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HIV and Infant Feeding

Operational Challenges of Achieving Safe Infant Feeding Practices

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Abstract
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This thesis assesses the uptake of the national Prevention of Mother to Child Transmission of HIV (PMTCT) programme in South Africa, and the challenges of achieving safe infant feeding practices in the context of HIV. The research studies contained in this thesis utilised a variety of quantitative and qualitative research methods in order to provide a full understanding of the challenges of moving from efficacy to effectiveness in PMTCT programmes. The first paper utilised a cross-sectional approach to a programme evaluation, papers two and three utilised qualitative methodologies, and paper four was based on a longitudinal cohort study design. The findings highlight the low uptake of PMTCT interventions and inappropriate infant feeding choices. The experiences of women with HIV provide an important insight into the difficulties of operationalising the WHO/UNICEF HIV and infant feeding recommendations in real life settings, where rates of HIV disclosure are low and mixed feeding is the norm. Several personal and environmental characteristics were identified that contributed to success in maintaining exclusive infant feeding practices. The research provides some guidance on the definition of appropriateness in infant feeding choices, and highlights the poor outcomes associated with formula feeding under unsafe conditions. Modifying infant feeding practices is essential in order to reduce postnatal HIV transmission and improve child survival. Interventions to improve infant feeding need to include improving the quality of counselling and support provided by health workers, with more structured assessments used to guide infant feeding choices. Efforts are also needed at the community level to increase rates of disclosure and to promote exclusive infant feeding as a norm.

Keywords: HIV/AIDS, Prevention of Mother to Child Transmission of HIV, infant feeding, child health, qualitative research, cohort study, programme evaluation, nutrition

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This thesis forms part of an ongoing collaboration in HIV and infant feeding research between Uppsala University and three institutions in South Africa; the University of the Western Cape, School of Public Health; the Health Systems Trust and the Medical Research Council, Health Systems Research Unit.

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List of publications

This thesis is based on the following papers which will be referred to in the text by their Roman numerals:

I. Doherty TM, McCoy D, Donohue S. 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. African Health Sciences 2005; 5 (3): 213-218.

II. Doherty T, Chopra M, Nkonki L, Jackson D, Greiner T. Effect of the HIV epidemic on infant feeding in South Africa: "when they see me coming with the tins they laugh at me". Bulletin of the World Health Organisation 2006; 84 (2): 90-96.

III. Doherty T, Chopra M, Nkonki L, Jackson D, Persson LA. A longitudinal qualitative study of infant feeding decision-making and practices amongst HIV positive women in South Africa. Journal of Nutrition 2006; 136 (9): 2421- 2426.

IV. Doherty T, Chopra M, Jackson D, Goga A, Colvin M, Persson LA. Infant feeding choices of HIV positive women. Do the WHO/UNICEF guidelines improve infant HIV-free survival? Submitted.

Contents

Abbreviations

3TC	The anti-retroviral drug lamivudine.
ANC	Antenatal Care
ARV	Anti-Retrovirals
CD4 count	The absolute CD4 cell count measures the number of CD4 T-cells in each cubic ml of blood.
CDC	Centers for Disease Control and Prevention, Atlanta, United States of America
DHIS	District Health Information System
EPI	Expanded Program of Immunisation
FP	Family Planning
GDP	Gross Domestic Product
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immunodeficiency Virus
IMCI	Integrated Management of Childhood Illnesses
IMR	Infant Mortality Rate
MCH	Mother-Child Health
M&E	Monitoring and Evaluation
NIH	National Institutes of Health
NVP	Nevirapine
MTCT	Mother to Child Transmission of HIV
OI	Opportunistic Infections
PACTG	Paediatric AIDS Clinical Trials Group
PCP	Pneumocystis carinii pneumonia
PCR	Polymerase Chain Reaction
PMTCT	Prevention of Mother to Child Transmission
RF	Replacement Feeding
STD	Sexually Transmitted Diseases
UNAIDS	The Joint United Nations Programme on HIV/AIDS
VCT	Voluntary Counselling and Testing
ZDV	Zidovudine
WHO	World Health Organisation

Introduction

Prevention of Mother to Child Transmission of HIV

The HIV/AIDS epidemic is having a devastating impact on women and children in sub-Saharan Africa. UNAIDS[1] estimated that during 2005 thirteen and a half million women and 540 000 children were newly infected with HIV, with 90% of these infections occurring in sub-Saharan Africa. South Africa is one of the countries with the greatest burden of HIV as a result of an explosive growth in the epidemic from a prevalence of less than 1% amongst pregnant women in 1990 to 30.2% in 2005[2] (Fig 1). Prevalence is highest amongst women aged 25 to 34 years where one in three is infected. Based on current birth rates and HIV prevalence amongst pregnant women, approximately 300 000 infants are exposed to HIV in South Africa each year.

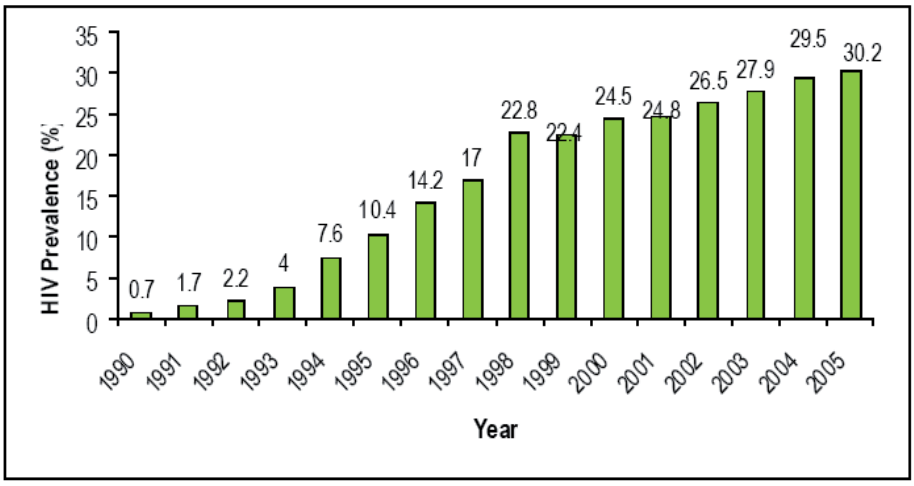

Figure 1. Prevalence of HIV amongst antenatal attendees in South Africa 1990-2005. Source: National Department of Health, National HIV and Syphilis annual antenatal survey 2006.

Mother to child transmission of HIV is the most significant route of HIV infection in children and is threatening to reverse previous gains in child survival. HIV transmission from mothers to infants can occur during pregnancy, labour and delivery, or during breastfeeding. In the absence of any intervention the risk of such transmission is 15-30% in non-breastfeeding populations. Breastfeeding by an infected mother increases the risk by 5-20% to a total of 20-45%[3].

In 2001, the United Nations General Assembly Special Session (UNGASS) on HIV/AIDS committed its signatories to the goal of reducing the proportion of children infected with HIV by 20% by the year 2005; and 50% by the year 2010, by ensuring access to effective interventions by 80% of pregnant women. Efforts to prevent mother to child transmission in developing country settings have focussed on reducing MTCT around the time of labour and delivery, which accounts for one to two thirds of overall transmission depending on whether the mother breastfeeds.

Several factors are known to increase the risk of early peri-partum MTCT. Maternal HIV-1 RNA levels have been shown in multivariate analysis to be the strongest independent predictor of intrapartum/very early HIV transmission[4-7]. Obstetric practices including mode of delivery, a prolonged period of rupture of membranes and practices that promote bleeding[5] (episiotomy, forceps or vacuum) are also well established risk factors as well as cervico-vaginal infections and sexually transmitted infections. Infant factors include prematurity[5] and low birth weight[8].

Since the early 1990s several randomised controlled trials have evaluated the efficacy of perinatal ARV prophylaxis regimens (Fig 2). The first of these, the PACTG 076 trial conducted in the United States and France, evaluated the efficacy of antenatal and intrapartum ZDV to the mother and 6 weeks of postnatal ZDV to infants versus placebo. All mothers fed their infants formula milk. At 18 months transmission was 7.6% in the ZDV group and 22.6% in the placebo group. This was the first randomised controlled trial to prove the efficacy of an intervention to reduce the incidence of HIV infection in infants.

When the results of the PACTG 076 trial became available, a number of randomised placebo controlled trials of ARVs to reduce MTCT were already underway in Africa and Thailand. In the late 1990s several researchers[9,10] questioned the need for placebo in these trials and argued for the 076 regimen to be the standard of care. The CDC, NIH, UNAIDS and a wide range of individuals rejected this view for several reasons. Firstly the 076 regimen was a complex, expensive, three-phase regimen that would be difficult to implement in resource poor settings; secondly the 076 trial was undertaken

in a non-breastfeeding population which is very different to the situation in African contexts where the majority of women breastfeed and other risk factors such as micronutrient deficiencies and sexually transmitted infections are more frequently present.

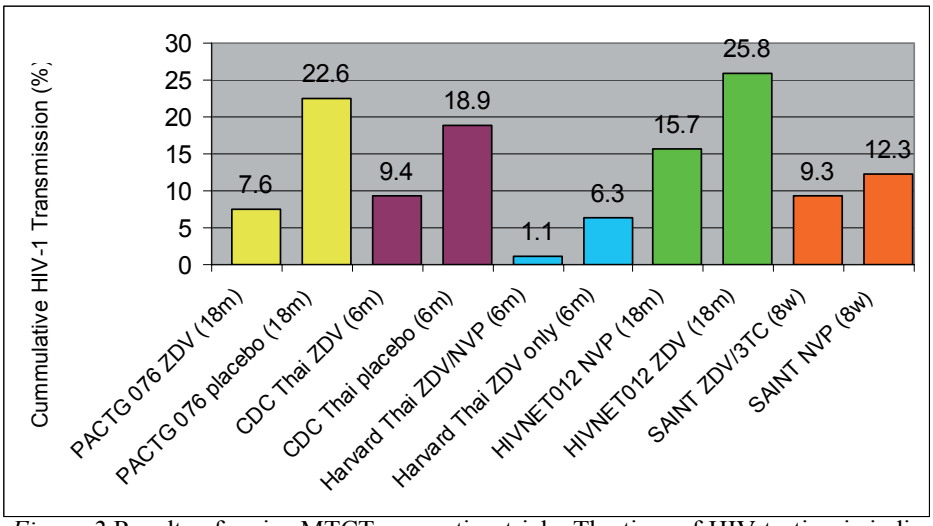

Figure 2 Results of major MTCT prevention trials. The time of HIV testing is indicated in parentheses next to each trial name.

During 1998, results of a trial in Thailand[11] which appeared more suited to developing country contexts were released. This trial assessed a short course of ZDV given orally during the last four weeks of pregnancy and oral doses during labour versus placebo amongst non-breastfeeding women. At six months transmission was 9.4% in the ZDV group and 18.9% in the placebo group. The claim that this regimen was appropriate for developing countries led to the discontinuation of the placebo arms of other major intervention studies, most notably the PETRA study in South Africa, Uganda and Tanzania. Although the Thai regimen was less costly and logistically easier to deliver than the 076 regimen, many unresolved problems relating to developing countries remained, most importantly the efficacy of these regimens in breastfeeding populations. There was still a need to find simple, cheap, short and effective regimens for these settings.

Subsequent trials assessed a variety of short course ARV regimens. Trials in the Ivory Coast[12] and Burkina Faso[13] compared ZDV to placebo. The PETRA study[14] assessed the efficacy of different regimens of ZDV and 3TC. The SAINT study[15] compared a combination of ZDV and 3TC to NVP. However the most influential trial was the HIVNET012 trial[16] in Uganda. A regimen of single dose NVP to mothers at the time of labour and to infants within 72 hours of birth was compared to ZDV during labour and for 7 days to infants, in a breastfeeding population. At 6-8 weeks the rate of transmis-

sion was 11.8% in the NVP group and 20% in the ZDV group. The early reduction in transmission with NVP was sustained at 18 months, with a rate of 15.7% compared to 25.8% in the ZDV group[17]. These encouraging findings of a simple, cost-effective and deliverable intervention to reduce MTCT in developing countries led to its support by the World Health Organisation and the announcement by the manufacturer, Boehringer Ingelheim, of free donations of NVP to developing countries for use in PMTCT programmes.

