

Acetaminophen Use During Pregnancy and Neurodevelopmental Disorders

Executive Summary

Acetaminophen, introduced in 1955 and made available over the counter in 1960, is a common medication, with about 50% of children exposed in utero and up to 90% by age two.

Actions by the U.S. Department of Health and Human Services (HHS) aiming to reduce the risks of neurodevelopmental disorders, such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), have spurred debate around the safety of acetaminophen, an essential pain and fever medication.

Current clinical practice guidelines recommend using only the minimally effective acetaminophen dose and duration, in keeping with general good principles in medication usage. Simply put – take the smallest dose you need, for the shortest time, which is the norm for all medications.

Although some of HHS’s proposed actions align with current best practices (i.e., taking the smallest dose for the shortest time), the mixed messages from national leaders related to autism and acetaminophen are causing confusion.

ECRI and many medical societies raised concerns that may discourage patients from using acetaminophen when needed, which can have negative effects on the mother and child.

As part of its mission to advance evidence-based healthcare, ECRI published this brief overview and appraisal of the clinical evidence and contemporary clinical practice guidance on acetaminophen’s potential effects during pregnancy on fetal neurocognitive development.

Evidence-Based Conclusion

Available evidence does not indicate that acetaminophen causes or contributes to neurodevelopmental disorders such as autism or ADHD.

ECRI and most clinical experts agree that current evidence does not warrant restrictions on acetaminophen use to treat pain and fever during pregnancy, especially considering that no suitable alternatives are available and that untreated fever poses significant risks to pregnancy.

Available guidance and expert consensus are consistent on their interpretation of clinical evidence pertaining to acetaminophen and neurodevelopmental disorders. Guidance and experts agree that pregnant patients should take acetaminophen only as needed (in keeping with safe medication use principles) and that a clinical professional should provide guidance to patients as needed.

Although epidemiologic studies show that acetaminophen use during pregnancy correlates with (or has an association with) adverse neurodevelopmental outcomes, this type of research is prone to producing false signals, misinterpretation and oversimplification, especially among patients. Importantly, correlation does not imply causation. Epidemiologic associations can arise from confounding factors—such as maternal illness, genetics, environmental exposures, or reporting bias—that are difficult to fully control. Observational designs cannot establish cause-and-effect relationships because they do not involve randomization or direct manipulation of variables. Therefore, while these findings may warrant further investigation, they should not be interpreted as evidence that acetaminophen use causes neurodevelopmental problems.

Actions by HHS

In April 2025, HHS announced a focused effort by the agency to identify environmental exposures as the leading cause of autism. On September 22, HHS announced actions on two potential exposures, acetaminophen and folate deficiency. On acetaminophen, FDA issued a recommendation to clinicians and initiated labeling changes aimed to reduce exposure in pregnant patients. HHS asserted that “the use of acetaminophen by pregnant women may be associated with an increased risk of neurological conditions such as autism and ADHD in children.”

Mixed messages have caused confusion. KFF’s Tracking Poll on Health Information and Trust found 77% of the public report having heard the claim that taking Tylenol during pregnancy can cause autism in children, and many are unsure whether it is true. Overall, just 4% of adults say it is “definitely true” that taking Tylenol during pregnancy increases the risk of the child developing autism, while 35% say the claim is “definitely false.” Most adults express uncertainty, saying the unproven claim is either “probably true” or “probably false.”

Medical Community’s Response

U.S. and international medical societies have issued statements unanimously reiterating that clinical evidence does not implicate acetaminophen in neurodevelopmental disorders and that acetaminophen remains an appropriate choice for treating pain and fever in pregnant patients. Some argued that promoting a hypothesis not supported by evidence may discourage necessary and timely treatments and put patients at risk. None of the responses disagree with limiting dosage and duration to what is strictly necessary, as this is already standard practice. *See Selected Resources.*

Unsubstantiated Theory

Some claims appear to give undue weight to inconclusive evidence by embracing the theory that in utero acetaminophen exposure increases the risk of ASD and ADHD. These actions align with the widely rejected position of a few clinical experts who suggest that increasing autism incidence (from 0.7% to 3.2% in the last 25 years) is driven by environmental exposures. Acetaminophen can produce neurotoxic metabolites, and animal studies suggest these may impair neurocognitive development; some epidemiologic studies have reported positive associations between prenatal acetaminophen exposure and neurodevelopmental disorders, ASD and ADHD.

