Title: Risk of mother-to-child HIV transmission among women under triple antiretroviral drugs in Sub-Saharan Africa: systematic review of published observational studies and explorative meta-analysis

A. Nikuze, J. Monarrez-Espino, A.M. Ekstr□m

Karolinska Institutet

Background: Intervention studies have shown the efficacy of triple antiretroviral drugs (ARVs) in preventing mother-to-child-transmission of HIV (MTCT). This work reviewed programme evaluation studies between 2000-2013 to determine the effect of triple ARVs on MTCT risk in Sub-Saharan Africa

Methods: A systematic review and explorative meta-analysis was undertaken. PUBMED and EMBASE were searched using relevant terms. The inclusion criteria for the systematic review, were: population, HIV-exposed infants and their mothers; intervention, triple ARVs treatment/prophylaxis; outcome, MTCT rate (proportion); study design, observational studies. Studies included in the meta-analysis had to have a minimum follow-up period of 6 months post-delivery and report the cumulative incidence proportion of MTCT when the infants were 6 months of age or older. The New-Castle Ottawa scale was used to assess the methodological quality. One reviewer (AN) selected the studies, assessed their quality and extracted the data and JME & AME supervised the process. For the meta-analysis, the MTCT rates found in the included studies were stabilized using the intermediate estimate of the direct method. Random-effect modeling was used to combine individual MTCT rates. Forest plots were used to summarize the results, and funnel plot was used to assess publication bias.

Results: Thirty studies were reviewed. Most were facility-based or child-testing data of intermediate quality. They were relatively similar in terms of exposure, but the outcome, sample size (10-5141), and type/number of covariates reported varied considerably. The review highlighted that MTCT rate in individual studies did not consider competing risks such as weaning, consequently resulting in an underestimation of the MTCT risk. The review also showed that all determinants of MTCT, particularly structural, socio-cultural and economic, were not systematically measured. Twelve studies were included in the meta-analysis leading to a pooled estimate of 4% (95% CI 1.6-7.3) with large variations in individual MTCT rates (0.9-11.9%); heterogeneity was also high (Q-statistic $p<0.000$; I^2-index 95% CI 92.9-96.5), and the funnel plot was asymmetric. Sources of heterogeneity could be explained by variation of bias in individual studies; variation in the design of the intervention in terms of: gestational age for the initiation of triple ARVs; study population differences in maternal age, immunologic, virologic and obstetric status of pregnant women at start of ARV therapy/prophylaxis; other PMTCT options in terms of prophylaxis to the infant or the mother during breastfeeding; proportion of infants with low birth weight and prematurity; etc.

Conclusion: Although the number of relevant studies on the subject was relatively large, major methodological differences between programme evaluation studies prevent meaningful comparisons, and limit the value of the pooled estimates on MTCT.