested the lower limit of the elective

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						delivery should be 37+0 weeks. Thus we recommended elective delivery for women with uncomplicated type 1 or type 2 diabetes between 37+0 and 38+6 weeks. In making this recommendation, we expect that, in practice, this would result in such women being routinely offered elective delivery nearer 38+6 weeks than 37+0 weeks.
Royal College of Obstetricians and Gynaecologists	9	Full	2.2	81	Point 21 states 'all other oral blood glucose lowering agents should be discontinued'. In 2.1.3 it states 'advise women on glibenclamide' . Glibenclamide is also an oral hypoglycemic agent. The 2 points seem to be conflicting.	Thank you for your comment. However, this recommendation is correct. Recommendation 55 on states that glibenclamide should be stopped. The footnote indicates that it is contraindicated in the first trimester in pregnancy. Thus it is good practice to stop it before pregnancy and for the first trimester. There is no evidence of harm from glibenclamide in second or third trimesters and so the guideline recommends it as an alternative to metformin for those trimesters.
Royal College of Obstetricians and Gynaecologists	10	Full	2.2	82	Recommendation 35 – suggest rewording from 'so that women can make' to 'to enable women to make an informed decision'	Thank you for your comment. This wording is consistent with NICE's use of plain English in recommendations and therefore a change cannot be made.
Royal College of Obstetricians and Gynaecologists	11	Full	2.2	82	Recommendation 36 – should it not state 'black and minority ethnic' and not 'minority ethnic'?	Thank you for your comment. The text of this recommendation was only amended in the 2015 update of the guideline to broaden the bullet point specifying particular family origins with a high prevalence of diabetes as a risk factor. The phrase 'minority ethnic family origin with high prevalence of diabetes' was agreed given the importance

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						of not overlooking risk factor assessment in women in groups other than those that were listed previously. The phrasing was not made more explicit (eg 'black and minority ethnic' as suggested) because the list would never be comprehensive.
Royal College of Obstetricians and Gynaecologists	12	Full	2.2	82 -83	In line with the RCOG life-course approach, suggest recommendation 44 – 'treatment should ALWAYS include changes in diet and exercise'.	Thank you for your comment. The guideline already recommends that all women are advised to make changes to their diet and exercise.
Royal College of Obstetricians and Gynaecologists	13	Full	2.2	84	Does recommendation 60 apply to both pre-existing diabetes and gestational diabetes? Please clarify.	Thank you for your comment. The stakeholder is correct - the recommendation applies to women with pre-existing Type 1 or Type 2 diabetes as well as those with gestational diabetes.
Royal College of Obstetricians and Gynaecologists	14	Full	2.2	85	Recommendation 68 states that HbA1c levels should be considered if the woman needs reassurance that her blood glucose control is optimised. Does this mean that all women with diabetes should be asked if they need reassurance?	Thank you for your comment. Several stakeholders raised similar concerns so we re-discussed the evidence in the draft guidance. We acknowledge that it is difficult to conduct a study that would determine target values for HbA1c. However, the GDG were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was

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						nonetheless a marker of risk of adverse outcome and could be of value in practice for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome. In the light of these considerations the GDG decided to amend their recommendations to reflect their conclusions that HbA1c should not be used in a diabetic pregnancy to assess glucose control, however, it should be used in specific circumstances to assess the risk in those pregnancies with 48mmol/mol (6.5%) as a threshold.
Royal College of Obstetricians and Gynaecologists	15	Full	2.2	86	Recommendation 85 - 'examination of the four chamber view of the fetal heart and outflow tracts.' change to 'examination of the fetal heart to include 4 chamber view and outflow tracts'. We are conducting an examination of the fetal heart. This includes standard views (4 chamber, outflows, 3 vessel, transverse arch, short axis) some of which are recommended as screening tests as part of FASP (4 chamber, outflows and/or 3 vessel).	Thank you for your comment. In the light of your suggestions we have changed the recommendation to: 'Offer women with diabetes an ultrasound scan for detecting fetal structural abnormalities including examination of the fetal heart (four chambers, outflow tracts and three vessels) at 20 weeks'.
Royal College of Obstetricians and Gynaecologi	16	Full	2.2	86	Recommendation 87 says that routine monitoring of fetal wellbeing is not recommended in pregnant women with diabetes, unless there is a risk of intrauterine growth restriction.	Thank you for your comments. This section was not prioritised in the scope for review in the guideline update. Nonetheless, we think the text and recommendation are clear with emphasis on the need to be especially

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sts					• The text in section 5.9.1.1 says that "women with diabetes are also at risk of having a baby that is small for gestational age". • The RCOG Guideline on Small for Gestational Age (Green-top guideline number 31) cites diabetes with vascular disease as a risk factor for small for gestational age and recommends monitoring. It would be good to clarify this recommendation and supporting text.	vigilant for fetal growth restriction in women with diabetes and vascular disease and/or nephropathy.
Royal College of Obstetricians and Gynaecologists	17	Full	2.2	87	Typo in recommendation 103 – remove 'blood'	Thank you for your comment. This has been corrected.
Royal College of Obstetricians and Gynaecologists	18	Full	2.2	87	Recommendation 93 – could the developers propose an insulin regime?	Thank you for your comment. However this topic was not prioritised for review in the scope for the guideline update. The text of the original recommendation was amended to put it into a more active form, consistent with NICE's current recommendation style.
Royal College of Obstetricians and Gynaecologists	19	Full	2.2	87	Recommendation 98 – add in 'if indicated' after CS	Thank you for your comment. This has been added to the recommendation.
Royal College of Obstetricians and Gynaecologists	20	Full	2.2	87	Recommendation 101 – add in 'spontaneous' before vaginal birth as IOL also aims for vaginal birth	Thank you for your comment. However, this recommendation was not prioritised in the scope for review during the update.

