

**PERSPECTIVE** OPEN ACCESS

# Paracetamol in Pregnancy: Uncertain Evidence, Certain Consequences

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## ABSTRACT

Autism diagnoses have increased over the past decade, prompting debate on potential causes. In September 2025, US President Donald Trump claimed that paracetamol is a 'big factor' in autism, citing a systematic review based solely on observational studies. The review's selective reporting, methodological flaws (including applying an environmental health rather than evidence-based medicine framework) and lack of causal evidence provided weak justifications for its conclusions and have fuelled public confusion about paracetamol safety in pregnancy. This article critically appraises the review and examines how scientific uncertainty can be manipulated and amplified within broader public health domains.

**JEL Classification:** Women's health, Statistics, epidemiology and research design, Health services administration, Environment and public health, General medicine, Anesthesia, analgesia and pain

## 1 | Introduction

On 22 September 2025, US President Donald Trump and senior health officials linked acetaminophen (paracetamol) use in pregnancy to rising autism diagnoses [1]. However, high quality studies do not support a causal link between paracetamol and neurodevelopmental disorders [2, 3]. The announcement spread globally, creating confusion about a widely used medicine and illustrating how scientific uncertainty can be amplified in ways that can erode trust in public health advice.

The claims drew on a systematic review by Prada and colleagues 2025 [4] (hereafter, the Prada review), which synthesised findings from 46 studies using the Navigation Guide, an environmental health framework that integrates human and non-human evidence [5]. While appropriate in regulatory contexts, such frameworks differ fundamentally from evidence-based

medicine approaches designed to guide public health and clinical decision-making. The Prada review emphasised studies reporting an association between prenatal paracetamol exposure and both attention-deficit/hyperactivity disorders (ADHD) and autism [6], while downplaying contradictory findings, including a large Swedish cohort study in which associations attenuated under sibling controls [7]. Health professionals responded swiftly to the Trump announcement, noting the lack of randomised evidence and the importance of findings from sibling-controlled designs that account for shared familial and genetic confounding.

Importantly, the significance of this debate extends beyond paracetamol safety in pregnancy. Selective use of studies in political and media discourse can shape perceptions of partisanship. In this case, expert concerns were met with counter-accusation of bias [8], shifting attention away from the methodological

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limitations of the Prada review to perceived political alignment. Similar dynamics have been observed across multiple contemporary public health domains, including vaccination, environmental exposure and pandemic response, where uncertainty is selectively framed to reinforce narratives, polarise debate and influence public perception and behaviour.

Subsequent high-quality systematic reviews conducted to evidence-based medicine standards have since clarified that the available evidence does not support a causal association between prenatal paracetamol exposure and neurodevelopmental disorders [9, 10]. The processes by which uncertainty was generated, amplified and communicated remain highly relevant. The Prada review provides a useful case study for examining how methodological choices, departures from established evidence-based medicine standards and narrative handling of uncertainty can confer unwarranted epistemic authority when scientific findings intersect with politicised health messaging.

Therefore, we critically appraise the methodological quality of the Prada review using evidence-based medicine standards, not simply to reassess its conclusions, but to illustrate how scientific uncertainty can be amplified beyond the literature, with implications for clinical practice and health communication.

## 2 | Scientific Assessment of the Prada Review

The Navigation Guide is a less established method for synthesising and appraising evidence. Although typically used for environmental exposures [11], and designed to combine human and non-human studies, the Prada review included only human observational data, despite available animal studies [12, 13]. More established and developed methodologies for synthesising observational data (Supporting Information: Section 1) are used by bodies such as Cochrane and the World Health Organization. We assessed the conduct of the Prada review using AMSTAR 2 (A Measurement Tool to Assess systematic Reviews, version 2) [14] and ROBIS (Risk of Bias in Systematic Reviews) [15] (Table 1 and Supporting Information: Section 2).

