Infant feeding, HIV transmission and mortality at 18 months: the need for appropriate choices by mothers and prioritization within programmes.

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Abstract

Objectives

To determine the late HIV transmission and survival risks associated with early infant feeding practices.

Design

A non-randomised interventional cohort.

Methods

HIV-infected pregnant women were supported in their infant feeding choices. Infant feeding data were obtained weekly; blood samples from infants were taken monthly to diagnose HIV infection. 18-month mortality and HIV transmission risk were assessed according to infant feeding practices at 6 months.

Results

1,193 live-born infants were included. Overall 18-month probability of death (95%CI) was 0.04 (0.03–0.06) and 0.53 (0.46–0.60) for HIV-uninfected and infected children, respectively. 18-month probability of survival was not statistically significantly different for HIV-uninfected infants breastfed or replacement fed from birth. In univariate analysis of infant feeding practices, the probability of HIV-free survival beyond the first 6 months of life in children alive at 6 months was 0.98 (0.89–1.00) amongst infants replacement fed from birth, 0.96 (0.90–0.98; p=0.25) and 0.91 (0.87–0.94; p=0.03) in those breastfed for less or more than 6 months, respectively. In multivariable analyses maternal unemployment and low antenatal CD4 counts were independently associated with more than three-fold increased risk of infant HIV infection or death.

Conclusions

Breastfeeding and replacement feeding of HIV uninfected infants were associated with similar mortality rates at 18 months. However, these findings were amongst mothers and infants who received excellent support to first make, and then practise, appropriate infant feeding choices. For programmes to achieve similar results, the quality of counselling and identification of mothers with low CD4 counts need to be the targets of improvement strategies.

MESH Keywords AIDS Serodiagnosis ; methods ; Adolescent ; Adult ; Anti-HIV Agents ; therapeutic use ; Breast Feeding ; adverse effects ; CD4 Lymphocyte Count ; Choice Behavior ; Developing Countries ; Female ; HIV Infections ; drug therapy ; mortality ; transmission ; HIV-1 ; Health Knowledge, Attitudes, Practice ; Health Priorities ; Humans ; Infant ; Infant Mortality ; Infant, Newborn ; Male ; Nevirapine ; therapeutic use ; Pregnancy ; Pregnancy Complications, Infectious ; drug therapy ; mortality ; Survival Analysis ; Young Adult

Author Keywords Mortality ; HIV infection ; transmission ; infant feeding ; maternal health ; Africa ; children

Introduction

The dilemma of how best to feed infants and young children of HIV-infected mothers living in high HIV prevalent communities remains complex. Exclusive breastfeeding carries a lower risk of HIV transmission over the first 6 months of life(1) but is infrequently practised by mothers or effectively supported by health systems(2 ;3). Replacement feeding avoids all postnatal HIV transmission but carries the risk of death(4 ;5) when given in household circumstances that are not ideal. Early data suggest that highly active antiretroviral

treatment (HAART) given to HIV-infected mothers during the period of breastfeeding can reduce transmission risks, even if she is already immunodeficient (6 –9). Yet despite 15 years of effective therapeutic interventions being available to reduce peripartum transmission of HIV, more than 500,000 children become infected by this route each year highlighting the gap between scientific evidence and feasibility or coverage of prevention of mother-to-child transmission of HIV (PMTCT) programmes.

Although not commonly measured in programmes, child survival without HIV infection, rather than avoidance of HIV infection alone, has emerged as the most important measure of PMTCT effectiveness(10). This acknowledges not only the availability and effectiveness of therapeutic interventions but also the competing threats to child survival. The quality of counselling to guide women in their choice of infant feeding practice and the practical support to enable these choices is frequently deficient(11 ;12). As a result, sub-optimal feeding practices have resulted in high mortality of HIV-exposed infants(13).

While the transmission risks of infant feeding practices of HIV-infected mothers in the first 6 months of life has been substantially researched, the pattern of feeding beyond this period is equally important in determining child survival. This paper describes the outcomes of infants that were part of an intervention cohort study in which feeding practices were intensively supported. We report the 18 month HIV-free survival of HIV-exposed infants according to infant feeding practices implemented at birth and secondly, by infant feeding practices between 0–6 months and subsequent feeding practices beyond 6 months of age.