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Royal College of Obstetricians and Gynaecologists	21	Full	2.2	88	Recommendation 107 – suggest re wording from 'skills' to 'facilities' as facility encompasses skills and equipment.	Thank you for your comment. This is a 2008 recommendation and was not identified in the scope for an update.
Royal College of Obstetricians and Gynaecologists	22	Full	2.2	90	Recommendation 130 – I believe there is an error in the 2nd dark bullet point. I think 86 should read 46 mmol/mol	Thank you for your comment. This has been corrected.
Royal College of Obstetricians and Gynaecologists	23	Full	Fig 2d	98	Lowest box says retinal assessment but deals with renal assessment	Thank you for your comment. This has been amended.
Royal College of Obstetricians and Gynaecologists	24	Full	3.9.3	238	We have concerns about the recommendation to avoid calcium channel blockers throughout – despite nifedipine being listed as a balance – it may steer people away from using them when in fact they are very safe.	Thank you for your comment. Although this section was not updated, the statement about stopping calcium channel blockers was only in the 'Evidence to recommendations section'. It was not a recommendation. Nevertheless, there was no evidence to support this statement and the GDG (2008) being on the safe side in the absence of evidence. However, as you point, the evidence base is now much stronger and they are a recommended option for women with hypertension in pregnancy (CG 107). Thus we have removed the paragraph.
Sanofi	1	Full	3.8.4	234	The draft guidelines state, 'the use of other rapid- and long-acting insulin analogues (glulisine, detemir and glargine) during pregnancy should be avoided until more data	Thank you for your comment. Insulin analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to

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					are available on their safety.' Whilst this section of the guideline was not reviewed as part of this guideline update, we consider that changes to the Summary of Product Characteristics (for insulin glargine and insulin detemir), since the original guideline was published, should be acknowledged in this update and physicians advised to consult these documents before making treatment decisions, or changes to treatments, for patients who become pregnant. (http://www.medicines.org.uk/emc/medicine/20123 and http://www.medicines.org.uk/emc/medicine/14584)	recommendation 23 that states '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'
The Royal College of Midwives	1	NICE	General	General	The RCM welcomes the update of this guideline and considers the new and updated recommendations to be appropriate.	Thank you for your comment.
The Royal College of Midwives	2	NICE	1.1	15	The new recommendations on information and advice for women with diabetes who are planning to become pregnant are very clear and highlight the value of beginning pregnancy in the best possible state of health.	Thank you for your comment.
The Royal College of Midwives	3	NICE	1.2.8	23	We are pleased to note that the draft has taken into account the potential impact on existing services when setting the diagnosis levels for OGTT. The change to fasting plasma glucose of 5.6 mmol/litre is a more appropriate level.	Thank you for your comment.
The Royal College of Midwives	5	NICE	1.3.9	26	There is some contradiction here - the first point recommends no routine testing of HbA1c in the second and third trimester but the second point	Thank you for your comment. Several stakeholders raised similar concerns so we re-discussed the evidence in the draft

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		Full	and 1.3.11 page 84 point 65 and 67		recommends testing HbA1c to identify women who are diagnosed with GDM and might have type 2 diabetes. This point needs clarification.	guidance. We acknowledge that it is difficult to conduct a study that would determine target values for HbA1c. However, the GDG were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was nonetheless a marker of risk of adverse outcome and could be of value in practice for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome.
The Royal College of Midwives	4	NICE	1.3.15	27	re the recommendation for ' sugar containing drinks' as a treatment for hypos. 'Glucose containing drinks' would be more appropriate as these work more quickly.	Thank you for your comment. The recommendation has been updated with the word sugar replaced with the word glucose.
The Royal College of Paediatrics and Child Health	2	NICE	General	General	Recommendations 115 and 116 I think are now outside clinical practice, and it may be possible to make some changes if enough people mention them.	Thank you for your comment. However, these are 2008 recommendations and have not been updated.
The Royal	3	NICE	Introducti	3	To state that complications for the baby are	Thank you for your comments. However,

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College of Paediatrics and Child Health			on		more common after pre-existing diabetes is misleading as the same occurs for most complications and gestational diabetes. It is too far down in the introduction to highlight that the guidance covers both pre-existing and gestational diabetes.	this statement is correct. Complications are more common in women and babies with pre-existing diabetes than in those with gestational diabetes. Thank you for your comment. However, we disagree: a) the title of the Guideline is 'Diabetes in pregnancy' (and does not exclude any forms), and b) the first paragraph mentions all three types - type 1 and 2 and gestational diabetes.
The Royal College of Paediatrics and Child Health	4	NICE	Patient centred care	5	As always, the well being of the baby is ignored along with the necessity for health professionals to at in the best interests of the baby once born.	Thank you for your comment. This is standard wording that is used in all NICE guidance. However the first sentence has been amended to include babies. The baby has a clear focus in the guideline. Much of the Pre-pregnancy care section is aimed at aiming for good glycaemic control prior to pregnancy so that the risk of congenital abnormalities in the first trimester is avoided. Similarly the Antenatal Care section has sections which deal with fetal surveillance. Finally Chapter 8 in the full guideline addresses neonatal care.
The Royal College of Paediatrics and Child Health	5	NICE	1.5 1.5.11	36	It is obvious given the section, but as written it sounds like it is the mother not the baby who has clinical signs	Thank you for your comment. However, we feel the recommendations are clear as they stand.
The Royal College of Paediatrics and Child Health	7	Full	General	General	There is often a reference to dextrose for treatment of hypoglycaemia. Dextrose is a historical term and is largely replaced by glucose in the modern pharmacopoeias, and the latter should be used	Thank you for your comment. Both terms are used within the guideline.

