Paracetamol (acetaminophen) Use During Pregnancy and Autism Risk: Evidence Does Not Support Causal Association

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Abstract

Recent political statements linking paracetamol use during pregnancy to autism spectrum disorders have created concern among patients and healthcare providers worldwide. This editorial critically examines the scientific evidence, highlighting that the largest and most methodologically rigorous population-based studies employing sibling control analyses demonstrate no causal association between prenatal paracetamol exposure and neurodevelopmental disorders. While some observational studies have suggested potential weak associations, these findings likely reflect confounding by indication and familial genetic factors rather than actual causal relationships. The most robust evidence comes from a Swedish population-based study of 2.48 million children that found no increased risk when familial confounding was controlled. Major international medical organisations, including ACOG, RCOG, FIGO, and regulatory agencies, including the European Medicines Agency, continue to recommend paracetamol as the safest analgesic option during pregnancy when clinically indicated. The established risks of untreated pain and fever during pregnancy significantly outweigh theoretical concerns based on methodologically limited studies. Healthcare providers should continue evidence-based counselling while avoiding unnecessary anxiety about this essential medication in obstetric practice.

Main Part

Political Claims

On September 22, 2025, President Donald Trump made unprecedented statements at the White House claiming that paracetamol (acetaminophen) use during pregnancy is linked to autism in children (1). This announcement, delivered alongside health officials including Robert F. Kennedy Jr., represents a concerning departure from evidence-based medical guidance that demands immediate professional response from the obstetric and gynaecological community.

President Trump asserted that the Food and Drug Administration (FDA) would be "notifying physicians that the use of acetaminophen during pregnancy can be associated with a very increased risk of autism," advising pregnant women to "fight like hell not to take it" (2). The administration referenced selective studies, including the Prada et al. 2025 review published in BMC Environmental Health, which have been documented as methodologically flawed (3,4).

These statements contradict established medical guidance from major obstetric organisations worldwide, which consistently recommend paracetamol as the safest analgesic option for pregnant women when used appropriately.

Scientific Evidence: The Swedish Population Study

The most comprehensive and methodologically sophisticated evidence on this topic comes from a Swedish population-based study published in JAMA in April 2024, analysing 2.48 million children born between 1995-2019 (5). This study employed sibling control analysis—a methodology that controls for shared genetic and environmental factors within families—representing the gold standard for addressing confounding in observational research.

The Swedish study's findings are clear: when familial confounding was properly controlled through sibling analysis, there was no evidence of increased risk for autism (hazard ratio 0.98, 95% CI: 0.94-1.02), attention-deficit/hyperactivity disorder (ADHD) (hazard ratio 0.98, 95% CI: 0.95-1.01), or intellectual disability (hazard ratio 1.01, 95% CI: 0.96-1.07) associated with paracetamol use during pregnancy (5).

This approach is particularly powerful given that siblings of children with autism have approximately a 20% likelihood of also receiving an autism diagnosis (6). Importantly, when conventional analytical models suggested marginal associations (hazard ratios of

1.05-1.07), these associations completely disappeared in sibling analyses, demonstrating that previously reported associations likely reflect familial confounding rather than causal relationships (5).

Supporting evidence comes from a Japanese population-based study of over 200,000 children that also employed sibling comparisons and found no link between acetaminophen use in pregnancy and autism, further reinforcing the reliability of the Swedish findings (7).

Critical Analysis of Conflicting Evidence

The Prada et al. (2025) review, cited by political figures, while employing the Navigation Guide methodology, suffers from fundamental methodological limitations that significantly compromise its reliability and clinical applicability (3). Although this analysis included 46 studies, some of the studies included are not considered high-quality and exhibit several critical limitations that undermine their validity.

The majority of the studies within the review rely on self-reported acetaminophen use with considerable potential for recall bias (8–14). This represents an essential flaw in exposure assessment that can lead to differential misclassification between cases and controls, where mothers of children with neurodevelopmental disorders may be more likely to recall or overreport medication use compared to mothers of typically developing children (15,16).

Some of the included studies feature limited or no information on dosage and duration of acetaminophen exposure, making it impossible to establish dose-response relationships or identify potential threshold effects (8–10,13,14). Without adequate characterisation of exposure patterns, timing, and dosage, any conclusions about causal relationships remain scientifically unfounded.

Furthermore, the review includes studies that employ different kinds of assessments of neurodevelopmental milestones over time, rather than using a single standardised, uniform assessment method (8–14,17). This methodological heterogeneity introduces significant variability and reduces the validity of pooled analyses, as combining studies with different outcome definitions and assessment methods can produce misleading results that do not reflect true biological relationships (18).

Most importantly, the majority of studies lack adequate controls for confounding factors, particularly the genetic and environmental factors that significantly influence both medications use patterns and neurodevelopmental outcomes (10,19,20). This represents a critical flaw in study design that prevents reliable causal inference, as unmeasured confounding variables may explain apparent associations between acetaminophen use and neurodevelopmental disorders (16).
The review is further compromised by conflict-of-interest concerns, as the senior author, Andrea Baccarelli, served as a paid expert witness in class-action litigation against paracetamol manufacturers in 2023, with his testimony ultimately rejected by the court as scientifically unfounded (21).

Earlier meta-analyses have reported pooled risk ratios of 1.34 for ADHD and 1.19 for ASD, but these studies exhibited substantial heterogeneity ($I^2 = 72\%$ for ADHD studies) and were limited by observational study designs susceptible to multiple sources of bias, including the same confounding factors addressed by the Swedish sibling control study (18).

