Risk of Mother-To-Child Transmission of HIV among Women on Triple Antiretroviral Drugs in Sub-Saharan Africa: Limitations of a Systematic Review and Meta-Analysis of Observational Studies

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Abstract

We report on data limitations when conducting systematic review and meta-analysis on the effect of triple antiretroviral drugs on mother-to-child transmission risk of HIV in sub-Saharan Africa. Data published since 2007 lag behind current prevention programme realities and long-term effectiveness studies are limited. There is considerable between-studies heterogeneity and the preventive effect is context specific. Competing risk for infection (weaning) is rarely considered in individual studies, leading to incorrect estimation of the postnatal transmission rate. Non-biomedical risk factors of transmission (e.g. adherence, health systems performance) are not usually reported. Studies using primary data and systematic review should consider these challenges.

KEYWORDS: HIV, effectiveness, antiretroviral, mother-to-child transmission, systematic review.

Introduction

Evaluation of the impact of prevention of mother-to-child transmission (PMTCT) of HIV programmes, particularly provision of triple antiretroviral drugs (ARVs) to pregnant women, is done at different levels: process (intervention carried out as intended), adherence (intervention worked as intended or compliance) and outcome (intervention decreased the health problem or effectiveness: real life as opposed to research settings) levels. While there are two systematic reviews with meta-analyses that reported on process and intermediary indicators (Nachega et al., 2012; Wettstein et al., 2012), to date no published review has summarized the ultimate effectiveness of triple ARVs given as therapy or prophylaxis, in reducing new HIV infections in children from Sub-Sahara African, using outcome indicators such as mother-to-child transmission (MTCT) rate. Here, we report some methodological challenges identified when conducting a systematic review and meta-analyses on this topic to illustrate the need for better studies to be able to determine the impact of such interventions in programmatic settings.

Findings

Search results

Table 1 shows the results of an online search performed in January and February 2013 using relevant key terms in PubMed and Embase that identified 30 studies on the effect of triple ARVs on MTCT rate (Cassim et al., 2010; Chama et al., 2007; Chama et al., 2010; Chibwesha et al., 2011; Cotton et al., 2009; Creek et al., 2008; Dryden-Peterson et al., 2011; Fitzgerald et al., 2010; Gartland et al., 2013; Geddes et al., 2011; Kesho Bora Study Group, 2010; Hoffman et al., 2010; Horwood et al., 2012; Hussain et al., 2011; Ibeziako et al., 2012; Ilboudo et al., 2010; Imade et al., 2010; Kouanda et al., 2010; Linguissi et al., 2012; Lussiana et al., 2012; Marazzi et al., 2010; Namukwaya et al., 2011; Njom Nlend et al., 2012; Nuwagaba-Biribonwoha et al., 2010; Nyandiko et al., 2010; Ruton et al., 2012; Tchendjou et al., 2010; Tonwe-Gold et al., 2007; Torpey et al., 2012; van Lettow et al., 2011). However, a search in two major HIV/AIDS conference proceedings (i.e. 6th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention in 2011 and the XIXth International AIDS Conference 2012) showed nine additional studies (Bosch et al., 2011; Carter et al., 2012; Diese et al., 2011; Dow et al., 2012; Kim et al., 2012; Kiptirim et al., 2011; Tchiakpe et al., 2011; Thompson et al., 2011; Tinoaga et al., 2011) pointing to the need to expand the search to less conventional data sources to obtain updated information and prevent publication bias. In addition, only eight studies looked at the long-term effectiveness after 18 months, even though this is the recommended time to accurately assess postnatal transmission (WHO, 2012).

Bias within studies and heterogeneity

Conventional quality assessment of studies relying on a tool like the New Castle Ottawa Scale (Wells et al., n.d.)] is inadequate to assess programme quality and surveillance bias, so that more ad hoc quality scales have to be developed for this purpose.

As expected, the heterogeneity across studies was very large (Q-statistic 221.6, $p<0.000$; I^2-index (95%CI 92.9-96.5%)). This can be explained by variations in a number of factors such as 1) whether ARVs intervention was of both therapeutic and preventive nature or used only therapeutic purposes, 2) gestational week at ARVs initiation, 3) mothers' virologic or immunologic status at initiation of therapy or prophylaxis, 4) bias due to loss to follow-up, 5) differences in timing of HIV testing in infants (age), 6) differences in breastfeeding patterns (exclusive breastfeeding vs. mixed or replacement feeding), 7) adherence to drugs intake, and 8) differences in study design (facility-based vs. population-based), and 9) variability in health systems performance and degree of programme implementation in reality. Further statistical analyses such as sensitivity analysis, meta-regression appear necessary for a better understanding of the heterogeneity between studies.

