Table S4: The full list of 60 indicative questions evidence search results completed over the period January to May 2020. Presented in groups by phase of pregnancy, with rank by groups. Darker grey indicates higher priority rank. Top ten are highlighted.

#	Phase of pregnancy	Indicative Question	FINAL RANK	Evidence (NICE NG3 and SIGN 116; Systematic Reviews 2017 onwards; Cochrane Reviews all-time)	Summary
1	Before pregnancy	What effect does diabetes, or previous gestational diabetes, have on a woman's fertility (ability to get pregnant and number of pregnancies)?	**40**	National Institute of Clinical Excellence National Guideline (NICE NG) 3: notes as common misconception that diabetes affects fertility. Reference in relation to use of oral contraceptives. Scottish Intercollegiate Guidelines Network (SIGN)116: None. Maresch CC, Stute D, Alves MG, Oliveira PF, de Kretser DM, Linn T. Diabetes-induced hyperglycemia impairs male reproductive function: a systematic review. Hum Reprod Update. 2018 Jan 1;24(1):86-105. doi: 10.1093/humupd/dmx033. Indirect relevance: Morley LC, Tang T, Yasmin E, Norman RJ, Balen AH. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev. 2017;11:CD003053. doi:10.1002/14651858.CD003053.pub6, 10.1002/14651858.CD003053.pub6	Guidelines – Notes negative effects of diabetes on fertility is a common misconception and no evidence to support. Systematic reviews (SRs) – 1 but in men with diabetes
2	Before pregnancy	How can a woman with diabetes best prepare for pregnancy? For example blood sugar level targets, nutrition.	**14**	NICE NG3: Chapter 3 - 3.6 and 3.7. Blood glucose control and targets. 3.4.1.2 A case–control study compared folate metabolism in 31 pregnant women with diabetes to that in 54 pregnant women without diabetes. The study found no significant differences for any measures of folate metabolism. 3.6. highlights a lack of pregnancy specific evidence to support target glucose ranges pre-conception. The guidelines were made in line with general type 1 diabetes population targets (as at 2015). SIGN116 : 7.3.1 moderate level evidence: showing the link between pre-gregnancy glucose levels (HbA1c) and the risk of congenital anomaly with tabulated presentation of absolute risk with HbA1c levels. In women with type 1 diabetes, suboptimal glucose management before and during pregnancy is associated with perinatal mortality and congenital malformations. However, "no HbA1c threshold for such effects was identified". Oral anti-diabetic agents for women with established diabetes/impaired glucose tolerance or previous gestational diabetes	Guidelines – Extensive pre-pregnancy preparation guidelines with varied evidence grade levels. Glucose targets: based on recommendations for type 1 diabetes for general population. No specific research in women with diabetes (any type) referenced. Research recommended on what can help women to achieve the best possible glycaemic management. Nutrition: none of relevance. SRs – Not done.

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				planning pregnancy, or pregnant women with pre-existing diabetes. Tieu J, Coat S, Hague W, Middleton P, Shepherd E. Cochrane Database Syst Rev. 2017 Oct 18;10:CD007724. doi: 10.1002/14651858.CD007724.pub3. Review. Hyperglycaemia and risk of adverse perinatal outcomes: systematic review and meta-analysis. Farrar D, Simmonds M, Bryant M, Sheldon TA, Tuffnell D, Golder S, Dunne F, Lawlor DA. BMJ. 2016 Sep 13;354:i4694. doi: 10.1136/bmj.i4694. Review. PMID: 27624087 Oteng-Ntim E, Mononen S, Sawicki O, Seed PT, Bick D, Poston L. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. BMJ Open. 2018;8(6):e018778. doi:10.1136/bmjopen-2017-018778, 10.1136/bmjopen-2017-018778 Interpregnancy weight change associated with risk of GDM and baby size.	
3	Before pregnancy	How much and for how long should women with diabetes take folic acid before pregnancy?	**57**	NICE NG3: 3.1.2, 3.2.2, 3.4.1.2 evidence for folic acid supplementation, but not the dose. No difference in metabolism of folate between women with and without diabetes. No folic acid supplementation preconception associated with poor pregnancy outcome. 3.4.2, 3.4.4 folic acid is particularly important for women with diabetes planning a pregnancy because of the increased risk of congenital malformations, which include neural tube defects. There is no evidence to suggest that these women would benefit from a larger dose than is recommended for women who do not have diabetes. However, women with diabetes should take the higher dose of 5 mg per day, as for other women with increased risk of neural tube defects, when intending to become pregnant. SIGN116: 7.3.2 moderate to high-grade evidence in population without diabetes for recommendation to supplement with 5mg folic acid pre-pregnancy and up to 12 weeks gestation.	Guidelines – Folic Acid: women with diabetes recommended to take the higher 5mg dose due to the higher risk of congenital abnormalities (as for any woman with high risk of neural tube defects). Although, no evidence of need/benefit in these women, nor on duration to take pre-pregnancy. SRs – None.
4	Before pregnancy	For women with diabetes, what factors	**55**	NICE NG3: Maternal age: Gestational diabetes incidence is increased with maternal age but inconsistent predictor for recurrence of GDM	Guidelines – Maternal age: Increased risk of developing GDM with increasing maternal age.

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		(i.e. their age, the duration they have had diabetes, contraception) may be important to consider when planning to have a family?		– low/moderate level evidence. Contraceptives: 3.3.5.3.4 no evidence of deterioration in glycaemia as assessed by HbA1c in women using oral contraceptives based on low quality studies. SIGN116: Maternal age: none. Contraceptives: none Duration of diabetes before pregnancy is not addressed.	Moderate evidence. None on pre-existing diabetes with age and risks. Duration diabetes pre-pregnancy: none. Contraception: 3 RCTs and a case control study that there is no consistent effect of hormonal contraception on average glycaemic control in women with diabetes. SRs – no evidence that advance maternal age increases the risk of recurrence of gestational diabetes. A lack of evidence for the effect of increased maternal age on the risk of the child developing diabetes. Otherwise none relevant on other elements.
5	**Before pregnancy**	**How can care and services be improved for women with diabetes who are planning pregnancy? For example, removing barriers to attending pre-pregnancy clinics.**	**10**	NICE NG3 – 3-preconception care. 2.3 Barriers to achieving blood glucose targets before and during pregnancy. Multiple recommendations on preconception care and barriers listed (low-moderate evidence). Identified key areas for improvement in the provision of preconception counselling there are no suggestions for how these can be improved. Research recommendations: "'What is the most clinically and cost-effective form of preconception care and advice for women with diabetes?"; "What are the barriers that women experience to achieving blood glucose targets?" ; "What are the roles of insulin pump therapy (continuous subcutaneous insulin infusion) and continuous glucose monitoring in helping women with diabetes to achieve blood glucose targets before pregnancy?" Preconception care for diabetic women for improving maternal and infant health. Tieu J, Middleton P, Crowther CA, Shepherd E. Cochrane Database Syst Rev. 2017 Aug 11;8:CD007776. Doi: 10.1002/14651858.CD007776.pub3. Review. PMID: 28799164 Free PMC Article. No relevant studies included Preconception Care Education for Women With Diabetes: A Systematic Review of Conventional and Digital Health Interventions.	Guidelines – Multiple recommendations on preconception care and barriers listed (low-moderate evidence). Research recommendation: 'What is the most clinically and cost-effective form of preconception care and advice for women with diabetes?' and 'What are the barriers that women experience to achieving blood glucose targets?' SRs – Not done

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#	Phase of pregnancy	Indicative Question	FINAL RANK	Evidence (NICE NG3 and SIGN 116; Systematic Reviews 2017 onwards; Cochrane Reviews all-time)	Summary
				Nwolise CH, Carey N, Shawe J. J Med Internet Res. 2016 Nov 8;18(11):e291. Review. PMID: 27826131. Reported that women receiving educational interventions via electronic methods (4 studies) had significantly improved levels of glycosylated haemoglobin.	
6	**During pregnancy**	**What is the best test to diagnose diabetes in pregnant women?**	**1**	NICE NG3: International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycaemia in pregnancy 2010 based on HAPO study. This is not uniformly used across the UK. NICE guidelines use cut offs based on Glycaemic index as well as cost modelling. Relevant research recommendation: "When should testing for gestational diabetes take place – in the first or second trimester?" SIGN116: used IADPS OGTT cut offs. Cochrane concluded There are insufficient randomised controlled trial data evaluating the effects of screening for GDM based on different risk profiles and settings on maternal and infant outcomes. Low-quality evidence suggests universal screening compared with risk factor-based screening leads to more women being diagnosed with GDM. Low to very low-quality evidence suggests no clear differences between primary care and secondary care screening, for outcomes: GDM, hypertension, pre-eclampsia, caesarean birth, large-for-gestational age, neonatal complications composite, and hypoglycaemia. Different strategies for diagnosing gestational diabetes to improve maternal and infant health, https://doi.org/10.1002/14651858.CD007122.pub4: concluded there is insufficient evidence to suggest which strategy is best for diagnosing GDM. Large randomised trials are required to establish the best strategy for correctly identifying women with GDM. Donovan BM, Nidey NL, Jasper EA, Robinson JG, Bao W, Saftlas AF, Ryckman KK. First trimester prenatal screening biomarkers and gestational diabetes mellitus: A systematic review and meta-analysis.	Guidelines – Advise only screening high risk women for GDM. No consensus on best test for GDM due to small trials. Guidelines vary even within region. Relevant research recommendation: 'When should testing for gestational diabetes take place – in the first or second trimester?' SRs – 1 reference, concluded insufficient evidence on which strategy is best for diagnosing GDM.

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				PLoS One. 2018 Jul 26;13(7):e0201319. doi: 10.1371/journal.pone.0201319. PMID: 30048548; PMCID: PMC6062092. Sweeting A, Park F, Hyett J. The first trimester: prediction and prevention of the great obstetrical syndromes. Best practice & research Clinical obstetrics & gynaecology. 2015;29(2):183–93. Epub 2014/12/09. 10.1016/j.bpobgyn.2014.09.006 Tieu J, McPhee AJ, Crowther CA, Middleton P, Shepherd E. Screening for gestational diabetes mellitus based on different risk profiles and settings for improving maternal and infant health. Cochrane Database of Systematic Reviews 2017. DOI: 10.1002/14651858.CD007222.pub4 Further, high-quality randomised controlled trials are needed to assess the value of screening for GDM, which may compare different protocols, guidelines or programmes for screening (based on different risk profiles and settings), with the absence of screening, or with other protocols, guidelines or programmes. Immanuel, J., Simmons, D. Screening and Treatment for Early-Onset Gestational Diabetes Mellitus: a Systematic Review and Meta-analysis. Curr Diab Rep 17, 115 (2017). https://doi-org.ezproxy.is.ed.ac.uk/10.1007/s11892-017-0943-7	
7	During pregnancy	What are the different types of diabetes that develop in pregnancy and how can they be promptly and accurately diagnosed?	**60**	NICE NG3: International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycaemia in pregnancy 2010 based on HAPO study. This is not uniformly used across the UK. NICE guidelines use cut offs based on Glycaemic index as well as cost modelling. SIGN116: used IADPS OGTT cut offs. National guidelines advise only screening high risk women (BMI, previous GDM, macrosomia, family history)	Guidelines – Recommendations on the diagnosis and classification of hyperglycaemia in pregnancy 2010 based on HAPO study. Advise only screening high risk women (BMI, previous GDM, macrosomia, family history). Low-grade evidence. None on screening for other types of diabetes. SRs – None relevant. Role of Metabolomic / Genetic biomarkers still remains uncertain.

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8	**During pregnancy**	**What is the best way to test for and treat diabetes in late pregnancy i.e. after 34 weeks?**	**7**	NICE NG3: 5.2.7.2 states "If a woman presents with gestational diabetes at 30 weeks and is set targets, it may be too late to prevent some poor outcomes and she may still have a large for gestational age baby or develop pre-eclampsia. If a woman has a high blood glucose at 30 weeks it is likely that it was also high at 20 weeks. This is an issue which is especially relevant for women with gestational diabetes. Existing guidance means that diagnosis of gestational diabetes is often not made until the third trimester. By this stage the argument that it is 'too late to affect adverse outcomes' may apply. This concern was specifically expressed in relation to the study by Rowan et al. (2010)." [evidence grade – consensus recommendation]. Relevant research recommendations: "What is the incidence in both unselected and high risk populations of previously undetected type 2 diabetes and gestational diabetes in the first trimester of pregnancy and the relationship to adverse pregnancy outcomes?"; "When should testing for gestational diabetes take place – in the first or second trimester?" Gomes, Delphina et al. Late-pregnancy dysglycemia in obese pregnancies after negative testing for gestational diabetes and risk of future childhood overweight: An interim analysis from a longitudinal mother-child cohort study." PLoS medicine vol. 15,10 e1002681. 29 Oct. 2018, doi:10.1371/journal.pmed.1002681 The Peaches study published evidence for GDM screening in late pregnancy in obese women who had -ve GDM screening in the 2nd/3rd TM. This demonstrated that 30% of obese women who had a -ve glucose tolerance test at <32+6 showed dysglycaemia at delivery, marked by an Hba1c > 39mmmol."	Guidelines – Commentary that existing guidance means that diagnosis of gestational diabetes is often not made until the third trimester, and that it is likely that BGs were high at 20 weeks, and late management may be too late to prevent some poor outcomes. Research recommendation: for RCTs to establish if testing, diagnosis and intervention in the first rather than the second trimester improves maternal, fetal and neonatal outcomes, including fetal hyperinsulinaemia. None on late pregnancy (after 28 weeks) testing and treatment. SRs – 1 relevant. No studies demonstrating validated reference ranges of OGTT/CGM/ Hba1c in the third TM/term. Additional evidence is needed on the consequences of late-pregnancy dysglycemia for long-term childhood and maternal outcomes.
9	During pregnancy	Does testing all pregnant women for gestational diabetes improve pregnancy outcomes?	**17**	National guidelines advise only screening women at high-risk (BMI, previous GDM, macrosomia, family history) - see related summary questions. Farrar D, Duley L, Dowswell T, Lawlor DA. Different strategies for diagnosing gestational diabetes to improve maternal and infant	Guidelines – Recommendation for assessing all women for risk factors and actively screening women at high risk. Low-level evidence. SRs – Insufficient randomised controlled trial data evaluating the effects of screening for

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				health. Cochrane Database of Systematic Reviews 2017, Issue 8. Art. No.: CD007122. DOI: 10.1002/14651858.CD007122.pub4. Concluded there are insufficient randomised controlled trial data evaluating the effects of screening for GDM based on different risk profiles and settings on maternal and infant outcomes. Low-quality evidence suggests universal screening compared with risk factor-based screening leads to more women being diagnosed with GDM. Low to very low-quality evidence suggests no clear differences between primary care and secondary care screening, for outcomes: GDM, hypertension, pre-eclampsia, caesarean birth, large-for-gestational age, neonatal complications composite, and hypoglycaemia.	GDM based on different risk profiles and settings on maternal and infant outcomes.
10	During pregnancy	Why do some women develop diabetes in pregnancy and others don't? Can this be predicted for individual women?	**30**	NICE NG3: 4.2 risk factors for gestational diabetes. Low-moderate grade evidence. SIGN116: 7.8.1 screening for GDM. The consensus group decided to set the threshold to detect 1.75-fold increase in risk of macrosomia. This reflects a diagnosis of 16-18% of the pregnant population. High-grade evidence for glycosuria and random glucose as risk factors for undiagnosed Type 2 diabetes. Garrison A. Screening, diagnosis, and management of gestational diabetes mellitus. Am Fam Physician. 2015 Apr 1;91(7):460-7. PMID: 25884746. Maternal age older than 35 years OR = 1.6. Petry CJ, Ong KK, Dunger DB. Age at menarche and the future risk of gestational diabetes: a systematic review and dose response meta-analysis. Acta Diabetol. 2018;55(12):1209-1219. doi:10.1007/s00592-018-1214-z, 10.1007/s00592-018-1214-z. Robust evidence that age at menarchy is associated with GDM risk. In Population-based cohort study using the UK Obstetric Surveillance System (UKOSS). Mat age >48 had an adjusted odds ratio [aOR] 4.81 for development of GDM. Lee, K.W., Ching, S.M., Ramachandran, V. et al. Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. BMC Pregnancy Childbirth 18, 494 (2018).	Guidelines – At a basic level the risk factors for GDM is well evidenced. However, could be addressed at a very complex level. SRs – Risk factors for developing GDM are well studied and there a great deal of consensus across studies, the risk of each factor will vary across different regions the world. There are studies (not SRs) showing promising prediction models but are small and limited to the population studied. Need further work on an individual's risk, plus looking wider than GDM subtype.

