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## COHORT PROFILE

# Cohort Profile: Mamanengane or the Africa Centre Vertical Transmission Study

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## How did the study come about?

From the mid-1990s, the success of antiretroviral prophylaxis to reduce HIV RNA viral load in plasma and avoidance of breastfeeding provided the real possibility that mother-to-child transmission (MTCT) of HIV-1 could be markedly reduced,<sup>1</sup> with an implicit understanding that these measures could be effectively applied to all HIV-infected women in developing countries.<sup>2,3</sup> The latter constitute the overwhelming majority of HIV-positive pregnancies resulting in approximately half a million new infant infections annually.<sup>4</sup> However, the inappropriate use of formula milks amongst impoverished populations resulted in major adverse effects; without the nutritional and immunological benefits of breastfeeding, growth failure, malnutrition, diarrhoea and infant death are common.<sup>5-7</sup>

Since 1996, a group at the Nelson Mandela School of Medicine, University of KwaZulu-Natal (UKZN), had been pursuing the idea of finding interventions to reduce breastfeeding transmission of HIV-1 that would be suitable and safe for populations living in resource-poor settings. The aim was to find efficacious, ethical, acceptable, feasible and sustainable approaches to prevent post-natal transmission, while preserving the critical practice of breastfeeding.

The presentation of preliminary evidence in 1999 from the UKZN group that exclusive breastfeeding (EBF) might be associated with lower HIV transmission than mixed breastfeeding (MBF) suggested that such an aim would be possible,<sup>8</sup> although considerable international scientific opposition to attempts to promote breastfeeding in an high HIV prevalence setting remained.<sup>9</sup> Subsequently, with support from the Wellcome Trust, UK, the availability of a population-based site at the Africa Centre for Health and Population Studies ([www.africacentre.ac.za](http://www.africacentre.ac.za)), and confluence of interests among a small number of individuals, the conditions were created for the Vertical Transmission Study (VTS), a non-randomized cohort intervention study, described here. ('Mamanengane' is the Zulu name for the study and means 'Mother and Child'.)

Ethical approval was granted by the Biomedical Research Ethics Committee of UKZN, pilot work began in 1999 and clinical follow-up of the study was completed in September 2006.

## Study objectives

The primary objectives were to determine the effect of infant feeding practices on HIV infection rates of infants at 6 and 22 weeks of age, and the infant survival rate at 24 months of age according to feeding practices and HIV status.

The secondary objectives were: to determine the HIV infection rate of infants as measured on a sample collected within 72 h of birth; the HIV transmission incidence attributable to the duration of different feeding practices; the cumulative incidence of MTCT in EBF, MBF and exclusively formula-fed (EFF) infants; to describe risk factors, other than feeding practice, for post-natal transmission of HIV, including maternal and infant morbidity and breast health; to assess the determinants of transmission in MBF

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adjusting for exposure factors e.g. type and age of introduction of other food/milk; to describe the morbidity and growth of infants in relation to feeding practices and HIV status; and to describe adherence rates to EBF following a breastfeeding support intervention.

### What does the study cover?

The study documents the feeding practices, HIV status, morbidity, mortality, growth and development of children born to HIV-infected and -uninfected women from birth to 2 years of age; and morbidity, mortality, breastfeeding difficulties and breast health problems of HIV-infected and -uninfected mothers from the antenatal period to 2 years post-partum.

### Where is the study area?

The study had two field sites. The first, and largest, was in the rural Umkhanyakude district of northern KwaZulu Natal, where enrolment commenced in August 2001 at eight clinics—one peri-urban and seven rural (Figure 1). In order to increase the rate of recruitment, enrolment began at an additional site on the outskirts of Durban in August 2003 (Figure 1). This site was urban and the population extremely mobile, with people migrating at short notice into and out of the area during pregnancy and post-delivery.

