Pre-existing diabetes

Introduction
Before the advent of insulin, the outlook for pregnant women with diabetes was poor; Elliot Joslin described 17 pregnancies between 1898 and 1917. Only four babies and seven women survived. The use of insulin in the 1920s and the recognition that glycaemic control influenced outcomes led to a progressive reduction in maternal and perinatal mortality. By the 1980s, perinatal mortality had reduced to 0.65% and maternal mortality to 0.5%, but remained 3–5 and 8–10 times above the background rate respectively.1–3

The teratogenicity of glucose was recognised in the 1980s when it was found that a woman with good glycaemic control is less likely to have a baby with a congenital abnormality than one with poor control. Since congenital abnormalities are a major factor contributing to perinatal mortality, and organogenesis occurs between weeks 3–8 of pregnancy, the key to improving pregnancy outcomes is the improvement of glucose control preconceptually.4–6

There have been many advances in diabetes and obstetrics care since the 1980s, and there was every expectation that pregnancy outcomes would improve. The 1989 St Vincent Declaration7 set a five-year target that the ‘Outcome of pregnancies of women with diabetes should approximate to those without diabetes in 5 years’. Over a decade later, the results of the Confidential Enquiry into Maternal and Child Health (CEMACH) – which examined the outcomes of pregnancies in women with diabetes between 2002–2003 in England, Wales and Northern Ireland – were disappointing. The incidence of neural tube and cardiovascular defects was three times, and of perinatal mortality 3.8 times, that of the background population.8,9 A further decade later, the National Pregnancy in Diabetes Audit, which last reported in October 2017,10 showed that only 8% of women were adequately prepared for pregnancy in that they had an HbA1c of <48mmol/mol, were on folic acid 5mg daily and were not on any medication that could cause adverse effects in pregnancy. The congenital abnormality rate remained five times, and stillbirths twice, that of the background population.

Disappointingly, there have been no changes since 2014, and it was noted that there was a wide variation in all of the findings. Clearly, much work still needs to be done to improve the outcomes of these pregnancies.

What is preconception care?
The 2015 NICE guidance on diabetes and pregnancy11 emphasised the importance of preconception care, and outlined the different components (summarised in Box 1). The aim is to counsel women as to the risks of diabetes and pregnancy, and
empower them to use contraception until they are optimally prepared for pregnancy, and so reduce risks to a background level. It also has the potential to make the pregnancy a less stressful experience.

The components are:

- Intensify glucose control: data from the North East demonstrated a continuous relationship between HbA1c above the upper limit of normal and congenital abnormality rate. Therefore, any improvement in control has the potential to reduce congenital abnormality risk, and the lowest risk is if glucose levels are in the non-diabetic range. This is why NICE set a preconception glucose target HbA1c of 48mmol/mol if safe. The aim is to achieve the tightest glucose control the individual can achieve without problematic hypoglycaemia. It is also important to avoid setting such unrealistic targets that the woman disengages. If control is poor (HbA1c >85mmol/mol), women are strongly advised to avoid pregnancy.
- Given the increased prevalence of neural tube defects, folic acid 5mg is prescribed for at least three months before conception.
- The risks and benefits for all other medication are considered and, if needed, medication is changed to those safe in pregnancy. For example, statins are discontinued because of their teratogenic risk. ACE inhibitors also have this risk, and NICE recommends that they are stopped, but the greater risk is to fetal renal function in the second trimester and, where renoprotective effects are significant, the ACE inhibitor is sometimes continued until conception. If the ACE inhibitor is for hypertension, then it is usually changed to labetalol or methyldopa.
- Complications are assessed and optimised.

**How has the problem been approached in Southern Derbyshire?**

Derby and Southern Derbyshire serve a population of 600,000 and handle 6000 deliveries/year, 60 of whom have pre-existing diabetes and 400 gestational diabetes. At the time of the CEMACH audit we undertook preconception care in the antenatal setting and saw 32% of the women preconceptually. There was a 10% congenital abnormality rate and a 6% stillbirth rate. We were also aware that 20% of women failed to attend follow-up appointments. In considering how we could effectively engage women in pregnancy planning, we reviewed the literature and discussed difficulties in attending preconception appointments with women who were attending our antenatal clinic. A number of themes emerged (summarised in Box 2).