International Professional Society Recommendations

The consensus among leading international obstetric organisations highlights a strong scientific agreement on the safety of paracetamol during pregnancy, based on thorough evaluations by expert committees knowledgeable in maternal-fetal medicine.

In a practice advisory released shortly after the government’s announcement, Acetaminophen Use in Pregnancy and Neurodevelopmental Outcomes, the American College of Obstetricians and Gynecologists (ACOG) affirms that "acetaminophen remains the safest first-line analgesic and antipyretic in pregnancy" and that “the current weight of evidence does not support a causal link between prenatal acetaminophen use and neurodevelopmental disorders“ (22). ACOG also stresses that "clinicians should continue to recommend its judicious use, provide evidence-based counselling, and reassure patients that current data do not support a causal link to neurodevelopmental disorders“ (22).

The Royal College of Obstetricians and Gynaecologists continues to recommend paracetamol as the first-line analgesic during pregnancy (23). Similarly, the International

Federation of Gynaecology and Obstetrics, through its published guidance, continues to recognise paracetamol as safe during pregnancy when clinically indicated (24).
The Society for Maternal-Fetal Medicine recommends paracetamol for treating fever and pain during pregnancy, emphasising that untreated fever can lead to miscarriage, birth defects, or premature birth, particularly in early pregnancy (25,26).

Regulatory Agency Positions

Similarly, International regulatory agencies have independently evaluated the evidence and maintain positions supporting paracetamol's continued use during pregnancy, though with updated labelling reflecting ongoing research. The UK Medicines and Healthcare products Regulatory Agency explicitly states, "there is no evidence that taking paracetamol during pregnancy causes autism in children" (27). The European Medicines Agency confirmed in September 2025 that current recommendations remain unchanged based on rigorous assessment of available evidence (28).
While the FDA initiated a label change process in September 2025, the agency carefully noted that "while an association between acetaminophen and neurological conditions has been described in many studies, a causal relationship has not been established and there are contrary studies in the scientific literature" (29). The FDA also emphasised that "acetaminophen is the only over-the-counter drug approved for use to treat fevers during pregnancy, and high fevers in pregnant women can pose a risk to their children" (29).
The Australian Therapeutic Goods Administration maintains paracetamol as a safe option during pregnancy when used as directed, and Health Canada continues to support its appropriate use (30,31).

Clinical Implications and Risk-Benefit Analysis

The clinical consequences of avoiding paracetamol during pregnancy are well-established and evidence-based. Untreated fever in early pregnancy is associated with increased risks of miscarriage, neural tube defects, cleft palate, and cardiac anomalies, and with increased risks of preterm birth and fetal growth restriction in later pregnancy (32).

Paracetamol is included on the World Health Organization's List of Essential Medicines, reflecting its fundamental importance in healthcare worldwide (33). Creating concerns about its safety during pregnancy could have devastating public health consequences,

particularly in resource-limited settings where alternative analgesics may be unavailable or contraindicated.

Understanding Methodological Challenges

The difficulty in determining definitively whether acetaminophen use in pregnancy causes neurodevelopmental disorders stems from fundamental methodological challenges. Most studies examining this relationship are retrospective and are inherently subject to human error, particularly recall bias, and confounding factors that cannot be adequately controlled for (16).

Genetic factors and environmental exposures play crucial roles in brain development during pregnancy and early childhood. These environmental links to neurodevelopmental outcomes warrant thorough exploration but have not been adequately controlled for in the majority of studies examining acetaminophen use in pregnancy (16,34). As practitioners committed to evidence-based medicine, we must distinguish between correlation and causation. The apparent associations noted in some observational studies likely reflect confounding by indication—women who require pain relief during pregnancy may have underlying conditions or genetic predispositions that independently influence neurodevelopmental outcomes in their children (3,5,16).

Professional Responsibility and Evidence-Based Practice

As obstetric and gynaecological professionals, we have a fundamental duty to our patients to provide guidance based on rigorous scientific evidence.

The broader pattern of anti-vaccine messaging accompanying these paracetamol claims further undermines public confidence in evidence-based healthcare. Decades of research have consistently found no correlation between vaccines and autism, yet these thoroughly debunked theories continue to resurface in political contexts, creating public health risks (35).

Recommendations for Practice

Healthcare providers should continue following established clinical guidelines regarding paracetamol use in pregnancy. When counselling patients, emphasise that:

- Paracetamol remains the safest analgesic option during pregnancy when used appropriately, supported by decades of clinical experience and the highest-quality epidemiological evidence.
- Untreated fever and pain pose documented risks to maternal and fetal health that are well-established in the literature.
- The largest and most methodologically rigorous studies to date found no causal relationship between paracetamol use and autism when proper controls for confounding factors were employed.
- Decisions regarding pain management should be individualised based on clinical assessment and evidence-based guidelines, not political statements or methodologically limited studies.
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Conclusion

The weight of scientific evidence, particularly from the largest and most methodologically rigorous studies employing sibling control designs, shows no causal relationship between paracetamol use during pregnancy and autism spectrum disorders. While some observational studies have suggested associations, these findings have fundamental methodological limitations, including recall bias, inadequate exposure characterisation, heterogeneous outcome assessment, and insufficient control for confounding factors.

Obstetric practice should be based on evidence-based medicine and careful evaluation of research methodology. Recent statements questioning paracetamol safety go against established scientific findings and may harm maternal and fetal health by discouraging use of this medication based on methodologically flawed research.

As obstetric professionals, we should maintain our focus on evidence-based practice and advocate for our patients based on rigorous scientific research and proper evaluation of study quality.

Healthcare providers should continue recommending paracetamol as the preferred analgesic during pregnancy when medically needed, counselling patients based on evidence while maintaining confidence in this medication's established safety profile.

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