The Africa Centre for Health and Population Studies ([www.africacentre.ac.za](http://www.africacentre.ac.za)) conducts a Africa Centre Demographic Information System (ACDIS), and individual HIV surveillance, in a sub-district of the Umkhanyakude district;<sup>10–13</sup> five of the VTS

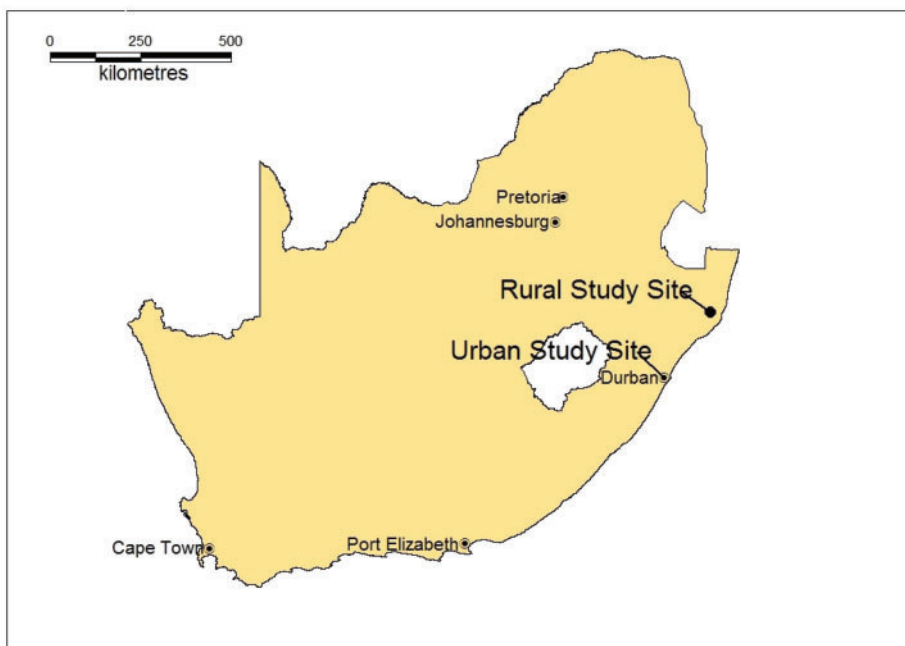
recruitment clinics are located within the Demographic Surveillance Area.

### Who is in the sample?

A total of 3445 women were enrolled during pregnancy: 2704 women from the eight clinics in Umkhanyakude and 741 women from the one clinic outside Durban. Eligibility criteria were: aged 16 years of age or older, planning to stay in the study area for at least 3 months after delivery, and provided written consent.

HIV-uninfected women were included to establish the effect of HIV status on adherence to EBF, and to avoid stigmatization of HIV-infected women in the community, as frequent home visits were part of the study protocol.

Initially, all HIV-infected women, and a systematic subsample of uninfected women, were offered enrolment in the study; 1 in 10 women who tested HIV negative were randomly and confidentially identified through a computer-based programme from batches of test results identified only with an encrypted study number. These women were offered enrolment when they were subsequently counselled after testing. From July 2003, all women attending antenatal clinics were offered enrolment before HIV testing. Although this resulted in a much larger cohort of HIV-negative women than originally planned, this negative comparison group is one of the strengths of the study, and has enabled us to conduct interesting analyses: for example, comparison of morbidity and growth between children of HIV-positive and -negative mothers, and comparisons of maternal morbidity and mortality between HIV-positive and -negative women. No other



**Figure 1** Rural and urban study sites in South Africa

mother and child cohort in sub-Saharan Africa has such a large comparative HIV-uninfected cohort with detailed data.