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				https://doi.org/10.1186/s12884-018-2131-4. A large review of GDM in Asian countries including >2million women identified women with a BMI ≥25 had a pooled OR of 3.27. David A. Sacks, MD1, David R. Hadden, MD2, Michael Maresh, MD3, Chaicharn Deerochanawong, MD4, Alan R. Dyer, PHD5, Boyd E. Metzger, MD6, Lynn P. Lowe, PHD5, Donald R. Coustan, MD7, Moshe Hod, MD8, Jeremy J.N. Oats, MD9, Bengt Persson, MD, PHD10, Elisabeth R. Trimble, MD11 and for the HAPO Study Cooperative Research Group.Frequency of Gestational Diabetes Mellitus at Collaborating Centers Based on IADPSG Consensus Panel–Recommended Criteria Frequency of Gestational Diabetes Mellitus at Collaborating Centres in the HAPO study showed a frequency of 14.4% in Hong Kong population, overall frequency was 17.8% Wan CS; Abell S; Aroni R; Nankervis A; Boyle J; Teede H.Journal Of Diabetes. 11(10):809-817, 2019 Oct. https://dx.doi.org/10.1111/1753-0407.12909 Ethnic differences in prevalence, risk factors, and perinatal outcomes of gestational diabetes mellitus: A comparison between immigrant ethnic Chinese women and Australian-born Caucasian women in Australia. Wu L; Han L; Zhan Y; Cui L; Chen W; Ma L; Lv J; Pan R; Zhao D; Xiao Z Prevalence of gestational diabetes mellitus and associated risk factors in pregnant Chinese women: a cross-sectional study in Huangdao, Qingdao, China. Asia Pacific Journal of Clinical Nutrition. 27(2):383-388, 2018. https://dx.doi.org/10.6133/apjcn.032017.03. Zhang F; Dong L; Zhang CP; Li B; Wen J; Gao W; Sun S; Lv F; Tian H; Tuomilehto J; Qi L; Zhang CL; Yu Z; Yang X; Hu G. Increasing prevalence of gestational diabetes mellitus in Chinese women from 1999 to 2008. Diabetic Medicine. 28(6):652-7, 2011 Jun. https://dx.doi.org/10.1111/j.1464-5491.2010.03205.x An older study 1998-2008 carried out in china (n=105,473) reported prevalence of 6.8% based on 2 step gtt - 50mg glucose 1 hr (BG > 7.8) followed by 2	

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				hr 75g OGTT (using WHO criteria Studies provide incidence in Migrant populations as well as Non-migrant populations. Chinese population in Australia had a 4-fold higher risk than Caucasians. Tieu J, Shepherd E, Middleton P, Crowther CA. Dietary advice interventions in pregnancy for preventing gestational diabetes mellitus. Cochrane Database Syst Rev. 2017 Jan 3;1(1):CD006674. doi: 10.1002/14651858.CD006674.pub3. PMID: 28046205; PMCID: PMC6464792. Very low-quality evidence from five trials suggests a possible reduction in GDM risk for women receiving dietary advice versus standard care, and low-quality evidence from four trials suggests no clear difference for women receiving low- versus moderate- to high-GI dietary advice. Han S, Middleton P, Crowther CA. Exercise for pregnant women for preventing gestational diabetes mellitus. Cochrane Database Syst Rev. 2012 Jul 11;(7):CD009021. doi: 10.1002/14651858.CD009021.pub2. PMID: 22786521. There is limited randomised controlled trial evidence available on the effect of exercise during pregnancy for preventing pregnancy glucose intolerance or GDM. Results from three randomised trials with moderate risk of bias suggested no significant difference in GDM incidence between women receiving an additional exercise intervention and routine care Shepherd E, Gomersall JC, Tieu J, Han S, Crowther CA, Middleton P. Combined diet and exercise interventions for preventing gestational diabetes mellitus. Cochrane Database Syst Rev. 2017 Nov 13;11(11):CD010443. doi: 10.1002/14651858.CD010443.pub3. PMID: 29129039; PMCID: PMC6485974. Moderate-quality evidence suggests reduced risks of GDM and caesarean section with combined diet and exercise interventions during pregnancy as well as reductions in gestational weight gain, compared with standard care. However, there were no clear differences in hypertensive disorders	

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				of pregnancy, perinatal mortality, large-for-gestational age, perineal trauma, neonatal hypoglycaemia, and childhood adiposity. Dodd JM, Grivell RM, Deussen AR, Hague WM. Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. Cochrane Database Syst Rev. 2018 Jul 24;7(7):CD010564. doi: 10.1002/14651858.CD010564.pub2. PMID: 30039871; PMCID: PMC6513233. Metformin may make little or no difference in the risk of women developing gestational hypertension. Barrett HL, Dekker Nitert M, Conwell LS, Callaway LK. Probiotics for preventing gestational diabetes. Cochrane Database Syst Rev. 2014 Feb 27;2014(2):CD009951. doi: 10.1002/14651858.CD009951.pub2. PMID: 24574258; PMCID: PMC6885033. One trial has shown a reduction in the rate of GDM when women are randomised to probiotics early in pregnancy but more uncertain evidence of any effect on miscarriage/IUFD/stillbirth/neonatal death. There are no data on macrosomia. At this time, there are insufficient studies to perform a quantitative meta-analysis. Crawford TJ, Crowther CA, Alsweiler J, Brown J. Antenatal dietary supplementation with myo-inositol in women during pregnancy for preventing gestational diabetes. Cochrane Database Syst Rev. 2015 Dec 17;2015(12):CD011507. doi: 10.1002/14651858.CD011507.pub2. PMID: 26678256; PMCID: PMC6599829. Evidence from four trials of antenatal dietary supplementation with myo-inositol during pregnancy shows a potential benefit for reducing the incidence of gestational diabetes. No data were reported for any of this review's primary neonatal outcomes. There were very little outcome data for the majority of this review's secondary outcomes. There is no clear evidence of a difference for macrosomia when compared with control.	
11	During pregnancy	What are the most effective ways (i.e. diet, lifestyle,	**26**	Han S, Middleton P, Crowther CA. Exercise for pregnant women for preventing gestational diabetes mellitus. Cochrane Database Syst Rev. 2012 Jul 11;(7):CD009021. doi:	Guidelines – None for prevention except limited economic evaluation of prevention vs treatment evidence. Recommendations on

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		medication) to prevent a woman developing diabetes in pregnancy?		10.1002/14651858.CD009021.pub2. PMID: 22786521. "There is limited randomised controlled trial evidence available on the effect of exercise during pregnancy for preventing pregnancy glucose intolerance or GDM." Directed preconception health programs and interventions for improving pregnancy outcomes for women who are overweight or obese. Opray N, Grivell RM, Deussen AR, Dodd JM Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD010932. DOI: 10.1002/14651858.CD010932.pub. Now studies identified – no evidence. Combined diet and exercise interventions for preventing gestational diabetes mellitus. https://doi.org/10.1002/14651858.CD010443.pub3. Moderate-quality evidence suggests reduced risks of GDM and caesarean section with combined diet and exercise interventions during pregnancy as well as reductions in gestational weight gain, compared with standard care. However, there were no clear differences in hypertensive disorders of pregnancy, perinatal mortality, large-for-gestational age, perineal trauma, neonatal hypoglycaemia, and childhood adiposity. Lifestyle interventions for the treatment of women with gestational diabetes. Women receiving lifestyle interventions were less likely to have postnatal depression and were more likely to achieve postpartum weight goals, but there were no trials that reported how health care professional and NHS services helps to promote and recruit women into lifestyle interventions Dietary advice interventions in pregnancy for preventing gestational diabetes mellitus. Cochrane Systematic Review - Intervention. 03 January 2017 https://doi.org/10.1002/14651858.CD006674.pub3. A trend towards a reduction in GDM was observed for women receiving dietary advice compared with standard care and subgroup analysis suggested a greater treatment effect for overweight and obese women receiving	optimising weight, nutrition and glucose before pregnancy in women with diabetes, and prevention of T2D in women with GDM postnatally. SRs – diet and exercise have been studied to target prevention of GDM. There has only been one drug intervention to look at preventing GDM. Due to the variability of the diet and exercise components tested in the included studies, the evidence has limited ability to inform practice. Future studies need to have the intervention standardised between studies. Other interventions showing trends toward reducing GDM include probiotics and myo-inositol. Nutritional status entering pregnancy, as reflected by pre-pregnancy BMI, is thought more important than pregnancy diet in development of GDM but there are inadequate number of studies.

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				dietary advice. Low-quality evidence from four trials suggests no clear difference in the risk of developing GDM for women receiving low- versus moderate- to high-GI dietary advice. Concluded that diet combined with exercise or diet alone enhances weight loss post-partum. Both pharmacological and intensive lifestyle interventions reduce onset of type 2 diabetes in people with impaired glucose tolerance, including women with previous gestational diabetes. In the review, they identified that Very low-quality evidence from five trials suggests a possible reduction in GDM risk for women receiving dietary advice versus standard care. Different types of dietary advice for women with gestational diabetes mellitus. https://doi.org/10.1002/14651858.CD009275.pub3. Evidence from 19 trials assessing different types of dietary advice for women with GDM suggests no clear differences for primary outcomes and secondary outcomes. Hypertensive disorders of pregnancy; caesarean section; type 2 diabetes mellitus; and child: large-for-gestational age; perinatal mortality; neonatal mortality or morbidity composite; neurosensory disability; secondary outcomes for the mother: induction of labour; perineal trauma; postnatal depression; postnatal weight retention or return to pre-pregnancy weight; and child: hypoglycaemia; childhood/adulthood adiposity; childhood/adulthood type 2 diabetes mellitus. Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. https://doi.org/10.1002/14651858.CD010564.pub2. Metformin probably makes little or no difference in the risk of women developing gestational diabetes. Review included 3 RCT's (2 RCT's considered low risk of bias)	
12	During pregnancy	What causes women with diabetes in pregnancy to have larger or smaller than	**38**	NICE NG3: 5.9 Macrosomia is a well-known complication of pregnancy with diabetes and linear association with maternal glucose levels. Evidence level low for different measures such as ultrasound fetal biometry, as predictors of LGA or SGA however.	Guidelines – Increased risk of macrosomia and IUGR and sub-optimal glycaemic management also association with vascular complications and pre-eclampsia. Low-grade evidence. Questions

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		average sized babies, and can it be prevented from happening?		SIGN116: 7.7 moderate-high level evidence of link between glucose levels and macrosomia or IUGR. Also increased risk of IUGR in women with retinopathy or nephropathy, and preclampsia. Shanshan Han, Philippa Middleton, Emily Shepherd, Emer Van Ryswyk, Caroline A Crowther. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Systematic Review - Intervention Version published: 25 February 2017. https://doi.org/10.1002/14651858.CD009275.pub3 Julie Brown,Gilles Ceysens, Michel Boulvain. Exercise for pregnant women with pre-existing diabetes for improving maternal and fetal outcomes. Cochrane Systematic Review - Intervention Version published: 21 December 2017 https://doi.org/10.1002/14651858.CD012696.pub2 Ruth Martis, Caroline A Crowther, Emily Shepherd, Jane Alsweiler, Michelle R Downie, Julie Brown. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews Cochrane Systematic Review - Overview Version published: 14 August 2018. https://doi.org/10.1002/14651858.CD012327.pub2 Joanna Tieu, Philippa Middleton, Caroline A Crowther, Emily Shepherd. Preconception care for diabetic women for improving maternal and infant health. Cochrane Systematic Review - Intervention Version published: 11 August 2017. https://doi.org/10.1002/14651858.CD007776.pub3 Czarnobay, Sandra Ana; Kroll, Caroline; Schultz, Lidiane F; Malinovski, Juliana; Mastroeni, Silmara Salete de Barros Silva et al. Predictors of excess birth weight in Brazil: a systematic review. Jornal de pediatria; 2019; vol. 95 (no. 2); p. 128-154. DOI 10.1016/j.jped.2018.04.006 Oteng-Ntim, Eugene; Mononen, Sofia; Sawicki, Olga; Seed, Paul T; Bick, Debra; Poston, Lucilla. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis.	over the effects of certain medications on fetal growth also. SRs – One systematic review showed that lifestyle changes showed possible health improvements for women and their babies. Some evidence regarding maternal non-glycaemic contributors to excess fetal growth, particularly lipids (triglycerides and free fatty acid) and gestational weight gain. Overall, very limited evidence regarding the contributors to macrosomia or how to prevent it. There were no systematic reviews specifically addressing the consequences of SGA in women with diabetes. There are some recent papers discussing the hypothesis of maternal diabetes that leads to metabolic disturbances during intrauterine growth restriction can modify the fetal programming and lead to the development of various chronic diseases later in life. Research is also needed in this area.

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				BMJ open; Jun 2018; vol. 8 (no. 6); p. e018778. DOI 10.1136/bmjopen-2017-018778 Viecceli, C; Remonti, L R; Hirakata, V N; Mastella, L S; Gnielka, V; Oppermann, M L R; Silveiro, S P; Reichelt, A J. Interpregnancy weight change and adverse pregnancy outcomes: a systematic review and meta-analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity; May 2017; vol. 18 (no. 5); p. 567-580. DOI 10.1111/obr.12521 Yamamoto, Jennifer M; Kellett, Joanne E; Balsells et al. Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight. Diabetes care; Jul 2018; vol. 41 (no. 7); p. 1346-1361. DOI 10.2337/dc18-0102" Goldstein, J A; Norris, S A; Aronoff, D M. DOHaD at the intersection of maternal immune activation and maternal metabolic stress: a scoping review. Journal of developmental origins of health and disease; Jun 2017; vol. 8 (no. 3); p. 273-283. DOI 10.1017/S2040174417000010.	
13	During pregnancy	For women with diabetes, what is the best way to monitor the baby's health during pregnancy? For example, timing of scans, in pregnancies where the baby is larger than average size, etc.	**23**	NICE NG3: 5.9 monitoring fetal growth and wellbeing, highlights “no clear consensus for monitoring fetal size in pregnant women with diabetes”, and that poor interpretation of surveillance measures may lead to inappropriate action. Research recommendation: “How can the fetus at risk of intrauterine death be identified in women with diabetes?” 5.10 Timetable of antenatal appointments includes fetal surveillance including plan during birth. SIGN116: 7.7 highlights “although regular fetal monitoring is common practice, no evidence has been identified on the effectiveness of any single or multiple techniques“. Puvaneswary Raman, Emily Shepherd, Therese Dowswell, Philippa Middleton, Caroline A Crowther. Different methods and settings for	Guidelines – Recommendations for regular monitoring by ultrasound, but other monitoring before 38 weeks is not recommended. Although regular fetal monitoring is common practice, no evidence has been identified on the effectiveness of any single or multiple techniques nor value in predicting fetal demise. SRs – 3 relevant. No strong clinical evidence available regarding ideal method of monitoring pregnancies complicated by macrosomia.