However, ECRI and most clinical experts do not share these positions for several reasons.

- While the etiology of ASD and ADHD remains unclear, genetic association studies have shown that heredity accounts for 50% to 90% of the disease burden.
- Increasing ASD incidence mostly reflects improved access to screening and changes in diagnostic criteria, including the recognition of autism as a behavioral spectrum rather than a discrete entity, a conclusion supported by recent trends identified by the U.S. Centers for Diseases Control and Prevention.
- Further, epidemiologic association provides only indirect evidence of etiologic involvement and is susceptible to “false signals” because association studies cannot exclude confounding by unknown factors. Such confounding is well documented in clinical literature, especially for associations identified in retrospective database review studies. Only randomized cohort studies can provide direct evidence of cause-effect relationship between exposures and outcomes.

Clinical Literature

We searched PubMed, Embase, and web-based resources for clinical literature published through September 23, 2025. We also searched ClinicalTrials.gov for ongoing trials. Because of the large retrieval, we focused our review on the best available evidence and included systematic reviews (SRs) and additional clinical studies published in the last five years. We identified four SRs and no additional studies published since the SRs. We also identified but excluded an umbrella review ([Kim et al. 2020](#)) that included a single relevant SR and meta-analysis ([Gou et al. 2019](#)), as all the studies included in the latter are also included in a more recent and comprehensive meta-analysis (Ricci et al. 2023). See Table 1 for a summary of included SRs.

Table 1. Clinical Literature

Study	Scope and Searches	Included Studies and Evidence Synthesis	Key Findings
Prada et al. Evaluation of the evidence on acetaminophen use and neurodevelopmental disorders using the Navigation Guide methodology. <i>Environ Health.</i> 2025;24(1):56. PubMed	To “examine the association between prenatal acetaminophen exposure and NDDs [neurodevelopmental disorders] and related symptomology in offspring.” Searched PubMed, Google Scholar, and Web of Science in February 2025.	44 observational cohort studies (n = 3,064,684) 2 case-control studies (n = 4,965). Qualitative synthesis with Navigation Guide methodology for risk of bias (ROB) and strength of evidence (SOE) assessment	“27 studies reported positive associations (significant links to NDDs), 9 showed null associations (no significant link), and 4 indicated negative associations (protective effects). Higher-quality studies were more likely to show positive associations.” “Our analyses using the Navigation Guide thus support evidence consistent with an association between acetaminophen exposure during pregnancy and increased incidence of NDDs.”
Pearce et al. Neurodevelopmental outcomes following paracetamol use for treatment of patent ductus arteriosus: A review. <i>Acta Paediatr.</i> 2024;113(11):2378-2383. PubMed Full text	“This review evaluates the evidence for the impact of paracetamol use for patent ductus arteriosus (PDA) treatment on neurodevelopmental outcomes in preterm infants.” Searched Embase, MEDLINE, and CINAHL for relevant studies (search date not reported).	2 randomized controlled trials (RCTs) (n = 100) 3 observational cohort studies (n = 679) 1 case-control study (n = 647) Narrative synthesis	“The studies varied in dosage, route, and duration of paracetamol administration and in the methods used to assess neurodevelopmental outcomes. None of the studies revealed different outcomes between paracetamol-exposed preterm infants and controls.” “Current low-to-moderate quality evidence suggests no association between paracetamol used for PDA treatment and adverse neurodevelopmental outcomes in preterm infants.”