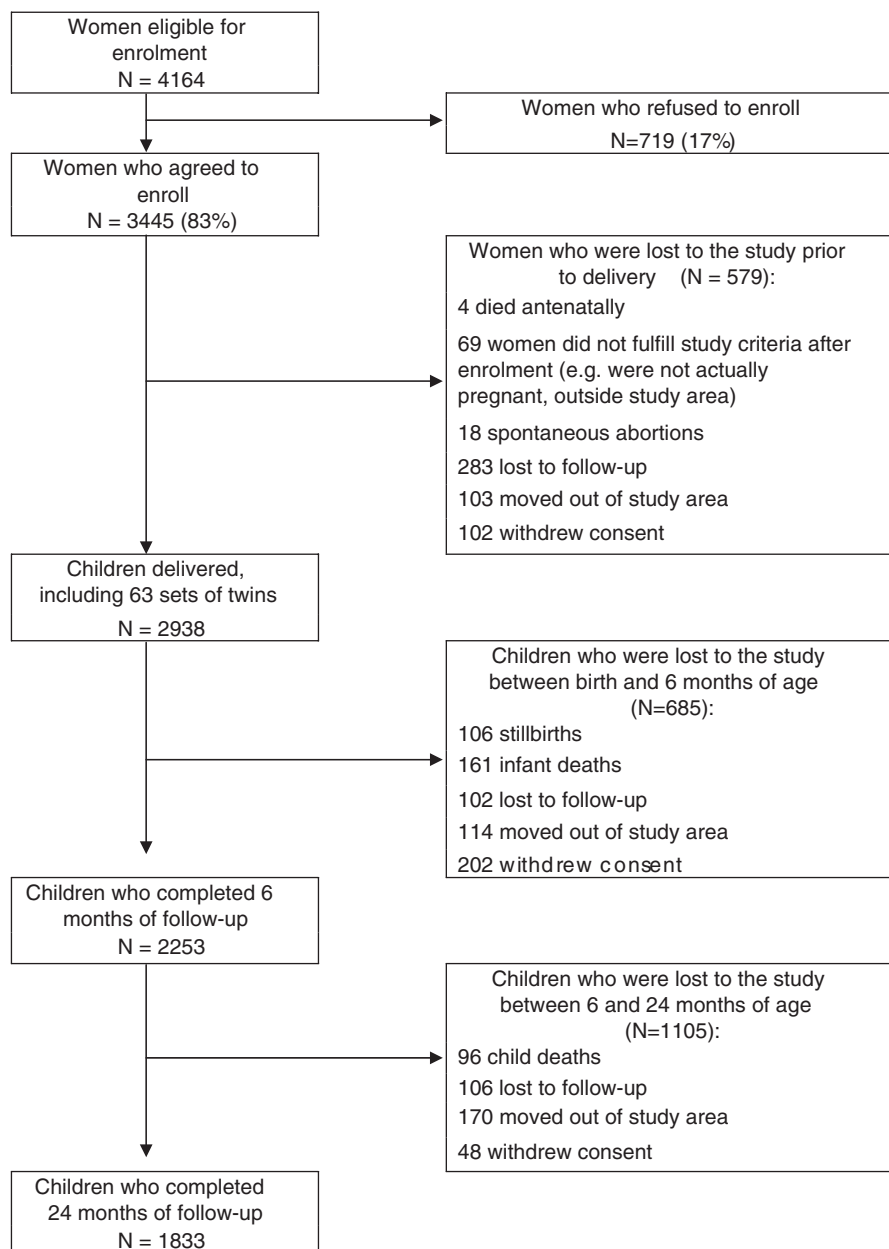
Figure 2 shows the number of women eligible for enrolment and numbers lost to follow-up at different time periods. Compared with women enrolling, those refusing to participate in the study were significantly more likely to live in the peri-urban area and to be HIV infected (Table 1).

Compared with women who remained active in the study, those who moved from the study area, withdrew consent or were lost to follow-up antenatally were significantly more likely to reside in the urban site at Durban and to have piped water in their home-steads; post-natally they were also significantly more

likely to live in the urban site, to be HIV positive and to have less than four previous pregnancies. There were no significant differences in terms of educational attainment or maternal income. Mobility of women in the urban setting was high, with many women coming to the area to join partners and to access antenatal care, but moving away to join their own families for delivery.