The HIVNET012 regimen became the standard protocol for use in PMTCT programmes in developing countries, although the WHO recommendations have changed subsequently in 2004[18] to recommend HAART for pregnant women with indications for ARV treatment and short course ZDV plus single dose NVP for women without indications for ARVs. This regimen was found in a trial in Thailand[19] to result in a rate of transmission of 1.1% versus 6.3% in the ZDV only group at six months.

Despite increasing evidence for the efficacy of dual and triple drug regimens in reducing early MTCT, the challenge remains to implement these interventions effectively in operational settings, and to address the issue of postpartum transmission through breastfeeding.

Operational effectiveness of PMTCT Programmes in Africa

Since 2001 governments in many African countries have started implementing prevention of mother to child HIV transmission (PMTCT) programmes. By 2005 however, only 9% of pregnant women living with HIV were receiving ARV prophylaxis for PMTCT[20]. For a PMTCT programme to be successful pregnant women must follow several sequential steps: (1) attend an antenatal clinic equipped to offer VCT; (2) accept pre-test counselling and HIV testing; (3) receive their test results; (4) accept ARV prophylaxis; (5) correctly receive and administer therapy; (6) receive infant feeding counselling and make an appropriate infant feeding choice; (7) participate in postpartum follow up care. At each step, losses occur which decrease the overall effectiveness of the programme (Fig 3).

Initial monitoring and evaluation of pilot PMTCT programmes in Africa consisted of reviews of routine indicators to determine the coverage and uptake of various components of the programme. Early evaluations highlighted deficiencies in these programmes within routine settings including uptake of HIV testing[21,22], receipt of test results[23], uptake of nevirapine prophylaxis[24-26], and postnatal follow up[27].

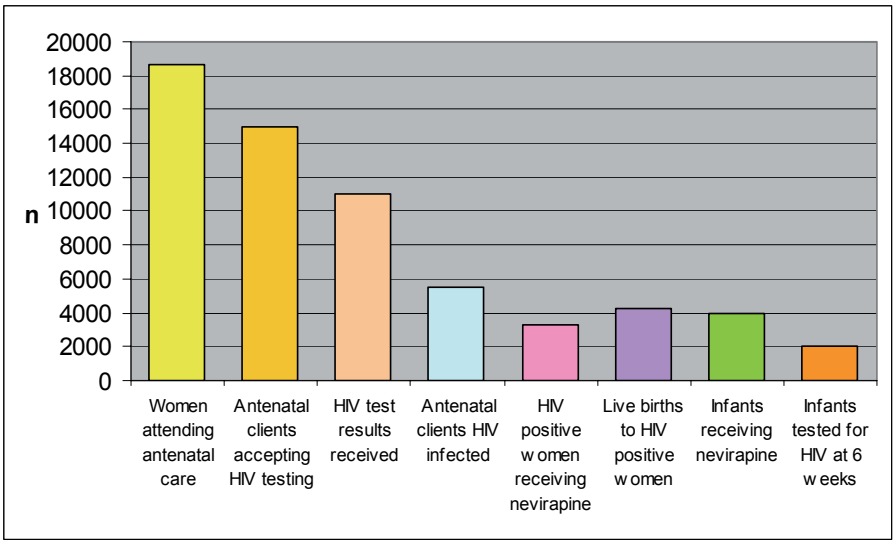

Figure 3. Example of the typical drop out at different stages of a PMTCT programme. Adapted from: WHO. Local Monitoring and Evaluation of the Integrated Prevention of Mother to Child HIV Transmission in Low Income Countries. 2001.

The South African PMTCT programme was largely introduced as a vertical programme to allow for central control and faster implementation; however the result is that it does not function integrally with broader maternal and child health services and many missed opportunities to prevent mother to child transmission are occurring. Underlying weaknesses in the health system such as the human resource crisis, poor drug and supply systems and weak health information systems have also hampered PMTCT implementation[22].

A similar situation has been found in other African countries. An observational study using routine data in Kenya[26] found that only 67% of pregnant women accepted HIV testing, and 20% of HIV positive women received nevirapine. Reasons for the low uptake were found to be shortages of trained staff to perform VCT, women not returning for test results, and lack of integration of MTCT services into routine antenatal care. A programme evaluation in Zambia[28] also found low uptake of nevirapine (57%) amongst HIV positive women. Stigma and fear of partner violence were found to contribute to women not returning for further care. Operational research in Zimbabwe[29] that assessed the implementation of a rural PMTCT programme found high (92.9%) uptake of HIV testing but low (24%) coverage of nevirapine. The high rate of testing has been attributed to the integration of VCT as a routine component of antenatal care. The low coverage of nevirapine

was possibly an underestimation due to the fact that some mothers delivered at home and it was not possible to verify whether they took nevirapine.

A routine review of a PMTCT programme in rural Malawi[27] found a cumulative loss to follow up of 55% by the 36-week antenatal visit, 70% by the first postnatal visit and 81% by the 6 month postnatal visit, resulting in only 19% of the mother-infant pairs who participated in the programme still receiving care. The progressive loss to follow up was associated with a centralised hospital-based PMTCT strategy in a rural setting with no public transport system. Many women therefore chose to deliver and attend postnatal care at a peripheral site without PMTCT services.

Similar deficiencies have been found in programmes in West Africa. An observational study in Ivory Coast[30] found a rate of HIV testing of 66.4% and an ARV coverage rate of 26.2% amongst women found to be HIV positive. Qualitative research[31] undertaken in Abidjan to determine women's reasons for not returning for care after receiving a positive HIV test result, found that disbelief of test results and negative experiences of interactions with health workers were important obstacles to programme participation.

Although these programme evaluations provide important insights into the coverage and uptake of programme components, the usefulness of the data is limited by the low rate of follow up and aggregated nature of the data, which makes it impossible to provide information on programme quality for individual mother-infant pairs or to determine programme outcomes such as vertical transmission rates.

A few longitudinal cohort studies have assessed the effectiveness of PMTCT programmes in operational settings. A study in Kenya[32] that assessed vertical transmission at 14-16 weeks in a nevirapine based programme, found a transmission rate of 18.1%., which was similar to the rate of 21.7% found before implementation of the PMTCT programme. The authors questioned the effectiveness of nevirapine in operational settings. However it is important to note that this study had a sample size of only 127 women, used historical controls, had incomplete uptake of NVP by mothers (85%) and, by testing at 14 weeks, will have included infants who were infected by breast feeding. In contrast, a study in South Africa[33], of a routine programme using a ZDV regimen from 34 weeks of pregnancy and during labour, with 99% of women using formula milk, had very encouraging findings. The rate of transmission at 6-10 weeks of age was 8.8% which is consistent with the findings of trials using the same regimen[11,15].

Enormous effort has gone into establishing PMTCT programmes in developing country contexts with evidence of effectiveness in reducing early mother

to child transmission. However, in contexts where avoidance of breastfeeding is not a safe option, further postnatal acquisition of infection through breastfeeding can substantially increase the overall rate of transmission to 20% or more[34]. The resulting challenge has been how to reduce HIV transmission through breastfeeding without undermining child survival.

HIV and Infant Feeding

Transmission of HIV from mother to child after birth has become one of the greatest challenges in HIV prevention. The transmission of HIV through breastmilk has created a dilemma: for each HIV positive woman the benefits of breastfeeding and the general health risks of not breastfeeding have to be weighed against the risk of HIV transmission through breastfeeding. Whilst intrauterine and intrapartum transmission can be substantially reduced through improved drug regimens, modifying infant feeding practices in order to reduce postnatal transmission is complex and proving difficult to achieve. MTCT rates of less than 2% are now reported from countries where antiretroviral prophylaxis, elective Caesarean section and refraining from breastfeeding can be applied[34], whilst in settings where refraining from breastfeeding is not feasible or safe, programmes for prevention of MTCT need to focus not only on preventing HIV transmission but also on improving child survival.

Benefits of breastfeeding

The single most effective way of saving the lives of millions of young children in developing countries would be the promotion of exclusive breastfeeding (EBF). A recent study found that 13% of under 5 deaths (approximately 1.3 million deaths per year) could be prevented if universal coverage of exclusive breastfeeding was increased to 90% amongst infants under 6 months.[35] Compared with the use of breast milk substitutes, breastfeeding has been consistently shown to reduce infant morbidity and mortality associated with infectious diseases in both resource-rich and resource-poor settings[36,37] particularly in the first months of life.

With regard to morbidity in resource poor settings, both risk of diarrhoeal and acute respiratory illness have been found to be associated with type of feeding. A large study of 9942 urban infants in the Philippines[38] followed from birth to the age of two years, found that deaths from diarrhoeal diseases were 10 times higher for infants under six months who were never breastfed or where breastfeeding was stopped, after controlling for demographic factors such as maternal education and socio-economic status. A study in Brazil[39] reported on the impact of type of feeding on infant hospital admissions

using a nested case-control design. Cases were 152 infants hospitalised for pneumonia and controls were 2391 community controls. After adjustment for socio-demographic factors, infants who were not breastfed had a 17-fold increased risk of hospitalisation for pneumonia (OR 16.7, 95% CI 7.7-36.0) compared with breastfed infants. Benefits of breastfeeding in terms of reduced morbidity have also been documented in settings with more resources. In a cluster randomised trial in Belarus with 17,046 mother-infant pairs, where half the sites implemented an intervention to encourage breastfeeding, increased breastfeeding rates were associated with a significant reduction in the risk of gastrointestinal infections (OR 0.6, 95% CI 0.4-0.9) in the first year of life[40].

"Infants aged 0-5 months who are not breastfed have seven-fold and five-fold increased risks of death from diarrhoea and pneumonia respectively, compared with infants who are exclusively breastfed. At the same age, non-exclusive rather than exclusive breastfeeding results in more than two-fold increased risks of dying from diarrhoea and pneumonia.[41]" This assertion, and related comments and findings are set out by the Bellagio Child Survival Group in a recent article series in the Lancet[35,41] summarising findings from international research of how best to reduce infant mortality in developing countries.

In addition to protection from morbidity and mortality associated with common infectious diseases, breastfeeding also provides a number of social, psychological[42] and economic benefits to both mother and baby. Exclusivity of breastfeeding also increases the duration of amenorrhoea which is positive for maternal health and birth spacing[43].

The benefits of breastfeeding and the negative effects of artificial feeding in resource-poor environments were clearly brought to public attention in the 1970's, backed by increasingly strong scientific support. As a result the International Code of Marketing of Breast-milk Substitutes and subsequent World Health Assembly Resolutions were agreed to in the 1980's to avoid marketing of infant foods, teats and bottles in ways that could interfere with breastfeeding. In the early 1990's, UNICEF started the "Baby-friendly Hospital Initiative" (BFHI), which decreased many of the practices in the health care system that had a negative impact on breastfeeding.

International policy also supports breastfeeding as the optimal infant nutrition. The WHO/UNICEF Global Strategy for Infant and Young Child Feeding, states that the optimal feeding pattern for overall child survival in the general population is exclusive breastfeeding for the first six months with continued breastfeeding for up to two years and beyond, with complemen-

tary feeding from age six months together with related maternal nutrition and support[44].

Risk of HIV transmission through breastmilk

The finding that HIV is present in breastmilk has led to a re-assessment of the benefits of breastfeeding and a reduction in global efforts to promote breastfeeding, especially in countries that would otherwise benefit the most.