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				glucose monitoring for gestational diabetes during pregnancy Cochrane Systematic Review - Intervention Version published: 29 October 2017 https://doi.org/10.1002/14651858.CD011069.pub2 Rao U, de Vries B, Ross GP, Gordon A. Fetal biometry for guiding the medical management of women with gestational diabetes mellitus for improving maternal and perinatal health. Cochrane Database Syst Rev. 2019;9:CD012544. doi:10.1002/14651858.CD012544.pub2, 10.1002/14651858.CD012544.pub2 Low quality studies. Conclude: "There is insufficient evidence to evaluate the use of fetal biometry (in addition to maternal blood glucose concentration values) to assist in guiding the medical management of GDM". Katherine AT Culliney, Graham K Parry, Julie Brown, Caroline A Crowther. Regimens of fetal surveillance of suspected large-for-gestational-age fetuses for improving health outcomes. Cochrane Systematic Review – Intervention. https://doi.org/10.1002/14651858.CD011739.pub2	
14	During pregnancy	How do we diagnose or predict problems with the baby in the womb caused by diabetes in pregnant women?	**42**	NICE NG3: 6.1.2.10 highlights current fetal surveillance methods have yet to be of value in predicting fetal demise. Research recommendation: "How can fetuses at risk of intrauterine death be identified in women with diabetes?" SIGN116: 7.7 FETAL ASSESSMENT. Low to moderate evidence around timing and reliability of scanning and to detect different fetal measures. Prediction of shoulder dystocia highlighted as specific gap. Parnell, Aimee S; Correa, Adolfo; Reece, E Albert. Pre-pregnancy Obesity as a Modifier of Gestational Diabetes and Birth Defects Associations: A Systematic Review. Maternal and child health journal; May 2017; vol. 21 (no. 5); p. 1105-1120 DOI 10.1007/s10995-016-2209-4 Rao U, de Vries B, Ross GP, Gordon A. Fetal biometry for guiding the medical management of women with gestational diabetes mellitus	Guidelines – There are various recommendations, however, they are mainly based on expert opinion. Research recommendation – 'How can fetuses at risk of intrauterine death be identified in women with diabetes?' SRs – There are limited evidence to guide regarding exact HbA1c threshold for congenital abnormalities.

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				for improving maternal and perinatal health. Cochrane Database Syst Rev. 2019;9:CD012544. doi:10.1002/14651858.CD012544.pub2, 10.1002/14651858.CD012544.pub2. Low quality studies. Conclude: "There is insufficient evidence to evaluate the use of fetal biometry (in addition to maternal blood glucose concentration values) to assist in guiding the medical management of GDM".	
15	During pregnancy	Can the risk of pregnancy loss (miscarriage, fetal death or stillbirth) be predicted in women with diabetes?	**27**	NICE NG3: Miscarriage: Evidence mainly in relation to causal, protective (e.g. metformin 3.8.1.1 – moderate grade evidence) or associated factors. 3.1 low grade evidence. State "good evidence that the degree of glycaemic control at the time of conception determines the risk of miscarriage." However, section 3.7.5 identifies low quality evidence for HbA1c relationship with poor outcomes including miscarriage and subsequent research recommendation 'Are other glycosylated molecules better than HbA1c at summarising blood glucose control in pregnancy?'. Further relevant research recommendation: 'What is the relationship between pre-pregnancy glucose control and ketonaemia and the risk of miscarriage?'. No evidence identified for hypoglycaemia (3.7.5.2.5) and e.g. miscarriage. IUFD: Risk with DKA and other associated factors. Research recommendation: 'How can fetuses at risk of intrauterine death be identified in women with diabetes?' Stillbirth: 6.1.1.5 highlights insufficient data on the gestation-specific risk. Risk of still-birth is the main driver for birth interventions e.g. caesarean and early induction. 6.1.2.10 highlights current fetal surveillance methods have yet to be of value in predicting fetal demise. SIGN116: 7.1 state national audits demonstrate higher rate of adverse pregnancy outcomes in women with diabetes compared with population without diabetes. As for NICE. Chiossi G, Pedroza C, Costantine MM, Truong VTT, Gargano G, Saade GR. Customized vs population-based growth charts to identify neonates at risk of adverse outcome: systematic review and Bayesian meta-analysis of observational studies. Ultrasound Obstet Gynecol.	Guidelines – Evidence is mainly in relation to causal, protective or associated factors. National audits demonstrate higher rate of adverse pregnancy outcomes in women with diabetes compared with population without diabetes. Predictive and causal factors are not well evidenced. Relevant research recommendations: 'Are other glycosylated molecules better than HbA1c at summarising blood glucose control in pregnancy?'; 'What is the relationship between pre-pregnancy glucose control and ketonaemia and the risk of miscarriage?'; How can fetuses at risk of intrauterine death be identified in women with diabetes?' SRs – 3 relevant, but focussed on specific angles. None conclusive. Steering group decision to focus on prediction of pregnancy loss rather than what the risk factors are.

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				2017;50(2):156-166. doi:10.1002/uog.17381, 10.1002/uog.17384 Concerning one factor – baby size – and does not look specifically in pregnant women with diabetes. Recommends further trials to compare the two approaches in babies small and large for gestational age. Rao U, de Vries B, Ross GP, Gordon A. Fetal biometry for guiding the medical management of women with gestational diabetes mellitus for improving maternal and perinatal health. Cochrane Database Syst Rev. 2019;9:CD012544. doi:10.1002/14651858.CD012544.pub2, 10.1002/14651858.CD012544.pub2. Low quality studies. Conclude: "There is insufficient evidence to evaluate the use of fetal biometry (in addition to maternal blood glucose concentration values) to assist in guiding the medical management of GDM". Lean SC, Derricott H, Jones RL, Heazell AEP. Advanced maternal age and adverse pregnancy outcomes: A systematic review and meta-analysis. PLoS ONE. 2017;12(10):e0186287. doi:10.1371/journal.pone.0186287, 10.1371/journal.pone.0186287 Advanced maternal age associated with increased risk of stillbirth, fetal death. However, trials in general population and diabetes is a factor looked at.	
16	During pregnancy	Does variation in a woman's blood sugar (level, range and duration) affect their pregnancy and baby, and if so, how?	**29**	NICE NG3: 5.2 very low grade evidence on target ranges. 5.3 covers HbA1c but no evidence, best practice recommendation only. Not clear that variability question is fully answered. Research recommendations include 'What is the role of CGM in helping women achieve blood glucose targets in pregnancy?' SIGN 116: 7.5 low or very low-grade evidence around monitoring. Reference NICE NG3 as high-grade evidence for optimisation of glucose levels in reducing complications and adverse events. Diabetes Metab Res Rev. 2002 Mar-Apr;18(2):96-105. Maternal hypoglycemia during pregnancy in type 1 diabetes: maternal and fetal consequences. ter Braak EW(1), Evers IM, Willem Erkelens D,	Guidelines – Targets are stated but seem to be based on very low grade evidence. Not clear that effects of glucose variability is answered. Research recommendation - 'What is the role of CGM in helping women achieve blood glucose targets in pregnancy?' SRs – 1 relevant, several clinical studies did not establish an association between maternal hypoglycaemia and diabetes-related embryopathy, but possible longer-term and

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				Visser GH. 'Several clinical studies did not establish an association between maternal hypoglycaemia and diabetic embryopathy. However, animal studies clearly indicate that hypoglycemia is potentially teratogenic during organogenesis. Increased rates of macrosomia continue to be observed despite near normal HbA1c levels. This may, at least in part, be the result of rebound hyperglycemia elicited by hypoglycemia. Exposure to hypoglycemia in utero may have long-term effects on offspring including neuropsychological defects.'	neuropsychological effects. Insufficient evidence.
17	During pregnancy	What factors aside from maternal blood sugar levels have an effect on pregnancy outcomes? Can these be tested for and used to improve the outcomes of the pregnancy?	**34**	NICE NG3: 5.1.2 covers ketone monitoring - no evidence, best practice recommendation only. SIGN116: none found.	Guidelines – Ketone monitoring recommendations but no evidence, best practice recommendation only. SRs – Not done. Sufficient uncertainty and wider factors to be identified and evidenced.
18	During pregnancy	For women with diabetes, does pregnancy affect their risks of diabetes-related complications? Does the risk change with further pregnancies?	**49**	NICE NG3: 5.6 Moderate level evidence for acceleration of retinopathy in pregnancy and more likely in those with severe retinopathy, suboptimal glycaemic management, and hypertension. Women who develop or experience progression of retinopathy do not tend to regress after birth. The magnitude of change in glucose levels with intensive management is a risk factor but highlights that an RCT to investigate gradual reduction in blood glucose levels is needed. 5.7 Low-moderate grade evidence to suggest pregnancy is not associated with development of nephropathy or accelerated progression except in pre-existing moderate to advanced disease. 8.1.5 recommends that women should continue to avoid taking medications for the treatment of diabetes complications that were stopped before pregnancy for safety. 3.9 low grade evidence on the use of antihypertensives and cholesterol lowering medications.	Guidelines – Main focus is on microvascular complications specifically retinopathy and neuropathy. Hypo unawareness, hypo rates and severity, and also DKA rates are also relevant complications specifically covered. Other areas such as neuropathy (except in the context of anaesthesia and analgesia for obstetric surgery 6.2 and briefly in relation to contraceptives 3.3.10) are not covered. Research recommendation: 'Should retinal assessment during pregnancy be offered to women diagnosed with gestational diabetes who are suspected of having pre-existing diabetes?' and also highlights that an RCT to investigate

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				Comparatively low risks to maternal complications out-weighed by potential risk of congenital abnormalities and preeclampsia. Research recommendation: 'Should retinal assessment during pregnancy be offered to women diagnosed with gestational diabetes who are suspected of having pre-existing diabetes?' SIGN116: 7.6.2 highlights increased risk of severe hypos and hypo unawareness, as well as more rapid development of DKA. 7.6.3 microvascular complications. Moderate level evidence for worsening retinopathy during pregnancy, although nulliparous women with diabetes have higher levels of retinopathy than parous women. Therefore recommends that women should continue tight glucose levels after pregnancy to reduce long-term risk of retinopathy. Nephropathy: proteinurea increases transiently during pregnancy, worsening nephropathy and preeclampsia main drivers of preterm delivery (high grade evidence).	gradual reduction in blood glucose levels is needed. Evidence level moderate. SRs – None in Cochrane.
19	During pregnancy	What is the best way to medically manage blood sugar levels during pregnancy for women with different types of diabetes? This includes finding new treatments.	**37**	NICE NG3: Relevant research recommendations: "What are the normal ranges for HbA1c in non-diabetic pregnancy?"; "Do new-generation CSII pumps offer an advantage over traditional intermittent insulin injections in terms of pregnancy outcomes in women with type 1 diabetes?". Extensive guidelines on the use of anti-diabetes medications during pregnancy with high-moderate level evidence. Evidence gaps (e.g. long acting insulin analogues) are highlighted in the safety and benefits of some medicines and treatment strategies/regimens in pregnancy. Guidelines refer to clinical requirement for treatment with medications and effectiveness of the medication to manage blood sugar levels as the main decision drivers. Also using alternatives if current treatment cannot be tolerated. Also at different stages e.g. insulin resistance. Caissutti C, Saccone G, Khalifeh A, Mackeen AD, Lott M, Berghella V. Which criteria should be used for starting pharmacologic therapy for management of gestational diabetes in pregnancy? Evidence from randomized controlled trials. J Matern Fetal Neonatal Med.	Guidelines – Extensive guidelines on the use of anti-diabetes medications during pregnancy with high-moderate level evidence. Evidence gaps (e.g. long acting insulin analogues) are highlighted in the safety and benefits of some medicines and treatment strategies/regimens in pregnancy. Guidelines refer to clinical requirement for treatment with medications and effectiveness of the medication to manage blood sugar levels as the main decision drivers. Also using alternatives if current treatment cannot be tolerated. Also at different stages e.g. insulin resistance. Relevant research recommendation: 'Do new-generation CSII pumps offer an advantage over traditional intermittent insulin injections in terms of

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				2019;32(17):2905-2914. doi:10.1080/14767058.2018.1449203, 10.1080/14767058.2018.1449203 Han S, Crowther CA, Middleton P. Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria. Cochrane Database Syst Rev. 2012 Jan 18;1:CD009037. doi: 10.1002/14651858.CD009037.pub2. PMID: 22258997. This review found interventions including providing dietary advice and blood glucose level monitoring for women with pregnancy hyperglycaemia not meeting GDM and T2DM diagnostic criteria helped reduce the number of macrosomic and LGA babies without increasing caesarean section and operative vaginal birth rates. It is important to notice that the results of this review were based on four small randomised trials with moderate to high risk of bias without follow-up outcomes for both women and their babies. Martis R, Crowther CA, Shepherd E, Alsweiler J, Downie MR, Brown J. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD012327. DOI: 10.1002/14651858.CD012327.pub2. States: Concludes: "There were insufficient data comparing oral anti-diabetic pharmacological therapies with placebo/standard care (lifestyle advice) to inform clinical practice. There was insufficient high-quality evidence to be able to draw any meaningful conclusions as to the benefits of one oral anti-diabetic pharmacological therapy over another due to limited reporting of data for the primary and secondary outcomes in this review. Short- and long-term clinical outcomes for this review were inadequately reported or not reported. Current choice of oral anti-diabetic pharmacological therapy appears to be based on clinical preference, availability and national clinical practice guidelines. The benefits and potential harms of one oral anti-diabetic pharmacological therapy compared with another, or compared with placebo/standard care remains unclear and requires further	pregnancy outcomes in women with type 1 diabetes?' SRs – Highlight insufficient high-quality evidence to effectively compare oral anti-diabetes drug therapies by short and long-term outcomes in women with GDM and their babies.

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				research. Future trials should attempt to report on the core outcomes suggested in this review, in particular long-term outcomes for the woman and the infant that have been poorly reported to date, women's experiences and cost benefit."	
20	**During pregnancy**	**For women with diabetes, what is the best way to manage blood sugar levels using diet and lifestyle during pregnancy? Wider factors to consider include maternity leave, dietitian services, safety and effectiveness of specific diets e.g. low carbohydrate, personalised diets.**	**3**	NICE NG3: 4.5 interventions in women with gestational diabetes. 4.5.8.5 Diet, 4.5.8.6 Exercise. Very low-moderate quality evidence. Research recommendation: "What is the optimum dietary and exercise strategy for the initial management of women diagnoses with gestational diabetes?" SIGN116: 7.4 dietetic advice recommended. High level evidence Systematic reviews: Mostly insufficient evidence and insignificant results. Difficult to find any specific evidence for weight management as an outcome in pregnant women with diabetes; two studies specifically looked at lifestyle interventions designed to reduce weight, but the outcome for both was prevention of GDM. Only three analyses specifically looking at low glycaemic index diets. Some evidence for significantly improved outcomes with diet, and some without significant results. No specific type of diet examined, other than low GI diets. Significant results found with exercise along with diet, points highlighted are the heterogeneity variety in studies and differences in control diets. Some significant differences found in maternal glycaemic control but not for fetal outcomes. Allehdan 2019, Dietary and exercise interventions and glycemic control and maternal and newborn outcomes in women diagnosed with gestational diabetes: Systematic review Bailey 2020, Are Lifestyle Interventions to Reduce Excessive Gestational Weight Gain Cost Effective? A Systematic Review. Found insufficient results and was unable to run a valid cost effectiveness assessment. Bennet 2018, Interventions designed to reduce excessive gestational weight gain can reduce the incidence of gestational diabetes mellitus:	Guidelines – Diet and exercise recommended as first-line treatment for women with GDM. High quality evidence on diet in the management of GDM. Low quality studies on calorie-restricted, low GI and low carb diets. Poor quality evidence on exercise and focussed on post-prandial. Personalised diets, dietician support (aside from economic cost modelling), maternity leave not covered. SRs – Multiple on diet, exercise and weight loss interventions but heterogeneous across studies and populations. Mostly in GDM. Further variables not searched.