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Ricci et al. In utero acetaminophen exposure and child neurodevelopmental outcomes: Systematic review and meta-analysis. <i>Paediatr Perinat Epidemiol.</i> 2023;37(5):473-484. PubMed Full text	“To summarise the literature on the association between in utero acetaminophen exposure and child neurodevelopmental outcomes, and assess the extent to which the association is due to confounding by indication.” Searched Embase, MEDLINE, CINAHL, and PsycINFO in August 2022.	22 observational cohort studies (n = 363,025) 1 case-control study (n = 4,750) Random-effects meta-analysis and ROB assessment with the Systematic Assessment of Quality in Observational Research tool	“Quality assessments resulted in 13.6% of studies being classified as high, 59.1% as medium, 22.7% as low, and 4.5% as very low quality.” “In utero acetaminophen exposure was associated with an elevated risk of ADHD [attention-deficit hyperactivity disorder] (unadjusted pooled RR 1.32, 95% confidence interval [CI] 1.20, 1.44; $I^2 = 47\%$, $n = 7$ studies), with little difference after adjusting for confounders, including indications for acetaminophen use (adjusted pooled RR 1.34, 95% CI 1.15, 1.55; $I^2 = 50\%$, $n = 4$ studies).” “Confounding by indication did not explain the association between in utero acetaminophen exposure and child ADHD.” “Studies examining other child neurodevelopmental outcomes were either too few or too heterogeneous in their measures to pool. However, overall, the narrative synthesis suggested stronger impacts of acetaminophen exposure were on ADHD and ASD [autism spectrum disorder], and weaker associations for other measures of neurodevelopment related to communication and motor delays.”

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Patel et al. Long-Term safety of prenatal and neonatal exposure to paracetamol: A systematic review. <i>Int J Environ Res Public Health</i> . 2022;19(4). PubMed	Searched Embase, MEDLINE, and Web of Science in August 2021 for “studies of any design that described the use of paracetamol in the prenatal or neonatal (within the first four weeks of life) periods and examined the occurrence of neurodevelopmental, atopic or reproductive adverse outcomes.”	12 observational cohort studies on prenatal exposure (n = 208,499) 2 RCTs on neonatal exposure (n = 105) 1 ecologic study on prenatal and neonatal exposure (geographic correlation between population exposure and outcome incidence estimates, 12 countries) Qualitative synthesis and ROB assessment with the Newcastle-Ottawa Scale and Cochrane RoB2 tool	“Behavioral, performance, intelligence, executive and psychomotor function problems, [ASD], [ADHD] and cerebral palsy (CP) were the neurodevelopmental outcomes assessed.” “All but three of the included observational studies received a rating between seven and nine, indicating a low risk of bias... We rated the risk of bias of the included RCTs as low and with some concerns.” “The results of the current systematic review suggest that prenatal exposure to paracetamol is associated with an increased risk of neurodevelopmental, atopic and reproductive adverse outcomes, independent of the timing and cumulative dosing of exposure. The ecologic study that examined the association between neonatal paracetamol exposure and neurodevelopmental adverse outcomes [ASD specifically] also demonstrated a correlation between neonatal exposure to paracetamol and neurodevelopmental adverse outcomes. However, neither of the two available RCTs on neonatal exposure to paracetamol showed an increased risk of neurodevelopmental [mental and psychomotor development scores] or atopic adverse outcomes.”

The limited evidence pointing to a possible cause-effect relationship between exposure and outcome consists of studies probing the correlation between the two, with the exposure occurring at the investigator’s discretion in interventional studies and in its natural setting in observational studies. Only interventional studies can provide definite evidence by ruling out confounding—that is, a circumstantial exposure-outcome association that reflects an association between the exposure and the outcome’s true cause (i.e., the confounder). To achieve this, investigators randomly assign subjects to exposure and control groups, so that even *unknown* confounders are equally distributed between the groups. Ideally, a randomized controlled trial (RCT) to examine acetaminophen’s safety in pregnancy would compare acetaminophen and placebo regimens in healthy pregnant subjects or in pregnant patients with an indication for taking the medication.