Synthesis results

Our pooled MTCT rate from the 12 studies measuring transmission after 6 months was 4.0% (95%CI 1.6-7.3%). However, the limitations in terms of interpreting the outcome are several: 1) The large heterogeneity observed limited the interpretation since this estimate can be thought of as a weighted mean effect around which the true effect varies. Had the studies been more homogenous, the summary estimate would have been interpreted as the best available estimate of the true effect. 2) Most of the studies included were facility-based and many suffered from considerable loss to follow-up for reasons

other than death, a common problem in PMTCT programmes, resulting in a major source of bias. 3) Most studies did not consider competing risk for HIV infection like weaning, as previously recommended (Alioum et al., 2001), leading to incorrect estimation of postnatal transmission rate. 4) Studies usually reported biomedical factors of transmission (i.e. duration of ARVs before birth, postnatal prophylaxis for children, breastfeeding, mode of delivery, maternal CD4 and viral load, maternal age, etc) but did not consider socio-cultural (i.e. male involvement, support network, disclosure), health systems (i.e. quality of care, home delivery), structural (i.e. education, income), and behavioural (i.e. readiness for ARVs, adherence) factors, which might play important roles in real-life effectiveness of various PMTCT strategies.

Conclusion and recommendations

The effect of triple ARVs on MTCT rate in programmatic settings in SSA very much depends on the context in which the intervention is implemented. Future studies on MTCT rates at country, provincial, programme, and facility levels should assess all possible risk factors associated with residual MTCT of HIV to allow development of targeted interventions to improve PMTCT programmes. These studies should also consider a standardization of reporting on weaning or breastfeeding. A comprehensive and rigorous systematic review and meta-analysis should then take in consideration the issues highlighted in this paper. Other important actions to be undertaken before and during a thorough systematic review of PMTCT include an extended grey literature search including programmes' reports and conference proceedings in addition to published studies in order to avoid publication bias and outdated reports, an adaptation of a quality assessment tool, a stabilization of individual MTCT rates taking in account competing risk like weaning and bias due to loss to follow up; and a categorization of possible heterogeneity's factors for a meta-regression.

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References

Alioum, A., Dabis, F., Dequae-merchadou, L., Haverkamp, G., Hudgens, M., Hughes, J., and Kesho Bora Study Group (2001). Estimating the efficacy of interventions to prevent mother-to-child transmission of HIV in breast-feeding populations : development of a consensus methodology. Statist. Med. 20, pp.3539–3556

Bosch, J. V. P., Haule, A., and Mwangomale, A. (2011). Roll out of prevention of mother-to-child transmission (PMTCT) services in Tanzania using a district approach : achievements , effectiveness , costs and lessons learned. Proceedings of 6th IAS Conference on HIV pathogenesis, treatment and prevention held in Rome. Available online at http://pag.ias2011.org/abstracts.aspx?aid=3219

Carter, R. J., Musoke, P., and Coutsoudis, A. (2012). Field efficacy of antiretroviral treatment and prophylaxis for prevention of mother-to-child transmission in resource limited settings. Proceedings of 19th International AIDS Conference held in Washington. Available online at http://pag.aids2012.org/abstracts.aspx?aid=5760

Cassim, S. M., and Botha, J. H. (2010). Prevention of mother-to-child transmission outcomes in the private sector in central durban. The Southern African Journal of HIV Medicine. 30, pp.6–7.

Chama, C., Gashau, W., and Oguche, S. (2007). The value of highly active antiretroviral therapy in the prevention of mother-to-child transmission of HIV. Journal of obstetrics and gynaecology. 27(2), pp.134–7

Chama, C. M., Bello, M., Ajayi, B. a, Zarma, S., and Gashau, W. (2010). The use of highly active antiretroviral therapy for the prevention of mother-to-child transmission of the human immunodeficiency virus in Nigeria. Journal of obstetrics and gynaecology. 30(4), pp.362–6

Chibwesha, C. J., Giganti, M. J., Putta, N., Chintu, N., Mulindwa, J., Dorton, B. J., and Stringer, E. M. (2011). Optimal time on HAART for prevention of mother-to-child transmission of HIV. J Acquir Immune Defic Syndr. 58(2), pp.224–8

Cotton, M., Kim, S., Rabie, H., and Coetzee, J. (2009). A window into a public programme for prevention of mother-to-child transmission of HIV; evidence from a prospective clinical trial. The Southern African Journal of HIV Medicine. pp.16–19.

