

**Patterns and predictors of exclusive breastfeeding
duration among women living with HIV in Cape Town,
South Africa**

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0. PREAMBLE

DECLARATION**MPH Mini Dissertation**

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Abstract

Breastmilk is the optimal source of infant nutrition, with exclusive breastfeeding provided until 4-6 months of age followed by the continuation of breastfeeding alongside nutritionally adequate complementary feeding. Breastmilk provides strong protection against infectious disease morbidity and mortality, particularly important for infants in low resources settings. However, some low resource settings such as South Africa have high prevalence of human immunodeficiency virus (HIV) infection, also among pregnant women. Over the last two decades, there have been ongoing debate regarding balancing the benefits of breastmilk and the risks of mother to child transmission of HIV (MTCT) through breastmilk. However, numerous large studies have shown that triple antiretroviral therapy (ART) substantially reduces the risk of MTCT during pregnancy and breastfeeding to less than 1%. The overwhelming evidence of maternal ART as optimal PMTCT, coupled with rapidly expanding global accessibility of ART, have resulted in HIV treatment guidelines now recommending universal, lifelong ART for all women ("Option B+"). During this time, accumulated evidence of the substantial mortality and morbidity risks of replacement feeding for children of HIV-infected mothers in resource limited settings, resulted in HIV infant feeding guideline shifts towards breastfeeding promotion (exclusive breastfeeding for 4-6 months, with continued breastfeeding alongside complementary feeding) as the optimal infant feeding choice in most settings. Following many years of pro-replacement feeding guidelines, South Africa in 2010 adopted breastfeeding as the new national infant feeding of choice for both HIV-infected and -uninfected mothers. In 2013, South Africa changed their national ART guidelines to Option B+ for PMTCT. However, since these dramatic policy shifts, there remain limited data on the breastfeeding practices of HIV-infected women under Option B+. A literature review completed on the 14th January 2017 identified 76

articles. However, only 8 studies (11 articles) fit the inclusion criteria and were included in the review. Of those that were included, all but one study took place prior to 2013 and the Option B+ and promotion of EBF guideline change. Prior to the shift, estimates of EBF from one cohort study reported 26% at 3 months and a median duration of 1 month. A single study that took place after 2013 provided estimates of EBF up to 6-week follow-up being 82%. However, the sample size in this study was very small, did not provide estimates for the entire 6 month duration of EBF, and South Africa had not yet implemented Option B+ at the time of their study. Our review indicated a need for updated estimates of EBF under the current policy and recommendation in South Africa.

The aim of this study was to examine early infant feeding practices among HIV-infected women in South Africa, with a specific focus on the first 6 months of life. This was a longitudinal analysis of data from the Maternal and Child Health AntiRetroviral Therapy (MCH-ART) study which took place between 2013 and 2015 in a peri-urban community in Cape Town, South Africa. MCH-ART study participants were HIV-infected pregnant women attending their first antenatal clinic, who were initiating ART and provided informed consent; and they were followed up through 18 months post-delivery. Infant feeding data were collected through clinical record forms based on maternal interview.

We found that of the 471 women enrolled for postnatal follow-up, 429 (91%) ever EBF. The median duration of EBF was 1.5 months (interquartile range, IQR 0.3-5.4); only 115/471 (24%) infants were EBF for 4 months or longer. Within the first week of birth, 8% of women reported some breast health issues; this figure increased to 22% of all women by 6 weeks. Lactation issues were common in our study sample and were predictive of suboptimal EBF.

Taken together, the literature review illustrates the lack of current estimates of EBF among HIV-infected women receiving lifelong ART – while the results presented illustrates multiple lactation issues and perseverance of suboptimal EBF practices.

For the children of HIV-infected women to benefit optimally from the current HIV and infant feeding guidelines, programmatic interventions are urgently needed to address lactation problems and support women at risk of suboptimal breastfeeding practices.

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A. RESEARCH PROTOCOL

Background

Knowledge regarding the beneficial and protective properties of breastfeeding on infants and adverse effects related to suboptimal breastfeeding are widely accepted and readily available. Newly released World Health Organization (WHO) recommendations reiterate that “mothers should exclusively breastfeed (EBF) for the first six months, introduce appropriate complementary feeds and continue breastfeeding until 24 months or beyond because of the many benefits for both mother and child” [1]. Breastfeeding in general and EBF in particular are key factors in reducing childhood mortality,[2] partly due to the provision of maternal antibodies that help protect infants from common childhood illnesses such as diarrhea and pneumonia [3]. A recent systematic review found that EBF infants were at an incrementally lower risk of all-cause mortality compared to infants who were predominantly, partially, or non-breastfed with the greatest risks observed in the latter two groups [4]. Breast milk is readily available and economical compared to formula milk, and further offers maternal health advantages including reductions in stress, risk of postpartum depression and some types of cancer [5]. If infants are EBF for the first 6 months, more than 800,000 neonatal deaths could be prevented each year [6]. EBF provides all the nutrients infants need during the first 6 months of life [7]. Though EBF is the ideal feeding strategy for infants, the estimates of EBF remains low globally. According to the United Nations Children’s Emergency Fund (UNICEF), global prevalence of EBF remains low at 43% [8]. South Africa is no exception. A cross-sectional study involving the general South African population, sampling from a total of 40 health facilities in four provinces, described a 12% prevalence of EBF until 6 months; 40% of mothers had stopped all breastfeeding by one month [9].

Breastfeeding duration and the prevalence of EBF are likely to be particularly low among HIV-infected South African women. Following years of controversy regarding the optimal infant feeding choices for HIV-infected women and their uninfected children, the newly released WHO guideline for HIV infant feeding in the context of maternal triple antiretroviral therapy (ART) promotes breastfeeding for settings with high rates of childhood mortality and morbidity due to infectious causes – such as most of sub-Saharan Africa [1]. This aligns HIV infant feeding guidelines to those for the general population. Specifically, HIV-infected women should EBF for the first four to six months, then introduce complementary foods, and continue to breastfeed until at least 12 months [1].

Early in the HIV epidemic in Africa, breastfeeding was controversial due to the risk of maternal to child transmission (MTCT) of HIV via breast milk. Indeed prior to 2010, South Africa distributed free formula milk for infants up to six months at public health facilities as part of the Prevention of Mother-to-Child transmission (PMTCT) strategy [10]. However, in response to the WHO infant feeding recommendations in 2010 [11], South Africa changed the infant feeding guidelines to recommend breastfeeding for all HIV-infected mothers [12]. Furthermore, building on substantial evidence highlighting the benefits of breastfeeding among HIV-infected women and the substantial reduction in MTCT risk in the context of universal maternal ART, the WHO since 2013 recommended lifelong antiretroviral therapy (ART) to all pregnant and breastfeeding women, with the promotion of breastfeeding in areas with high risk of childhood infectious diseases, such as South Africa [13]. In response to these guideline changes, the South Africa National Department of Health withdrew the

free formula milk program and adopted breastfeeding as the optimal infant feeding strategy [14].

Yet before these guideline changes, data from a South African randomized intervention study found that 40% of HIV-infected women had stopped all breastfeeding by 12 weeks postpartum despite breastfeeding support [14]. Reasons for early cessation of breastfeeding generally and EBF specifically differ substantially between individuals and settings. These can include the understanding of the term “exclusive” breastfeeding, cultural practices, and infants who cry or cannot sleep at night [15]. There are many possible reasons for breastfeeding mothers to switch to formula feeding or to start complementary feeding before six months. These poor EBF practices could severely impact child health and survival.

Optimal breastfeeding with maternal ART is an important aspect of PMTCT strategies that seek to promote HIV-free survival in areas with high infectious mortality and morbidity in childhood, such as South Africa [1]. In addition to poor general uptake of breastfeeding and EBF in South Africa, additional challenges are likely to exist following years of conflicting feeding advice [16]. To truly optimize HIV-free survival among the children of HIV-infected women, current breastfeeding practices under the newly implemented guidelines need to be established. In addition, risk factors for early cessation of breastfeeding and EBF need to be identified to aid the urgently needed development of interventions that improve the rates of EBF among both HIV-infected and HIV-uninfected South African women.

Study Aim

The main purpose of this study is to investigate the prevalence and duration of EBF among HIV-infected women that have initiated ART as part of PMTCT care at the Gugulethu Midwife Obstetric Unit (MOU) in Cape Town, South Africa.

The study has two main objectives:

OBJECTIVE 1: To describe the prevalence and duration of EBF among HIV-infected women receiving ART in the postnatal period

OBJECTIVE 2: Identify potential maternal and environmental factors that contribute to early cessation of EBF among HIV-infected women receiving ART in the postnatal period

Identifying and investigating indicators and predictors will allow public health workers to develop area specific programmatic interventions to improve duration of EBF among HIV-infected women in peri-urban South Africa.

Methodology

Study design

This study will be a secondary data analysis using data collected prospectively from the maternal and child health antiretroviral therapy (MCH-ART) cohort study (UCT HREC reference 451/2012, Appendix A), which enrolled participants from March 2013 to June 2014 and followed up participants for 18 months. The study took place in a large public sector primary healthcare facility in Cape Town, South Africa. The healthcare facility is surrounded by high levels of poverty and unemployment, and high HIV prevalence [17]. The MCH-ART study used both observational and experimental components. The MCH-ART study had three interrelated phases: Phase 1 was a cross sectional evaluation of HIV-infected women at their first antenatal visit at Gugulethu midwife obstetrics unit (MOU); Phase 2 was an observational cohort of women taken from Phase 1 that were eligible for ART initiation; and Phase 3 was a randomised trial of two different strategies for delivering ART to postpartum women. Phase 1 consecutively enrolled all HIV-infected pregnant

women attending their first antenatal visit in order to characterized the health status of HIV-infected pregnant women seeking antenatal care at Gugulethu MOU [17]. Phase 2 included all of Phase 1 women who were eligible for ART initiation, followed up from their second antenatal clinic visit through their first postpartum clinic visit (conducted within 7 days postpartum) to provide detailed description of ART initiation and antenatal follow-up [17]. Women were approached at their last Phase 2 visit, to participate in Phase 3. Phase 3 was a randomised trial of two different strategies for delivering ART to women during the postpartum period: referral to the general adult ART services from 4-6 weeks postpartum (the local standard of care) or continued receipt of ART in the antenatal clinic [17]. Women in Phase 3 returned for 6 additional study visits at 6 weeks, 3, 6, 9, 12, and 18 months postpartum [17].

The main aim of the MCH-ART study was to evaluate two different strategies for delivering HIV care and treatment services during the postpartum period. Data for the current study will come from baseline and longitudinal interview questionnaires conducted during pregnancy and in the early postpartum period until age of 6 months. The infant feeding questionnaire was based on a validated infant feeding questionnaire from other PMTCT studies. Questionnaires included in this study were those concerning infant feeding, maternal demographics and general health, and maternal mental health.

Study population

Inclusion criteria for MCH-ART included a minimum age of 18 year, maternal HIV infection, antenatal care sought at the Gugulethu MOU (Appendix B). The study population will be participants from Phases 2 and 3 of the MCH-ART study; inclusion criteria are limited to women in Phase 2 who presented with their infants for study follow-up before the age of 6

months. All those who participated in phase 3 postnatal follow up were included in this analysis.

Data collection methods

Data have been collected through the MCH-ART clinical record forms (CRFs). All MCH-ART CRFs were translated into isiXhosa and back translated to English by trained Xhosa-speaking staff. Study visits included interviewer administered questionnaires in private rooms and venipuncture for viral load testing [17]. The measure of EBF will be calculated from maternal interview data provided on the infant feeding CRF collected during visits up to 6 months (Appendix C and Appendix D).

Data safety and monitoring

As per MCH-ART protocol, participant data are anonymous, with only participant identification numbers that were systematically assigned; data were captured without personal information attached to the files. Database files are kept on a password encrypted external hard drive, locked in a safe at the study site and at the office at the University of Cape Town.

Data analysis

All statistical will be done using STATA SE version 12.0 (Stata Corporation, College Station, Texas). Descriptive statistics will be used to investigate the frequency of overall breastfeeding cessation practices with bar graphs, stacked column bar graphs, and tables. To test the relationship between duration of EBF and different maternal characteristics that may affect cessation time, a logistic regression model will be implemented using a combined

binary indicator for EBF of <4 months and \geq 4 months. All analysis will be conducted by supervisor and summarized and interpreted by the student.

Ethical Considerations

Description of risks and benefits

The Columbia University Medical Center Institutional Review Board (CUMC-IRB) and the University Of Cape Town Faculty Of Health Services Research Ethics Committee (UCT-HREC) have approved the MCH-ART study (Appendix A). This secondary analysis will only go through the UCT-HREC (Appendix E). There are no direct risks or benefits for this study because there is no direct contact, laboratory work, or follow up will be done directly with study participants; only secondary analysis of the de-identified data, as has already been collected.

Informed consent process

Participants for this study were consented through the MCH-ART consent process (Appendix F and Appendix G). The informed consent process was done with an interviewer in the local language (isiXhosa) with a standardized form. The standardized forms were translated English to isiXhosa and back to English by two different isiXhosa speakers. During the informed consent process, participants were educated on the study purpose and procedures and were given an opportunity to ask the interviewer questions regarding the study as well as their role. Participation was strictly voluntary. For the purposes of this study, no extra consent is needed.

Privacy and confidentiality

For this analysis, there will be no contact with participants.

List of abbreviations

EBF: exclusive breastfeeding, exclusively breastfed

WHO: World Health Organization

HIV: human immunodeficiency virus

ART: antiretroviral therapy

MCH-ART: maternal and child health antiretroviral therapy cohort study

PMTCT: prevent of mother-to-child transmission

EPDS: Edinburgh Postnatal Depression Scale

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B. LITERATURE REVIEW

INTRODUCTION

In low-and middle-income countries (LMIC) where resources are limited and the burden of disease is high, infant mortality rates continue to be high. Since replacement feeding is not a safe option for most; benefits of breastfeeding, especially exclusively breastfeeding (EBF), are crucial for health and survival of both mother and infant [1]. The greatest child survival and health benefits of breastfeeding are seen among children who are EBF for the first 4-6 months of life, with breastfeeding continued thereafter along with nutritionally adequate complementary foods [2].

However, 2016 global rates of EBF remains at a low 43% according to the United Nations Children's Emergency Fund (UNICEF) [3]. In areas of high childhood mortality risks due to infectious causes, such as South Africa, the benefits of breastfeeding and EBF are most evident yet EBF is not practiced widely [2].

In the early years of the HIV pandemic, HIV-infected women were discouraged from breastfeeding to avoid mother-to-infant transmission of HIV (MTCT) [4]. In the past two decades there have been multiple drastic HIV infant feeding guideline changes [1, 5, 6], causing much confusion among health workers, women and their families [7-11].

With ample evidence that triple antiretroviral therapy (ART) minimizes HIV transmission through breastfeeding [12-16], the World Health Organization (WHO) now recommends that all pregnant women be on life-long ART to achieve HIV viral suppression, thus preventing new paediatric infections (Option B+) [17]. Alongside these recommendations, the WHO HIV infant feeding guidelines have been updated to recommend breastfeeding as best infant feeding choice for HIV-infected women from settings with high infant mortality;

the recommendations are to EBF for the first six months of life, then continue breastfeeding thereafter along with providing nutritionally adequate complementary foods [1].

South Africa has adopted Option B+ PMTCT approaches in 2015, and since 2010 promote breastfeeding (with EBF until 6 months) as the best national infant feeding choice for both HIV-uninfected and HIV-infected women [18]. The new, uniform infant feeding guidelines which align recommendations for both HIV-infected and uninfected women, may improve the consistency of breastfeeding encouragement and support across health-care settings and communities. In turn, increased uptake of breastfeeding may positively impact rates of EBF. In this new era of prevention of mother-to-child transmission (PMTCT) of HIV (with universal maternal ART) and infant feeding (with universal promotion of breastfeeding) in South Africa, previous estimates of EBF are obsolete. The improved and now uniform infant feeding guidelines in the context of widespread maternal viral suppression and thus low risk of breastfeeding-related MTCT may improve EBF rates – simultaneously, this combination might not be sufficient to bring successful breastfeeding practices to the PMTCT setting. It is therefore imperative that estimates of EBF are updated and that potential risk factors that may prevent uptake of and/or adherence to EBF practices in the current PMTCT era be identified. This can facilitate evaluation of the guideline's implementation success, and allow the development of targeted interventions so that all infants can fully benefit from the new national strategies.

Objectives

The main objective of this review is to evaluate changes in estimates of EBF prevalence, duration and determinants among HIV-infected South African women over the last 20 years.

In particular, to evaluate if there have been improvements in these estimates under current recommendations of universal ART with encouragement of breastfeeding.

METHODOLOGY

Search strategy

This literature review aims to identify the prevalence and duration of, and factors associated with, EBF in South Africa. The literature search was done (final search in Pubmed/MEDLINE, on 14 January 2017) restricted to English language without restriction on publication date.

The search was narrowed down based on study population of interest (HIV-infected women), geographic location (South Africa), and whether any EBF estimates were presented (at least one of prevalence, duration, or potential predictors of EBF). The search terms were combined as (((“breastfeeding” OR “breastfed” OR “breastfeed” OR “breast feed”) AND (“exclusive” OR “exclusively”)) AND (((“HIV” AND (“positive” OR “infected”)) AND (“women” OR “mother”) AND “South Africa”)) (Figure 1). Only original research studies in South Africa that provided estimates of EBF prevalence, duration, or predictors of cessation or uptake among HIV-infected women were included in this literature review, as shown in Figure 1 and summarized in Table 1. Excluded studies with reasons for exclusion are shown in Table 2. A single author conducted the search and extracted the data under supervision of a senior author.

Definition of exclusive breastfeeding

The WHO definition of EBF most commonly used globally is “only breast milk without any other liquids or solids, not even water, except for oral rehydration solution or drops or syrups of vitamins, minerals or medicines” [1]. Most of the studies included in this review

followed the WHO definition of EBF, with the exception of the Vertical Transmission Study (VTS) which “allowed water or formula milk to be given for up to three days” [19].

RESULTS

The search strategy yielded a total of 76 articles on EBF among HIV-infected women in South Africa. Of these, 58 records were excluded (Figure 1 and Table 2) following screening of titles and abstracts. Eighteen full text articles were screened, of which 7 were excluded (no desired estimates, n=2; review article, n=2; did not provide separate indicators of SA EBF, n=1; no differentiation between HIV-infected or uninfected women, n=2). Eleven publications are included in the review, from 8 studies. These are summarized in Table 1.

Prevalence of exclusive breastfeeding among HIV-infected women in South Africa

Analysis from the Vitamin A study (randomized controlled trial of maternal vitamin A supplementation to HIV-infected pregnant women, South Africa 1995-1998; no access to ART), assessed MTCT risk by feeding practices from delivery to 3 months [4]. Among 391 breastfeeding women, 191 (48.8%) EBF until one month then dropped to 103 (26.3%) EBF at three months [4]. The Vertical Transmission Study (VTS) was a large non-randomized intervention conducted in KwaZulu-Natal from 2001-2005; although the majority of HIV-infected women and infants received single-dose Nevirapine for PMTCT, a few women enrolled after 2004 received ART for severe HIV-related disease. The VTS reported much higher prevalence of EBF among HIV-infected mothers – over 80% EBF at 1 month and 60% at 5.5 months [20]; they also found that the majority of women started EBF at birth (83%) [19]. Notably, the intervention for this study was intensive breastfeeding counselling and support throughout the early postpartum period. An observational cohort study of selected

PMTCT sites in South Africa conducted between 2002 and 2003, reported EBF prevalence of 42% at 3 weeks [21]. In 2009, a cross sectional survey of 815 HIV-infected women, with a mean infant age of 4.5 months, found that 35.6% of women were EBF [22]. The prevalence of EBF among the women who participated in the cross-sectional survey had infants anywhere between three and six months old and difficult to determine age of infants when EBF ceased. Estimates of EBF have generally been low, except where intensive feeding counselling and support were provided in the VTS intervention.

Duration of exclusive breastfeeding among HIV-infected women in South Africa

In the Vitamin A trial, median duration of EBF was only one month [4], and the probability of still EBF at one month was only 0.49; 0.29 at 3 months, and only 0.04 at 6 months [23].

Similarly, in the observational study by Goga et al., it was reported that 130 women were EBF (42%) of the 309 women practicing any breastfeeding at three weeks, where-after the estimates dropped to 30% by 7 weeks and only 18% at 12 weeks [21]. Per contra, a report from the VTS by Coovadia et al. reported 83% of women EBF at birth, declining to 82% at 6 weeks, 67% for at least 3 months, then only 40% EBF for 6 months with a median duration of EBF estimated at 159 days (IQR 122-174)[19]. A later analysis from the VTS demonstrated that among the 851 of 941 (90.4%) infants of HIV-infected women who had at least one day of EBF, the median duration of EBF was 175 days (IQR 137-180), or just under 6 months [20].

Another VTS analysis by Rollins et al. reported similar estimates up to 3 months; 81.4% of HIV-infected women were still EBF at 6-8 weeks, and 61.8% still EBF at 3-4 months [24] but they did not report estimates at 6 months. As can be seen from these findings of studies conducted prior to the introduction of current PMTCT guidelines, median duration of EBF varied from 3 weeks to 5.5 months in South Africa, bearing in mind that the 5.5 month

duration reported by the VTS study was within an intervention cohort providing comprehensive breastfeeding counselling and support.

Risk factors for suboptimal feeding

HIV-infected mothers face many challenges of adherence. Different studies in South Africa have identified various different factors that potentially affect EBF duration. Socioeconomic factors are often explored in relation to health outcomes and have commonly been associated with EBF. Having electricity appears to reduce the prevalence of EBF: hazard for cessation of EBF among VTS cohort participants [20] was increased by 60% (adjusted Hazard Ratio, AHR 1.64 95% CI 1.24-2.17). Similar results were found in the Vitamin A study [25]. This is probably because women who have electricity have replacement feeding as an option because of the ease of preparation and refrigeration. The analysis of the Vitamin A study, at 14 weeks, reported fewer (57%) women who EBF had electricity compared to other groups (77%) combined [25] and the analysis of the VTS study also found that women who had electricity, gas, or paraffin (AOR 1.69 95%CI 1.16-2.46) were less likely to adhere to EBF intentions [26]. These findings suggest that women without electricity, gas or paraffin are more likely to EBF than those who do have electricity. This might be because women who have electricity, gas, or paraffin are able to easily boil water and also have refrigeration; they are able to easily prepare and store the replacement milk. They seem to appear of higher socioeconomic status and likely are also able to more easily afford to buy infant formula. While most studies found an association between having electricity has an effect on EBF, Coutsooudis et al. found that the duration of EBF was not consistently related to the socioeconomic indicators they investigated [4]. It is possible that the socioeconomic indicators they investigated were different than the ones the other studies used, or more

likely, that the extensive breastfeeding counselling and support negated the use of replacement feeding among those of higher socio-economic situations.