However, our searches and the SRs we reviewed identified no such studies, likely because of the ethical barriers to conducting them. The included SRs (Pearce et al. 2024 and Patel et al. 2022) describe two RCTs; however, these compared acetaminophen and placebo in preterm newborns treated for patent ductus arteriosus. Neither RCT found an association between exposure and neurodevelopmental outcomes; however, this evidence may not support conclusions for several reasons. First, the study may not capture drug effects on early brain development, which according to some hypotheses, are the main link between acetaminophen and neurodevelopmental disorders. Furthermore, the exposure was short and may not reflect longer or repeated exposure in typical acetaminophen use for pain and fever. Also, while preterm newborns’ brains develop as they would in utero, they are no longer exposed to maternal and placental factors that may mediate the drug’s effects. Finally, the studies involved a small sample at a single study center each and may thus not fully

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represent the population's characteristics and risk factors. Our searches identified three ongoing RCTs of acetaminophen in preterm infants with patent ductus arteriosus; ([NCT05340582](#), [NCT06601114](#), and [NCT06152796](#)); however, none list neurodevelopmental disorders among planned study outcomes. In contrast, many observational studies have reported on the association between acetaminophen and neurodevelopmental disorders. The most recent and comprehensive SR (Prada et al. 2025) included 46 observational studies and conducted a qualitative synthesis according to the [Navigation Guide](#) methodology, an epidemiologic evidence synthesis framework based on GRADE. While some of the studies' findings disagree, the authors found the evidence conclusive because most of the studies, as well as most of the high-quality studies, reported a positive association, and the overall quality of the evidence (i.e. risk of bias) was adequate. Two other SRs (Ricci et al. 2025 and Patel et al. 2022) reached similar conclusions, but a fourth SR (Pearce et al. 2024) concluded there was no association. Ricci et al. 2025 and Patel et al. 2022 overlap with Prada et al. and included fewer patients; however, Ricci et al. found data on ADHD incidence suitable for meta-analysis. The authors estimated a pooled ADHD risk ratio of 1.34 (95% confidence interval 1.15 to 1.55) for exposed and control groups. Given that about 11% of children have a diagnosis of [ADHD in the U.S.](#) and assuming that 50% are exposed to acetaminophen in utero, the pooled estimate translates to ADHD rates of 12.5% versus 9.5% in the exposed and nonexposed populations, a modest but clinically significant difference.

The most important limitation to this evidence body is the possibility of confounding. Observational studies can account for designated confounders in several ways (e.g., by matching patient characteristics across groups or using mathematical models to remove confounder effects), but the possibility of *unknown* confounders makes observational studies inadequate for demonstrating a cause-effect relationship. Many well-described epidemiologic associations result from such confounding. For example, an observational study by [Clark et al. \(2008\)](#) showed that asthma treatment with intravenous (rather than inhaled) steroids is associated with higher hospitalization risks, which contradicted the results of several well-designed RCTs. In this case, the confounding factor was asthma severity (i.e., patients with worse symptoms are more likely to receive intravenous therapy), which Clark et al. Confirmed by stratifying data to only compare patients with similar asthma severity. In another classic example, the inverse association between [beta-carotene intake and lung cancer risk](#) has been confirmed by over 30 observational studies, while RCTs of beta-carotene supplementation have failed to show any protective effects. While the exact confounder remains unknown, clinical experts broadly agree that this is an example of "healthy user bias": higher beta-carotene intake often results from healthy eating habits and is associated with other healthy traits (active lifestyle, healthy weight), all of which may reduce overall cancer risk.

Nonetheless, controlling for confounders strengthens the evidence and is thus useful to support decision-making. Most studies described in the SRs accounted for potential confounders, such as mother's age, race, ethnicity, socioeconomic level, underlying etiology and comorbidities, and acetaminophen dosage and duration. However, residual confounding is likely because of inaccurate or incomplete data or methodologic limitations. For instance, studies that sought to account for underlying etiologies (confounding by indication) grouped them, out of necessity, in broad categories (e.g., fever, pain, inflammation). However, grouping may mask the effect of specific etiologies. If, for instance, ASD were to result from infection by a few specific viral strains, grouping all viral infections may mask the association, leading to residual confounding. A potentially important confounder that many studies did not examine is acetaminophen exposure during *infancy* (i.e., after birth), which almost all children experience by age two in industrialized countries. Postnatal acetaminophen exposure may affect the result of studies focusing on prenatal exposure depending on the timing of the drug's adverse effects. While outside of this review's scope, conflicting results on postnatal exposure are described in the SRs by Pearce et al. and Patel et al. and in additional published studies (e.g., [Alemany et al. 2021](#), [Bittker and Bell 2020](#)). Another group of incompletely controlled potential confounders includes genetic factors and early-life environmental factors, such as diet, parenting, and familial interactions. Of note, Prada et al. identified three sibling comparison studies, which can account for known and unknown confounders in these categories; however, the studies had limited statistical power and reported inconsistent results (two with association, one without).

