# Optimising pregnancy outcomes for women with pre-gestational diabetes in primary health care

Glynis P Ross

**Preconception care for women with pre-existing diabetes (type 1 or type 2) is critical to optimise pregnancy outcomes and reduce the risk of adverse outcomes, including miscarriage, congenital anomalies, hypertension, caesarean deliveries and perinatal mortality. Pre-gestational diabetes is present in approximately 1% of pregnant women in Australia, and the prevalence is increasing. Women with pre-gestational diabetes need to be informed on the availability and importance of preconception care, which can be provided by both primary care and specialised diabetes services. The key elements of preconception care for women with diabetes are outlined in this article with two case examples to illustrate.**

RACGP QI&CPD Accredited Activity CATEGORY 2

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## Learning objectives

After reading this article, the participant should be able to:

1. Identify the increased risks of adverse pregnancy outcomes to mother and baby that are associated with pre-gestational diabetes.
2. Describe the ideal preconception care consultation and the key elements of care that a pregnant woman with pre-existing diabetes should receive.
3. Implement a checklist for preconception care for women with diabetes.

## Key words

- Preconception care
- Pre-gestational diabetes
- Pregnancy
- Type 1 diabetes
- Type 2 diabetes

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Women with pre-gestational type 1 or type 2 diabetes are at high risk of complications during pregnancy and of adverse outcomes including miscarriage, congenital anomalies and perinatal mortality. Despite advances in diabetes management, rates of congenital anomalies are 2–4 times higher than that of the background population and there is a 3–5 fold increased risk of stillbirth and perinatal mortality for births to women with diabetes (Macintosh et al, 2006; Dunne et al, 2009; Kitzmiller et al, 2010). Data from the Australian Institute of Health and Welfare (2010) show that in 2005–2007, more than half of all Australian women with pre-gestational diabetes underwent caesarean delivery (59%; 71% type 1 and 56% type 2 diabetes), compared to a third of women without diabetes. Following birth, 58% of infants born to women with diabetes were admitted to a special care nursery or neonatal intensive care unit, compared to 14% of babies born to mothers without diabetes.

Glycaemic control in early pregnancy is strongly associated with the risk of adverse pregnancy outcomes (Nielsen et al, 2004; Guerin et al, 2007, Jensen et al, 2009). Research shows that for every 10.93 mmol/mol (1%) increase in $HbA_{1c}$ above 53 mmol/mol (7%), there is a 5.5% increase in risk of adverse outcomes (Nielsen et al, 2004). The American Diabetes Association (2017) states that the lowest rates of adverse pregnancy outcomes are seen in association with an early gestation $HbA_{1c}$ of 42–48 mmol/mol (6.0–6.5%).

Preconception care for women with existing diabetes provides an opportunity to optimise glycaemic control, as well as other aspects of maternal health such as folic acid supplementation, diabetes complications screening and discontinuation of teratogenic medications prior to conception (McElduff et al, 2005; Mahmud and Mazza, 2010; Egan et al, 2015). Attendance at diabetes-specific preconception care has been associated with a reduction in congenital anomalies (relative risk [RR], 0.25), perinatal mortality (RR, 0.35) and reduced first trimester $HbA_{1c}$ by an average of 26 mmol/mol (2.4%; Wahabi et al, 2010).

## Advice

Preconception planning and assessment is recommended for all women considering pregnancy, but it is particularly important for women with diabetes or other medical disorders. Primary health care providers are well placed to complete most of the preconception screening and risk assessment, and can facilitate many of

the interventions and appropriate referrals that may be required. A checklist, such as below, may be useful when undertaking pre-pregnancy counselling.

