

## Comparative safety of antiepileptic drugs for neurological development in children exposed during pregnancy and breast feeding: a systematic review and network meta-analysis

### Summary

Anti-epileptic drugs (AEDs) are used by pregnant women for various health conditions. AED use during pregnancy and breastfeeding years poses severe risks to the fetus and/or infant. However, there is a lack of sufficiently powered studies that assess the impact of AEDs on neurodevelopment in children of women exposed to these agents. This study was the first that compared and ranked the safety of AEDs on neurodevelopment of infants/children exposed in-utero or during breastfeeding, including comparative safety of treatments that have not been directly compared. Our results show that valproate alone or combined with another AED is associated with the greatest odds of adverse neurodevelopmental outcomes. AEDs associated with increased occurrence of autism include oxcarbazepine and lamotrigine.

### Implications

We found that AEDs are associated with an increased risk of adverse neurodevelopmental outcomes. More evidence from long-term follow-up studies is required for further insight on neurodevelopmental risks in children.

**Reference:** Veroniki AA, Rios P, Cogo E, et al. Comparative safety of antiepileptic drugs for neurological development in children exposed during pregnancy and breast feeding: a systematic review and network meta-analysis. *BMJ Open*. 2017;7(7):e017248.

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### What is the current situation?

- Anti-epileptic drugs (AEDs) are used by pregnant women for various health conditions.
- AED use during pregnancy and breastfeeding years poses potentially severe risks to the fetus and/or infant, the extent of which are not clear based on current research

### What is the objective?

- Compare the safety of AEDs for the neurodevelopment of infants/children exposed in-utero or during breastfeeding.

### How was the review conducted?

- MEDLINE, EMBASE, and the Cochrane CENTRAL Register of Controlled Trials were searched until March 2014 and updated in April 2017
- Studies reporting at least one outcome of interest that included pregnant/breastfeeding women taking AEDs for any indication were eligible
- Two reviewers independently performed study selection, data abstraction, and quality appraisal of included articles. All discrepancies were resolved by a third reviewer.
- Bayesian random-effects network meta-analysis (NMA) was conducted. Statistical analysis was performed according to the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) guidelines

### What did the review find?

- 112 studies were eligible for the overall review, of these, 29 articles reported one or more relevant neurological outcomes with 5100 patients included in the analysis
- Valproate alone or in combination with another AED was associated with significantly increased odds of developing autism or dyspraxia, language delays, cognitive developmental delays, and psychomotor developmental delays
- Oxcarbazepine and lamotrigine (alone or with valproate) were associated with significantly increased odds of developing autism or dyspraxia
- Results should be interpreted with caution as the analyses may be underpowered due to missing data and a number of factors that may influence outcomes such as family medical history, occurrence of seizures during pregnancy, type of maternal epilepsy, and in utero exposure to other substances (e.g., alcohol or tobacco) were not reported in the included studies
- Counselling is advised for women considering pregnancy to tailor the safest medication regime

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