Transmission of HIV through breastfeeding has been well documented. The first reports indicating the possibility of HIV transmission through breastmilk were of breastfed infants of women who had been infected postnatally through blood transfusion or through heterosexual exposure[45,46]. Other reports related to infants with no known exposure to HIV other than wet-nursing or pooled breastmilk[47]. HIV has been cultured in breastmilk; however, the exact mechanism for HIV transmission during breastfeeding is unknown. Possible portals of virus entry include M cells in the tonsils or overlying the intestinal lymphoid Peyer's patches, direct infection of the enterocyte or possibly direct passage through disruptions in mucosa or between immature mucosal junctions[48]. The roles of cell-free and cell associated virus in transmission and the association between virus levels in plasma and in milk have not been reliably quantified.

Several factors are known to increase the risk of HIV transmission through breastmilk[48]. The maternal factors include high plasma viral load, low CD4 count, breast pathology (including mastitis and abscesses), mode of infant feeding and prolonged duration of breastfeeding (more than 6 months). In particular recent HIV infection is an important risk factor for HIV transmission through breastmilk as it doubles the risk compared to a woman with earlier established infection due to the high viral load associated with recent infection[49].

The risk of transmitting HIV through breastfeeding is strongly associated with HIV RNA levels in breastmilk[50]. In South Africa[50] and Malawi[51], women with a detectable RNA viral load in their milk at any time during the first six months postpartum were more likely to transmit HIV than were women who did not have detectable virus in their milk. In West Africa, the rate of late postnatal transmission increased 2.6 times for every $\log_{10}$ increase in plasma RNA viral load measured in late pregnancy[52]. Research in South Africa[53,54] indicates that, in general, RNA viral load in milk is lower than in plasma and often lower than the detectable limit of the assays used.

Clinical and sub-clinical mastitis are also associated with HIV transmission risk[51,55]. Sub-clinical mastitis is not necessarily an infection and may occur

with milk stasis and breast engorgement, and may be associated with increased milk HIV RNA load and cytokines.

Infant factors known to increase the risk of transmission through breastfeeding include damage to the mucous membranes (e.g. by oral thrush), damage to the intestinal mucosa by cow's milk or allergic reactions to complementary foods, and mixed feeding which may affect intestinal permeability[56]. Exclusively breastfed infants may have a less permeable gut lining than those not breastfed.

Two factors make it difficult to determine the precise timing of HIV transmission and whether transmission occurred during delivery or through early breastfeeding: one is the persistence of maternal antibodies and the other is that during a certain period infection is undetectable by current technology. One study has suggested that the first several weeks of life may be the highest-risk period for transmission. A trial in Nairobi[57] where infants were randomised to breastfeed or formula feed found that most of the cumulative difference in HIV infection rates had occurred by six weeks of age: the difference between groups was 10% at 6 weeks and 16% at 24 months. However there were differences in the transmission rates at birth between the breastfed and formula fed groups suggesting that randomisation had not produced equivalent groups and hence a comparison of cumulative rates is problematic.

Breastmilk can transmit HIV at any time during lactation, therefore the rate of HIV infection in breastfed infants is cumulative and increases with duration of breastfeeding. An individual patient data meta-analysis[58] estimated that the cumulative probability of late postnatal transmission between 4 weeks and 18 months of age was 9.3% or 9 infections per 100 child years of breastfeeding, and that the risk of transmission was constant throughout breastfeeding. In this meta-analysis, approximately 42% of all HIV infections in children were attributable to breastfeeding.

Mode of feeding and HIV transmission

Current approaches to reducing or preventing postnatal transmission through breastfeeding include the avoidance of all breastfeeding through the use of exclusive replacement feeds, or exclusive breastfeeding for a limited duration with early and rapid cessation of breastfeeding as soon as it is feasible.

The most commonly recommended infant feeding options for HIV positive women in South Africa are replacement feeding with commercial infant formula, or exclusive breastfeeding with early cessation. Home modified

animal milks, heat treatment of breastmilk and breast milk banks are rarely used.

Exclusive breastfeeding with early cessation

Exclusive breastfeeding means nourishing an infant on breastmilk alone with no other liquids or solid foods except for prescription medicines and vitamin-mineral supplements. Exclusive breastfeeding has been found to result in a lower rate of postnatal HIV transmission compared to mixed breastfeeding. A study in South Africa[59] was the first to assess exclusive breastfeeding in a cohort of HIV positive women. The study found that infants who received both breastmilk and other feeds were significantly more likely to be HIV infected by 15 months of age (36%) than those who had been exclusively breastfed for the first three months (25%) or formula fed (19%). There have been some criticisms of this study and it is not consistent with another study[60] conducted in the same setting a few years earlier which found similar rates of transmission and mortality amongst exclusively breastfed infants compared with infants who were mixed fed. However, the Coutsoudis et al. study may have used a stricter definition of exclusive breastfeeding than the previous South African study.

A similar finding to that of Coutsoudis et al. was reported from the ZVITAMBO trial in Zimbabwe in 2005[61]. In this study, amongst 2060 HIV positive mothers with infants who were HIV-PCR negative at 6 weeks, compared with exclusive breastfeeding, early mixed feeding was associated with a 4.03 (95%CI 0.98-16.61), 3.79 (95%CI 1.40–10.29), and 2.60 (95% CI 1.21–5.55) greater risk of postnatal transmission at 6, 12, and 18 months, respectively.

A recent study from South Africa confirms earlier findings regarding exclusive breastfeeding and HIV transmission. This study, undertaken in a rural area in KwaZulu-Natal province, found a cumulative postnatal HIV transmission risk of 4.04% after five months of exclusive breastfeeding. Infants who were fed both breast and formula milk at age twelve weeks were twice as likely as exclusively breastfed infants to be infected (HR 1.82, 95% CI: 0.98-3.36)[62].

All but one study investigating HIV transmission and mode of infant feeding have been cohort study designs in which women self selected their feeding methods, and in many the investigation of feeding mode and HIV transmission was a secondary analysis and not the main outcome of the studies. For example, the Coutsoudis study was a randomized trial to assess the effect of vitamin A supplementation on MTCT.

The WHO recommends[63] early cessation of breastfeeding for HIV positive women as soon as replacement feeding is acceptable, feasible, affordable, sustainable and safe as a strategy to reduce the risk of HIV transmission by limiting the infant's exposure to HIV infection through breastmilk. Recent data have highlighted the dangers of early cessation of breastfeeding under conditions of underlying poor socio-economic status and food insecurity. A cross sectional study in Mozambique[64] found that most (78%) HIV positive women had stopped breastfeeding their infants by six months of age and less than 10% reported regular consumption of iron-rich, animal source foods. Linear programming results indicated that commonly consumed, locally available foods would not meet the nutritional needs of non-breastfed infants between 6-12 months of age; furthermore, replacing breastmilk with local foods would double the estimated daily cost of feeding a 6-12 month infant.

The ZVITAMBO study in Zimbabwe[65], a randomized trial to assess the impact of Vitamin A supplementation on MTCT, also found inadequate feeding of infants weaned early from breastfeeding. Most diets only met 58% of the infant's energy needs and were insufficient in animal milks or formula. This research suggested that it would be extremely difficult for HIV positive women in Zimbabwe to safely wean their infants from breastmilk unless special food supplements (such as Plumpy'nut) were provided.

The question of how HIV positive mothers can wean safely and whether early and abrupt weaning is feasible still remains largely unanswered, particularly strategies to ensure adequate nutrition during the first year of life.

Exclusive replacement feeding

Replacement feeding means feeding an infant a diet that provides the necessary nutrients while receiving no breastmilk. Exclusive replacement feeding with no breastmilk given eliminates the risk of postnatal HIV transmission. It is therefore the preferred infant feeding method for HIV positive mothers in developed country contexts. However in low and middle income countries, replacement feeding is not considered to be the automatic choice for HIV positive women due to socio-economic environments that may not enable safe replacement feeding.

In the general population the risks of formula feeding are well described. A pooled-meta analysis conducted by WHO[37] of studies in developing countries in populations with a low HIV prevalence, found that infants who are not breastfed and receive formula milk or other replacement feeding have a 6-fold increased risk of dying in the first 2 months of life, a 4-fold increase between 2-3 months, and a 2.5 fold increase between 4 and 5 months compared with those who are breastfed.

There is limited operational data on the risks of replacement feeding in the context of PMTCT but it is understood that these risks vary depending on individual and environmental circumstances.

One randomized controlled trial conducted in an urban PMTCT setting in Kenya found that infants in the formula feeding group, whose mothers had access to clean water, free formula and frequent support by health workers, had a 40% lower risk of HIV transmission but their 24 month mortality was similar to that in the breastfed group[66]. During the first three months infants in the formula fed group had an increased risk of diarrhea (RR 2.7; 95% CI, 1.6-4.6) dehydration (RR11.9; 95% CI, 1.6-91.9), and upper respiratory infections (RR 1.3; 95% CI, 1.1-1.7). Similarly the cumulative mortality at 6 weeks and 3 months was higher in the formula fed group than the breastfed group (3.9 versus 1.0% at 6 weeks, and 6.4 versus 4.1% at 3 months). Mortality of infants uninfected with HIV in the first 6 months of life was higher for formula fed infants (5%) than for breastfed infants (0.8%). This suggests that in areas of high HIV prevalence, any gains from preventing HIV transmission through formula feeding were negated by deaths from other causes.

A more recent study from Kenya[67] followed infants identified as HIV infected, in a perinatal cohort, in order to determine predictors of mortality during the first two years of life. One of the predictors of infant mortality in addition to biological factors was formula feeding (HR 4.0, p =0.01). All deaths amongst the non-breastfed infants occurred during the first six months of life and these infants were more likely to be of low weight for age at age one month compared to breastfed infants.

The MASHI study in Botswana[68] was a randomised controlled trial that compared the efficacy of exclusive breastfeeding plus six months of infant ZDV prophylaxis versus formula feeding plus one month of infant ZDV. Cumulative HIV transmission rates at seven months were 5.6% in the formula fed group and 9.0% in the breastfed plus ZDV group. The cumulative incidence of infant death by month 7 was significantly higher in the formula fed group than in the breastfed plus ZDV group (9.3% vs 4.9%; P=0.003). However, by eighteen months there were no significant differences between the formula fed and breastfed plus ZDV group in the combined outcome HIV infection or mortality (13.9% vs 15.1%; P=0.60). Both strategies therefore resulted in a comparable HIV-free survival at 18 months.

The DITRAME PLUS study[69] conducted in Ivory Coast found a more positive outcome with formula feeding in an urban setting with high levels of support. In this study women were randomised to ZDV from 36 weeks of pregnancy plus single dose nevirapine with no postnatal prophylaxis versus

ZDV and 3TC from 32-36 weeks of pregnancy with single dose nevirapine during labour and 3 days postnatal ZDV and 3TC. Women could choose to formula feed their infants with replacement feeds and supplies provided free for nine months, or exclusive breastfeeding with early weaning. This study found no significant difference in rates of infant illness and death at twenty four months between breastfed and formula fed infants, and suggests that safe formula feeding can be achieved in settings where women have access to clean water, free health care, free transport to health facilities, free formula milk and formula feeding supplies.

Evidence of the dangers of formula feeding in non-research settings has recently been found in Botswana. Between November 2005 and February 2006 there were unusually heavy rains and flooding which led to an increase in infant diarrhoea and mortality. The CDC was brought in to investigate the outbreak. They found widespread contamination of the public water supply in four northern districts of the country. The most significant risk factor for diarrhoea was not breastfeeding (AOR 50 (95% CI 4.5 – 100). Most of the deaths were amongst HIV exposed infants whose mothers were receiving free formula milk through the PMTCT programme. Among hospitalised infants 51% had poor growth before the illness[70].

Current data on the risks of formula feeding reinforce the importance of individual assessments of home circumstances in the process of decision making. Based on available evidence, formula feeding can be an appropriate feeding choice for women in urban settings with intensive counselling, adequate water supply and where formula is provided free.