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					in the guidance.	
The Royal College of Paediatrics and Child Health	8	Full	2.2	87	Although the guideline recommends the administration of antenatal steroids to enhance fetal lung maturation (typically before 35 weeks of pregnancy), there is no mention about the administration of steroids to prevent respiratory morbidity in neonates. The RCOG guidance recommends antenatal corticosteroids for women undergoing elective caesarean section before 38+6 weeks1. As steroid administration is known to significant worsening of glycaemic control in pregnant women, there is ongoing concern about the relevance of this recommendation to the women with diabetes undergoing elective CS. A recent report from Newcastle however showed that the rate of admission of babies born by elective CS to women with diabetes without corticosteroid cover was in fact lower than that in the general population undergoing elective CS before 38+6 weeks (1.38% vs. 4.7%)[2]. In view of these conflicting observations, a firm recommendation about the advisability of corticosteroid administration to women undergoing elective CS before 38+6 weeks would be helpful. 1. Royal College of Obstetricians and and gynaecologists. Green-top Guideline No.7. Antenatal corticosteroids to reduce neonatal mortality and morbidity. 2010 (https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-7.pdf) 2. Hodson K, Lyon-Dea C, Marshall S,	Thank you for your comment. The recommendation regarding steroids were not prioritised for update and hence we are not in a position to amend this although we note that diabetes is not a contraindication for their use and therefore no specific recommendations for women with diabetes would be necessary unless preterm delivery was contemplated.

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					MacDougal M. Antenatal corticosteroid for women with diabetes undergoing elective lower uterine segment caesarean section between 38+0-38+6, are they worth it? doi: 10.1136/archdischild-2013-303966.286	
The Royal College of Paediatrics and Child Health	1	Full	2.2 (summary recommendations)	88 recs 115 and 116	The threshold for escalating the treatment of hypoglycaemia in babies is very low at 2.0 mmol/l. This has not been updated in the new version as the evidence was not reviewed again. It is important that the guidelines are safe and so these recommendations should be changed in the light of current safe practice as they are currently unsafe. A threshold of either 2.6 mmol/l or 3.0 mmol/l (given that this hypoglycaemia is hyperinsulinaemic and the baby will therefore not have the benefit of ketones for brain metabolism) should be used.	Thank you for your comment. However, this section and topic were not prioritised in the scope for this guideline update Your comment been passed onto the Surveillance Review team at NICE.
The Royal College of Paediatrics and Child Health	6	Full	2.2	561	Should this recommendation be specific about the timing of blood glucose determination – e.g. pre-feed? The guidance provides for the timing of the first blood glucose determination after birth but none for continuing monitoring of glycaemic status. Perhaps some guidance about the duration of such monitoring would be useful.	Thank you for your comment. As this section was not prioritised for update, we are not able to make the amendment suggested.
University Hospital Birmingham NHS Foundation Trust	1	NICE	1.2.2	22	Please consider introducing age as a risk factor for GDM	Thank you for your comment. A review of the risk factors for gestational diabetes was not prioritised during scoping for the guideline update. Age was not specified as a risk factor in the 2008 guideline and has therefore not been included as a risk factor in this update.
University Hospital Birmingham	2	NICE	1.3.4	25	Although I understand that women with GDM/T2DM are at risk of DKA if severely unwell, does this really justify routine ketone-	Thank you for your comment. Thank you for your comment. Amendments to this recommendation and the next

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NHS Foundation Trust					testing education? Although home testing is necessary in T1DM, in others I'd have thought the clinical scenario would be one requiring hospital assessment and home testing would add no benefit.	recommendation (now Recommendations 1.3.20 and 1.3.21) were made in line with your comment following consultation. Recommendation 1.3.20 restricts use of blood ketone testing strips and meters for ketonaemia testing to pregnant women with type 1 diabetes. In recommendation 1.3.21, pregnant women with type 2 diabetes or gestational diabetes are advised to seek urgent medical advice if they become hyperglycaemic or unwell, but home testing for ketonaemia is not recommended for these women. The final recommendation (1.3.22) is that women with any form of diabetes who is hyperglycaemic or unwell should be tested for ketonaemia.
University Hospital Birmingham NHS Foundation Trust	3	NICE	1.3.8	26	Please consider whether it is necessary to introduce a 2 hour target while advising 1 hour testing?	Thank you for your comment. We felt that to have both 1h and 2h targets would allow women greater flexibility in terms of the timing of their postprandial test.
University Hospital Birmingham NHS Foundation Trust	4	NICE	1.3.9	26	Please consider routine 28 week HbA1c testing for T1 and T2 diabetes; CEMACH data showed that routine testing of 3rd trimester HbA1c would supply a risk factor for stillbirth	Thank you for your comments. Several stakeholders raised similar concerns so we re-discussed the evidence in the draft guidance. CEMACH data were sought for inclusion in the guideline early in development but were not available in the public domain. The GDG were aware of several observational studies with large cohorts of women with pre-existing diabetes where there were associations between increasing levels of HbA1c and worsening outcomes for women and their babies including stillbirth (Tennant 2014, Glinianaia 2012, Murphy 2011). In other words, we