Thus, while clinical evidence demonstrates there is an association between prenatal acetaminophen exposure and neurodevelopmental problems, its significance and implications for clinical practice remain unclear, and postnatal exposure complicates data interpretation. Interventional studies and complex observational studies designed to minimize the risks of bias and confounding, such as Mendelian randomization studies and sibling comparison studies, may be needed to address the evidence's limitations and gaps. However, our search of ClinicalTrials.gov identified no ongoing observational studies probing the association between acetaminophen and neurodevelopmental outcomes. However, observational studies and retrospective registry or chart review studies may not be registered in ClinicalTrials.gov or other trial databases.

Guidelines, Position and Consensus Statements

We searched PubMed, Embase, ECRI Guidelines Trust®, and prominent specialty societies for clinical practice guidelines, consensus statements, and position statements discussing acetaminophen use during pregnancy. We excluded responses to the new HHS statements and included documents published through September 22, 2025. To include all expert viewpoints, we also included guidance from independent expert panels not sponsored or endorsed by medical societies or professional organizations. We identified seven documents. See Table 2 for details. All addressed the use of acetaminophen during pregnancy, but only five of the seven specifically mentioned its potential neurodevelopmental harms.

Table 2. Guidelines, Position and Consensus Statements

Source	Key Recommendations or Statements
Guidance and Statements Supported by Systematic Literature Review	
American College of Obstetricians and Gynecologists (ACOG). ACOG Clinical Practice Guideline No. 3: Headaches in pregnancy and postpartum: Obstet Gynecol. 2022	“ACOG recommends acetaminophen 1,000 mg orally as initial therapy for the treatment of acute migraine (STRONG RECOMMENDATION, VERY LOW-QUALITY EVIDENCE).” “ACOG suggests use of acetaminophen combined with caffeine for treatment of migraine headache in pregnancy, but with some caution for potential fetal effects at caffeine doses exceeding 200 mg per day. (CONDITIONAL RECOMMENDATION, VERY LOW-QUALITY EVIDENCE).” “Total clearance of acetaminophen progressively increases across pregnancy, peaking during the third trimester, and is 1.8-fold greater than in nonpregnant adults. However, conversion to the toxic metabolite N-acetyl-p-benzoquinone-imine also increases in pregnancy, enhancing the risk of maternal hepatotoxicity with acetaminophen overdose. Total 24-hour exposure should be kept at or below the U.S. Food and Drug Administration–recommended maximum dosage of 4 g.” <i>The guideline does not discuss the potential association between acetaminophen and neurodevelopmental disorders</i>
ACOG. ACOG Clinical Consensus No. 1. Pharmacologic stepwise multimodal approach for postpartum pain management. 2021	“Acetaminophen and ibuprofen are first-line analgesics for postpartum pain for individuals intending to provide breast milk to their infants.” “Orally administered acetaminophen and NSAIDs are excreted into breast milk in low concentrations, with peak RID [relative infant dose] estimates (which vary by time after administration and phase of milk production) of approximately 2% and 0.6%, respectively.” <i>The guideline does not discuss the potential association between acetaminophen and neurodevelopmental disorders</i>
Bauer et al. Paracetamol use during pregnancy - a call for precautionary action. 2021	“In this Consensus Statement, we summarize research showing adverse neurological, urogenital and reproductive outcomes associated with maternal and perinatal use of APAP. Based on this experimental and epidemiological literature, we believe the potential for harm from continued inaction exceeds the harm that might arise from precautionary action. We recognize the limitations of the existing epidemiological literature and the need for rigorous meta-analyses and therefore we call for a focused research effort.” “We recommend that women be counselled prior to or early in pregnancy with the following guidance: • Pregnant women should forego APAP use unless medically indicated. • Pregnant women should consult with their physician or pharmacist if they are uncertain whether use is indicated and before using on a long-term basis. • Pregnant women should minimize risk by using the lowest effective APAP dose for the shortest possible time.