Modelling the risks of different infant feeding options

Prevention of HIV transmission associated with breastfeeding needs to be considered in a broad context that takes into account the need to promote breastfeeding of infants and young children in the general population. Several researchers have attempted to use mathematical models to guide policy makers in weighing the relative risks and benefits of breastfeeding and other infant feeding options. These models are limited by the scarcity of data on the risks associated with various methods of infant feeding, particularly in the first weeks of life, the risks associated with not breastfeeding in populations where HIV is prevalent, and by the inability of models to take into account all the factors that influence individual decisions about infant feeding.

Kuhn and colleagues[71] modelled the expected frequency of adverse outcomes (HIV infections and infant deaths) in the first year of life associated with different infant feeding practices (optimal breastfeeding, complete

avoidance of breastfeeding and early cessation of breastfeeding). The following parameters were varied in the models: HIV prevalence amongst pregnant women, HIV incidence, infant mortality rates, HIV transmission rates through breastfeeding, relative risk of infant death if no or less breastfeeding. They found that given infant mortality rates below 100 per 1000 and a relative risk of dying set at 2.5 for non breastfed compared to optimally breastfed (up to 12 months or longer) infants, the lowest frequency of adverse outcomes would occur if no HIV positive women breastfed and all HIV negative women breastfed optimally. For known HIV positive women fewer adverse outcomes would result from early cessation (by 3 months of age) than prolonged breastfeeding if the hazard of HIV transmission through breastfeeding after 3 months is 7% or more, even at high mortality rates, given relative risks of dying set at 1.5 for early cessation compared with optimal duration of breastfeeding. This model used a fairly moderate risk associated with artificial feeding (RR 2.5) that may be an under-estimate for many of the highest HIV prevalence countries. Furthermore the hazard of HIV transmission through breastfeeding is likely to be considerably lower with exclusive breastfeeding.

A more recent model[72] estimates the effect of three different infant feeding scenarios for HIV positive women (replacement feeding from birth, exclusive breastfeeding from birth to 6 months followed by early cessation, and prolonged breastfeeding) on infant HIV free survival at 24 months in settings with different infant mortality rates. It differs from the earlier model by Kuhn and colleagues in that is uses more recent data on risks of postnatal HIV transmission for mixed and exclusive breastfeeding. The findings suggest that in settings where the IMR is <25/1000 live births, replacement feeding results in the greatest HIV free survival to 24 months, exclusive breastfeeding produces the best outcome where IMR is >25/1000 live births, and replacement feeding results in a lower HIV free survival than no intervention where IMR is >101/1000.

Adapting this model to South Africa suggests that in seven of the nine provinces, safer breastfeeding (defined as exclusive breastfeeding followed by rapid cessation) results in the greatest HIV free survival at 12 months. In the Western Cape and Gauteng, where infant mortality rates (IMR) are low, no breastfeeding produced a similar outcome to safer breastfeeding. However, in poorer settings like the Oliver Tambo district in the Eastern Cape, where IMR is above 80/1000 live births, universal adoption of replacement feeding would lead to a lower HIV-free survival than no intervention (Unpublished results, Chopra et al).

A major limitation of these models and their practical application is the assumption that all mothers will comply with the feeding scenarios. The im-

pact of imperfect behavioural compliance on postnatal HIV transmission and non-HIV related child deaths will vary depending on which behaviour is examined i.e. lower compliance with EBF or lower compliance with replacement feeding. These models are also based on population level IMR data, although IMRs may vary substantially among different sub-populations within countries. For example, in South Africa, vastly different socio-economic groups (extremely poor and working class) live in close proximity to each other and may use the same health facilities. A provincial or national policy on infant feeding would not take such diversities into account and further emphasises the need for individual assessment as part of infant feeding counselling.

Infant feeding practices in the general population in South Africa

WHO/UNICEF infant feeding recommendations for women of unknown HIV status are six months of exclusive breastfeeding with continued breastfeeding and complementary feeding until age 2 years[73].

Although most infants in South Africa are breastfed, the most recent Demographic and Health Survey[74] found that only 12% of infants below four months and 2% of infants 4-6 months were exclusively breastfed, based on a 24 hour recall. A baseline survey of infant feeding practices in PMTCT and non-PMTCT clinics in South Africa found even lower rates of exclusive breastfeeding of 4.7% in infants under 10 weeks dropping to 1.2% for children aged more than 10 weeks. Mixed breastfeeding was the most common practice with a rate of 75.2% amongst infants less than 10 weeks of age and 87.4% amongst infants more than 10 weeks of age. The survey also found a high rate of formula usage with 64.8% of the urban infants aged less than ten weeks receiving formula milk, either exclusively or simultaneously with breastmilk (Unpublished paper, McCoy et al).

It is against this background that infant feeding recommendations for women with HIV are being implemented. If women with HIV are to succeed in practising exclusive infant feeding, then improvements in infant feeding practices in the general population are necessary to ensure that exclusive breastfeeding is the norm rather than an exception.

Infant feeding counselling of HIV positive mothers

Reducing MTCT through improved infant feeding requires greater attention to the quality of counselling and support provided to mothers. International guidelines[75] recommend that all HIV positive women should receive counselling which includes general information about the risks and benefits of

various infant feeding options and specific guidance in selecting the option most likely to be suitable for their situation.

In many countries, shortcomings in the implementation of these guidelines have been found. Inadequate training of health workers, particularly infant feeding counsellors, about the relative risks associated with infant feeding in the context of HIV, lack of culturally sensitive counselling tools, and the stigma associated with replacement feeding, all make appropriate and effective infant feeding counselling difficult. Even after training, health workers are often unsure of the risks of different feeding options. For example, an evaluation of the WHO/UNICEF infant feeding training in South Africa[76] found low levels of knowledge amongst both participants and trainers. Most participants (88%) over-estimated the risks of breastfeeding for HIV positive women and very few (10%) knew of the health risks of formula feeding. Participants' confidence in counselling following training was also disappointing with 44% being uncomfortable counselling women experiencing breastfeeding difficulties.

A similar cross-sectional assessment of health worker knowledge was undertaken in a rural area of KwaZulu-Natal, South Africa[77]. This study found that 71% of doctors would recommend water and 50% solids to breastfed infants under 6 months of age. The most commonly given responses by all health workers to problems of infants being thirsty or unsatisfied was to supplement with other fluids or feeds.

A qualitative interview study undertaken with 19 health workers in Malawi[78] found that none had received formal training, although many reported counselling mothers on infant feeding. There was generally good knowledge of the definition of exclusive breastfeeding, and all the health workers had concerns about early cessation of breastfeeding despite this being the national recommendation for HIV positive women.

Within the context of busy antenatal clinics, it is not surprising that the quality of infant feeding counselling has generally been found to be poor. Staff shortages and the associated lack of time to counsel properly, even for those adequately trained in infant feeding counselling, are important barriers to the provision of informed infant feeding choices.

In contrast, an intervention study in a rural area in KwaZulu-Natal, South Africa[79] that provided intensive training and support to counsellors, found appropriate feeding choices being made by HIV positive women. Women initiating replacement feeding were more likely to be the main income provider and to have a CD4 cell count below 200 cells per ml. This study con-

firms that well trained and supported counsellors are able to provide high quality infant feeding counselling according to international guidelines.

Infant feeding counselling is one of the most important components of PMTCT programmes. Done well it could result in significant reductions in child mortality through decreased postnatal HIV transmission and improved infant feeding practices. Done badly, it could lead to deaths from diarrhoea and other infections, and the spread of poor infant feeding practices into the general population.

HIV and infant feeding policy environment

In order to guide health workers in assisting women to make appropriate infant feeding choices, WHO and UNICEF developed the Global Strategy for Infant and Young Child Feeding[75]. The recommendation for women known to be HIV positive is avoidance of all breastfeeding if replacement feeding is acceptable, feasible, affordable, sustainable and safe. Otherwise exclusive breastfeeding for the first months of life is recommended, and should be discontinued as soon as it is feasible, when conditions for safe replacement feeding can be met. These are global guidelines which countries have adapted and modified to suit their own circumstances.

The South African Department of Health PMTCT Protocol[80], has its own specific recommendations relating to HIV and infant feeding. The recommendation is that "where safe and adequate formula feeding is possible, and where ongoing support for mother and monitoring of an infant is available, formula feeding is the principal recommended method of feeding. The risks of feeding the infant with breast milk substitutes (mainly formula) must be balanced against the risks of HIV transmission through breastfeeding." It further suggests that HIV infected women who choose to breast feed be counselled and supported to exclusively breastfeed. For women who choose to formula feed, the South African protocol makes provision for 6 months of free commercial formula milk.

Infant feeding recommendations for HIV positive women should ideally be situated within a broader policy framework for infant and young child feeding. Unfortunately, there has been little progress in terms of general infant feeding policies in South Africa. Several important policies are still in draft form and are awaiting cabinet approval. The most important of these is the Infant and Young Child Feeding Policy which would provide guidance on infant feeding recommendations for the general population.

Another key strategy to support infant feeding is the Baby Friendly Hospital Initiative (BFHI) which is a WHO/UNICEF approach to support appropriate infant feeding practices in hospitals. At the end of 2005 there were only 178 hospitals (24%) in South Africa that had BFHI accreditation. There is a modified BFHI policy that takes into account the needs of HIV positive women in terms of allowing formula use in hospitals but this is also currently in draft form.

The second policy that requires urgent legalisation is the WHO/UNICEF Code of Marketing of Breastmilk substitutes[81]. This code applies to the marketing of breastmilk substitutes, including infant formula, when marketed or otherwise represented to be suitable for use as a partial or total replacement of breastmilk. The code deals with information and education needs concerning the feeding of infants, advertising or other forms of promotion to the general public, and standards for product labelling and quality. The Code is currently a discussion paper in South Africa and has been for several years, despite the fact that the government is providing free formula milk for the PMTCT programme.

It is against this policy background that infant feeding recommendations for HIV positive women are being introduced. With no firm policy guidance on general infant feeding practices, especially the encouragement of exclusive breastfeeding for the general population, achieving high quality infant feeding counselling and safe practices amongst HIV positive women will continue to be a challenge.

Equity considerations

The HIV and infant feeding dilemma provides a clear example of the disadvantaged position of poor women in developing countries. For an HIV positive woman living in Sweden for example, to breastfeed would be considered child endangerment. However, in developing country contexts where the resources to ensure safe replacement feeding are not always available to women, the risks and benefits of breastfeeding versus replacement feeding are not as straightforward.

The current WHO/UNICEF recommendations provide clear guidance on conditions that should be met in order for formula feeding to be a safe and feasible option. The families who satisfy these criteria for formula feeding are likely to be relatively advantaged in relation to the rest of the population. Consequently, for poor women without access to clean water and other conditions amenable to safe formula feeding, the most appropriate choice would be exclusive breastfeeding. However, in a context such as South Africa

where free formula milk is provided by the health system, it is questionable whether reasoned choice is possible or whether the free subsidy induces inappropriate choices. The current policy of providing free formula milk to women who choose not to breastfeed, with no equivalent support for women who choose to breastfeed leads to further inequity and exacerbates poor choices.

This issue necessitates strong community level advocacy regarding basic resources and infrastructure. In a country such as South Africa with a GDP of over $4 000 per capita, it should be a human rights priority that all women have access to education, clean water, and fuel in order to allow for free and reasoned choice in terms of infant feeding options.

Current research priorities

Current research into the prevention of MTCT is concerned primarily with preventing postnatal HIV transmission through modifying breastfeeding practices, and with the effect of antiretroviral prophylaxis on transmission. Research into prophylaxis has focused on the timing and duration of its administration; whether it is given to the mother or infant or both; drug resistance and other health consequences for mothers and infants. The safety of replacement feeding after early cessation of breastfeeding using locally available foods or supplements is another important research question.

HIV RNA viral load and advanced maternal HIV disease are the most important risk factors for HIV transmission through breastmilk. Studies are therefore underway to explore the impact of antiretroviral therapy given to the mother who is breastfeeding or to the infant for the period of breastfeeding or to both. The aim is to prevent HIV transmission to infants during the period of breastfeeding by reducing breastmilk viral load, or providing ARV prophylaxis to infants to reduce sero-conversion[82].

