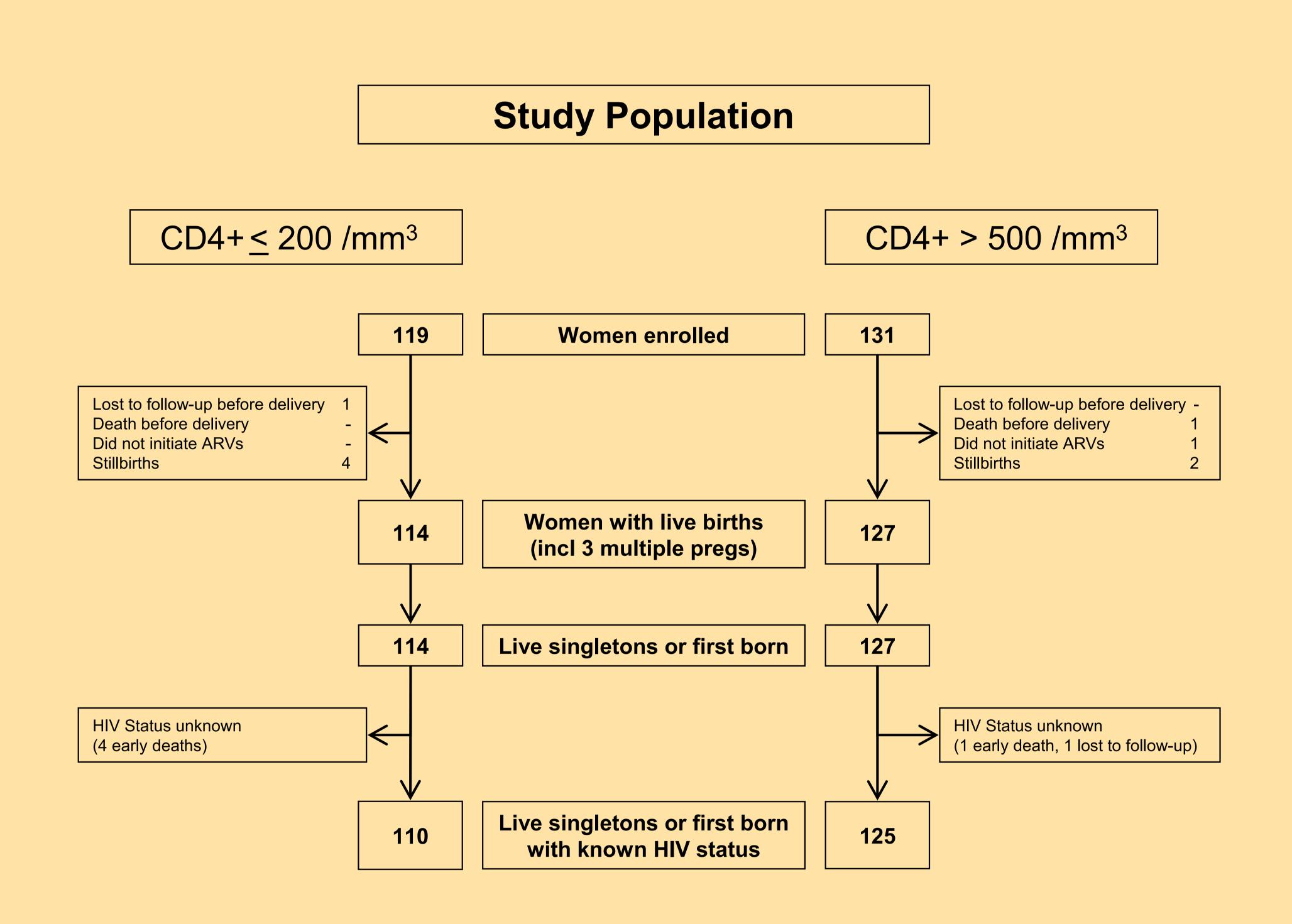
HIV-Free Survival at 12 Months among Children Born to HIV-Infected Women Receiving Antiretrovirals (ARVs) from 18-36 Weeks of Pregnancy The Kesho Bora Study Group*

BACKGROUND

The Kesho Bora ("A better future", Swahili) study conducted at 5 sites in Africa is recruiting HIV-infected pregnant women with CD4+ 200-500 cells/mm³ to participate in a randomized clinical trial to assess the efficacy of maternal antiretrovirals given during breastfeeding to reduce postnatal transmission of HIV.

