1 National Drug and Alcohol Research Centre, Faculty of Medicine and Health, University of New South Wales, Australia

2 Mater Research, South Brisbane, Queensland, Australia

3 Australian Injecting and Illicit Drug Users League, Canberra, Australia

Correspondence to: D Thuy Tran
Danielle.Tran@unsw.edu.au

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Treatments for opioid use disorder during pregnancy

Reassuring evidence on neurodevelopmental outcomes

Duong Thuy Tran, [1] Bianca Varney, [1] Julee Oie, [2] Jess Doumany, [3] Alys Havard[1]

Opioid use disorder during pregnancy poses substantial risks of harm to maternal and fetal health, including overdose, preterm birth, neonatal complications, and maternal and fetal death.[1 2] Methadone and buprenorphine are the recommended medications for opioid use disorder (MOUD).[1 -3] Methadone has been the standard treatment in pregnancy for more than three decades, but buprenorphine is increasingly used in many settings.[3] This shift reflects buprenorphine's pharmacological advantage as a partial opioid agonist[2] with a lower risk of sedation and respiratory depression, together with early evidence suggesting favourable neonatal outcomes.[1 2] Yet, uncertainty has persisted about the comparative effects of opioid use on the neurodevelopment of children.

The linked study by Friedrich and colleagues (doi:10.1136/bmj-2025-087321) addresses this evidence gap.[4] Using nationwide Medicaid data from the US, the authors compared the risk of neurodevelopmental disorders during the first eight years of life among children prenatally exposed to buprenorphine versus methadone. Their findings are reassuring: exposure to buprenorphine was not associated with an increased risk of overall or specific neurodevelopmental disorders compared with exposure to methadone.

The study is large scale and methodologically rigorous. Drawing on a population based cohort of 18 025 MOUD treated pregnancies resulting in live births, the study examined the risk of clinically important neurodevelopmental disorders with greater precision than previous studies. Adjustment for age, race, severity of opioid use disorder, co-occurring substance use diagnoses, comorbidities, concomitant medications, and prenatal care reduced the likelihood of between group differences arising from underlying maternal factors. Extensive sensitivity analyses confirmed the robustness of the findings across distinct definitions and subgroups with potentially different vulnerabilities. Importantly, trimester specific analyses provided reassurance that exposure later in pregnancy—when cognition, memory, and behaviour develop rapidly—was not associated with increased neurodevelopmental risk.

However, as with all observational research, residual confounding cannot be completely ruled out. In the US, individuals receiving buprenorphine tend to be more socioeconomically advantaged than those receiving methadone.[5 6] Although Friedrich and colleagues' study adjusted for the socioeconomic status of the mother's residential area, unmeasured individual level factors, such as education, employment, and income, may remain imbalanced.

Taken together, well designed population based studies such as that by Friedrich and colleagues[4] provide the most reliable evidence currently available to guide clinical decisions. Studies using human brain organoids (in vitro stem cell derived culture) suggest that methadone may impair growth and neuronal activity to a greater extent than buprenorphine[7]; however, preclinical data do not reliably predict neurodevelopmental outcomes in humans. Randomised trials have faced substantial barriers in recruitment and attrition; the landmark MOTHER (Maternal Opioid Treatment: Human Experimental Research) trial retained only 96 children at 36 months for neurodevelopmental assessment.[8] Earlier observational studies were constrained by small cohort sizes and inadequate control for confounding.[9]

Beyond this new evidence showing equivalent neurodevelopmental risks, evidence to date suggests buprenorphine is associated with improved birth outcomes and reduced severity of neonatal abstinence syndrome compared with methadone.[9 10] These findings cannot be considered conclusive, however, given the imprecise risk estimates and high likelihood of residual confounding.[9] Furthermore, there has been little investigation of the comparative risk of harms related to opioid use disorder, which may be greater among individuals receiving buprenorphine due to higher treatment drop-out typically seen for buprenorphine.[11 -13] Accordingly, while buprenorphine can be considered a reasonable initial treatment option for many individuals, how it compares to methadone across all clinically relevant domains is not yet fully established. In settings dominated by illicitly manufactured fentanyl, careful induction and close monitoring of buprenorphine are critical to prevent precipitated withdrawal or treatment discontinuation.[14] Methadone remains essential for individuals with higher opioid tolerance or more complex clinical and social needs.[15]

From the perspective of individuals with lived experience of MOUD during pregnancy, access to safe and effective medications is vital, as is autonomy of choice. High quality evidence on the risks and benefits of different MOUDs is critical to making this choice. A need also exists to address stigma, fragmented services, and structural inequities that undermine engagement in care for people with opioid use disorder. Meaningful improvements in maternal and child outcomes require continuity of care, social and wellbeing support, and coordinated services.[16] Irrespective of which MOUD is chosen, children with prenatal exposure to opioids should be given opportunities for developmental monitoring and early intervention.

This new evidence should increase confidence in buprenorphine as an option during pregnancy. Nevertheless, further research is needed to evaluate other clinically important outcomes and emerging formulations. Long acting injectable buprenorphine is becoming increasingly available in high income countries,[17] yet unstudied in pregnancy, underscoring the onus for ongoing investigation to ensure clinical recommendations remain evidence based and responsive to evolving options for MOUD.

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