## ADVICE AND CONSIDERATIONS FOR ALL WOMEN CONSIDERING PREGNANCY

- ☐ Appropriate contraception until optimal situation for pregnancy.
- ☐ Review ALL current medications and ensure they are safe and appropriate for pregnancy.
- ☐ Check blood pressure.
- ☐ *(For women not known to have diabetes, assess risk, and test appropriately for abnormal glucose tolerance.)*
- ☐ Promote a healthy lifestyle with regard to diet, exercise and optimal weight – this is also advisable for partners!
- ☐ Encourage smoking cessation.
- ☐ Advise to cease alcohol intake.
- ☐ Advise to stop any recreational drug use.
- ☐ Reduce caffeine intake.
- ☐ Dental check.
- ☐ Complete breast check and pap smear.
- ☐ Assess immunity to rubella and varicella zoster, and, if necessary, organise vaccinations with appropriate waiting periods before conception.
- ☐ Consider vaccinations for influenza and whooping cough.
- ☐ Commence folic acid 3 months prior to pregnancy at 0.5 mg daily (see below for dose adjustments for women with known diabetes).
- ☐ Commence an iodine-containing supplement (unless active thyrotoxicosis is present).
- ☐ Consider checking thyroid function, iron, B12 (especially if vegetarian or taking metformin) and vitamin D status (if at risk).

## ADDITIONAL ADVICE AND CONSIDERATIONS FOR WOMEN WITH PRE-GESTATIONAL DIABETES CONSIDERING PREGNANCY

- ☐ **Refer to a diabetes specialist or team** if not already under their care for assessment.
- ☐ **Optimise glycaemic control**
  - ☐ In type 1 diabetes, pre-pregnancy $HbA_{1c}$ should ideally be <53 mmol/mol (7%). A slightly higher $HbA_{1c}$ target is appropriate in pregnancy to balance the benefit of tighter glycaemic control against risk of severe hypoglycaemia.
  - ☐ In type 2 diabetes, pre-pregnancy $HbA_{1c}$ should ideally be ≤42 mmol/mol (6%).
  - ☐ Minimise risk of hypoglycaemia.
  - ☐ Minimise glycaemic excursions.
- ☐ **Review diabetes medications**
  - ☐ In type 1 diabetes, insulin management should be by multiple daily insulin (MDI) or subcutaneous insulin pump therapy. If MDI, check the insulins are approved for pregnancy – note, Lantus® and Apidra® do not have regulatory approval for pregnancy.
  - ☐ In type 2 diabetes, insulin may be initiated and titrated if glucose levels are not adequately controlled with lifestyle measures and metformin.
- ☐ **Review diabetes self-management skills and knowledge, ideally with a diabetes educator.**
  - ☐ Fingerprick blood glucose level (BGL) with/without continuous glucose monitoring system (CGMS) or flash glucose monitoring as adjuncts.
  - ☐ Hypoglycaemia prevention and management (including glucagon administration).
  - ☐ Appropriate National Diabetes Services Scheme (NDSS) registration.
  - ☐ Sick day management.
  - ☐ Driving risks and recommendations and appropriate glycaemic assessment and management.
- ☐ **Dietitian review**
- ☐ **Assessment of diabetes complications**
  - ☐ Eyes: ensure any retinopathy is treated and is stable prior to conception.
  - ☐ Kidneys: arrange renal assessment preconception if overt proteinuria or hypertension is present. Antihypertensive medication needs to be appropriate for pregnancy.
  - ☐ Autonomic neuropathy: specialist assessment is strongly advised. Discuss the impact this will have on pregnancy.
  - ☐ Consider cardiac assessment for women with multiple cardiovascular risk factors or known cardiac disease.
- ☐ **Start high-dose folic acid** at 5 mg daily 3 months prior to pregnancy (consider 5 mg alternate days if taking another pregnancy supplement containing folic acid).
- ☐ Refer women with type 1 diabetes for **coeliac screening and thyroid function tests**. *Note: women on thyroxine pre-pregnancy should be advised to increase the dose by ~30% once they have a positive pregnancy test in view of the increased demand for thyroxine in early pregnancy. Women with reduced thyroid reserve (e.g. underlying autoimmune thyroid disease) may need thyroxine replacement in pregnancy.*

**Page points**

1. Preconception care should be individualised.
2. Women should be advised to continue to use effective contraception until the best possible conditions for a safe pregnancy and birth are achieved.
3. Regular monitoring and recording of blood glucose levels during the preconception stage and pregnancy can be helpful in optimising pregnancy outcomes.