Creek, T., Tanuri, A., Smith, M., Seipone, K., Smit, M., Legwaila, K., and Shaffer, N. (2008). Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission. Pediatr Infect Dis J. 27(1), pp.22–6

Diese, M., Kikumbih, N., and Perchal, P. (2011). The efficacy of triple antiretroviral treatment during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 : hospital setting experience from Tanzania. Proceedings of 6th IAS Conference on HIV pathogenesis, treatment and prevention held in Rome. Available online at http://pag.ias2011.org/abstracts.aspx?aid=2119

Dow, D. E., Schimana, W., and Feng, S. (2012). PMTCT Performance among HIV-Exposed Infants in Tanzania. Proceedings of 19th International AIDS Conference held in Washington. Available online at http://pag.aids2012.org/EPosterHandler.axd?aid=15626

Dryden-Peterson, S., Jayeoba, O., Hughes, M. D., Jibril, H., Keapoletswe, K., Tlale, J., and Lockman, S. (2011). Highly Active Antiretroviral Therapy versus Zidovudine for prevention of mother-to-child transmission in a programmatic setting, Botswana. J Acquir Immune Defic Syndr. 58(3), pp.353–7

Fitzgerald, F. C., Bekker, L.-G., Kaplan, R., Myer, L., Lawn, S. D., and Wood, R. (2010). Mother-to-child transmission of HIV in a community-based antiretroviral clinic in South Africa. S Afr Med J. 100(12), pp.827–31

Gartland, M. G., Chintu, N. T., Li, M. S., Lembalemba, M. K., Mulenga, S. N., Bweupe, M., and Chi, B. H. (2013). Field effectiveness of combination antiretroviral prophylaxis for the prevention of mother-to-child HIV transmission in rural Zambia. AIDS. 27, pp.000–000

Geddes, R., Giddy, J., Butler, L. M., Van Wyk, E., Crankshaw, T., Esterhuizen, T. M., and Knight, S. (2011). Dual and triple therapy to prevent mother-to-child transmission of HIV in a resource-limited setting - lessons from a South African programme. S Afr Med J. 101(9), pp.651–4.

Group, The Kesho Bora Study (2010). Eighteen-month follow-up of HIV-1-infected mothers and their children enrolled in the Kesho Bora study observational cohorts. J Acquir Immune Defic Syndr. 54(5), pp.533–41

Hoffman, R. M., Black, V., Technau, K., van der Merwe, K. J., Currier, J., Coovadia, A., and Chersich, M. (2010). Effects of highly active antiretroviral therapy duration and regimen on risk for mother-to-child transmission of HIV in Johannesburg, South Africa. J Acquir Immune Defic Syndr. 54(1), pp.35–41

Horwood, C., Vermaak, K., Butler, L., Haskins, L., Phakathi, S., and Rollins, N. (2012). Elimination of paediatric HIV in KwaZulu-Natal, South Africa: large-scale assessment of interventions for the prevention of mother-to-child transmission. Bull World Health Organ. 90(3), pp.168–75

Hussain, A., Moodley, D., Naidoo, S., and Esterhuizen, T. M. (2011). Pregnant women's access to PMTCT and ART services in South Africa and implications for universal antiretroviral treatment. PloS one. 6(12), e27907

Ibeziako, N. S., Ubesie, A. C., Emodi, I. J., Ayuk, A. C., Iloh, K. K., and Ikefuna, A. N. (2012). Mother-to-child transmission of HIV: the pre-rapid advice experience of the university of Nigeria teaching hospital Ituku/Ozalla, Enugu, South-east Nigeria. BMC Research Notes. 5(1), pp.305

Ilboudo, D., Simpore, J., Ouermi, D., Bisseye, C., Sagna, T., Odolini, S., and Musumeci, S. (2010). Towards the complete eradication of mother-to-child HIV/HBV coinfection at Saint Camille Medical Centre in Burkina Faso, Africa. Braz J Infect Dis. 14(3), pp.219–224