Another risk factor that has emerged is maternal mental health. A retrospective cohort study found that prenatally depressed women were less likely to EBF at 6 weeks (adjusted odds ratio, AOR 0.68 95% CI 0.49-0.95) although EBF practices appeared not to be influenced by partum depression [27]. However, this study only looked at EBF until 6 weeks, not through six months of EBF, thus the effects of postpartum depression on later estimates of EBF may have been underestimated.

An important risk factor for early EBF cessation is breast health concerns. An analysis of the VTS study between 2001 and 2003, which investigated the HIV transmission rate by infant feeding practices while providing intensive feeding support and home visits, found that reported breast problems can affect duration of EBF. The study reported breast health to be a major determinant of EBF cessation (AHR 4.12 95% CI 2.50-6.80) and that women who practice EBF experienced fewer breast health problems [20]. They also reported having feeding difficulties in the previous two weeks (AHR 1.75 95% CI 1.42-2.16) as increasing the hazard of EBF cessation [20].

Many different risk factors emerged from these various studies in South Africa that may have affected prevalence and/or duration of EBF, some were similar while others were contradictory. However, there is consensus that HIV-infected women face many different challenges and factors that affect their infant feeding choices as well as duration of breastfeeding practices, although intensive breastfeeding counselling and support appears to enable women to surmount many of the obstacles to successful EBF.

Possible ways to fill in the gaps

There have been numerous studies that have investigated intervention strategies that have shown to increase or improve prevalence and/or duration of EBF in South Africa. In the PMTCT intervention cohort of scheduled home visits, Bland et al found that at one month, HIV+ women who were part of the intervention group that received the scheduled number of home visits were more than twice as likely to still be EBF at that time (AOR 2.29; 95%CI: 1.60–3.28) and again at two and four months, especially in HIV-infected women [20]. A more recent cluster randomized intervention trial by Ijumba et al. evaluated an integrated PMTCT package that included two visits during pregnancy and five postnatal home visits. In this study, the intervention was associated with doubling of exclusive breastfeeding (OR 2.29, 95%CI 1.8-2.92 at 12 weeks postpartum [28].

It has been emphasized that better counselling support of EBF can improve EBF rates when counsellors are well informed [28]. In order for HIV-exposed infants to experience the full benefits of EBF through the new guidelines of Option B+, targeted intervention strategies have shown to improve EBF adherence and need to be developed and implemented in Option B+ PMTCT settings as soon as possible.

Exclusive breastfeeding in Africa

As these various studies in South Africa have illustrated, the prevalence of EBF among HIV-infected women is extremely low in the absence of intensive breastfeeding counselling and support, and the duration is unacceptably short. However, low EBF rates among HIV-infected women is not limited to South Africa; other countries in Africa, like Botswana, Zambia, Tanzania, Burkina Faso, Uganda, and Kenya, also experience similarly low

prevalence and short duration of EBF among HIV-infected women. A cross-sectional population-based study from Tanzania reported that the prevalence of EBF was 88.3% at one month, 65.5% at three months, and only 20.7% by 6 months [29]. An analysis of the MASHI study in Botswana, a clinical PMTCT trial, found that by 5 months, there was only 17.5% of women still EBF [30]. In the Six Week Extended-Dose Nevirapine (SWEN) study, which analysed data from three randomized control trial from Ethiopia, India, and Uganda, reported a 28% EBF prevalence at six months in all three countries [31]. A study completed in an urban informal settlement in Nairobi, Kenya reported only 2% EBF at six months [32]. The median duration of EBF by study site in the multi-country Kesho Bora study, comparing different antiretroviral interventions in the prevention of MTCT in Burkina Faso, Kenya, and South Africa, was 3.4 months in Burkina Faso, 1.4 and 1.8 months in two cities in Kenya [33]. They reported the median duration of EBF in South Africa was 5.3 months, however, only 65% of the combined South African cohorts were ever breastfeeding [33]. Comparable to the estimates from Kenya, the median duration for HIV-infected women in Zambia, during the early 2000s when Nevirapine was given during the time of delivery to decrease MTCT, was 1.5 weeks [34]. There are many possible factors that contribute to the prevailing low prevalence and duration of EBF in South Africa as well as Africa.

Many common risk factors for early EBF cessation have been identified across Africa. In the cross-sectional study in Zambia, women were more likely to EBF if they have adequate knowledge of EBF (AOR 5.4 95%CI 2.5, 11.6), delivered in health facilities (AOR 3.0 95% CI 1.7, 5.4), or not experienced breast health problems (AOR 6.6 95%CI 3.2, 13.6) [35]. Similarly to findings in South Africa, women in Western Tanzania with breast health problems in the first 6 months were 86% less likely to EBF compared to those that did not experience breast

health problems (OR 0.14 95% CI 0.07, 0.26) [35]. Another study in Tanzania identified that women are more likely to EBF up to six months if she receives advice on breastfeeding after delivery (AOR 2.6 95% CI 1.5, 4.6) [29]. A cross-sectional study in Ethiopia also found that women who receive antenatal and postnatal counselling were more likely to EBF than those who do not [36]. Mgongo et al. also reported that single women (AOR 0.4 95% CI 0.2, 0.9) and women who drink alcohol (AOR 0.4 95% CI 0.3, 0.7) are less likely to EBF up to six months compared to married/cohabiting women and those who do not drink alcohol [29]. A systematic review and meta-analysis of breastfeeding and maternal health outcomes found that there is not a clear and consistent association between breastfeeding and maternal depression [37]; this might however not be applicable to all settings and situations, as evidenced by recent South African data from Tuthill et al., which reported that prenatally depressed women were less likely to breastfeed at 6 weeks [27].

Although EBF practices appear to be suboptimal in many settings in sub-Saharan Africa, it is not ubiquitous. For example, EBF is a common practice in Malawi. It has been postulated that EBF is not stigmatized because it is widely promoted and accepted within the general population [38], unlike the rest of SSA and specifically in South Africa. The Breastfeeding, Antiretroviral, and Nutrition (BAN) study in Malawi, which was a randomized control trial examining an antiretroviral and nutritional intervention among breastfeeding HIV-infected women, reported a high adherence rate of EBF at 24 weeks in all three groups: 90% in the infant-Nevirapine group, 89% for the maternal-antiretroviral, and 88% in the control group [39]. Women in the BAN study were individually advised on EBF and received group counselling sessions by the WHO standardized protocol on breastfeeding training and counselling [39]. Although EBF prevalence and duration remains largely undesirable across

most of Africa, the situation in Malawi does provide insight and optimism, suggesting that even in low-resource settings, it is possible to increase EBF rates.

The various studies and data illustrated the dire situation of EBF in Africa which led to the present WHO recommendation of Option B+. However limited data exists for current estimates. Similarly to most other countries in Africa, South African EBF prevalence and duration among HIV-infected women were low and risk factors diverse, prior to the 2010 shift in infant feeding practices and the 2013 shift towards ART-based PMTCT strategies.

CONCLUSION

Since the drastic shifts in feeding recommendations, data on EBF patterns among HIV-infected women under the new PMTCT and ART guidelines are limited, in Africa and specifically in South Africa. Though HIV-infected women on ART are able and encouraged to breastfeed, many still do not. In examining the literature on current EBF estimates in South Africa, it can be concluded that current data, since the policy shift, is scarce. The data that are available are outdated and reported mixed results. Furthermore, risk factors for suboptimal infant feeding - particularly lack of or early cessation of EBF – among HIV-infected women and their infants are unknown in the current era of PMTCT. Data are urgently needed to guide potential interventions in this setting and this population. Quantitative studies are necessary to provide estimates of current EBF rates while qualitative studies could further identify social, economic, and cultural factors that impede prevalence and duration of EBF.

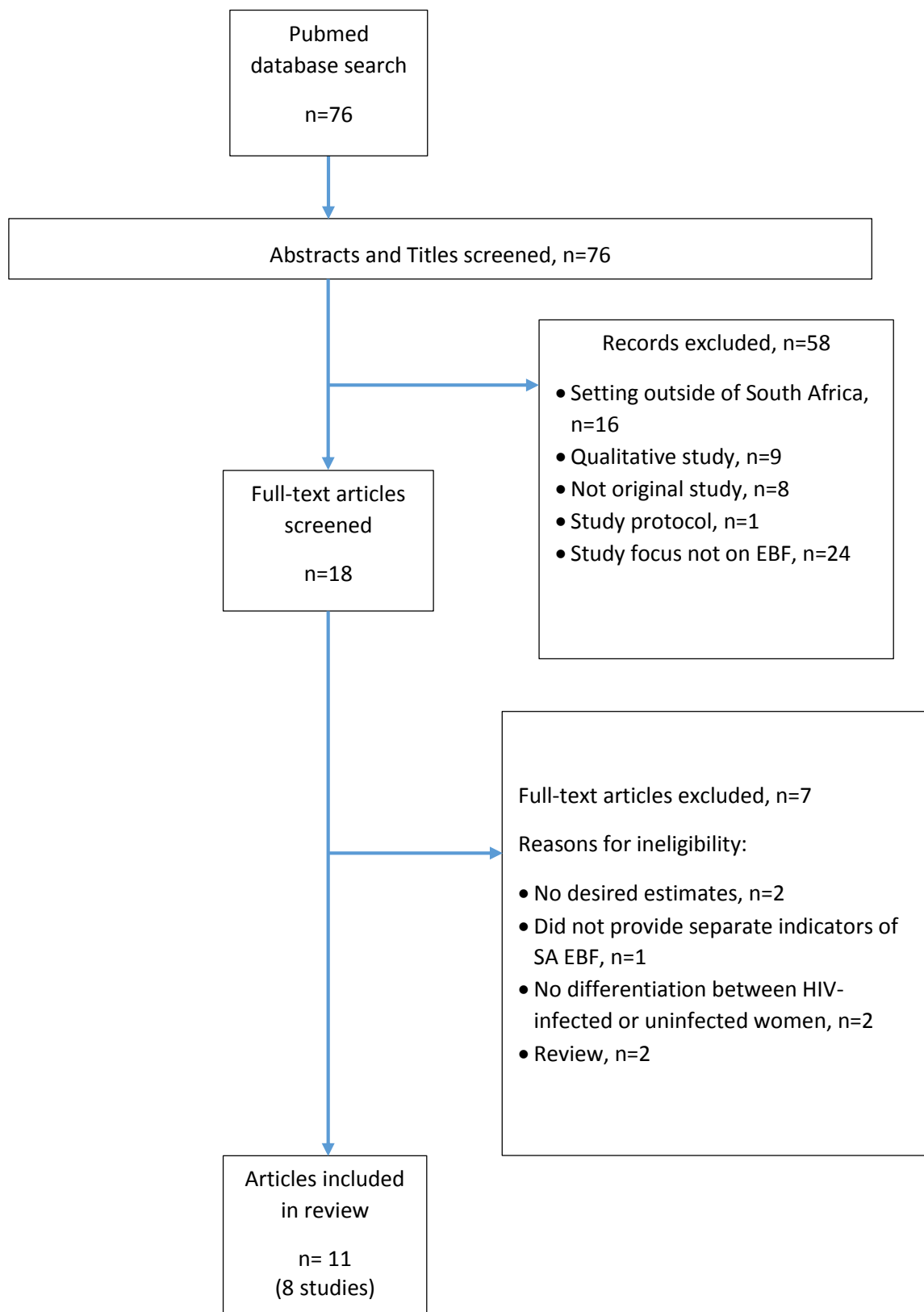
Figure 1. Flowchart of study selection process

Table 1. Summary of included articles

First author, publication year	Time of study	Type of study	Setting	Participants	PMTCT practices	Prevalence of EBF initiation after birth	Average duration of EBF	Factors associated with BF and EBF	Other findings/comment
Coutsoudis 1999 ¹	Jul 1995- Apr 1998	Prospective cohort from PMTCT Vitamin A RCT. This paper presented preliminary results for transmission rates between different feeding practices at 3 month	Antenatal clinics of 1 tertiary hospital and 1 semi-private hospital in Durban, Kwa-Zulu Natal (KZN) South Africa	549 HIV+ women and their singleton infants Mean age 27 (SD 4.8)	No use of ARVs. Infant feeding counselling, informed maternal choice. Those who chose BF, encouraged to EBF	Among the 391 who ever BF, 191(49%) EBF to 1 month; 103 (26%) EBF to 3 months	Median duration of EBF was 1 month (IQR 0–3)	Among BF women, EBF duration was not consistently related to socioeconomic indicators. Those initiating BF had less education, no electricity, no water source in home than those not BF	EBF associated with significantly lower HIV transmission than MF, with a transmission risk similar to that of no breastfeeding
Coutsoudis 2001 ¹	1995- 1998	Prospective cohort from PMTCT Vitamin A RCT. This paper provided a fuller report of	Antenatal clinics of 1 tertiary hospital and 1 semi-private hospital in	551 HIV+ pregnant women 3 groups: 157 (29%) FF, 118 (21%) EBF 3+	No use of ARVs. Infant feeding counselling, informed maternal	394 initiated BF; 103 (26%) EBF for 3+ months. 155 (39%) EBF <3 months. Of	Median duration of EBF was 3 weeks (95%CI 2 weeks, 1 month), EBF	Compared to never breastfeeding mothers, those who EBF were less likely to have completed high school (25% vs 50%), be employed (31%	Those still EBF at 3 months were more likely to BF for longer (median 13 months 95%CI 11-15 months); those who

Abbreviations – RCT: randomized control trial; EBF: exclusive breastfeeding (breastmilk and medicine only, no other fluids or solids); BF: breastfeeding; MF: mixed feeding; FF: formula feeding; PMTCT: prevention of mother-to-child transmission; ARV: antiretroviral drugs not in triple; ART: antiretroviral therapy; VCT: voluntary counselling and testing; KZN, Kwa-Zulu Natal, a province in South Africa; OR: odds ratio; AOR: adjusted odds ratio; AHR: adjusted hazard ratio; IQR: interquartile range; SD: standard deviation; sdNVP, single dose Nevirapine

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First author, publication year	Time of study	Type of study	Setting	Participants	PMTCT practices	Prevalence of EBF initiation after birth	Average duration of EBF	Factors associated with BF and EBF	Other findings/comment
		transmission rates between different feeding practices at 3 month	Durban, KZN, South Africa	months, 276 (50%) MF Mean age 27 (SD 4.8)	choice. Those who chose BF, encouraged to EBF	103 who ever EBF, 93 (90%) EBF for 3 months	probability at 1 month was 0.49, at 3 months was 0.29, and at 6 months was 0.04	vs. 44%) or have electricity in the home (57% vs.79%); they were also slightly younger (25.8 years vs. 27 years)	did not EBF to 3 months are likely to BF for shorter overall duration (median 9.25 months (95%CI 7.5-10 months)
Rollins 2001 ¹	1995-1998	Prospective cohort from PMTCT Vitamin A RCT. This paper investigated possible explanations for previous results, and examined urinary	Antenatal clinics of 1 tertiary hospital and 1 semi-private hospital in Durban, KZN, South Africa	265 Pregnant HIV+ women between 28-32 weeks' gestation. (sample size limited by availability of urine samples)	No use of ARVs. Infant feeding counselling, informed maternal choice. Those who chose BF, encouraged to EBF	47% EBF at 1 week postpartum	Median duration of EBF 3 weeks (95%CI 2 weeks to 1 month) and 103/394 EBF for 3+ month	Fewer women who EBF had electricity (57%) or a refrigerator (44%), compared to women who mixed BF or FF (77% had electricity; 56% and 69% had refrigeration, respectively). Compared to MF, EBF infants had	Feeding mode did not affect neopterin excretion, and no difference in intestinal permeability comparing EBF vs. MF

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		neopterin and lactulose/ mannitol ratio		Mean age 27 (SD 4.8)				lower birthweight (3.09kg vs 3.41kg); EBF mothers were slightly younger (median 26 vs 29 years).	
Coovadia 2007 ²	Oct 2001- Apr 2005	Non-randomized intervention cohort study - Vertical Transmission Study (VTS), examined MTCT by infant feeding while providing intensive feeding support and home visits	9 antenatal clinics: 7 rural, 1 semi urban, 1 urban) in KZN, South Africa	1372 HIV-infected pregnant women; 1345 HIV-uninfected. Median age overall, 25.1 (IQR 16.1-45.8)	sdNVP; informed maternal feeding choice with intensive counselling and support; EBF for 6 months, or formula if AFASS ³ ; free formula	EBF 1132/1372 (83%)	Median EBF duration was 159 days (IQR 122-174). Of 1034 BF, 847 (82%) EBF at least 6 weeks; 688 (67%) EBF at least at 3 months; 415 (40%) EBF for at least 6 months	Compared to those who exclusively FF, mothers who EBF were less likely to live in urban settings (18% vs. 32%), have a flush toilet (18% vs. 26%), have piped water (39% vs. 50%), be the main income provider (10% vs. 18%), and more likely to have an infant with birthweight >3500g (22% vs. 31%)	HIV+ women, if provided with good support, will adopt appropriate and optimum feeding practices Infants who received formula milk in addition to BF were nearly twice as likely to become HIV+

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					provided at clinics				
Bland 2007 ²	Aug 2001 -Sep 2004	VTS; this paper examined appropriateness of infant feeding choices, and ability to adhere to antenatal choices	9 antenatal clinics: 7 rural, 1 semi urban, 1 urban in KZN, South Africa	2491 pregnant women enrolled before testing: HIV+ women 1253 and 1238 HIV-. Median age of HIV+ is 25 (range 15-45)	sdNVP; informed maternal feeding choice with intensive counselling and support; EBF for 6 months, or formula if AFASS ³ ; free formula provided at clinics	Of 1253 HIV+ women, 911 (73%) intended to EBF; of those 911, 707 (78%) EBF adhered at 1 week.	Only reported on feeding practice in the first week	Among those HIV+ women intending to EBF, having access to electricity, gas, or paraffin was associated with non-adherence to antenatal infant feeding intentions, (AOR 1.69 95%CI 1.16-2.46); similarly, fewer antenatal counselling visits were associated with non-adherence (1 visit vs 4, AOR 1.69,95%CI 1.04-2.76)	Sufficient maternal income, with access to water, fuel and a refrigerator were taken to indicate meeting "AFASS" criteria; of all women planning replacement feed, only 8% (9/113) had access to all four resources

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Bland 2008 ²	Between 2001-2004	VTS; this paper focused on the design and effects of the intervention on success of BF during the first 6 months after delivery	9 antenatal clinics: 7 rural, 1 semi urban, 1 urban in KZN, South Africa	1219 infants of HIV+ and 1217 infants of HIV- women, Median age 25.1 (IQR 16.1-45.9)	sdNVP; informed maternal feeding choice with intensive counselling and support; EBF for 6 months, or formula if AFASS ³ ; free formula provided at clinics	561 HIV+ women stopped EBF before 180 days; 316 resumed EBF within a median of 2 days. Over 80% EBF at 1 months and 60% at 5.5 months. Cumulative probability of EBF at 6 months was 40%	Median EBF duration among HIV+ women, 175 days (IQR 137–180)	Probability of stopping EBF is associated with having electricity: AHR 1.64 (95% CI 1.24-2.17); urban setting: AHR 0.68 (95% CI 0.48-0.98); breast health AHR 4.12 (95% CI 2.50-6.80); or feeding difficulties AHR 1.75 (95% CI 1.42-2.16) in the previous 2 weeks	At 1 month, HIV+ women with scheduled number of visits were more than 2 times as likely to still be EBF when compared to those who missed any scheduled visits: AOR 2.29 (95%CI: 1.60–3.28). Similar results were found for likelihood of EBF at 2 & 4 months

Abbreviations – RCT: randomized control trial; EBF: exclusive breastfeeding (breastmilk and medicine only, no other fluids or solids); BF: breastfeeding; MF: mixed feeding; FF: formula feeding; PMTCT: prevention of mother-to-child transmission; ARV: antiretroviral drugs not in triple; ART: antiretroviral therapy; VCT: voluntary counselling and testing; KZN, Kwa-Zulu Natal, a province in South Africa; OR: odds ratio; AOR: adjusted odds ratio; AHR: adjusted hazard ratio; IQR: interquartile range; SD: standard deviation; sdNVP, single dose Nevirapine

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Ladzani 2011	Jan 2009 - Mar 2009	Cross-sectional PMTCT survey study	47 sub district clinics in Mpumalanga province, South Africa	815 HIV+ mothers, babies 3-6 months. Median age of mothers 27 (IQR 23-32)	VCT, counselling on infant-feeding, sdNVP & free infant formula if AFASS ³ criteria met	368 (47%) reported having started EBF within 1 hour of delivery; 36% were EBF at the time of the survey	Only one visit done, did not report duration of EBF	MF was associated with: Having a vaginal delivery (AOR 1.39; 95%CI 0.70-2.76), infant hospital admissions (AOR 2.95; 95%CI 1.61-5.43), and currently pregnant (AOR 3.69; 95%CI 1.13-12.06). FF was associated with: being older (AOR 1.04; 95%CI 1.00-1.09), knowing the HIV status of the infant (AOR 0.61; 95%CI 0.41-0.93) and higher knowledge on HIV transmission through BF	115 (15%) did not receive infant feeding counselling within 72 hours of delivery.