Research trials providing prolonged prophylaxis to infants of HIV positive mothers have shown promising results. The MITRA study in Tanzania[83] was a non-randomised study where mothers were given combivir (ZDV/3TC) from week 36 of pregnancy to 1 week after delivery and infants were given combivir for 1 week, and daily 3TC (4 mg/kg) throughout the breastfeeding period. Mothers were counselled to stop breastfeeding by 6 months. At 6 months, 4.9% of infants were HIV positive, compared to 11.9% in the historical control group (p=0.003).

Whether HAART beginning in late pregnancy, at delivery, or after delivery reduces the risk of postnatal infection of the infant also needs to be carefully

examined. A multi-country study supported by WHO, known as the Kesho Bora study, is underway in four countries and aims to assess the impact of maternal HAART on mother to child transmission and maternal health. Women with CD4 counts < 200/mm³ or clinical AIDS will all be offered life-long HAART. Women with CD4 counts > 500/mm³ who are at low risk of HIV transmission to infants and high risk of HAART toxicity and development of resistance will be offered short-course MTCT prophylaxis. Women with CD4 counts 200-500/mm³ where the risk-benefit balance between risks of HAART, reducing MTCT, and the health benefits for mothers is not known will be randomised to receive either short-course MTCT prophylaxis or triple-ARV MTCT prophylaxis during late pregnancy and breastfeeding. This study has recently been started so results are unlikely to be available for several years.

Rationale for this study

Mother to child transmission of HIV is the main source of HIV infection in children and has resulted in declines in child survival in many of the worst affected countries[84]. Since 1998 the efficacy of various antiretroviral regimens for the prevention of peripartum mother to child transmission (MTCT) has been demonstrated[15,16,19,85]. Soon after the results of these trials became available, governments in many high HIV prevalence countries started implementing PMTCT programmes. Translating protocols from clinical trials into operational programmes proved to be a considerable challenge. South Africa introduced a PMTCT programme in 2001. At the time of its introduction a research framework was developed to monitor the effectiveness of the programme. The research presented in this thesis forms part of the national research framework.

During the period of my PhD studies I was working as a researcher for a non-governmental research organisation, the Health Systems Trust. As a member of the national PMTCT steering committee, I participated from an early stage in the development of the national research framework for PMTCT. I was involved in the writing of the proposals for the studies that contributed to this thesis, in securing funding for the research, development of research tools, training and supervision of field staff, data analysis and report writing.

PMTCT programmes have largely been introduced into already weak health systems and although evidence from many clinical trials has shown the efficacy of the drug component of the intervention, very little operational research existed to describe how the programme would perform under routine health service conditions. Furthermore, international recommendations on

HIV and infant feeding have been developed, with little guidance on how to apply these guidelines in practical counselling situations.

This research aimed to assess the implementation of the PMTCT programme in South Africa and the challenges of achieving safe infant feeding practices in the context of HIV. The studies contributing to this thesis utilise a variety of quantitative and qualitative research methodologies. This mix of research designs was chosen in order to provide a full understanding of the challenges of moving from efficacy to effectiveness and has allowed for insights to be gathered at both a national level and an individual level.

The research began with a health systems evaluation of district level data on overall programme functioning, moved to an in-depth assessment of individual HIV positive women's experiences of infant feeding, and finally to a quantitative assessment of the outcomes of infant feeding choices in order to guide policy making.

Local and international guidelines regarding PMTCT and infant feeding continue to be revised, whilst there is little research describing operational experiences of these interventions. This research aims to inform policy development, and to provide practical recommendations to improve the counselling and postpartum support to women.

Study aim

The overall aim of this research was to assess the implementation of the PMTCT programme in South Africa and the challenges associated with achieving safe infant feeding practices in the context of HIV.

Specific objectives

- To assess the uptake and coverage of the South African national PMTCT pilot programme. (Paper I)
- To explore how HIV has impacted on the infant feeding experiences of HIV positive mothers. (Paper II)
- To describe the challenges that HIV positive women face at different stages of early infant feeding and to identify characteristics of women and their environments that contribute to success in maintaining either exclusive breast or exclusive formula feeding. (Paper III)
- To identify criteria to guide appropriate infant feeding choices, and to assess the effect of inappropriate choices on infant HIV-free survival. (Paper IV)

Research methods

Study designs

The research presented in this thesis arises out of two larger studies; firstly a national evaluation of the South African PMTCT pilot programme and secondly a prospective cohort study of mother to child HIV transmission (Good Start study) in South African pilot sites. Both quantitative and qualitative research designs were used. Quantitative health systems research methods were used for the national programme evaluation (Paper I) and a prospective cohort study design was used for the assessment of infant feeding choices and outcomes as part of the Good Start study (Paper IV). Qualitative methods which are best suited to a deeper understanding of individual experiences and behaviours[86,87], were used for the sub-studies of the Good Start cohort reported in Papers II and III, which sought to explore infant feeding experiences of HIV positive women.

National PMTCT evaluation

The national PMTCT evaluation was commissioned by the national Department of Health in South Africa and was undertaken one year following implementation of the national PMTCT pilot programme. The initial implementation of PMTCT services occurred at eighteen pilot sites, two in each of the nine provinces (one urban and one rural site). This cross-sectional evaluation utilised a health systems approach to assessing programme performance by evaluating uptake and coverage of each step in the programme and identifying bottlenecks to optimal programme effectiveness.

In health systems research, health services are considered as a complex system consisting of numerous components that are essential to optimal functioning. These components include but are not limited to; human resources, physical infrastructure, drugs and supplies, transportation systems, management and supervision. A health systems approach to programme evaluation includes an assessment of each of these components in order to improve the understanding and interpretation of broad programme indicators, such as HIV testing rate.

Habicht et al.[88] propose a framework for choosing an evaluation design based on an understanding of the purpose of the evaluation. One of the key objectives of this evaluation was to identify constraints or bottle-necks to optimal functioning of the PMTCT programme in order to provide information that would inform national plans for scale-up. This objective could be answered with an assessment design focused on programme utilisation and coverage, with the performance compared to previously established criteria such as WHO/UNAIDS targets for HIV testing uptake and ARV coverage. Habicht et al. refer to this as an adequacy evaluation. Adequacy assessments require no control groups as results are compared with set criteria and they are most commonly cross-sectional. The main purpose of this design is usually to provide evidence that expected programme goals are being met in order for policy makers to make decisions on continued support or expansion.

The main indicators that were measured in this evaluation therefore focused on utilisation and coverage of the programme, for example, coverage of nevirapine amongst women identified to be HIV positive. Health service coverage has been defined as "the extent of interaction between the health service and the people for whom it is intended[89]". For the measurement of coverage, several key steps in an intervention need to be identified and a coverage measure for each step needs to be defined. The South African PMTCT programme[80] includes counselling and HIV testing using an opt-in model, antenatal infant feeding counselling, single dose nevirapine to women and infants, and infant testing at 12 months using a rapid antibody test. The evaluation assessed the uptake and coverage of each of these steps of the programme.

The evaluation of coverage allows health service managers to identify bottle-necks in the operation of a service, to analyse constraining factors responsible for such bottle-necks, and to identify strategies for improvement. Whilst an assessment of coverage is useful to determine whether a programme has achieved set criteria, such as an HIV testing uptake rate of over 50% amongst pregnant women, the next step would be to measure the impact of achieved coverage, for example, whether a high coverage of nevirapine resulted in a lower vertical transmission rate. This required a more complex evaluation design as undertaken in the Good Start study.

Good Start study

Cohort study

The importance of rigorously evaluating pilot programmes such as the PMTCT programme led the South African Department of Health to support a prospective cohort study of 665 HIV positive mother-child pairs with active follow-up to determine the impact of the PMTCT programme on vertical transmission rates. An observational cohort study design was best suited to the objectives of this study for several reasons. Firstly, little was known about the infant feeding practices of HIV positive women and these needed to be documented in order for appropriate interventions to be developed. Secondly, long term follow up is needed to determine infants' exposure to HIV and the outcomes of that exposure i.e. HIV transmission. Thirdly, the prospective nature of the design enabled an assessment of temporal sequence between exposure and disease i.e. timing of transmission, which would not have been possible with a cross-sectional design. Fourthly, the study aimed to assess the effectiveness of the current PMTCT programme under routine conditions, therefore it would not have been appropriate to randomise mothers to different antiretroviral regimens or modes of feeding. Finally, a cohort design allowed for the assessment of multiple effects from a single exposure, for example, the relationship between exposure of infants to HIV and HIV transmission, growth and mortality.

Several disadvantages of the observational cohort design deserve mention[90]. Firstly, such studies take a long time and are considerably more costly than a cross-sectional design. Secondly, they are prone to bias due to loss to follow up. Thirdly, secular changes could take place during the course of the study (i.e. changes in treatment regimen) which may not be measured. Lastly, the exposed and unexposed groups may differ in aspects other than the exposure i.e. possible confounders such as access to health services.

A research consortium including the Health Systems Trust, Medical Research Council and University of the Western Cape was provided with a grant by the National Department of Health to implement this study. Women (and their infants) were recruited prior to, or at the time of delivery and followed until the infants were 36 weeks of age. HIV testing of the child took place at 3 weeks, 6 months and 9 months.

The study was undertaken at three sites (Paarl, Rietvlei and Umlazi) which were among the eighteen national pilot sites. Paarl (Western Cape province) is a peri-urban/rural area situated in a commercial farming region. It has a relatively well functioning public health system and an antenatal HIV prevalence of 9%[91] (photo of site, Fig 4). Rietvlei (Eastern Cape province) is a rural area in one of the poorest regions of South Africa with a 28% antenatal

HIV prevalence and a very weak health service (photo of site, Fig 5). Umlazi (KwaZulu-Natal province), is a peri-urban township area on the outskirts of Durban (Fig 6) with formal and informal housing and is considered to be intermediate with regard to health resources compared to the other two sites. The antenatal HIV prevalence is 47%. Figure 7 shows the locations of all three sites.

Figure 4. Children playing in Mbekweni informal settlement, part of the Paarl Good Start study site.

Figure 5. Houses within Umlazi site of the Good Start study.

Figure 6. Rietvlei Hospital.

Figure 7. Map of South Africa showing the three sites for the Good Start Study.

Qualitative sub-studies

The cohort study was designed to collect quantitative information on infant feeding patterns and HIV transmission rates. This information alone is not sufficient to understand the challenges women face in implementing these feeding options. In order to help inform programme planning, research also needs to focus on the experiences of mothers in the PMTCT programme and the socio-cultural determinants of infant feeding practices. Given that PMTCT programmes worldwide are relatively new interventions, much of the research is focusing on clinical outcomes in order to design treatment regimens. Consequently, women's experiences of these programmes have been a neglected focus of inquiry.

The experience of mothers in the PMTCT programme, the socio-cultural influences on feeding choices, and disclosure of HIV status are complex issues that have a substantial impact on the ability of women to provide safe and appropriate feeding for their infants. Exploration of these issues is best suited to a qualitative research design. Furthermore, a greater understanding of these issues allows for a fuller analysis of quantitative outcomes such as HIV-free survival rates, which are regarded as the ultimate measure of the effectiveness of a PMTCT programme, yet provide limited information on their own. This cohort provided a unique opportunity to capture in-depth information from women that have experienced the PMTCT programme. Provision was therefore made for qualitative sub-studies that could explore these issues in further depth.

Several researchers have attempted to define qualitative research. One definition that fits well with the use of qualitative research in this thesis is: "…qualitative implies a direct concern with experience as it is 'lived' or 'felt' or 'undergone'…qualitative research, then, has the aim of understanding as nearly as possible as its participants feel it or live it"[92].

The theoretical framework for most qualitative research emerges from an interpretivist perspective, a paradigm that attempts to examine the experiences, feelings and perceptions of the people under study rather than imposing frameworks which might distort the ideas of the participants. When exploring a programme, project or service, as in this research, statements in the reporting person's own words can provide an accurate picture of their reality, and their experience of the programme.