Imade, P. E., Uwakwe, N. O., Omoregie, R., and Eghafona, N. O. (2010). Effect of Prevention of the Mother to Child Transmission Program on the Prevalence of Postnatal HIV Infection in Benin City, Nigeria. Fooyin J Health Sci. 2(2), pp.58–61

Kim, M. H., Ahmed, S., & Bhalakia, A. (2012). Low rates of early mother-to-child transmission in a routine programmatic setting in Lilongwe, Malawi. Proceedings of 19th International AIDS Conference held in Washington. Available online at http://pag.aids2012.org/abstracts.aspx?aid=13318

Kiptirim, W. K., Akach, E., & Mumba, S. (2011). A retrospective study of the effectiveness of HIV prevention of mother to child transmission in Kibera informal settlement in Kenya. Proceedings of 6th IAS Conference on HIV pathogenesis, treatment and prevention held in Rome. Available online at http://pag.ias2011.org/abstracts.aspx?aid=2489

Kouanda, S., Tougri, H., Cisse, M., Simpore, J., Pietra, V., Doulougou, B., and Sondo, B. (2010). Impact of maternal HAART on the prevention of mother-to-child transmission of HIV: results of an 18-month follow-up study in Ouagadougou, Burkina Faso. AIDS care. 22(7), pp.843–50

Linguissi, L. S. G., Bisseye, C., Sagna, T., Nagalo, B. M., Ouermi, D., Djigma, F. W., and Simpore, J. (2012). Efficiency of HAART in the prevention of mother to children HIV-1 transmission at Saint Camille medical centre in Burkina Faso, West Africa. Asian Pacific journal of tropical medicine. 5(12), pp.991–4

Lussiana, C., Clemente, S. V. L., Ghelardi, A., Lonardi, M., Pulido Tarquino, I. A., and Floridia, M. (2012). Effectiveness of a prevention of mother-to-child HIV transmission programme in an urban hospital in Angola. PloS one, 7(4), e36381.

Marazzi, M. C., Liotta, G., Nielsen-Saines, K., Haswell, J., Magid, N. a, Buonomo, E., and Palombi, L. (2010). Extended antenatal antiretroviral use correlates with improved infant outcomes throughout the first year of life. AIDS. 24(18), pp.2819–26

Nachega, J. B., Uthman, O. A., Anderson, J., Peltzer, K., Wampold, S., Cotton, M. F., and Mofenson, L. M. (2012). Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. AIDS, 26(16), pp.2039–52

Namukwaya, Z., Mudiope, P., Kekitiinwa, A., Musoke, P., Matovu, J., Kayma, S., and Fowler, M. G. (2011). The impact of maternal highly active antiretroviral therapy and short-course combination antiretrovirals for prevention of mother-to-child transmission on early infant infection rates at the Mulago national referral hospital in Kampala, Uganda, January 20. J Acquir Immune Defic Syndr. 56(1), pp.69–75

Njom Nlend, A. E., Same Ekobo, C., Bitoungui, M., Bagfegue Ekani, B., Tchokoteu, P., Lyeb, S., and The Mother and Child Network (2012). Early outcomes of HIV exposed children in the first district-wide programme using extended regimens for the prevention of mother-to-child transmission of HIV, in Yaounde, Cameroon. Journal of tropical pediatrics, 58(4), pp.297–302

Nuwagaba-Biribonwoha, H., Werq-Semo, B., Abdallah, A., Cunningham, A., Gamaliel, J. G., Mtunga, S., and Abrams, E. J. (2010). Introducing a multi-site program for early diagnosis of HIV infection among HIV-exposed infants in Tanzania. BMC pediatrics. 10, pp.44.

Nyandiko, W. M., Otieno-Nyunya, B., Musick, B., Bucher-Yiannoutsos, S., Akhaabi, P., Lane, K., and Wools-Kaloustian, K. (2010). Outcomes of HIV-exposed children in western Kenya: efficacy of prevention of mother to child transmission in a resource-constrained setting. J Acquir Immune Defic Syndr, 54(1), pp.42–50

Ruton, H., Mugwaneza, P., Shema, N., Lyambabaje, A., de Dieu Bizimana, J., Tsague, L., and Binagwaho, A. (2012). HIV-free survival among nine- to 24-month-old children born to HIV-positive mothers in the Rwandan national PMTCT programme: a community-based household survey. Journal of the International AIDS Society. 15(1), pp.4