Abbreviations – RCT: randomized control trial; EBF: exclusive breastfeeding (breastmilk and medicine only, no other fluids or solids); BF: breastfeeding; MF: mixed feeding; FF: formula feeding; PMTCT: prevention of mother-to-child transmission; ARV: antiretroviral drugs not in triple; ART: antiretroviral therapy; VCT: voluntary counselling and testing; KZN, Kwa-Zulu Natal, a province in South Africa; OR: odds ratio; AOR: adjusted odds ratio; AHR: adjusted hazard ratio; IQR: interquartile range; SD: standard deviation; sdNVP, single dose Nevirapine

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								(AOR 0.61; 95%CI 0.41-0.93).	
Goga 2012	Sept 2002 -Aug 2003	Data from prospective observational cohort study	3 study sites: <u>Paarl</u> : well-resourced commercial farm area <u>Rietvlei</u> : poverty stricken deep rural area <u>Umlazi</u> : a peri-urban area	Consecutive 665 HIV+ and 218 HIV- pregnant women. 586 HIV+ and 197 HIV- remained at 3 weeks and follow up until 36 weeks postpartum. Median age 25 (IQR 21-29)	PMTCT: sdNVP; infant feeding counseling with replacement feeding recommended if AFASS ³ criteria met	309 HIV+ women BF, 130 (42%) EBF at 3 weeks; At 7 weeks: EBF 67 (30%). At 12 weeks EBF 35 (18%)	Summary estimates of duration not provided; 18% HIV+ women were still EBF by 12 weeks	BF initiation significantly different by sites: Umlazi 226 (70%) vs Rietvlei 72 (32%) & Paarl 37(25%)	HIV+ women were significantly more likely to EBF at 3 weeks (OR 2.4 95% CI 1.7, 3.3), 5 weeks (OR 1.6 95% CI 1.1, 2.6), 7 weeks (OR 2.2 95% CI 1.4, 3.4), 9 weeks (OR 2.7 95% CI 1.5, 4.9), 12 weeks (OR 5.2 95% CI 2.1, 13), and 24 weeks (OR 2.2 95% CI 1.6, 2.7) than HIV- women
Rollins 2013 ²	Oct 2001 - Apr 2005	VTS; this paper examined	9 antenatal clinics: 7 rural,	1082 singleton infants born to	sdNVP for majority; a	HIV+ 81.4% were EBF at 6-	2097 started EBF; median	Examined the consequences of not	Infants who were EBF for shorter durations

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		diarrhoeal morbidity and all-cause mortality by infant feeding modality	1 peri-urban, 1 urban in KZN, South Africa	HIV+ mothers, with feeding data available at 6 months: and 1155 born to HIV-mothers. Median age 23.6 (IQR 20.0-28.9)	few mothers with advanced disease accessed ART as of 2004; informed maternal feeding choice with intensive counselling and support; EBF for 6 months, or formula if AFASS ³ ; free formula provided at clinics	8 weeks, & 61.8% at 3-4 months	cessation of all BF 171 days (IQR 82-180). HIV+ (81.4%) were EBF at 6-8 weeks, & 61.8% at 3-4 months	EBF, not risk factors of EBF cessation.	had an increased risk of death compared to those EBF for 5-6 months AHR 2.18 (95% CI, 1.56-3.01)

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Ijumba 2015	Jun 2008 – Jul 2011	Cluster randomized trial, 15 clusters to evaluate integrated package (2 pregnancy & 5 postnatal home visits)	Study site was in a semi-urban area in KZN, South Africa	Both HIV+ and HIV- pregnant women (1894 intervention and 2243 control), 750 HIV+ per arm Median age 23 (IQR 20-27)	VCT; HIV+ received sdNVP & replacement feeding if AFASS ³	Intervention was associated with EBF at 12 weeks (441/1629, 27%), EBF in control (260/1865, 14%); AOR 2.31 (95%CI 1.82-2.93)	Data was collected at a single time point	Community-based counselling (study intervention) was associated with EBF at 12 weeks, in both HIV+, AOR 1.70 (95% CI 1.32-2.20); and in HIV- women, AOR 2.70 (95% CI 2.01-3.70)	None
Tuthill 2016	Mar 2014 -Feb 2015	Retrospective cohort study, from an RCT, to identify perinatal depression in HIV+ and relationship	Two rural public health service clinics in KZN, South Africa	Enrolled 68 HIV+ pregnant women; 58 completed 6 week postpartum follow up and included in analyses.	Option B: pregnant women ART & Nevirapine while BF. EBF for 6 months	N=44/58 (76%)	Only analyzed till 6 weeks; 82% still EBF at 6 weeks	Prenatally depressed women were less likely to EBF at 6 weeks, AOR 0.68 (95% CI 0.49, 0.95). Women living with their mothers were more likely to EBF at 6 weeks,	None

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		between perinatal depression and infant feeding outcomes		Median age 28 (IQR 26-39)	and BF for up to 2 years			AOR 51.77 (95% CI 1.32, 2034.62)	

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Table 2. Characteristics of studies excluded following full-text review

First author	Year of publication	Title	Journal	Reason for exclusion
Bobat	1997	Breastfeeding by HIV-1-infected women and outcome of their infants: a cohort study from Durban, South Africa	AIDS	Examined transmission rate between feeding methods. Estimates of HIV-infected and HIV-uninfected mothers were not stratified by HIV status
Bland	2002	Breastfeeding practices in an area of high HIV prevalence in rural South Africa	Acta Paediatr	Review of 2 different studies: longitudinal study and cross sectional study
Bland	2003	Maternal recall of exclusive breast feeding duration	Arch Dis Child	Does not distinguish between HIV+ and HIV- women. EBF estimates are not stratified by HIV status
Doherty	2005	Health system constraints to optimal coverage of the prevention of mother-to-child HIV transmission programme in South Africa: lessons from the implementation of the national pilot programme	Afr Health Sci	Review of PMTCT programme in SA
Patel	2010	Breastfeeding, HIV status and weights in South African children: a comparison of HIV-exposed and unexposed children	AIDS	Does not provide EBF estimates of interest
Cournil	2013	Relationship between mortality and feeding modality among children born to HIV-infected mothers in a research setting: the Kesho Bora study	AIDS	Does not provide separate indicators for SA EBF
Rochat	2016	Exclusive Breastfeeding and Cognition, Executive Function, and Behavioural Disorders in Primary School-Aged Children in Rural South Africa: A Cohort Analysis	PLoS Med	Examined long term effects of EBF. Does not provide EBF estimates of interest

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C. MANUSCRIPT¹

¹ This manuscript is prepared for International Journal of Breastfeeding submission. The instructions for this journal is included as Appendix H. This journal requires that line numbering be used; this has not been inserted in this manuscript for dissertation purposes.

Patterns and predictors of exclusive breastfeeding duration among women living with HIV in Cape Town, South Africa

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² The final manuscript for publication submission will include several co-authors, but presented here with one single author (MPH candidate) as per degree requirements.

ABSTRACT

Background

Exclusive breastfeeding (EBF) is the international gold standard for infant feeding in the first 4-6 months of life. In sub-Saharan Africa, breastfeeding has been adversely affected by the HIV epidemic, due to breastmilk-associated mother-to-child transmission (MTCT) risk in the absence of triple antiretroviral therapy (ART). However, with rapidly expanding global accessibility of ART, HIV treatment and infant feeding guidelines now recommend universal ART for all women (“Option B+”) with breastfeeding as the optimal infant feeding choice in most settings. Data is scarce on breastfeeding practices in this context. This project seeks to describe early infant feeding practices among HIV-infected women initiating ART in an Option B+ PMTCT clinic in peri-urban Cape Town, South Africa.

Methods

The Maternal-and-Child-Health-Antiretroviral (MCH-ART) study (2013-2016) enrolled HIV-infected women initiating ART in pregnancy; breastfeeding mother-infant pairs were followed until 18 months. Data were collected via interviews at scheduled study visits, including repeated measures of infant feeding practices (24-hour recall). EBF duration was defined from delivery date to date of last visit reporting EBF. A *priori*-defined maternal-infant characteristics potentially associated with early EBF cessation (< 4 months/never) were evaluated using exploratory data analysis and multivariable logistic regression.

Results

Of 471 breastfeeding mother-infant pairs, 429 (91%) were ever EBF. Median duration of EBF was 1.5 months (interquartile range, IQR 0.3-5.4); only 115/471 (24%) were EBF for 4 months or longer. Median maternal age was 28 years (IQR 24-32); 41% were married/co-habiting; 58% delivered at primary care level. Within the first week of birth, 8% of women

reported some breast health issues, increasing to 22% of all women by 6 weeks. The most commonly reported lactation concern was cracked nipples (43/96 women, 45% of all lactation problems). After adjusting for maternal age, marital status, education, poverty, gravidity, place of delivery, anxiety and alcohol use, lactation concerns remained somewhat predictive of suboptimal EBF, adjusted OR (AOR) 1.70, 95% CI 0.93-3.14.

Conclusions

Exclusive breastfeeding is sub-optimal in this setting. Lactation problems are common, and associated with premature EBF cessation. Additional lactation support is urgently required in PMTCT settings promoting breastfeeding.

Trial registration

ClinicalTrials.gov NCT01933477

KEY WORDS

Exclusive breastfeeding; HIV; PMTCT; Africa

MANUSCRIPT

Background

Optimal breastfeeding practices are strongly associated with improved child survival and health across nations [1-3]. The greatest benefits of breastfeeding are seen among children who exclusively breastfeed (EBF) for the first 4-6 months of life, with breastfeeding continued thereafter along with nutritionally adequate complementary food [2]. Due to risks of mother-to-child transmission (MTCT) of HIV via breastmilk [4, 5], these recommendations have not been universally applied to HIV-infected women. Until recently the optimal feeding choice for HIV-exposed infants had been a widely debated global health dilemma [6-8]. Early World Health Organization (WHO) human immunodeficiency virus (HIV) infant feeding guidelines focused primarily on prevention of mother to child transmission of HIV (PMTCT), and included recommendations involving replacement feeding where “affordable, feasible, acceptable, sustainable and safe (AFASS)” with early, abrupt weaning when breastfeeding was the only option [3, 9]. Some national PMTCT programmes provided free infant formula to HIV-infected women during this time, including Botswana and South Africa [10].

However, in line with findings from the pre-HIV era [11], several large studies subsequently demonstrated substantial childhood mortality and morbidity associated with replacement feeding for HIV-exposed infants in most settings [3, 12-14]. Breastfeeding reduces the risk of these adverse outcomes, with evidence of a benefit gradient where mixed feeding (breastfeeding with other items) provides some protection while EBF provides optimal protection. A recent systematic review, analysing the effects of optimal breastfeeding on infant survival among HIV-unexposed infants, found an almost threefold higher mortality

risk among partially breastfed infants, RR 2.84, 95% CI 1.63–4.97, and a 14-fold higher risk among non-breastfeeding infants (RR 14.4, 95% CI 6.13–33.9), compared to EBF infants. [15]. Similar results have been described for HIV-exposed infants, with a consistent picture emerging of improved HIV-free survival among breastfeeding infants [16, 17]. In terms of infectious morbidity, a systematic review by Zunza et al. showed that HIV-exposed breastfeeding infants experienced less diarrhoea than those that are formula fed, risk ratio (RR) 0.31; 95% CI 0.13-0.74 [18]. In keeping with these findings, a large cohort study of HIV-exposed South African infants [19] found that EBF offers higher diarrhoeal protection than predominant (adjusted hazard ratio (AHR) 1.38, 95%CI 0.96-1.97), partial (AHR 1.19, 95%CI 1.02-1.53), and no breastfeeding (AHR 1.35, 95%CI 1.17-1.53).

Concurrently, several large PMTCT studies demonstrated dramatic reductions in MTCT risk among women receiving triple antiretroviral therapy (ART) [14, 20, 21]. Accumulated evidence presented in a 2011 Cochrane review showed that MTCT can be less than 1% with maternal viral suppression under triple antiretroviral therapy (ART) during pregnancy and breastfeeding [22].

The primary focus of PMTCT and infant feeding guidelines had shifted to HIV-free child survival rather than only MTCT, and ART was increasingly available across resource-limited settings. Consequently, the WHO ART, PMTCT and HIV infant feeding guidelines were updated to reflect these encouraging findings, and now recommend lifelong triple ART for all pregnant and breastfeeding HIV-infected women (“Option B+” PMTCT strategy), with breastfeeding for at least 12 months (EBF for first 4-6 months) as optimal feeding choice in most settings where HIV is highly prevalent [23]. From the beginning of the HIV epidemic, conflicting changes in infant feeding guidelines for HIV-infected women and their infants

resulted in health workers disseminating mixed messages to women [24]. Now, the infant feeding guidelines are the same for both HIV-infected and uninfected women. South Africa phased out free infant formula after 2010 [10], adopted Option B+ in 2015 and now promote breastfeeding (with EBF until 6 months) as best national infant feeding choice for both HIV-uninfected and HIV-infected women, provided the latter are receiving ART [25, 26]. The new, uniform infant feeding guidelines which align recommendations for both HIV-infected and uninfected women, may improve the consistency of breastfeeding encouragement and support across health-care settings; in turn, this may improve the rates of exclusive breastfeeding.

Since 2013, substantial progress has been made in providing ART to pregnant and breastfeeding HIV-infected women across South Africa [27]. However little data exists on the successful implementation of the accompanying infant feeding recommendations. Indeed, there is reason to expect poor uptake of these recommendations, given the suboptimal breastfeeding statistics for the general South African population [28]. There are limited published data on EBF prevalence and duration among South African women receiving universal ART, as per the recently introduced guidelines. Furthermore, many widely recognized risk factors for suboptimal breastfeeding such as poor family support, maternal anxiety, depression and substance abuse may be particularly common among women recently diagnosed with HIV [29, 30]. Identification of indicators and predictors of EBF among this potentially vulnerable population will allow public health workers to develop area-specific programmatic interventions to improve breastfeeding practices under conditions of ART, with the aim to optimize HIV-free survival and health of HIV-exposed children.

The main objective of this analysis is therefore to describe the prevalence, predictors and duration of exclusive breastfeeding among HIV-infected South African women initiating universal, lifelong ART during pregnancy.

Methodology

Study design

The Maternal and Child Health AntiRetroviral Therapy (MCH-ART) study was conducted between 2013 and 2015 in a peri-urban community in Cape Town, South Africa. The MCH-ART study used both observational and experimental components. The MCH-ART study had three interrelated phases: Phase 1 was a cross-sectional evaluation of HIV-infected women at their first antenatal visit at Gugulethu midwife obstetrics unit (MOU); Phase 2 was an observational cohort of women taken from Phase 1 that were eligible for ART initiation; and Phase 3 was a randomised trial of two different strategies for delivering ART to postpartum women [31]. MCH-ART study design and procedures have been described in detail elsewhere [31]. In short, consecutively enrolled HIV-infected women seeking antenatal care and initiating ART during pregnancy were enrolled and followed through pregnancy, and with their breastfeeding infants until 18 months postpartum [31]. Besides interviews conducted in isiXhosa, MCH-ART study visits also included viral load testing, and maternal and infant anthropometry [31].

This analysis used perinatal data collected during pregnancy and the first 6 months after birth. Women attended up to three antenatal visits, and between birth and 6 months, up to four visits. The postnatal visits occurred at approximately < 7 days, 6 weeks, 3 and 6 months since birth. Trained field workers interviewed mothers and completed questionnaires on maternal and infant characteristics and health.

Study setting

Recruitment and enrolment into MCH-ART took place between April 2013 and June 2014 at a dedicated research site located next to but separate from the Community Health Centre and midwife and obstetric unit (MOU) in Gugulethu, a peri-urban township of Cape Town, South Africa. Study follow-up was conducted at the same research site. The health centre and MOU serve a broader community with high levels of poverty and unemployment.

Limited breastfeeding and EBF data from the general population in South Africa show that 88% of women initiate breastfeeding after birth, however, more than 70% of infants receive other liquids and food before six months of age, and only about 8% are EBF at six months [32, 33].

Study participants were enrolled from the midwife and obstetric unit (MOU), which functions as a 24-hour primary care obstetric unit. The MOU is currently certified as a baby-friendly hospital [9, 34]. Referrals for complicated pregnancies and/or deliveries are made to nearby tertiary care centres including the Mowbray Maternity Hospital and Groote Schuur Hospitals; both centres have facilities for assisted and caesarean section deliveries, maternal and neonatal intensive care units, and kangaroo mother care units. Breastfeeding is promoted by health care workers, and lactation consultants are available on request.

Study participants

Inclusion criteria for prospective follow-up in MCH-ART included maternal HIV infection and ART initiation in pregnancy, with antenatal care sought at the Gugulethu MOU at a minimum age of 18 years (Appendix B). Maternal HIV status was ascertained and documented by trained HIV testing and counselling staff with two finger-prick rapid tests at the MOU. Maternal viral load was tested at study measurement visits for adherence

measurements, not as part of the inclusion criteria. Postnatal follow-up was limited to breastfeeding mother-infant pairs who presented for a neonatal study visit before the age of 2 months. From the 589 women followed through pregnancy, 471 women and their infants were eligible for postnatal follow-up and are included in this analysis (Figure 1).

Study measures

Extensive infant feeding questionnaires were used to determine infant exposure to solid food or liquids other than breastmilk within 3 days after birth, and at each study visit (24-hour recall). The infant feeding questionnaire was based on a validated infant feeding questionnaire from other PMTCT studies. Mothers were also asked to recall the infant's age at first introduction of any item other than breastmilk or medicine, and to report any breast health related concerns, such as cracked nipples, engorgement, mastitis/abscess, and insufficient milk supply. Those who reported having stopped all breastfeeding were asked the principle reasons for breastfeeding cessation. Maternal depression was measured using the Edinburgh Postnatal Depression Scale (EDPS) at antenatal and postnatal study visits, a 10-item self-reported screening questionnaire for depressive symptoms [35]. Antenatal maternal anxiety was measured and calculated using the Kessler Psychological Distress Scale (K-10), where items are scored between 1 and 5 [36]. The Alcohol Use Disorders Identification Test was used to identify hazardous alcohol consumption (AUDIT-C) [37]. Antenatal ultrasound measures were used to estimate gestational age, supplemented with reports of last menstrual period where indicated. Samples for maternal viral load testing were collected at each study visit for batched analysis.

Data analysis

Definitions: outcome

This analysis characterized EBF in accordance with the WHO definition, as “the infant receives only breast milk without any other liquids or solids, not even water, except for oral rehydration solution or drops or syrups of vitamins, minerals or medicines” [23].

Breastfeeding practices were defined cross-sectionally at each study visit, and categorized as no breastfeeding, some breastfeeding but not exclusively, or EBF. Loss of EBF status was considered irreversible. The last study visit at which EBF was reported was conservatively assumed to be the last day of any EBF, and the last study visit at which any breastfeeding was reported was taken as the last day of breastfeeding. Duration of EBF was defined as infant date of birth subtracted from date of visit with last reported EBF; for analysis, a combined binary indicator was created to indicate (1) EBF for 4 months or longer (“optimal EBF practices”), vs (2) never EBF or EBF for less than 4 months (“suboptimal EBF practices”).

Definitions: potential risk factors

Successful EBF is strongly related to lactation problems in the early postnatal period [38].

We categorized maternal complaints of breast health issues or maternal reasons for breastfeeding cessation into the following broad categories: painful or engorged breasts; cracked nipples; mastitis (painful or engorged breasts treated with antibiotics) or breast abscess; and/or maternal impression of inadequate breast milk supply (including maternal concerns regarding poor infant growth, excessive crying or small volumes of expressed breast milk).

Generally, breastfeeding can be influenced by multiple maternal, infant and environmental factors [39]. For this analysis, we decided *a priori* to explore the association between exclusive breastfeeding and a variety of factors as follows: maternal enrolment characteristics included age; education (highest grade completed); marital status

(married/cohabiting with a partner vs. not married/cohabiting with a partner); degree of poverty (poverty score calculated using a standardized asset score based on dwelling type, access to a flush toilet, running water in the home, electricity, refrigerator, television, telephone; and combined with employment status); pregnancy intentions (unplanned pregnancy); parity and gravidity; and timing of HIV diagnosis with relation to index pregnancy. Maternal HIV disease severity close to delivery was expressed as HIV viral load <50 copies/ml. Antenatal mental health measures included: EPDS score ≥ 13 to identify women with major depressive symptoms [35]; maternal anxiety, a K-10 score of ≥ 21.5 ; hazardous drinking, AUDIT-C score ≥ 3 . Birth and delivery characteristics included place (delivery at a primary care facility including the MOU vs. hospital facilities vs. delivery before arrival at a facility, BBA) and method (caesarean section vs. vaginal delivery at a facility vs. BBA vaginal delivery). Gestational age at delivery was categorized into ≥ 37 completed weeks; 34 to <37 weeks; and <34 weeks. Infant birth weight was abstracted from the Road to Health Booklet (patient-held record for South African children); those born at less than the 10th percentile expected for gestational age were classified as being “small-for-gestational-age” (SGA).

Analysis

Exploratory data analysis was used to identify patterns of exclusive breastfeeding, including frequency tables and bar graphs. Relationships between EBF duration (as a continuous measure and binary) were explored using the chi² statistic or t-tests as applicable. Logistic regression analysis was used to test relationships identified in exploratory analysis. Variables which improved model fit according to the Akaike’s Information Criterion were included in the final logistic regression model, working on the principle of parsimony. All analyses were

done using Stata 12.0 (StataCorp, College Station, TX, USA); estimates are presented with corresponding 95% confidence intervals.

Sample size

A specific power analysis was not indicated for this secondary data analysis, but all results are presented with 95% confidence intervals to demonstrate achieved precision [40].

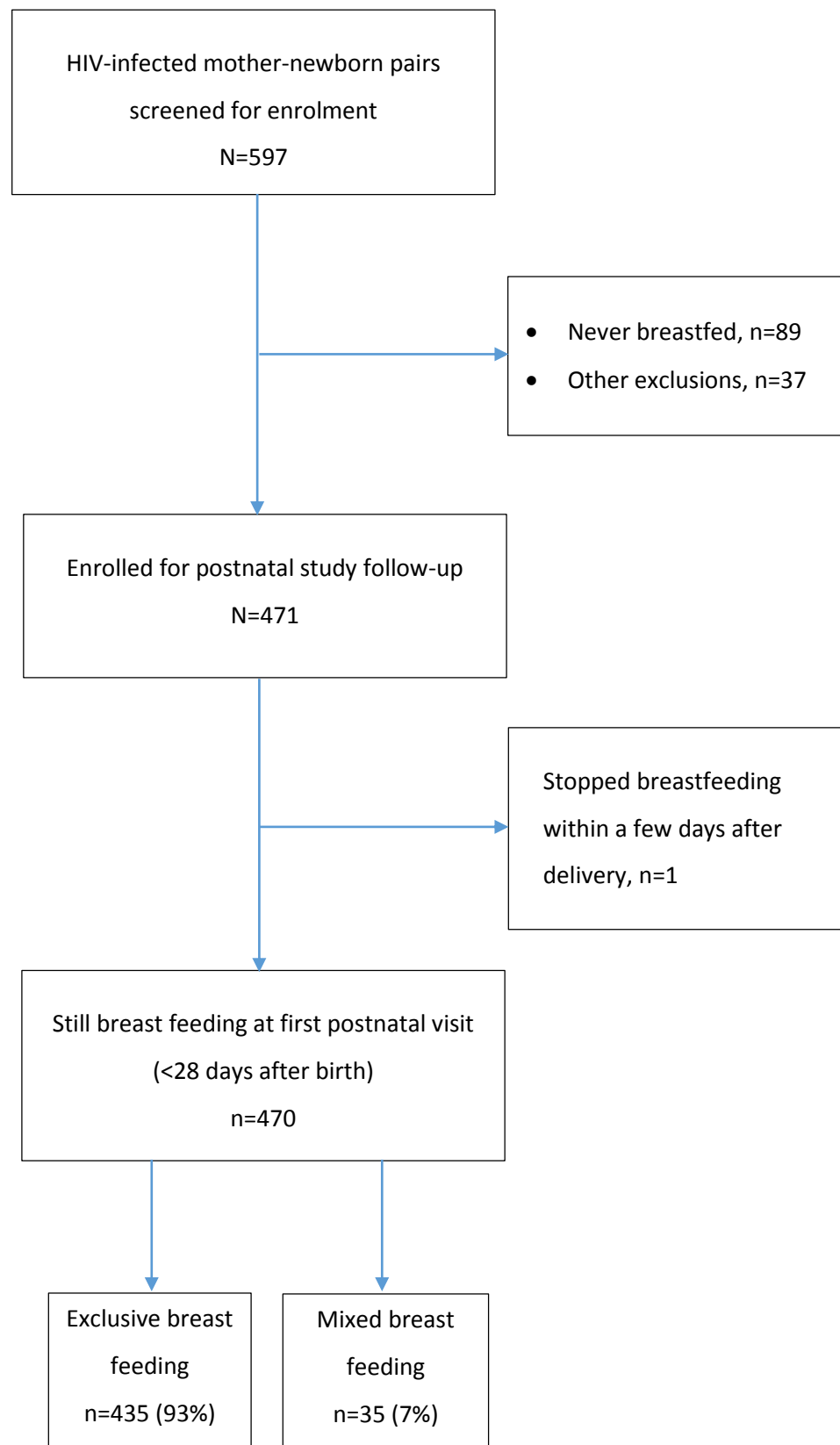
Original sample size calculations were based on requirements to determine a significant difference between the MCH-ART main trial arms for the primary study aims [31].