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				A systematic review and meta-analysis of randomised controlled trials. Found significant improvement in GDM prevention with diet and exercise but the effect varied by region and BMI. Brown 2017, Lifestyle interventions for the treatment of women with gestational diabetes. Looking at GDM management found significant results but advised cost effectiveness analysis needed. Garcia-Patterson 2019, Usual dietary treatment of gestational diabetes mellitus assessed after control diet in randomized controlled trials: subanalysis of a systematic review and meta-analysis. Highlight that diets varied widely. Guo 2019, Improving the effectiveness of lifestyle interventions for gestational diabetes prevention: a meta-analysis and meta-regression. Looked at diet and exercise to prevent GDM including 47 RCTs with 15745 patients, and found significant results - main message was targeting high risk groups, early interventions, correct regimes, and managing maternal weight gain. Han S, Middleton P, Shepherd E, Van Ryswyk E, Crowther CA. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD009275. DOI: 10.1002/14651858.CD009275.pub3. Looked at different types of diet and concluded that there was no significant impact on maternal and fetal outcomes with any particular diet, highlighting that the review was limited by a small number of studies with small sample sizes and variable methodological quality - need for more adequately powered studies." Miyazaki 2017, Nonpharmacological interventions to prevent type 2 diabetes in women diagnosed with gestational diabetes mellitus: a systematic overview" Ojo 2019, The Effects of a Low GI Diet on Cardiometabolic and Inflammatory Parameters in Patients with Type 2 and Gestational Diabetes: A Systematic Review and Meta-Analysis of Randomised	

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				Controlled Trials. Looked at cardiometabolic and inflammatory markers in patient with GDM but also at patients with T2DM who were not pregnant; found no significant difference with GDM. Tsirou 2019, Guidelines for Medical Nutrition Therapy in Gestational Diabetes Mellitus: Systematic Review and Critical Appraisal. Commented that diets varied widely, the review was flawed and there is a need for better unbiased guidelines. Xu 2020, Influence of low-glycemic index diet for gestational diabetes: a meta-analysis of randomized controlled trials. Looked at GDM only, 6 RCTs - found significantly reduced 2hr post prandial blood sugar, but no impact on other maternal or fetal outcomes such as insulin requirement, birth weight. Wan 2019 Dietary intervention strategies for ethnic Chinese women with gestational diabetes mellitus: A systematic review and meta-analysis. Looked at GDM but in Chinese patients only, and diets also were fibre enriched - did find improved glucose control and outcomes but commented need direct comparison trials for just low GI diet and just fibre enriched. Importantly other studies looking at diet commented on the fact that the control diets of different populations varied widely and so looking only at Chinese means the data is not likely to be generalisable. " Yamamoto 2018, Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight.	
21	During pregnancy	What is the best way to monitor blood sugar levels of pregnant women with diabetes?	**44**	NICE NG3: 5.1 monitoring blood glucose and ketones during pregnancy. Very low-moderate evidence for different monitoring regimes. Research recommendation: "Do women with gestational diabetes achieving good glucose control with diet, exercise and metformin need to have blood glucose tested as frequently as women taking insulin?"; "Post-meal blood glucose testing in women with diabetes in pregnancy: is the 1 hour test more acceptable than	Guidelines – High quality but conflicting evidence on the monitoring regimen/methods and use of e.g. CGM around pregnancy, and in different diabetes types. CGM for T1D pregnancy evidence level high – single landmark trial.

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				the 2 hour test?"; "What is the optimum frequency of blood glucose testing in pregnancy in women with pre-existing diabetes who are not taking insulin?"; "Are other glycosylated molecules better than HbA1c at summarising blood glucose control in pregnancy?"; "What are the barriers to testing blood glucose frequently in pregnancy?"; "Which is the optimum timing of the post-prandial blood glucose test in pregnancy – 1, 1.5 or 2 hours?". 2018 update to reflect moderate-high grade evidence including CONCEPTT trial (Feig DS, Donovan LE, Corcoy R, Murphy KE, Amiel SA, Hunt KF, Asztalos E, Barrett JFR, Sanchez JJ, de Leiva A, Hod M, Jovanovic L, Keely E, McManus R, Hutton EK, Meek CL, Stewart ZA, Wysocki T, O'Brien R, Ruedy K, Kollman C, Tomlinson G, Murphy HR; CONCEPTT Collaborative Group. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. Lancet. 2017 Nov 25;390(10110):2347-2359. doi: 10.1016/S0140-6736(17)32400-5. Epub 2017 Sep 15. Erratum in: Lancet. 2017 Nov 25;390(10110):2346. PMID: 28923465; PMCID: PMC5713979.) Reserach recommendation: "In women with type 1 diabetes who are already pregnant, what is the most effective method of glucose monitoring to improve maternal and infant outcomes: • continuous glucose monitoring• flash glucose monitoring?" SIGN116: 7.5.1 highlights limited evidence re: pre- and post-prandial testing, continuous glucose monitoring. Low grade evidence. Jones LV, Ray A, Moy FM, Buckley BS. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2019, Issue 5. Art. No.: CD009613. DOI: 10.1002/14651858.CD009613.pub4. 1). Self-monitoring versus standard care (two studies, 43 women): there was no clear difference for caesarean section (risk ratio (RR) 0.78, 95% confidence interval (CI) 0.40 to 1.49; one study, 28 women) or glycaemic control (both very low-quality), and not enough	SRs – The evidence base for the effectiveness of monitoring techniques is weak and additional evidence from large well-designed randomised trials is required to inform choices of glucose monitoring techniques.

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				evidence to assess perinatal mortality and neonatal mortality and morbidity composite. Hypertensive disorders of pregnancy, large-for-gestational age, neurosensory disability, and preterm birth were not reported in either study. 2. Self-monitoring versus hospitalisation (one study, 100 women): there was no clear difference for hypertensive disorders of pregnancy (pre-eclampsia and hypertension) (RR 4.26, 95% CI 0.52 to 35.16; very low-quality: RR 0.43, 95% CI 0.08 to 2.22; very low-quality). There was no clear difference in caesarean section or preterm birth less than 37 weeks' gestation (both very low quality), and the sample size was too small to assess perinatal mortality (very low-quality). Large-for-gestational age, mortality or morbidity composite, neurosensory disability and preterm birth less than 34 weeks were not reported. 3. Pre-prandial versus post-prandial glucose monitoring (one study, 61 women): there was no clear difference between groups for caesarean section (RR 1.45, 95% CI 0.92 to 2.28; very low-quality), large-for-gestational age (RR 1.16, 95% CI 0.73 to 1.85; very low-quality) or glycaemic control (very low-quality). The results for hypertensive disorders of pregnancy: pre-eclampsia and perinatal mortality are not meaningful because these outcomes were too rare to show differences in a small sample (all very low-quality). The study did not report the outcomes mortality or morbidity composite, neurosensory disability or preterm birth. 4. Automated telemedicine monitoring versus conventional system (three studies, 84 women): there was no clear difference for caesarean section (RR 0.96, 95% CI 0.62 to 1.48; one study, 32 women; very low-quality), and mortality or morbidity composite in the one study that reported these outcomes. There were no clear differences for glycaemic control (very low-quality). No studies reported hypertensive disorders of pregnancy, large-for-gestational age, perinatal mortality (stillbirth and neonatal mortality), neurosensory disability or preterm birth.	

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				5.CGM versus intermittent monitoring (two studies, 225 women): there was no clear difference for pre-eclampsia (RR 1.37, 95% CI 0.52 to 3.59; low-quality), caesarean section (average RR 1.00, 95% CI 0.65 to 1.54; I^2 = 62%; very low-quality) and large-for-gestational age (average RR 0.89, 95% CI 0.41 to 1.92; I^2 = 82%; very low-quality). Glycaemic control indicated by mean maternal HbA1c was lower for women in the continuous monitoring group (mean difference (MD) -0.60 %, 95% CI -0.91 to -0.29; one study, 71 women; moderate-quality). There was not enough evidence to assess perinatal mortality and there were no clear differences for preterm birth less than 37 weeks' gestation (low-quality). Mortality or morbidity composite, neurosensory disability and preterm birth less than 34 weeks were not reported. 6. Constant CGM versus intermittent CGM (one study, 25 women): there was no clear difference between groups for caesarean section (RR 0.77, 95% CI 0.33 to 1.79; very low-quality), glycaemic control (mean blood glucose in the 3rd trimester) (MD -0.14 mmol/L, 95% CI -2.00 to 1.72; very low-quality) or preterm birth less than 37 weeks' gestation (RR 1.08, 95% CI 0.08 to 15.46; very low-quality). Other primary (hypertensive disorders of pregnancy, large-for-gestational age, perinatal mortality (stillbirth and neonatal mortality), mortality or morbidity composite, and neurosensory disability) or GRADE outcomes (preterm birth less than 34 weeks' gestation) were not reported."	
22	During pregnancy	How can diabetes and pregnancy management be tailored for individual women during their pregnancy? Taking into account, for example, different	**45**	NICE NG3: 1.3.4 recommends agreeing individualised targets for self-monitoring of blood glucose, taking into account the risk of hypoglycaemia. Recommends individualised dietary advice (3.4.5), blood glucose targets to avoid hypos (1.3.4; 3.6.5.4; 3.6.7; 3.2.8; 4.5.10.2) taking into account risk of hypoglycaemia; monitoring of fetal growth and wellbeing (5.9.6); overall care plan pre-post pregnancy (5.10.1.1). The grouping of different types of diabetes for clinical recommendations is raised for consideration due to the	Guidelines – Clinical requirement for treatment with medications and effectiveness of the medication to manage blood sugar levels as the main decision drivers. There is also tolerability of side-effects and setting individualised blood glucose targets managing risk of hypoglycaemia. Subtypes of GDM not covered although stratification of treatment with risk levels. None

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		types of diabetes, the phase or type of pregnancy, risk to pregnancy, or women's own preferences.		differences in risk profiles for different factors and stages of pregnancy etc. and the paucity of evidence for different areas with different diabetes types e.g. 6.1.2.7.5, 6.1.2.8, 6.1.2.10, 3.3.13.3. Middleton P, Crowther CA, Simmonds L. Different intensities of glycaemic control for pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD008540. DOI: 10.1002/14651858.CD008540.pub4: The review compared: tight (≤ 5.6 mmol/L FBG); moderate (5.6 to 6.7 mmol/L); and loose (6.7 to 8.9 mmol/L) Martis R, Crowther CA, Shepherd E, Alsweiler J, Downie MR, Brown J. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD012327. DOI: 10.1002/14651858.CD012327.pub2. 1)Ineffective or possibly harmful: Lifestyle versus usual care; Exercise versus control; Insulin versus oral therapy (insulin increases the risk of induction of labour);Lifestyle versus usual care(The evidence for childhood adiposity kg/m² (RR 0.91, 95% CI 0.75 to 1.11; 3 RCTs, N = 767; GRADE moderate-quality) and hypoglycaemia was inconclusive (average RR 0.99, 95% CI 0.65 to 1.52; 6 RCTs, N = 3000; GRADE moderate-quality);Exercise versus control (The evidence for caesarean section (RR 0.86, 95% CI 0.63 to 1.16; 5 RCTs, N = 316; GRADE moderate quality) and perinatal death or serious morbidity composite was inconclusive (RR 0.56, 95% CI 0.12 to 2.61; 2 RCTs, N = 169; GRADE moderate-quality); Insulin versus oral therapy (The evidence for the following outcomes was inconclusive: pre-eclampsia (RR 1.14, 95% CI 0.86 to 1.52; 10 RCTs, N = 2060), caesarean section (RR 1.03, 95% CI 0.93 to 1.14; 17 RCTs, N = 1988), large-for-gestational age (average RR 1.01, 95% CI 0.76 to 1.35; 13 RCTs, N = 2352), and perinatal death or serious morbidity composite (RR 1.03; 95% CI 0.84 to 1.26; 2 RCTs, N = 760). GRADE assessment was moderate-quality for these outcomes); Insulin versus diet (The	on different subtypes of GDM, or on multiple pregnancy. SRs – Different intensities for glycaemic control. Trials in women with type 2 diabetes, and exploring the experiences of women are needed.

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				evidence for perinatal mortality was inconclusive (RR 0.74, 95% CI 0.41 to 1.33; 4 RCTs, N = 1137; GRADE moderate-quality).; Insulin versus insulin (The evidence for insulin aspart versus lispro for risk of caesarean section was inconclusive (RR 1.00, 95% CI 0.91 to 1.09; 3 RCTs, N = 410; GRADE moderate quality)" States "Current choice of oral anti-diabetic pharmacological therapy appears to be based on clinical preference, availability and national clinical practice guidelines. The benefits and potential harms of one oral anti-diabetic pharmacological therapy compared with another, or compared with placebo/standard care remains unclear and requires further research. Future trials should attempt to report on the core outcomes suggested in this review, in particular long-term outcomes for the woman and the infant that have been poorly reported to date, women's experiences and cost benefit." Different intensities of glycaemic control for women with gestational diabetes mellitus. https://doi.org/10.1002/14651858.CD011624.pub2. No evidence of how stratify women into high risk of low risk women. One trial showed that Strict glycaemic targets were associated with an increase in the use of pharmacological therapy (identified as the use of insulin in this study) (33/85; 39%) compared with liberal glycaemic targets but this does not specifically address question. Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes. [Review] Brown J; Martis R; Hughes B; Rowan J; Crowther CA. Cochrane Database of Systematic Reviews. 1:CD011967, 2017 01 25.	
23	During pregnancy	What psychological interventions can help motivate or support pregnant women in their diabetes management?	**31**	NICE NG3: 8.2.1.3 – General support (e.g. groups), motivation and behaviour mentioned but not specific intervention options. SIGN116: states research on efficacy of psychological interventions is in its infancy and lacking long-term implications, representativeness and valid screening/measuring tools.	Guidelines – General support (e.g. groups), motivation and behaviour mentioned but not specific intervention options. Psychology section in SIGN guideline states research on efficacy of psychological interventions is in its infancy and lacking long-term implications,

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				Byerley BM, Haas DM. A systematic overview of the literature regarding group prenatal care for high-risk pregnant women. BMC Pregnancy Childbirth. 2017;17(1):329. doi:10.1186/s12884-017-1522-2, 10.1186/s12884-017-1522-2 Studies in women with diabetes demonstrated that fewer women required treatment with medication when exposed to group prenatal care, and even reduced the dose of insulin they needed. However, lack of studies and of high quality, further research is needed. Carolan-Olah M, Duarte-Gardea M, Lechuga J. A systematic review of interventions for Hispanic women with or at risk of Gestational diabetes mellitus (GDM). Sex Reprod Healthc. 2017;13:14-22. doi:10.1016/j.srhc.2017.02.006, 10.1016/j.srhc.2017.02.006 Intensive nutritional counselling as an adjunct to other treatments in hispanic women with GDM was identified as most effective. However, low number and heterogeniety of studies. Bgeginski R, Ribeiro PAB, Mottola MF, Ramos JGL. Effects of weekly supervised exercise or physical activity counseling on fasting blood glucose in women diagnosed with gestational diabetes mellitus: A systematic review and meta-analysis of randomized trials. J Diabetes. 2017;9(11):1023-1032. doi:10.1111/1753-0407.12519, 10.1111/1753-0407.12519 Supervised exercise and physical activity counselling in women with GDM is effective. Although this doesn't directly address the question.	representativeness and valid screening/measuring tools. Some high quality but very specific trials referenced. SRs – Very limited in scope, number and relevance.
24	During pregnancy	Are diabetes medications (e.g. metformin, insulin) safe in pregnancy and for the baby in the short and long term?	**33**	NICE NG3 3.8 - Safety of medicines for diabetes before and during pregnancy. Recommends research on safety of metformin and glibencamide, as well as certain insulin analogues. NICE and SIGN guidelines do not include any recommendations specifically about use of metformin in growth-restricted pregnancies. SIGN116 7.3.2 and 7.5.2 - SRs on observational studies to indicate metformin and sulphonyl ureas do not increase certain pregnancy and fetal risks. Highlights no consistent safety concerns with respect to maternal or neonatal outcomes with rapid-acting insulin	Guidelines – Recommend research on safety of metformin and glibencamide, as well as certain insulin analogues. Highlights no consistent safety concerns with respect to maternal or neonatal outcomes with rapid-acting insulin analogues. No high quality supporting evidence for the use of long-acting basal analogues. Human insulins licensed for use in pregnancy, but analogues and oral glucose-lowering agents

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				analogues. Lispro and aspart recommended, however, no high quality supporting evidence for the use of long-acting basal analogues. Human insulins licensed for use in pregnancy, but analogues and oral glucose-lowering agents are not. NICE and SIGN guidelines do not include any recommendations specifically about use of metformin in growth-restricted pregnancies. Tieu J, Coat S, Hague W, Middleton P, Shepherd E. Oral anti-diabetic agents for women with established diabetes/impaired glucose tolerance or previous gestational diabetes planning pregnancy, or pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD007724. DOI: 10.1002/14651858.CD007724.pub3. Brown J, Grzeskowiak L, Williamson K, Downie MR, Crowther CA. Insulin for the treatment of women with gestational diabetes. Cochrane Database of Systematic Reviews 2017, Issue 11. Art. No.: CD012037. DOI: 10.1002/14651858.CD012037.pub2. Brown J, Martis R, Hughes B, Rowan J, Crowther CA. Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD011967. DOI: 10.1002/14651858.CD011967.pub2. Martis R, Crowther CA, Shepherd E, Alsweiler J, Downie MR, Brown J. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD012327. DOI: 10.1002/14651858.CD012327.pub2. O'Neill SM, Kenny LC, Khashan AS, West HM, Smyth RMD, Kearney PM. Different insulin types and regimens for pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD011880. DOI: 10.1002/14651858.CD011880.pub2.	are not. Also do not include any recommendations specifically about use of metformin in growth-restricted pregnancies. SRs – No studies in fetal growth and long-term outcomes. Further work is needed to look at the direct effects on fetal growth and specifically the safety of use in growth-restricted pregnancy, as well as the longer-term implications.