Tchendjou, P., Same-Ekobo, C., Nga, A., Tejiokem, M., Kfutwah, A., Nlend, A. N., and Dabis, F. (2010). Effectiveness of multidrug antiretroviral regimens to prevent mother-to-child transmission of HIV-1 in routine public health services in Cameroon. PloS one. 5(4), e10411

Tchiakpe, E., Lafia, B., & Métadokou, D. (2011). Contribution of blotting paper in the decentralization of Early HIV-1 diagnosis infection in Benin. Proceedings of 6th IAS Conference on HIV pathogenesis, treatment and prevention held in Rome. Available online at http://pag.ias2011.org/abstracts.aspx?aid=272

Thompson, D., Edmonds, A., & Lusiama, J. (2011). Field Evaluation of a Prevention of Mother-to-Child Transmission Program in the Democratic Republic of Congo using DNA PCR Test Results – Implications for Increased Intervention Impact. Proceedings of 6th IAS Conference on HIV pathogenesis, treatment and prevention held in Rome. Available online at http://pag.ias2011.org/abstracts.aspx?aid=4233

Tinoaga, O. L., Savadogo, L. G. B., and Meda, N. (2011). Residual vertical transmission of HIV in mother-infant pairs receiving PMTCT program in Ouagadougou , Burkina Faso. Proceedings of 6th IAS Conference on HIV pathogenesis, treatment and prevention held in Rome. Retrieved from http://pag.ias2011.org/abstracts.aspx?aid=2427

Tonwe-Gold, B., Ekouevi, D. K., Viho, I., Amani-Bosse, C., Toure, S., Coffie, P. a, and Dabis, F. (2007). Antiretroviral treatment and prevention of peripartum and postnatal HIV transmission in West Africa: evaluation of a two-tiered approach. PLoS medicine. 4(8), e257

Torpey, K., Mandala, J., Kasonde, P., Bryan-Mofya, G., Bweupe, M., Mukundu, J., and Welsh, M. (2012). Analysis of HIV early infant diagnosis data to estimate rates of perinatal HIV transmission in Zambia. PloS one. 7(8), e42859

Van Lettow, M., Bedell, R., Landes, M., Gawa, L., Gatto, S., Mayuni, I., and Schouten, E. (2011). Uptake and outcomes of a prevention-of mother-to-child transmission (PMTCT) program in Zomba district, Malawi. BMC public health. 11(1), pp.426

Wells, G., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., and Tugwell, P. (n.d.). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available online at http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

Wettstein, C., Mugglin, C., Egger, M., Blaser, N., Vizcaya, L. S., Estill, J., and Keiser, O. (2012). Missed opportunities to prevent mother-to-child-transmission: systematic review and meta-analysis. AIDS. 26(18), pp.2361–73

WHO. (2012). A SHORT GUIDE ON METHODS: Measuring the impact of national PMTCT programmes: towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive. Geneva: World Health Organization.

Table 1. Characteristics of reviewed studies on triple antiretroviral drugs and mother-to-child HIV transmission in Sub-Saharan Africa

First author, year	Country	Data period[1]	Regimen[2]	CD4[3]	Infants[4]	Diagnosis test	Time[5]	N[6]	Rate (95% CI)[7]
Chama, 2007[10]	Nigeria	07.02-12.04	ART	<200	Single dose	Rapid test	16-24 m	22	9.1
Tonwe-Gold, 2007[10]	Ivory Coast	08.03-04.05	ART	<200	Short	Rapid test/PCR	<3 m	95	1 (0.0-3.1)
							3-6 m	86	3.3 (0.0-6.9)
							7-15 m	86	3.3 (0.0-6.9)
Creek, 2008	Botswana	06.05-12.05	ART	<200	Medium	PCR	<24 m	175	0.6
Cotton, 2009	South Africa	04.05-05.06	ART	<200	Short	PCR	3-6 m	57	1.8
Cassim, 2010	South Africa	01.04-06.05	ART/tARVs	Any	Long	PCR/ELISA	16-24 m	92	2.2
Chama, 2010	Nigeria	01.07-12.08	ART	Any	Long	PCR	3-6 m	446	1.1
Fitzgerald, 2010	South Africa	09.02-03.08	ART	<200/<250		PCR	3-6 m	214	5.1 (2.8-9.0)
Hoffman, 2010	South Africa	01.04-08.08	ART	<200	Single dose	PCR	<3 m	873	4.9
Ilboudo, 2010	Burkina Faso	01.07-04.09	ART			PCR	3-6 m	115	0
Imade, 2010	Nigeria		ART			PCR	<3 m	201	8.96
K-Bora Study, 2010[10]	Burkina Faso/Kenya	01.05-09.06	ART	<200	Single dose	PCR	<3 m	104	3.7 (1.4-9.5)
							3-6 m	97	5.6 (2.5-12)
							7-15 m	94	7.5 (3.8-14.5)
							16-24 m	83	7.5 (3.8-14.5)