### 2.1 | Critical Appraisal With Evidence-Based Medicine Standards

#### 2.1.1 | Methods Prespecification and Study Selection

The Prada review did not prespecify its methods, and no protocol was registered or published. Its search strategy lacked sufficient detail for replication, unpublished studies were not sought and no excluded studies list was provided. The senior author, Andrea Baccarelli, Dean of the Harvard TH Chan School of Public Health, declared a conflict as an expert witness in litigation concerning paracetamol and neurodevelopmental disorders. But the review did not explain how this conflict was managed. The case was later dismissed for insufficient evidence. The judge from this case also noted that his testimony failed to acknowledge the 'role of genetics in aetiology' [16] for autism. Without transparent study selection and clear management of declared conflicts, readers cannot be confident that the review's conclusions are not shaped by selective

inclusion of studies, or investigator bias rather than the totality of the available evidence.

#### 2.1.2 | Risk of Bias Assessment

The methods used to assess risk of bias were not consistent with current standards and offered minimal justifications. However, some domains, such as confounding, were addressed by the reviewers, that is, adjustment for key variables, use of propensity score matching and evaluation of residual confounding. Domain-level assessments were converted to numerical scores and averaged, a practice widely discouraged [17] because it can mask domains with critical risk of bias. In four autism studies, averaging suggested low risk of bias despite some domains being rated as critical. These departures from established risk of bias assessment can obscure serious methodological flaws in studies, giving a misleading impression of the overall strength of evidence.

#### 2.1.3 | Synthesis of Studies

A meta-analysis was not conducted due to the diversity of the included studies, in terms of their populations, methods of assessing paracetamol use and time frames of recall. This decision is not unreasonable; a meta-analysis of observational studies is challenging, and can yield misleading summary estimates [18]. However, the Prada review uses vote counting based on the statistical significance of study results, classifying studies as showing a positive association, null association or mixed, without a clear definition of 'mixed'. Vote counting based on statistical significance is widely considered inappropriate [17, 19], and much the same diversity that precluded a meta-analysis should also prevent the use of vote counting to infer an overall direction of effect across the included studies. Although sources of heterogeneity were identified (e.g., maternal self-reports vs. biomarkers, timing and duration of exposure, outcome measures and confounder adjustment approaches), their impact was not systematically assessed. Instead, heterogeneity was discussed narratively, creating scope for selective emphasis that can align with prior assumptions. In the absence of a structured heterogeneity analysis, such discussions risk serving as post hoc justification and limit confidence in any inferred direction or magnitude of effect.

#### 2.1.4 | Certainty of the Evidence

The Prada review reported using GRADE (Grading of Recommendations Assessment, Development and Evaluation) to assess the certainty of the evidence, but deviated substantially from published guidance, applying selective domains and assessing individual studies with a non-standard scoring system [19]. Studies were rated from very strong to very weak based on criteria partly drawn from GRADE components, such as large relative effect and dose-response. These ratings were summed into a 'strength of evidence' score with little clarity on derivation. The use of a non-standard certainty of the evidence rating without transparent justifications may overstate confidence in the overall findings of the review. Furthermore, the authors removed the lowest-scoring studies, and an unclear 'expert

**TABLE 1** | A Measurement Tool to Assess Systematic Reviews Version 2 (AMSTAR 2) checklist [14] of Prada et al. 2025 [4].

