

## Comparative safety and effectiveness of perinatal antiretroviral therapies for HIV-infected women and their children: Systematic review and network meta-analysis including different study designs

### Summary

We conducted a systematic review and network meta-analysis (NMA) including randomized control trials (RCTs), quasi-RCTs, non-RCTs, interrupted-time-series, controlled before-after studies, and observational studies (cohort, case-control) to compare the safety and effectiveness of antiretroviral (ART) drugs in children exposed to maternal human immunodeficiency virus (HIV) and ART (or no ART) during pregnancy, delivery, and breastfeeding. Our findings suggest that none of the ART drugs examined were associated with a significant increase in congenital malformations (CMs), yet some may increase adverse birth events. An NMA examining mother-to-child transmission (MTCT) of HIV found that zidovudine administered once or twice was associated with significantly reduced risk of MTCT.

### Implications

Our study is the first comprehensive systematic review and NMA, including both RCTs and observational studies, comparing the safety and effectiveness of ART drugs in infants/children exposed to ART. Our results can be used by patients who are taking these medications during pregnancy, as well as their clinicians and policy-makers who make decisions about these drugs at a population or regulatory level.

**Reference:** Veroniki AA, Antony J, Straus SE, et al. Comparative safety and effectiveness of perinatal antiretroviral therapies for HIV-infected women and their children: Systematic review and network meta-analysis including different study designs. *PLoS One*. 2018 Jun 18;13(6):e0198447.

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### What is the current situation?

- In 2014, 2.6 million children aged 15 and younger were living with HIV and there were 220,000 newly infected youth.
- Many infected youth acquire HIV through mother-to-child transmission (MTCT).
- Anti-retroviral therapy (ART) can be used to reduce MTCT; however, evidence of its effectiveness and harms in infants and children is unclear.

### What is the objective?

- To examine the comparative safety and effectiveness of ART drugs in children exposed to maternal HIV and ART through a systematic review and NMA.

### How was the review conducted?

- MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials were searched from inception until December 7, 2015.
- Studies examining children whose mothers were HIV positive during pregnancy and treated with any of the 24 ART medications approved for national use were included.
- Comparators included: placebo, no ART, or any of the 24 ART medications alone or in combinations.
- Pairs of reviewers independently performed screening, data abstraction, and quality appraisal of included articles; discrepancies were resolved through discussion.
- Bayesian random-effects pairwise meta-analysis and network meta-analysis models were conducted for each outcome.
- ART medications were ranked using the surface under the cumulative ranking curve.

### What did the review find?

- 17 RCTs, 1 case-control study, and 72 cohort studies ( $N=90,563$ ) that were published between 1995 and 2015 were included.
- NMA found that none of the ART drugs examined were associated with a significant increase in congenital malformations.
- Zidovudine administered with lamivudine and indinavir was associated with increased risk of preterm births.
- Zidovudine administered with nevirapine was associated with increased risk of stillbirths.
- Lamivudine administered with stavudine and efavirenz was associated with increased risk of low birth weight.
- Zidovudine administered once or twice significantly reduced the risk of MTCT of HIV.

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