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						were of the view that, whilst there was no evidence that routine HbA1c testing in pregnancy would be useful in assessing blood glucose control it was nonetheless a marker of risk of adverse outcome and could be of value in practice for that purpose. Whilst it is difficult to establish the normal reference ranges for pregnancy because of the impact of anaemia and increased red cell turnover, the data from the above observational studies indicates that a HbA1c value in pregnancy above 48mmol/mol (6.5%) is associated with an increasing risk of adverse outcome. In the light of these considerations the GDG decided to amend their recommendations (1.3.7 to 1.3.11) to reflect their conclusions that HbA1c should not be used in a diabetic pregnancy to assess glucose control, however, it should be used in specific circumstances to assess the risk in those pregnancies with 48mmol/mol (6.5%) as a threshold.
University Hospital Birmingham NHS Foundation Trust	8	NICE	1.3.27	29	Please consider: "Diabetic retinopathy should not routinely be considered a contraindication to vaginal birth" in order to retain the option of CS when proliferative retinopathy remains unstable (eg recent vitreous haemorrhage)	Thank you for your comment. However, this topic was not prioritised for review in this guideline update during scoping.
University Hospital Birmingham NHS Foundation Trust	9	NICE	1.3.24	29	Please consider clarifying the recommendation on first retinal screening. It suggests that early pregnancy retinal screening is not required if screening has occurred in the last 12 months. This would risk missing retinopathy which had developed or progressed in, say, 11 months-	Thank you for your comment. This was discussed following consultation and amendments have been made to Table 1 and to the corresponding recommendation 1.3.24 to address your concern.

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					especially if the woman's glycaemic control had tightened in preparation for pregnancy	
University Hospital Birmingham NHS Foundation Trust	5	Full	5.4.5	447	Given that 5.4.2 says "The NICE technology appraisal relating to insulin pump therapy (CSII) for people with type 1 diabetes states that insulin pumps can be used in pregnancy even if there is good glycaemic control on MDI regimens" it is disappointing that you have retained in 5.4.5 the need to justify pump therapy with "disabling" hypoglycaemia rather than frequent/troublesome and/or nocturnal hypoglycaemia or hypoglycaemia unawareness. Please consider removing "significant disabling".	Thank you for your comment. However, this section and topic were not prioritised in the scope for this guideline update.
University Hospital Birmingham NHS Foundation Trust	6	Full	5.5.10	464	Please reconsider introducing intermittent cgm in T1DM. The Murphy et al paper " Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial BMJ 2008" is dismissed as "very low quality" but I can't imagine much of what we do has a better trial behind it. Your restrictions on cgm ignore the benefits accrued in this trial from using short spells of cgm as a diagnostic and educational tool and makes it unlikely that those of us who have taken this trial evidence and found it useful will be able to secure funding for it.	Thank you for your comment. The GRADE method used does not assess the quality of the Murphy paper as 'very low', but rather assesses the outcomes within the paper as they relate to the review protocol as 'very low'. We do not believe that this will have an effect on securing funding for the stakeholders research interests
University Hospital Birmingham NHS Foundation Trust	7	Full	5.5.10	464	What is the evidence for the necessity for cgm users to have "24-hour contact with a member of the diabetes care team who is expert in its use"? It will be unrealistic for most teams and it is difficult to understand why you've introduced this but not similar support for pump users. If you retain this clause please consider specifying that this applies to those using cgm for therapeutic rather than educational/diagnostic purposes.	Thank you for your comment. We discussed the recommendation and agreed that whilst the provision of support was essential for women using CGM from someone who was expert in its use, it was not necessary to stipulate that this had to be 24h support from a diabetologist. The recommendation has been amended accordingly.
Welsh	4	Full	General	General	Insulin levemir is licensed in pregnancy.	Thank you for your comment. Insulin

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Endocrine and Diabetes Society						analogues were not prioritised for review in this guideline update during scoping. However, a footnote has been added to recommendation 23 that states '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'.
Welsh Endocrine and Diabetes Society	6	Full	General	General	Aspirin after week 12 of pregnancy is not mentioned compared to other NICE guidance.	Thank you for your comment. We have now acknowledged and made a link to the Hypertension in pregnancy clinical guidance (CG107) regarding offering LDA (75mgs daily) to all women with diabetes. We have retained the recommendation about increased LDA dose in women with proteinuria.
Welsh Endocrine and Diabetes Society	2	Full	4.3.2	253	Those with risk factors only will be screened. This approach is known to miss large numbers with GDM. The ADA have adopted the IADPSG recommendation of screening all.	Thank you for your comment. Our UK/Australian HAPO dataset suggested that the patients missed without risk factors would have milder disease than those patients detected with risk factors. The health economic analysis did not find it was cost-effective to treat the sub-group of

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						gestational diabetes women without risk factors.
Welsh Endocrine and Diabetes Society	1	Full	4.4.8	313	The diagnostic criteria for gestational diabetes are given as fasting > 5.6 mmol/l and 2 hour > 7.8 mmol/l. This is not consistent with other diagnostic criteria (e.g. WHO and ADA have accepted the IADPSG criteria of fasting > 5.1, 1 hour > 10, 2 hour > 8.5) and subsequently may give rise to confusion.	Thank you for your comment. Whilst the new IADPSG diagnostic criteria are supported by many, they are not universally accepted and remains controversial. Furthermore, it is widely accepted that IADPSG diagnostic criteria would greatly increase the woman diagnosed with gestational diabetes and it is important in NICE guidelines that increased use of scarce NHS resources is supported by evidence that this would be cost-effective. Some commentators have criticised the arbitrary nature of IADPSG diagnostic thresholds and those thresholds were certainly not developed using any formal consideration of whether any additional benefits of diagnosing more women would justify the additional costs. We accept that the criteria recommended by this guideline differ from the new WHO criteria. However, we noted that the strength of the WHO recommendation was weak and that the WHO guideline suggests a rapid update of the criteria may be necessary in the light of new health economic evidence.
Welsh Endocrine and Diabetes Society	5	Full	5.5.10	464	There is a suggestion that a patient receiving continuous glucose monitoring in pregnancy should have 24 hour access to her specialist team however the rationale for this is not clear and is of doubtful necessity.	Thank you for your comment. We discussed the recommendation and agreed that whilst the provision of support was essential for women using CGM from someone who was expert in its use, it was not necessary to stipulate that this had to be 24h support from a diabetologist. The