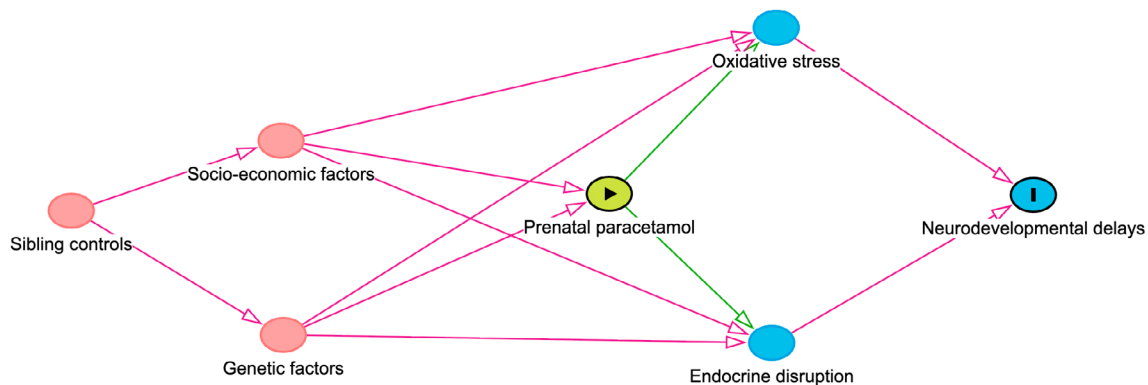
AMSTAR 2 Checklist question			Overall
Did the research questions and inclusion criteria for the review include components of PICO?	For yes <input checked="" type="checkbox"/> Population <input checked="" type="checkbox"/> Exposure <input checked="" type="checkbox"/> Comparator <input checked="" type="checkbox"/> Outcome <input type="checkbox"/> Timeframe (Optional)		Yes
Did the report of the review contain an explicit statement that the review methods were established before the conduct of the review and did the report justify any significant deviations from the protocol?	For partial yes The authors state they have followed a written protocol or guide that included all the following <input type="checkbox"/> review question(s) <input type="checkbox"/> a search strategy <input type="checkbox"/> Inclusion/exclusion criteria <input type="checkbox"/> a risk of bias assessment <input type="checkbox"/> Timeframe (Optional)	For yes As for partial yes, plus the protocol should be registered and should also be specified <input type="checkbox"/> a meta-analysis/synthesis plan <input type="checkbox"/> a plan for investigating heterogeneity <input type="checkbox"/> a plan for investigating causes of heterogeneity	No
Did the review authors explain their selection of the study designs for inclusion in the review?	For yes, the review should satisfy one of the following <input type="checkbox"/> a explanation for including only RCTs <input type="checkbox"/> OR explanation for including only non-randomised studies <input type="checkbox"/> OR explanation for including both RCTs and non-randomised studies		Yes
Did the review authors use a comprehensive literature search strategy?	For partial yes (all the following) <input checked="" type="checkbox"/> Searched at least 2 relevant databases <input checked="" type="checkbox"/> provided key word and/or search strategy <input type="checkbox"/> justified publication restrictions	For yes, should also have (all the following) <input type="checkbox"/> searched the reference lists of included studies <input checked="" type="checkbox"/> searched trial/study registries – not relevant <input type="checkbox"/> included/consulted content experts in the field <input type="checkbox"/> Where relevant, searched grey literature <input checked="" type="checkbox"/> conducted search within 24 months of completion of the review	No
Did the review authors perform study selection in duplicate?	For yes, either one of the following <input checked="" type="checkbox"/> At least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include <input type="checkbox"/> OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80%), with the remainder selected by one reviewer		Yes
Did the review authors perform data extraction in duplicate?	For yes, either one of the following: <input checked="" type="checkbox"/> at least two reviewers achieved consensus on which data to extract from included studies <input type="checkbox"/> OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.		Yes
Did the review authors provide a list of excluded studies and justify the exclusions?	For partial yes <input type="checkbox"/> provided a list of all potentially relevant studies that were read in full-text form but excluded from the review	For yes, must also have <input type="checkbox"/> Justified the exclusion from the review of each potentially relevant study	No
Did the review authors describe the included studies in adequate detail?	For partial yes (all the following) <input checked="" type="checkbox"/> described populations <input checked="" type="checkbox"/> described exposure <input checked="" type="checkbox"/> described comparator <input checked="" type="checkbox"/> described outcomes <input checked="" type="checkbox"/> described research design	For yes, should also have all the following <input checked="" type="checkbox"/> described populations in detail <input checked="" type="checkbox"/> described exposure in detail <input checked="" type="checkbox"/> described comparator in detail <input checked="" type="checkbox"/> described study's setting <input checked="" type="checkbox"/> Timeframe for follow-up	Yes
Did the review authors use a satisfactory technique for assessing risk of bias (RoB) in individual studies that were included in the review.	For partial yes, must have assessed RoB <input checked="" type="checkbox"/> from confounding and	For yes, must also assessed RoB <input checked="" type="checkbox"/> Methods used to ascertain exposure and outcomes, and <input type="checkbox"/> selection of the reported results among multiple measurements or analyses of a specified outcome	No
Did the review authors report on the sources of funding for the studies included in the review	For yes <input type="checkbox"/> Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies		No
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	For non-randomised studies For yes <input type="checkbox"/> The authors justified combining the data in a meta-analysis <input type="checkbox"/> AND they used appropriate weighted technique to combine study results, adjusting for heterogeneity if present <input type="checkbox"/> AND they statistically combined effect estimates from non-randomised studies that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates are not available <input type="checkbox"/> AND they reported separate summary estimates for RCTs and non-randomised studies separately when both included in the review.		No meta-analysis conducted