Source	Key Recommendations or Statements
	We recommend the following specific actions to implement the goals of raising awareness amongst patients and health-care providers: • The 2015 FDA Drug Safety Communication recommendations should be updated based on evaluation of all available scientific evidence, including both epidemiological and experimental evidence. • The EMA Pharmacovigilance Risk Assessment Committee should review the most recent research and issue an updated Drug Safety Communication¹⁰, including both epidemiological and experimental evidence. • Obstetric and gynaecological associations should review all available research and update their guidance. • The Acetaminophen Awareness Coalition ("<u>Know Your Dose</u>" Campaign) should be expanded to include standardized warnings including that pregnant women should forego APAP use unless medically indicated. • All sales of APAP-containing medications, regardless of country, should be accompanied by recommendations for use in pregnancy. This information should include warning labels on packaging of all APAP-containing medications. If possible, APAP should be sold only from pharmacies (as is currently done in France, Spain, Sweden, Finland and Iceland)." <i>Note: Please see the European Network of Teratology Information Services (ENTIS) response to this statement, cited below.</i>
Other Documents	
European Medicines Agency (EMA). Pharmacovigilance Risk Assessment Committee (PRAC). PRAC recommendations on signals. 2019	"Having considered the available evidence from literature, including non-clinical and epidemiological studies, regarding the signal of prenatal exposure to paracetamol and the impact on the urogenital apparatus or neurodevelopmental disorders in offspring, and the comments received from the MAHs [marketing authorisation holders], the PRAC concluded that the studies are inconclusive, but nevertheless, the summary of product characteristics (SmPC) of paracetamol containing medicinal products should be amended in order to reflect the current state of scientific knowledge, as detailed below... Summary of product characteristics 4.6. Fertility, pregnancy and lactation A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency. 5.3. Preclinical safety data Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available. Package leaflet 2. What you need to know before you use [product name] Pregnancy and breast-feeding <u>if necessary</u>, can be used during pregnancy. You should use the lowest possible dose that reduces your pain and/or your fever and use it for the shortest time possible. Contact your if the pain and/or fever are not reduced or if you need to take the medicine more often."