Methods

The study design and methods have been described previously(1). In brief, HIV-infected pregnant women attending rural and semi-urban antenatal clinics in KwaZulu Natal (KZN) were enrolled into a non-randomised intervention cohort study. All women were counselled antenatally regarding infant feeding options and supported in their choice(14); those who chose to formula feed their infants were visited at home antenatally and shown how to safely prepare feeds(14). Mothers were visited at home by infant feeding counsellors three or four times in the first two weeks of life and every two weeks thereafter until the infant was 6 months of age(1). Mothers who chose to replacement feed and who encountered problems were principally supported by the infant feeding supervisor or study nurses when refered by infant feeding counsellors following a home visit or when they visited the study clinics. Mothers and infants were followed-up at the study clinic when the infant was 6 weeks old, every month thereafter until the infant was 9 months of age and then three monthly until 18 months of age. At each visit a dried blood spot sample was collected for determination of HIV status by quantitative HIV RNA assay (Nuclisens HIV-1 QT, Organon Teknika, Boxtel, The Netherlands and Nuclisens EasyQ HIV-1, Biomerieux, Boxtel, The Netherlands)(15 ;16). HIV status was determined at 5 months to guide counselling on infant feeding practices after 6 months. An independent group of field monitors visited mothers at home every week from birth until the infant was 9 months of age and documented all feeds and morbidity episodes for each day of the preceding week.

When infants were 5 months old, breastfeeding mothers were counselled to stop breastfeeding (at 6 months) of infants that were confirmed HIV uninfected; mothers were counselled to continue breastfeeding infants who were already HIV infected(17). All mothers were counselled regarding the introduction of complementary feeds. Single-dose nevirapine was provided to all HIV-infected women and their infants for use during labour and delivery and cotrimoxazole was provided to all HIV exposed infants. Six months supply of commercial infant formula was offered free through the KZN PMTCT programme from the end of 2002(1 ;18). CD4 counts were performed on HIV-infected women antenatally but were not routinely considered in infant feeding counseling. At each clinic visit, all mothers were checked for symptoms and weight, and referred to the local hospital for diagnostic services if indicated. At the time of the study, HAART was not available through the Provincial health services. The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (T050/01).

Statistical methods

Analysis was based on a database created in April 2007, and included live-born children of HIV-infected mothers. Cumulative HIV-free survival probabilities in the first 18 months of life were assessed by Kaplan-Meier analysis(19); associations with maternal and infant variables were quantified in Cox regression analysis(20). The following variables were tested in univariable analysis to assess the determinants of HIV infection and death: multiple birth outcome, sex of the child, maternal education, water access, low birth weight (<2.5kg), maternal employment, maternal antenatal CD4 count. Variables with a p-value <0.20 were included in multivariable analysis(20).

Feeding categories were determined from the analytical database by applying algorithms that first classified infants' feeding practices on each day of life and then determined the cumulative pattern from birth. World Health Organization definitions for exclusive breastfeeding, mixed breastfeeding and replacement feeding were used to classify children from the time of introduction of these fluids or feeds(21 –23). A child who was only ever breastfed by his/her mother while having never received any other drink, food or non-human milk with the exception of drops or syrups consisting of vitamins, mineral supplements or medicines was defined as exclusively breastfed.

A child who was breastfed at a given age while also having received water-based drinks, food-based fluid, solid food or non-human milk was mixed breastfed from the date of introduction of these fluids or foods. Replacement feeding was defined as giving any non-human milk and the exclusion of all breastmilk, with or without other liquids or solids.

18-month HIV-free survival was assessed according to firstly, infant feeding practices implemented at birth, and secondly, on cumulative feeding recall histories. If exclusively breastfed infants were given additional fluid or milk even on one occasion, they were immediately reclassified as mixed feeding, irrespective of subsequent feeding practices. Infants with no feeding or test data were excluded from the analyses. In case of missing data, information was censored at the time the infant was last seen. To assess HIV-free survival in children breastfed for less and more than 6 months, we had to take into account survival bias, since children needed to be alive at 6 months of age to be breastfed beyond that age. We thus calculated the probability of HIV-free survival between 7 and 18 months of age, according to infant feeding practices from birth until 6 months of age, among children who were still alive, HIV uninfected at 6 weeks and still being followed-up in the cohort at 6 months of age.