Kouanda, 2010[10]	Burkina Faso	01.03-12.06	ART		Single dose	Rapid test/PCR	7-15 m	28	0
							16-24 m	195	0
Marrazi, 2010[10]	Malawi/Mozambique	07.05-12.09	ART/tARVs	<350		PCR	<3 m	3081	0.8
							3-6 m	2926	0.9[8]
							7-15 m	2536	0.3[8]
Nuwagaba-B, 2010	Tanzania	10.06-03.07	ART		Single dose	PCR	3-6 m	10	0
Nyandiko, 2010[10]	Kenya	02.02-07.07	ART/tARVs	<250	Single dose	PCR/ELISA	<3 m	733	3.6
							16-24m	416	6.5[8]
Tchendjou, 2010	Cameroon	10.04-03.08	ART	<200/≤350	Short/medium	PCR/ELISA	<3 m	73	2.7 (0.5-8.8)
Chibwesha, 2011	Zambia	01.07-03.10	ART	<350		PCR	<3 m	1813	3.3 (2.5-4.2)
Dryden-Peterson, 2011	Botswana	02.09-04.10	ART	<250	Medium	PCR	3-6 m	252	0.4 (0-2.2)
Geddes, 2011	South Africa	03.04-02.07	ART	<200	Short	PCR	3-6 m	373	2.1
Hussain, 2011	South Africa	02.10-05.10	ART	<200		ELISA/PCR	<3 m	-	2.7
Namukwaya, 2011	Uganda	01.07-05.09	ART	<350	Short	PCR	<3 m	788	1.7 (0.8-2.8)
Van Lettow, 2011	Malawi	08.09-12.09	ART	<250	Single dose	Rapid test/PCR	<24 m	13	0
Horwood, 2012	South Africa	05.08-04.09	ART	<200	Short/medium	Rapid test/PCR	<3 m	396	5.1
Ibeziako, 2012[10]	Nigeria	03.06-09.08	ART		Long	Rapid test/PCR	16-24 m	178	3.9 (1.1-6.7)
Linguissi, 2012	Burkina Faso	09.10-	ART		Medium	PCR	<3 m	114	0

		07.11							
Lussiana, 2012[10]	Angola	03.07-08.10	ART	<350	Medium	Rapid test	16-24 m	66	1.5
Njom Nlend, 2012	Cameroon	03.08-03.10	ART	<350	Short/medium	PCR	<3 m	285	1.75
Ruton, 2012[10]	Rwanda	02.09-05.09	ART/tARVs	<350	Medium	Rapid test/PCR	16-24 m	384	1.9
Torpey, 2012[9,10]	Zambia	09.07-07.10	ART	≤350		PCR	<3 m	1966	4.2 (3.3-5.1)
							3-6m	5141	4.7 (4.1-5.3)
							7-15 m	1591[10]	11.8 (10.2-13.4)
Gartland, 2013[10]	Zambia	04.09-01.11	tARVs	Any	Short	PCR	<3 m	127	0.8
							3-6 m	113	0.9
							7-15 m	104	1

[1] Period during which data were collected

[2] For the mother, ART: Antiretroviral therapy, tARVs: Triple antiretroviral prophylaxis

[3] CD4 count threshold from which women were eligible for treatment

[4] Child's prophylaxis, Single dose (SD): Nevirapine within 72 h of birth, Short: SD nevirapine & 7 d of zidovudine, Medium: SD nevirapine & 4 wk zidovudine, Long: SD nevirapine plus 6 wks zidovudine

[5] Age of the infants at HIV testing, <3, 3- 6 months, 7-15, 16-24, and <24 months

[6] Total number of infants tested

[7] Proportion of infected with HIV

[8] Not cumulative incidence proportion, but prevalence at time of outcome measurement

[9] Study with different cohorts defined based on the time at outcome measurement

[10] Studies included in the meta-analysis