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						recommendation has been amended accordingly.
Welsh Endocrine and Diabetes Society	3	Full	5.10.3	497	The recommended scheduling of appointments for pre-existing diabetes starts at 10 weeks. There should be a recommendation for intervention to improve glycaemic control as soon as possible in pregnancy if this was not possible pre-conception.	Thank you for your comment. However, we think the scheduling of appointments which is covered in Tables 70 and 73 in the Full Guideline and Table 1 in the NICE version do address this point. In Table 73 (Full Guideline) or 1 (NICE version) it says '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.' That 'review of medicines' will include adjustment of her treatment regimen to aim for target glucose values recommended elsewhere in the guideline.
Whittington Hospital NHS Foundation Trust	1	NICE	General	General	We believe there should be more emphasis on the fact that pre-existing diabetes carries far greater risks for the mother and the fetus than gestational diabetes. Percentages for risk of complications in both groups may be helpful to stress this point.	Thank you for your comments. However, we consider the balance between established diabetes and gestational diabetes is appropriate. We think it is wrong to emphasise the importance of the condition. Apart from congenital abnormalities, women with gestational diabetes are at increased risk of the same complications as women with established diabetes. Also the majority of women with diabetes in pregnancy have gestational diabetes. Finally, some of the women with that diagnosis in fact have type 2 diabetes which is only picked up in pregnancy.
Whittington Hospital NHS	2	NICE	1.1.17	10	Advising all women with diabetes who are planning to become pregnant to aim for glucose values the same as all people with diabetes	Thank you for your comment. However, the target glucose values recommended in the consultation draft of the updated NICE

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Foundation Trust					belittles the added risks associated in the early prenatal period to the fetus and the mother. This statement as a 'stand alone' statement gives the wrong message. ie 'it's no more important in the preconception period, than any other time of your life, to have near perfect glucose values'. Of course people with diabetes should always aim for the best control possible at all times but the reality of this is low. To assume otherwise we believe is unrealistic and inappropriate.	clinical guidance 15 'Type 1 diabetes: the diagnosis and management of type 1 diabetes in adults' are much more stringent than previously. The GDG felt that these were sufficiently strict and, if followed, would improve the outcomes in early pregnancy. The consultation draft of the updated NICE CG 15 is available from the NICE website http://www.nice.org.uk/guidance/indevelopment/gid-cgwaver122/consultation Consultation closes at 5pm on 4 March 2015
Whittington Hospital NHS Foundation Trust	3	NICE	1.2.8	10 and 23	We do not agree with the diagnostic criteria for OGTT for GDM. We believe the FBG should be lower and the 2 hr cut off higher. The evidence to support risk with a 2 hr cut off as low as 7.8 mmol/L is weak. We support IADPSG /ADA criteria. HAPO included 20,000 women which is probably a larger number of women than all studies quoted in the full document put together.	Thank you for your comment. However, it is not clear on what basis the claim that the 'evidence to support risk with a 2 hr cut off as low as 7.8 mmol/L is weak' is made. These recommendations were informed by a health economic model which used logistic regression analysis to derive a prediction model to estimate risk based on fasting, 1 hour and 2 hour OGTT blood glucose values in addition to other variables. This health economic model was explained in detail in Chapter 9 of the consultation version of the guideline. We are aware that the HAPO study included over 20,000 women but there it is not clear how the data from that study was used to derive IADPSG diagnostic thresholds. It has been argued that the IADPSG criteria are arbitrary. In contrast, the prediction model in the Guideline was based on data from over 6,000 women in the UK and Australia, who were included in the HAPO dataset.

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						Whilst smaller than the complete HAPO dataset they more closely reflect the characteristics of the population for which NICE recommendations are made. Furthermore, uncertainty in prediction coefficients was addressed through probabilistic sensitivity analysis. The prediction model suggested that 2 hour blood glucose values was a stronger predictor than fasting blood glucose for most outcomes (see Chapter 9 of the Full Guideline). Finally, it should be noted also that the proposed fasting diagnostic threshold for gestational diabetes is substantially lower than the fasting threshold used in the 2008 NICE guideline.
Whittington Hospital NHS Foundation Trust	4	NICE	1.4.4	13 and 33	There is no good evidence reported suggesting benefit in all women with GDM being advised to give birth by 39 +6 weeks. At our unit we sometimes allow diet, well controlled and uncomplicated pregnancies to progress up to 40+6 weeks. As outlined on p544 of full document, the increased number of inductions of labour has cost and fetal and maternal well being implications	Thank you for your comment. We reconsidered the recommendation about timing of birth in response to stakeholder comments. We felt that the evidence justified making separate recommendations for the timing of birth for women with type 1 or type 2 diabetes and for women with gestational diabetes. For women with gestational diabetes, the data from Rosenstein (2012) demonstrated that there was a significant rise in stillbirth rate after 40+6 days. Whereas the Kjos (1993) study showed that the incidence of babies weight more than 4000g rose after 39+6 days. Given that avoidance of stillbirth was the philosophy underpinning the timing of delivery, the GDG felt that in women with