All statistical analyses were carried out using SAS software (version 9.1; SAS Institute, http://www.sas.com).

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Results

Overall 18-month HIV-free survival

Details of the cohort are shown in Table 1 . 1193 live-born infants from HIV-infected mothers born between end-October 2001 and mid-April 2005 were included. By 18 months of age, 147 children died and 237 were diagnosed as HIV-infected; 113 deaths (77%) occurred among HIV-infected children. The overall estimated 18-month probability of death (95% confidence interval) was 0.04 (0.03–0.06) for HIV-uninfected and 0.53 (0.46–0.60) for infected children. Infected children were 17-times more likely to die than uninfected children (unadjusted hazard ratio: 16.9 [11.5–24.8]). By 18 months an estimated 21% (19%–23%) of children born to HIV-infected mothers would have acquired HIV infection. Combined, the overall probability of remaining free from HIV infection and death by 18-month was 0.76 (0.73–0.78). The overall estimated risk exposure for breastfeeding over the 18 month period was 9.1 cases per 100 child-years of breastfeeding (95%CI: 5.8–12.5).

In univariate analyses low birth weight (<2.5kg), maternal unemployment and low maternal antenatal CD4 count were associated ($p<0.20$) with increased child death or HIV-infection and were therefore included in a multivariable analysis. Overall adjusted hazard ratios (AHR) of HIV infection/death were 1.5 (1.1–2.2, $p=0.03$) for low birth-weight children, 1.9 (1.3–2.9, $p=0.004$) for children of unemployed mothers and 2.4 (1.7–3.2, $p<0.001$) for children of mothers with an antenatal CD4 count below 200 cells/ml.

18-month HIV-free survival according to infant feeding practices implemented at birth

Among the 1,193 infants, infant feeding practices implemented at birth were: 937 (78%) exclusively breastfed, 105 (8.8%) mixed fed of whom 75 (71.4%) received breastmilk plus water based drinks or solids and 30 (28.6%) breastmilk plus formula milk, and 118 (10%) had received replacement milk only. 33 infants were excluded as they had received only water or were fed intravenously from birth (13) or were missing infant feeding data (20).

Table 2 shows the probability of remaining free from HIV infection and death, as well as the probability of survival according to infant feeding practices implemented at birth. By 18 months of age an estimated 25% of infants ever exclusively breastfed born to HIV infected mothers would have acquired HIV infection or have died, compared to 20% of never breastfed infants ($p=0.05$). This difference is mostly due to acquisition of infection through breastfeeding. The 18-month probability of survival among HIV-uninfected children was 96% (94%–97%) regardless whether they were breastfed or replacement fed from birth.

HIV-free survival according to infant feeding practices from birth until age 6-months

Of the 893 children included (not HIV-infected peripartum and still alive at 6 months -Table 1), 69 (8%) were never breastfed, 136 (15%) were breastfed for less than 6 months, and 688 (76%) breastfed beyond 6 months of age. Cumulative feeding practices at three and six months of age are shown in Table 3 .

Of the 688 children who received breastmilk beyond 6 months of age, 278 (31%) had been exclusively breastfed throughout the first 6 months of life, 42 (5%) received liquids other than non-human milks at least once and 368 (40%) received food-based fluid, solid food or

non-human milk in the first 6 months of life. Amongst these 688 children the overall median duration of breastfeeding was 283 days (inter-quartile range: 206–491) and the Kaplan-Meier probabilities (95%CI) of still being breastfed at 7, 9, 12 and 18 months of age were 0.74 (0.71–0.78), 0.58 (0.54–0.61), 0.45 (0.41–0.49), 0.22 (0.19–0.25), respectively.

Univariable and adjusted analyses of the risk of HIV infection or death between 7 and 18 months in 893 infants alive at 6 months showed a 2.7 increased risk for infants who continued to be breastfed beyond 6 months compared to the group who were either replacement fed, exclusively breastfed up to 6 months or ceased all breastfeeding any time before 6 months (Table 4). In a similar analysis but stratified on antenatal maternal CD4 count: the adjusted hazard ratio for infants breastfed beyond 6 months was 4.3 (0.9–18.0; p=0.06) among women with CD4 count below 200 cells/ml and 2.5 (1.0–6.2; p=0.05) among women with CD4 over 200 cells/ml. Mothers who breastfed for less than 6 months (n=136) were more often unemployed than the mothers who continued to breastfeed beyond 6 months (n=688) (19.9% vs. 11.5%, p=0.001); they also tended to more often have access to piped water inside their home (9.5% vs. 7.7%, p=0.25).