It was clear that the service needed to be taken out of the antenatal clinic environment and provide more flexibility in the appointments system. We were fortunate in gaining funding from the Health Foundation’s SHINE programme to pilot the first integrated model for preconception care: PROCEED (Preconception Care for Diabetes in Derby and Derbyshire). PROCEED has two components (Figure 1): raising preconception awareness and delivering care.

It was important we devised a model that addressed as many of these points as possible. PROCEED is a flexible integrated model that took preconception care out of the hospital to accessible community-based venues. It was funded for 12

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**Box 1. Components of preconception care**

- Contraception
- HbA1c target <48mmol/mol if safe
- Folic acid 5mg daily
- Review medication and change to those safe in pregnancy
- Review and optimise complications
- General lifestyle advice

**Box 2. Barriers to accessing preconception care**

- Lack of knowledge – user and professionals
- Denial
- Distressing environment – e.g. antenatal clinic following miscarriage or when undergoing infertility treatment
- Travel, parking, access
- Time off work
- Attending a preconception appointment when employers are not aware pregnancy is planned
- Health professionals being judgemental, setting unrealistic targets

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**Figure 1. PROCEED: raising awareness, and delivering care**

- Mental health problems are identified and supported according to local pathways.
- Women are given general lifestyle advice such as risks of smoking, alcohol and recreational drug use, as well as the benefits of weight reduction.

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**A. Raising awareness**

- Pharmacy
- Health visitors
- Family planning clinics
- Practice nurses/GPs
- Educators

**B. Delivering care**

- Consultant role
- Cross boundaries
- 6 Cs
- Competent
- Consistent
- Choice
months by the Health Foundation’s SHINE programme and has two equally important components, as shown in Figure 1.

Details of PROCEED have been previously published. In summary, all professions in contact with women with diabetes of childbearing age, including the primary care team, are encouraged to use every opportunity to discuss and document pregnancy plans and advise on contraception use (Figure 1A). We specifically targeted community pharmacists who use their new medications and medicines review services to discuss preconception in general. We also worked closely with the infertility clinic so that treatment is given once women are prepared for pregnancy. Pregnancy is included in structured education for patients and education for practices, and is also discussed during community nurse specialist practice visits. Women were sent leaflets, and posters were put up in GP practices. If a woman is considering pregnancy, then she is referred to the PROCEED clinic. As we were initially externally funded and subsequently commissioned through the block contract for integrated diabetes care, the referral process is flexible, using NHS mail, SystmOne, paper referral or self-referral by phone or email.

PROCEED involves working across organisational boundaries, using all competent resources – for example, previous members of the antenatal team who now work in the community. Women are offered a choice of community-based venues and flexibility about when they are seen. After an initial care planning appointment, they work with the clinician who would best support their needs. Through close team working consistency of information is ensured, and a member of the antenatal team works in each PROCEED clinic ensuring continuity from the preconception to the antenatal period. The consultant role has changed from seeing every patient to providing an overview to ensure women were progressing and so maximising the efficiency of the service. Once the woman is prepared for pregnancy, she comes off contraception, and contacts the team as soon as she is pregnant. She is reviewed in the antenatal clinic within seven days.

PROCEED also reviews women postnatally, especially those who have not received preconception care, to remind them to seek our advice before their next pregnancy and discuss contraception use. Within 12 months, PROCEED doubled the numbers seen preconceptually, and reduced the failure-to-attend rates from 18 to 5%. Women were better prepared for pregnancy, with 97% taking folic acid 5mg conceptually compared with none if they had not received preconception care; a mean first trimester HbA1c was 54mmol/mol as opposed to 69mmol/mol for those who did not access preconception care. Congenital abnormalities reduced from 10% to 4% and we saw three stillbirths over five years. Figure 2 demonstrates the sustainability of the project, and we continue to see 55–60% of women before pregnancy.

The service has been well received by our users, with 95% rating it as excellent or good. Short videos of their experiences can be viewed through the Health Foundation website via https://www.health.org.uk/improvement-projects/pre-pregnancy-care-in-diabetes.