## Case studies

Outlined on the following two pages are two case studies illustrating some of the considerations to address during the preconception period. Given the range of situations that may be encountered, all care needs to be individualised. Ideally, most women with diabetes should be assessed before conception by a diabetes specialist or team with expertise in diabetes and pregnancy. This is particularly important when there are diabetes complications or additional medical disorders. For women in rural and remote areas, review in a regional centre or via telehealth with a specialist centre may be an appropriate option. This is especially important for women with more complex situations such as type 1 diabetes, type 2 diabetes requiring multiple medications, diabetes vascular complications and/or other vascular risk factors.

### Case 1

Maria is a 41-year old woman and has come to see you for a pap smear. You last saw her 4 months ago when she wanted a script for the oral contraceptive pill (OCP). On routine questioning when you are completing the pathology request for cervical cytology she says that she is considering having a break from the pill as she and her husband are thinking about having another baby.

#### History

Maria has two children aged 9 and 12 years. The first pregnancy was uncomplicated and she had spontaneous vaginal delivery at term. Her daughter weighed 3450 g and was breastfed for 12 months. Before her second pregnancy, Maria had gained 8 kg in weight and her BMI was 28 kg/m$^2$. At 28 weeks during her second pregnancy, Maria was diagnosed with gestational diabetes. She was able to manage this with diet modification alone and had spontaneous vaginal delivery at 39$^{+3}$ weeks of a 3720 g son. He was also breastfed for 12 months.

Three years ago (age 38 years), Maria's weight had risen and her BMI was 31 kg/m$^2$ (class 1 obesity range). Her fasting glucose was 7.2 mmol/L and her $HbA_{1c}$ was 49 mmol/mol (6.6%) and a diagnosis of type 2 diabetes was made. Initially she was treated with metformin XR 2 g daily. Despite the metformin and Maria trying to follow dietary guidelines, 4 months ago her $HbA_{1c}$ was 62 mmol/mol (7.8%) and so empagliflozin was added to her regimen. She continued to struggle to find time to exercise.

Maria has a strong family history of type 2 diabetes (both parents, her older brother and all grandparents) and hypertension (father and paternal grandmother). Her father had a myocardial infarct at the age of 39 years with subsequent stenting. For 7 years, Maria has also been treated for hypertension with telmisartan, and dyslipidaemia for which she is taking atorvastatin and fenofibrate. She and her husband smoke, but Maria has said she is trying to stop so is only smoking in the evenings after dinner.

#### Discussion

Maria has several factors that increase her risk of adverse pregnancy outcomes. She is of advanced maternal age, is obese, a smoker, and has type 2 diabetes, hypertension, dyslipidaemia and a family history of early-onset ischaemic heart disease.

Her glycaemic control is not satisfactory for pregnancy, and although metformin can be continued during pregnancy, empagliflozin will need to be stopped and insulin therapy commenced and titrated. She will need to increase her blood glucose monitoring and recording of results, preferably including dietary information. Review with a dietitian, diabetes educator and preferably an exercise physiologist is advisable. She should be seen by a diabetes physician with expertise in diabetes and pregnancy.

She has multiple vascular risk factors and is at a higher risk of developing pre-eclampsia in pregnancy. She should be appropriately counselled regarding smoking cessation. The medication she is on for hypertension needs to be changed and the lipid management will need to be stopped for pregnancy. As she has hypertension it would be preferable that she is also seen by a renal or obstetric medicine physician, especially if she fails to achieve blood pressure targets or if she has overt proteinuria. Given the multiple vascular risk factors, she should have a pre-pregnancy cardiac assessment.

### Advice

You advise Maria that she should stay on the OCP for the time being and that preconception planning is needed in view of her multiple medical conditions and medications. If she still wishes to become pregnant, she should commence high-dose folic acid and have routine pre-pregnancy checks. If she conceives, her contraception choice should be reviewed following the pregnancy as it is not advisable for her to continue on the OCP given her age and vascular risk status.

## Case 2

Jennifer has come to see you for a referral letter to her gynaecologist. She wants to have her intrauterine contraceptive device (IUCD) removed as she is keen to start a family. Jennifer is a 30-year-old woman who has had type 1 diabetes for 21 years. For the last 3 years, she has been using insulin pump therapy. Jennifer's most recent $HbA_{1c}$ of 70 mmol/mol (8.6%) was higher than usual after a recent overseas holiday with her husband.