In 3 of the sites, women not eligible for the RCT were enrolled in a prospective cohort study to assess the effectiveness and safety of current international recommendations: long-term ARVs for women with advanced stage of HIV infection and short-course ARV prophylaxis for women in early stage disease.

We report infant HIV-free survival and cumulative risk of infection at age 12 months according to infant feeding choice from the prospective cohort.



METHODS

From January 2005 to August 2006, women with CD4+ counts < 200 cells/mm³ or with HIV disease stage 4 initiated life-long ARV therapy (ART; ZDV/3TC/NVP) from 18-36 weeks pregnancy. Those with CD4+ > 500 and asymptomatic received zidovudine alone from 34-36 weeks pregnancy until delivery plus a single-dose of nevirapine (sd-NVP) at delivery (short-course MTCT prophylaxis). All infants received sd-NVP at birth. Infant HIV infection status was assessed using PCR.

Infant feeding pattern was assessed through regular interview at all scheduled visits. Mothers were seen weekly from enrolment till delivery and women and children were seen at 2, 4, 6, 8 weeks postpartum and then monthly till one year postpartum

Kaplan-Meier analyses were used to assess 12-month mortality, HIV transmission rate and HIV-free survival. Cox proportional hazards regression models were used to compute the effect of breastfeeding, adjusted for centre and CD4 count at enrolment.

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Characteristics of enrolled women

	CD4+ ≤ 200/mm³ (n=119)	CD4+ > 500/mm ³ (n=131)	P
Centre - Bobo Dioulasso - Nairobi - Mombasa	47 35 37	50 62 19	
Age [mean] (years)	28.9	26.7	<0.001
Parity (% primigravida)	7.6%	21.4%	0.002
CD4+ [median and IQR] (cells/mm3) - At enrolment - At delivery (data missing for 23) - At 12 months	134 [91 - 170] 184 [129 - 277] 305 [228 - 419]	621 [559 - 731] 740 [603 - 906] 676 [540 - 870]	<0.001 <0.001
Time on ARV before delivery (Not applicable 1 death and 1 lost to follow-up before delivery) Median duration on ARV [IQR] (weeks) - % on ARV for at least 4 weeks - % on ARV for 2 - 4 weeks - % on ARV for less than 2 weeks	6.9 [8.9 - 5.0] 85.7% 10.9% 2.5%	5.1 [7.0 - 4.0] 77.1% 18.3% 3.8%	<0.001
Adherence to ARVs (% who took > 95% of prescribed ARVs before delivery) (data missing for 13)	88.9 %	85.0 %	0.44
Deaths	4	1 (before delivery)	NS

Characteristics of live born infants

	CD4+ ≤ 200/mm³ (n=114)	CD4+ > 500/mm ³ (n=127)	P
Sex (% male)	56.1%	46.5%	0.17
Birth weight ≤ 2500g (data missing for 21)	19.4%	12.0%	0.14
Ever breastfed (BF) Duration of breastfeeding in weeks if ever breast fed Median [IQR]	57.0% 20.9 [13.1 - 26.1]	77.2% 17.8 [9.0 - 24.9]	<0.001
Grade 3 or 4 anaemia - At birth: Hb<12g/I (data missing for 53) - At 3 month: Hb<7g/I (data missing for 43)	17.4% 2.2%	9.4% 0%	0.13 0.21

Infant outcomes at 12 months

	CD4+ ≤ 200/mm ³ (n=114)	CD4+ > 500/mm ³ (n=127)
Deaths before 12 months	14	11
Lost to FU before 12 months	1	7
Infected - By 6 weeks - Additional infections by 12 months	8 4 4*	7 6 1*