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						uncomplicated gestational diabetes elective delivery could be delayed until 40+6 days. For women with type 1 or type 2 diabetes the limited data demonstrated that the stillbirth rate rose after 38+6 weeks. Thus such women should be offered elective delivery by 38+6 weeks. We felt that a lower limit should be also included in the recommendation to avoid women with uncomplicated type 1 or type 2 diabetes being advised to have an elective preterm delivery with its associated complications for the woman (such as failed induction of labour and caesarean section) and the baby (such as respiratory distress syndrome and admission to the neonatal unit). The data from Holman (2014) suggested the lower limit of the elective delivery should be 37+0 weeks. Thus we recommended elective delivery for women with uncomplicated type 1 or type 2 diabetes between 37+0 and 38+6 weeks. In making this recommendation, we expect that, in practice, this would result in such women being routinely offered elective delivery nearer 38+6 weeks than 37+0 weeks.
Whittington Hospital NHS Foundation Trust	5	NICE	1.2.4	22	A statement of 'consider OGTT when there is glycosuria in pregnancy, particularly first trimester', is unhelpful. If we do in all, this may be more costly than screening at risk groups for undiagnosed type 2 diabetes or impaired glucose tolerance with FBG or HbA1c	Thank you for your comment. In summary, the evidence relating to glycosuria as a predictor of glucose intolerance in pregnancy is that there is no evidence of its value as a population screening test, but, there is observational data that glycosuria increases the likelihood of gestational diabetes. Because of the screening

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						evidence (or lack of it) the original guideline and the ANC guideline do not recommend it for population screening in pregnancy. However, we recognise that urinalysis is undertaken routinely in pregnancy using reagent strips that not only record the presence of protein but other substances including glucose. Thus we have made a recommendation based on the observational data presented in the original guideline. No health economic evaluation was undertaken as part of this review. The text of the guideline and the recommendations have been amended to make these points clearer.
Whittington Hospital NHS Foundation Trust	6	Full	4.4.7.3	311	Locally we have adopted the IADSPAG criteria. We asked our biochemist to review previous OGTTs in our population of pregnant women. We found that although lowering the FBG, (previously 5.5 mmol/L locally), by raising the cut off of the 2hr value (previously 8.0 mmol/L locally), numbers of women diagnosed with GDM did not alter greatly. We believe the number of units using old WHO criteria for GDM is less than 50% (accepting FBG of > 6.0 mmol/L as 'normal in pregnancy' goes against much of the evidence available). Therefore the economics arguments applied by the GDG are flawed and are based on an incorrect baseline data.	Thank you for this your comment. The impact of different thresholds on the number of women diagnosed is considered in considerable detail in Section 9.2.3.1 of the consultation version of the guideline across a number of centres. It is not clear to us that the premise that less than 50% of units are using old WHO criteria for gestational diabetes, which may well be true, implies the economic arguments are flawed or are based on incorrect baseline data. The health economic model considers 14 different diagnostic thresholds in addition to a strategy of no diagnosis/treatment. It uses individual patient data and a prediction model to estimate a baseline risk for various maternal and neonatal outcomes. It then applies a treatment effect, derived from intervention studies, to that woman's risk if they are identified as having gestational

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						diabetes by a particular strategy. In that way the model estimates the costs and benefits of all diagnostic strategies and uses standard NICE decision criteria to determine whether the more effective strategies do so at acceptable cost.

These organisations were approached but did not respond:
5 Borough Partnership NHS Foundation Trust
5 boroughs NHS Foundation Trust Partnership
A.Menarini Pharma U.K. S.R.L.
Abbott Laboratories
Action on Pre-Eclampsia
Airedale NHS Trust
Alere
All Wales Dietetic Advisory Committee
Allocate Software PLC
Aneurin Bevan Health Board
Anglian Community Enterprise
Arrowe Park Hospital
Association for Improvements in the Maternity Services
Association of Ambulance Chief Executives
Association of British Clinical Diabetologists
Association of British Healthcare Industries
Association of Clinical Pathologists
Association of Radical Midwives
Astrazeneca UK Ltd
Baby Lifeline
Bayer plc
Becton Dickinson
Belfast Health and Social Care Trust
Berkshire Local Pharmaceutical Committees
Best Beginnings
Betsi cadwaladr
BirthChoice UK

Black and Ethnic Minority Diabetes Association
Bliss
Boehringer Ingelheim
Bolton Hospitals NHS Trust
Boots
Bradford District Care Trust
Bradford Royal Infirmary
Breastfeeding Network - Scotland
Bristol Health Services Plan
Bristol-Myers Squibb Pharmaceuticals Ltd
British Association of Perinatal Medicine
British Association of Prosthetists & Orthotists
British Dietetic Association
British Infection Association
British Maternal & Fetal Medicine Society
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Pharmacological Society
British Psychological Society
British Red Cross
BSN Medical
Buckinghamshire Hospitals NHS Trust
C. R. Bard, Inc.
Cambridge University Hospitals NHS Foundation Trust
Camden Link
Capsulation PPS
Capsulation PPS
Cardiff and Vale University Health Board
Care Quality Commission
Cegedimrx
Central & North West London NHS Foundation Trust
Central London Community Health Care NHS Trust
Central London Community Health Care NHS Trust
Children England
Children, Young People and Families NHS Network
CHKS Ltd