Short-term cost savings were £66,000/year, but when the lifetime costs from reducing abnormalities were considered £18 million could be saved every year.

PROCEED became the first commissioned diabetes preconception service.

What is the role of primary care?

Preconception awareness. Florence Nightingale stated: ‘Let whoever is in charge keep this simple question in their head: not how can I always do this right thing myself, but how can I provide for this right thing to be always done?’

With an increasing number of women taking teratogenic drugs, and having other comorbidities, most would regard preconception care as a specialist area. However, in accordance with Florence Nightingale’s beliefs, all professionals in contact with women with diabetes have a responsibility to raise preconception awareness, so that women are aware they need to ask for support and be advised by them on contraception use.

Primary care is ideally placed in this, as the annual diabetes review or medication reviews provide an opportunity for these discussions and for signposting women to the local preconception service if they are planning pregnancy. There is considerable variation in the provision of such services ranging from the integrated model described above, to care within a diabetes or obstetrics service only. In some centres there is no dedicated preconception service at all, and the primary care team may find themselves in the situation of having to address as many of the components...
listed in Box 1 as they are competent to do, and involve diabetes specialists to support glucose intensification or an obstetrician to discuss the safety of medications as needed.

Increasingly, women with type 2 diabetes are being managed with medication that should not be used in pregnancy – such as GLP-1 analogues, SGLT-2 inhibitors, statins and ACE inhibitors. Pregnancy plans and contraception use should be considered when prescribing any of these agents.

Preparing for pregnancy is important for any long-term condition, and the approach to discussing pregnancy plans described above could be extended to long-term conditions generally. Public Health England is encouraging professionals to take a system-wide approach to pregnancy planning, be it working with education, sexual health clinics, cervical screening programmes, and specialists as well as primary care.

Postnatal care. The six-week postnatal check is an opportunity to raise preconception awareness and advise on effective contraception, particularly if teratogenic drugs are to be recommenced.

What if a woman presents pregnant? It is inevitable that some women with diabetes will present with pregnancies without preconception care. Box 3 summarises what to do under these circumstances. It is important to emphasise that, while there is insufficient evidence for the safe use of newer agents in pregnancy, discontinuing these agents may result in a rapid escalation of glucose levels during the critical period of organogenesis which may result in congenital abnormalities. Locally, we advise that these agents be continued as specialist advice is available the same day, and the woman seen within 48 hours if necessary. The aim in pregnancy is to manage diabetes according to the 2015 NICE guidance,11 and use lifestyle advice, metformin and insulin (although in certain situations glibenclamide can be used), and discontinue other medication for diabetes without destabilising glucose control.

I hope that in the future, by working together, the vision of the St Vincent Declaration will finally be realised and the outcomes of pregnancies in women with diabetes will be similar to those of women without diabetes.

Gestational diabetes

Background

The National Diabetes Data Group15 defined gestational diabetes (GDM) as 'any degree of hyperglycaemia at onset or first recognition during pregnancy'. This includes women with undiagnosed diabetes as well as those with transient hyperglycaemia due to pregnancy-induced insulin resistance. Those with an underlying predisposition to insulin resistance – such as the obese, some ethnic groups and those with a family history of diabetes – are predisposed to GDM. The prevalence of GDM varies according to the diagnostic criteria used and the populations studied. The Born in Bradford study16 showed prevalence rates between 2–24%, depending on the ethnicity of the groups studied and the six diagnostic criteria used. Irrespective of the criteria used, increasing obesity means GDM prevalence is increasing.

Gestational diabetes poses a number of risks to mother and baby, including pregnancy-induced hypertension, pre-eclampsia, shoulder dystocia, macrosomia and neonatal hypoglycaemia.17 In the longer term, mothers are at increased risk of diabetes, and risks vary between 2.6–70%, depending on the populations studied and the length of follow up. The greatest risk is in the first five years.18 Their offsprings’ risk of diabetes is over and above that expected from genetic factors, suggesting there may be in utero programming as a result of maternal hyperglycaemia.19,20

How is GDM diagnosed?

