Does Prenatal Exposure to Acetaminophen and Antibiotics Increase the Risk of Autism Spectrum Disorder?

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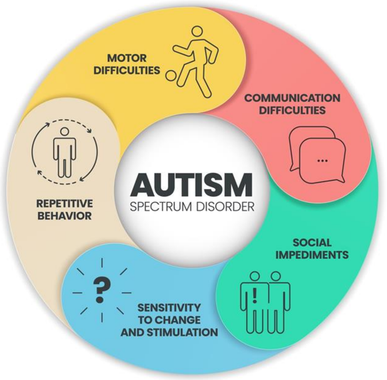
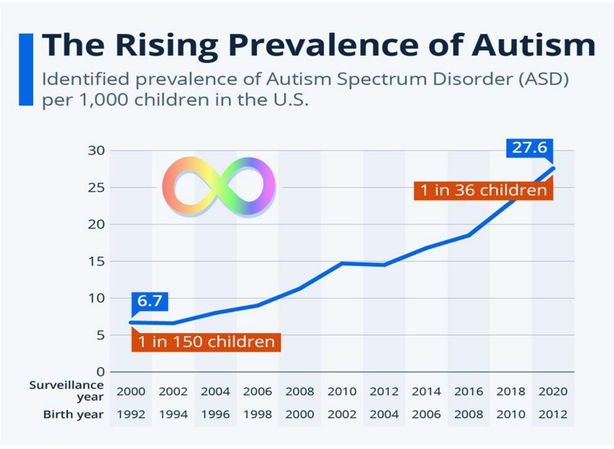
Introduction/Background

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition that typically emerges in early childhood and has lifelong effects on cognitive development, social interaction, and quality of life. Over the past two decades, there has been a prevalence increase worldwide in the number of individuals diagnosed with ASD, which has led to the evaluation of genetic and environmental factors. Research studies investigate the possibility that prenatal drug exposures, such as acetaminophen and antibiotic use, may increase the risk of ASD in children. However, there is much controversy around this correlation because of underlying maternal conditions, including infection, fever, and pain, which may also play a role in fetal neurodevelopment. In this study, we review current evidence from cohort studies, biomarker analyses, and sibling-comparison studies to assess whether prenatal medication exposure solely contributes to ASD risk or whether observed associations are largely explained by confounding maternal and familial factors.



https://phoenixautism.com/understanding-autism-spectrum-disorder-key-facts-every-parent-should-know/



https://www.statista.com/chart/29630/identified-prevalence-of-autism-spectrum-disorder-in-the-us/

Study Objective

- Evaluate whether the use of acetaminophen and antibiotics during pregnancy is associated with an increased risk of ASD.
- Examine the impact of maternal illness and the potential issues of confounding by indication regarding the association found.
- Compare evidence from different studies to determine whether the observed risk is due to medication or shared familial factors.

Methods

- A literature review was conducted to evaluate primary and secondary sources.
- The sources included cohort studies, biomarker-based studies, sibling comparison studies, and meta-analysis related to prenatal exposure to medication and ASD.

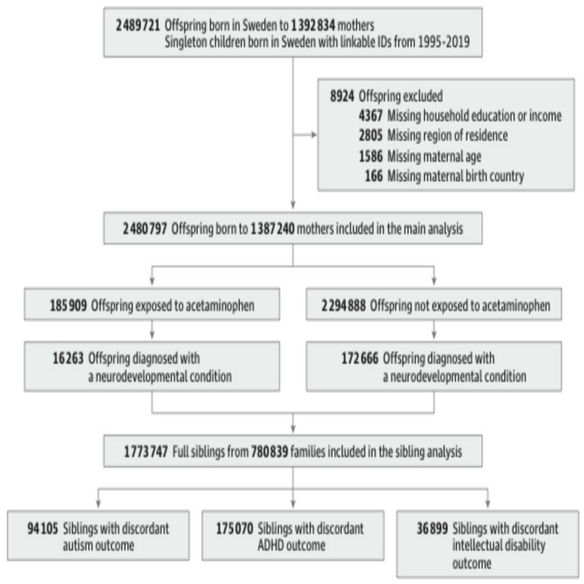


Figure 1. Flow of participants in a Study of Acetaminophen Use During Pregnancy and Risk of Neurodevelopmental Disorders (Siblings Control Analysis). The study included singleton children born in Sweden between 1995 and 2019 with linkable identification records. 8924 participants with missing demographic information were excluded before the final cohort division. The figure also shows the number of offspring diagnosed with different neurodevelopmental conditions at the bottom (Ahlqvist VH et al., 2024).