Mothers in both groups had similar levels of education and access to toilets. The mean antenatal CD4 count was slightly lower in mothers who breastfed less than 6 months (487 vs. 514, p=0.24) and the proportion of women with CD4 counts below 200 was also similar (BF<6 months 10.8% vs. BF>6 months 8.1%, p=0.31). In multivariable analyses maternal employment was associated with a three-fold increased likelihood of HIV-free survival between 7 and 18 months in children alive at 6 months (Table 4); antenatal maternal CD4 count below 200 cells/ml was associated with a 3.6-fold increased risk of HIV infection or death. Although low birthweight was associated with survival early in life, this was not the case for HIV-free survival between 7 and 18 months of age (p=0.52).

The probabilities of death and postnatal HIV acquisition between 7 and 18 months of age are shown separately in Figure 1 . Univariably, the probability of HIV-free survival (no corresponding figure) at 18 months (conditional on survival to 6 months and including postnatal transmissions) was 0.98 (0.89–1.00) in the 69 replacement fed from birth infants, 0.96 (0.90–0.98) in 136 children that were breastfed for any period up to 6 months (p=0.25), and 0.91 (0.87–0.94) in 688 children who were breastfed for more than 6 months (p=0.03). Overall, the probability of HIV-free survival was significantly lower in children who were breastfed for more than 6 months than in the combined group of children replacement fed or breastfed for less than 6 months (0.91 (0.88–0.93) vs. 0.96 (0.93–0.98), p=0.001).

Overall, breastfeeding beyond 6 months increased the risk of HIV acquisition (AHR 3.3; CI: 1.0–10.5, p=0.05) compared with durations of breastfeeding less than 6 months. However, in multivariable analysis allowing for infant's HIV infection (data not shown), with replacement feeding only from birth as reference, the probability of survival beyond 6 months of age (excluding deaths in the first 6 months) did not differ by breastfeeding duration: infants breastfed for less than 6 months AHR 1.2 (0.1–11.9, p=0.86); breastfed for more than 6 months AHR 0.9 (0.1–7.1, p=0.92).

Among the infants breastfed beyond 6 months of age, although the differences in overall probability of death or HIV infection between 7–18 months in these three groups did not reach statistical significance, those who were exclusively breastfed in the first 6 months tended to do better than those mixed-fed.

Discussion

The most striking, though not new, message from these data is that HIV infection is the major driver of childhood mortality in these rural and urban communities. About 53% of infants who became infected would have died by 18 months compared with 4% of infants who were not. This again emphasizes the gains for child survival if effective PMTCT programming were achieved(24 ;25).

In this population, replacement feeding of HIV-uninfected infants between 7 and 18 months, or those who were switched earlier, did not increase mortality compared to infants who continued to receive breastmilk. It is essential however, to contextualize these findings including the circumstances that guided the initial feeding choices of these mothers(14) and the support available to them, before simple generalizations are drawn. Mothers who had limited access to safe water, poor sanitation at home, as well as higher CD4 counts tended to initiate breastfeeding; mothers with lower CD4 counts and access to personal income tended to start replacement feeds(14). Mothers also received ongoing guidance and support in their feeding choice and had immediate access to study teams at clinics. The sum of these ' interventions' are likely to have optimized the environment in which these feeding choices were practised and reduced potential morbidity and mortality. This is evidenced by results of an operational study describing the South African national PMTCT programme(3) in which infants of women who were given replacement feeds under inappropriate conditions experienced the highest risk of HIV transmission or death (AHR 3.63; 95%CI 1.48–8.89) in comparison to those who received replacement feeds under appropriate circumstances.