There has been little agreement as to the diagnostic criteria and therapeutic targets for GDM. It was hoped that the Hyperglycaemia and Adverse Pregnancy Outcome Study21 would facilitate a consensus. It was a large, multi-centred study involving over 25,000 women looking at outcomes in GDM. The study reported in 2008 and showed a continuous relationship between fasting, 1- and 2-hour postprandial glucose and adverse outcome.

On the basis of this study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) arrived at a consensus for a diagnosis of GDM based on fasting, 1- and 2-hour glucose thresholds following a 75g glucose tolerance test.22 These criteria were adopted by the World Health Organisation (WHO) and by many centres in the UK. The reality of adopting the IADPSG criteria is that there would be at least a 2–3-fold increase in numbers diagnosed with GDM, and concern was expressed as to the cost effectiveness of treating those with minimally-elevated glucose levels.23

Following a cost-effective analysis, NICE published guidance in 2015 with diagnostic threshold and treatment targets that differed from the IADPSG and WHO guidance.11 Some welcomed the attempt to balance risk at a time of limited resources, whereas others are concerned that some women at risk may ‘slip through the net’.24 This has resulted in a variation in practice with the Scottish SIGN guidelines,25

<table>
<thead>
<tr>
<th>Box 3. Women who present with pregnancy without preconception care</th>
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<tbody>
<tr>
<td>• Don’t stop oral hypoglycaemic agents until insulin is in place</td>
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<tr>
<td>• Do prescribe 5mg folic acid</td>
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<tr>
<td>• Stop ACE inhibitors, and change to labetalol or methyldopa if hypertensive</td>
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<tr>
<td>• Stop statins</td>
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<tr>
<td>• Refer to diabetes obstetrics clinic urgently and discuss any other medication being taken</td>
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<tr>
<th>Box 4. Risk factors for screening for gestational diabetes at 24–28 weeks</th>
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<tr>
<td>• BMI &gt;30kg/m²</td>
</tr>
<tr>
<td>• Previous baby &gt;4.5kg</td>
</tr>
<tr>
<td>• Previous gestational diabetes</td>
</tr>
<tr>
<td>• Family history in 1st degree relative</td>
</tr>
<tr>
<td>• Family origin from a group with a high prevalence of diabetes</td>
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and several centres in the rest of the UK choosing to continue to use the IADPSG guidance, whereas others adopted NICE.

Both guidelines advocate screening for GDM for those at risk, using a 75g glucose tolerance test at 24–28 weeks gestation. The risk factors are listed in Box 4. The two guidelines differ in how the general population is screened: the SIGN guidance recommends a fasting glucose at 24–28 weeks, whereas NICE advocates an oral glucose tolerance test (GTT) if 1+ glycosuria is present on more than one occasion or 2+ once. While the treatment targets differ (see Table 1), the principles of management with diet, lifestyle and the options to use metformin and insulin as well as glibenclamide are similar.

### What is the role of primary care?

As pregnant women present initially to the primary care team, it will be the primary care or community midwifery team that will be undertaking population screening and identifying risk factors. It is essential that all clinicians who review pregnant women, particularly the community midwifery team, are familiar with local guidance and referral processes. For example, in Derby, we follow the NICE guidance, and the community midwifery team identify those at risk. The diabetes specialist midwife coordinates the GTT and is responsible for identifying positive results and booking women to the next available new patient group session within one week with follow up in a multidisciplinary clinic thereafter, with the intensity of follow up dependent on individual risk. While a diagnosis of GDM results in consultant-led care, we encourage continuing contact with the community midwifery team, as they will be undertaking postnatal care and support.

As with pre-existing diabetes, there is considerable variation in service provision for women with GDM and, in some centres, the service is midwife and nurse specialist led. In these situations, the primary care team, particularly the general practitioner, may have a greater role in the management of these women – for example, in supporting prescribing and the management of comorbidities.

Once a woman has been delivered, and overt hyperglycaemia is excluded, women undergo a postnatal evaluation of their glucose tolerance. The SIGN guidance continues to advocate a GTT six weeks postpartum, whereas NICE recommends a fasting glucose from six weeks onwards or, if this is not done, an HbA1c from 13 weeks onwards.