### How often have they been followed up?

Follow-up took place both at clinics and women's homes, with the same frequency for HIV-infected



**Figure 2** Flow diagram of women eligible for enrolment and numbers lost to follow-up during the study

**Table 1** Characteristics of eligible women who enrolled in the study and those who declined to participate

Variable	Women who enrolled N = 3445	Women who declined enrolment N = 719	P-value for difference between groups of women
<b>Residence</b>			
Rural	1586 (46%)	257 (35.8%)	<0.001
Semi-urban	1119 (32.5%)	462 (64.2%)	
Urban	740 (21.5%)	0	
<b>Maternal HIV status</b>			
Positive	1769 (51.4%)	452 (63.4%)	<0.001
Negative	1662 (48.3%)	259 (36.3%)	
Indeterminate	12 (0.3%)	2 (0.3%)	
<b>Highest level of education attained</b>			
None	224 (6.5%)	55 (7.7%)	0.479
Primary	1196 (34.7%)	253 (35.2%)	
Secondary	2025 (58.8%)	411 (57.1%)	
<b>Number of previous pregnancies</b>			
0	1228 (35.6%)	240 (33.4%)	0.3
1–4	1981 (57.5%)	434 (60.3%)	
4–11	211 (6.1%)	43 (6%)	
Missing	25 (0.8%)	2 (0.3%)	

**Table 2** Training provided to study staff

Staff group	Training provided
Clinic assistants	40-h WHO breastfeeding counselling course <sup>14</sup> Training in anthropometry
HIV counsellors	40-h HIV counselling course (local course) 40-h WHO breastfeeding counselling course <sup>14</sup> 15-h WHO HIV and infant feeding counselling course <sup>24</sup>
Breastfeeding counsellors	40-h WHO breastfeeding counselling course <sup>14</sup>
Field monitors	IMCI training on respiratory and diarrhoeal disease
Study nurses	40-h WHO breastfeeding counselling course <sup>14</sup> 15-h WHO HIV and infant feeding counselling course <sup>24</sup> 24-h WHO Complementary feeding counselling course <sup>38</sup> Training in anthropometry

All staff received basic training in numeracy, HIV education, research methods, study protocol, family planning, sexually transmitted infections, life skills, growth charts, recognition of a sick child.

and -uninfected women. A large operational study staff (numbering 140 persons at peak) was required to conduct this rigorous follow-up over a wide geographical area. Most study staff were local Zulu women, with no tertiary education, who were specifically trained for the study (Table 2).

All pregnant women were tested for HIV and counselled at the antenatal clinic, by lay HIV counsellors, on infant feeding options according to the WHO/UNAIDS recommendations available at the time.<sup>14,15</sup> HIV-uninfected women were counselled to exclusively

breastfeed for the first 6 months of life with sustained breastfeeding to at least 2 years. The option of replacement feeding (commercial formula feeds) or EBF for the first 6 months of life was discussed with HIV-infected women who made decisions based on their home circumstances. At 5 months, HIV-infected breastfeeding women were counselled to stop breastfeeding (at 6 months) of infants who were confirmed not to be HIV-infected; mothers were counselled to continue breastfeeding infants who were already HIV-infected.<sup>16</sup> Women were

encouraged to cease breastfeeding as rapidly as possible; relatively large numbers (>70%) of HIV-infected women continued to breastfeed beyond 6 months, despite counselling and access to replacement feeds.<sup>17</sup>

Single-dose nevirapine was provided for all HIV-infected women and their infants any time after first booking or 28 weeks gestation.<sup>18</sup> Six months supply of commercial infant formula was offered free through the KwaZulu Natal PMTCT programme from the end of 2002, and HIV-infected mothers could choose to access this supply any time in the first 12 months of the infants' life.<sup>18</sup> For those initiating formula milk from birth, an initial supply was provided antenatally. At the time of the study, highly active antiretroviral treatment was not available through the provincial health services.