(Continues)

**TABLE 1** | (Continued)

AMSTAR 2 Checklist question		Overall
If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	For yes <input type="checkbox"/> included only low risk of bias RCTs <input type="checkbox"/> OR, if the pooled estimated was based on RCTs and/or non-randomised studies at variable RoB, the authors performed analyses to investigate possible impact of RoB on the summary estimates of effect.	No meta-analysis conducted
Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?	For yes <input type="checkbox"/> Included low risk of bias RCTs <input checked="" type="checkbox"/> OR, if RCTs with moderate or high RoB, or non-randomised studies were included the review provided a discussion of the impact of RoB on the results	Partial yes
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	For yes <input type="checkbox"/> There was no significant heterogeneity in the results <input checked="" type="checkbox"/> OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in results and discussed the impact of this on the results of the review	No
If they performed quantitative synthesis did the review authors carry out adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review	For yes <input type="checkbox"/> performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	No, vote counting used and no examination of publication bias
Did the review authors report any potential conflict of interest, including any funding they received for conducting the review?	For yes <input type="checkbox"/> The authors reported no competing interests OR <input type="checkbox"/> The authors described their funding sources and how they managed potential conflicts of interest	No

Abbreviations: PICO, Population, Intervention, Comparator, Outcome; RCT, randomised controlled trial; RoB, risk of bias.



**FIGURE 1** | Directed acyclic graph illustrating how the Prada et al. review [4] hypothesised relationships between prenatal paracetamol exposure, neurodevelopment outcomes, shared familial factors and proposed biological mediators (oxidative stress and endocrine disruption). Sibling-controlled designs account for shared familial factors. Arrows represent hypothesised causal relationships.

opinion score’ was added, but its purpose and calculation were not well explained. The authors appear to have reweighted criteria based on their assessment of study flaws, blurring the distinction between evidence appraisal and expert opinion.

### 2.1.5 | Risk of Bias in Interpretation

The review’s discussion focused heavily on criticising the two sibling-matched studies [7]. The Swedish study [7] was rated with a high risk of bias due to a lack of specificity in measuring paracetamol exposure, relying on routinely collected midwife interviews without questions on paracetamol use, resulting in presumed underreporting (~7.5%) of paracetamol use in pregnancy versus other studies (~50%) [20]. Most studies relied on maternal self-report, introducing potential recall bias; only a few used biomarkers, such as paracetamol concentrations in core blood or the meconium. Prada and colleagues argued that sibling controls may introduce bias by relying on discordant pairs for exposure and outcome, reducing statistical power. However,

the Swedish study [7] retained over 31,000 participants from the initial 2.48 million, mitigating this concern. Sibling controls may cause non-differential exposure misclassification if recall is similar across pregnancies for siblings. Prospectively collected midwife data may reduce this risk. While sibling controls address socio-economic status and genetic confounding, they may also adjust for shared mediators. Sibling controls may also attenuate associations if biological mechanisms (e.g., increased oxidative stress and endocrine disruptions) are partly shared within families. In such cases, shared components may be removed, potentially obscuring true effects (Figure 1). However, this depends on the underlying causal pathway, which has not been established.

