Efficacy of antiretroviral drugs in reducing mother-to-child transmission of HIV in Africa: 
a meta-analysis of published clinical trials

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CRD summary
This review concluded that antiretroviral drugs were effective in reducing mother-to-child transmission of HIV at four to six weeks after birth in Africa and were well tolerated. The authors’ conclusions appeared to support the evidence, but given the small number of placebo controlled trials and the methods of data synthesis, they should be interpreted with caution.

Authors’ objectives
To assess the effectiveness of antiretroviral drugs in reducing mother-to-child transmission of human immunodeficiency virus (HIV) in Africa.

Searching
MEDLINE via PubMed, EMBASE and The Cochrane Library were searched for articles published up to December 2006. Search terms were reported. In addition, references of systematic reviews were searched.

Study selection
Clinical antiretroviral drug studies conducted in Africa that assessed antiretroviral drugs and reported primary data that measured the transmission of HIV from mother-to-child were eligible for inclusion. Studies of pregnant women of young age, abnormal blood counts or abnormal liver function tests were excluded. Phase one and two trials were also excluded.

Included trials were carried out in West, East and Southern Africa. Trials included zidovudine and nevirapine administered at different regimens and different time points (antepartum, intrapartum, postpartum to the mother, postpartum to the baby). Most studies measured HIV transmission at four to six weeks; others measured transmission at six to eight weeks or 14 to 16 weeks. Comparators included placebo, zidovudine, nevirapine, lamivudine and no placebo. Most trials included women who breastfed. Some studies were of antiretroviral naïve women. Most studies used DNA and/or RNA (ribonucleic acid) tests to measure transmission rates. Studies used a nucleic acid assay to identify infection in babies.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Methodological quality was assessed using the Jadad scale (criteria on randomisation, blinding and loss to follow-up), but a quantitative score was not assigned to each study. The authors did not state how the validity assessment was performed.

Data extraction
One reviewer extracted raw data on HIV transmission rates to babies (using a standardised form developed a priori) under the supervision of a second reviewer. Event rates and standard errors were calculated, with their 95% confidence intervals (CIs). Where raw data were not reported or were incomplete, transmission rate estimates calculated from survival analysis were used. Before and during birth transmission rates were captured at four to six weeks following birth. Where data at four to six weeks were not reported, data nearest to four weeks (no less than three weeks were extracted). The efficacy of antiretroviral drugs to reduce mother to child transmission was also calculated. Discrepancies were resolved by discussion with all authors.

Methods of synthesis
A random-effects model was used to combine event rates separately for intervention and placebo arms. A fixed-effect
model was used to assess sensitivity. Heterogeneity was assessed using the $\chi^2$ and $I^2$ tests for study trial arms separately and combined. Sensitivity analysis was conducted by removing one study at a time. Publication bias was assessed using funnel plots, Duval and Tweedie’s trim and fill procedure, Begg, Mazumdar’s and Egger’s tests. Orwin’s method was used to calculate the number of studies with a 25% transmission that would be needed to bring the transmission rate to 20% (the assumed transmission rate without antiretroviral drugs).

Results of the review
Ten randomised clinical trials (RCTs) (n=7,165) were included in the review; four included placebo arms. Sample sizes ranged from 139 to 1,797 participants. Most studies were reported to be of high quality, although only one study reported double blinding.

The combined event rate for arms that used antiretroviral drugs was 10.6% (95% CI 8.6 to 13.1) compared with 21.0% (95% CI 15.5 to 27.7) for arms that used placebo; this translated into a reduction in mother-to-child transmission of approximately 50% using antiretroviral drugs. Sensitivity analysis did not identify any individual study bias. There was evidence of significant statistical heterogeneity for antiretroviral drug treatment arms ($p<0.001$ and $I^2=87\%$) and some evidence of statistical heterogeneity between placebo arms ($p=0.029$ and $I^2=67\%$). The authors reported no evidence of publication bias ($p>0.07$).

Nine of 10 studies reported that study drugs were well tolerated.

Authors’ conclusions
Antiretroviral drugs were effective in reducing mother-to-child transmission transmission of HIV at four to six weeks after birth in Africa and were well tolerated.

CRD commentary
The review question was clear and supported by appropriate, but broad inclusion criteria. A satisfactory literature search was undertaken, but the search was restricted to published studies and so it was possible that potentially relevant studies may have been missed. Various tests showed no evidence of publication bias. Validity was assessed using reliable methods and studies were reported to be of high quality. Although the review process for data extraction was reported, this was not the case for study selection or validity assessment, thus reviewer error and bias cannot be ruled out. The separate pooling of intervention and placebo data was questionable. It may have been more informative to present comparative statistics for the placebo controlled trials to show direct comparisons. There was evidence of significant statistical heterogeneity between studies. Patient characteristics were not presented, but were reported to be comparable for placebo and non-placebo studies. The authors’ conclusions appeared to support the evidence, but it was difficult to determine the reliability of their conclusions (particularly given the small number of placebo controlled trials included in the review) and so these should be interpreted with caution.

Implications of the review for practice and research
The authors did not report any implications for practice or research.

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Record Status
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