### History

In her teens, Jennifer struggled with her diabetes control but in the past 5 years has been managing quite well. Her last episode of diabetic ketoacidosis was 18 months ago when there was a problem with insulin delivery through her pump. She has not had severe hypoglycaemia (requiring the assistance of another person) for 5 years and is using a continuous glucose monitoring system (CGMS) with predictive low-glucose suspend, as she knows that she does not reliably sense hypoglycaemia.

Jennifer has diabetic retinopathy that has previously required laser photocoagulation. However, she has not had her eyes checked for about 2 years as she missed an appointment and did not find time to reschedule. She has overt proteinuria (0.5 g per day) and is on ramipril for nephroprotection. Her eGFR is 62 mL/min/1.73 $m^2$ and she has previously been assessed for other causes of renal disease by a nephrologist. Her blood pressure and lipids are normal. She has a moderate degree of asymptomatic peripheral neuropathy with loss of distal sensation to light touch and vibration, as well as loss of ankle reflexes. She senses a monofilament and has had no diabetes-related foot complications.

### Discussion

If conception is successful, this will be Jennifer's first pregnancy. As she is on insulin pump therapy and uses a CGM device, she will already be under a specialist diabetes team. Her glycaemic control is sub-optimal and significantly increases her risk of adverse pregnancy outcomes, including miscarriage and congenital anomalies. Even though the recommended $HbA_{1c}$ target for women with type 1 diabetes in the preconception stage is ≤53 mmol/mol (7%), given her long duration of type 1 diabetes and poor hypoglycaemic awareness, it may not be safe to reduce her $HbA_{1c}$ below 58 mmol/mol (7.5%) due to the increasing risk of severe hypoglycaemia at lower levels. She needs specific specialist assessment and advice regarding her $HbA_{1c}$ as well as review of all aspects of her diabetes self-management (e.g. diet, exercise, BGL testing and recording, insulin pump settings review, pump management skills, driving considerations, and hypoglycaemia and diabetic ketoacidosis prevention and management).

Jennifer also needs an urgent diabetes eye review. If there is active proliferative retinopathy or macular oedema she will need to delay pregnancy plans until the retinopathy has been treated and is stable. As she has overt proteinuria, she should be assessed pre-pregnancy by a renal or obstetric medicine physician who will be able to continue to manage her in pregnancy. Her risk of pre-eclampsia and poor fetal outcomes, including intrauterine growth restriction (IUGR), will be increased. Although she is not known to have autonomic neuropathy, she should be assessed for this by her diabetes specialist.

### Advice

You advise Jennifer to not have the IUCD removed yet and that preconception planning is needed in view of her complex diabetes situation – especially her overall glycaemic control, nephropathy and retinopathy. You also ask her whether she has discussed pregnancy with her endocrinologist and check the date of her next scheduled appointment. Following diabetes complications assessment and optimising glycaemic management, Jennifer should commence high-dose folic acid and have routine pre-pregnancy checks.

***"If a woman has been diagnosed with retinopathy, it is important to ensure it has been treated and is stable prior to pregnancy."***

*"Primary health care providers have critical roles to play in the assessment and management of contraception, pre-pregnancy assessment and care."*

## Conclusion

Women of child-bearing age with pre-gestational type 1 or type 2 diabetes need to be counselled on the need for appropriate contraception at all times unless trying for pregnancy in the best possible circumstances to avoid adverse pregnancy outcomes. Most women with pre-gestational diabetes are able to have successful pregnancies. However, they are at much higher risk of having adverse pregnancy outcomes than women without diabetes (Macintosh et al, 2006; Dunne et al, 2009). It has been shown that women who have had optimal pre-pregnancy care and best practice management of their diabetes, both before and throughout pregnancy, will have a substantially lower rate of adverse outcomes (Ray et al, 2001; Wahabi et al, 2010).