The authors of the Prada review concluded that there was ‘strong evidence of a likely association between prenatal paracetamol use and increased risk of ADHD, autism and neurodevelopment delays in children’. They argued that triangulation with earlier reviews [21, 22] strengthened their conclusions, although those reviews pre-dated the Swedish study [7, 23]. Prada

and colleagues acknowledged possible residual confounding but argued that their evaluation of exposure assessment, the use of variable adjustments and negative controls made confounding unlikely. The authors advised judicious paracetamol use in pregnancy but acknowledged its favourable safety profile compared with other analgesics, such as non-steroidal anti-inflammatory drugs.

### 3 | Conclusions

Our assessment identified major methodological issues in the Prada review [4] that limit confidence in its conclusions. Readers cannot be assured that all relevant studies were included or that risk of bias, certainty in the evidence or between-study differences were appropriately assessed. Reviews that do not meet systematic review standards should not guide practice. Although the Prada review raises valid concerns regarding sibling controls, the extent to which these concerns meaningfully affect causal interpretation remains unclear.

More recent umbrella and systematic reviews [9, 10] have since clarified that associations between paracetamol and neurodevelopmental outcomes are attenuated once key sources of bias are addressed. These reviews consistently highlight residual confounding, including maternal infection, inflammation or fever, which both prompt paracetamol use and independently influence neurodevelopment. Importantly, these analyses were conducted using established evidence-based medicine standards, including structured assessment of risk of bias, confounding, heterogeneity assessment and evaluating the certainty of the evidence.

The contrast between these reviews and the Prada review underscores the importance of systematic review methods. The Prada review was misleading, not only because of its conclusions, but because the methodological choices allowed for presentation of findings with authority disproportionate to the underlying certainty of the evidence. The more recent reviews [9, 10] contextualised uncertainty, highlighted the limitations of observational data and resisted causal claims with insufficient evidence. This comparison illustrates how different methodological choices and different narrative handling of uncertainty can shape scientific and public understanding.

The downstream consequences of such misinterpretation can be substantial. Incorrect or selectively framed health information from political and regulatory leaders risks harm and erodes public trust. Statements by the Trump Administration and Federal Drug Administration may prompt pregnant women to avoid treating fever or select less safe alternatives, despite paracetamol remaining the safest option in pregnancy, while others may increase use unnecessarily. Untreated fever itself poses risks, and other painkillers carry the risk of fetal harms. Families may also experience anxiety about past exposures, which may adversely affect the mother-child relationship. These reactions demonstrate the tangible consequences of politicised health communication and underscore the importance of consistent messaging from trusted sources. Misinformation, whether deliberate or unintentional, can exploit structural weaknesses in our institutions and health systems. Clinical and public health recommendations should

follow established processes, like evidence-to-decision frameworks [19], which weigh benefits and harms, values, acceptability, equity and resource implications.

Although Australia is less polarised than the United States, similar risks exist. After the Trump announcement, Australian institutions responded swiftly, with bodies such as the Australian Academy of Health and Medical Research [2] and Royal Australian and New Zealand College of Obstetricians and Gynaecologists [3] providing reassurance about paracetamol safety in pregnancy. Continued reliance on these organisations is essential, but addressing the current gap will require more formalised and stronger mechanisms. Strengthening rapid-response evidence-appraisal infrastructure, modelled on the National Clinical Evidence Taskforce, would support timely, rapid evidence updates. Improved coordination of national and state health communications to ensure consistent messaging would help clinicians access clear guidance and counter misinformation. The success of Australia's coronavirus disease living guidelines demonstrates the feasibility and value of such structures [24]. Similar proactive approaches will be crucial in maintaining public confidence in evidence-based healthcare.

#### Author Contributions

**David J. Tunnicliffe:** conceptualisation, formal analysis, and writing of the original draft, and reviewing and editing the manuscript. **Miranda Cumpston:** formal analysis, writing and editing the manuscript. **Debra Kennedy:** writing and editing the manuscript. **Margie Danchin:** writing and reviewing the manuscript. **Armando Teixeira-Pinto:** conceptualisation, reviewing the editing of the manuscript.

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#### Disclosure

Not commissioned; externally peer reviewed.