Thereafter women were followed up by three separate study teams:

- field monitoring (by field monitors)
- breastfeeding counselling (by breastfeeding counsellors)
- clinic follow-up (by nurses, clinic assistants and HIV counsellors)

In the rural site the field monitoring and breastfeeding counselling visits were conducted at women's homes. In the urban site, owing to concerns about staff security, separate counselling and monitoring visits were carried out at the clinic, with the same frequency as home visits in the rural area.

### Breastfeeding counselling

Breastfeeding counsellors visited all enrolled women at home, antenatally, to discuss study logistics, explain again the study protocol and ensure women wanted to participate. Any woman who chose to replace feed was referred to the study infant feeding specialist for support; those choosing to breastfeed received up to three further antenatal home visits to discuss breastfeeding issues.

Within 72 h of delivery, all women received one home visit from the breastfeeding counsellor, irrespective of antenatal feeding intention. Mothers initiating breastfeeding received a further three home visits in the first 2 weeks, and fortnightly thereafter, until the infant was 6 months old. The counsellors supported women to exclusively breastfeed, and also recorded information on breast health and breastfeeding technique (positioning and attachment), but no data on infant feeding practices, to avoid potential recording bias. Support for formula-feeding mothers was provided by study nurses at the clinics, and home visits as required.

### Field monitoring

Infant feeding practices were reported to independent field monitors who visited every week and documented all feeds (milks and solids), fluids, drugs, morbidity episodes, hospitalization and attendances at health

facilities for every day of the preceding week. Mothers kept food-intake and morbidity diaries for use during the field-monitor interview to corroborate the verbal report. If a mother or main care giver was not present for a counselling or monitoring visit, the study team returned on up to 2 consecutive days. Thereafter, the visit was considered to be a missed visit. Mothers kept food-intake and morbidity diaries for use during the field visit to corroborate the verbal report.

Neither feeding counsellors nor field monitors were aware of the mothers' HIV status. Home visits by the breastfeeding counsellors (for women who were breastfeeding) ceased at 6 months; and monitoring visits by the field monitors (for all women—breastfeeding or replacement feeding), at 9 months, post-delivery.

### Clinic follow-up

Study staff (study nurse, clinic assistant), based at health facilities, aimed to see infants as soon as possible after delivery to record birth data and obtain a dried blood spot.

Further clinic visits were scheduled to coincide with routine infant immunizations to avoid unnecessary visits—at 6, 10, 14, 18, 22, 26 weeks and then 7, 8, 9, 12, 15, 18, 21, 24 months after delivery. If infants did not attend at around 6 and 26 weeks post-delivery, attempts were made to trace the women, and if necessary, to bring them and their infant to the clinic for assessment.

At every visit, the study nurse documented a medical history, examined and conducted anthropometry on mother and infant and obtained biological specimens. At each visit, a dried blood spot sample was obtained by heel prick from the infant. HIV status was established by quantitative HIV RNA assay with a sensitivity of 80 copies of HIV RNA per millilitre of blood (equivalent to 1600 copies HIV RNA per 50 µl dried blood spot). A breastmilk sample from each breast was obtained from breastfeeding mothers. Venous blood samples were collected at 6 months from mothers and infants.

## What has been measured?

Examples of data collected are shown in Table 3. There was relatively little missing data for the key variables, specifically daily feeding practices in the first 6 months. For the main transmission analyses, infants were excluded if there were >5 days of missing feeding data in any 30-day period.<sup>19</sup>

Feeding data were collected in line with recommended practices, and after discussion with investigators involved in feeding trials at other sites, including Zimbabwe,<sup>20</sup> Zambia<sup>21</sup> and Cote d'Ivoire.<sup>22</sup> Strict World Health Organization definitions of feeding were used.<sup>23,24</sup> This similarity in data collection methods has allowed not only comparisons of our