We were unable to determine if there had been changes in household circumstances from the antenatal period that might have influenced mothers' decisions to switch from breastfeeding to non-breastfeeding in the postpartum period. Antenatal demographic and socio-economic characteristics were available, but although counsellors and nurses would have learned of changes in mothers' circumstances and this would have influenced subsequent counselling, this information was not systematically captured in the database. All HIV-infected mothers had been counselled, both antenatally and postpartum, to stop breastfeeding around 6 months, as long as there was a safe and nutritionally adequate alternative. In spite of this, 688 (77%) mothers of infants uninfected at 6 months decided to continue

breastfeeding. Amongst this group 22% would have continued to at least 18 months. For these infants, although at continued risk of HIV infection, this strategy might still have been correct to promote their long term overall survival. Given that this was not a randomized trial, we are unable to determine what might have happened if those same mothers had chosen to stop breastfeeding earlier and adopt a feeding practice that could not have been safely supported.

Continued breastfeeding resulted in significantly more infections over the 18 month period. Children who were breastfed for more than 6 months were 2.7 times more likely to become infected compared to infants who were breastfed for less than 6 months. The low risk of death, apart from HIV transmission, highlights the feasibility of supporting good infant feeding to promote child survival. HIV-free survival could be achieved, even in rural settings, if strategies to reduce the risk of postnatal infection such as HAART to breastfeeding mothers are demonstrated to be effective and feasible at scale.

In this study, amongst infants that never became infected, early feeding practices did not influence long term survival. As in previous analyses of this cohort(1), numbers of infants in the mixed feeding categories in the first 6 months were too small to make statistical comparisons regarding transmission, including the risk of mixed feeding in the first 6 months versus the risk of receiving breastmilk and complementary feeds beyond 6 months. The overall estimated risk exposure for breastfeeding over the 18 month period (9.1 cases per 100 child-years of breastfeeding) was similar to previous estimates(26). Among the infants breastfed beyond 6 months of age and allowing for maternal CD4 counts, although the differences in overall probability of HIV-free survival between 7–18 months did not reach statistical significance, those who were exclusively breastfed in the first 6 months tended to do better than those mixed-fed.

Maternal health remained a major determinant of HIV infections and mortality of exposed infants throughout the 18 month period. Overall, the probability of HIV infection or death was highest amongst infants born to mothers with low antenatal CD4 counts but also significantly higher if the mother was unemployed antenatally. Unemployment could represent several independent influences including dependency and lack of autonomy to make choices about infant feeding practices, impaired nutrition and lack of resources e.g. taxi fares to access to health services. Low birth-weight of exposed infants also increased the likelihood of adverse outcomes in early life and may similarly reflect poor maternal health and antenatal care. Perhaps surprisingly, infant outcomes between 7 and 18 months were more substantially determined by these maternal factors than by feeding practices.

We were surprised by the relatively large number of mothers who continued to breastfeed beyond 6 months, despite counselling, planning and access to replacement feeds. That so many mothers opted to continue breastfeeding likely reflects the socio-demographics of the study population and cultural issues within the communities. These mothers presumably weighed up the complexities and relative inconvenience of safe replacement feeding and decided that continued breastfeeding was still preferable. PMTCT programmes need to offer better counselling and support throughout this time if overall child health and survival are to improve.

Methodologically, we did not permit any lapses whatsoever when allocating infants to specific feeding practices. If an infant received water, non-human milk or solids even for one day, the infant was reclassified as mixed feeding. In comparison with our analysis of HIV transmission in the first 6 months(1), in which we permitted up to 3 lapsed days before exclusion to another category, this approach significantly reduced the number of infants within the exclusive breastfeeding group. Also, because in this analysis we were interested in transmission and survival by initial feeding mode, or feeding mode up to a certain age, we did not censor when the child dropped out of the initial feeding mode.

The question remains how best to identify and support the optimal infant feeding strategy beyond 6 months for individual HIV-infected women. Any approach must consider a mother's prevailing or changing household circumstances as well as her own disease status, to determine if, or when she should stop breastfeeding. Programmes need to remain in contact with mothers to assist with the process of stopping breastfeeding and offer advice on complementary feeding. Amidst the many difficult contextual issues remains the greatest opportunity, namely to identify the women with low CD4 counts and start them on HAART for life. Where HAART is not available for this group of women, the balance of evidence suggests that where possible and safe, stopping breastfeeding at 6 months or before will increase the child's long term prospects of survival. The ability of international recommendations, national policies, individual programmes and community responses to promote and protect the equality and autonomy of women and mothers, to benefit from employment and access to health interventions, will be measured by the most tangible of child health outcomes, namely whether they live or die.