#### Conflicts of Interest

The authors declare no conflicts of interest.

#### Data Availability Statement

No new datasets were generated or analysed in this study. This work appraises a previously published systematic review, and all data can be accessed through the original article as cited.

## References

1. J. Bhattacharya, M. Makary, and M. Oz, "The Trump Administration's New Steps to Tackle Autism," *Politico*, 2025, <https://www.politico.com/news/magazine/2025/09/22/autism-trump-nih-fda-cms-op-ed-00575420>.
2. Australian Academy of Health & Medical Sciences, "Autism: An Evidence Brief," Australian Policy Observatory, 2025, <https://aahms.org/wp-content/uploads/2025/12/AAHMS-Autism-Evidence-Brief.pdf>.
3. Royal Australian and New Zealand College of Obstetricians and Gynaecologists, "Paracetamol Use in Pregnancy not Linked to Autism or ADHD, RANZCOG Asserts," 2025, [updated 2025/09/23], Viewed 23rd September 2025, [http://ranzocg.edu.au/news/paracetamol-use-in-pregnancy/?fbclid=IwY2xjawNSrfdleHRuA2F1bQ1xMABicmlkETE1aDhzenNNQ1F5YzlwRXA1AR7SpDyZh83PF40e9IEN7GBYMOvOeeqKwYHBYJfpOixQq8c1NhJRhxub7pp1BA\\_aem\\_oUqoEHglAFXW9Bx4neAgsq](http://ranzocg.edu.au/news/paracetamol-use-in-pregnancy/?fbclid=IwY2xjawNSrfdleHRuA2F1bQ1xMABicmlkETE1aDhzenNNQ1F5YzlwRXA1AR7SpDyZh83PF40e9IEN7GBYMOvOeeqKwYHBYJfpOixQq8c1NhJRhxub7pp1BA_aem_oUqoEHglAFXW9Bx4neAgsq).
4. D. Prada, B. Ritz, A. Z. Bauer, and A. A. Baccarelli, "Evaluation of the Evidence on Acetaminophen Use and Neurodevelopmental Disorders Using the Navigation Guide Methodology," *Environmental Health* 24, no. 1 (2025): 56.
5. T. J. Woodruff and P. Sutton, "The Navigation Guide Systematic Review Methodology: A Rigorous and Transparent Method for Translating Environmental Health Science Into Better Health Outcomes," *Environmental Health Perspectives* 122, no. 10 (2014): 1007–1014.
6. Z. Liew, M. A. Kioumourtzoglou, A. L. Roberts, É. J. O'Reilly, A. Ascherio, and M. G. Weisskopf, "Use of Negative Control Exposure Analysis to Evaluate Confounding: An Example of Acetaminophen Exposure and Attention-Deficit/Hyperactivity Disorder in Nurses' Health Study II," *American Journal of Epidemiology* 188, no. 4 (2019): 768–775.
7. V. H. Ahlqvist, H. Sjöqvist, C. Dalman, et al., "Acetaminophen Use During Pregnancy and Children's Risk of Autism, ADHD, and Intellectual Disability," *Journal of the American Medical Association* 331, no. 14 (2024): 1205–1214.
8. The White House, "FACT: Evidence Suggests Link Between Acetaminophen, Autism [Article]," 2025, Viewed 22nd September 2025, <https://www.whitehouse.gov/articles/2025/09/fact-evidence-suggests-link-between-acetaminophen-autism/>.
9. J. Sheikh, J. Allotey, S. Sobhy, et al., "Maternal Paracetamol (Acetaminophen) Use During Pregnancy and Risk of Autism Spectrum Disorder and Attention Deficit/Hyperactivity Disorder in Offspring: Umbrella Review of Systematic Reviews," *BMJ* 391 (2025): e088141.
10. A. Béard, J. Cottin, L. F. Leal, et al., "Systematic Review and Meta-Analysis: Acetaminophen Use During Pregnancy and the Risk of Neurodevelopmental Disorders in Childhood," *Journal of the American Academy of Child and Adolescent Psychiatry* 65, no. 4 (2025): 484–504.