City Hospitals Sunderland NHS Foundation Trust
Clarity Informatics Ltd
Cochrane Pregnancy & Childbirth Group
Colchester Hospital University NHS Foundation Trust
Community Diabetes Consultants
Co-operative Pharmacy Association
Countess of Chester Hospital NHS Foundation Trust
Coventry and Warwickshire Cardiac Network
Croydon Clinical Commissioning Group
Croydon Council
Croydon Health Services NHS Trust
Croydon University Hospital
Cumbria Partnership NHS Foundation Trust
Cumbria Partnership NHS Trust
CWHHE Collaborative CCGs
Cytyc UK Limited
Daiichi Sankyo UK
Deaf Diabetes UK
Department for Communities and Local Government
Department of Health
Department of Health, Social Services and Public Safety - Northern Ireland
Derbyshire County Council
Det Norske Veritas - NHSLA Schemes
Diabetes Management and Education Group
Dieticians in obesity management
Doncaster and Bassetlaw Hospitals NHS Foundation Trust
Doula UK
Dudley Group Of Hospitals NHS Foundation Trust
Durham County Council
Ealing Hospital NHS Trust
Ealing Public Health
East and North Hertfordshire NHS Trust
East Kent Hospitals University NHS Foundation Trust
East Midland Ambulance Services NHS
East Riding of Yorkshire Council
Eastbourne District General Hospital
Economic and Social Research Council
Elcena Jeffers Foundation

Elective Cesarean
English National Forum of LSA Midwifery Officers
Equalities National Council
Ethical Medicines Industry Group
European Atherosclerosis Society
Evidence based Midwifery Network
Expert Patients Programme CIC
Faculty of Dental Surgery
Faculty of Public Health
FBA and Brook
Federation of Ophthalmic and Dispensing Opticians
Ferring Pharmaceuticals
Fibroid Network Charity
Five Boroughs Partnership NHS Trust
George Eliot Hospital NHS Trust
Gloucestershire LINk
GP update / Red Whale
Great Western Hospitals NHS Foundation Trust
Greater Manchester West Mental Health NHS Foundation Trust
Group B Strep Support
Guy's and St Thomas' NHS Foundation Trust
Health and Care Professions Council
Health and Social Care Information Centre
Healthcare Improvement Scotland
Healthcare Infection Society
Healthcare Quality Improvement Partnership
Healthwatch East Sussex
HemoCue Ltd
Hertfordshire Partnership NHS Trust
Herts Valleys Clinical Commissioning Group
Hindu Council UK
Hockley Medical Practice
Homerton Hospital NHS Foundation Trust
HQT Diagnostics
Humber NHS Foundation Trust
InDependent Diabetes Trust
Independent Healthcare Advisory Services
Independent Midwives Association

Innermost Secrets Ltd
INPUT Patient Advocacy
Institute for Womens Health
Institute Metabolic Science
Institute of Biomedical Science
Institute of Health and Society
Insulin Pump Awareness Group - Scotland
Janssen
JBOL Ltd
Johnson & Johnson
Johnson & Johnson Medical Ltd
Juvenile Diabetes Research Foundation
karimahs cuisina
KCl Europe Holding B.V.
KCl Medical Ltd
Kidney Research UK
King Fahd Military Medical Complex
King's College Hospital - Weston Education Centre
Kingston Hospital
Kingston University and St Georges, University of London
La Leche League GB
La Leche League Great Britain
Lactation Consultants of Great Britain
Lancashire Care NHS Foundation Trust
Launch Diagnostics
Leeds Community Healthcare NHS Trust
Leeds North Clinical Commisioning Group
Leeds South and East Clinical Commissioning Group
Leeds Teaching Hospitals NHS Trust
Lesbian, gay, bisexual and trans domestic abuse forum
Lewisham University Hospital
LifeScan
Lilly UK
Liverpool PCT Provider Services
Liverpool Women's NHS Foundation Trust
Local Government Association
London Labour Ward Leads Group
Luton and Dunstable Hospital NHS Trust

MacDonald UK Obstetric Medicine Society
Maidstone and Tunbridge Wells NHS Trust
Maidstone Hospital
Maquet UK Ltd
Maternity Action
Maternity and Health Links
McCallan Group, The
McDonald Obstetric Medicine Society
medical directorate DMS
Medicines and Healthcare products Regulatory Agency
Medway NHS Foundation Trust
Menarini Diagnostics UK
Merck Serono
Merck Sharp & Dohme UK Ltd
Mid and West Regional Maternity Service Liasion Committee
Mid Staffordshire NHS Foundation Trust
midwifeexpert.com
Midwives Information and Resource Service
Ministry of Defence (MOD)
Multiple Births Foundation
National Association of Primary Care
National Childbirth Trust
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Concern for Healthcare Infection
National Deaf Children's Society
National Diabetes Inpatient Specialist Nurse
National Federation of Women's Institutes
National Institute for Health Research
National Institute for Health Research Health Technology Assessment Programme
National Kidney Research Foundation
National Obesity Forum
National Patient Safety Agency
National Perinatal Epidemiology Unit
National Pharmacy Association
National Public Health Service for Wales

NDR UK
Neonatal & Paediatric Pharmacists Group
Nester Healthcare Group Plc
NHS Barnsley Clinical Commissioning Group
NHS Blood and Transplant
NHS Clinical Knowledge Summaries
NHS Connecting for Health
NHS Cornwall and Isles Of Scilly
NHS County Durham and Darlington
NHS Cumbria Clinical Commissioning Group
NHS Derbyshire county
NHS Fetal Anomaly Screening Programme
NHS Greater Manchester Commissioning Support Unit
NHS Halton CCG
NHS Hardwick CCG
NHS Health at Work
NHS Improvement
NHS Kirklees
NHS London
NHS Manchester
NHS Medway Clinical Commissioning Group
NHS Midlands and East
NHS Milton Keynes
NHS Newcastle
NHS North Somerset CCG
NHS Plus
NHS Plymouth
NHS Sheffield
NHS South Central
NHS South Cheshire CCG
NHS Sussex
NHS Trafford CCG
NHS Wakefield CCG
NHS Warwickshire North CCG
NHS West Cheshire CCG
North Bristol Trust
North Cheshire Hospitals NHS Trust
NORTH EAST LONDON FOUNDATION TRUST