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Source	Key Recommendations or Statements
European Network of Teratology Information Services (ENTIS). <u>Position statement on acetaminophen (paracetamol) in pregnancy.</u> 2021	“Paracetamol during pregnancy – call for precautionary action. The 13 authors call for caution and suggest that there is now a growing body of evidence to support the hypothesis that in utero exposure to paracetamol (or acetaminophen, APAP) alters fetal development.” “While endorsed by 78 signatories, this paper reflects the views of the authors and is not endorsed by regulatory authorities or medical specialty organizations.” “On face value, the conclusions by the authors can hardly be disagreed upon and could be used for any drug. These are, however, trivial: Nobody should use drugs without appropriate considerations on indication, efficacy & adverse reactions, and this even outside of pregnancy.” “These conclusions are preceded by seven pages in which the authors detail evidence they argue substantiate that APAP during pregnancy comes with non-trivial and disturbing risks to the fetus and long-term developmental risks. Some principal methodological points to consider in the portfolio of studies presented: - Drawing clinical conclusions using data from which causality cannot be effortlessly inferred. - Use of unvalidated outcome measurements [i.e., parent or- teacher filled questionnaires on a Likert scale being transformed into continuous quantitative scales representing neurodevelopment]. 3 This applies to many of the underlying studies and these questionnaires are neither developed nor validated for the purpose and context in which they are used. - Not accounting for hereditary aspects of neurodevelopment, ASD and ADHD and the ensuing importance of this as confounder - On urogenital development, the underlying studies are unconvincing and some of the data in the original studies does not appear to support the authors’ interpretation. - Confirmation bias: Uncritical appraisal of studies supporting the narrative of the authors. One example: A recent study from the Boston Birth Cohort is assigned much weight by the authors to substantiate APAP exposure using umbilical cord plasma concentrations and correlating this to childhood ADHD, ASD and other neurodevelopmental diagnoses. This study has severe issues with external and internal validity. APAP or metabolites were detected in every single of the 996 umbilical cord samples. This does not compare well to our knowledge on the use of APAP during pregnancy. Among the 996 children, an unprecedented large proportion were diagnosed with ADHD/ASD (37%) and only 33% had no “developmental disability” diagnosis. Population prevalence estimates of ADHD is around 3-5%. The validity of the exposure construct “burden of APAP exposure” is undocumented and actual levels are not presented. Analytical methods are insufficiently accounted for including stability from up to 20 years of sample storage. - Preclinical data may support some mechanistic aspects of a hypothesis. It cannot be summoned to support a clinical recommendation.” “ENTIS acknowledges the authors right to hold their position. ENTIS does not share this position and believes the supporting evidence brought forward is weak, inconsistent and to a large extent fundamentally flawed. The media headlines and social media reactions were predictable, and ENTIS believes that this paper and the ensuing reaction will promote unwarranted uncertainty, fear, and guilt among pregnant women. It will also likely result in use of less safe alternatives during pregnancy.”

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Source	Key Recommendations or Statements
ACOG response to consensus statement on paracetamol use during pregnancy , September 2021	“A consensus statement that was recently published in the journal <i>Nature Reviews Endocrinology</i> claims that a growing body of research shows that prenatal exposure to paracetamol, or acetaminophen, may alter fetal development and increase the risks of neurodevelopmental, reproductive, and urogenital disorders.” “ACOG and obstetrician-gynecologists across the country have always identified acetaminophen as one of the only safe pain relievers for pregnant individuals during pregnancy. This consensus statement, and studies that have been conducted in the past, show no clear evidence that proves a direct relationship between the prudent use of acetaminophen during any trimester and fetal developmental issues.” “The authors are not recommending anything counter to what is already done by obstetrician-gynecologists when prescribing acetaminophen for a given clinical condition. ACOG’s clinical guidance remains the same and physicians should not change clinical practice until definitive prospective research is done. Most importantly, patients should not be frightened away from the many benefits of acetaminophen. However, as always, any medication taken during pregnancy should be used only as needed, in moderation, and after the pregnant patient has consulted with their doctor.”
Society for Maternal-Fetal Medicine (SMFM). Prenatal acetaminophen use and outcomes in children . 2017	“We believe that the weight of evidence is inconclusive regarding a possible causal relationship between acetaminophen use and neurobehavioral disorders in the offspring. As with all medication use during pregnancy, communication regarding the risks versus the benefits of prescription and over-the-counter medications use should occur between patient and provider. The SMFM Publications Committee continues to advise that acetaminophen be considered a reasonable and appropriate medication choice for the treatment of pain and/or fever during pregnancy.”

We identified three documents supported by an SR of the clinical literature on acetaminophen’s safety and effectiveness. Two are evidence-based practice guidelines by the American College of Obstetricians and Gynecologists on pain management; authors followed a GRADE-based framework to assess the evidence and derive practice recommendations. Both guidelines recommend acetaminophen as first-line medication for pain control during pregnancy and breastfeeding because of its favorable pharmacokinetic profile and the known risks of NSAIDs. However, neither discusses the possible link between acetaminophen and neurodevelopmental disorders.

The third document is a 2021 expert review and position statement (Bauer et al. 2021) by an independent, international expert panel endorsed by 78 clinical professionals and published in a peer-reviewed journal. Authors reviewed clinical evidence alongside preclinical studies and epidemiology and utilization data but did not use a formal evidence assessment and synthesis framework; the authors presented their review and conclusions as a narrative synthesis and discussion. [The authors state that the association between prenatal acetaminophen exposure and neurodevelopmental disorder incidence does not support changes to the medication’s indication for use but warrants greater restraint to minimize reasonably avoidable exposure.](#) Authors outline specific actions to this end, including evidence-based guidance updates and changes to the medication’s labeling and commercial distribution.