**Table 3** Examples of data collected

<b>Variables</b>	<b>Comments where applicable</b>
<b>Socio-demographic factors</b>	
Maternal age at delivery	
Maternal education	Collected in the antenatal period.
Maternal employment	Collected in the antenatal period.
Type of water supply, ownership of fridge, cooking fuel	Collected in the antenatal period.
<b>Pregnancy and birth details</b>	
Parity and gravidity	Collected at antenatal clinic.
Date of last menstrual period	Collected at antenatal clinic.
Gestation at booking visit	Collected at antenatal clinic.
Previous infant feeding practices	Collected at antenatal clinic.
Gestational age at birth	Collected from the delivery facility and delivery maternity records.
Mode of delivery	Collected from the delivery facility and delivery maternity records.
Duration of labour	Collected from the delivery facility and delivery maternity records.
Duration of rupture of membranes	Collected from the delivery facility and delivery maternity records.
Apgar scores	Collected from the delivery facility and delivery maternity records.
Birth weight, length, head circumference	Weight: from the delivery maternity records; and also measured by study staff if not too long after delivery. Length and head circumference from maternity records.
<b>Infant feeding practices</b>	
Daily feeding practices	Daily information documented at weekly intervals at home. All foods and fluids given to infant recorded for each day of the preceding week. Approximate volumes of other food and fluids given in previous 24h documented.
Maternal breast health problems	Daily information documented at 2-weekly intervals at home. All breast health pathology, per breast, recorded for each day of the preceding week.
Breastfeeding difficulties	Information on breastfeeding difficulties documented since last visit at 2-weekly intervals at home.
<b>Infant morbidity</b>	
Diarrhoea	Daily information documented at weekly intervals at home, and at scheduled clinic visits. <sup>a</sup>
Respiratory illness	Daily information documented at weekly intervals at home, and at scheduled clinic visits.
Hospitalizations	Daily information documented at weekly intervals at home, and at scheduled clinic visits.
Other morbidity	Daily information documented at weekly intervals at home, and at scheduled clinic visits.
Drugs given (prescribed)	Daily information documented at weekly intervals at home, and at scheduled clinic visits.
Drugs given (non-prescribed)	Daily information documented at weekly intervals at home, and at scheduled clinic visits.
Clinical diagnosis	At scheduled clinic visits by study nurse.
Treatment given (if any)	At scheduled clinic visits by study nurse.
<b>Infant growth and development</b>	
Weight, length and head circumference	Measured on standardized equipment at each scheduled clinic visit. <sup>a</sup>
Development	Modified Denver Developmental assessment conducted at each scheduled clinic visit, including gross motor, fine motor/vision, social, language/hearing

(continued)

Table 3 Continued

Variables	Comments where applicable
<b>Maternal health</b>	
Weight and mid-upper arm circumference	Measured on standardized equipment at each scheduled clinic visit. <sup>a</sup>
Morbidity	Intervening morbidity documented at scheduled clinic visits.
Hospitalizations	Any hospitalizations documented at scheduled clinic visits.
Clinical diagnosis	If unwell, diagnosis recorded by nurse at scheduled clinic visits.
Contraception	Contraception used since last visit and at last sex documented at scheduled clinic visit.
<b>Laboratory markers</b>	
Maternal HIV antibody	Antenatal at booking visit, ELISA.
Maternal CD4 count	Antenatal and 6 months post-natal (September 2001–March 2003; FACScan, Becton Dickinson and Co., NJ, USA; thereafter Epics XL, Beckman Coulter, CA, USA).
Maternal viral load	6 months post-delivery.
Infant HIV status	Dried blood spot taken at each scheduled clinic visit. Quantitative HIV RNA assay (Nuclisens HIV-1 QT, Organon Teknika, Boxtel, the Netherlands, and Nuclisens EasyQ HIV-1, Biomerieux, Boxtel, the Netherlands) with a sensitivity of 80 copies of HIV RNA per millilitre of blood (equivalent to 1600 copies HIV RNA per 50 µl dried blood spot. <sup>39</sup>
Infant CD4 count	6 months of age.
Infant haemoglobin	Taken if clinically indicated.
Breastmilk samples	Sample from right and left breast taken from breastfeeding women at each scheduled clinic visit.