Results

Demographics

Four-hundred-and-seventy-one breastfeeding mother-infant pairs were enrolled into postnatal follow-up and are represented in this analysis (Figure 1). The first postnatal study visit occurred at a median of 5 days after birth (interquartile range, IQR 4-7 days); the second study visit at 6 weeks (IQR, 6-6.1 weeks); third, at 3 months (IQR 3-3.1 months) and fourth, at 6 months (IQR 6-6.1 months). The total number of infant feeding data available was different at different study visits due to some attrition: at 1st, 2nd, 3rd and 4th study visits data was available for 471 (100%), 444 (94%), 372 (79%), and 407 (86%) mother-infant pairs, respectively. At enrolment, median maternal age was 28 years (IQR 24-32). Less than half of the women 193 (41%) were married or cohabiting with a partner and 25% had completed secondary school. More than half of the women (58%) delivered at a hospital; approximately a third (30%) had caesarean sections. At delivery, the median gestational age was 39 weeks (IQR 38-40); 88% delivered at ≥ 37 weeks. Overall, women who EBF for 4 months or greater (median duration of EBF 6 months, IQR 6-6) were slightly older, and were

less likely to be employed, single, primigravida or to report antenatal depression/anxiety (Table 1). Almost a quarter (24%) of women who did not EBF/EBF<4 months reported any lactation issues in the first 6 weeks, compared to 15% of those who EBF≥4 months (Table 1).

Figure 1. Exclusive breastfeeding among HIV-infected women: study flow diagram

EBF, exclusive breastmilk and medicine only; BF, breastfeeding: categories based on maternal self-report with 24-hour recall

Study visits at <7 days (median age 5 days, interquartile range/IQR, 4-7); 6 weeks (IQR, 6-6); 3 months (IQR, 3-3) and 6 months (IQR, 5.9-6.1)

Table 1. Characteristics of HIV-infected women and their HIV-exposed infants, by initiation and duration of exclusive breastfeeding in the first 6 months of life

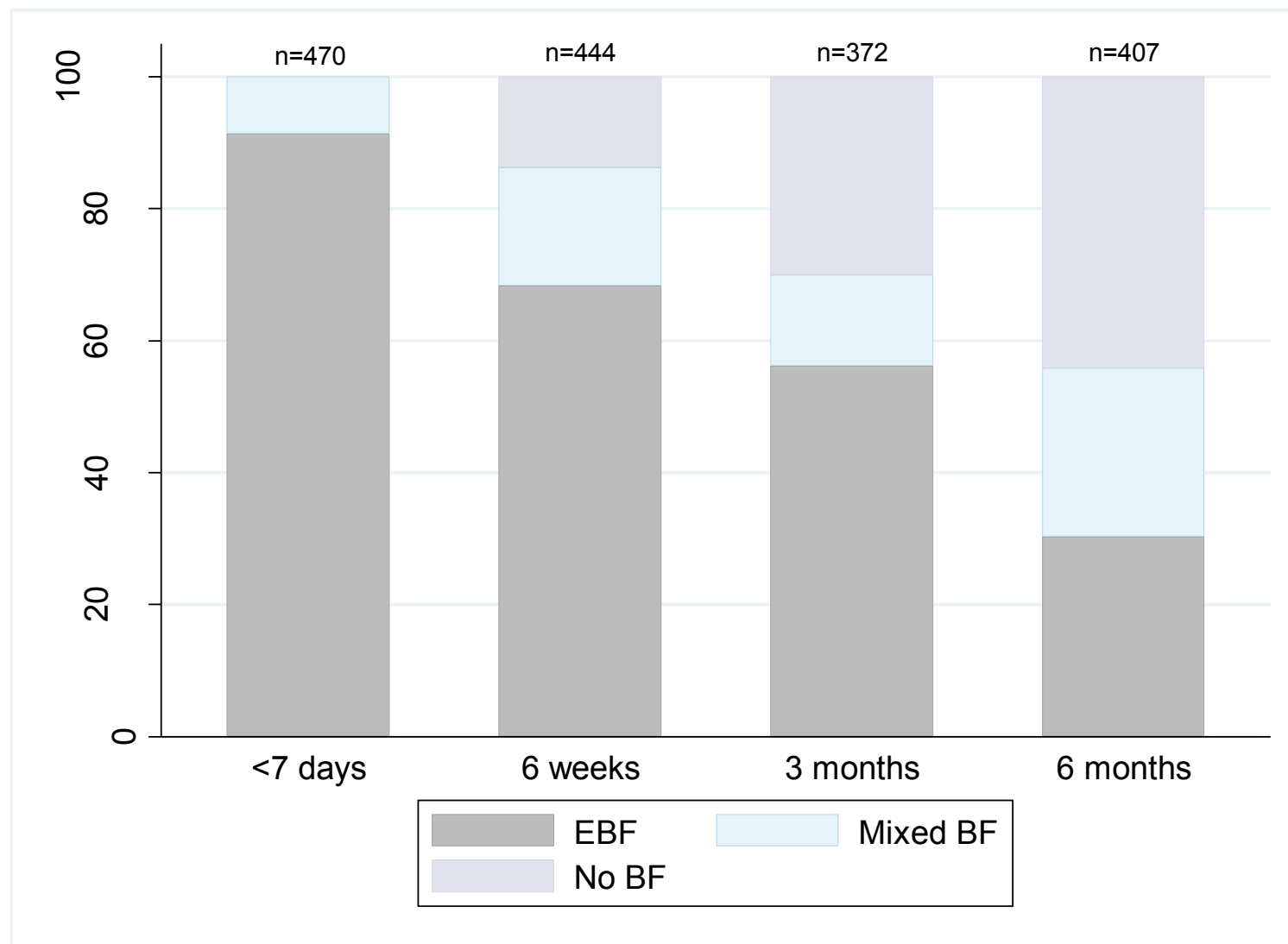
	EBF < 4 months or never EBF (N=356)	EBF ≥ 4 months (N=115)	Total (N=471)
Maternal demographics			
Age in years ¹	27.4 (24.1, 31.7)	28.9 (25.4, 33.6)	27.8 (24.5, 32.3)
Married or cohabiting ¹	128 (36)	65 (57)	193 (41)
Highest grade complete ¹	11 (10, 11.5)	11 (10, 11)	11 (10, 11)
Employed ¹	146 (41)	38 (33)	184 (39)
House/formal dwelling ¹	177 (50)	47 (41)	224 (48)
Poverty score ¹	0.5 (-0.5, 1.3)	0.5 (-0.5, 1.3)	0.5 (-0.5, 1.3)
Primigravida	70 (20)	12 (10)	82 (17)
Intended pregnancy	100 (28)	33 (29)	133 (28)
HIV diagnosis during this pregnancy	210 (59)	58 (50)	268 (57)
Viral suppression <50 copies/mL ¹	269 (76)	88 (77)	357 (76)
EPDS threshold ≥13 ²	41 (12)	7 (6)	48 (10)
K-10 threshold ≥21.5 ²	25 (7)	2 (2)	27 (6)
AUDIT-C threshold ≥3 ²	31 (9)	11 (10)	42 (9)
Delivery/birth characteristics			
Gestational age (weeks)	39 (38, 40)	39 (38, 40)	39 (38, 40)
<i>Premature, ≤ 37 weeks</i>	43 (12)	14 (12)	57 (12)
Log ₁₀ HIV viral	1.6 (1.6, 1.7)	1.6 (1.6, 1.7)	1.6 (1.6, 1.7)
Place of delivery			
<i>Primary care</i>	138 (39)	48 (42)	186 (39)
<i>Hospital care</i>	207 (58)	64 (56)	271 (58)
<i>Born before arrival</i>	11 (3)	3 (3)	14 (3)
Caesarean section delivery	105 (29)	36 (31)	141 (30)
Female	184 (52)	50 (43)	234 (50)
Infant birthweight (kg)	3.1 (2.8, 3.4)	3.2 (2.7, 3.4)	3.1 (2.8, 3.4)
<i>Small for gestational age³</i>	41 (12)	12 (10)	53 (11)
Breastfeeding characteristics			
Put to breast within 1 hour of delivery	309 (87)	100 (87)	409 (87)
Lactation issues in first 6 weeks of life	80 (24)	16 (15)	96 (22)
Duration of EBF (in months)	1.4 (0.2, 2.9)	6.0 (6.0, 6.0)	1.5 (0.3, 5.4)

Values are median (IQR) or n (%); Abbreviations – EBF: exclusive breastfeeding; BF: breastfeeding; GA: gestation age; EPDS: Edinburgh Postnatal Depression Scale – 10-item self-report scale to screen for postnatal depression; threshold used; K-10: Kessler Psychological Distress Scale, Items scored between 1 and 5; AUDIT-C: Alcohol Use Disorders Identification Test–Consumption, Included scores of questions 1-3 only

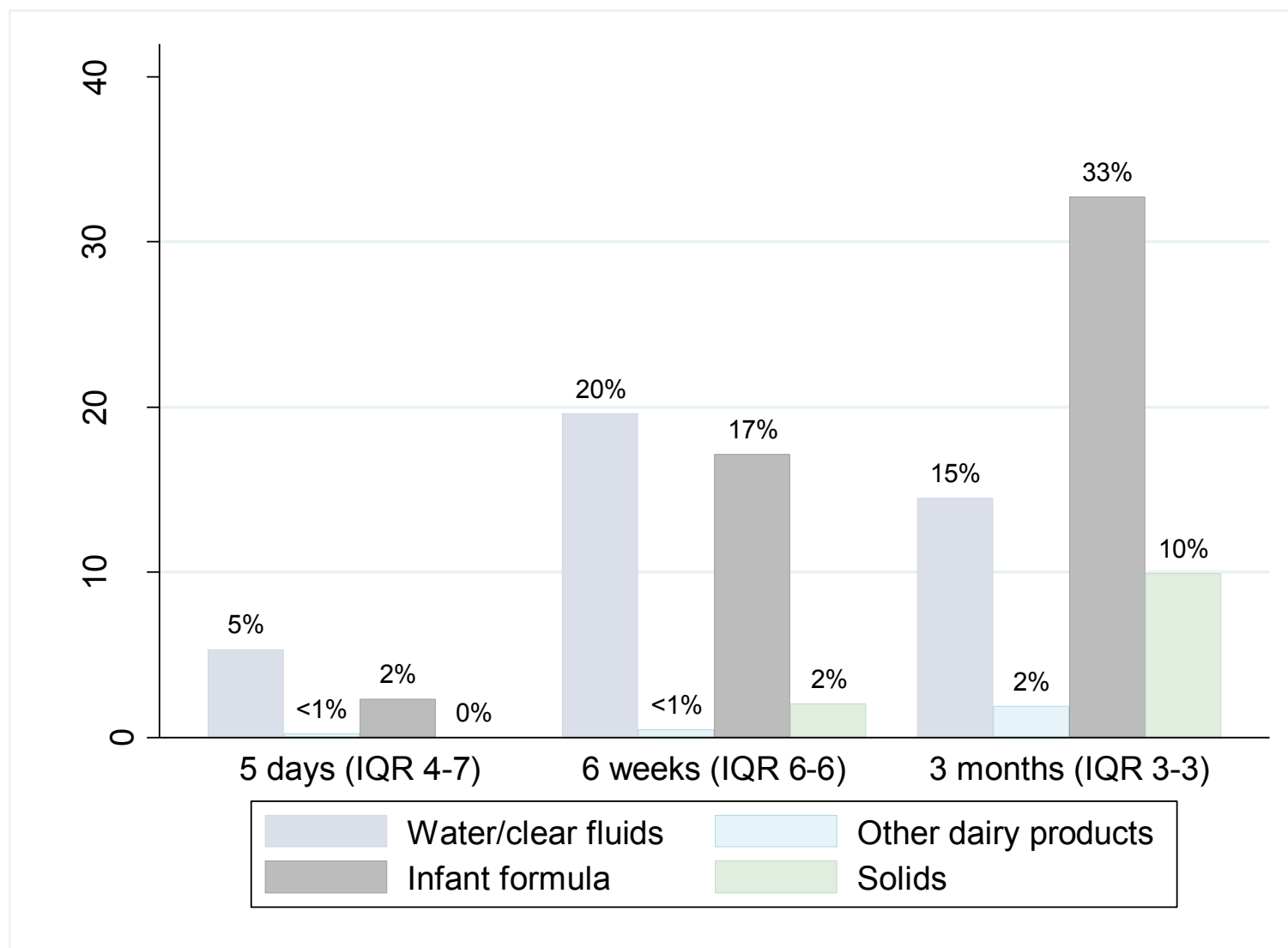
¹: Measure taken at study enrolment; ²: Measure taken during antepartum; ³: <10 percentile for birth weight

Breastfeeding indicators

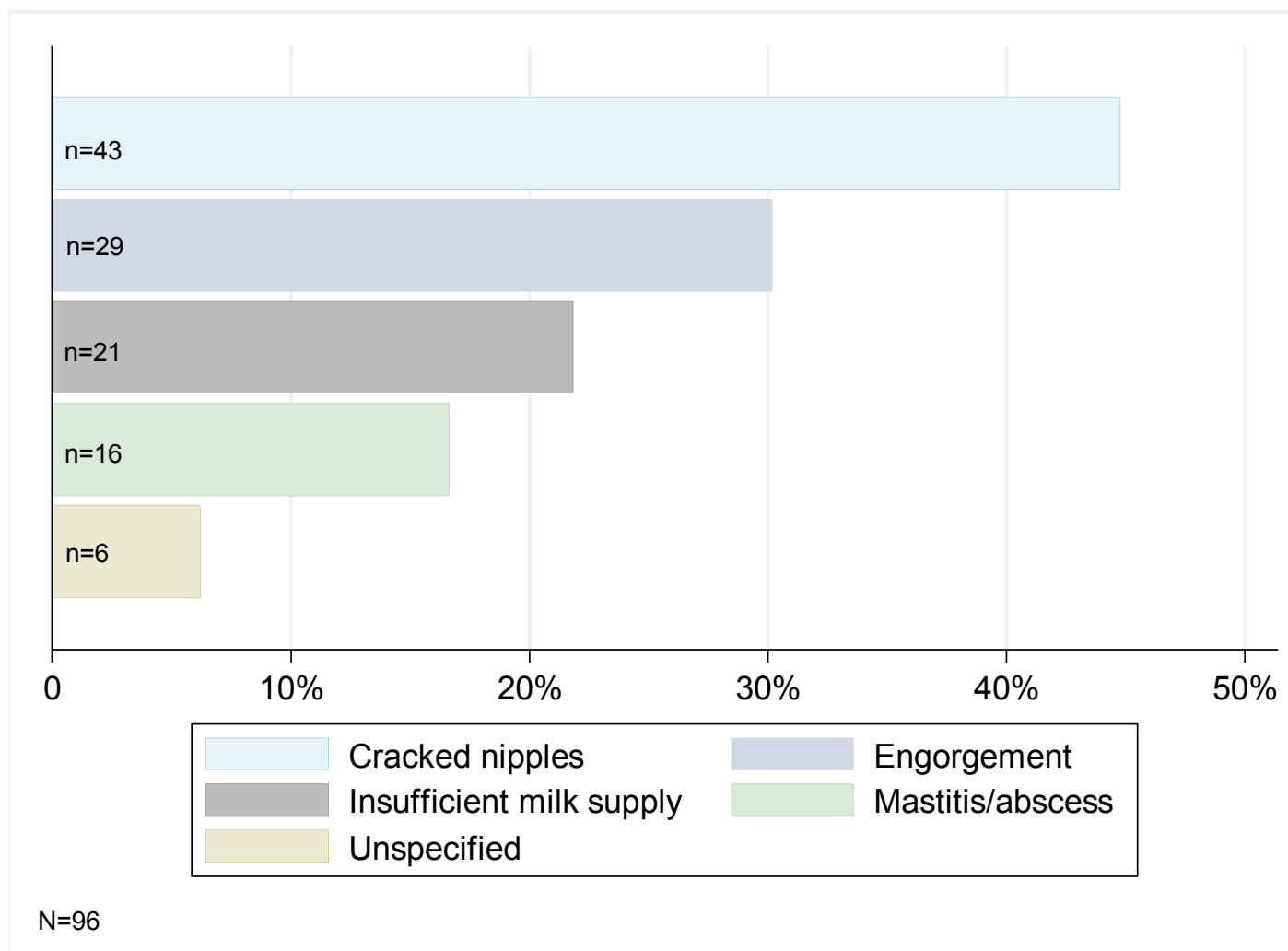
Overall, the median duration of EBF was 1.5 months (IQR 0.33-5.36). Although 91% of mother-infant pairs were EBF at the first study visit, only about a quarter (115, 24%) of women continued to EBF for 4 or more months. Proportions of mother-infant pairs practicing EBF vs. some breastfeeding vs. no breastfeeding at each study visit are shown in Figure 2. Only 2% of mothers had introduced infant formula milk (FF) in the first week but by 3 months of age, 33% of infants were receiving FF (Figure 3) while 37 (10%) of infants had already received some solids. There were 409 (87%) babies breastfeeding within one hour of delivery (Table 1). Within the first week of birth, 8% of women reported some breast health issues, increasing to 22% of all women by 6 weeks. The most commonly reported lactation concern was cracked nipples (43/96 women, 45% of all lactation problems), followed by engorgement/painful breasts (Figure 4). In univariable analysis, various factors, seen in Table 2, were predictive of suboptimal EBF. However, after adjusting for maternal age, marital status, education, poverty, gravidity, place of delivery, anxiety and alcohol use, lactation concerns remained somewhat predictive of suboptimal EBF, adjusted OR (AOR) 1.70, 95% CI 0.93-3.14; (Table 2). Overall, lactation issues appeared to mediate the relationships of many of the identified risk factors with EBF practices, although formal mediation analysis was not conducted.

Figure 2. Proportion mother-infant pairs per breastfeeding category over time

Study visits occurred at <7 days (median age, 5 days with interquartile range, IQR 4-7); 6 weeks and 3 months of age. Cumulative proportions based on maternal self-report (24-hour recall at study visit)

Figure 3. Distribution of non-breast milk fluid and/or solid food intake during the first 3 months of life, by study visit

Cumulative proportions, from maternal self-report (24-hour recall) at study visits; median age (interquartile range) at study visits 1-3 presented

Figure 4. Prevalence of common lactation problems reported during first 6 weeks of life

Self-reported breast health at first (median infant age, 5 days; interquartile range, IQR 4-7) and/or second study visit (median age 6 weeks, IQR 6-6)

Table 2. Predictors of suboptimal exclusive breastfeeding (EBF) practices (EBF for less than 4 months or never EBF), among HIV-infected women: results from logistic regression analysis

Predictors	Univariable		Multivariable	
	OR	95% CI	aOR	95% CI
Maternal age in years ¹	0.95	0.91 - 0.98	0.96	0.92 - 1.00
Married/co-habiting ¹	0.43	0.28 - 0.66	0.50	0.31 - 0.79
School grade ¹	0.99	0.85 - 1.14	0.86	0.73 - 1.03
Poverty score ¹	1.20	0.99 - 1.45	1.21	0.98 - 1.51
Primigravida	2.10	1.09 - 4.03	1.43	0.67 - 3.06
Planned pregnancy	0.97	0.61 - 1.55	-	-
EPDS threshold ≥ 13 ²	2.02	0.88 - 4.64	-	-
K-10 threshold ≥ 21.5 ²	4.29	1.00 - 18.41	3.93	0.89 - 17.26
AUDIT-C threshold ≥ 3 ²	0.89	0.43 - 1.84	0.75	0.34 - 1.62
Lactation issues in first 6 weeks of life	1.84	1.03 - 3.31	1.70	0.93 - 3.14
Gestation at delivery	0.96	0.87 - 1.05	-	-
Primigravida	2.10	1.09 - 4.03	1.44	0.68 - 3.06
Primary care delivery (reference)	1.00		-	-
Hospital	1.12	0.73 - 1.73	1.40	0.88 - 2.24
BBA	1.28	0.34 - 4.77	2.20	0.55 - 8.76
Vaginal delivery, facility (reference)	1.00		-	-
Vaginal delivery, BBA	1.16	0.32 - 4.27	-	-
Caesarean section	0.92	0.58 - 1.46	-	-
Infant gender (male vs female)	1.39	0.91 - 2.12	-	-
Small for gestational age ³	1.12	0.57 - 2.21	-	-
Put to breast within 1 hour of delivery	0.99	0.53 - 1.84	-	-

OR: odds ratio; aOR: adjusted odds ratio from logistic regression analysis; CI – confidence interval; EPDS: Edinburgh Postnatal Depression Scale – 10-item self-report scale to screen for postnatal depression; threshold used; K-10: Kessler Psychological Distress Scale, Items scored between 1 and 5; AUDIT-C: Alcohol Use Disorders Identification Test–Consumption, Included scores of questions 1-3 only; BBA: born before arrival, delivery not in a facility

¹: Measure taken at study enrolment; ²: Measure taken during antepartum; ³: <10 percentile for birth weight

Discussion

In this novel study population, we describe good initiation of EBF with a sharp drop off after 6 weeks, and suboptimal duration of EBF overall. Although 91% of mothers practiced EBF in the first few days of life, by 3 months almost half had introduced other items and only one quarter of women completed at least 4 months of EBF.