There has been increasing recognition of the importance of qualitative methods in health systems research and a subsequent rise in the reporting of qualitative research studies in medical and related journals[93]. Furthermore, traditional qualitative methodologies such as phenomenology, ethnography

or grounded theory have been applied in more pragmatic, action-oriented approaches to create a style of qualitative research rather than a specific method[94]. Applied qualitative research is undertaken to inform action and enhance decision making on practical issues, unlike basic or purist qualitative research which is usually undertaken to generate theory[95].

Two qualitative studies are included in this thesis. Both of these studies utilised an exploratory descriptive qualitative design as little was known on the topic under study, namely infant feeding experiences of HIV positive women, in the South African context. Qualitative research methods are ideally suited to this type of exploration as they provide inductive insights into social practices by moving from observations and open questions to theme areas and general conclusions.

The two qualitative studies included in this thesis utilised different approaches to exploring HIV positive women's experiences of infant feeding. The first (Paper II) utilized a cross-sectional approach whereby women were interviewed once during the postnatal period in order to describe their experiences of infant feeding decision-making and practices and the sociocultural influences on them. The second study (Paper III) utilised a longitudinal approach whereby women were interviewed on five occasions beginning in the antenatal period and ending at twelve weeks postpartum. This allowed for an exploration of experiences during key stages of the antenatal and early postpartum period. These two approaches provide a fuller understanding of important challenges and enabling factors in infant feeding in the context of HIV.

Sampling

For the national PMTCT evaluation (Paper I) all eighteen PMTCT pilot sites were sampled. These sites consisted of various levels of care including tertiary hospitals, district hospitals, community health centres and clinics. The primary sampling unit was all women attending antenatal care at these PMTCT facilities between January and December 2002. One hospital and one of its associated feeder clinics in each of the provinces was visited for data verification and individual interviews. Semi-structured interviews were conducted with health workers implementing the programme at these facilities and with the PMTCT programme manager at the provincial level in each of the nine provinces. Purposive sampling was used to identify health workers at the facility level with responsibility for PMTCT implementation, for example the nurse in charge of the labour ward and the nurse in charge of the antenatal clinic. Approximately 2-3 health workers were interviewed at each facility that was visited.

For the Good Start study and qualitative sub-studies (Papers II, III & IV), the three sites were purposively selected from amongst the eighteen PMTCT pilot sites. The selection was made to enable an assessment of programme effectiveness in areas with different HIV prevalence rates, geographic locations and health system functioning.

For the Good Start study HIV-positive mothers were recruited from the local hospital or clinic offering the PMTCT programme by a qualified field researcher either antenatally or postpartum prior to discharge from the hospital. Mothers who did not receive antenatal care at a National PMTCT pilot programme site selected for the study, did not deliver at a designated facility or refused informed consent were excluded from the study. Other exclusion criteria included multiple births, congenital malformations or other serious newborn illness. Recruitment over a period of 12 months yielded a total sample size of 665 mother-infant pairs as follows: Paarl 149, Rietvlei 192, and Umlazi 324. The full sample of HIV positive women in the cohort study was used for the analysis in Paper IV.

Sampling for the first qualitative sub-study (Paper II) was from the larger cohort of HIV positive women. Women who had achieved some success in exclusivity of early infant feeding practices were identified from the larger cohort sample and asked by a field worker to participate in an additional in-depth interview about infant feeding. Recruitment continued until no new information was emerging from the interviews (sometimes referred to as data saturation[96]) and the final sample was forty women. Focus group discussions were also held with the community workers who regularly visited women in the cohort study to collect data on infant feeding practices. One focus group was held per site and all of the community workers in each of the sites (8-10 people) participated in the focus group discussions.

For the second qualitative study (Paper III) HIV positive women were sampled from the same three sites as the Good Start study but only once recruitment for the cohort study was complete. As this qualitative study had a longitudinal design, women participating in the cohort study were not included because they were already receiving regular data collection visits for the larger study and these extra in-depth visits may have been too burdensome and time consuming for them. Pregnant women, at least 34 weeks gestation, who had been through voluntary counselling and testing (VCT) and who had received an HIV positive test result were informed about the study by a clinic nurse and if they agreed to participate were introduced to a field researcher. Purposive sampling (a method of selecting individuals with qualities of interest to the research question[97]) was used to select the first three to five HIV positive women who intended to formula feed and the first three to five HIV positive women who intended to breastfeed at each site. This sam-

ple size was used as a guide to enable different experiences of these feeding options to be captured in the three sites. The final sample consisted of 11 women who intended to breastfeed and 16 women who intended to formula feed. Sample size was determined after data collection began and was based on a review of the interview transcripts in order to determine the point of data saturation.

Data collection

Data collection methods utilized in these studies included routine data reviews, structured interviews, semi-structured in-depth interviews and focus group discussions.

Routine data reviews

The primary source of data collection for the national PMTCT evaluation (Paper I) was routine monthly PMTCT data from the facilities included in the review. Registers and tick sheets for the collection of aggregated PMTCT data were designed by the national Department of health and there was little opportunity for input from researchers. These registers were completed on a daily basis by health workers and then compiled into monthly summary sheets. The data items and indicators collected as part of the routine data and included in the evaluation are listed in Table 1.

The monthly summary sheets were sent to the provincial health department and were captured by study staff into the District Health Information System (DHIS). The DHIS is accepted as the national standard for district-level anonymised health data.

There were several shortcomings of using routine health data for this evaluation. The main weakness was that the data was collected by health workers in the facilities and not by researchers. The information system for PMTCT was also initially a separate system that was not integrated into the routine essential primary health care data set. This system was chosen in order to allow for central level reporting at the early stages of the programme but resulted in this extra data requirement being burdensome and time consuming for health workers leading, to problems with data quality.

The aggregated nature of the data also did not allow for the assessment of programme outcomes for individual mother-infant pairs but provided a general overview of programme coverage.

Table 1. *Routine PMTCT indicators.*

Indicator	**Numerator**	**Denominator**
Proportion antenatal clients tested for HIV	Antenatal clients tested for HIV	Antenatal 1st visits
HIV test results received	Antenatal clients receiving HIV test results	Antenatal clients tested for HIV
HIV prevalence amongst antenatal clients tested	Antenatal client tested HIV positive – new	HIV test done on antenatal client
Nevirapine uptake rate amongst pregnant women with HIV	Nevirapine dose to woman at antenatal or labour	Antenatal client tested HIV positive - new
Nevirapine uptake rate rate among babies born to women with HIV	Nevirapine dose to baby born to woman with HIV	Live birth to woman with HIV
Formula feeding intention rate	HIV positive women intending to formula feed at discharge from hospital	Live birth to woman with HIV
Exclusive breastfeeding intention rate	HIV positive women intending to exclusively breastfeed at discharge from hospital	Live birth to woman with HIV
HIV testing rate of baby	HIV 1st test of baby at 12 months	Live birth to woman with HIV
HIV vertical transmission rate	HIV 1st test positive of baby born to HIV positive woman	HIV 1st test of baby born to HIV positive woman

In order to verify the quality of the data several strategies were adopted. Firstly, researchers made visits to the sites in order to review registers and correct errors found in monthly summary sheets. Secondly, where data quality was suspect, other routine data collected by the site was examined. For example, the number of 1st antenatal visits recorded in the PMTCT data set should be the same as the number of 1st antenatal visits reported by the facility for the primary health care data set. The indicator that was the most problematic was the nevirapine coverage. Health workers recorded nevirapine dispensed to HIV positive pregnant women either at antenatal clinics or at the point of delivery. In many cases the data was collected and recorded at both sites. The data demonstrated both gaps and double counting and in many instances the original registers at both places had to be checked. Researchers also attended the national PMTCT steering committee meeting where provincial coordinators from all nine provinces present their programme data on a quarterly basis. This meeting provided an opportunity to verify data errors with the managers through joint review and interrogation of indicators.

Structured interviews

For the Good Start study, data was collected using structured interviews with mothers in their homes or the study office. Data was collected by either: trained field researchers or trained community health workers (CHWs). All interviews were in the preferred language of the subject (Xhosa, Zulu, Afrikaans or English). Community health workers were blinded to the HIV status of the mother. The schedule of visits and scope of data collection is shown in Table 2.

An initial interview was conducted by a trained field researcher at recruitment to explain the study and gain signed informed consent from each participant mother. This interview concentrated on plans for infant feeding and care of the infant, plans for disclosure of HIV status, basic knowledge of HIV/AIDS and MTCT, as well as explaining the home visits and obtaining clear directions to the mother's home. This interview took approximately 30 minutes. A medical record review was also conducted on all relevant antenatal, intra-partum, post-partum, PMTCT and other records.

Table 2. *Data Collection & Scope of Data for the Good Start study.*

Recruitment and informed consent by qualified field researcher	• Either antenatally at 34-36 weeks (preferred) or after delivery, prior to discharge
Perinatal medical record review by qualified field researcher	• Post-delivery - including antenatal, intra-partum, post-partum, PMTCT and any other relevant records
Semi-structured questionnaire and observation conducted by qualified field researcher (0.5 – 1 hour)	• After delivery, prior to discharge • 3 weeks post-delivery • 24 weeks post-delivery • 36 weeks post-delivery
HIV status of infants of HIV-positive mothers (dried blood spots for DNA PCR)	• 3 weeks post-delivery • 24 weeks post-delivery • 36 weeks post-delivery
Viral load of HIV-positive mothers (dried blood spots for RNA PCR)	• 3 weeks post-delivery • 36 weeks post-delivery
Structured questionnaire conducted by local community health workers during home visits	• Fortnightly for first 9 weeks • Monthly from 12 weeks to 9 months

Subsequent home visits were made by a trained field researcher at 3 weeks, 24 weeks, and 36 weeks post-delivery. These visits took approximately 1 hour each and the questionnaires included data on infant diet, cessation of breastfeeding (if applicable), influences on decisions around infant feeding choices, child care practices, socio-demographic data, participation in and satisfaction with PMTCT, health status and health visits (formal and traditional) for mother and infant, issues related to disclosure, and family/social

support. In addition, anthropometric measurements (weight and length) of infants were obtained at the 3, 24 and 36 week visits (Fig 8 shows a typical interview).

Figure 8. Field researcher interviewing a mother in the Good Start study.

Home visits by trained CHW field staff were completed every 2 weeks until 9 weeks and then monthly thereafter until 36 weeks (5, 7, 9, 12, 16, 20, 28, 32 weeks). CHWs completed a simple structured questionnaire on infant diet, infant health, formula availability, and visits to health facilities.

Laboratory data collection

Blood collection in infants was obtained from dried blood spots collected on Guthrie cards by means of a heel prick during home visits at 3, 24 and 36 weeks. HIV infection in infants was determined by quantitative HIV-1 RNA NASBA (Nuclisens ECL, Biomerieux) and qualitative HIV-1 DNA PCR assay (Amplicor V.1.5, Roche). Children were defined as infected with HIV-1 if they had either a detectable viral load above 10 000 copies or were positive on DNA testing.

Maternal HIV status was initially determined from routine PMTCT medical records. However, in cases where a mother recorded as being HIV positive had no detectable viral load, a repeat laboratory ELISA was done (Biomerieux Uniform 2 HIV-1 Assay followed by Biorad HIV-1 Assay).

Quality control testing was performed on 5% of the samples by an independent laboratory.

Semi-structured interviews

Interviews with health workers and provincial managers for the national PMTCT evaluation

In order to capture the experiences of health workers implementing PMTCT, semi-structured interviews were held with health workers at one hospital and one of its associated feeder clinics in each of the nine provinces. An interview was also held with the programme manager in each province.

Two questionnaires were developed for the evaluation, one for the facility level, and the other for the provincial level. The facility questionnaire addressed management, training, counselling and testing, antenatal care, infant feeding, monitoring and follow up, procurement of supplies, and community involvement. The provincial questionnaire addressed provincial management, information management, plans for expansion of the programme, and expenditure.