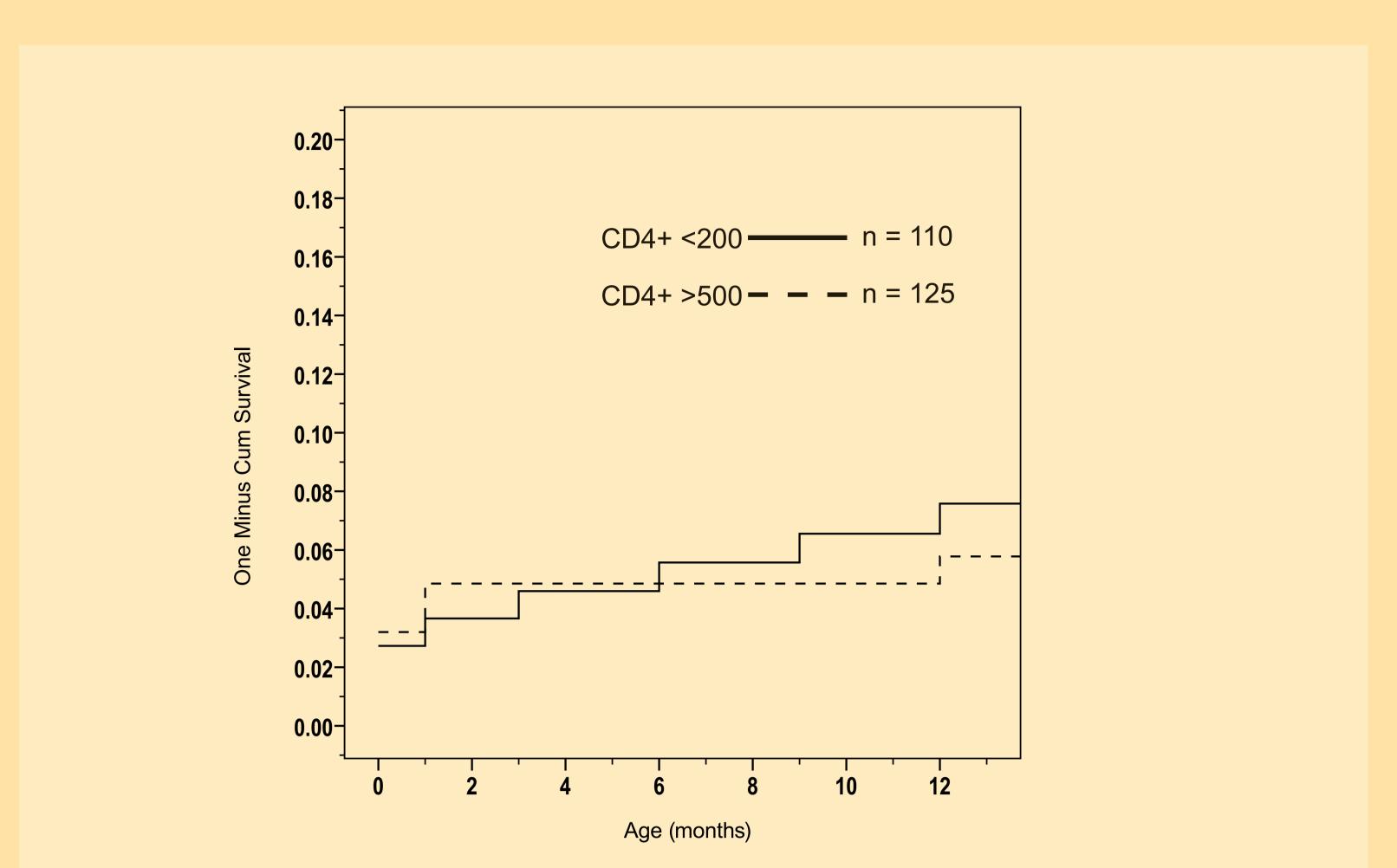
* Including 1 late infection in each group in babies reported weaned more than 6 months before the 1st positive PCR test result

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Study sites: (1) Bobo Dioulasso, Burkina-Faso (Centre Muraz): Nicolas Meda (Principal Investigator), Paulin Fao, Odette Ky-Zerbo, Clarisse Gouem (Study Coordinators), Paulin Sombda, Hervé Hien, Elysée Ouedraogo (Investigators), Diane Valea (Laboratory Coordinator), Sayouba Ouedraogo (Data Manager), Francois Rouet (Site Laboratory Coordinator). (2) Mombasa, Kenya (International Centre for Reproductive Health): Stanley Luchters (Principal Investigator), Eunice Irungu (Study Coordinator), Christine Katingima and Gina Ouattara (Investigators), Kishor Mandaliya (Laboratory Coordinator), Mary Thiongo (Data Manager). (3) Nairobi, Kenya (NARESA): Ruth Nduati (Principal Investigator), Judy Kose (Study Coordinator), Ephantus Njagi (Laboratory Coordinator), Peter Mwaura (Data Manager);