These findings are in keeping with earlier EBF data among women from several other resource-limited settings. A prospective observational study in South Africa under previous PMTCT guidelines reported 18% EBF by 3 months [41] and similarly, the Vitamin A study reported that only 26% of HIV-infected South African women EBF for more than three months [42], possibly influenced by the then prevalent PMTCT recommendations of complete breastfeeding avoidance and free infant formula programme under “AFASS” principles. A study in the early 2000s in Zambia, which included HIV-infected and HIV-uninfected women, reported a low 37% that were still EBF at four months [43], while in an analysis of the MASHI study in Botswana, Shapiro et al. reported that only 17.5% of HIV-infected women still EBF at five months [44]. The multi-country SWEN (Six Week Extended-dose Nevirapine) study, which analysed daily dose of nevirapine and the transmission rate of HIV through breastfeeding from three RCT in Ethiopia, India, and Uganda, reported a 28% EBF overall prevalence at six months [45], which is similar to our results at six months. The low prevalence of these studies are not unexpected, partly as a result of previous PMTCT recommendations for HIV-infected women and partly due to the known – substantial – social and contextual barriers against EBF that exist across most of Southern African populations [46, 47]. However, the low 6 months EBF prevalence in our cohort is concerning in the light of current PMTCT recommendations to promote and support EBF, especially as

our study population were women attending a BFHI facility, who had voluntarily chosen to breastfeed their infants and from whom more optimal breastfeeding practices might have been expected.

Some studies in resource-limited settings have reported more favourable prevalence of EBF; of note is that these were studies centred on providing in-depth nutritional counselling with support for breastfeeding mothers. The Vertical Transmission Study (VTS) in 2001 to 2004 in South Africa reported 60% EBF at 5.5 months [38]. The Breastfeeding, Antiretroviral, and Nutrition (BAN) study in Malawi reported even higher prevalence of EBF among all three study groups: 90% in the infant-nevirapine group, 89% for the maternal-antiretroviral, and 88% in the control group [48]. Results of these studies show that intense breastfeeding counselling and support could yield successful EBF results.

In our cohort, the median duration of EBF was only 1.5 months, which is substantially shorter than the WHO recommendation of 6 months. This result is comparable to the Vitamin A study by Coutsooudis et al. in the late 1990s, which reported a median duration of 1 month in a South African population of HIV-infected women [49]. The analysis of the multi-country Kesho Bora study [50], which compared different antiretroviral interventions in prevention of MTCT in Burkina Faso, two cities in Kenya, and rural and semi-urban cities in South Africa, reported dissimilar median durations of EBF by study sites, ranging from 1.4 months in Kenya to 5.3 months in South Africa. It should however be noted that only 65% of the combined South African cohorts ever breastfed [51]. Overall, median durations of EBF appear to vary between countries and settings, but a consistent picture emerges of suboptimal EBF initiation and/or duration among populations without specific interventions

or counselling aimed at improving breastfeeding practices, even when the national infant feeding policies include EBF.

Lactation issues were commonly reported in our cohort, and associated with suboptimal EBF practices. Between 2001 and 2004 when the PMTCT strategy was single-dose nevirapine coupled with EBF for six months, Bland et al. found that in South Africa the probability of early EBF cessation was strongly associated with lactation problems: breast health issues, AHR (adjusted hazard ratio) 4.12, 95% CI 2.50-6.80 and feeding difficulties, AHR 1.75, 95% CI 1.42-2.16 were both factors strongly associated with increased hazard of EBF cessation [38].

A sub-group analysis from the PROMISE-EBF study reported that 21% of HIV-infected women experienced some form of breast issues in the first six weeks postpartum and were three times as likely to stop breastfeeding before three months, AOR 3.1, 95% CI 1.7-5.7 [52]. Similarly, in Tanzania among both HIV-infected and HIV-uninfected women, 17% experienced breast issues during breastfeeding and those women were 86% less likely to EBF compared to women who did not experience those issues, OR: 0.14, 95% CI 0.07, 0.26 [53]. Lactation and breast issues are common and strongly associated with early EBF cessation, despite substantial evidence that EBF support interventions are available and have been shown to be highly effective [54].

Lactation issues can be overcome with adequate EBF support. The nonrandomized intervention control cohort (VTS) study found that women who were not EBF were more likely to have breast health issues than women who were EBF (time-dependent variable; AOR 1.4, 95% CI 1.13-1.87) [55]. The study, which achieved high rates of EBF, examined the effect of a counselling intervention strategy and found that most breast health issues occurred during the first month; and that breast health issues were inversely related to the

quality of support from the trained breastfeeding counsellors [55]. In this study, breastfeeding counsellors assisted the women with breastfeeding and diagnosed breast health issues before they become serious issues [55]. A cross-sectional study in Ethiopia found that women that were counselled postnatally were more likely to EBF than those that were not, AOR 2.12, 95 % CI 1.28, 3.54 [56]. If well-trained EBF support was available and provided to breastfeeding women, lactation issues could be minimized or diagnosed and treated as the breastfeeding counsellors did in the intervention cohort. In keeping with this, the PROMISE-EBF study showed that frequent peer counselling can improve EBF practice in Burkina Faso, Uganda, and South Africa [57]. The WHO guidelines adopted in South Africa recommends Option B+ for HIV-infected women with promotion and support of breastfeeding, EBF in particular [23]. Although removing the promotion of infant formula from the South African PMTCT programme has been a strongly positive step, our results indicate the need for more lactation support.

Hospital delivery, marital status, and antenatal anxiety were associated with suboptimal EBF in our cohort. In our context, marital status is probably a marker of improved social and economic support. This is in keeping with findings from Tuthill et al, who demonstrated that women living with their mothers were more likely to EBF [58]. Our study also found that women who delivered in a hospital facility were more likely to sub-optimally EBF, possibly in part the residual result of more than a decade of health workers recommending complete breastfeeding avoidance by HIV-infected women and/or lack of quality breastfeeding counselling in large, busy postnatal wards. Women with antenatal anxiety may be less likely to continue breastfeeding due to fear of HIV transmission; conversely, maternal anxiety reduces self-efficacy as well as negatively affecting breast milk composition [59], even in the absence of maternal HIV infection. Identification of women at risk of peripartum mental

health problems is increasingly recognized as an important determinant of adherence to ART [29]; our data highlights the additional importance of maternal mental health in terms of adherence to breastfeeding recommendations. Along with factors examined, timing of the study execution and the time of transition to policy of breastfeeding might possibly explain in part the study findings.

Limitations

Our measurements of infant feeding practices were based on maternal recall. Although the risk of recall bias is reduced when utilizing 24-hour recall, our estimates of EBF are likely to be overestimations, given the social desirability of EBF in PMTCT settings. Our data may also not be broadly generalizable. Study participants were limited to women who attended antenatal care (and therefore had received some infant feeding counselling), had voluntarily chosen to breastfeed, and had returned for study follow-up. For these reasons, our findings may present an overestimation of EBF prevalence and duration for broader HIV-infected populations in this setting. Despite this, we describe suboptimal EBF practices, which raises concern for the true practices in our PMTCT settings. South African breastfeeding and EBF practices are most suboptimal in peri-urban settings where high levels of employment exist and infant formula is widely available [57]; our study participants' experiences and practices are unlikely to reflect practices in rural areas. As is expected in observational research, some attrition resulted in missing data, however, the total proportions of women with available data were high, and it is unlikely that those who did not return for follow-up represented more favourable breastfeeding practices. Breastfeeding is a complex anatomical, physical and social interaction between mothers, infants and their families and communities. In recognition of the complex nature of

breastfeeding, we evaluated multiple potentially influential factors despite some sample size limitations. Some of our estimates have low precision, and the role of chance must be considered when interpreting our point estimates. Nonetheless, our findings are in keeping with breastfeeding literature from non-HIV infected populations.

Conclusions

This study demonstrates that most HIV-infected women receiving care at a reasonably well-resourced PMTCT program, which provides ART and actively promotes breastfeeding, still fail to maintain optimal EBF practices. Preventable and treatable lactation problems were highly prevalent. To optimize the benefits of current ART and infant feeding guidelines, programmatic interventions to target lactation problems and identify women at risk of practicing suboptimal breastfeeding are urgently needed. Further qualitative research could help identify and address obstacles that hinder optimal breastfeeding practices among HIV-infected women and their families.

Declarations

Ethics approval and consent to participate

The MCH-ART study was approved by the Columbia University Medical Center Institutional Review Board (CUMC-IRB) and the Human Research Ethics Committee of University of Cape Town (HREC REF Number 451/2012). This subgroup analysis of EBF data was approved for submission for a Master's degree in Public Health at the University of Cape Town (HREC REF: 876/2016).

The MCH-ART study is registered at ClinicalTrials.gov Trial number: NCT01933477

Consent for publication

Not applicable

Availability of data and material

The datasets generated in this analysis are not publicly available due to ongoing study activities and other analyses-in-process, but are available from the principle investigators upon reasonable request.

Competing interests

The authors have no competing interests to declare.

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Authors' contributions

Kelly Nguyen conceived of the structure of this sub-analysis, wrote the protocol and drafted the manuscript. Dr Stanzi le Roux was a co-investigator for all infant aspects of the MCH-ART study, conducted the analyses for this paper and was the main supervisor for the mini-dissertation. Professors Landon Myer and Elaine Abrams were co-principal investigators for the main research study; Professor Myer was also the co-supervisor for the mini-dissertation. Tammy Phillips was the study coordinator and Kirsty Brittain was in charge of data management of the main research study.

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List of abbreviations

BF: breastfeeding, breastfeed, breastfed

EBF: exclusive breastfeeding, exclusively breastfed

WHO: World Health Organization

HIV: human immunodeficiency virus

ART: antiretroviral therapy

MCH-ART: maternal and child health antiretroviral therapy cohort study

PMTCT: prevent of mother-to-child transmission

EPDS: Edinburgh Postnatal Depression Scale

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D. APPENDICES

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Appendix A –

MCH-ART study HREC approval



FHS016: Annual Progress Report / Renewal - 5 OCT 2016

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below			
<input checked="" type="checkbox"/> Approved	Annual progress report	Approved until/next renewal date	30.10.2017
<input type="checkbox"/> Not approved	See attached comments		
Signature Chairperson of the HREC	signature removed	Date Signed	7/10/16

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	03 Oct 2016		
HREC REF Number	451/2012	Current Ethics Approval was granted until	30 OCT 2016
Protocol title	Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study		
Protocol number (if applicable)	N/A		
Are there any sub-studies linked to this study?	<input checked="" type="checkbox"/> YES		
If yes, could you please provide the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.	<p>HREC REF 194/2013 Estimation of delivery dates using obstetric ultrasound in the MCH-ART study</p> <p>HREC REF 550/2015 Childbearing, family planning and relationships among women living with HIV in Gugulethu, Cape Town.</p>		
Principal Investigator	Prof Landon Myer		
Department / Office Internal Mail Address	CIDER, School of Public Health and Family Medicine, Faculty of Health Sciences		

1.1 Does this protocol receive US Federal funding?	<input checked="" type="checkbox"/> Yes	<input type="checkbox"/> No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No



1.3 Has sponsorship of this study changed? If yes, please attach a revised summary of the budget.	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
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2. List of documentation for approval

1. Protocol version 2.2 08 May 2015	
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3. Protocol status (tick ✓)

<input type="checkbox"/>	Open to enrolment	
<input checked="" type="checkbox"/>	Closed to enrolment (tick ✓)	
	Research-related activities are ongoing	
	Research-related activities are complete, long-term follow-up only	
<input checked="" type="checkbox"/>	Research-related activities are complete, data analysis only	
<input type="checkbox"/>	Main study is complete but sub-study research-related activities are ongoing	
<input type="checkbox"/>	Study is closed → Please submit a Study Closure Form (FHS010)	



4. Enrolment

Number of participants enrolled to date	Phase 1: 1554 Phase 2: 628 Phase 3: 472
Number of participants enrolled, since last HREC Progress report (continuing review)	Phase 1: 0 Phase 2: 0 Phase 3: 26
Additional number of participants still required	Phase 1: 0 Phase 2: 0 Phase 3: 0

5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	Phase 1: 0 Phase 2: 2 Phase 3: 8
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6. Cumulative summary of participants

Total number of participants who provided consent	Phase 1: 1554 Phase 2: 628 Phase 3: 472
Number of participants determined to be ineligible (i.e. after screening)	Phase 1: 286 Phase 2: 899 Phase 3: 125
Number of participants currently active on the study	Phase 1: 0 Phase 2: 0 Phase 3: 0
Number of participants completed study (without events leading to withdrawal)	Phase 1: 1527 Phase 2: 597 Phase 3: 463
Number of participants withdrawn at participants' request (i.e. changed their mind)	Phase 1: 0 Phase 2: 3 Phase 3: 5
Number of participants withdrawn by PI due to toxicity or adverse events	N/A
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	Phase 1: 26 (were never pregnant) 1 (incorrectly enrolled) Phase 2: 0 Phase 3: 1 (incorrectly enrolled)
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up.	Phase 1: 1 Phase 2: 28 Phase 3: 25



Phase 1: she completed informed consent late on the day of booking and was unable to stay to complete phase 1 CRFs. She was scheduled to return the following day but did not return. No contact details were collected at Phase 1 so unable to recall her.

Phase 2:

12 moved out of Cape Town

5 had a miscarried/stillbirth and did not return for final study visit - we were unable to track them by phone or home visits

11 had no successful contact after repeated telephone calls and home visits. Follow up was discontinued when the mother would have been out of the window for the postpartum phase

Phase 3:

25 women had no successful contact after repeated telephone calls and home visits. Active follow up attempts were discontinued when the mother would have been at least 20 months postpartum

Number of participants no longer taking part for reasons not listed above.
Please provide reasons below:

Phase 1: 0

Phase 2: 1

Phase 3: 3

Phase 2: 1 participant died

Phase 3: 1 participant relocated permanently out of South Africa

2 participants died

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:

Currently we have completed follow-up for all three phases and we are at data analysis. The primary outcomes have been finalized using dummy allocations and subsequently the random allocations have been unblinded.

Since the last annual renewal work from this study has been presented at international conferences and submitted for publication in peer reviews journals. All study outputs are described in the tables attached. The primary trial outcomes have been submitted for presentation at the 2017 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle, USA.

Please see attached list of abstracts and posters and submitted as well as manuscripts published in various journals.

8. Protocol violations and exceptions (tick ✓ all that apply)

✓	No prior violations or exceptions have occurred since the original approval
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<input type="checkbox"/>	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved
<input type="checkbox"/>	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

<input checked="" type="checkbox"/>	No prior amendments have been made since the original approval
<input type="checkbox"/>	Prior amendments have been reported since the last review and have already been approved
<input type="checkbox"/>	New protocol changes/ amendments are requested as part of this continuing review (See note below)

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS006).

Specific changes in the amended protocol and consent/assent forms must be **bolded**, *italicised* or tracked and all changes must include a rationale.



10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.

No study related adverse events reported.

10.2 Have participants received appropriate treatment/ follow-up/ referral when indicated (e.g. in the case of abnormal or incidental clinical findings, distress or anxiety)?

Yes No Not applicable

If yes, please describe:

Women were referred to appropriate care services as necessary for counselling and support and/or ART services.

11. Summary of Monitoring and Audit Activities (tick ✓)

11.1 Was this study monitored or audited by an external agency (e.g. MCC, FDA)?

Yes No Not applicable

11.2 Did a Data and Safety Monitoring Board publish a report?

Yes No Not applicable

11.3 If yes, please identify the agency and attach a summary of the findings.

Agency Name	Report attached	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Not applicable
	DSMB report attached	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Not applicable

11.4 Has there been any agency, institutional or other inquiry into non-compliance in this study, or any finding of non-compliance concerning a member of the research team?

Yes No

If yes, please explain:



12. Level of risk (tick ✓)

12.1 In light of your experience of this research, please indicate whether the level of risk to participants has:	
<input type="checkbox"/>	Increased
<input type="checkbox"/>	Decreased
<input checked="" type="checkbox"/>	Shown no change
If there has been a change, please explain:	

12.2 Please provide a narrative summary of recent relevant literature that may have a bearing on the level of risk.
N/A

13. Statement of conflict of interest

Has there been any change in the conflict of interest status of this protocol since the original approval? (tick ✓)	
<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
If yes, please explain and if necessary attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form FHS013):	

14. Signature

My signature certifies that the above is complete	
Signature of PI	signature removed
Date	4/10/2014

Appendix B –

MCH-ART inclusion/exclusion criteria

Inclusion and Exclusion Criteria

Phase 1: All HIV infected women booking for antenatal care at Gugulethu MOU who are:

- Age 18 years or older
- Documented HIV-infection according to two finger-prick rapid tests using different test types (per routine protocol in this setting) or documentation of HIV status for those women self-reporting HIV diagnosis.
- Confirmed pregnancy according to urine pregnancy test, ultrasound or clinical assessment
- Has not initiated triple-drug antiretroviral therapy or AZT for PMTCT during the current pregnancy
- Able to provide informed consent for research (Informed Consent #1)

Phase 2: All of the phase 1 women who were eligible to initiate lifelong ART

- Consented and participated in Phase 1
- Documented ART eligibility based on current local guidelines
- Started or scheduled to start ART at Gugulethu MOU in the current pregnancy (women started on AZT for PMTCT during the current pregnancy are eligible)
- Women who were previously receiving lifelong ART must have not used ART for at least 6 months.
- Able to provide informed consent for research (Informed Consent #2)

Phase 3: All of the phase 2 women who were breastfeeding their babies at the <7days postpartum study visit

- Consented and participated in Phase 2
- Initiated ART during the antenatal period
- Currently breastfeeding within <7 days postpartum (with an allowable window of up to 28 days postpartum)
- Willingness to be randomized and return for postnatal study visits
- Able to provide informed consent for research (Informed Consent #3)

Exclusion criteria

Individuals meeting any of the following exclusion criteria at the point in the study will be excluded:

- Not currently pregnant (Phases 1 and 2) or loss of pregnancy/neonate (Phase 3) at the time of eligibility determination
- Intention to relocate out of Cape Town permanently during the study period (Phase 2 and 3 only)
- Any medical, psychiatric or social condition which in the opinion of the investigators would affect the ability to consent and/or participate in the study (all phases), including:
 - Refusal to take ART/ARVs
 - Denial of HIV status

Appendix C –

MCH-ART Phase 2, infant feeding intentions/practices questionnaire

Visit Date: ____/____/____	
Ukuqalisa ukuncancisa <i>Initiation of breastfeeding:</i>	
1. Wakhe waluncancisa ibele usana lwakho? <i>Have you ever given breast milk to your baby?</i>	Hayi No = 0 → Gqithela ku Q5 <i>SKIP to Q5</i> Ewe Yes = 1
2. Ulubeke nini usana ebeleni emva kokuba ubelekile? <i>When did you put the baby to the breast after birth?</i>	Kwiyure yokuqala =1 <i>Within the first hour</i> Emva kweyure yokuqala ukya kwiyure ezi-12=2 <i>After the first hour and up to 12 hours</i> Emva kweyure ezi-12 ukuya kwiyure ezi-24=3 <i>After 12 hours and up to 24 hours</i> Emva kweyure ezi-24 ukuya kwiyure ezi-48(usuku lwe-2)=4 <i>After 24 hours and up to 48 hours (2nd day)</i> Emva kweyure ezi-48 ukya kwiyure ezi-72(usuku lwe-3)=5 <i>After 48 hours and up to 72 hours (3rd day)</i> Emva kweyure ezi-72(emva kosuku lwe-3)=6 <i>After 72 hours (After the 3rd day)</i>
3. Ubisi lokuqala ulunike usana okanye ulikhamile walilahla? <i>Did you give the first milk to the baby or did you express and discard it?</i>	Ndilunikile usana=1 <i>Gave the first milk</i> Ndilikhamile, ndalulahla elokuqala=2 <i>Expressed and discarded the first milk</i> Omabini ndimnikile ndakhama=3 <i>Both gave and expressed it</i> Enye=4, cacisa: _____ <i>Other, specify</i>
4. Emva kwentsuku ezi-3 ubelekile, usana lwanikwa enye into ngaphandle kobisi lwebele? <i>Within the first three days after birth, was your baby given anything to drink other than breast milk?</i>	Hayi No = 0 → Gqithela ku Q6 <i>SKIP to Q6</i> Ewe Yes = 1 Andazi= 9 → Gqithela ku Q6 <i>Don't know SKIP to Q6</i>
5. Usana lwanika ntoni ukuba lincance kwintsuku ezi-3 lubelekiwe? <i>What was the child given to drink within the first 3 days after birth?</i> Rhangqa zonke awazingcamliswa <i>Read all, circle all that apply</i>	a. Amanzi <i>Water</i> b. Amanzi aneswekile <i>Water with sugar (or glucose)</i> c. Amanzi anetyuwa <i>Water with salt</i> d. Ubisi lwenkomo oluxutyiweyo <i>Diluted cow's milk</i> e. Ubisi lwenkomo olungaxutywanga <i>Not diluted cow's milk</i> f. Ubisi olungumgubo labantwana <i>Infant formula</i> g. Olungolunye ubisi olungumgubo <i>Any other powdered milk</i> h. Ipapa <i>Any porridge</i> i. Isophu <i>Any soup</i> j. Nayaphi na into engemanzi ibiyinxalezye yesiko <i>Any liquid as part of a ritual.</i> k. Utywala <i>Alcohol</i> l. Iyeza lesintu <i>Traditional medicine</i> m. Amayeza angekhoyo kuluhlu <i>Non-prescribed medicine</i> chaza/specify: _____ n. Amayeza akuluhlu avunyiweyo <i>Prescribed medicine,</i> chaza/specify: _____ o. Ubusi <i>Honey</i> p. Amanye <i>Other,</i> chaza/specify: _____