In order to ensure standardisation amongst researchers, the same tools were used in all provinces and the same categories of health workers were interviewed across all provinces. Brief notes were made on the tools and open ended questions were expanded into full interview transcripts as soon as possible after the interviews.

In-depth interviews for the two qualitative studies

Semi-structured discussion guides were developed for the individual interviews undertaken for Papers II & III. Existing tools for assessing infant feeding were consulted in the development of these discussion guides. The interview questions were open ended and began with an initial question to start discussions on a particular theme area such as, ‘Can you tell me about your experiences of the counselling you received during antenatal care?’ Ongoing discussion was minimally directive in that the researcher would probe and ask further questions based on the interviewee’s responses. The interview guides focused on infant feeding counselling experiences, previous breastfeeding experiences, infant feeding decision-making, and early infant feeding practices.

For the second qualitative study (Paper III) interviews were held with HIV positive women antenatally and at one, four, six and twelve weeks postpartum. Interview guides were developed for each interview which focused on unique experiences and challenges related to infant feeding during these

distinct phases of the postnatal period. The antenatal interview focussed on infant feeding intentions, involvement of key people in decision-making, and disclosure of HIV status. The one week interview focused on experiences of delivery, infant feeding initiation, and early experiences in the home environment. The four week interview focused on introduction of other fluids, infant growth and well-being, and involvement of key people in infant feeding. The six week interview focused on growth spurts, HIV disclosure, sustainability of formula (for women using formula milk) and plans for breastfeeding cessation (for women who were breastfeeding). The twelve week interview focused on mother's activities and time away from the infant, breastfeeding cessation, and maternal and infant health.

The interviews for both qualitative studies were conducted by three trained field researchers with experience in qualitative interviewing. Interviews were conducted in the participants' preferred language (Xhosa, Zulu or Afrikaans) and lasted between 30 and 60 minutes. All interviews were audio taped, transcribed verbatim and translated into English. Transcripts of interviews were anonymised with only a participant code.

An important consideration in qualitative research is the need for more than one method of data collection in order to portray accurately the situation under analysis. Brink[98] advocates the use of a variety of methods of data collection to enable concurrent validation. Such variety provides "triangulation", whereby several different methods are employed to broaden the understanding of information obtained during a study. In the first qualitative study, (Paper II) focus group discussions were undertaken to validate and enrich the data from individual interviews.

Focus group discussions

Focus group discussions were held in the first qualitative study (Paper II) as a means to gather information on normative infant feeding practices and community perceptions about PMTCT from a group of individuals who live in the same communities as the HIV positive women.

The focus group method has been widely used in social science research[99]. It is a purposive discussion of a specific topic or related topics taking place between six to eight individuals with a similar background and common interests. The group interaction consists of verbal and non-verbal communication and interplay of perceptions and opinions that will stimulate discussion. The focus group interview enables the researcher to develop concepts, generalisations and theories that are grounded in or reflect the intimate knowledge of the people participating in the group. Focus groups also permit

access to attitudes and perceptions which are more likely to surface by virtue of the interaction within the group.

A discussion guide was developed for the focus groups following initial analysis of the individual interviews. This enabled issues from the individual interviews that required further exploration or understanding to be included. One focus group was conducted in each site with approximately 8-10 community health workers (CHWs). The groups were conducted approximately mid way through the cohort study in order for the CHWs to have time to develop both a relationship with the mothers they were visiting and an awareness of family and socio-cultural dynamics operating in the household. The groups were facilitated by the same field researchers who conducted the individual interviews in the local language spoken by the participants. The discussion flowed from an opening question, "Can you tell me about your work?" Group interactions and critical reflections were facilitated through ongoing discussion. The focus groups lasted approximately one hour. They were tape recorded, transcribed and translated into English.

Data analysis

Analysis of routine PMTCT data

The routine PMTCT data was collected from monthly provincial summary sheets and entered into the District Health Information System (DHIS). This programme allows for data cleaning and analysis. The data items that were collected were identified from the national routine PMTCT monitoring indicators (Table 1). Indicators were classified according to their measure of effectiveness, for example, uptake of HIV testing was classified as an initial use indicator, coverage of nevirapine was classified as a continuity indicator and infant feeding intentions were classified as quality indicators.

Pivot tables were generated and indicators were plotted on a graph showing the monthly means of key indicators across provinces for the time period January to December 2002. This enabled the researchers to visualise the degree of fulfilment of programme targets, to assess changes in coverage over time, and to identify at which level the operational problems hampering implementation were occurring. For example, of the women who tested HIV positive, only 55% were dispensed nevirapine. The reasons for this low coverage had to be further explored through analysis of individual interviews. Indicators were also compared within (using time trends) and between provinces and considered against national and international targets, for example, the WHO/UNICEF target for HIV testing amongst pregnant women is at

least 50% and for ARV coverage at least 75%[100]. Sub-analyses were also done by geographic region, for example, infant feeding intentions were compared between urban and rural sites.

Analysis of qualitative interviews

Analysis of interviews with health workers and provincial managers for the national PMTCT evaluation

The notes from the semi-structured interviews with facility and provincial managers were read by the members of the research team and key themes were identified and grouped together to form categories. The findings from these interviews were used to provide contextual insight into the programme indicators. For example, the findings from individual interviews in relation to HIV disclosure amongst mothers assisted with the understanding of the low nevirapine uptake levels in some provinces.

Analysis of interviews for the two qualitative studies

The interviews from both qualitative studies were analysed using the same methodological approach. Data analysis was undertaken concurrently with data collection in order to guide further interviews and to determine final sample size[101]. Analysis was done manually without the assistance of any computer programmes.

Following transcription and translation, interview transcripts were read by all of the researchers and sections of text were marked and linked to sections of text from other interviews that covered similar issues or experiences. In this way recurrent themes were identified inductively i.e. the themes were identified gradually from the data not a priori. A theme can be described as "a statement of meaning that runs through all or most of the pertinent data, or one in the minority that carries heavy emotional or factual impact"[102]. Notes were also written in the margins of the interview to record first thoughts and feelings on the interview as a whole. During this process the researcher attempts to search for the core meanings of the thoughts, feelings and behaviours described in the text.

Emerging themes were discussed in group meetings in order to define the final descriptive categories and interpretations. Data analysis continued until the team determined that no new information was emerging, i.e. a stage of data saturation. The focus group data was transcribed and analysed in the same manner as described above.

Analysis of quantitative cohort data

Quantitative data from the cohort study was entered into MS ACCESS using double data entry at a central site (MRC Durban). After validation the database was exported to Stata (v8.0) for data management and analysis.

HIV-free survival was chosen as the primary outcome for this analysis and for the main analysis of the cohort study (the composite end-point of HIV transmission or death was used). The choice of HIV-free survival was influenced by review of papers published by the Ghent MTCT research group[103,104]. The Ghent group point out that the methods they advocate, Turnbull's adaptation of the Kaplan-Meier, are not appropriate for exploratory analyses to investigate risk factors for HIV-transmission or death. In order to investigate the effect of an infant feeding choice on HIV-free survival under various conditions, Cox's proportional hazards regression models were fitted, using Efron's method for adjusting for tied survival times as there were a high proportion of ties due to having only three HIV testing points.

Adherence to formula feeding was a secondary outcome and was defined as never introducing breastmilk amongst women who intended to formula feed. Baseline characteristics were compared between women intending to formula feed and women intending to breastfeed using chi-square tests for categorical variables and one-way analysis of variance for continuous variables.

In order to determine which criteria should be included in a measure of appropriateness for infant feeding choices according to the WHO/UNICEF guideline, Cox's proportional hazards regression models were run to determine which factors individually predicted infant HIV-free survival amongst women who intended to formula feed. The factors assessed were the availability of piped water, availability of electricity, gas or paraffin as a source of fuel, HIV status disclosure, access to a fridge, and household employment. In order to determine predictors of formula adherence, using ever breastfeeding as a marker of non-adherence, a second analysis was done using logistic regression to determine which of the above criteria were predictors of adherence to exclusive formula feeding. A balance between protective effect (i.e. which criteria best predicted HIV-free survival and formula adherence) and not being too restrictive (i.e. that very few women met the criteria) was sought in the selection of appropriate criteria for recommending formula feeding.

Potential confounding factors that were examined included maternal age, parity, maternal education, maternal viral load, site, and household asset score using a data based approach (i.e. greater than 10% change in between

group hazard ratios)[105]. Maternal education was found to play a confounding role for the outcome HIV transmission or death but not for the outcome of formula adherence. Maternal viral load was not found to be a confounder as it changed the hazard ratios by less than 10%. The HIV transmission/death estimates were therefore adjusted for maternal education only. Site was found to be an effect modifier of the relationship between the criteria (exposure) and the outcome formula adherence therefore no adjustment was made for site. However due to limited numbers it was not possible to present site specific estimates.

Validity, Reliability and Trustworthiness

Qualitative Studies

Qualitative research work has often been criticised by empirical researchers who believe that there is a lack of control over the quality of the findings. Criteria used to assess the quality of quantitative research such as generalisability, validity, reliability and precision are inherently different from criteria used to assess the quality of qualitative research which aims to explore, discover and understand experiences and behaviour. In a qualitative study, terms such as credibility, transferability, dependability and trustworthiness are used to describe processes to ensure quality[95]. In qualitative research the researcher is the interpretative instrument. It is therefore of critical importance that certain measures are taken to ensure the quality of the data collected. Several measures were taken in these studies to ensure the trustworthiness of the research findings.

Triangulation is one method of increasing the credibility of qualitative data and involves the use of a number of methods of gathering data and several approaches to ongoing data analysis[93]. Triangulation characteristically depends on the convergence of data gathered by different methods. In the first qualitative study both individual interviews and focus group discussion methods were used. The use of more than one method provides a rich and complex picture of the phenomenon being studied.

Interview transcripts and initial analysis were subjected to peer review as a form of co-analysis[101]. A team approach to analysis increases the dependability of qualitative findings as it helps to offset the subjective bias of one researcher. Individuals involved in this process included one of my supervisors and two other colleagues. This allowed for the interpretations to be challenged or new interpretations presented.

Another criterion for credibility in qualitative research is to engage in collecting data for a sufficient period of time to enable a full understanding of

the subject under study. The term 'saturation' is often used to describe the stage in data collection and analysis when data repeats itself and no new data is forthcoming. According to Ely et al[102] it is at this stage that the researcher needs to trust that it is time to stop. Finding that moment, and then having the confidence and skill to define it and to use it well, is key to qualitative research. During these studies data collection and analysis continued until a stage when the data was becoming similar and when the team felt that we had exhausted the data these studies would yield.

Transferability is the qualitative analogue to the concept of generalisability. Because qualitative analysis is firmly rooted in specific contexts, some researchers believe that it is not possible to make inferences to other populations, however others believe that it is possible to apply lessons learned in one context to similar contexts[95]. In this research the sample of women was carefully selected from different geographic regions including rural and urban areas and included HIV positive women practising both breastfeeding and formula feeding. This data could therefore be conceptually transferable to HIV positive women living in similar contexts.

Quantitative studies

In the Good Start study various measures were taken to ensure validity and reliability of the data collected. The data collectors underwent intensive training to ensure standardisation of practices across sites, particularly with anthropometric measurements. Practice interviewing was also undertaken to ensure that all interviewers asked questions in the same manner and with the same meaning. In order to ensure the validity of questionnaires, existing validated tools on infant feeding were consulted in the development of questions and all questionnaires were piloted to ensure that questions were valid and understandable. All study activities were described in standard operating procedure (SOP) guides that were kept at all three sites and an external quality control specialist performed two study audits during the course of the study to ensure that field staff was adhering to study SOPs.

To ensure reliability of the anthropometric measurements electronic scales were used and all scales were checked regularly for accuracy with a standard weight (see Figs 9 and 10). To ensure accurate measurement of the main outcome, HIV transmission, tests suitable for detecting HIV DNA and RNA were used as opposed to ELISA tests which would have detected maternal antibodies and therefore would not have been a true measure of actual infant infection status. The DNA PCR Assay detects proviral cell-associated DNA with a sensitivity of 95-99% and a specificity of 98%[106,107].

