

Microvascular outcomes in type 2 diabetes

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lower than 5.1 mmol/L in the first trimester of pregnancy.² This finding further supports the evidence for a linear effect of hyperglycaemia on offspring adiposity, a differential effect of hyperglycaemia in different ethnic populations, and a potential role of non-glucose factors.

As Sweeting and colleagues point out, it is urgent that we call for high-quality evidence to establish the optimum test and glycaemic thresholds for the diagnosis and treatment of gestational diabetes in early pregnancy. However, gestational diabetes affects an estimated 21.4 million livebirths worldwide and more than 90% of these births happen in low-income and middle-income countries.³ It is important to keep this in mind in designing studies, and we feel that now is the time to raise these hard questions: who are we interested in treating—the mother or the offspring? The biggest benefit for the mother during pregnancy seems to be reducing pre-eclampsia. Is this really due to managing hyperglycaemia? On the contrary, the gestational diabetes label in routine care increases the induction and caesarean section rates.⁴ Second, if our interest is the offspring, should we not move away from simple birthweight-based outcomes (eg, large and small for gestational age) to adiposity outcomes? And finally, does a single threshold work for different ethnic groups? What is the cost-effectiveness of diagnosing and managing gestational diabetes in low-income and middle-income countries? Can these countries afford and establish screening programmes based on oral glucose tolerance tests?

We also believe that the disorder should be relabelled as “hyperglycaemia in pregnancy” and that the debate should be stopped about where to draw a line to define “normal or abnormal” that can be applied universally. It is time to do studies to create population-specific diagnostic and treatment strategies that include detailed economic evaluation to inform policy makers

in respective low-income and middle-income countries. Some of these studies are recently funded and in progress.^{5,6} Until these studies are completed, energy should be focused on detecting undiagnosed overt diabetes in all pregnant women and on educating high-risk women about pre-pregnancy care.

We declare no competing interests.

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In the individual participant data meta-analysis by Zoungas and colleagues,¹ more compared with less intensive glucose control reduced the risk of kidney and eye events, but not nerve events. However, we are concerned that not all endpoints used are of direct relevance for the clinic.

The kidney events outcome included development of macroalbuminuria,

development of an estimated glomerular filtration rate lower than 30 mL/min per 1.73 m², end-stage kidney disease, and renal death. Of these, only end-stage kidney disease and renal death are true clinical events. However, there was no effect on these outcomes. The positive effect found on kidney events was driven primarily by the effect on macroalbuminuria, which is an important prognostic indicator but not a clinical event. Similarly, the effect on eye events was driven by the effect on retinopathy progression (not a clinical event), and not by effects on clinical events such as retinal photocoagulation therapy, vitrectomy, or development of proliferative retinopathy. In addition, it is unclear to us why macular oedema, blindness, vision deterioration, and cataract extraction were included only as secondary outcomes, and not in the primary outcome. After all, these are true clinical events. Finally, the nerve events outcome was entirely non-clinical. Especially data for painful neuropathy and neuropathic ulcer would have been extremely valuable. As pointed out in the accompanying Comment,² a strategy of intensive glycaemic control must weigh benefits on macrovascular and microvascular events against harms, notably severe hypoglycaemia. In this crucial trade-off, all clinical events should be taken into consideration, and all events taken into consideration should first and foremost be clinical.

We declare no competing interests.

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