<p>6. Kwintsuku zokuqala usana lunikwe into lungcamle;amaqabaza ento okanye nganeno kunomlomo ogcweleyo? <i>Within the first days did the baby get anything to taste; a few drops of something or less than a mouth full?</i></p>	<p>Hayi <i>No</i> = 0 → Gqithela ku Q8 <i>SKIP to Q8</i> Ewe <i>Yes</i> = 1 Andazi= 9 → Gqithela ku Q8 <i>Don't know SKIP to Q8</i></p>
<p>7. Ukuba ewe, Yintoni eyanikwa usana lungcamle kwintsuku ezi-3 luzzelwe. <i>If yes, what was the child given to taste within the first 3 days after birth</i> Rhangqa zonke awazingcamliswa <i>Read all, circle all that apply</i></p>	<p>a. Amanzi <i>Water</i> b. Amanzi aneswekile <i>Water with sugar (or glucose)</i> c. manzi anetyuwa <i>Water with salt</i> d. Ubisi lwenkomo oluxutyiweyo <i>Diluted cow's milk</i> e. Ubisi lwenkomo olungaxutywanga <i>Not diluted cow's milk</i> f. Ubisi olungumgubo labantwana <i>Infant formula</i> g. Olungolunye ubisi olungumgubo <i>Any other powdered milk</i> h. Ipapa <i>Any porridge</i> i. Isophu <i>Any soup</i> j. Nayaphi na into engemanzi ibiyinxalezye yesiko <i>Any liquid as part of a ritual.</i> k. Utywala <i>Alcohol</i> l. Iyeza lesintu <i>Traditional medicine</i> m. Amayeza angekhoyo kuluhlu <i>Non-prescribed medicine</i> chaza/specify: _____ n. Amayeza akuluhlu avunyiweyo <i>Prescribed medicine,</i> chaza/specify: _____ o. Ubusi <i>Honey</i> p. Amanye <i>Other,</i> chaza/specify: _____</p>
<p>Ukukhumbula indlela zokondla usana <i>Infant feeding recalls:</i></p>	
<p>8. Uyaluncancisa ibele usana lwakho kude kube ngoku <i>Are you currently breastfeeding your baby</i></p>	<p>Hayi <i>No</i> = 0 Ewe <i>Yes</i> = 1 → <i>SKIP TO Q14</i></p>
<p>9. Uluncancise ibele usana lwakho ixesha elingakanani <i>For how long did you breastfeed your child?</i></p>	<p>Zange lube sebeleni=0 <i>Never breastfed</i> lintsuku: _____ <i>Days</i> Andiyazi =9 <i>Do not know</i></p>
<p>10. Zeziphi izizathu ezibangele uyeke ukuluncancisa usana/okanye ungaluncancisi <i>What were your reasons for stopping to breastfeed/not breastfeed your child?</i> <i>Read all, circle all that apply</i></p>	<p>a. Umsebenzi <i>Work</i> b. Imfundo <i>Education</i> c. Ukugula, ngaphandle kwengxaki zokuncancisa <i>Illness, other than lactation problems</i> d. Ingxaki zokuncancisa <i>Lactation problems</i> e. Usana alukhuli kakuhle <i>Child not grow well</i> f. Usana lukhala kakhulu <i>Child crying a lot</i> g. Ubisi lwebele alwanelanga <i>Not enough breast milk</i> h. Andifuni ukumosulela ngentsholongwane <i>Did not want to give my baby HIV infection</i> i. lingcebiso/ukunyanzeliswa ngabanye <i>Advice/pressure from others</i> j. Ezinye, cacisa: _____ <i>Other, specify</i></p>

<p>11. Uyeke njani ukuncancisa? <i>How did you stop breastfeeding?</i></p>	<p>Andizanga ndancancisa=0 Never breastfed Ndimlumile kancinci ndamnika olunye ubisi emva kwentsuku ezimbalwa=1 <i>Gradually changed to other replacement milk over a period of days</i> Ndimlumile kancinci ndamnika ubisi emva kweveki ezimbalwa=2 <i>Gradually change to other replacement milk over a period of weeks</i> Ndimlumile kancinci ndamnika ubisi mva kwenyanga ezimbalwa=3 <i>Gradually change to other replacement milk over a period of months</i> Ndiluhambisile usana iintsuku ezimbzlw=4 <i>Sent the child away for some days</i> Ndiqabe into ebeleni usana alwalifuna ibele=5 <i>Put something on breast to make child refuse breast</i> Ndiluncancise ebusuku kuphela=6 <i>Only breastfed at night</i> Ndifumene iyeza ekliniki lokunqamla ubisi=7 <i>Got medicine from clinic to stop milk</i> Ndisebenzise iyeza lesi Xhosa lokunqamla/irati yokunqamla=8 <i>Took traditional medicine/remedy medicine to stop milk</i> Lingcebiso/uxizelelo ngabaye=9 <i>Advice/pressure from others</i> Ezinye=10,cacisa: _____ <i>Other , specify</i></p>
<p>12. Ikuthathe ixesha elingakanani ukumyeka umphelelo? <i>How long did it take you to stop all breastfeeding?</i></p>	<p>lintsuku: _____ <i>Days</i></p>
<p>13. Uceba ukuluncancisa olu sana kaphinda? <i>Are you planning on breast feeding this baby ever again?</i></p>	<p>Hayi No = 0 Ewe Yes = 1 Andazi=9 <i>Don't know</i></p>
<p>14. Aye acandeka aphuma ubumdaka amabele,okanye wanengxaki emabeleni oko uhte walubeleka usana ? <i>Have you had any infection, or problem with your breasts since this child has been born?</i></p>	<p>Hayi No = 0 → Gqithela ku- 17 “dietary 24 hour recall” <i>SKIP to Q17</i> Ewe Yes = 1</p>
<p>15. Ukuba ewe,ngxakini le? <i>If yes, what problem did you have?</i> Funda zonke , urhangqe ezenzekileyo <i>Read all, circle all that apply</i></p>	<p>a. Ukudumba kwamabele <i>Engorgement (swollen painful breasts)</i> b. lingono ezichachambileyo <i>Cracked nipples</i> c. isilonda ebeleni <i>Abscess (sore on the breast)</i> d. ulosuleleko <i>Infection</i> e. Uqhaqho <i>Operation</i> f. Umothuko <i>Trauma</i> g. Ezinye, cacisa <i>Other, specify: _____</i></p>

<p>16. Usana lwakho belunangaphi ukwenzeka kwa le nto? <i>How old was your baby when this occurred?</i></p>	<p>lintsuku : _____ Days</p>
<p>Dietary 24hr recall <i>We will now ask you some questions about your baby's feeding since yesterday morning</i></p>	
<p>17. Ukuvuka kwakho izolo ekuseni kude ibe kukuvuka kwakho namhlanje ekuseni uye waluncancisa usana? <i>From the time you woke up yesterday morning till you woke up this morning did you breastfeed your baby?</i></p>	<p>Hayi No = 0 → Gqithela ku- 20 <i>SKIP to Q20</i> Ewe Yes = 1</p>
<p>18. Ukuvuka kwakho izolo ekuseni wade walala ebusuku ,uluncancise kangaphi usana? <i>From the time you woke up yesterday morning till you went to bed last night, how many times did you breastfeed?</i></p>	<p>a. _____ amaxa # of times b. _____ usana lulilela ibele # of on demand feedings</p>
<p>19. Ngelixesha uya kulala izolo kwade kwaba kukuvuka kwakho namhlanje ekuseni,uluncancise kangaphi usana? <i>From the time you went to bed last night till you woke up this morning, how many times did you breastfeed?</i></p>	<p>c. _____ amaxa # of times d. _____ usana lulilela ibele # of on demand feedings</p>
<p>20. Ukuvuka kwakho izolo ekuseni kude kube kukuvuka kwakho namhlanje ekuseni:Ulunikile usana ezinye zezi zinto. Rhangqa zonke omnike zona. <i>From the time you woke up yesterday morning till you woke up this morning: Did you give any of the following items to the child?</i></p> <p><u>Read ALL; please circle all that apply.</u></p> <p>Ukuba umnikile ,sixelele umnike kangaphi? <i>And if you did, will you please tell how many times you gave it?</i></p>	<p>a. Amanzi: Water, # _____ b. Amanzi aneswekile Any water with sugar or glucose, # _____ c. Ijusi yeziqhamo Any fruit juice, # _____ d. Ingcambu emanzini Any herbs in water, # _____ e. Iti engenabisi Any tea without milk, # _____ f. Iti enobisi Any tea with milk, # _____ g. amanzi erayisi Rice water, # _____ h. Ubisi lwenkomo oluxutyiweyo Diluted cow's milk, # _____ i. Ubisi lwenkomo olungaxutywanga # _____ <i>Non diluted cow's milk,</i> j. Ubisi olungumgubo labantwana Infant formula, # _____ k. Olungolunye ubisi olungumgubo # _____ <i>Other powdered milk,</i> l. Ezinye izinto njenge yogati,itshizi,ikhrim # _____ <i>Any other dairy product like yoghurt, cheese or cream,</i> m. Ubisi lwebhokhwe Goat's milk # _____ n. Ipapa yabantwana,ipapa,okanye isonka, # _____ <i>Cereals, porridge or bread,</i> o. Iziquhamo/vegi Any fruits/vegetables, # _____ p. Inyama ,intlanzi Any meat or fish, # _____ q. Amaqanda Eggs, # _____ r. iGripe water Gripe water, # _____ s. Amayeza abhalwe ngugqira <i>Any prescribed medicine, # _____</i> t. Amayeza angabhalwanga ngugqira, # _____ <i>Any non-prescribed medicine,</i> u. Into ebutywalara njenge bhiya,umqombothi, # _____ <i>Any alcohol like beer or brew,</i> v. Ezinye, cacisa: _____ # _____ <i>Other, specify</i> w. Nanye kwezi zikhankanywe ngentla <i>None of the above</i></p>

Formula feeding	
<i>We would also like to ask you some questions about using infant formula milk</i>	
21. Umnika umntwana ubisi lomgubo? <i>Is the mother formula feeding?</i>	Hayi No = 0 → Gqithela ku-39 "leaving the child" <i>SKIP to Q39</i> Ewe Yes = 1
22. Yeyiphi indlela eqhelekileyo yokunika usana ubisi lomgubo? <i>What is the usual way that you feed the child formula milk?</i> Mthundeze xa iyimfuneko. <i>Prompt when necessary.</i>	Ibhotile = 1 <i>Bottles</i> Ikomityi necephe=2 <i>Cup and spoon</i> Ikomityi evulekileyo asele=3 <i>Open cup and drinking</i> Ikomityi enomngxunya wokusela=4 <i>Cup with drinking spout</i> Ezinye=5 <i>Other</i> Andazi=9 <i>Don't know</i>
23. Zingaphi ezinye zezi zinto onazo ezisetyenziselwa ukondla usana? <i>How many of each of the following items do you have that are for infant feeding?</i> Nika inani lonazo ngento nganye. <i>Provide a number for each item that applies.</i>	a. Ibhotile <i>Bottles</i> : # _____ b. Ikomityi <i>Cups</i> : # _____ c. Ikomityi zokondla ezinemingxuma yokusela <i>Feeding cups with drinking spouts</i> : # _____ d. Ititi <i>Teats</i> : # _____ e. Ezinye, cacisa into : _____ # _____ <i>Other, specify item</i>
Kuyakhuthazwa ukuxuba/ulungise isidlo esinye sobisi lomgubo ngexesha, kwaye ungalugcini olushiyeluley ubisi, kodwa abanye omama bafumanisa kulula kwaye kungabizi ukuxuba ubisi olungu mgubo lwabantwana olwanele ngaphezu kwesidlo esinye, banika inxenye yobisi kwisidlo esinye kwaye bongele isininzi sobisi isidlo esilandelayo. Ngoku sizakubuza eminye imibuzo malunga nokuba ukukhetha ukuxuba kwaye utyise ngayo umntwana wakho amaxesha amaninzi: <i>It is recommended to only mix/prepare one feed of formula milk at a time, and not store left over milk. However, some mothers find it easier, and cheaper, to mix enough formula for more than one feed; they give some of the milk for one feed and save the rest of the milk for the next feed. We are now going to ask some questions about how you choose to mix and feed your baby most of the time:</i>	
24. Kukangaphi ngemini (iiyure ezi -24)ulungisa ubisi lomgubo xa usana luza kuncanca. (Kukangahpi uxuba ubisi lomgubo,hayi amaxa omncancisa ngawo) <i>How many times during a day (i.e. in a 24 hour period) is the formula normally prepared for the child? (Number of times the formula is mixed, not number of times given)</i>	_____ amaxesha <i>times</i>
25. Lubisi olungakanani lomgubo wabantwana oqhele ukululungisa ngexesha elinye (hayi ubungakanani obutyisa umntwana kwisidlo esinye)? <i>How much formula is normally prepared at one time (not how much is fed to the baby in one feed)?</i> Mthundeza xa kuyimfuneko <i>Prompt when necessary.</i>	75ml 100ml 125ml (1/2 yebhotile=1bhotile encinci) 150ml 175ml 200ml 250ml (1 bhotile enkulu) 500ml 1 litre Eminye, cacisa : _____ (mls) <i>Other, specify</i> Andazi/ Don't know = 9

<p>26. Umncancisa ubisi lomgubo olungakanani ngexesha? <i>How much formula is fed to the child each time?</i></p>	<p>_____ (mls)</p>
<p>27. Xa ubisi lomgubo wabantwana selulungisiwe (luxutyiwe), ulubekaphi ubisi oselulungisiwe kude ube uyamtyisa umntwana/phakathi kokutyisa umntwana?? <i>When the formula has been prepared (mixed), where is the prepared formula stored until/between feeding the baby?</i></p> <p>Mthundeze xa kuyimfuneko. <i>Prompt when necessary.</i></p>	<p>Egumbini: luggqunyiwe=1 <i>Room; covered</i> Egumbini ;lungagqunywanga=2 <i>Room; uncovered</i> Kwisikhencisi=3 <i>Refrigerator</i> Eflaskini lupholisiwe=4 <i>Flask: cooled first</i> Andilugcini,ndilunika ngoko=5 <i>Do not store, give it directly</i> Ezinye=6 cacisa: _____ <i>Other, specify</i> Andazi=9 <i>Don't know</i></p>
<p>28. Anjani amanzi owenza ngawo ngesiqhelo ubisi? <i>How was the water you use for the child's formula feeds normally prepared?</i></p> <p>Aphendule kubekanye ungamthundezi <i>One response only, do not prompt.</i></p>	<p>Billisa phambi kokunika usana=1 <i>Boil before each feed</i> Bilisa kanye ngemini agcinwe:egqunyiwe=2 <i>Boil once a day and store it: covered</i> Hluza=3 <i>Filter</i> Linda acwenge=4 <i>Allow to settle</i> Galela iblitshi=5 <i>Bleach</i> Andenzi nto=6 <i>Nothing</i> Bilisa,gcine amanzi ashushu eflaskini=7 <i>Boil, store hot water in flask</i> Ezinye=8 cacisa: _____ <i>Other, specify</i> Andazi=9 <i>Don't know</i></p>
<p>29. Ubisi lomgubo ulufumana esibhedlele /kliniki losana lwakho? <i>Are you currently receiving formula milk from the hospital/clinic for your infant?</i></p>	<p>Hayi No = 0 →SKIP to Q32 Ewe Yes = 1</p>
<p>30. Oko usana lwakho walubeleka ukhe waya ekliniki uyokulanda ubisi wafumanisa lungakho? <i>Since your baby was born have you been to the clinic to collect milk and found that they were out of stock?</i></p>	<p>Hayi No = 0 → Gqithela ku-32 <i>SKIP to Q32</i> Ewe Yes = 1</p>
<p>31. Yenzeke kangaphi le nto oko walubeleka usana? <i>How many times has this happened since your baby was born?</i></p>	<p>_____ amaxesha <i># times</i></p>
<p>32. Oko usana walubeleka sewukhe waluthenga ubisi? <i>Since your child's birth have you purchased any formula milk for your infant?</i></p>	<p>Hayi No = 0 Ewe Yes = 1</p>

<p>33. Oko usana walubeleka wakhe waphelelwa lubisi? <i>Since your child's birth have you run out of formula milk?</i></p>	<p>Hayi No = 0 → Gqithela ku-36 <i>SKIP to Q36</i> Ewe Yes = 1</p>
<p>34. Ithathe ixesha elingakanani? <i>How many days did this last?</i></p>	<p>Iintsuku : _____ <i>Days</i></p>
<p>35. Uluncancise ntoni usana ngeli xesha? <i>What did you feed the baby during this time?</i></p> <p>Rhangqa zonke omnike zona <i>Circle all that apply</i></p>	<p>a. Ubisi lwebele <i>Breast milk</i> b. Ipapa <i>Porridge</i> c. Amanzi <i>Water</i> d. Amanzi aneswekile <i>Sugar and water</i> e. Iti <i>Tea</i> f. Ndiluthengile <i>Purchased formula</i> g. Ijusi <i>Juice</i> h. Ezinye,cacisa: _____ <i>Other, specify</i></p>
<p>36. Unalo ubisi lomgubo namhlanje endlini? <i>Do you have any formula in the house today?</i></p>	<p>Hayi No = 0 Ewe Yes = 1</p>
<p>37. Wakhe waluncancisa usana lwakho oko waluzala ,umz.xa luza kulala,ebusuku ebhedini,xa lulila? <i>Have you ever put your baby to the breast since birth e.g. to go to sleep, in bed at night time, when crying?</i></p>	<p>Hayi No = 0 Ewe Yes = 1</p>
<p>38. Wakhe wabona ezikliniki amaphepha apapasha ngobisi lomgubo? <i>Have you seen adverts at any health clinic advertising formula milks?</i></p>	<p>Hayi No = 0 Ewe Yes = 1</p>
<p>Questions about leaving the child</p>	
<p>39. Sewukhe wohlukana nosana lwakho oko walubeleka kwenzeka ancanciswe ngomnye umntu? <i>Have you ever been separated from your child since childbirth so that someone else has fed the child?</i></p>	<p>Hayi No = 0 → <i>SKIP TO Q41</i> Ewe Yes = 1</p>
<p>40. Luye lwancanciswa ntoni usana oku kokugqibela ungekho? <i>What did they feed the child the last time you were away?</i></p> <p>Rhangqa zonke ezenziweyo <i>Circle all that apply</i></p>	<p>a. Umxube wamanzi <i>Water based liquids</i> b. Umxube wobisi/ukutya okuthambileyo <i>Milk based liquids/semi-solid feeds</i> c. Ubisi lwam lwebele ebendilukhamile <i>My own expressed breast milk</i> d. Usana beluncanciswe ibele ngomnye umdlezana <i>The child was "wet nursed" (breastfed by another woman)</i> e. Ubisi lomgubo <i>Formula milk</i> f. Ukutya ebendikuhlafunile kosana <i>Food that I chewed for the baby</i> g. Andazi <i>Do not know</i> h. Enye,cacisa : _____ <i>Other, Specify</i></p>

Last questions about formula and breastfeeding:	
<i>We will now ask you only five more questions about formula and breastfeeding</i>	
<p>41. Ngawaphi kulamayeza atyiwa lusana lwakho: Which of these medicines is your baby currently receiving:</p> <p><i>Show the mother a range of possible medicines: multivitamins, iron drops, nevirapine, cotrimoxazole, TB treatment and antibiotics</i></p> <p>Rhangqa zonke ezenziweyo <i>Circle all that apply</i></p>	<p>a. Multivitamins (eg. Kiddievite) b. Iron drops c. Zinc syrup d. Nevirapine e. Co-trimoxazole (or Bactrim/Trimethoprim-Sulphamethoxazole / Resmed / Iantibiotic ukukhusela ulwasuleleko lwesifuba (<i>antibiotic to prevent chest infection</i>)) f. TB drugs g. Antibiotics h. Enye, cacisa <i>Other, specify</i> _____ i. Umntwana akanamayeza awatyayo <i>Baby is not currently on any medication</i></p>
<p>42. Ebengakanani umntwana ukuqala kwakho ukumnika ezinye izinto ngaphandle kwebisi lebele okanye amayeza? Ngamany'amazwi, ebengakanani yena xa wayeqala ukufumana amanzi okanye ukutya okanye ubisi lomgubo wabantwana?</p> <p><i>How old was the baby when you FIRST gave him/her anything other than breast-milk or medicine to drink? In other words, how old when he/she first had any water or food or formula milk?</i></p>	<p>Zange ndamnika enye into umntwana ngaphandle kwebisi lwebele = 0 → Phela apha/ END <i>Have only given baby breastmilk and medicine since birth</i> OR Indicate age in weeks: # _____ Andiqinisekanga <i>Unsure</i> = 9</p>
<p>43. Ukusuka kwixesha ovuke ngalo kusasa izolo kude kuye ekuvukeni kwakho kusasa nje, ubukhe wamnika umntwana wakho ubisi olungumgubo lwabantwana?</p> <p><i>From the time you woke up yesterday morning till you woke up this morning did you give your baby any formula milk?</i></p>	<p>Hayi <i>No</i> = 0 → Phela apha/ END Ewe <i>Yes</i> = 1</p>
<p>44. Ukusuka kwixesha ovuke ngalo kusasa izolo kude kubelixesha lakho lokulala, umncancise kangaphi umntwana wakho ubisi olungumgubo lwabantwana?</p> <p><i>From the time you woke up yesterday morning till you went to bed last night, how many times did you feed your baby formula milk?</i></p>	<p>_____ amaxa # of times</p>
<p>45. Ukusuka kwixesha ovuke ngalo kusasa izolo kude kube kukuvuka kwakho kusasa nje, umncancise kangaphi umntwana wakho ubisi olungumgubo lwabantwana?</p> <p><i>From the time you went to bed last night till you woke up this morning, how many times did you feed your baby formula milk?</i></p>	<p>_____ amaxa # of times</p>

Date completed: ___ / ___ / _____

Signed counsellor completing CRF: _____

Date of QC: ___ / ___ / _____

Signed measurement nurse: _____

Appendix D –

MCH-ART Phase 3, infant feeding intentions/practices questionnaire

		Visit Date: ___/___/_____
<i>Infant feeding recalls:</i>		
1.	Are you currently breastfeeding your baby?	No = 0 Yes = 1 → SKIP to Q7
2.	For how long did you breastfeed your baby?	Days: _____ Weeks: _____ Do not know
3.	What were your reasons for stopping to breastfeed/not breastfeed your baby? <i>Read all, circle all that apply</i>	a. Work b. Education c. Illness, other than lactation problems d. Lactation problems e. Child not grow well f. Child crying a lot g. Not enough breast milk h. Did not want to give my baby HIV infection i. Advice/pressure from others j. Other, specify: _____
4.	How did you stop breastfeeding?	Gradually changed to other replacement milk over a period of days = 1 Gradually change to other replacement milk over a period of weeks = 2 Gradually change to other replacement milk over a period of months = 3 Sent the child away for some days = 4 Put something on breast to make child refuse breast = 5 Only breastfed at night = 6 Got medicine from clinic to stop milk = 7 Took traditional medicine/remedy medicine to stop milk = 8 Advice/pressure from others = 9 Other = 10, specify: _____
5.	How long did it take you to stop all breastfeeding?	Days: _____
6.	Are you planning on breast feeding this baby ever again?	No = 0 Yes = 1 Don't know = 9
7.	Have you had any infection, or problem with your breasts since this child has been born?	No = 0 → SKIP to "Dietary 24hr recall" 10 Yes = 1
8.	If yes , what problem did you have? <i>Read all, circle all that apply</i>	a. Engorgement (swollen painful breasts) b. Cracked nipples c. Abscess (sore on the breast) d. Infection e. Operation f. Trauma g. Other, specify: _____
9.	How old was your baby when this occurred?	Days: _____ Weeks: _____