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				Dodd JM, Grivell RM, Deussen AR, Hague WM. Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. Cochrane Database of Systematic Reviews 2018, Issue 7. Art. No.: CD010564. DOI: 10.1002/14651858.CD010564.pub2. Rev Bras Ginecol Obstet. 2019 Feb;41(2):104-115. doi: 10.1055/s-0038-1676510. Epub 2019 Feb 20. Effectiveness of Insulin Analogs Compared with Human Insulins in Pregnant Women with Diabetes Mellitus: Systematic Review and Meta-analysis. Santos LL et al. PLoS Med. 2019 Aug 6;16(8):e1002848. doi: 10.1371/journal.pmed.1002848. eCollection 2019 Aug. Neonatal, infant, and childhood growth following metformin versus insulin treatment for gestational diabetes: A systematic review and meta-analysis. Tarry-Adkins JL et al. Diabetes Ther. 2018 Oct;9(5):1811-1829. doi: 10.1007/s13300-018-0479-0. Epub 2018 Aug 30. Long-Term Effects of Oral Antidiabetic Drugs During Pregnancy on Offspring: A Systematic Review and Meta-analysis of Follow-up Studies of RCTs van Weelden W et al. Diabet Med. 2017 Jan;34(1):27-36. doi: 10.1111/dme.13150. Epub 2016 Jun 8. Short- and long-term outcomes of metformin compared with insulin alone in pregnancy: a systematic review and meta-analysis. Kalafat, E., Sukur, Y.E., Abdi, A., Thilaganathan, B. and Khalil, A. (2018), Metformin for prevention of hypertensive disorders of pregnancy in women with gestational diabetes or obesity: systematic review and meta-analysis of randomized trials. Ultrasound Obstet Gynecol, 52: 706-714. doi:10.1002/uog.19084 Risk of pre-eclampsia in women taking metformin: a systematic review and meta-analysis	

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				A. Alqudah M. C. McKinley R. McNally U. Graham C. J. Watson T. J. Lyons L. McClements First published: 16 October 2017 https://doi.org/10.1111/dme.13523 Diabet. Med. 35, 160– 172 (2018) Farrar D, Simmonds M, Bryant M, et alTreatments for gestational diabetes: a systematic review and meta-analysisBMJ Open 2017;7:e015557. doi: 10.1136/bmjopen-2016-015557 Ye Feng & Huixia Yang (2017) Metformin – a potentially effective drug for gestational diabetes mellitus: a systematic review and meta-analysis, The Journal of Maternal-Fetal & Neonatal Medicine, 30:15, 1874-1881, DOI: 10.1080/14767058.2016.1228061 Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes Cochrane Systematic Review - Intervention Version published: 24 July 2018 https://doi.org/10.1002/14651858.CD010564.pub2 Oral anti-diabetic agents for women with established diabetes/impaired glucose tolerance or previous gestational diabetes planning pregnancy, or pregnant women with pre-existing diabetes. [Review] Tieu J; Coat S; Hague W; Middleton P; Shepherd E. Cochrane Database of Systematic Reviews. 10:CD007724, 2017 10 18. Neonatal, infant, and childhood growth following metformin versus insulin treatment for gestational diabetes: A systematic review and meta-analysis. Tarry-Adkins JL; Aiken CE; Ozanne SE. PLoS Medicine / Public Library of Science. 16(8):e1002848, 2019 08. Priya G, Kalra S. Metformin in the management of diabetes during pregnancy and lactation. Drugs Context. 2018;7:212523. Published 2018 Jun 15. doi:10.7573/dic.212523	
25	During pregnancy	What is the best way to manage sickness/vomiting in	**51**	NICE NG3: 1.1.3 states information should be given on how nausea and vomiting in pregnancy can affect blood glucose management.	Guidelines – Acknowledged that hyperemesis will affect glucose level. No research evidence.

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		pregnancy with diabetes? For example, hyperemesis in women with type 1 diabetes.		SIGN 116: No information on emesis (nausea/vomiting) in pregnancy Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD000145. DOI: 10.1002/14651858.CD000145.pub2. has been withdrawn. Boelig RC, Barton SJ, Saccone G, Kelly AJ, Edwards SJ, Berghella V. Interventions for treating hyperemesis gravidarum. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD010607. DOI: 10.1002/14651858.CD010607.pub2. Studies were mixed and limited interpretation possible of results. Variability in definition of hyperemesis was highlighted, as well as the requirement for validated outcome measures and larger trials.	SRs – None specifically relating to pregnancy with diabetes, however, 2 results for management in pregnancy generally. Studies were mixed and limited interpretation possible of results. Variability in definition of hyperemesis was highlighted, as well as the requirement for validated outcome measures and larger trials.
26	During pregnancy	How can the diagnosis and management of preeclampsia be improved for pregnant women with diabetes with and without diabetes-related complications e.g. diabetic nephropathy?	**56**	NICE NG3: 5.7 full guidance highlights strong evidence for pre-eclampsia association with nephropathy, and has updated renal function testing timeframes, and parameters for diagnosis of renal disease. It presents moderate level evidence for the use of antihypertensive treatment of nephropathy and reduction in pre-eclampsia incidence. The guidance (1.3.28 updated in 2015) for renal assessment and when to refer to nephrologist and when to start thromboprophylaxis is clearly delineated. SIGN116: 7.1 highlights strong evidence for increased risk of pre-eclampsia in women with diabetes, with reduced incidence with post-meal monitoring (7.5.1) Association of hypertension/pre-eclampsia with nephropathy (7.6.3) both of which are common causes of pre-term delivery in women with diabetes. Recommendation for careful monitoring and management of blood pressure in women with diabetes-related nephropathy and use of appropriate antihypertensive agents. Evidence considered moderate (C - with 2+ graded). The risk of growth restriction of the fetus is greater in women with vascular complications of diabetes	Guidelines – Research recommendation: 'Does identification of microalbuminuria during pregnancy offer the opportunity for appropriate pharmacological treatment to prevent progression to pre-eclampsia in women with pre-existing diabetes?' Introducing testing of kidney function in pregnant women with (pre-existing) diabetes prophylactic treatment of pre-eclampsia in women at high risk i.e. with nephropathy (microalbuminaemia) SRs – The evidence is strong in the understanding of risks and incidence of pre-eclampsia particularly in association with diabetes complications, such as diabetes-related nephropathy. However, the differentiation of and relationship between diabetes-related microvascular complications such as nephropathy, and pre-eclampsia may need further work (to improve the diagnosis and management).The use or inhibition of

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				(retinopathy, nephropathy) or when pre-eclampsia develops. (low grade 3 evidence. 7.7) Cavero-Redondo I, Martinez-Vizcaino V, Soriano-Cano A, Martinez-Hortelano JA, Sanabria-Martinez G, Alvarez-Bueno C. Glycated haemoglobin A1c as a predictor of preeclampsia in type 1 diabetic pregnant women: A systematic review and meta-analysis. Pregnancy Hypertens. 2018;14:49-54. doi:10.1016/j.preghy.2018.04.004, 10.1016/j.preghy.2018.04.004 Concludes good evidence to support HbA1c as a predictor of preeclampsia and testing particularly in first trimester (suggest further resaerch in the feasibility of testing). Davenport MH, Ruchat SM, Poitras VJ, et al. Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. BJSM online. 2018;52(21):1367-1375. doi:10.1136/bjsports-2018-099355, 10.1136/bjsports-2018-099355 Supports the use of exercise in reducing risks of developing preeclampsia (standalone rather than with diabetes). Kalafat E, Sukur YE, Abdi A, Thilaganathan B, Khalil A. Metformin for prevention of hypertensive disorders of pregnancy in women with gestational diabetes or obesity: systematic review and meta-analysis of randomized trials. Ultrasound Obstet Gynecol. 2018;52(6):706-714. doi:10.1002/uog.19084, 10.1002/uog.19084 Low quality and heterogeneity in the studies. However, supports the association of reduced incidence of hypertensive disorders of pregnancy compared with other treatments or placebo in women with gestational diabetes. Recommends further prospective trials needed. Alqudah A, McKinley MC, McNally R, et al. Risk of pre-eclampsia in women taking metformin: a systematic review and meta-analysis. Diabet Med. 2018;35(2):160-172. doi:10.1111/dme.13523, 10.1111/dme.13523	certain anti-hypertensives during pregnancy appears to be based on low-moderate grade evidence and as such warrants further research.

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				Concludes metformin associated with reduced incidence of preeclampsia if taken alongside insulin rather than insulin alone. However, does not include any studies on T1D. Recommends trials of metformin in GDM, T2D, and T1D, with preeclampsia as primary outcome. Vestgaard M, Sommer MC, Ringholm L, Damm P, Mathiesen ER. Prediction of preeclampsia in type 1 diabetes in early pregnancy by clinical predictors: a systematic review. J Matern Fetal Neonatal Med. 2018;31(14):1933-1939. doi:10.1080/14767058.2017.1331429, 10.1080/14767058.2017.1331429 Pre-existing hypertension and microangiopathy (small vessel disease) - specifically nephropathy with microalbuminuria, and diabetic retinopathy, were found to be key predictors of pre-eclampsia in women with T1D. They raise a level of heterogeneity in the studies included, but supports clinical practice to act on hypertension and albumin excretion. Further research/evaluation of the effects of the treatment strategy is highlighted. The effect of pregnancy on the development or changes in pre-existing diabetic nephropathy are considered to be out of scope of this question but in "In women with diabetes, what effect does pregnancy have on pre-existing and the development of diabetes complications, such as retinopathy, later on in their life?"	
27	During pregnancy	How can we optimise the benefits and reduce the risks of steroid administration in pregnant women with diabetes?	**52**	NICE NG3: 5.12.2.1 pre-term labour and antenatal steroids in women with diabetes. Steroids given antenatally for fetal lung maturation in women with diabetes is not contraindicated, and that additional insulin should be given for women on insulin (according to agreed protocol and with close monitoring) for treatment of their diabetes. SIGN116: 7.9 Delivery section states women at risk of pre-term delivery should get corticosteroids under supervision of experienced team to regulate glucose levels. High level evidence.	Guidelines – High grade evidence for administration of steroids for pre-term delivery with diabetes specialist supervision to manage glucose. The evidence acknowledges significant effects of steroids on glucose levels and supports close management of glucose levels, but not how best to do this. There are no reviews of use of steroids in this population. SRs – None.

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				No specific guidance/evidence on timing of steroid administration nor, specifically, in relation to elective c-section around 37-39 weeks. No indications at all supporting general administration of steroids to all women at 28 wks.	
28	During pregnancy	In women with diabetes, does diabetic neuropathy affect the woman's ability to feel and detect movements of their baby in the womb? What impact does this have on risks and outcomes?	**59**	No evidence found in guidelines. Carroll L, Gallagher L, Smith V. Risk factors for reduced fetal movements in pregnancy: A systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2019;243:72-82. doi:10.1016/j.ejogrb.2019.09.028, 10.1016/j.ejogrb.2019.09.028 Indicates that diabetes was not predictive of reduced fetal movements, but low study numbers and heterogeneity means this is not a reliable finding.	Guidelines – None. SRs – 1 relevant. Indicates that diabetes was not predictive of reduced fetal movements, but low study numbers and heterogeneity means this is not a reliable finding.
29	Labour and birth	In women with diabetes, what is the best way to manage their blood sugar levels during labour and delivery? For example, blood sugar targets, women managing their diabetes themselves, insulin infusions/sliding scale, use of diabetes management/monitoring technology.	**15**	NICE NG3: 6.3 No clinical studies evaluating the optimal method of glycaemic management. Targets are based on neonatal hypoglycaemia and fetal distress risks. Research recommendation: 'What is the optimal method for controlling glycaemia during labour and birth?'; "What are the normal ranges for HbA1c in non-diabetic pregnancy?" SIGN116: 7.9 No evidence presented for the recommendations.	Guidelines – Complicating factors such as analgesia and anaesthesia were not included within the scope of this question. No strong evidence for optimal diabetes management methods. Targets are based on neonatal hypoglycaemia and fetal distress risks (multiple moderate level studies). SRs – None.
30	Labour and birth	Why does being on diabetes medications in pregnancy affect	**47**	No evidence found.	Guidelines – None. SRs – None.

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		the way women can give birth?			
31	Labour and birth	When is it safe for pregnant women with diabetes to have a vaginal birth compared to e.g. a caesarean section?	**48**	NICE NG3: 6.1.1 mode of birth. Small number of studies ranging from high to very low quality comparing different modes of delivery and association with outcome measures. The studies also included populations without diabetes or did not distinguish diabetes types, or focussed on GDM. Fetal macrosomia should not be considered an indication for inducing birth. Moderate level study showed no advantage in pre-term caesarean in women with GDM. 6.2.6 Research recommendations: 'What are the risks and benefits associated with analgesia and anaesthesia in women with diabetes?' SIGN116: None found. Mitric C, Desilets J, Brown RN. Recent advances in the antepartum management of diabetes. F1000Res. 2019;8. doi:10.12688/f1000research.15795.1 No new evidence on the induction of labour – work to-date show lack of evidence for induction. Biesty LM, Egan AM, Dunne F, et al. Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants. Cochrane Database Syst Rev. 2018;1:CD012910. doi:10.1002/14651858.CD012910 Lack of evidence for planned birth vs expectant approach. Biesty LM, Egan AM, Dunne F, Smith V, Meskell P, Dempsey E, Ni Bhuinneain GM, Devane D. Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012948. DOI: 10.1002/14651858.CD012948. Lack of evidence for planned birth vs expectant approach.	Guidelines – Small number of studies ranging from high to very low quality comparing different modes of delivery and association with outcome measures. Expectant management vs elective delivery regimens seem to have different benefits/risks depending on a number of factors including diabetes type (pre-existing vs GDM). However, evidence is sparse and heterogeneous. Further research is needed. Relevant research recommendation: 'What are the risks and benefits associated with analgesia and anaesthesia in women with diabetes?' SRs – Limited search, 3 relevant which recommend further research as not enough evidence to conclude.
32	Labour and birth	Is it always necessary for pregnant women	**18**	NICE NG3: 6.1.1 mode of birth includes regimens for inducing labour with high grade study demonstrating no difference in outcomes for	Guidelines – No indication of requirement for induction for all women with diabetes.