North Essex Mental Health Partnership Trust
North Middlesex University Hospital NHS Trust
North of England Commissioning Support
North Tees and Hartlepool NHS Foundation Trust
North West London Hospitals NHS Trust
North West London Perinatal Network
Northamptonshire county council
Northern Health and Social Care Trust
Northumbria Diabetes Service
Northumbria Healthcare NHS Foundation Trust
Nottingham City Hospital
Nova Biomedical UK
Nursing and Midwifery Council
Nutrition and Diet Resources UK
Nutrition Society
Obstetric Anaesthetists' Association
One to One
Optical Confederation, The
Owen Mumford Ltd
Oxford Centre for Diabetes, Endocrinology and Metabolism
Oxford Health NHS Foundation Trust
Oxford University Hospitals NHS Trust
Oxfordshire Clinical Commissioning Group
Pennine Acute Hospitals NHS Trust
PERIGON Healthcare Ltd
Perinatal Institute
Pfizer
PharmaPlus Ltd
Plymouth Hospitals NHS Trust
Powys Local Health Board
PrescQIPP NHS Programme
Primary Care Dermatology Society
Primary Care Diabetes Society
Primary Care Pharmacists Association
Primary Care Women's Health Forum
Primrose Bank Medical Centre
Programme development Group in Maternal and Child Nutrition
Public Health Agency

Public Health England
Queen Elizabeth Hospital
Queen Mary's Hospital NHS Trust
RCM Consultant Midwives Forum
Regional Maternity Survey Office
RioMed Ltd.
Royal Berkshire NHS Foundation Trust
Royal Brompton Hospital & Harefield NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners in Wales
Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition
Royal College of Pathologists
Royal College of Physicians
Royal College of Physicians and Surgeons of Glasgow
Royal College of Physicians of Edinburgh
Royal College of Psychiatrists
Royal College of Psychiatrists in Scotland
Royal College of Radiologists
Royal College of Speech and Language Therapists
Royal College of Surgeons of England
Royal Cornwall Hospitals NHS Trust
Royal Free Hospital NHS Foundation Trust
Royal National Institute of Blind People
Royal Pharmaceutical Society
Royal Society of Medicine
Royal Surrey County Hospital NHS Trust
Royal United Hospital Bath NHS Trust
Royal West Sussex NHS Trust
Saint Mary's Hospital
Salford Royal Foundation Hospital
Sands, the stillbirth and neonatal death charity
Sandwell and West Birmingham Hospitals NHS Trust
Scarborough and North Yorkshire Healthcare NHS Trust
School of Midwifery
Scottish Government
Scottish Intercollegiate Guidelines Network
Sheffield Teaching Hospitals NHS Foundation Trust

SNDRi
Social Care Institute for Excellence
Society and College of Radiographers
Society for Endocrinology
Society for the Protection of Unborn Children
South Asian Health Foundation
South Belfast Partnership Board
South Devon Healthcare NHS Foundation Trust
South East Coast Ambulance Service
South Eastern Health and Social Care Trust
South London & Maudsley NHS Trust
South Tees Hospitals NHS Trust
South West commissioning Support
South West London Maternity Network
South West Yorkshire Partnership NHS Foundation Trust
Southend Hospitals NHS Foundation Trust
Southern Health & Social Care Trust
Southport and Ormskirk Hospital NHS Trust
Spirit Healthcare
St Mary's Hospital
Staffordshire and Stoke on Trent Partnership NHS Trust
Stockport Clinical Commissioning Group
Stockport Clinical Commissioning Pathfinder
Suffolk County Council
Sunderland Royal Hospital
Sure Start Tamworth
Swansea NHS Trust
Swansea University
Tameside Hospital NHS Foundation Trust
The Association of the British Pharmaceutical Industry
The British In Vitro Diagnostics Association
The Natural Ketosis Company
The Patients Association
The Princess Alexandra Hospital NHS Trust
The Rotherham NHS Foundation Trust
Tiny Tickers
Tommy's - The Baby Charity
UCL/UCLH Institute for Women's Health

UK Anaemia
UK Clinical Pharmacy Association
UK National Screening Committee
UK Specialised Services Public Health Network
UK Thalassaemia Society
United Lincolnshire Hospitals NHS
University College London
University College London Hospital NHS Foundation Trust
University College London Hospitals NHS Foundation Trust
University Hospital of North Staffordshire NHS Trust
University Hospitals Birmingham
University Hospitals Bristol NHS Foundation Trust
University of Huddersfield
University of Leicester
University of Salford
University of Sheffield
Vifor Pharma UK Ltd
Walsall Local Involvement Network
Weight Concern
Welsh Government
Welsh Scientific Advisory Committee
West Hertfordshire Hospital Trust
West Herts Hospitals NHS Trust
West Middlesex University Hospital NHS Trust
West Midlands Antenatal Diabetes Association
West Midlands Perinatal Institute
Western Health and Social Care Trust
Western Sussex Hospitals NHS Trust
Wigan Borough Clinical Commissioning Group
Wirral University Teaching Hospital NHS Foundation Trust
Wockhardt UK Ltd
Women's Support Network
WORCESTER ROYAL HOSPITAL
Worcestershire Acute Hospitals Trust
Worcestershire Health and Care NHS Trust
Worthing Hospital
Wrightington, Wigan and Leigh NHS Foundation Trust
Wye Valley NHS Trust

Yeovil District Hospital NHS Foundation Trust
York Hospitals NHS Foundation Trust
Yorkshire and Humber Strategic Clinical Network
Yorkshire and The Humber Maternity Network
Young Diabetlolgists Forum