<i>Dietary 24hr recall</i> We will now ask you some questions about your baby's feeding over the last 24 hours		
10.	From <u>the time you woke up yesterday morning till you woke up this morning</u> did you breastfeed your baby?	No = 0 → SKIP to Q13 Yes = 1
11.	From <u>the time you woke up yesterday morning till you went to bed last night</u> , how many times did you breastfeed?	a. _____ # of times b. _____ # of on demand feedings
12.	From <u>the time you went to bed last night till you woke up this morning</u> , how many times did you breastfeed?	a. _____ # of times b. _____ # of on demand feedings
13.	From <u>the time you woke up yesterday morning till you woke up this morning</u> : Did you give any of the following items to the child? Please circle all that apply. And if you did, will you please tell how many times you gave it?	a. Water, # _____ b. Any water with sugar or glucose, # _____ c. Any fruit juice, # _____ d. Any herbs in water, # _____ e. Any tea without milk, # _____ f. Any tea with milk, # _____ g. Rice water, # _____ h. Diluted cow's milk, # _____ i. Non diluted cow's milk, # _____ j. Infant formula, # _____ k. Other powdered milk, # _____ l. Any other dairy product like yoghurt, cheese or cream, # _____ m. Goat's milk, # _____ n. Cereals, porridge or bread, # _____ o. Any fruits/vegetables, # _____ p. Any meat or fish, # _____ q. Eggs, # _____ r. Gripe water, # _____ s. Any prescribed medicine, # _____ t. Any non-prescribed medicine, # _____ u. Any alcohol like beer or brew, # _____ v. Other, specify: _____ # _____ w. None of the above
<i>Formula Feeding</i> We would also like to ask you some questions about using infant formula milk		
14.	Is the mother formula feeding?	No = 0 → SKIP to "leaving the child" Q32 Yes = 1
15.	What is the usual way that you feed the child formula milk? Prompt when necessary.	Bottles = 1 Cup and spoon = 2 Open cup and drinking = 3 Cup with drinking spout = 4 Other = 5 Don't know = 9

16.	<p>How many of each of the following items do you have that are for infant feeding?</p> <p><i>Provide a number for each item that applies.</i></p>	<p>a. Bottles: # _____ b. Cups :# _____ c. Feeding cups with drinking spouts: # _____ d. Teats: # _____ e. Other, specify item: _____ # _____</p>
17.	<p>How many times during a day (i.e. in a 24 hour period) is the formula normally prepared for the child? (Number of times the formula is mixed, not number of times given)</p>	<p>_____ times</p>
18.	<p>How much formula is normally prepared at one time?</p> <p>Prompt when necessary.</p>	<p>75ml 100ml 125ml (1/2 big bottle = 1 small bottle) 150ml 175ml 200ml 250ml (1 big bottle) 500ml 1 litre Other, specify: _____ (mls) Don't know</p>
19.	<p>How much formula is fed to the child each time?</p>	<p>_____ (mls)</p>
20.	<p>Where is the prepared formula stored?</p> <p>Prompt when necessary.</p>	<p>Room; covered = 1 Room; uncovered = 2 Refrigerator = 3 Flask: cooled first = 4 Do not store, give it directly = 5 Other = 6, specify _____ Don't know = 9</p>
21.	<p>How was the water you use for the child's formula feeds normally prepared?</p> <p>One response only, do not prompt.</p>	<p>Boil before each feed = 1 Boil once a day and store it: covered = 2 Filter = 3 Allow to settle = 4 Bleach = 5 Nothing = 6 Boil, store hot water in flask = 7 Other = 8, specify: _____ Don't know = 9</p>
22.	<p>Are you currently receiving formula milk from the hospital/clinic for your infant?</p>	<p>No = 0 Yes = 1</p>
23.	<p>Since your baby was born have you been to the clinic to collect milk and found that they were out of stock?</p>	<p>No = 0 → SKIP to Q25 Yes = 1</p>
24.	<p>How many times has this happened since your baby was born?</p>	<p>_____ # of times</p>

25.	Since your child's birth have you purchased any formula milk for your infant?	No = 0 Yes = 1
26.	Since your child's birth have you run out of formula milk?	No = 0 → SKIP to Q29 Yes = 1
27.	How many days did this last?	Days: _____
28.	What did you feed the baby during this time? <i>Circle all that apply</i>	a. Breast milk b. Porridge c. Water d. Sugar and water e. Tea f. Purchased formula g. Juice h. Other, specify: _____
29.	Do you have any formula in the house today?	No = 0 Yes = 1
30.	Have you ever put your baby to the breast since birth e.g. to go to sleep, in bed at night time, when crying?	No = 0 Yes = 1
31.	Have you seen adverts at any health clinic advertising formula milks?	No = 0 Yes = 1
Questions about leaving the child		
32.	Have you ever been separated from your child since childbirth so that someone else has fed the child?	No = 0 → SKIP to Q34 Yes = 1
33.	What did they feed the child the last time you were away? <i>Circle all that apply</i>	a. Water based liquids b. Milk based liquids/semi-solid feeds c. My own expressed breast milk d. The child was "wet nursed" (breastfed by another woman) e. Formula milk f. Food that I chewed for the baby g. Do not know h. Other, Specify: _____
Last questions about formula and breastfeeding: <i>We will now ask you only five more questions about milk feeding</i>		
34.	Which of these medicines is your baby currently receiving: <i>Please show the mother a range of possible medicines: multivitamins, iron drops, nevirapine, cotrimoxazole, TB treatment and antibiotics</i> <i>Circle all that apply</i>	a. Multivitamins (eg Kiddievite) b. Iron drops c. Zinc syrup d. Nevirapine e. Co-trimoxazole f. TB drugs g. Antibiotics h. Other – specify _____ i. Baby is not currently receiving any medicine

35.	How old was the baby when you FIRST gave him/her anything other than breast-milk or medicine?	# weeks old _____ OR Have only given baby breast-milk and medicine since birth = 0 → END 1. Unsure = 9 → END
36.	From the time you woke up yesterday morning till you woke up this morning did you give your baby any formula milk?	Hayi No = 0 → END Ewe Yes = 1
37.	From the time you woke up yesterday morning till you went to bed last night, how many times did you feed your baby formula milk?	_____ # of times
38.	From the time you went to bed last night till you woke up this morning, how many times did you feed your baby formula milk?	_____ # of times

Date completed: ___ / ___ / _____

Signed counsellor completing CRF: _____

Date of QC: ___ / ___ / _____

Signed measurement nurse: _____

		Visit Date: ___/___/_____
<i>Infant feeding recalls:</i>		
1.	Are you currently breastfeeding your baby?	No = 0 Yes = 1 → SKIP to Q7
2.	For how long did you breastfeed your baby?	Days: _____ Weeks: _____ Do not know
3.	What were your reasons for stopping to breastfeed/not breastfeed your baby? <i>Read all, circle all that apply</i>	a. Work b. Education c. Illness, other than lactation problems d. Lactation problems e. Child not grow well f. Child crying a lot g. Not enough breast milk h. Did not want to give my baby HIV infection i. Advice/pressure from others j. Other, specify: _____
4.	How did you stop breastfeeding?	Gradually changed to other replacement milk over a period of days = 1 Gradually change to other replacement milk over a period of weeks = 2 Gradually change to other replacement milk over a period of months = 3 Sent the child away for some days = 4 Put something on breast to make child refuse breast = 5 Only breastfed at night = 6 Got medicine from clinic to stop milk = 7 Took traditional medicine/remedy medicine to stop milk = 8 Advice/pressure from others = 9 Other = 10, specify: _____
5.	How long did it take you to stop all breastfeeding?	Days: _____
6.	Are you planning on breast feeding this baby ever again?	No = 0 Yes = 1 Don't know = 9
7.	Have you had any infection, or problem with your breasts since we last saw you?	No = 0 → SKIP to "Dietary 24hr recall" 10 Yes = 1
8.	If yes , what problem did you have? <i>Read all, circle all that apply</i>	a. Engorgement (swollen painful breasts) b. Cracked nipples c. Abscess (sore on the breast) d. Infection e. Operation f. Trauma g. Other, specify: _____
9.	How old was your baby when this occurred?	Days: _____ Weeks: _____

<i>Dietary 24hr recall</i> <i>We will now ask you some questions about your baby's feeding over the last 24 hours</i>		
10.	From <u>the time you woke up yesterday morning till you woke up this morning</u> did you breastfeed your baby?	No = 0 → SKIP to Q13 Yes = 1
11.	From <u>the time you woke up yesterday morning till you went to bed last night</u> , how many times did you breastfeed?	a. _____ # of times b. _____ # of on demand feedings
12.	From <u>the time you went to bed last night till you woke up this morning</u> , how many times did you breastfeed?	a. _____ # of times b. _____ # of on demand feedings
13.	From <u>the time you woke up yesterday morning till you woke up this morning</u> : Did you give any of the following items to the child? Please circle all that apply. And if you did, will you please tell how many times you gave it?	a. Water, # _____ b. Any water with sugar or glucose, # _____ c. Any fruit juice, # _____ d. Any herbs in water, # _____ e. Any tea without milk, # _____ f. Any tea with milk, # _____ g. Rice water, # _____ h. Diluted cow's milk, # _____ i. Non diluted cow's milk, # _____ j. Infant formula, # _____ k. Other powdered milk, # _____ l. Any other dairy product like yoghurt, cheese or cream, # _____ m. Goat's milk, # _____ n. Cereals, porridge or bread, # _____ o. Any fruits/vegetables, # _____ p. Any meat or fish, # _____ q. Eggs, # _____ r. Gripe water, # _____ s. Any prescribed medicine, # _____ t. Any non-prescribed medicine, # _____ u. Any alcohol like beer or brew, # _____ v. Other, specify: _____ # _____ w. None of the above
<i>Formula Feeding</i> <i>We would also like to ask you some questions about using infant formula milk</i>		
14.	Is the mother formula feeding?	No = 0 → SKIP to "leaving the child" Q32 Yes = 1
15.	What is the usual way that you feed the child formula milk? Prompt when necessary.	Bottles = 1 Cup and spoon = 2 Open cup and drinking = 3 Cup with drinking spout = 4 Other = 5 Don't know = 9

16.	<p>How many of each of the following items do you have that are for infant feeding?</p> <p><i>Provide a number for each item that applies.</i></p>	<p>a. Bottles: # _____ b. Cups :# _____ c. Feeding cups with drinking spouts: # _____ d. Teats: # _____ e. Other, specify item: _____ # _____</p>
17.	<p>How many times during a day (i.e. in a 24 hour period) is the formula normally prepared for the child? (Number of times the formula is mixed, not number of times given)</p>	<p>_____ times</p>
18.	<p>How much formula is normally prepared at one time?</p> <p>Prompt when necessary.</p>	<p>75ml 100ml 125ml (1/2 big bottle = 1 small bottle) 150ml 175ml 200ml 250ml (1 big bottle) 500ml 1 litre Other, specify: _____ (mls) Don't know</p>
19.	<p>How much formula is fed to the child each time?</p>	<p>_____ (mls)</p>
20.	<p>Where is the prepared formula stored?</p> <p>Prompt when necessary.</p>	<p>Room; covered = 1 Room; uncovered = 2 Refrigerator = 3 Flask: cooled first = 4 Do not store, give it directly = 5 Other = 6, specify _____ Don't know = 9</p>
21.	<p>How was the water you use for the child's formula feeds normally prepared?</p> <p>One response only, do not prompt.</p>	<p>Boil before each feed = 1 Boil once a day and store it: covered = 2 Filter = 3 Allow to settle = 4 Bleach = 5 Nothing = 6 Boil, store hot water in flask = 7 Other = 8, specify: _____ Don't know = 9</p>
22.	<p>Are you currently receiving formula milk from the hospital/clinic for your infant?</p>	<p>No = 0 Yes = 1</p>
23.	<p>Since we last saw you have you been to the clinic to collect milk and found that they were out of stock?</p>	<p>No = 0 → SKIP to Q25 Yes = 1</p>
24.	<p>How many times has this happened since we last saw you?</p>	<p>_____ # of times</p>

25.	Since we last saw you have you purchased any formula milk for your infant?	No = 0 Yes = 1
26.	Since we last saw you have you run out of formula milk?	No = 0 → SKIP to Q29 Yes = 1
27.	How many days did this last?	Days: _____
28.	What did you feed the baby during this time? <i>Circle all that apply</i>	a. Breast milk b. Porridge c. Water d. Sugar and water e. Tea f. Purchased formula g. Juice h. Other, specify: _____
29.	Do you have any formula in the house today?	No = 0 Yes = 1
30.	Since we last saw you have you ever put your baby to the breast e.g. to go to sleep, in bed at night time, when crying?	No = 0 Yes = 1
31.	Since we last saw you have you seen adverts at any health clinic advertising formula milks?	No = 0 Yes = 1
Questions about leaving the child		
32.	Have you been separated from your child since we last saw you so that someone else has fed the child?	No = 0 → SKIP to Q34 Yes = 1
33.	What did they feed the child the last time you were away? <i>Circle all that apply</i>	a. Water based liquids b. Milk based liquids/semi-solid feeds c. My own expressed breast milk d. The child was "wet nursed" (breastfed by another woman) e. Formula milk f. Food that I chewed for the baby g. Do not know h. Other, Specify: _____
Last questions about formula and breastfeeding: <i>We will now ask you only five more questions about milk feeding</i>		
34.	Which of these medicines is your baby currently receiving: <i>Please show the mother a range of possible medicines: multivitamins, iron drops, nevirapine, cotrimoxazole, TB treatment and antibiotics</i> <i>Circle all that apply</i>	a. Multivitamins (eg Kiddievite) b. Iron drops c. Zinc syrup d. Nevirapine e. Co-trimoxazole f. TB drugs g. Antibiotics h. Other – specify _____ i. Baby is not currently receiving any medicine

35.	How old was the baby when you FIRST gave him/her anything other than breast-milk or medicine?	# weeks old _____ OR Have only given baby breast-milk and medicine since birth = 0 → END Unsure = 9 → END
36.	From the time you woke up yesterday morning till you woke up this morning did you give your baby any formula milk?	No = 0 → END Yes = 1
37.	From the time you woke up yesterday morning till you went to bed last night, how many times did you feed your baby formula milk?	_____ # of times
38.	From the time you went to bed last night till you woke up this morning, how many times did you feed your baby formula milk?	_____ # of times
Questions about introduction of complementary foods <i>We will now ask you about feeding your baby food other than milk</i>		
39.	Do you give your baby any meals or snacks besides milk?	No = 0 → END Yes = 1
40.	At what age did you FIRST give your baby any meals or snacks besides milk? <i>Choose one option</i>	a. Within 1 week of birth b. 1-4 weeks old c. 1-2 months old d. 2-3 months old e. 4-5 months old f. 6 months old g. Older than 6 months, # months age: _____ h. Unsure
41.	How many times PER DAY do you <u>usually</u> feed your baby food other than milk? (both snacks and meals)	# _____ times per day
42.	How many times did you give your baby food other than milk <u>yesterday</u> ? (both snacks and meals)	# _____ times per day
43.	How much food (other than milk) does your baby <u>usually</u> eat per meal? ** Please show mother the study-specific cups (full cup, half cup, quarter cup) and teaspoon	a. A teaspoon or less b. ¼ - ½ cup c. ½ - 1 cup d. >1 cup e. Other, please specify: _____ f. Unsure

Date completed: ___ / ___ / _____

Signed counsellor completing CRF: _____

Date of QC: ___ / ___ / _____

Signed measurement nurse: _____

Appendix E –

Dissertation study HREC approval



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: larnees.emledi@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

23 December 2016

HREC REF: 876/2016

Dr S Le Roux
Public Health & Family Medicine
Falmouth Building
Medical School

Dear Dr Le Roux

PROJECT TITLE: PATTERNS AND PREDICTORS OF EXCLUSIVE BREASTFEEDING DURATION AMONG WOMEN LIVING WITH HIV IN CAPE TOWN, SOUTH AFRICA (MPH-candidate-K Nguyen)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30th December 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period. (Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledges that the following MPH Candidate, K Nguyen, will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate Institutional approval before the research may occur.

Yours sincerely

PP signature removed
PROFESSOR M. BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 876/2016

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Appendix F –

MCH-ART Phase 2 informed consent form

TITLE OF RESEARCH: **Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study**

WHAT IS THE PURPOSE OF THIS STUDY?

We are from the University of Cape Town and ICAP at Columbia University. You are being asked to take part in a study that is being conducted at the Gugulethu Midwife Obstetric Unit (MOU). The purpose of this study is to understand how to improve health care services for HIV-positive women during their pregnancy and after they deliver the baby.

We know that it is important for their own health as well as the health of their baby, that HIV-positive women receive the HIV care and treatment that they need both during and after delivery. Information learned in this study will help us to improve HIV services for pregnant women.

You are being asked to take part in this study because you are a pregnant woman with known HIV infection who is about to start taking HIV drugs (antiretroviral therapy) and you took part in the first phase of the study. The purpose of this consent form is to give you information to help you decide if you want to take part in the next phase of this study.

WHAT DO I HAVE TO DO IF I AGREE TO TAKE PART?

If you agree to take part, you will come in for up to 3 visits. These visits will take place today while you are in the clinic, when you are getting close to delivering your baby and within one week of delivering your baby. These study visits are separate from the usual clinic visits that you will have for your pregnancy and HIV care. Study visits will be timed so that they take place on the same days that you come in for your usual pregnancy and/or HIV care. Each visit will take about 30-45 minutes.

At the two visits that are conducted *while you are pregnant*, you will do the following:

- Answer questions about your recent pregnancy- and HIV-related health care, HIV disclosure, and use of HIV drugs (including side effects and adherence).
 - At different visits, we will ask you additional questions about HIV, stigma, social support, infant feeding practices, family planning, experiences of partner violence, and mental health (including drug and alcohol use).
- Have 5mLs (1 teaspoon) of blood drawn from your arm each time

One-week after delivery

One week after you give birth to your baby, you will come to the clinic for a visit that will include the following:

- Answer questions about your recent pregnancy- and HIV-related health care, HIV disclosure, and use of HIV drugs (including side effects and adherence).
 - At this visit, we will ask you additional questions about family planning after delivery, how you felt about the HIV care that you received, infant feeding practices and infant health and health care.
- Have 5mLs (1 teaspoon) of blood drawn from your arm

NOTE: The blood that is drawn today will be stored and used to check your viral load (this is the amount of HIV in your blood) at a later time. Results from these tests will not be available to you, the clinic, or the study staff. When the health care providers at the clinic need to check your viral load, they will take a separate blood specimen. When it is stored, your blood and test results will not have your name or any other way of identifying you attached to it.

Follow-up of missed visits

You will be asked to provide contact information so that we may get in touch with you during the study. Study staff will talk with you about the best way to contact you. In the event that you miss one of the scheduled study visits, a member of the study staff will contact you in order to find another day and time to complete your visit. If you repeatedly miss study visits or the staff is unable to contact you using the information that you provide, it may be necessary to visit you at home in order to reschedule the missed study visit.

Contact for future study

After the completion of the visit one week after delivery, *it is possible that we will contact you again at your next clinic visit or at another time in the future to take part in additional research studies. At that time, you would be asked to review and sign another consent form. You can choose to not take part in any future studies if you are asked.* You will be asked to provide contact information so that we may get in touch with you regarding additional research studies. Study staff will talk with you about the best way to contact you.

WHAT ARE THE POTENTIAL RISKS?

You may feel uncomfortable about some of the personal questions you are asked. You may refuse to answer any question that you do not want to answer. There is some risk in sharing personal and medical information. We will be careful to keep all your information as private as possible.

Drawing blood is normally done as part of routine medical care and presents a slight risk of discomfort. Experienced staff will draw blood under sterile conditions in order to protect you against these risks.

WHAT ARE THE POTENTIAL BENEFITS?

There is no direct benefit to you if you take part in this study. The information gained in this study may help to improve ART services for HIV-infected pregnant women in Cape Town, the Western Cape Province, and across South Africa.

WHAT ARE THE ALTERNATIVES TO TAKING PART?

The alternative to taking part in this study is to continue with your usual care at the MOU.

WHAT ABOUT CONFIDENTIALITY?

If you agree to take part, all information collected during the study will be kept strictly confidential. Your name will not be written on the study forms and will not be used in connection with any information or lab specimens that are collected as part of the study.

All study materials will be stored in locked filing cabinets. Only study staff and personnel involved in routine audits will have access to these materials. All staff involved in data collection and management will get specific training in confidentiality.

Even with these procedures in place, if the study staff learns that you are a risk to yourself or someone else or of possible child abuse and/or neglect, study staff will tell the proper authorities.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

At the end of each visit, you will be given R20 in cash to cover the transport cost to your next scheduled study visit, and an R80 grocery voucher. You will also receive a small gift for the first visit after birth and refreshments will be provided at all visits.

ARE THERE ANY COSTS?

There is no cost for being in this study.

CAN I LEAVE THE STUDY?

You have the right to decide not to take part in the study, to refuse to answer any questions, or to withdraw from the study at any time without any penalty. It will have no effect on the care that you receive at the Gugulethu MOU or any other health facility.

FUTURE USE OF SPECIMENS:

If you agree, any leftover blood from the samples you have provided for this research project may be used for future HIV related research. It is possible that these stored samples may be tested to see if the HIV in your blood is resistant to any types of HIV medications or to look at other questions related to HIV.

At this time, we cannot provide details of when this testing may be conducted. However, additional testing will not be done using these stored samples without the approval of the appropriate ethics committees involved in this research.

If you agree to let us keep your stored samples for future research, they may be kept in a locked freezer for up to 5 years. If we do use your samples in the future, your name or other identifiers will not be included with this information (as with the rest of the information we collect for this study).

