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Abstract Title

Prenatal Exposure to Third-Generation Antiseizure Medication and Offspring ADHD: A Systematic Review

Authors

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Background

Third-generation antiseizure medications (ASMs) are increasingly used during pregnancy, but their long-term neurodevelopmental safety remains largely unclear.

Objective

We aimed to summarize the existing evidence on prenatal exposure to third-generation ASMs and the risk of attention-deficit/hyperactivity disorder (ADHD) in offspring.

Methods

MEDLINE, Embase, PsycINFO, Scopus, and the Cochrane Library were searched from inception to June 24, 2026. Human studies reporting offspring ADHD following prenatal third-generation ASM exposure were eligible regardless of exposure trimester or comparator. Two reviewers independently screened records, extracted data, and assessed methodological quality using the Newcastle-Ottawa Scale. The protocol was registered in PROSPERO (CRD420261454098).

Results

Of 2,222 records screened, four records published from 2023 onwards were included. All were retrospective cohort studies using data from Denmark, Finland, Norway, Sweden, the United Kingdom (including a separate Welsh cohort), and the United States. Three studies reported ADHD estimates for pregabalin and one for lacosamide. Quality scores ranged from 6 to 9 out of 9. The number of prenatally exposed children ranged from 219 to 2,872. Compared with no ASM exposure, one Nordic study found a modestly increased ADHD risk following pregabalin exposure (adjusted hazard ratio [aHR] 1.29, 95%

confidence interval [CI] 1.03-1.63), but the estimates were attenuated with active comparators. A study using UK and Swedish data reported a lower risk (aHR 0.67, 95% CI 0.55-0.83). Two studies reported no statistically significant associations with pregabalin (aHR 1.67, 95% CI 0.54-5.20) and lacosamide (aHR 2.66, 95% CI 0.77-9.21).

Conclusion

The available evidence is recent and limited to pregabalin and lacosamide, with no consistent evidence of increased offspring ADHD risk. Potential residual confounding and wide confidence intervals limit causal interpretation. Future studies should use indication-matched active comparators to better address confounding by indication and follow children through at least 6 years of age to allow sufficient time for ADHD ascertainment.

Table/Figure File

PRISMA Flow Diagram.pdf

Table 1 - Inclusion and exclusion table.pdf

Table 2 - Study Characteristics .pdf

Appendix 1. Database Search Strategies.pdf