We also identified four additional documents without accompanying literature reviews. Two are statements by the European Medicines Agency (EMA) and the Society for Maternal-Fetal Medicine that predate Bauer’s et al. statement. EMA and the Society for Maternal-Fetal Medicine (SMFM) acknowledge available evidence on acetaminophen and neurodevelopmental disorder association and maintained recommendations that acetaminophen use for pain and fever. Both statements encourage pregnant patients to seek medical advice on acetaminophen use. EMA’s recommendation, in the form of proposed labeling changes, also encourages pregnant patients to use the minimally effective acetaminophen dosage and duration. Unlike Bauer et al., however, EMA and SMFM adopted a reassuring tone and proposed no further action.

The other two documents are direct responses to Bauer et al. from ACOG and the European Network of Teratology Information Services (ENTIS). While agreeing with Bauer et al.’s main takeaway, ACOG and ENTIS criticize Bauer et al. for

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their stance, which ENTIS judges unnecessarily alarming given that that limiting reasonably avoidable acetaminophen exposure in pregnant women is already standard clinical practice. ACOG and ENTIS also point out that the additional actions proposed by Bauer et al. risk discouraging patients from indicated acetaminophen use, which may result in avoidable health risks. Furthermore, ENTIS points out important flaws in Bauer et al.'s recommendation development, including overinterpreting and overweighing preclinical and epidemiologic data and not using a formal framework for study quality and evidence assessment, which may result in biased conclusions.

In summary, available guidance and expert consensus agree on the significance of clinical evidence but disagree on the proposed approaches for encouraging appropriate acetaminophen use by pregnant patients. Additional research to clarify the association between acetaminophen and neurodevelopmental disorders is needed; in the meantime, reviewing clinical practice and utilization data and using formal methods to assess the potential impact of proposed policies may support broader consensus.

Selected Resources

Statements by the U.S. Dept of Health and Human Services (HHS)

- [Autism announcement fact sheet](#). Reviewed 2025 Sep 25.
- [President Trump, Secretary Kennedy announce bold actions to tackle autism epidemic](#). 2025 Sep 22.

Statements by FDA

- [FDA responds to evidence of possible association between autism and acetaminophen use during pregnancy](#). 2025 Sep 22.
- [Notice to physicians on the use of acetaminophen during pregnancy](#). 2025 Sep 22.

Medical Association Responses to HHS Acetaminophen/Pregnancy Guidance

- Agenzia Italiana Del Farmaco (AIFA). [Use of paracetamol during pregnancy: European recommendations confirmed](#). 2025 Sep 23.
- American Academy of Pediatrics (AAP). [AAP Statement on White House autism announcement](#). 2025 Sep 22.
- American College of Obstetrics and Gynecology (ACOG). [Practice advisory]. [Acetaminophen use in pregnancy and neurodevelopmental outcomes](#). 2025 Sep.
- ACOG. [ACOG affirms safety and benefits of acetaminophen during pregnancy](#). 2025 Sep 22.
- European Medicines Agency (EMA). [Use of paracetamol during pregnancy unchanged in the EU](#). 2025. Sep 23.
- Health Products Regulatory Agency (HPRA – Ireland). [HPRA statement on use of paracetamol medicines during pregnancy](#). 2025 Sep 23.
- Society for Maternal and Fetal Medicine (SMFM). [SMFM response to administration announcement on acetaminophen use during pregnancy and autism](#). 2025 Sep 25.
- SMFM. [SMFM statement on acetaminophen use during pregnancy and autism](#). 2025 Sep 5.
- Society of Obstetricians and Gynaecologists of Canada. [SOGC position statement on the use of acetaminophen for analgesia and fever in pregnancy](#). 2025 Sep 12.

Policy Statement

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