Results

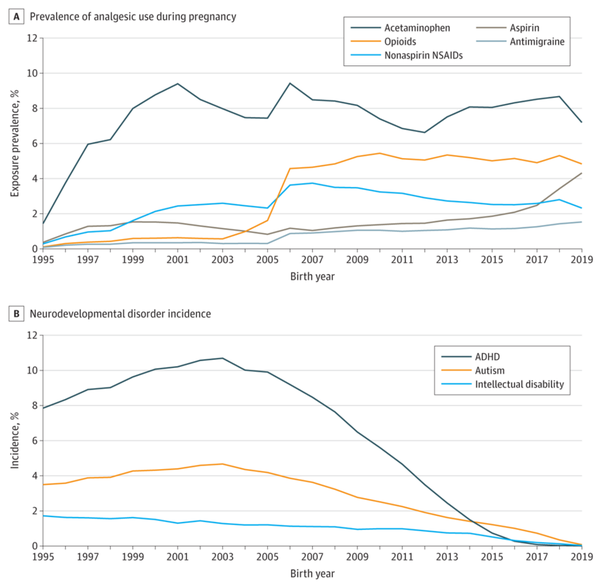


Figure 2. Analgesics usage prevalence among pregnant women and neurodevelopmental disorders incidence by birth year in Sweden (1995-2019). (A) Trends of acetaminophen, opioids, aspirin, non-aspirin NSAIDs, and antimigraine drugs during pregnancy. Acetaminophen was most commonly used throughout the study period. (B) Occurrence of ADHD, autism, and intellectual disability among children born during the study period. The declining trend in incidence in later birth cohorts may be caused by a shorter follow-up period among younger participants(Ahlqvist VH et al., 2024).

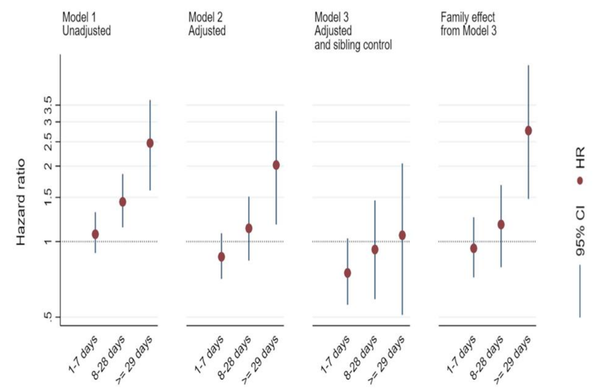


Figure 3. Hazard ratio with 95% confidence intervals demonstrating the relationship between the duration of exposure to acetaminophen during pregnancy and the risk of neurodevelopmental disorder in children. Model 1 indicates an unadjusted analysis, while Model 2 adjusts for maternal and pregnancy-related variables. Model 3 further adjusts for shared familial factors using sibling control. The trend toward lower hazard ratios across all three models indicates that most of the observed association may be explained by familial and maternal confounding rather than exposure to acetaminophen (Gustavson et al., 2021).

Conclusion

- Several studies have indicated potential links between prenatal exposure to acetaminophen and antibiotics and a higher chance of developing ASD, but the results are still inconclusive.
- Many of these associations may be explained by confounding factors like maternal infections, fever, inflammation, genetic factors, and other environmental factors present during pregnancy.
- Sibling and family-based comparison studies often refer to a weaker association, suggesting that the medications themselves may not lead to ASD.
- Current studies do not provide enough evidence for the existence of a causal relationship between prenatal drug use and the development of ASD.

Future Directions

- More longitudinal and sibling-based comparisons are required to clearly differentiate the impact of exposure to medication during pregnancy from other influences, such as genetics, environment, and health problems like infections and inflammation in mothers.
- Future research should focus on how the timing, dosing, and duration of acetaminophen and antibiotics used by pregnant women can affect fetal neurodevelopment.
- Improved approaches to methodologies for measuring fetal exposure through biomarkers like cord plasma analysis could help clarify insights into the biological pathways of autism spectrum disorder.

Acknowledgement

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References