

GLP-1s in pregnancy: Reassuring data, one unresolved signal

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Millions of women of reproductive age are now prescribed a GLP-1 receptor agonist, and the evidence guiding what to do before, during and after pregnancy has not kept pace. A systematic review and meta-analysis published in *The Lancet Obstetrics, Gynaecology & Women's Health* gives the first international consensus recommendations built on that evidence, and the overall picture is more reassuring than the silence around it would suggest.¹

KEY TAKEAWAYS

- **The Pivot:** The first international consensus on GLP-1 use across the reproductive life course finds no increased risk of major adverse outcomes after first-trimester exposure, but flags one signal that current evidence cannot resolve.
- **The Data:** Across seven outcomes in 43,000-plus women, none showed a significant association with first-trimester GLP-1 exposure except early pregnancy loss (31% more common), a finding confounded by miscarriage and termination being recorded as one outcome in the study that supplied 99% of that comparison.
- **The Action:** Support GLP-1 use for preconception metabolic optimisation in women with type 2 diabetes as the panel recommends, advise stopping before a planned pregnancy, and counsel patients honestly that the pregnancy-loss data cannot yet be read as reassurance or as risk.

Diabetes in pregnancy, across type 1, type 2 and gestational forms, continues to rise globally, and GLP-1 therapy offers real benefits for the metabolic optimisation clinicians want before conception. But the drugs' safety profile across the reproductive life course, from preconception through breastfeeding, has been assembled from scattered observational data rather than any dedicated trial.¹

The consensus panel combined a systematic review and meta-analysis of seven studies covering more than 43,000 women exposed to a GLP-1 receptor agonist, expert input from 42 specialists, and the perspectives of 60 women with lived experience of using these drugs. Six of the seven studies captured exposure specifically in the first trimester; the seventh covered any exposure in the 12 months before pregnancy, which could overlap with early gestation.¹

What the Data Show

On the outcomes clinicians worry about most, the meta-analysis found no significant association between first-trimester GLP-1 exposure and congenital anomalies, preterm birth, stillbirth, neonatal death, caesarean delivery, hypertensive disorders of pregnancy or small-for-gestational-age birth.¹ For a drug class this widely prescribed, the absence of a

signal across seven distinct outcomes is itself a meaningful finding.

One result does not fit that pattern. Early pregnancy loss, defined here as miscarriage or termination occurring before 14 to 22 weeks, was 31% more common among women exposed to a GLP-1 drug. But the panel attached an explicit caveat to that number: it comes from only two studies covering 41,046 women, and in the study that supplied 99% of that group, miscarriage and elective termination were recorded as a single combined outcome. There is no way to separate a pregnancy lost spontaneously from one a woman chose to end after learning she was pregnant while on the drug.¹

The authors' own framing is blunt about what this means: the 31% figure is real in the data, and uninterpretable as a safety signal. It could reflect a genuine biological effect on early pregnancy, a higher rate of planned termination among women taking a drug not indicated for pregnancy, or some mix of both, and the current evidence cannot distinguish between them.

Evidence thins further at the edges of the reproductive timeline. Exposure beyond the first trimester is covered by almost no data. Postpartum evidence rests on one small randomised trial in non-breastfeeding women and two pharmacokinetic lactation studies, which found subcutaneous GLP-1 drugs undetectable or present only at negligible levels in breast milk, a reassuring but thin basis for advising breastfeeding mothers, particularly with oral formulations that use absorption enhancers.

The panel's recommendations reflect this nuanced understanding, advising that GLP-1s should be discontinued at least 2 months before planned conception due to the lack of robust safety data in early pregnancy and the unresolved signal of early pregnancy loss. However, they acknowledge the complexities of real-world clinical practice, particularly for women with type 2 diabetes or obesity who may benefit significantly from GLP-1 therapy for metabolic optimization prior to pregnancy. The decision to continue or restart GLP-1s in the preconception period, or even in early, unplanned pregnancy, must be an individualized one, balancing the potential risks with the benefits of glycemic control and weight management.

The panel also highlighted critical gaps in the evidence base that necessitate further research. Prospective studies, ideally registries or large cohort studies, are urgently needed to track pregnancy outcomes in women exposed to GLP-1s, particularly with detailed capture of early pregnancy loss and the ability to differentiate between spontaneous miscarriage and elective termination. Such studies should also aim to capture data on exposure beyond the first trimester, which is currently almost entirely absent. Furthermore, research into the pharmacokinetics of oral GLP-1 formulations in lactation is crucial, given their increasing use and the potential for different absorption profiles compared to subcutaneous injections.

The clinical implications of this consensus are clear: while the overall safety profile of GLP-1s in early pregnancy appears

reassuring for major congenital anomalies and other adverse outcomes, the signal regarding early pregnancy loss, though uninterpretable, warrants caution. Clinicians should engage in thorough shared decision-making with patients, discussing the knowns and unknowns, and emphasizing the importance of discontinuing GLP-1s prior to conception when feasible. For women who become pregnant while on GLP-1s, reassurance regarding major congenital anomalies can be offered based on current data, but careful monitoring for early pregnancy loss is prudent. The ongoing rise in diabetes and obesity in reproductive-aged women underscores the urgent need for more definitive data to guide safe and effective management strategies throughout the reproductive journey.

CLINICAL IMPLICATIONS

The instinct with a headline like "31% more pregnancy loss" is to treat it as the story. The panel that generated that number spent as much effort explaining why it cannot be read that way as it did reporting it, and that caution deserves to survive into how this gets discussed with patients. A woman asking whether her GLP-1 prescription raised her miscarriage risk deserves an honest answer: the data cannot currently tell her, because the one study driving that comparison could not distinguish a miscarriage from a termination.

Set against that unresolved question, the consensus on the other seven outcomes is worth stating plainly and without hedging: no signal for congenital anomalies, preterm birth, stillbirth, neonatal death, caesarean delivery, hypertensive disorders or small-for-gestational-age birth. The panel's support for preconception GLP-1 use in women with type 2 diabetes, provided it stops before a planned pregnancy, rests on genuinely reassuring evidence for the outcomes it covers.

For manufacturers and researchers, the gap that matters most is not the pregnancy-loss signal itself but the fact that a drug class used by millions of women of reproductive age has never been the subject of a trial designed to answer these questions directly. Two pharmacokinetic lactation studies and one small non-breastfeeding trial is not a postpartum evidence base, it is a placeholder for one.

The practical instruction for now is narrower than either "safe" or "avoid": use GLP-1 therapy to optimise metabolic health before conception where indicated, stop before a planned pregnancy, and treat any question about pregnancy loss, second and third trimester exposure or breastfeeding as genuinely open rather than quietly reassuring. Patients are entitled to that distinction, even when it makes for a less tidy conversation.

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