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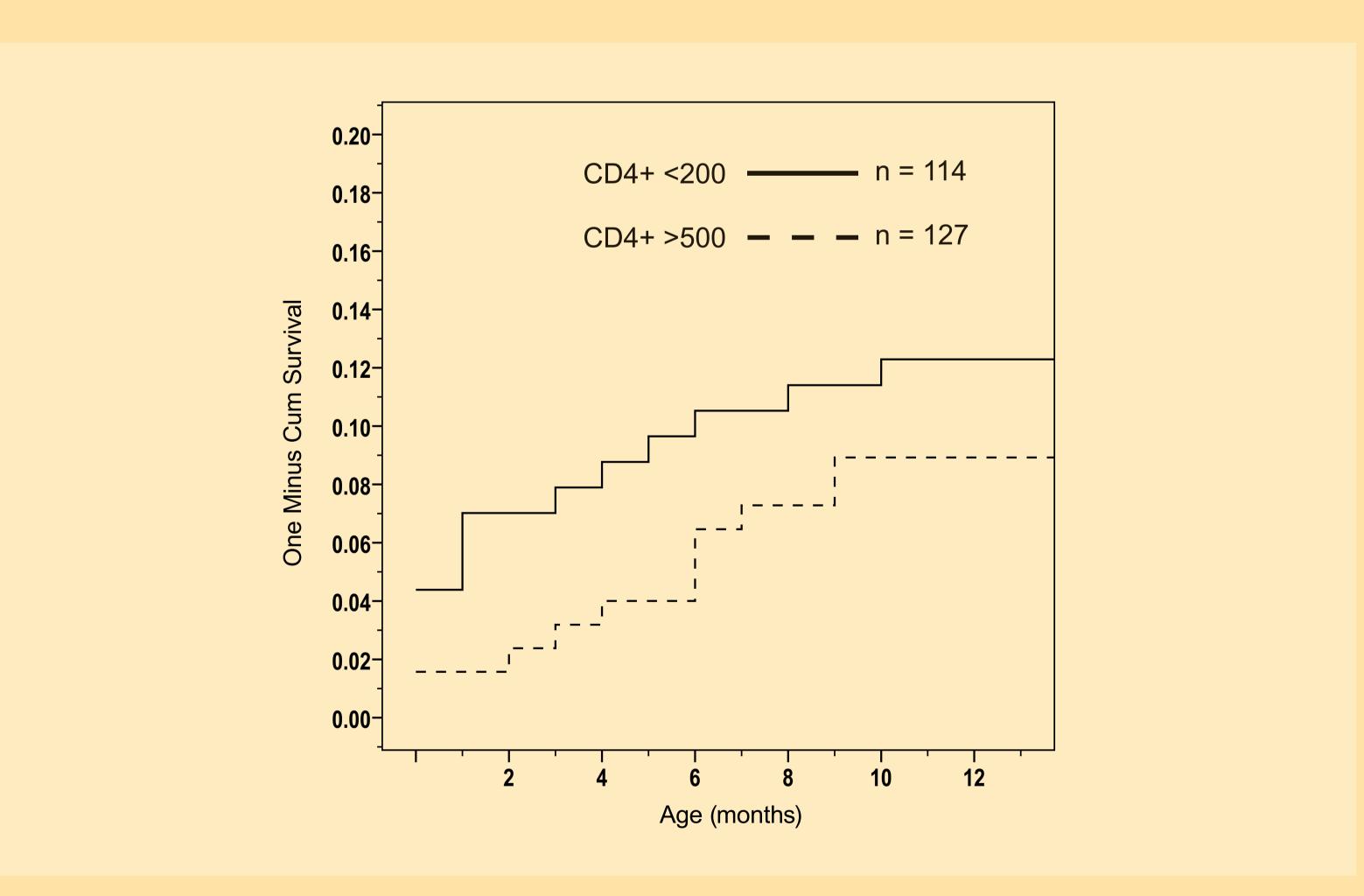
Cumulative risk of HIV infection



