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HIGHLIGHT NOTICE: ADDRESSING PRE-PREGNANCY GESTATIONAL DIABETES

Scope

Diabetes UK welcomes applications investigating feasibility of a randomised study of significant weight loss prior to pregnancy among women who experienced GDM in a previous pregnancy. The study will acquire pilot data on effectiveness to inform a subsequent large, randomised study.

Background

Gestational diabetes (GDM) is a high-risk condition that poses considerable problems for both mother and baby. Recent insights into the pathophysiological basis of type 2 diabetes (T2D) and previous studies on GDM suggest a practical approach that is likely to prevent GDM and improve outcomes for both mother and baby. Additionally, there are potential benefits both for future family eating patterns and for women without diabetes who wish to prepare optimally for pregnancy.

The problem

GDM affects at least 5% of pregnancies in the UK and causes major complications for both mother and baby. Women with GDM are more likely to have large-for-gestational-age babies, instrumented deliveries, and Caesarean sections. Their babies are more likely to require admission to neonatal intensive care units, especially for hypoglycaemia. Higher BMI in pregnant women increases the risk of Caesarean sections, neonatal hypoglycaemia, and macrosomic infants (1, 2). GDM also increases prenatal care costs by 5-16% (3).

Causation of GDM

Like type 2 diabetes (T2D), GDM is more likely in individuals with higher weight and can be seen as a first manifestation of T2D triggered by the metabolic stress of pregnancy. In normal pregnancy, insulin resistance increases during the second trimester and maternal insulin sensitivity is reduced significantly by about 50% - to a degree comparable with that in non-pregnant people with type 2 diabetes. The rise

in plasma triglyceride during pregnancy which favours glucose delivery to the baby (4, 5), is a key mediator of these changes (6). Elevated plasma triglycerides expose all tissues to excess fatty acids. The Twin Cycle Hypothesis suggests that surplus triglycerides in the pancreas lead to T2D, a theory supported by other studies such as Counterpoint, Counterbalance, DiRECT, and ReTUNE (7-10). Prolonged fat exposure suppresses glucose-stimulated insulin secretion, which likely develops months or years before pregnancy-related fatty acid increases can impair pancreatic function. This suppression only affects those with beta cells genetically prone to excess fat.

The opportunity to prevent GDM

The WellBabe study showed that calorie restriction upon GDM diagnosis around 28 weeks gestation could reverse some pathophysiological changes (11) but not beta cell dysfunction. This suggests that the window to prevent GDM is before the early pregnancy rise in plasma triglycerides. Weight loss of 10-15kg in the first trimester is not feasible, so it must be achieved pre-pregnancy.

New understanding of T2D pathophysiology indicates that chronic positive calorie balance, in the presence of two genetic susceptibility factors, causes T2D. These two factors are limitation of metabolically safe storage of fat in the subcutaneous depots and susceptibility to suppression of beta cell function by fat. Successful correction of the causative factor at the population level has been demonstrated for T2D (12), and similar principles can be applied to prevent GDM. Women with previous GDM have elevated liver triglyceride levels, and weight loss has been shown to prevent GDM even in women with previous T2D which resolved after bariatric surgery (13-17).

Ethical Considerations

Both safety of weight loss even during pregnancy and absence of any adverse effect upon subsequent eating behaviours have been established (19, 20). The benefits of pre-pregnancy weight loss make a strong case for its implementation, but establishing feasibility and effectiveness of weight loss in this circumstance is necessary as proof of principle for a larger randomised study. Current guidelines support weight control before and during pregnancy but not the extent of weight loss shown to be necessary to normalise dysglycaemia. The proposed study could lead to changes in guidelines and healthcare practices.

Research Priority

Research which facilitates whether 10-15kg weight loss prior to pregnancy prevents GDM, potentially improving outcomes in a subsequent singleton pregnancy. The research should:

- Involve women who developed GDM in a previous pregnancy.
- Establish an evidence base using a randomised controlled trial. Multicentre involvement is likely to be necessary to achieve suitable numbers possibly involving delivery of the intervention currently provided via the NHSE T2D Path to Remission Programme. Must use a dietary method already shown to achieve sustained 10-15kg weight loss in more than one population-based study.
- Primary outcomes should include proportion of women agreeing to be randomised and extent of weight loss achieved.
- Secondary outcomes should include assessment of metabolic state during the weight loss period and collection from NHS records of subsequent pregnancy outcomes including incidence of GDM
- Protocol is likely to include OGTT at baseline and after weight loss; with measurement of plasma insulin, HbA1c; fasting triglyceride; ALT & GGT.

Funding

Diabetes UK invites research proposals that address this knowledge gap in line with our project grant scheme which provides funding of up to £500,000 over five years. Note they do not have ringfenced funding, and these applications are in open competition with all the other applications we receive.

Applicants are encouraged to show evidence of substantial patient and public involvement in all stages of the development and delivery of their project, and should ensure that equity, diversity and inclusion is embedded within the design of the project.

Deadline

1 June 2026 17:00 hrs (Committee meets October 2026)

How to apply

Apply for a Diabetes UK grant through our online portal and select "ADDRESSING PRE-PREGNANCY GDM"

For further details please contact the Diabetes UK Research team at research@diabetes.org.uk

Application assessment process

Applications will be assessed by the scientific panel on the following criteria:

- Potential difference the research will make to the lives of women at risk of GDM.
- Scientific excellence and potential impact.
- Track record of the applicants.
- Value for money.

Applications will be assessed by the Grants Advisory Panel of people with lived experience on the following criteria:

- Relevance to women at risk of GDM and its potential impact.
- The projected timeframe for the research project to start delivering benefits to women at risk of GDM.
- The extent of involvement of women at risk of GDM in the development and the management of the study.

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