Phase 2 Informed Consent Form

Please initial below to indicate whether or not you give permission for your specimens to be used for future research. You may still remain in the study, no matter which you choose.

_____ (initial) I agree to have my blood stored for future research.

_____ (initial) I agree to have my blood stored for future research related to this study ONLY.

_____ (initial) I do NOT agree to the storage of my blood for future use.

DO YOU HAVE ANY QUESTIONS?

If there is anything that is unclear or if you need further information, please ask us and we will provide it.

Do you have any questions?

FOR ADDITIONAL INFORMATION:

If you have any questions or have any problems while taking part in this research study, you should contact:

Dr Landon Myer
School of Public Health and Family Medicine
Faculty of Health Sciences, University of
Cape Town
Tel: 021 406 6661
Email: Landon.Myer@uct.ac.za

Dr Elaine Abrams
ICAP, Columbia University
Mailman School of Public Health
College of Physicians and Surgeons
Tel: +1 212 342 0543
Email: eja1@columbia.edu

If you have any questions about your rights as a research participant, you may contact the following member of the ethics committee:

Prof Marc Blockman
Chair, Human Research Ethics Committee
Faculty of Health Sciences, University of Cape
Town
Tel: 021 406 6338

Columbia University Medical Center IRB
Tel: +1 212 305 5883

Phase 2 Informed Consent Form

CONSENT STATEMENT:

I have read this form, or someone has read it to me. I have been offered a copy of this consent form. I was encouraged and given time to ask questions. I agree to be in this study. I know that after choosing to be in this study, I may withdraw at any time. My being in the study is voluntary. I understand that whether or not I participate will not affect my health care services received today, or at any time in the future.

Please indicate your consent with your signature.

Volunteer's name _____

Signature of Volunteer Date

Staff member's name _____

Signature of study staff Date

If the volunteer is unable to read or write the entire counselling process must be observed by an independent witness who can then confirm the procedure once the she has given consent.

Fingerprint of volunteer:

Witness:

I confirm that I am independent of the study and that I witnessed the entire informed consent counselling process in the home language of the volunteer

Name: _____

Signature: _____

Date: _____

Thank you.

Appendix G –

MCH-ART Phase 3 informed consent form

TITLE OF RESEARCH: Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study

WHAT IS THE PURPOSE OF THIS STUDY?

We are from the University of Cape Town and ICAP at Columbia University. You are being asked to take part in a study that is being conducted at the Gugulethu Midwife Obstetric Unit (MOU). The purpose of this study is to compare two different ways of providing HIV treatment to women after they deliver a baby.

We know that it is important for their own health as well as the health of their baby, that HIV-positive women receive the HIV care and treatment that they need both during and after delivery. Information learned in this study will help us to improve HIV services for pregnant women.

You are being asked to take part in this study because you are woman with known HIV infection who is currently breastfeeding a baby and who is taking HIV drugs. In addition, you have taken part in the previous phases of this study. The purpose of this consent form is to give you information to help you decide if you want to continue to take part in the last phase of this study.

WHAT DO I HAVE TO DO IF I AGREE TO TAKE PART?

If you agree to take part, you will be randomized (like a flip of a coin) to one of two places to receive your ART, as described below:

1. MCH-focused ART services group: Women assigned to this group will continue to receive HIV care and medicines here, at the MOU, as they did during their pregnancy. Their babies will also receive their routine baby care here at the MOU. When they have stopped breastfeeding, women in this group will be referred to their nearest general ART clinic, and their babies to their nearest City of Cape Town clinic for routine baby care
2. General ART services group: Women assigned to this group will be referred to the nearest ART clinic for HIV care and to continue their HIV medicines. Their babies will be referred to their nearest clinic for routine baby care.

This is currently the standard of care for all HIV-positive women and their babies attending the MOU.

“Randomized” means that you will have a 50% chance of being in the group that will stay at the MOU to receive care. You will also have a 50% chance of being in the group that gets referred to an ART clinic. Neither the study staff nor you can choose which group you will be assigned to. The decisions are made by a computer and put into an envelope. The staff does not know which group is in each envelope.

Phase 3 Informed Consent Form

This randomization will occur today and you and your baby will then come in for up to 6 additional study measurement visits at 6 weeks after delivery and 3, 6, 9, 12 **and 18 months** after delivery. These study visits are separate from the usual clinic visits that you will have for your postpartum and HIV care. Study visits will be timed so that they take place on the same days that you come in for your usual postpartum and/or HIV care. Each visit will take about 30-60 minutes.

These visits will include the following:

- Answer questions about your recent pregnancy- and HIV-related health care, HIV disclosure, and use of HIV drugs (including side effects and adherence).
 - At selected visits, we will ask you additional questions about HIV, stigma, and mental health (including drug and alcohol use), family planning, infant feeding practices, infant health and health care and how you feel about the HIV care that you have received.
- Have 5mLs (1 teaspoon) of blood drawn from your arm
- Measurement of weight, length, head circumference and mid-upper arm circumference of your baby.
- Measurement of your height at the first visit and your weight and mid-upper arm circumference at all study visits

NOTE: The blood that is drawn at each visit will be stored and used to check your viral load (this is the amount of HIV in your blood) at a later time. Results from these tests will not be available to you, the clinic, or the study staff. When the health care providers at the clinic need to check your viral load, they will take a separate blood specimen. When it is stored, your blood and test results will not have your name or any other way of identifying you attached to it.

At both the 12 and 18 month visits, we will also draw blood from your baby:

- Baby will undergo a blood draw to collect up to 5ml of blood (no more than 1 teaspoon).
- This blood will be used to check your baby's HIV status.
 - We will return the results of this test to you as soon as it is available.

Follow-up of missed visits

You will be asked to provide contact information so that we may get in touch with you during the study. Study staff will talk with you about the best way to contact you. In the event that you miss one of the scheduled study visits, a member of the study staff will contact you in order to find another day and time to complete your visit. If you repeatedly miss study visits or the staff is unable to contact you using the information that you provide, it may be necessary to visit you at home in order to reschedule the missed study visit.

Contact for future study

After the completion of your last visit at **18 months postpartum**, it is possible that we will contact you again at your next clinic visit or at another time in the future to take part in additional research studies. At that time, you would be asked to review and sign another consent form. You can choose to not take part in any future studies if you are asked. You will be asked to provide contact information so that we may get in touch with you regarding additional research studies. Study staff will talk with you about the best way to contact you.

WHAT ARE THE POTENTIAL RISKS?

You may feel uncomfortable about some of the personal questions you are asked. You may refuse to answer any question that you do not want to answer. There is some risk in sharing personal and medical information. We will be careful to keep all your information as private as possible.

Drawing blood is normally done as part of routine medical care and presents a slight risk of discomfort. Experienced staff will draw blood under sterile conditions in order to protect you against these risks.

WHAT ARE THE POTENTIAL BENEFITS?

There is no direct benefit to you if you take part in this study, but if we identify any health care problem for you or your baby during the course of the study, we will make sure you are referred to the appropriate health care services. In addition, the information gained in this study may help to improve ART services for HIV-infected pregnant women in Cape Town, the Western Cape Province, and across South Africa.

WHAT ARE THE ALTERNATIVES TO TAKING PART?

The alternative to taking part in this study is to continue with the standard of care for all HIV-positive pregnant women, which means you will be referred from the MOU to your nearest general ART clinic, and your baby will be referred to your nearest clinic for routine baby care, as soon as possible.

WHAT ABOUT CONFIDENTIALITY?

If you agree to take part, all information collected during the study will be kept strictly confidential. Your name will not be written on the study forms and will not be used in connection with any information or lab specimens that are collected as part of the study.

All study materials will be stored in locked filing cabinets. Only study staff and personnel involved in routine audits will have access to these materials. All staff involved in data collection and management will get specific training in confidentiality.

Even with these procedures in place, if the study staff learns that you are a risk to yourself or someone else or of possible child abuse and/or neglect, study staff will tell the proper authorities.

WHAT ABOUT INSURANCE?

There are no experimental medicines being used in this study. Therefore no insurance has been obtained. However you will be protected in terms of the study staffs' personal malpractice insurance or that of the university in the event of injury or illness that is caused by you taking part in this study.

If you sign this form, you do not give up any of the legal rights that you and your child have as research participants.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

At the end of each visit, you will be given R20 in cash to cover the transport cost to your next scheduled study visit, and an R80 grocery voucher. Refreshments will be provided at all visits. You will also receive a small gift, up to the value of R50, at the final study visit when your baby is 12 months old.

ARE THERE ANY COSTS?

There is no cost for being in this study.

CAN I LEAVE THE STUDY?

You have the right to decide not to take part in the study, to refuse to answer any questions, or to withdraw from the study at any time without any penalty. It will have no effect on the care that you receive at the Gugulethu MOU or any other health facility.

FUTURE USE OF SPECIMENS:

If you agree, any left over blood from the samples you have provided for this research project and the sample taken from your baby at the 12 and **18 month study visit**, may be used for future HIV and maternal and child health related research. It is possible that these stored samples may be tested to see if the HIV in your blood is resistant to any types of HIV medications or to look at other questions related to HIV. It is also possible that the stored blood from you and your baby may be used to look at other questions related to maternal and child health.

At this time, we cannot provide details of when this testing may be conducted. However, additional testing will not be done using these stored samples without the approval of the appropriate ethics committees involved in this research.

If you agree to let us keep your and/or your baby's stored samples for future research, they will be kept in a locked freezer for up to 5 years. If we do use the samples in the future, your name, your baby's name or other identifiers will not be included with this information (as with the rest of the information we collect for this study).

Please initial below to indicate whether or not you give permission for your and/or your baby's specimens to be used for future research. You may still remain in the study, no matter which you choose.

Phase 3 Informed Consent Form

Consent for storage of your blood:

_____ (initial) I agree to have my blood stored for future research.

_____ (initial) I agree to have my blood stored for future research related to this study ONLY.

_____ (initial) I do NOT agree to the storage of my blood for future use.

Consent for storage of your baby's blood taken at the 12 and 18 month visit:

_____ (initial) I agree to have my baby's blood stored for future research.

_____ (initial) I agree to have my baby's blood stored for future research related to this study ONLY.

_____ (initial) I do NOT agree to the storage of my baby's blood for future use.

DO YOU HAVE ANY QUESTIONS?

If there is anything that is unclear or if you need further information, please ask us and we will provide it.

Do you have any questions?

FOR ADDITIONAL INFORMATION:

If you have any questions or have any problems while taking part in this research study, you should contact:

Dr Landon Myer
School of Public Health and Family Medicine
Faculty of Health Sciences, University of
Cape Town
Tel: 021 406 6661
Email: Landon.Myer@uct.ac.za

Dr Elaine Abrams
ICAP, Columbia University
Mailman School of Public Health
College of Physicians and Surgeons
Tel: +1 212 342 0543
Email: ejal@columbia.edu

If you have any questions about your rights as a research participant, you may contact the following member of the ethics committee:

Prof Marc Blockman
Chair, Human Research Ethics Committee
Faculty of Health Sciences, University of Cape
Town
Tel: 021 406 6338

Columbia University Medical Center IRB
Tel: +1 212 305 5883

Appendix H –

International Journal of Breastfeeding manuscript instructions

General formatting guidelines

- [Preparing main manuscript text](#)
- [Preparing illustrations and figures](#)
- [Preparing tables](#)
- [Preparing additional files](#)

Preparing main manuscript text

Quick points:

- Use double line spacing
- Include line and page numbering
- Use SI units: Please ensure that all special characters used are embedded in the text, otherwise they will be lost during conversion to PDF
- Do not use page breaks in your manuscript

File formats

The following word processor file formats are acceptable for the main manuscript document:

- Microsoft word (DOC, DOCX)
- Rich text format (RTF)
- TeX/LaTeX (use BioMed Central's TeX template)

Please note: editable files are required for processing in production. If your manuscript contains any non-editable files (such as PDFs) you will be required to re-submit an editable file when you submit your revised manuscript, or after editorial acceptance in case no revision is necessary.

Note that figures must be submitted as separate image files, not as part of the submitted manuscript file. For more information, see [Preparing figures](#) below.

Additional information for TeX/LaTeX users

Please use [BioMed Central's TeX template](#) and BibTeX stylefile if you use TeX format. When submitting TeX submissions, please submit your TeX file as the main manuscript file and your bib/bbl file as a dependent file. Please also convert your TeX file into a PDF and submit this PDF as an additional file with the name 'Reference PDF'. This PDF will be used by our production team as a reference point to check the layout of the article as the author intended. Please also note that all figures must be coded at the end of the TeX file and not inline.

All relevant editable source files must be uploaded during the submission process. Failing to submit these source files will cause unnecessary delays in the production process.

TeX templates
BioMedCentral_article (ZIP format) - preferred template
Springer article svjour3 (ZIP format)
birkjour (Birkhäuser, ZIP format)
article (part of the standard TeX distribution)
amsart (part of the standard TeX distribution)

Style and language

For editors and reviewers to accurately assess the work presented in your manuscript you need to ensure the English language is of sufficient quality to be understood. If you need help with writing in English you should consider:

- Visiting the [English language tutorial](#) which covers the common mistakes when writing in English.
- Asking a colleague who is a native English speaker to review your manuscript for clarity.
- Using a professional language editing service where editors will improve the English to ensure that your meaning is clear and identify problems that require your review. Two such services are provided by

our affiliates [Nature Research Editing Service](#) and [American Journal Experts](#).

Please note that the use of a language editing service is not a requirement for publication in the journal and does not imply or guarantee that the article will be selected for peer review or accepted.

Data and materials

For all journals, BioMed Central strongly encourages all datasets on which the conclusions of the manuscript rely to be either deposited in publicly available repositories (where available and appropriate) or presented in the main paper or additional supporting files, in machine-readable format (such as spread sheets rather than PDFs) whenever possible. Please see the list of [recommended repositories](#) in our editorial policies.

For some journals, deposition of the data on which the conclusions of the manuscript rely is an absolute requirement. Please check the Instructions for Authors for the relevant journal and article type for journal specific policies.

For all manuscripts, information about data availability should be detailed in an 'Availability of data and materials' section. For more information on the content of this section, please see the Declarations section of the relevant journal's Instruction for Authors. For more information on BioMed Centrals policies on data availability, please see our [editorial policies].

Formatting the 'Availability of data and materials' section of your manuscript

The following format for the 'Availability of data and materials' section of your manuscript should be used:

"The dataset(s) supporting the conclusions of this article is(are) available in the [repository name] repository, [unique persistent identifier and hyperlink to dataset(s) in http:// format]."

The following format is required when data are included as additional files:

"The dataset(s) supporting the conclusions of this article is(are) included within the article (and its additional file(s))."

BioMed Central endorses the Force 11 Data Citation Principles and requires that all publicly available datasets be fully referenced in the reference list with an accession number or unique identifier such as a DOI.

For databases, this section should state the web/ftp address at which the database is available and any restrictions to its use by non-academics.

For software, this section should include:

- Project name: e.g. My bioinformatics project
- Project home page: e.g. <http://sourceforge.net/projects/mged>
- Archived version: DOI or unique identifier of archived software or code in repository (e.g. enodo)
- Operating system(s): e.g. Platform independent
- Programming language: e.g. Java
- Other requirements: e.g. Java 1.3.1 or higher, Tomcat 4.0 or higher
- License: e.g. GNU GPL, FreeBSD etc.
- Any restrictions to use by non-academics: e.g. licence needed

Information on available repositories for other types of scientific data, including clinical data, can be found in our [editorial policies](#).

References

See our [editorial policies](#) for author guidance on good citation practice.

All references, including URLs, must be numbered consecutively, in square brackets, in the order in which they are cited in the text, followed by any in tables or legends. The reference numbers must be finalized and the reference list fully formatted before submission. For

further information including example references please read our reference preparation guidelines.

What should be cited?

Only articles, clinical trial registration records and abstracts that have been published or are in press, or are available through public e-print/preprint servers, may be cited.

Unpublished abstracts, unpublished data and personal communications should not be included in the reference list, but may be included in the text and referred to as "unpublished observations" or "personal communications" giving the names of the involved researchers. Obtaining permission to quote personal communications and unpublished data from the cited colleagues is the responsibility of the author. Footnotes are not allowed, but endnotes are permitted. Journal abbreviations follow Index Medicus/MEDLINE.

Any in press articles cited within the references and necessary for the reviewers' assessment of the manuscript should be made available if requested by the editorial office.

How to format your references

Examples of the BioMed Central reference style are shown below. Please ensure that the reference style is followed precisely; if the references are not in the correct style, they may need to be retyped and carefully proofread.

Web links and URLs: All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database.
<http://tumor.informatics.jax.org/mtbwi/index.do>. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

Authors may wish to make use of reference management software to ensure that reference lists are correctly formatted.

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Smith JJ. The world of science. Am J Sci. 1999;36:234-5.

Article within a journal (no page numbers)

Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. BMC Med. 2013;11:63.

Article within a journal by DOI

Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.

Article within a journal supplement

Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. Blood 1979;59 Suppl 1:26-32.

Book chapter, or an article within a book

Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.

OnlineFirst chapter in a series (without a volume designation but with a DOI)

Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. *Top Curr Chem*. 2007. doi:10.1007/128_2006_108.

Complete book, authored

Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.

Online document

Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999.
[http://www.rsc.org/dose/title of subordinate document](http://www.rsc.org/dose/title%20of%20subordinate%20document). Accessed 15 Jan 1999.

Online database

Healthwise Knowledgebase. US Pharmacopeia, Rockville. 1998.
<http://www.healthwise.org>. Accessed 21 Sept 1998.

Supplementary material/private homepage

Doe J. Title of supplementary material. 2000.
<http://www.privatehomepage.com>. Accessed 22 Feb 2000.

University site

Doe, J: Title of preprint. <http://www.uni-heidelberg.de/mydata.html> (1999). Accessed 25 Dec 1999.

FTP site

Doe, J: Trivial HTTP, RFC2169. <ftp://ftp.isi.edu/in-notes/rfc2169.txt> (1999). Accessed 12 Nov 1999.

Organization site

ISSN International Centre: The ISSN register. <http://www.issn.org> (2006). Accessed 20 Feb 2007.

Dataset with persistent identifier

Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, et al. Genome data from sweet and grain sorghum (*Sorghum bicolor*). GigaScience Database. 2011. <http://dx.doi.org/10.5524/100012>.

Preparing figures

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- Tables should NOT be submitted as figures but should be included in the main manuscript file.
- Multi-panel figures (those with parts a, b, c, d etc.) should be submitted as a single composite file that contains all parts of the figure.
- Figures should be numbered in the order they are first mentioned in the text, and uploaded in this order.
- Figures should be uploaded in the correct orientation.
- Figure titles (max 15 words) and legends (max 300 words) should be provided in the main manuscript, not in the graphic file.
- Figure keys should be incorporated into the graphic, not into the legend of the figure.
- Each figure should be closely cropped to minimize the amount of white space surrounding the illustration. Cropping figures improves accuracy when placing the figure in combination with other elements when the accepted manuscript is prepared for publication on our site. For more information on individual figure file formats, see our detailed instructions.
- Individual figure files should not exceed 10 MB. If a suitable format is chosen, this file size is adequate for extremely high quality figures.

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Figure file types

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- EPS (suitable for diagrams and/or images)
- PDF (suitable for diagrams and/or images)
- Microsoft Word (suitable for diagrams and/or images, figures must be a single page)
- PowerPoint (suitable for diagrams and/or images, figures must be a single page)
- TIFF (suitable for images)
- JPEG (suitable for photographic images, less suitable for graphical images)
- PNG (suitable for images)
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- width of 600 pixels (standard), 1200 pixels (high resolution).

Figures in the final PDF version:

- width of 85 mm for half page width figure
- width of 170 mm for full page width figure
- maximum height of 225 mm for figure and legend
- image resolution of approximately 300 dpi (dots per inch) at the final size

Figures should be designed such that all information, including text, is legible at these dimensions. All lines should be wider than 0.25 pt when constrained to standard figure widths. All fonts must be embedded.

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- Vector figures should if possible be submitted as PDF files, which are usually more compact than EPS files.
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- Tables larger than one A4 or Letter page in length can be placed at the end of the document text file. Please cite and indicate where the table

should appear at the relevant location in the text file so that the table can be added in the correct place during production.

- Larger datasets, or tables too wide for A4 or Letter landscape page can be uploaded as additional files. Please see [below] for more information.
- Tabular data provided as additional files can be uploaded as an Excel spreadsheet (.xls) or comma separated values (.csv). Please use the standard file extensions.
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- Title of data
- Description of data

Additional files should be named "Additional file 1" and so on and should be referenced explicitly by file name within the body of the article, e.g. 'An additional movie file shows this in more detail [see Additional file 1]'.

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Preparing your manuscript

Research article

Criteria

Research articles should report on original primary research.

International Breastfeeding Journal strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's [information on recommended repositories](#). Where a widely established research community expectation for data archiving in public repositories exists, submission to a community-endorsed, public repository is mandatory. A list of data where deposition is required, with the appropriate repositories, can be found on the [Editorial Policies Page](#).

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Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

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The title page should:

- present a title that includes, if appropriate, the study design e.g.:
 - "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"

- or for non-clinical or non-research studies a description of what the article reports
- list the full names, institutional addresses and email addresses for all authors
- if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the “Acknowledgements” section in accordance with the instructions below
- indicate the corresponding author

Abstract

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the [CONSORT](#) extension for abstracts. The abstract must include the following separate sections:

- **Background:** the context and purpose of the study
- **Methods:** how the study was performed and statistical tests used
- **Results:** the main findings
- **Conclusions:** brief summary and potential implications
- **Trial registration:** If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration number and date of registration should be in stated in this section. If it was not registered prospectively (before enrollment of the first participant), you should include the words 'retrospectively registered'. See our [editorial policies](#) for more information on trial registration

Keywords

Three to ten keywords representing the main content of the article.

Background

The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

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The methods section should include:

- the aim, design and setting of the study
- the characteristics of participants or description of materials
- a clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses
- the type of statistical analysis used, including a power calculation if appropriate

Results

This should include the findings of the study including, if appropriate, results of statistical analysis which must be included either in the text or as tables and figures.

Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.

Conclusions

This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.

List of abbreviations

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and material
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
- Authors' information (optional)

Please see below for details on the information to be included in these sections.

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Ethics approval and consent to participate

Manuscripts reporting studies involving human participants, human data or human tissue must:

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If your manuscript does not contain data from any individual person, please state “Not applicable” in this section.

Availability of data and materials

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FTP site

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from sweet and grain sorghum (*Sorghum bicolor*). GigaScience
Database. 2011. <http://dx.doi.org/10.5524/100012>.

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