Mother Status	All Infants*	Ever breastfed	Never breastfed	RR ever vs. never breastfed (95% CI)§
CD4+ ≤ 200/mm ³	8/110 7.6% [2.5 to 12.6]	4/64 6.4% [0.3 to 12.4]	4/46 9.3% [0.6 to 18.1]	0.90 (0.22 – 3.75) P = 0.887
CD4+ > 500/mm ³	7/125 5.8% [1.6 to 9.9]	7/97 7.5% [2.2 to 12.8]	0/28 0%	-

* Including 1 late infection in each group in babies reported weaned more than 6 months before the 1st positive PCR test result § adjusted for centre and enrolment CD4 count

Cumulative risk of death



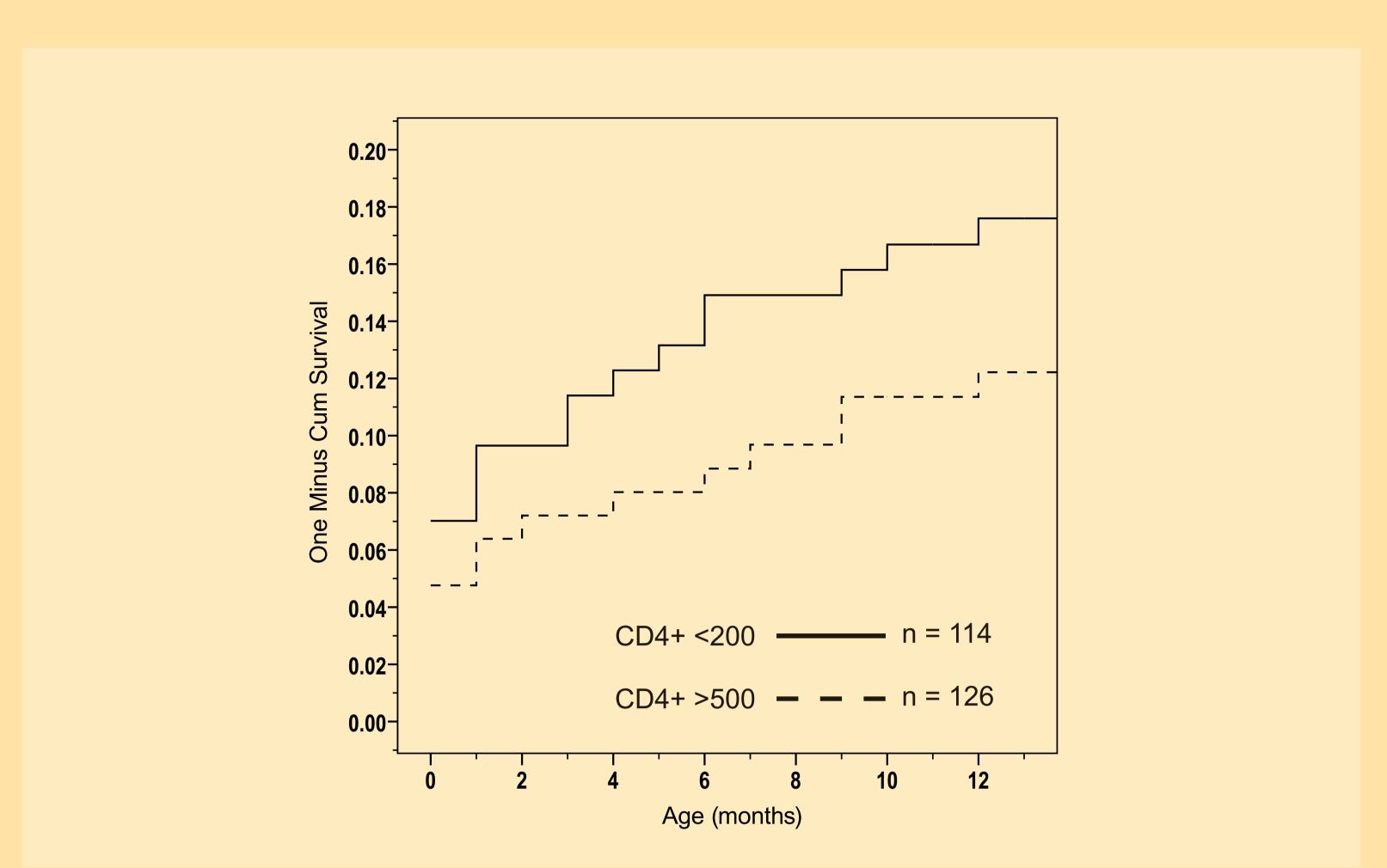
Mother Status	All Infants	Ever breastfed	Never breastfed	RR ever vs. never breastfed (95% CI)§
CD4+ ≤ 200/mm ³	14/114	3/65	11/49	0.18 (0.05 – 0.69)
	12.3% [6.3 to 18.3]	4.6% [0 to 9.7]	22.5% [10.8 to 34.2]	P = 0.012
CD4+ > 500/mm ³	11/127	10/98	1/29	3.37 (0.42 – 27.0)
	8.9% [3.9 to 14.0]	10.5% [0.4 to 16.6]	3.6% [0 to 10.4]	P = 0.252