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		with diabetes to be induced?		expectant delivery vs induced labour, however this study concluded induction of labour at 38 weeks should be considered for women who need insulin. As for Q30. 6.1.2.10 Research recommendation: 'What is the relationship between timing of elective delivery in women with diabetes and the outcome in the baby?'; 'What is the optimum gestation for delivering women with uncomplicated gestational diabetes?' SIGN116: None found. Mitric C, Desilets J, Brown RN. Recent advances in the antepartum management of diabetes. F1000Res. 2019;8. doi:10.12688/f1000research.15795.1 No new evidence on the induction of labour – work to-date show lack of evidence for induction. Biesty LM, Egan AM, Dunne F, et al. Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants. Cochrane Database Syst Rev. 2018;1:CD012910. doi:10.1002/14651858.CD012910 Lack of evidence for planned birth vs expectant approach. Biesty LM, Egan AM, Dunne F, Smith V, Meskell P, Dempsey E, Ni Bhuinneain GM, Devane D. Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012948. DOI: 10.1002/14651858.CD012948. Lack of evidence for planned birth vs expectant approach.	However, there is discussion on the timing of birth via elective delivery by induction or caesarean section (see Q 34) and how induction may be performed. Research recommendation: 'What is the relationship between timing of elective delivery in women with diabetes and the outcome in the baby?'; 'What is the optimum gestation for delivering women with uncomplicated gestational diabetes?' SRs – Limited search, 3 relevant which recommend further research as not enough evidence to conclude.
33	Labour and birth	In pregnant women with diabetes, how does diabetes affect whether inducing birth will work?	**54**	NICE NG3: 6.1.1.3 and 6.1.1.7 No evidence that induction of labour should be conducted differently in women with diabetes vs non-diabetes (including oxytocin protocols and EFM). There are considerations for surgical birth (e.g. caesarean) but his is not within the scope of this question. 6.1.2.7.2 states higher risk of failed induction with elective delivery.	Guidelines – No evidence that induction of labour should be conducted differently in women with diabetes vs non-diabetes (including oxytocin protocols and EFM). There are considerations for surgical birth (e.g. caesarean) but his is not within the scope of this

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				SIGN116: None.	question. Elective delivery associated with higher rates of induction failure. SRs – None.
34	**Labour and birth**	**When is it safe for pregnant women with diabetes to give birth at full term compared with early delivery via induction or elective caesarean? For example, factors may include managing timing of delivery according to changes in blood sugar levels, insulin requirements, size of the baby.**	**5**	NICE NG3: 6.1.2 Quality of studies low-very low. No studies looking at fetal mortality rates. Differences with timing of elective delivery in women with T1 and T2D vs GDM in relation to stillbirth and complications risks such as macrosomia. GDM related research was comparatively weaker than T1 and T2D. 6.2.6 Research recommendations: What are the risks and benefits associated with analgesia and anaesthesia in women with diabetes? 6.1.2.10 'What is the relationship between timing of elective delivery in women with diabetes and the outcome in the baby?'; 'What is the optimum gestation for delivering women with uncomplicated gestational diabetes?' SIGN116: 7.9 states no clear evidence identified to inform timing of delivery. Biesty LM, Egan AM, Dunne F, et al. Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants. Cochrane Database Syst Rev. 2018;1:CD012910. doi:10.1002/14651858.CD012910 Biesty LM, Egan AM, Dunne F, Smith V, Meskell P, Dempsey E, Ni Bhuinneain GM, Devane D. Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012948. DOI: 10.1002/14651858.CD012948. Lack of evidence for planned birth vs expectant approach.	Guidelines – Translated as timing of birth. No reference to using changes in insulin requirements to inform timing. Low quality and few studies to inform practice however highlighted different risk for stillbirth between T1 and T2D vs GDM resulting in different gestation periods before recommending elective delivery. Research recommendations: 'What are the risks and benefits associated with analgesia and anaesthesia in women with diabetes?; 'What is the relationship between timing of elective delivery in women with diabetes and the outcome in the baby?'; 'What is the optimum gestation for delivering women with uncomplicated gestational diabetes?' SRs – 2 relevant comparing planned birth vs expectant approach in women with GDM or women with T1 and T2D. Lack of evidence to conclude.
35	Labour and birth	When is it safe for women with diabetes to give birth at home or in a midwifery	**24**	NICE NG3: 6.1.1.5 mentions for women who choose not to deliver in a consultant-led obstetric unit that arrangements should be in place for rapid transfer if needed	Guidelines – None. Only guidelines for birthing in consultant-led maternity unit with neonatal intensive care facilities. SRs – None.

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		unit/birthing centre compared with a hospital birth?		SIGN116: 7.9 consensus statement that women with diabetes should be delivered in consultant-led maternity units under combined care of a physician with interest in diabetes, obstetrician and neonatologist. No evidence - moderate evidence of higher rates of caesarean needed in women with diabetes accounting fo confounders. 7.10 opens that labour and delivery should only be undertaken in a maternity unit supported by neonatal intensive care facilities. No evidence referenced. Related but not addressing the question SRs which may provide a starting point: Mitric C, Desilets J, Brown RN. Recent advances in the antepartum management of diabetes. F1000Res. 2019;8. doi:10.12688/f1000research.15795.1, 10.12688/f1000research.15795.1 Biesty LM, Egan AM, Dunne F, et al. Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants. Cochrane Database Syst Rev. 2018;2:CD012948. doi:10.1002/14651858.CD012948, 10.1002/14651858.CD012948	
36	Labour and birth	Do all women with diabetes need continuous Electronic Fetal Monitoring during labour?	**35**	NICE NG3: 6.1.1.5 Continuous electronic fetal monitoring should be offered to all women with diabetes during labour. Refers also to the NICE intrapartum care guideline for recommendations and that when conducted as part of induction should be no different to women without diabetes. However, low grade evidence which focuses on the mode of delivery as opposed to specifically the use of electronic fetal monitoring. Further sections on cardiotocography in general fetal wellbeing monitoring during pregnancy, but not in terms of continuous monitoring. SIGN 116: 7.9 recommends monitoring as for other high risk women to include continuous electronic fetal monitoring. No evidence to support.	Guidelines – Low grade or no evidence for recommendation to offer continuous electronic fetal monitoring to all women with diabetes. SRs – None.

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37	Labour and birth	Is it possible to predict shoulder dystocia in pregnant women with diabetes, and does this improve pregnancy and birth outcomes?	**43**	NICE NG3: There is a range of work presented with shoulder dystocia is an outcome measure in certain cohorts. There is no specific mention of predictability and prediction of shoulder dystocia for improving outcomes. SIGN116: 7.7 highlights that prediction of shoulder dystocia in the population without diabetes is poor and evidence in the population with diabetes limited (low grade evidence). Chiossi G, Pedroza C, Costantine MM, Truong VTT, Gargano G, Saade GR. Customized vs population-based growth charts to identify neonates at risk of adverse outcome: systematic review and Bayesian meta-analysis of observational studies. Ultrasound Obstet Gynecol. 2017;50(2):156-166. doi:10.1002/uog.17381, 10.1002/uog.17381. Growth charts for identifying baby's at risk of a range of adverse outcomes including shoulder dystocia. They found babies that are large for gestational age are more at risk of shoulder dystocia. Further reference: http://www.shoulderdystociainfo.com/anticipated.htm	Guidelines – References evidence with shoulder dystocia as an outcome measure. State prediction of shoulder dystocia in population without diabetes is poor and that in the population with diabetes is limited. Low grade evidence. SRs – A good body of work exists looking at predictability of shoulder dystocia in general population with mixed results (http://www.shoulderdystociainfo.com/anticipated.htm). The specific risks associated with mode of delivery, fetal factors e.g. gestational age size, and some maternal factors. However, there does not seem to be any recent systematic reviews looking specifically at the prediction of shoulder dystocia in women with diabetes.
38	**Labour and birth**	**What are the labour and birth experiences of women with diabetes, and how can their choices and shared decision making be enhanced?**	**9**	NICE NG3: 6.1.1.5 highlights that some women's experience of a "medicalised" and high interventional labour and delivery is a negative one. Encourage involvement in decision making and kept informed. SIGN116: 7.9 consensus recommendation to have a mutually agreed written plan for insulin management at time of delivery. None otherwise. Biesty LM, Egan AM, Dunne F, Smith V, Meskell P, Dempsey E, Ni Bhuinneain GM, Devane D. Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012948. DOI: 10.1002/14651858.CD012948.	Guidelines – None. SRs – None. 2 indirectly relevant.

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				Biesty LM, Egan AM, Dunne F, Dempsey E, Meskell P, Smith V, Ni Bhuinneain GM, Devane D. Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD012910. DOI: 10.1002/14651858.CD012910.	
39	After pregnancy and birth	How does breastfeeding affect diabetes management for the mother? How can women with diabetes be better supported during breastfeeding?	**32**	NICE NG3: 8.1.2 states there are no high-quality studies that show that breastfeeding affects glycaemic control. SIGN116: 7.10 states glycaemic control at six weeks in women with type 1 diabetes, who exclusively breast fed, has been found to be significantly better than those who bottle fed. Low grade evidence. Ma S et al. Metabolic effects of breastfeed in women with prior gestational diabetes mellitus: A systematic review and meta-analysis. Diabetes Metab Res Rev. 2019 Mar;35(3):e3108. A systematic review of 23 observational studies in women with gestational diabetes. The main finding was that "compared with women with shorter breastfeeding, those with longer breast feeding manifested more favourable metabolic parameters, including significant lower body mass index, fasting glucose, triglyceride, and higher insulin sensitivity index."	Guidelines – No high quality evidence for breastfeeding effects on glycaemic control. SRs – 1 relevant in women with GDM only looking at maternal metabolic effects in relation to breastfeeding.
40	After pregnancy and birth	What effect does diabetes have on breastmilk and breastfeeding? For example, the safety of diabetes medications, and low-carbohydrate diets.	**41**	NICE NG3: 7.2.1.4 effect of diabetes on initiating and maintaining breast-feeding. Low grade evidence. 7.2.1.3 Effects of diabetes on breast milk composition. Low grade evidence indicates no significant difference in breast milk from mother with diabetes compared to controls. 7.2.1.3 Effect of milk from mothers with diabetes on the neonate. Low grade evidence indicating higher ketone, lower glucose and higher gluconeogenic substrate levels in breastfed babies. 8.1.1.2 Oral hypoglycaemic agents. Low/moderate grade evidence to indicate safety and compatibility of e.g. metformin, glibenclamide, glipizide, acarbose, nateglinide, pioglitozone, rosiglitazone, glimepiride with breastfeeding. However, reference guide level	Guidelines – Effect of diabetes on breastfeeding and on breast milk.Breastfeeding: Low grade evidence that women with diabetes more likely to experience difficulties establishing and continuing breastfeeding. Interestingly, this was attributed to practical impositions rather than biological e.g. hospital neonatal monitoring protocols, caesarean, sleepy baby. Breastmilk: Low grade evidence that no difference in glucose levels, but higher in ketones. Anti-diabetes drugs: compatibility of most medications with breastfeeding summarised

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				evidence for possible toxicity of repaglinide, chlorpropamide and tolbutamide. SIGN116: 7.10 states Insulin, metformin and glibenclamide are considered compatible with breast feeding, although the infant should be observed for signs of hypoglycaemia. Evidence: reference works.	with evidence from reference works and small scale studies – overall considered compatible.Ketosis: None. SRs – None relevant.
41	After pregnancy and birth	How effective is collecting colostrum/breast milk before birth in improving clinical outcomes for the baby when born? When is the best time to collect this?	**28**	NICE NG3: 7.2.1.5 Banking colostrum before birth. States "A narrative non-systematic review concluded that expressing and storing colostrum is advantageous to babies and confidence building for women and should, therefore, be supported for any condition which healthcare professionals consider to be relevant [EL-4]" SIGN116: None found. East CE, Dolan WJ, Forster DA. Antenatal breast milk expression by women with diabetes for improving infant outcomes. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD010408. DOI: 10.1002/14651858.CD010408.pub2. Although relevant to the question found no studies to include in the review.	Guidelines – Low grade evidence for expressing and storing colostrum as advantageous to babies and confidence building for women. None on clinical outcomes specifically. SRs – 1 relevant, but the authors found no studies to include in it.
42	After pregnancy and birth	Does diabetes in the mother affect the short and long-term risk of the child (and future generations) developing diabetes and can it be prevented?	**12**	NICE NG3: 4.2 GDM risk factor is family history of diabetes with first degree relative (moderate grade evidence). SIGN116: 5.1.1 moderate grade Type 1 risk with first degree family history and for GDM as NG3. Twelve to fifteen per cent of young people under the age of 15 years with diabetes mellitus have an affected first degree relative (a positive family history). - Ref: Factors influencing glycemic control in young people with type 1 diabetes in Scotland: a population-based study (DIABAUD2). Diabetes Care 2001;24(2):239-44 - Evidence level: large observational study	Guidelines – Moderate level evidence on incidence of diabetes with first degree relative with diabetes. Generational predictors not covered. SRs – None. The search identified no relevant studies to answer the question. The one study that was identified as potentially relevant used only patients with diabetes and so can not be used to calculate the risk of developing type 1 diabetes given a positive family history.
43	After pregnancy and birth	What are the long-term effects on the child (apart from risk	**11**	NICE NG3: 3.6 research recommendation: 'What is the long term impact for children born to women with different degrees of preconception glycaemic control?'	Guidelines – Two aspects to this question, direct diabetes impact and treatment/intervention impacts on long-term

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		of diabetes) due to the mother having diabetes during pregnancy? For example, weight in the short and long term, and mental development.		SIGN116: None found. Xu Q, Xie Q. Long-term effects of prenatal exposure to metformin on the health of children based on follow-up studies of randomized controlled trials: a systematic review and meta-analysis. Arch Gynecol Obstet. 2019;299(5):1295-1303. doi:10.1007/s00404-019-05124-w Exposure to metformin associated with increased offspring weight. Aurich B, Martin-Montoya T, Zhang D, Jacqz-Aigrain E. Reporting of offspring data in diabetes, HIV infection and hypertension trials during pregnancy: a systematic review. Arch Dis Child Fetal Neonatal Ed. 2020;105(2):215-221. doi:10.1136/archdischild-2019-316982 Identifies underreporting in trials which prevents effective assessment of risk/benefit ration of treatment options during pregnancy. Kawasaki M, Arata N, Ogawa Y. Obesity and abnormal glucose tolerance in the offspring of mothers with diabetes. Curr Opin Obstet Gynecol. 2018;30(6):361-368. doi:10.1097/GCO.0000000000000479 Intrauterine exposure to hyperglycaemia is associated with offspring obesity and abnormal glucose tolerance; possibly determined by timing and degree of exposure. Further studies needed. Moen GH, Sommer C, Prasad RB, et al. MECHANISMS IN ENDOCRINOLOGY: Epigenetic modifications and gestational diabetes: a systematic review of published literature. EUR. J. ENDOCRINOL.. 2017;176(5):R247-R267. doi:10.1530/EJE-16-1017 Epigenetic modifications in the mother and offspring may be impacted by GDM. Further research needed. Butalia S, Gutierrez L, Lodha A, Aitken E, Zakariasen A, Donovan L. Short- and long-term outcomes of metformin compared with insulin alone in pregnancy: a systematic review and meta-analysis. Diabet Med. 2017;34(1):27-36. doi:10.1111/dme.13150,	outcomes for the offspring of women with diabetes. Long-term implications of the range of factors referred to throughout, but no specific references to evidence answering this question. Research recommendation: 'What is the long term impact for children born to women with different degrees of preconception glycaemic control?' Neonatal hypoglycaemia is covered in Q44. SRs – Advise further research is needed to understand the impact of diabetes and of interventions for diabetes in pregnancy on the long-term health of the child. Weight and exposure to metformin and maternal hyperglycaemia indicate possible adverse effects long term. Multiple areas of child health to consider not touched on in SRs.