Ideally, care should involve services that are specialised in diabetes in pregnancy. However, primary health care providers also have critical roles to play in the assessment and management of contraception, pre-pregnancy assessment and care, coordination of specialist services and ongoing support prior to, as well as throughout and following, the pregnancy. ■

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# Online CPD activity

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1. What percentage of pregnant women are affected by pre-gestational diabetes? **Select ONE option only.**
   A. 0.1%
   B. 1%
   C. 2.5%
   D. 5%
   E. 10%

2. A woman with type 2 diabetes has an $HbA_{1c}$ of 69 mmol/mol (8.5%) in early pregnancy. **Which ONE of the following statements is NOT true?**
   A. She is at increased risk of miscarriage.
   B. She is at increased risk of hypertension in late pregnancy.
   C. She is at increased risk of developing retinopathy in pregnancy.
   D. She will not have an increased risk of pregnancy complications unless she is obese.
   E. It is safe for her to continue taking metformin.

3. A 31-year-old woman with type 2 diabetes has just found she is pregnant. She is currently being treated with gliclazide and metformin. Which of the following options is most appropriate? **Choose ONE option only.**
   A. Stop gliclazide immediately
   B. Continue gliclazide and metformin initially
   C. Check $HbA_{1c}$
   D. Start self-monitoring of blood glucose (finger-prick testing)
   E. B, C and D

4. Attendance at diabetes-specific preconception care has been associated with which one of the following? **Choose ONE option only.**
   A. A reduction in congenital anomalies
   B. A reduction in perinatal mortality
   C. A reduction in first trimester $HbA_{1c}$
   D. A, B and C
   E. None of the above

5. Rachel has long-standing type 1 diabetes. Her most recent $HbA_{1c}$ is 70 mmol/mol (8.6%). She is keen to conceive soon. Which of the following statements is INCORRECT? **Select ONE option only.**
   A. She should avoid pregnancy until her $HbA_{1c}$ is close to 53 mmol/mol (7%) while still minimising hypoglycaemia risk.
   B. She should start taking folic acid 5 mg daily at least 3 months before she starts trying to conceive.
   C. She should be referred to a specialist diabetes and pregnancy unit to optimise her diabetes management prior to conceiving.
   D. She should be advised to terminate the pregnancy if she falls pregnant before her $HbA_{1c}$ has improved as risk to her and the fetus would be unacceptable.
   E. She should delay pregnancy plans if she has active retinopathy until it has been treated.

6. A 43-year-old woman with type 2 diabetes is currently 6 weeks pregnant. She has a past medical history that includes pernicious anaemia, hypertension and hyperlipidaemia. Which of her medications, if any, should she now STOP? **Choose ONE option only.**
   A. Metformin
   B. Hydroxocobalamin 1 mg 3-monthly
   C. Labetalol 200 mg twice daily
   D. Simvastatin 20 mg daily
   E. None of the above

7. Which of the following antidiabetes agents, if any, are SAFE to prescribe for a woman with type 2 diabetes planning pregnancy? **Choose ONE option only.**
   A. A sodium–glucose co-transporter 2 (SGLT2) inhibitor
   B. A dipeptidyl peptidase-4 (DPP-4) inhibitor
   C. A glucagon-like peptide-1(GLP-1) receptor agonist
   D. Thiazolidinedione
   E. Insulin

8. A 37-year-old woman with pre-gestational type 2 diabetes is advised to monitor her blood glucose levels as she has recently commenced insulin to control her diabetes. Which of the following is the most appropriate to monitor her glycaemia? **Choose ONE option only.**
   A. $HbA_{1c}$
   B. Self-monitoring of blood glucose (finger-prick testing)
   C. Fructosamine
   D. Continuous blood glucose monitoring
   E. A and B

9. Which of the following insulins does not have regulatory approval for use during pregnancy? **Select ONE option only.**
   A. Insulin glulisine (Apidra®)
   B. Protaphane/Humulin NPH
   C. Insulin detemir (Levemir®)
   D. Insulin aspart (Novorapid®)
   E. None of the above; they are all approved for use in pregnancy

10. Ideally, what should the pre-pregnancy $HbA_{1c}$ target for women with type 2 diabetes be? **Choose ONE option only.**
    A. <31 mmol/mol (5%)
    B. ≤42 mmol/mol (6%)
    C. ≤48 mmol/mol (6.5%)
    D. <53 mmol/mol (7%)
    E. Maintain current $HbA_{1c}$ to avoid unstable blood glucose levels