11. E. J. Rugel and M. Brauer, "Quiet, Clean, Green, and Active: A Navigation Guide Systematic Review of the Impacts of Spatially Correlated Urban Exposures on a Range of Physical Health Outcomes," *Environmental Research* 185 (2020): 109388.
12. E. Mirrasekhian, J. Nilsson, K. Shionoya, et al., "The Antipyretic Effect of Paracetamol Occurs Independent of Transient Receptor Potential Ankyrin 1-Mediated Hypothermia and Is Associated With Prostaglandin Inhibition in the Brain," *FASEB Journal* 32, no. 10 (2018): 5751–5759.
13. D. Angelis, R. C. Savani, J. Jagarapu, J. Hu, P. Wan-Huen, and L. Chalak, "Part I. Mechanisms of Actions and Metabolism of Acetaminophen Related to the Neonatal Brain," *Early Human Development* 159 (2021): 105406.
14. B. J. Shea, B. C. Reeves, G. Wells, et al., "AMSTAR 2: A Critical Appraisal Tool for Systematic Reviews That Include Randomised or Non-Randomised Studies of Healthcare Interventions, or Both," *BMJ (Clinical Research Ed.)* 358 (2017): j4008.
15. P. Whiting, J. Savović, J. P. Higgins, et al., "ROBIS: A New Tool to Assess Risk of Bias in Systematic Reviews Was Developed," *Journal of Clinical Epidemiology* 69 (2016): 225–234.
16. A. S. Gerstein and E. F. Niederhelman, "Harvard's Public Health Dean Was Paid \$150,000 to Testify Tylenol Causes Autism.C Health," *The Harvard Crimson*, 2025, <https://www.thecrimson.com/article/2025/9/24/autism-dean-public-health/>.
17. M. Cumpston, T. Li, M. J. Page, et al., "Updated Guidance for Trusted Systematic Reviews: A New Edition of the Cochrane Handbook for Systematic Reviews of Interventions," *Cochrane Database of Systematic Reviews* 10, no. 10 (2019): Ed000142.
18. S. Metelli and A. Chaimani, "Challenges in Meta-Analyses With Observational Studies," *Evidence-Based Mental Health* 23, no. 2 (2020): 83–87.
19. I. Neumann and H. Schünemann, *The GRADE Book (Version 1.0, Updated August 2025)* (GRADE Working Group, 2025), <https://book.gradepr.org>.
20. M. M. Werler, A. A. Mitchell, S. Hernandez-Diaz, and M. A. Honein, "Use of Over-The-Counter Medications During Pregnancy," *American Journal of Obstetrics and Gynecology* 193, no. 3 Pt 1 (2005): 771–777.
21. C. Ricci, C. M. Albanese, L. A. Pablo, et al., "In Utero Acetaminophen Exposure and Child Neurodevelopmental Outcomes: Systematic Review and Meta-Analysis," *Paediatric and Perinatal Epidemiology* 37, no. 5 (2023): 473–484.
22. R. Masarwa, H. Levine, E. Gorelik, S. Reif, A. Perlman, and I. Matok, "Prenatal Exposure to Acetaminophen and Risk for Attention Deficit Hyperactivity Disorder and Autistic Spectrum Disorder: A Systematic Review, Meta-Analysis, and Meta-Regression Analysis of Cohort Studies," *American Journal of Epidemiology* 187, no. 8 (2018): 1817–1827.
23. K. Gustavson, E. Ystrom, H. Ask, et al., "Acetaminophen Use During Pregnancy and Offspring Attention Deficit Hyperactivity Disorder—A Longitudinal Sibling Control Study," *JCPP Advances* 1, no. 2 (2021): e12020.
24. T. Millard, J. H. Elliott, S. Green, et al., "Awareness, Value and Use of the Australian Living Guidelines for the Clinical Care of People With COVID-19: An Impact Evaluation," *Journal of Clinical Epidemiology* 143 (2022): 11–21.

## Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** [mja270203-sup-0001-supinfo.pdf](#).