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				10.1111/dme.13150 No long-term data. Guillemette L, Durksen A, Rabbani R, et al. Intensive gestational glycemic management and childhood obesity: a systematic review and meta-analysis. Int J Obes (Lond). 2017;41(7):999-1004. doi:10.1038/ijo.2017.65, 10.1038/ijo.2017.65 Too few studies. Further long-term follow-up of trials needed to measure childhood metabolic risk profiles. van Weelden W, Wekker V, de Wit L, et al. Long-Term Effects of Oral Antidiabetic Drugs During Pregnancy on Offspring: A Systematic Review and Meta-analysis of Follow-up Studies of RCTs. Diabetes Ther. 2018;9(5):1811-1829. doi:10.1007/s13300-018-0479-0, 10.1007/s13300-018-0479-0 Prenatal exposure to metformin associated with increased offspring weight. Further larger follow-up studies needed to assess implications.	
44	After pregnancy and birth	What is the best way to prevent, monitor, and manage low blood sugar levels of babies born to mothers with diabetes during pregnancy?	**22**	NICE NG3: 7.1.1.2 highlights no studies identified that address the assessments that babies should undergo. 7.2 focusses on prevention and treatment of hypoglycaemia. Highlights absence of high-quality evidence in the prevention and treatment of neonatal hypoglycaemia. Breast feeding within 30min of delivery is recommended. Low sensitivity and specificity of blood strip glucose testing for neonatal hypoglycaemia highlighted and recommendation to test with validated lab testing. Relevant research recommendation: 'Is systematic banking of colostrum antenatally of any benefit in pregnancies complicated by diabetes?' SIGN116: 7.10 very low to moderate evidence on the impact of hypoglycaemia on neonatal neuro/cognitive outcomes. Highlights insufficient evidence on the preferred method for blood glucose measurement in the baby except to confirm by lab test.	Guidelines – Although frequent monitoring is recommend the methods for testing are not well-evidenced as well as the prevention and treatment of neonatal hypoglycaemia. Relevant research recommendation: 'Is systematic banking of colostrum antenatally of any benefit in pregnancies complicated by diabetes?' Multiple applicable elements in relation to prevention from the management of maternal diabetes perspective as covered mostly in the other questions E.g. Moderate level evidence for maintaining BG within set range during labour achieved through a range of methods but no consensus on optimal way. Randomised controlled trials are needed to evaluate the safety of intermittent insulin injections and/or

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				Weston PJ, Harris DL, Battin M, Brown J, Hegarty JE, Harding JE. Oral dextrose gel for the treatment of hypoglycaemia in newborn infants. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD011027. DOI: 10.1002/14651858.CD011027.pub2. Dextrose gel as first line treatment recommended. However, low to moderated grade studies. Also recommends further studies looking at episodes of hypos and potential effects on brain injury. East CE, Dolan WJ, Forster DA. Antenatal breast milk expression by women with diabetes for improving infant outcomes. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD010408. DOI: 10.1002/14651858.CD010408.pub2. No studies found to complete this review.	CSII during labour and birth compared with that of intravenous dextrose plus insulin. This would fall into the scope of Q29 too. SRs – Multiple with neonatal hypo as an outcome measure which may need to be considered in terms of preventative strategies. However, directly addressing only 2 found. Very limited.
45	After pregnancy and birth	In women with diabetes, what effect does pregnancy have on diabetes-related complications (pre-existing and new) later on in their life?	**39**	NICE NG3: 5.6 Women who develop or experience progression of retinopathy do not tend to regress after birth. The magnitude of change in glucose levels with intensive management is a risk factor but highlights that an RCT to investigate gradual reduction in blood glucose levels is needed. SIGN116: 7.6.3 microvascular complications. Moderate level evidence for nulliparous women with diabetes have higher levels of retinopathy than parous women. Therefore recommends that women should continue tight glucose levels after pregnancy to reduce long-term risk of retinopathy. SRs – None found.	Guidelines – Main focus is on microvascular complications specifically retinopathy and neuropathy changes during pregnancy as opposed to post-pregnancy. SRs – None.
46	**After pregnancy and birth**	**In women with gestational diabetes, what is best way to reduce their risk or prevent them from developing other types of diabetes any time after pregnancy?**	**8**	NICE NG3: Chapter 8. Research recommendation: 'Are there effective long-term pharmacological interventions that can be recommended post-natally for women who have been diagnosed with gestational diabetes to prevent the onset of type 2 diabetes?' 8.2.1.2 Identifies no clear pattern for risk factors including family history, previous history of GDM, etc. (moderate grade). Studies are heterogeneous and further work on the duration of risk and factors themselves is still needed. References the same study as SIGN116 on drug and	Guidelines – Although there is consensus that GDM is a strong risk factor for developing T2D later, there is some inconsistency in effects of confounding factors e.g ethnicity, age etc. Evidence for risk factors – although diabetes type does not seem to be distinguished. Prevention strategies still needs further work. Research recommendation: 'Are there effective

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				lifestyle interventions, however, was in general population not GDM, and long-term follow-up data not available. SIGN116: 7.12 low-moderate grade evidence for risk of developing T2D with a GDM diagnosis (15-50% cumulative incidence at 5 years); and reduced progression to T2D through intensive lifestyle and drug-based interventions. Screening practice post-natally is still unclear for most effective monitoring of risk and diagnosis. Song C, Lyu Y, Li C, et al. Long-term risk of diabetes in women at varying durations after gestational diabetes: a systematic review and meta-analysis with more than 2 million women. Obes Rev. 2018;19(3):421-429. doi:10.1111/obr.12645, 10.1111/obr.12645 Evidence for risk factors – although diabetes type does not seem to be distinguished Tieu J, Shepherd E, Middleton P, Crowther CA. Interconception care for women with a history of gestational diabetes for improving maternal and infant outcomes. Cochrane Database of Systematic Reviews 2017, Issue 8. Art. No.: CD010211. DOI: 10.1002/14651858.CD010211.pub3. Recommends further research on interconception care protocols. Brown J, Ceysens G, Boulvain M. Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD012202. DOI: 10.1002/14651858.CD012202.pub2. Recommend further research on different types of exercise interventions for short and long-term outcomes. Han S, Middleton P, Shepherd E, Van Ryswyk E, Crowther CA. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD009275. DOI: 10.1002/14651858.CD009275.pub3. No studies looking at long-term outcomes – research recommended.	long-term pharmacological interventions that can be recommended post-natally for women who have been diagnosed with gestational diabetes to prevent the onset of type 2 diabetes?' Not clear if risks of T1D or others has been assessed. SRs – When to implement interventions and which are most effective still needs to be determined. Acceptability, emotional and behavioural factors are relatively untouched aspects. Steering group noted that no evidence of risk of diabetes post-GDM in UK population.

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				Middleton P, Crowther CA. Reminder systems for women with previous gestational diabetes mellitus to increase uptake of testing for type 2 diabetes or impaired glucose tolerance. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD009578. DOI: 10.1002/14651858.CD009578.pub2. Concludes: 'important to determine whether increased test uptake rates also increase women's use of preventive strategies such as lifestyle modifications.' Others: Jones EJ, Fraley HE, Mazzawi J. Appreciating Recent Motherhood and Culture: A Systematic Review of Multimodal Postpartum Lifestyle Interventions to Reduce Diabetes Risk in Women with Prior Gestational Diabetes. Matern Child Health J. 2017;21(1):45-57. doi:10.1007/s10995-016-2092-z, 10.1007/s10995-016-2092-z Dennison RA, Ward RJ, Griffin SJ, Usher-Smith JA. Women's views on lifestyle changes to reduce the risk of developing Type 2 diabetes after gestational diabetes: a systematic review, qualitative synthesis and recommendations for practice. Diabet Med. 2019;36(6):702-717. doi:10.1111/dme.13926, 10.1111/dme.13926 Pedersen ALW, Terkildsen Maindal H, Juul L. How to prevent type 2 diabetes in women with previous gestational diabetes? A systematic review of behavioural interventions. Prim Care Diabetes. 2017;11(5):403-413. doi:10.1016/j.pcd.2017.05.002, 10.1016/j.pcd.2017.05.002 van Weelden W, Wekker V, de Wit L, et al. Long-Term Effects of Oral Antidiabetic Drugs During Pregnancy on Offspring: A Systematic Review and Meta-analysis of Follow-up Studies of RCTs. Diabetes Ther. 2018;9(5):1811-1829. doi:10.1007/s13300-018-0479-0, 10.1007/s13300-018-0479-0	

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47	After pregnancy and birth	In women with gestational diabetes, what are the long-term effects of diabetes on their health, such as heart disease, any time after pregnancy? Can this be prevented?	**19**	NICE NG3: None. Mostly around long-term implications of treatment or non-diagnosis of diabetes. SIGN116: None found. Xie C, Wang W, Li X, Shao N, Li W. Gestational diabetes mellitus and maternal breast cancer risk: a meta-analysis of the literature. J Matern Fetal Neonatal Med. 2019;32(6):1022-1032. doi:10.1080/14767058.2017.1397117, 10.1080/14767058.2017.1397117 GDM may have protective effects on maternal risk of breast cancer. No association with GDM as a causative/related factor of breast cancer. Li J, Song C, Li C, Liu P, Sun Z, Yang X. Increased risk of cardiovascular disease in women with prior gestational diabetes: A systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;140:324-338. doi:10.1016/j.diabres.2018.03.054, 10.1016/j.diabres.2018.03.054 Adjustments for high heterogeneity of studies, but conclude women with prior GDM have increased risk of CVD, CAD and stroke. However, limitations in the populations and settings of the studies means further research is warranted to assess the magnitude of risk and over time and in follow-up to interventions. Jones EJ, Hernandez TL, Edmonds JK, Ferranti EP. Continued Disparities in Postpartum Follow-Up and Screening Among Women With Gestational Diabetes and Hypertensive Disorders of Pregnancy: A Systematic Review. J Perinat Neonatal Nurs. 2019;33(2):136-148. doi:10.1097/JPN.0000000000000399, 10.1097/JPN.0000000000000399 Post-partum screening for at-risk women for hypertensive disorders was found to vary substantially and were suboptimal. Moen GH, Sommer C, Prasad RB, et al. MECHANISMS IN ENDOCRINOLOGY: Epigenetic modifications and gestational diabetes: a systematic review of published literature. EUR. J. ENDOCRINOL..	Guidelines – None. SRs – 4 relevant. Each look at different factors e.g. breast cancer, cardiovascular, and hypertension. Significant gaps in understanding wider health risks as well as needing further research in these areas. Also some indication that epigenetic modification may be affected.

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				2017;176(5):R247-R267. doi:10.1530/EJE-16-1017 Epigenetic modifications in the mother and offspring may be impacted by GDM. Further research needed.	
48	**After pregnancy and birth**	**What are the specific postnatal care and support needs of women with diabetes and their infants? For example, breastfeeding, recovery from childbirth, managing diabetes with a newborn.**	**6**	NICE NG3: Chapter 8 No studies on information and follow-up of women with T1 and 2D postnatally. SIGN116: 7.10 Encourages breastfeeding, but should support the feeding method of mother's choice. 8.2.1.4 Highlights concerns on postnatal glycaemic management, inadequate plans for care after discharge, lack of contact with diabetes team, lack of contraceptive advice in T1 and 2D women (low grade evidence). Jones EJ, Fraley HE, Mazzawi J. Appreciating Recent Motherhood and Culture: A Systematic Review of Multimodal Postpartum Lifestyle Interventions to Reduce Diabetes Risk in Women with Prior Gestational Diabetes. Matern Child Health J. 2017;21(1):45-57. doi:10.1007/s10995-016-2092-z, 10.1007/s10995-016-2092-z Although not directly addressing the question, the review highlights personalised interventions and care are more effective.	Guidelines – Focus on post-natal follow-up from a clinical management perspective. None on wider support needs. SRs – 1 relevant but indirectly. Highlights need for further research for interventions that engage women with prior GDM by addressing socio-cultural determinants on women's lifestyle behaviours.
49	After pregnancy and birth	What is the best way to follow-up and screen women with gestational diabetes after their pregnancy?	**25**	NICE NG3: 8.3 reviews evidence for test types used and the timing of testing. All very low quality. Research recommendations: 'What is the efficacy of HbA1c as a diagnostic test for detecting impaired glucose tolerance in the postnatal period?'; 'What is the optimal timing of an HbA1c test for detecting diabetes and/or glucose intolerance in the postnatal period?'; 'What is the optimal timing of an HbA1c test for detecting diabetes and/or glucose intolerance in the postnatal period?'; 'Why women do not engage with postnatal glucose tolerance testing? Surveillance of uptake in the postnatal test for diabetes'; 'Does the diagnosis of IGT influence the uptake of life style changes after birth in a woman with previous GDM'. 9.1.4 highlights economically beneficial to test at longer intervals, but also lower detection rates.	Guidelines – Very low grade evidence found and multiple research recommendations on the topic: Research recommendations: 'What is the efficacy of HbA1c as a diagnostic test for detecting impaired glucose tolerance in the postnatal period?'; 'What is the optimal timing of an HbA1c test for detecting diabetes and/or glucose intolerance in the postnatal period?'; 'What is the optimal timing of an HbA1c test for detecting diabetes and/or glucose intolerance in the postnatal period?'; 'Why women do not engage with postnatal glucose tolerance testing? Surveillance of uptake in the postnatal test for diabetes'; 'Does the diagnosis of IGT

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				SIGN116: 7.12 No robust evidence for when follow-up testing should be done. Low grade recommendation evidence on what testing and follow-up should be done. Tieu J, Shepherd E, Middleton P, Crowther CA. Interconception care for women with a history of gestational diabetes for improving maternal and infant outcomes. Cochrane Database of Systematic Reviews 2017, Issue 8. Art. No.: CD010211. DOI: 10.1002/14651858.CD010211.pub3. Middleton P, Crowther CA. Reminder systems for women with previous gestational diabetes mellitus to increase uptake of testing for type 2 diabetes or impaired glucose tolerance. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD009578. DOI: 10.1002/14651858.CD009578.pub2. Jones EJ, Hernandez TL, Edmonds JK, Ferranti EP. Continued Disparities in Postpartum Follow-Up and Screening Among Women With Gestational Diabetes and Hypertensive Disorders of Pregnancy: A Systematic Review. J Perinat Neonatal Nurs. 2019;33(2):136-148. doi:10.1097/JPN.0000000000000399, 10.1097/JPN.0000000000000399 Tieu J, Coat S, Hague W, Middleton P, Shepherd E. Oral anti-diabetic agents for women with established diabetes/impaired glucose tolerance or previous gestational diabetes planning pregnancy, or pregnant women with pre-existing diabetes. Cochrane Database Syst Rev. 2017;10:CD007724. doi:10.1002/14651858.CD007724.pub3, 10.1002/14651858.CD007724.pub3 Jones EJ, Fraley HE, Mazzawi J. Appreciating Recent Motherhood and Culture: A Systematic Review of Multimodal Postpartum Lifestyle Interventions to Reduce Diabetes Risk in Women with Prior Gestational Diabetes. Matern Child Health J. 2017;21(1):45-57. doi:10.1007/s10995-016-2092-z, 10.1007/s10995-016-2092-z	influence the uptake of life style changes after birth in a woman with previous GDM'. SRs – Focus mainly on screening for diabetes rather than any other aspects which may need attention. Touch on sociocultural aspects. Lack of evidence highlighted. Need for further trials on interconception care and acceptability of interventions.

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50	**Cross-cutting**	**How can diabetes technology be used to improve pregnancy, birth, and mother and child health outcomes? For example, continuous and glucose flash monitoring, insulin pumps, closed loop systems, apps, etc.**	**1**	NICE NG3: research recommendation: 2.1 Preconception care for women with diabetes: insulin pump therapy and continuous glucose monitoring "What are the roles of insulin pump therapy (continuous subcutaneous insulin infusion) and continuous glucose monitoring in helping women with diabetes to achieve blood glucose targets before pregnancy?' Research recommendation: 'What is the role of CGM in helping women achieve blood glucose targets in pregnancy?' Mitric C, Desilets J, Brown RN. Recent advances in the antepartum management of diabetes. F1000Res. 2019;8. doi:10.12688/f1000research.15795.1 Indicates positive advances in the use of technology and platforms for the management of diabetes.	Guidelines – Significant uncertainty remains. Continuously developing area. Further checks not required.Research recommendation: 'What are the roles of insulin pump therapy (continuous subcutaneous insulin infusion) and continuous glucose monitoring in helping women with diabetes to achieve blood glucose targets before pregnancy?; 'What is the role of CGM in helping women achieve blood glucose targets in pregnancy?' SRs – Not done.
51	Cross-cutting	How effective (clinically and cost) is the use of continuous glucose monitoring in pregnant women with diabetes?	**36**	NICE NG3: 5.5 CGM section and 2018 surveillance update. 5.2.9 Research recommendation: What is the role of CGM in helping women achieve blood glucose targets in pregnancy?' SIGN116: 7.5.1. Limited evidence that CGM may be of benefit during pregnancy in T1 and 2D, no benefit seen in GDM – moderate grade evidence. Jones LV, Ray A, Moy FM, Buckley BS. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. Cochrane Database Syst Rev. 2019;5:CD009613. doi:10.1002/14651858.CD009613.pub4, 10.1002/14651858.CD009613.pub4 Raman P, Shepherd E, Dowswell T, Middleton P, Crowther CA. Different methods and settings for glucose monitoring for gestational diabetes during pregnancy. Cochrane Database Syst Rev. 2017;10:CD011069. doi:10.1002/14651858.CD011069.pub2, 10.1002/14651858.CD011069.pub2 Further trials needed for different monitoring methods and systems in women with diabetes (reviews cover T1 T2 and GDM).	Guidelines – High quality but conflicting evidence on the use of CGM around pregnancy, and in different diabetes types. Research recommendation: What is the role of CGM in helping women achieve blood glucose targets in pregnancy?'. Landmark trial in CGM in T1D pregnancy. SG members have highlighted further significant questions remain. SRs – 2 relevant, conclude further trials needed for different monitoring methods and systems in women with diabetes (reviews cover T1 T2 and GDM).

