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**Universal ART among pregnant and post-partum HIV-infected women  
would improve maternal health and decrease postnatal HIV transmission**

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In a recent issue of AIDS, the Zvitambo study group from Zimbabwe showed increased post-partum mortality among HIV-infected women with high CD4 count who were not eligible for and not receiving antiretroviral therapy (ART), compared to HIV-uninfected post-partum women from the same population [1]. In the two years post-partum, the adjusted mortality hazard ratio (95% confidence interval) was 7.3 (3.6-15.1) among HIV-infected women with baseline CD4 between 600 and 800 cells/ml, compared to the reference category of HIV uninfected women [1]. The authors therefore argued the case for early ART initiation among all pregnant and post-partum women in Africa, irrespective of CD4 count or treatment eligibility. We entirely agree with this interpretation of their findings, in particular because such a strategy would also contribute to the elimination of paediatric HIV in breastfeeding populations.

To prove this point, we combined data from two cohorts in South [2] and West Africa [3] to evaluate mother-to-child transmission (MTCT) risk through breastfeeding [4]. Similar to the Zvitambo trial, maternal ART was unavailable at the time of the study in these two populations. In this pooled analysis, breastfeeding duration was a median of 6.4 months (inter-quartile range: 4.4-12.4), shorter than usually observed in African settings; postnatal transmission rates were thus similarly lower than seen elsewhere. Overall, 70% of these HIV-infected pregnant breastfeeding women had CD4 counts above 350 cells/ml (Table 1), and would therefore not have been eligible for ART for their own health according to the most recently agreed international recommendations [5]. In the absence of ART intervention, the cumulative risk of HIV transmission through breastfeeding in the first 18 months of life was substantial in this group (4.8%), despite their high CD4 count, accounting for 53% of all cases of breastfeeding transmission (the remaining 47% of postnatal transmission cases occurred among women with <350 CD4 cells/ml). Further, even women with baseline CD4 counts above 500 or above 700 cells/ml were at substantial risk of postnatal transmission (Table 1). These findings highlight the crucial need for antiretroviral-based interventions also among women with higher CD4 counts, so that the risk of HIV transmission can be significantly reduced for all HIV-exposed infants. If ART had been provided to these women with CD4 counts over 350, the expected MTCT rate would have been at least halved, as per European experience [6].

In the recently released WHO guidelines on the use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants, two options of similar efficacy are offered for women with CD4 count above the 350 CD4 treatment eligibility threshold [7]. Option A consists in providing maternal zidovudine prophylaxis from the second trimester of pregnancy until delivery, followed by daily oral nevirapine to the breastfed infant until all

breastfeeding has ceased. Option B consists of the provision of maternal triple antiretroviral prophylaxis (as per ART for treatment) starting from the second trimester of pregnancy until all exposure to breast milk has ended.

The new results from the Zvitambo study clearly support the initiation of triple antiretroviral prophylaxis among all pregnant women and continued throughout breastfeeding exposure, following option B, not only to prevent mother-to-child HIV transmission and enable safer breastfeeding practices, but importantly also to improve maternal health. Both eligible and ineligible women would then be receiving the same triple antiretroviral regimen, which would make this universal strategy easier to implement at a population level [8]. However, in a context where all pregnant women would be offered triple antiretroviral regimens, the question of whether and when to stop this intervention in women who are not eligible for ARV treatment according to the current international guidelines is of particular interest. The risk for maternal health of stopping maternal triple ARV prophylaxis after breastfeeding cessation among women with high CD4 count is unknown. Hence, this strategy would need to be assessed in carefully conducted field studies in terms of acceptability, efficiency and maternal and infant safety.

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**Table 1.** 18-month postnatal HIV transmission risk among uninfected children at four weeks of age according to different thresholds of maternal antenatal CD4 count. Pooled analysis of the Vertical Transmission Study (South Africa, 2001-2007) and the ANRS 1202 Ditrane Plus Study (Côte d'Ivoire, 2001-2005). N=1151. *Adapted from Becquet et al. PLoS One 2009 [4].*

Antenatal maternal CD4 count	N	Number of children acquiring HIV through breastfeeding	HIV postnatal transmission rate (%)	95% confidence interval
< 350	353	38	12.6	9.3-16.9
≥ 350	798	34	4.8	3.4-6.6
< 500	673	56	8.3	7.5-12.3
≥ 500	478	16	3.4	2.3-6.0
< 700	952	63	6.6	6.0-9.7
≥ 700	199	9	4.5	2.6-9.2