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Authors contributions	
Nigel Rollins	Design, implementation and project management of the study, analysis of data and drafted manuscript
Renaud Becquet	Analysis of data and drafted manuscript
Ruth Bland	Design, implementation and project management of the study, analysis of data and reviewed manuscript
Anna Coutsoudis	Conceptualisation, design and implementation of the study, and drafted the manuscript

Hoosen Coovadia	Conceptualisation, design and implementation of the study, and drafted the manuscript
Marie-Louise Newell	Design of study, analysis of data and drafted manuscript

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Figure 1

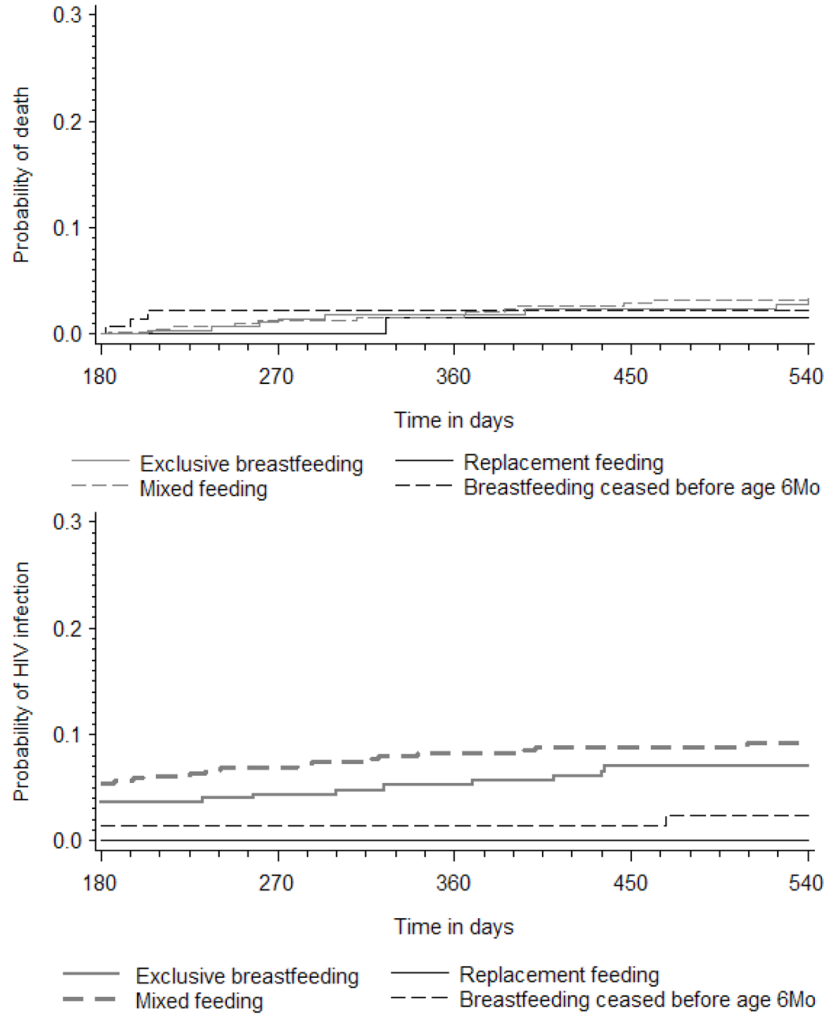

Table 1

Cohort profile.

Pregnant women enrolled	3,445
Exclusion of women not infected with HIV-1 or HIV-1 status not confirmed	1,679
Exclusion of HIV-1 infected women lost to follow-up or dead before delivery or who had spontaneous abortion	306
HIV-1 infected women having delivered	1,460
Birth outcomes	1,496
Exclusion of second/third born of twins/triplets	36
Exclusion of stillbirths	60
Single or first births, live born infants from HIV-infected mother	1,400
Exclusion of infants lost to follow-up immediately after birth	82
Exclusion of infants not tested for HIV infection	125
Mother-infant pairs included in the 18 months outcomes analyses according to infant feeding practices implemented at birth	**1,193**
Exclusion of infants HIV-infected in peri-partum or with unknown timing of HIV-infection	173
Exclusion of infants dead by 3 months of age	12
Exclusion of infants lost to follow-up by 3 months of age	56
Mother-infant pairs included in the 18 months outcomes analyses according to infant feeding practices from birth until 3 months of age	**952**
Exclusion of infants dead between 3 and 6 months of age	14
Exclusion of infants lost to follow-up between 3 and 6 months of age	45
Mother-infant pairs included in the 18 months outcomes analyses according to infant feeding practices from birth until 6 months of age	**893**

Table 2

Probability of remaining free from HIV infection and death according to infant feeding practices implemented at birth (n=1,160, with information on all variables).