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52	Cross-cutting	How safe and effective is the use of closed loop systems (also known as artificial pancreas) in improving outcomes of pregnancy and birth?	**50**	NICE NG3: None found. SIGN116: None found. Yamamoto JM, Murphy HR. Emerging Technologies for the Management of Type 1 Diabetes in Pregnancy. Curr Diab Rep. 2018;18(1):4. Published 2018 Jan 30. doi:10.1007/s11892-018-0973-9 Reviewed evidence on a range of technologies including closed-loop in pregnancy. Highlights the need for further larger scale research, with wider diversity and also in pre-pregnancy. T1D only.	Guidelines – None. SRs – None. Other – 1 relevant review. Reviewed evidence on a range of technologies including closed-loop in pregnancy. Highlights the need for further larger scale research, with wider diversity and also in pre-pregnancy. T1D only.
53	**Cross-cutting**	**What are the emotional and mental well-being needs of women with diabetes before, during, and after pregnancy, and how can they best be supported?**	**4**	NICE NG3: 3.1.6 Refers to the standard set by the NSF for diabetes for empowering and supporting women with diabetes in pregnancy, including ensuring a positive experience, by providing care which promotes physical and psychological wellbeing and keeping women and their partners fully informed and involved in the decision making through pregnancy and childbirth. 6.3.3 raises the possible psychological benefits of women feeling in control of their glucose management during labour. 5.1.1.7.2 recognises that women may experience anxiety as a result of the intensive self-monitoring and management expected through pregnancy. In numerous places, the guidelines raise the risk of undue anxiety in women wrongly tested or with false positives, and also the fear of hypoglycaemia. There is no direct reference to maternal psychological and social well-being, anxiety or depression and care of generally. SIGN 116: describes research on the efficacy of psychological interventions as in its infancy. Section 4 covers psychosocial factors and the findings and limitations of the research conducted in the area. There is no specific detail in the guideline on pregnancy-related needs and research. Julie Brown et al. Lifestyle interventions for the treatment of women with gestational diabetes. Cochrane Systematic Review - Intervention Version published: 04 May 2017. doi.org/10.1002/14651858.CD011970.pub2	Guidelines – No direct reference to maternal psychosocial wellbeing, anxiety or depression, and care of women in this regard generally. SRs – None relevant. Multitude of SRs report studies using post-partum depression as an outcome for an intervention.

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				Identified a decreased risk of postnatal depression in women given lifestyle interventions such as healthy eating, physical activity and self-monitoring of blood glucose. Ruth Martis et al. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews. Cochrane Systematic Review - Overview. 14 August 2018. doi.org/10.1002/14651858.CD012327.pub2 Postnatal depression risk as an outcome for lifestyle interventions in women with GDM - low or very low quality evidence to comment on effectiveness. Dennison RA, Ward RJ, Griffin SJ, Usher-Smith JA. Women's views on lifestyle changes to reduce the risk of developing Type 2 diabetes after gestational diabetes: a systematic review, qualitative synthesis and recommendations for practice. Diabet Med. 2019;36(6):702-717. doi:10.1111/dme.13926, 10.1111/dme.13926. A qualitative study review looking at experiences of women with GDM, but in relation to adopting and maintaining a healthy lifestyle (post-partum) rather than their psychosocial needs more generally. It highlights many factors affect and block, and that the needs and experiences of women needs to be considered when developing support tools and interventions. Jones EJ, Fraley HE, Mazzawi J. Appreciating Recent Motherhood and Culture: A Systematic Review of Multimodal Postpartum Lifestyle Interventions to Reduce Diabetes Risk in Women with Prior Gestational Diabetes. Matern Child Health J. 2017;21(1):45-57. doi:10.1007/s10995-016-2092-z, 10.1007/s10995-016-2092-z As above, focussing on the mulitmodal lifestyle interventions after birth in women with GDM. Highlights need to address sociocultural factors which affect risk of diabetes and lifestyle behaviours. Again, does not look specifically at womens' support needs. Azami M, Badfar G, Soleymani A, Rahmati S. The association between gestational diabetes and postpartum depression: A systematic review	

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				and meta-analysis. Diabetes Res Clin Pract. 2019;149:147-155. doi:10.1016/j.diabres.2019.01.034, 10.1016/j.diabres.2019.01.034 Findings support GDM as a risk factor for post-partum depression and recommends examination for post-partum depression in women with GDM. Arafa A, Dong JY. Gestational diabetes and risk of postpartum depressive symptoms: A meta-analysis of cohort studies. J Affect Disord. 2019;253:312-316. doi:10.1016/j.jad.2019.05.001, 10.1016/j.jad.2019.05.001 Confirms GDM as a risk factor for post-partum depression. Recommends further prospective studies. Brown J, Alwan NA, West J, et al. Lifestyle interventions for the treatment of women with gestational diabetes. Cochrane Database Syst Rev. 2017;5:CD011970. doi:10.1002/14651858.CD011970.pub2, 10.1002/14651858.CD011970.pub2 As above, lifestyle interventions in the treatment of women with GDM reduces incidence of post partum depression. Recommends further research in the longer-term effects of interventions in the mother and baby, further work on specific interventions and the way these are delivered. Craig L, Sims R, Glasziou P, Thomas R. Women's experiences of a diagnosis of gestational diabetes mellitus: a systematic review. BMC Pregnancy Childbirth. 2020;20(1):76. doi:10.1186/s12884-020-2745-1, 10.1186/s12884-020-2745-1 Is there an increased risk of perinatal mental disorder in women with gestational diabetes? A systematic review and meta-analysis C. A. Wilson J. Newham J. Rankin K. Ismail E. Simonoff R. M. Reynolds N. Stoll L. M. Howard First published: 06 November 2019 https://doi.org/10.1111/dme.14170 Diabet. Med. 37, 602– 622 (2020) "found an increased risk of probable antenatal and postnatal	

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				depression (and possibly anxiety) in women with GDM. Future research would usefully focus on risk for other mental disorders, including those occurring prior to pregnancy and in early pregnancy prior to the onset of GDM, and on exploring possible mechanisms"	
54	Cross-cutting	How can support networks i.e. family and friends, help to support women with the challenges they face in pregnancy? Also, how can support networks themselves be supported?	**58**	NICE NG3: Recommends involving and informing partners and family members in preconception care, how diabetes affects pregnancy and how pregnancy affects diabetes, and providing information in a supportive environment by encouraging family members and partners to attend appointments and be involved in decision making. It also recommends instructing the woman as well as her partner or other family member of the increased risk of hypoglycaemia and hypo unawareness in pregnancy, how to prevent it, and recognising and treating hypos, including the use of glucagon where needed (5.4.4). (No specific research.). 3.10.1 Looks at the relationship with the partner as a factor in preconception care highlighting higher satisfaction and feelings of being well supported in women who planned their pregnancy with most feeling their partners were well-informed about diabetes and pregnancy issues before the pregnancy. They were more likely to have planned the pregnancy and attended the appointments together. Unplanned pregnancies were associated more with unsupportive partners. (Moderate evidence level) The support needs of partners/family was not covered. SIGN116: 7.6.2 Education for women and their partners on the management of hypos, including using glucagon, and also recognition and prevention of ketoacidosis.	Guidelines – No research evidence. General recommendation to encourage involvement of partners/family in information giving, particularly in risks and management of hypoglycaemia, and decision making through pregnancy. Moderate level evidence on partner support and involvement in planned vs unplanned pregnancies in women with diabetes. Nothing on support needs for partners/family. SRs – Not done.
55	Cross-cutting	How should diabetes specialists and clinics be involved at all stages, pre-pregnancy to after birth, for women with diabetes?	**46**	NICE NG3: 5.11.5.1 Multidisciplinary team compared to standard antenatal care. Recommendation is a consensus. Quality of evidence very low. 5.4.1.3 Study in DKA (general population). People treated by diabetes specialist had shorter length of stay, lower rate of readmission, faster glucose recovery. Moderate grade evidence. 5.10 antenatal appointments.	Guidelines – Low to moderate level evidence for the provision of care via a multidisciplinary team compared to standard antenatal care. Recommendation is a consensus. SRs – None.¶

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				SIGN 116: Recommendation that an experienced multidisciplinary team with diabetes specialisms should care from pre-pregnancy to postnatal review. 7.3. Moderate level evidence for strong recommendation	
56	Cross-cutting	How can remote clinics (telemedicine) be used to improve care for pregnant women with diabetes?	**13**	NICE NG3: Research recommendation: 'What is the role of telemedicine in helping women achieve blood glucose targets in pregnancy?' Research should be undertaken in the acceptability and understanding of the use of telemedicine, and use in primary care and specialist referral services to ascertain efficacy of remote patient monitoring. SIGN116: none found. Jones LV, Ray A, Moy FM, Buckley BS. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2019, Issue 5. Art. No.: CD009613. DOI: 10.1002/14651858.CD009613.pub4. Raman P, Shepherd E, Dowswell T, Middleton P, Crowther CA. Different methods and settings for glucose monitoring for gestational diabetes during pregnancy. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD011069. DOI: 10.1002/14651858.CD011069.pub2. Fantinelli S, Marchetti D, Verrocchio MC, Franzago M, Fulcheri M, Vitacolonna E. Assessment of Psychological Dimensions in Telemedicine Care for Gestational Diabetes Mellitus: A Systematic Review of Qualitative and Quantitative Studies. Front Psychol. 2019;10:153. Published 2019 Feb 5. doi:10.3389/fpsyg.2019.00153 Mitric C, Desilets J, Brown RN. Recent advances in the antepartum management of diabetes. F1000Res. 2019;8. doi:10.12688/f1000research.15795.1, 10.12688/f1000research.15795.1 SRs identified hetergeneous and small studies looking at telemedicine vs standard care. Further research is necessary.	Guidelines – Research recommendation: 'What is the role of telemedicine in helping women achieve blood glucose targets in pregnancy?' Research should be undertaken in the acceptability and understanding of the use of telemedicine, and use in primary care and specialist referral services to ascertain efficacy of remote patient monitoring. SRs – 4 relevant. Small trials and heterogeneity in methodology. Future RCTs are recommended comparing with standard care.

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57	Cross-cutting	How can community care services for pregnant women with diabetes be improved?	**53**	NICE NG3: 7.1.6. and 4.4.1 Transfer of mother (GDM) and baby to community care (including midwifery) care recommendations driven by evidence. 4.4.8.5 refers to involvement of GPs alongside midwives in the care of women diagnosed with GDM. Refers to NICE antenatal care general guidance. Relevant research recommendations: Achieving glycaemic targets pre-pregnancy – what is the role of telemedicine?' and 'Why women do not engage with postnatal glucose tolerance testing? Surveillance of uptake in the postnatal test for diabetes'. None directly answering the question. SIGN116: 7.1 recommends multidisciplinary team. No evidence referred to. Tieu J, McPhee AJ, Crowther CA, Middleton P, Shepherd E. Screening for gestational diabetes mellitus based on different risk profiles and settings for improving maternal and infant health. Cochrane Database of Systematic Reviews 2017, Issue 8. Art. No.: CD007222. DOI: 10.1002/14651858.CD007222.pub4. Primary care and secondary care screening practice for GDM. No difference but low quality studies. Multiple settings and pathways not covered. Question remains pertinent.	Guidelines – Recommendations on the transfer of the mother and baby into community care, and post-natal monitoring of the mother with GDM. Relevant research recommendations: Achieving glycaemic targets pre-pregnancy – what is the role of telemedicine?' and 'Why women do not engage with postnatal glucose tolerance testing? Surveillance of uptake in the postnatal test for diabetes'. None directly answering the question. SRs – Primary care and secondary care screening practice for GDM. No difference but low quality studies. Multiple settings and pathways not covered. Question remains pertinent.
58	Cross-cutting	Why do standards and advice for pregnant women with diabetes vary across NHS Trusts?	**16**	NICE NG3 – 5.3.1.7.4 identifies variation in practice and following guidance from the 2008 guideline for the targets and monitoring of maternal blood glucose. Raises and assesses guideline limitations as opposed to local/service level. Question not addressed. SRs – Not done. Other - NPID 2018: Highlights variation at unit level for a range of parameters in mothers and babies. Many possibly down to variation in clinical practice, but many are also down to maternal characteristics.	Guidelines – Question not addressed. Identifies variation in practice and following guidance for the targets and monitoring of maternal blood glucose. Raises and assesses guideline limitations as opposed to local/service level. SRs – Not done Other - NPID 2018: Highlights variation at unit level for a range of parameters in mothers and babies. Many possibly down to variation in clinical practice, but many are down to maternal characteristics.

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59	Cross-cutting	How can continuity of care and support services be improved for women with diabetes before, during and after pregnancy?	**20**	NICE NG3: 3.1.8 consensus recommendations on supporting and empowering women to have a positive experience of pregnancy and childbirth. 4.5.10.1.4 Continuity of care for women with GDM for post-natal follow-up and testing for T2D – references NICE guideline on patient experience in adult NHS services in relation to continuity of care. 5.10.1.1 and 5.10.2 CEMACH enquiry low grade evidence recommending care plan for the full pre-post pregnancy pathway by multidisciplinary team together in the same clinic. This is focussed on 1-2 weekly contact and monitoring during pregnancy. Research recommendation: 'Achieving glycaemic targets pre-pregnancy – what is the role of the health care professional?'; 'Achieving glycaemic targets pre-pregnancy – what is the role of telemedicine?'; 'What is the experience for women with type 1 and type 2 diabetes going through preconception and pregnancy?'. SIGN116: 7.1 recommends experienced multidisciplinary team…should provide comprehensive care from pre-pregnancy to postnatal review. 7.11 postnatal follow-up recommended from a clinical management perspective but not maternal support needs. 7.12 Low-moderate grade evidence on post-partum pharmacological and lifestyle interventions to reduce onset of type 2 diabetes in women with GDM. No evidence on timing of follow-up. SRs – Not done	Guidelines – Focus on post-natal follow-up from a clinical management perspective. None on wider support needs. Research recommendation: 'Achieving glycaemic targets pre-pregnancy – what is the role of the health care professional?'; 'Achieving glycaemic targets pre-pregnancy – what is the role of telemedicine?'; 'What is the experience for women with type 1 and type 2 diabetes going through preconception and pregnancy?' SRs – Not done
60	Cross-cutting	What information e.g. on risks or complications, should be given to women with diabetes during their pregnancy? What is the best way to give this information?	**21**	NICE NG3: 3.1.5 identifies lack of discussion of fetal risks in pregnancy with diabetes as a risk factor for adverse outcomes (low grade evidence). 3.1.8 lists information about diabetes vs pregnancy and vv. 3.10 and 3.11.1 reviews a range of education programmes but withholds recommendations on any specific preconception care and advice method due to limitations in data. 3.12 research recommendation: 'What is the most clinically and cost-effective form of preconception care and advice for women with diabetes?' 5.10.28 recommendation on information at first antenatal appointment and at 36 weeks' covering a range of areas. 2.1.3 and 5.10.2	Guidelines – None on how information, particularly in relation to complications, should be offered and delivered. Recommendation for women to enter structured education programmes (focussing on self-management of diabetes, moderate evidence) from the time they contemplate pregnancy. Some limited guidance on what information to offer at certain time points in the perinatal period.

Table S4: The full list of 60 indicative questions evidence search results completed over the period January to May 2020. Presented in groups by phase of pregnancy, with rank by groups. Darker grey indicates higher priority rank. Top ten are highlighted.

#	Phase of pregnancy	Indicative Question	FINAL RANK	Evidence (NICE NG3 and SIGN 116; Systematic Reviews 2017 onwards; Cochrane Reviews all-time)	Summary
				Recommends that women should be offered information and education opportunities throughout the antenatal period. Chapter 8. Focusses on glucose and medicines management in relation to breastfeeding, post-GDM monitoring, and information and follow-up after birth. Table 73 – booking appointment (by 10 weeks) discuss information, education and advice about how diabetes will affect the pregnancy, birth and early parenting i.e. breastfeeding and initial care of the baby. References NG17 for structured education for T1D generally: https://www.nice.org.uk/guidance/ng17/resources/type-1-diabetes-in-adults-diagnosis-and-management-pdf-1837276469701. Lifestyle/education interventions to prevent development of T2D in the post-natal period for women with GDM are also reviewed. SIGN116: 7.3 No evidence was identified on structured education specifically for pre-pregnant women. Women contemplating pregnancy should have access to structured education in line with the recommendations for adults with diabetes (see sections 3.2.1 and 3.2.3). 7.13 lists information provision – no evidence. SRs – Not done	SRs – Not done