<sup>a</sup>Scheduled clinic visits: weeks 6, 10, 14, 18, 22, 26; then months 7, 8, 9, 12, 15, 18, 21, 24.

data with other studies, but also a pooled analysis of the VTS data with the West African cohort.<sup>25</sup>

All data were documented on study forms that were optically scanned (Teleform, Cardiff, San Diego, CA, USA), rather than being manually entered, which reduced human error in data entry.

Data were stored in a Microsoft SQL Server database with custom written applications.

## What has been found?

### Pregnancy outcomes

Compared with HIV-uninfected women, infected women are at a significantly increased risk of adverse pregnancy outcomes; adverse pregnancy outcome was independently associated with HIV infection, urban enrolment and non-hospital delivery, and with a CD4 count <200 cells/ml among HIV-infected women.<sup>26</sup>

### Infant feeding practices

After infant feeding counselling, the majority of HIV-infected women chose to breastfeed, and >80% initiated EBF from birth. Most HIV-infected women did not have the resources for safe replacement feeding and chose appropriately to exclusively

breastfeed.<sup>27–30</sup> EBF rates were high in both HIV-infected and -uninfected women, and counselling visits were strongly associated with adherence to cumulative EBF: the median duration of EBF was 177 and 175 days in HIV-negative and -positive women, respectively. Breast health problems were rare in all women. The cost of rolling out the breast-feeding intervention to the province of KwaZulu-Natal, South Africa, has been calculated.

### Post-natal HIV transmission

With regard to post-natal HIV transmission, Kaplan-Meier estimated risk of acquisition of infection between 4–6 weeks and 6 months of age was 4%.<sup>31</sup> Breastfed infants who also received solids were 11 times more likely to acquire infection than were EBF children; infants who at 12 weeks received both breastmilk and formula milk were twice as likely to be infected. The few HIV-infected women who experienced any serious breast health problem were approximately 3 times more likely to transmit HIV post-natally to their infant.

All publications can be found on the Africa Centre website: [www.africacentre.ac.za](http://www.africacentre.ac.za). The main study results have been disseminated widely, and contributed to revisions in the World Health Organization guidelines on HIV and infant feeding made after a

consultation in October 2006.<sup>32</sup> EBF for 6 months is now recommended for HIV-infected mothers unless formula feeds can be provided in a safe, sustainable and feasible manner.

Further analyses are in progress to examine infant growth, morbidity and development and maternal morbidity related to different feeding modalities and HIV status. There is increasing evidence that HIV exposed, but uninfected children, are at higher risk of morbidity, poor growth and development, compared with unexposed children, but there are few cohorts with such detailed data on daily feeding and morbidity patterns, and with a large control group of children born to HIV-uninfected women, which can explore these issues.

We have also been granted ethics permission to link the children from the VTS to the Demographic Surveillance System (DSS). Whilst the VTS data provides a rich set of antenatal and early life data, it has limited data on household composition, household income, migration, family deaths, other household shocks and subsequent pregnancies in the study mother, all factors which impact on child growth and development between 6 and 24 months of age. The latter are all collected routinely by the DSS and there have been three rounds of data collection during the period of 2-year follow-up for each enrolled VTS mother. Linkage will facilitate novel analyses on the impact of family support, household structure and location on child growth and development and life course studies of the role of early life antecedents in outcomes in later childhood and adulthood.

## What are the main strengths and weaknesses of the study?

The study design was intensely debated—whether it should be a randomized trial or cohort study. After considered thought, and taking into account opinions of experts, we decided it would be unethical in this setting to randomize HIV-infected women to EBF or EFF. First, feeding practice is a personal choice, and a woman's right. A woman is more likely to successfully adhere to a feeding option if she feels committed and convinced about her chosen option. We followed WHO/UNAIDS guidelines on infant feeding counselling for HIV-positive women, helping women to make appropriate choices according to their situations.<sup>24</sup> Secondly, given the socio-demographic profile of the community, randomizing women to formula feeding would likely have resulted in significant morbidity and mortality risks.<sup>6,7,33,34</sup> Thirdly, the post-natal HIV transmission risk in EFF infants is known to be zero. We could, therefore, compare any transmission found in EBF infants, or MBF, against zero.