	Age 3 Months	Age 6 Months	Age 9 Months	Age 12 Months	Age 18 Months
Numbers at risk	**908**	**841**	**766**	**703**	**592**
Probability of remaining free from HIV-infection and death (95%CI) [1]					
Exclusive Breastfeeding group (n=937)	0.82 (0.79–0.84)	0.79 (0.77–0.82)	0.78 (0.75–0.80)	0.76 (0.74–0.79)	0.75 (0.72–0.78)
Mixed feeding group (n=105)	0.84 (0.75–0.89)	0.81 (0.71–0.87)	0.81 (0.71–0.87)	0.81 (0.71–0.87)	0.79 (0.70–0.86)
Replacement feeding group (n=118)	0.85 (0.77–0.90)	0.82 (0.74–0.88)	0.81 (0.73–0.87)	0.80 (0.72–0.87)	0.80 (0.72–0.87)
Probability of survival (95%CI) [2]					
Exclusive Breastfeeding group (n=937)	0.96 (0.95–0.97)	0.93 (0.91–0.94)	0.90 (0.89–0.92)	0.89 (0.86–0.90)	0.86 (0.83–0.88)
Mixed feeding group (n=105)	0.98 (0.92–0.99)	0.97 (0.91–0.99)	0.96 (0.89–0.98)	0.94 (0.86–0.97)	0.87 (0.78–0.93)
Replacement feeding group (n=118)	0.96 (0.91–0.99)	0.91 (0.84–0.95)	0.91 (0.84–0.95)	0.89 (0.81–0.93)	0.87 (0.78–0.92)

1 Log-Rank test between the 3 groups, p=0.43

2 Log-Rank test between the 3 groups, p=0.74

Note 1,193 infants were eligible for this analysis, but 33 infants had not been fed during their first 2 days of life or had missing infant feeding data and were excluded from this analysis.

Table 3

Infant feeding practices between birth and 3 or 6 months of age

Infant feeding modality[1]	From birth until age 3-month n (%)[2]	From birth until age 6-month n (%)[3]
Exclusive breastfeeding	533 (56)	278 (31)
Mixed feeding	259 (27)	410 (46)
breastmilk and water only	71 (7)	42 (5)
breastmilk plus solids	32 (3)	135 (15)
breastmilk plus non-human milks	122 (13)	99 (11)
breastmilk plus two other things	34 (4)	134 (15)
Breastfeeding ceased before age 3 or 6-month	82 (9)	136 (15)
Replacement feeding (never breastfed)	78 (8)	69 (8)

[1] According to strict WHO definitions.

[2] Among N=952 children not HIV-infected in peri-partum, and still alive at 3 months of age.

[3] Among N=893 children not HIV-infected in peri-partum, and still alive at 6 months of age.

Table 4

Determinants of HIV infection or death of infants between 7 and 18 months of age, n=893

Variables	N	Univariable analysis			Multivariable analysis		
		Hazard Ratio	95% CI	p	Adjusted hazard ratio	95% CI	p
Infant feeding practices between birth and age 6Mo							
Breastfeeding ceased before age 6Mo or replacement feeding from birth	205	1	-	0.01	1	-	0.01
Breastfeeding beyond age 6Mo	688	2.7	1.2–5.8		2.7	1.2–6.0	
Mother employed							
Yes	122	1	-	0.03	1	-	0.04
No	771	3.5	1.1–11.2		3.4	1.1–11.0	
Sex of the child							
Male	445	1	-	0.11	1	-	0.09
Female	448	0.7	0.4–1.1		0.7	0.4–1.1	
Maternal CD4 count							
≥200 cells/ml	767	1	-	<0.001	1	-	<0.001
< 200 cells/ml	82	3.0	1.7–5.3		3.6	2.0–6.4	
Missing	44	1.4	0.5–4.0		1.5	0.5–4.1	