In Derby, a form for HbA1c is given to the woman at 36 weeks; she is asked to attend for a blood test at the time of the baby’s 12-week immunisation – the results are reviewed by the consultant and the practice informed. In many centres, the responsibility of postpartum evaluation of glucose tolerance rests with the primary care team, so familiarisation of local pathways and responsibilities is essential.

All women with a history of GDM are at risk of diabetes, particularly, as discussed above, in the first five years. It is an opportunity for the primary care and community teams to use the diagnosis and a point of change in the women’s lives positively, and engage them and their families in making diet and lifestyle alterations. Women should be aware that a study of 1000 women showed that breastfeeding halved their likelihood of developing diabetes over two years.25 The Diabetes Prevention Trial,26 which recruited people with pre-diabetes, reduced diabetes risk by 58% in the lifestyle group and by 31% in the metformin group. Irrespective of the postnatal glucose tolerance, a history of GDM can be regarded as pre-diabetes. A subgroup analysis of 350 women with GDM28 demonstrated benefit from lifestyle advice and metformin, whereas the control group benefited from the former alone. This demonstrates the benefits of intervention in women with a history of GDM to prevent diabetes and raises the question of the use of metformin as well as lifestyle changes in

### Table 1. SIGN and NICE guidance: population and early screening, later screening, and treatment target.

<table>
<thead>
<tr>
<th>SIGN (based on WHO / IADPSG)</th>
<th>NICE</th>
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<tr>
<td><strong>Population and early screening</strong></td>
<td><strong>Later screening</strong></td>
</tr>
<tr>
<td>Fasting glucose or HbA1c in those at risk at booking to exclude overt diabetes</td>
<td>Fasting glucose low risk women at 24–28 weeks</td>
</tr>
<tr>
<td>Repeat GTT at 24–28 weeks if the diagnosis remains unclear</td>
<td>75g GTT 24–28 weeks if at risk</td>
</tr>
<tr>
<td>Fasting glucose in all women at 24–28 weeks</td>
<td>Diagnosis if any of the following plasma glucose criteria are met: Fasting ≥5.1mmol/L 1 hour ≥10mmol/L 2 hour ≥8.5mmol/L</td>
</tr>
<tr>
<td><strong>Treatment targets</strong></td>
<td><strong>GDM = gestational diabetes; GTT = oral glucose tolerance test; IADPSG = International Association of Diabetes and Pregnancy Study Groups; NICE = National Institute for Health and Care Excellence; SIGN = Scottish Intercollegiate Guidelines Network; WHO = World Health Organization.</strong></td>
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<tr>
<td>≥5.5mmol/L pre-prandial or ≥7mmol/L post-prandial &lt;35 weeks</td>
<td>≥5.5mmol/L pre-prandial or ≥8mmol/L 2 hours post-prandial &gt;35 weeks</td>
</tr>
<tr>
<td>Any post-prandial ≥9mmol/L</td>
<td>Fasting &lt;5.3mmol/L and 1 hour post-prandial &lt;7.8mmol/L OR 2 hour &lt;6.4mmol/L</td>
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</table>

GDM = gestational diabetes; GTT = oral glucose tolerance test; IADPSG = International Association of Diabetes and Pregnancy Study Groups; NICE = National Institute for Health and Care Excellence; SIGN = Scottish Intercollegiate Guidelines Network; WHO = World Health Organization.
diabetes prevention in this group. So a diagnosis of GDM is an opportunity to signpost them to local or national group interventions.

Both NICE and SIGN agree that those with a history of GDM should be screened annually for diabetes; so, initiating an annual recall at the point of receiving the postnatal discharge summary would facilitate this.

Finally, if postnatal or subsequent screening identifies diabetes, then it is important to raise preconception awareness, the need to use reliable contraception, and the need to seek advice from the local preconception service to minimise risks.

To conclude, the primary care team has a key role in the identification and support of women with gestational diabetes during and after pregnancy, as well as in preventing diabetes – not only in the mother but potentially in her offspring too.

Declaration of interests
There are no conflicts of interest declared.

References