A cohort study provides a realistic life setting for infant feeding in the context of HIV. We showed that high rates of EBF were possible amongst women

choosing this option.<sup>28</sup> Women who chose to formula feed in general made this choice appropriately. To our knowledge, there has only been one previous randomized study, from Kenya, examining infant feeding and HIV transmission. In that study, there was 70% compliance to feeding mode in the formula feeding arm, with 30% of the women practising mixed feeding, with more loss to follow-up in the formula feeding than the breastfeeding arm.<sup>35</sup>

## Strengths

Previous studies were not designed to examine HIV transmission by feeding mode; the primary aim of this study was to determine the effect of infant feeding practices on HIV infection rates of infants at 6 and 22 weeks of age. A further important strength of this study is the large sample size of both HIV-infected and -uninfected women, and the high proportion of women who succeeded to exclusively breastfeed. There were concerns at the start of the study, based on results of pilot work,<sup>36</sup> that it would be extremely difficult to support women to exclusively breastfeed in a society where mixed feeding was the norm from soon after birth.

Data on infant feeding were meticulously collected. Previous studies had relied on cross-sectional surveys of infant feeding, at various time points (e.g. when the child was 3 and 6 months of age). In these surveys, mothers were asked what foods and drinks they have given to their child over the past 24 hours ('24 hour recall') or what they have given since birth until the present time. Both methods have problems, and are likely to misclassify cumulative feeding practices.<sup>37</sup> The WHO has well-defined definitions of infant feeding,<sup>23,24</sup> which were used in the study, and enabled comparisons with other studies. Furthermore, we used a separate group of field workers to collect the detailed feeding data (field monitors) from those who supported breastfeeding (breastfeeding counsellors), to minimize bias in mothers' reported practices.

Infants were tested for HIV at monthly intervals, allowing timing of HIV infection, in those infants who did sero-convert, to within a month in the first 9 months of life.

## Weaknesses

As this study was designed to examine the effect of EBF on post-natal transmission of HIV, we went to extraordinary lengths to promote and support EBF for women choosing this feeding option. At the start of the study, we knew from previous pilot work that EBF was rare in this population, and that MBF was the norm in our area.<sup>36</sup> Promotion of EBF was so successful that there were few women who mixed fed, and this group was too small for multivariate

regression analyses, or to address some of the original objectives (e.g. the cumulative incidence of MTCT in MBF infants or the determinants of transmission in MBF infants adjusting for exposure factors, e.g. type and age of introduction of other food/milk—see Study Objectives section). In retrospect, we could have randomized the support given to breastfeeding women, with some receiving half the number of home visits by the breastfeeding counsellors as others. We could have then modelled more accurately the effect of the number of visits on adherence to breastfeeding, and provided helpful guidance to programme and policy makers.

In hindsight, it would have been interesting and useful to have collected information on the partnership arrangements of the women, and whether they were married, had a current partner or were resident with the father of the child; and also whether the women had disclosed their HIV status to anyone, and if so, to whom. This would have enabled exploring what support there is available within the home and it would have been interesting to examine adherence to EBF in relation to disclosure of HIV, and presence in the home of the child's father.

## Can I get hold of the data? Where can I find out more?

The VTS SQL database is well documented (including definition of variables and the questionnaires used for data collection). Information can be obtained from the Africa Centre website ([www.africacentre.ac.za](http://www.africacentre.ac.za)). Requests to use data require the completion of a data use request form, which is accompanied by an analysis plan. For further information regarding data use please contact [rbland@africacentre.ac.za](mailto:rbland@africacentre.ac.za)

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**Conflict of interest:** None declared.

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