§: adjusted for centre and enrolment CD4 count.

RR of death per additional 50 CD4 cell count at enrolment in babies born to mothers with CD4 count < 200: 0.52 (0.29 – 0.94)

Cécile Cames (Nutrition Coordination). (3) National Institute of Child Health and Human Development, National Institutes of Health, USA: Jennifer Read (Sponsor Representative and Co-investigator). (4) Agence Nationale de Recherche sur le SIDA, France: Brigitte Bazin and Claire Rekacewicz (Sponsor Representatives). (5) Centers for Disease Control and Prevention, USA: Michael Thigpen, Mary Glenn Fowler, Denise Jamieson (Sponsor Representatives and Co-investigators). (6) International Centre for Reproductive Health Ghent: Patricia Claeys, Marleen Temmerman. (7) Study coordination: World Health Organization, Geneva, Switzerland: Isabelle de Vincenzi (Study Coordinator), Philippe Gaillard (Site Coordinator), Tim Farley (Project Manager), Eduardo Bergel (Statistician), Roselyne Vallo and Sihem Landoulsi (Data Management).

Cumulative risk of HIV infection or death



Mother Status	All Infants	Ever breastfed	Never breastfed	RR ever vs. never breastfed (95% CI)§
CD4+ ≤ 200/mm ³	20/114	7/65	13/49	0.41 (0.16 – 1.08)
	17.6% [10.6 to 24.6]	10.8%§ [3.2 to 18.3]	26.7%§ [14.3 to 39.1]	P = 0.071
CD4+ > 500/mm ³	15/126	14/98	1/28	4.24 (0.55 – 33.0)
	12.2% [6.4 to 18.0]	14.7% [7.6 to 21.9]	3.6% [0 to 10.4]	P = 0.167

§: adjusted for centre and enrolment CD4 count.

RESULTS

CD4+ <**200/mm³:** Women who require ART were less likely to breastfeed than healthier women. Although CD4+ counts were still low at delivery (median 184 cells/mm³) despite ART, the risk of transmission in this group was low whether or not infants were breastfed (6.4% and 9.3%, respectively). The overall infant mortality was somewhat higher than in babies born to healthier mothers (12.3% and 8.3%, respectively). Compared with babies born to mothers in this group who were breastfed, the mortality rate in those never breastfed was 5.4-fold higher (95% confidence interval 1.5 – 20.4, P = 0.012). Three of the 11 deaths were in babies too ill to initiate breastfeeding and two babies born to mothers too ill to breastfeed.

CD4+ >500/mm³: The 1-year cumulative risk of infection was low (5.8%) in this subgroup. Only one late post-partum infection was observed, in a baby reported weaned at least six months before the first positive PCR result, suggesting a potential source of infection other than breastfeeding or unreliable maternal reports on infant feeding patterns. Four of ten deaths in ever breastfed babies occurred within 3 months of weaning.

CONCLUSION

CD4+<200/mm³: Identification of women in need of long-term ART early in pregnancy and active referral to HIV treatment clinics for prompt ARV initiation should be encouraged. Advanced maternal disease and poor infant health were factors that prevented breastfeeding initiation in some babies and may have contributed to the high mortality observed among those never breastfed.

CD4+>500/mm³: Given the low risk of transmission with short-course MTCT-prophylaxis, the potential additional benefit of prolonging prophylaxis during lactation must be carefully weighed. Further investigation of infant feeding patterns is required to identify risks associated with breastfeeding cessation.

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