Figure 9. Infant participating in the Good Start study being weighed during a home visit.

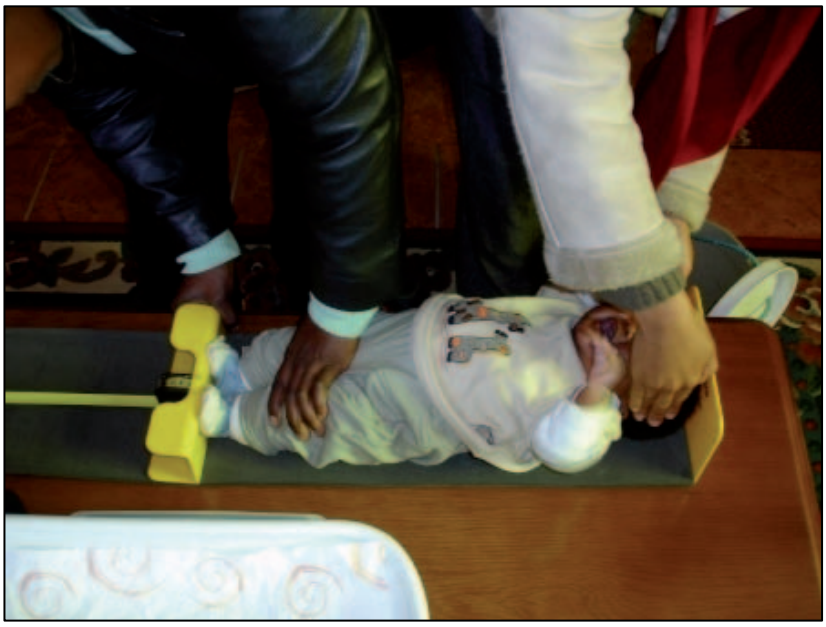

Figure 10. Infant participating in the Good Start study having his length measured during a home visit.

Ethical considerations

All of the studies described in this thesis were reviewed by a recognised ethics committee. The national PMTCT evaluation was reviewed by the committee at the national Department of Health, the Good Start study was reviewed by the ethics committee of the University of KwaZulu-Natal and the two qualitative sub-studies were reviewed by the ethics committee of the University of the Western Cape and the World Health Organisation who were the funders.

For the national PMTCT evaluation verbal consent was obtained from health workers and programme managers for interviews. All interview notes were anonymised and no identifying information about respondents was used in study reports or papers.

For the Good Start cohort study, signed informed consent was obtained at enrolment, with verbal informed consent at each home visit. Compensation for interview time was based on local norms in the sites and took the form of food vouchers, cash or food parcels.

An ethical dilemma facing the study team at the start of this study was whether to provide results of infant HIV tests real time or to store samples till the end of the follow-up period and to test them retrospectively. Testing all samples at the end was the cheaper and more efficient option as only infants who tested HIV positive at 36 weeks would need earlier samples to be tested (24 and 3 weeks) to determine timing of infection. In the PMTCT programme at the time the standard of care with regards to infant testing was to conduct testing at 12 months, therefore giving results at 36 weeks was earlier than the current standard. Furthermore, there was some concern that providing test results earlier might be an intervention in itself which could lead to behaviour change in terms of infant feeding practices and would mean that the study would no longer be truly observational. After much discussion it was decided that testing would be done on completion of follow up and this information was given to mothers during the informed consent process.

For the first qualitative sub-study, although the respondents were already enrolled in the larger cohort study, an additional consent process was followed and mothers were informed that refusal to participate in the sub-study would not compromise their participation in the larger study. Informed consent was also obtained from community health workers who participated in the focus group discussions.

For the second qualitative study mothers were informed about the purpose of the research, the timing of interview visits and were given the option of having interviews in their homes or in the study office depending on where they felt most comfortable. If a woman agreed to participate she was asked to sign an informed consent form.

To maintain the confidentiality of participants in both qualitative studies, transcripts of interviews were labelled with only a participant code and these codes were used in all reporting of the data.

Findings

In this section the main findings across the four papers will be summarised. The findings highlight important challenges to the operational effectiveness of PMTCT programmes at a health systems and an individual level. Detailed results can be found in the individual papers.

Low coverage of PMTCT interventions in operational settings (Paper I)

This research highlighted the many missed opportunities to prevent mother to child HIV transmission due to the drop out of women at various stages of the intervention.

HIV testing provides the entry point to the PMTCT programme and it was therefore assessed as a key indicator of PMTCT implementation. This research has found that the uptake of HIV testing within the pilot sites differed greatly, with some sites achieving high uptake and others consistently low uptake. This has resulted in many women not having the opportunity to benefit from this intervention. The average testing uptake rate across the 18 pilot sites was 56%. Several factors were identified which could have contributed to the low testing uptake, including the 'opt-in' model of testing, the availability of lay counsellors, and interruptions in the supply of test kits and consumables.

At the next stage of the intervention, provision of antiretroviral prophylaxis, further loss occurred as just over half of the women who tested HIV positive were recorded to have received nevirapine. This low rate could be due to problems with data recording and compilation as nevirapine is dispensed in both antenatal clinics and labour ward settings. Fears of disclosing their status may have resulted in women self-administering nevirapine at home and not informing labour ward staff, hence the dose would not be recorded in the routine records.

Coverage of nevirapine to infants was generally found to be high, most likely due to the fact that they are a 'captive audience' in the hospital as the dose is due soon after delivery. It is important to note that this indicator only includes infants born to women who were known to be HIV positive during labour. The denominator is therefore most likely to be an underestimate of total births to HIV positive women, as women who did not disclose their HIV status in labour, and home deliveries, are not included.

This evaluation captured data on the recorded infant feeding intentions of HIV positive women antenatally or postpartum, prior to discharge from the hospital. In community obstetric units in South Africa, following a normal vaginal delivery, discharge usually occurs 6-8 hours following delivery. This research found that almost 10% of HIV positive women were still undecided about how they would feed their infants around the time of delivery. Of the women who did make a decision, over half (58%) planned to use formula milk. In provinces where intensive HIV and infant feeding counselling had taken place, more women opted for exclusive breastfeeding. The finding of a high rate of intention to formula feed in rural sites (67%) is cause for concern as many of these areas do not have access to safe water.

Operational problems with the distribution of free formula included supplies running out, supplies given to mothers not lasting until their scheduled return date to the clinic, and concerns amongst health workers regarding how to counsel mothers on infant feeding from six months when the free supply of formula ends.

The largest drop out in the PMTCT programme occurred in the follow up of mothers and infants postnatally. Only half of the infants born to HIV positive women were followed to 12 months for rapid HIV testing. The infants who remained in the system could be different, in terms of risk factors for transmission, from those who were lost to follow up e.g. they could be more likely to be formula fed as this requires more regular contact with health facilities. Furthermore, the HIV status of the infants who died before 12 months will be unknown. Consequently, the large drop out means that the ultimate effectiveness of the programme cannot be determined from routine data and requires more intensive longitudinal follow up of individual mother-infant pairs.

Infant feeding experiences of HIV positive women (Paper II)

The findings from this study are presented in five key themes that characterised the infant feeding experiences of women with HIV. These women, who were mostly young and single, were struggling to make a decision about an infant feeding option in the context of a recent HIV positive diagnosis and new information about risks of HIV transmission to their infants. They faced an enormous dilemma between providing what they felt was the best infant feeding option and protecting their children from HIV. In this context with many uncertainties, the power and influence of health workers over infant feeding choices was found to have increased.

In the postpartum period, breastfeeding women face enormous pressure from family members and partners to introduce other fluids and foods from an early age. Fear of disclosure of HIV status and stigma has weakened the ability of HIV positive mothers to resist these entrenched family and community norms that encourage mixed feeding, despite attempts to provide plausible explanations for their non-normative feeding practices.

Women who chose to exclusively formula feed had difficulties accessing formula milk and 80% had run out of formula supplies at least once in the first 12 weeks. Inflexible clinic policies, power dynamics in relationships with health workers, and erratic supplies were contributing factors.

An HIV positive diagnosis led to social isolation and powerlessness for many women. Limited postpartum support worsened the situation and resulted in low levels of self-efficacy, particularly related to maintaining exclusive infant feeding practices.

The challenge of achieving exclusive infant feeding practices (Paper III)

The findings of this paper highlight the large drop-off from exclusive feeding similar to that found in quantitative studies. In this study just under half of the women who initiated breastfeeding maintained exclusivity to twelve weeks, and two thirds of the women who initiated formula feeding maintained exclusivity.

The longitudinal nature of the study allowed for key enabling factors at critical stages from the antenatal to postpartum period to be identified. During the antenatal stage, many of the women who subsequently maintained exclu-

sive breastfeeding, recalled having a positive counselling experience and receiving key information about HIV transmission which they could use to explain their infant feeding practices to family members.

During the early postnatal period women faced pressures in the hospital to change from their intended infant feeding practice, sometimes due to the fact that the health workers were unaware of the mother's HIV status. Between four and six weeks postpartum, breastfeeding women faced pressures from family members to introduce other fluids and foods. In some instances women had to spend time away from their infants and had little control over what their family would give their children. For women choosing to formula feed, almost a third had run out of formula at least once by this stage.

At twelve weeks postpartum, some of the women who had chosen to breast-feed had abruptly weaned their infants and switched to formula feeding. According to the South Africa PMTCT protocol, HIV positive women are advised to wean from exclusive breastfeeding between 3 and 4 months and this is considered optimal breastfeeding practice.

Key characteristics of women who achieved success in exclusivity were identified. Amongst women who maintained exclusive breastfeeding, a strong belief in the benefits of breastfeeding, the ability to resist pressure from family to introduce other fluids, and a supportive home environment that enabled women to stay with their infants was important. For women using formula milk, disclosure to a partner or family member reduced fears of stigmatisation; furthermore, having resources such as electricity, a kettle and flask made feeding at night easier. Cash resources to purchase formula milk when clinic supplies were unavailable were also important.

Determining appropriateness in the context of infant feeding choices (Paper IV)

This paper attempts to define the concept of appropriateness in the context of infant feeding choices of HIV positive mothers and to assess the effect of inappropriate choices on infant HIV-free survival. The results show that women choosing formula feeding and those choosing exclusive breastfeeding were similar in terms of basic characteristics and home environments. Most women had received antenatal infant feeding counselling and two thirds had four or more antenatal visits; however, despite the counselling received, the home circumstances of these women did not appear to influence their infant feeding choices.

In order to define the concept of appropriateness as it applies to the WHO/UNICEF infant feeding recommendations, the following criteria were identified: piped water, electricity, gas or paraffin as a source of fuel, access to a fridge, household income, and HIV status disclosure.

These criteria were assessed individually and then in scores in regression models to determine predictors of HIV-free survival and formula adherence amongst women intending to formula feed. The score with piped water, electricity, gas or paraffin as a source of fuel and HIV disclosure was found to be the most predictive of HIV-free survival and adherence amongst women choosing to formula fed and was therefore used as the definition of appropriateness for further analysis.

A key finding of this analysis was that according to these defined criteria of appropriateness, over two thirds (67.4%) of women intending to formula feed made an inappropriate choice and just under a third (30.5%) of women who intended to breastfeed made an inappropriate choice.

The main finding from this analysis that has relevance for infant feeding policy is that infants of women who were classified as inappropriate formula feeders had a 3 times greater risk of HIV transmission or death. Similarly, infants of women who were classified as inappropriate breastfeeders also had a greater risk of HIV transmission or death (HR 2.72; 95% CI 1.38 – 5.35) compared to appropriate formula feeders. The risk of HIV transmission or death as compared to appropriate formula feeding was similar in the appropriate and inappropriate breastfeeding groups (HR 2.74 vs. 2.72), suggesting a consistent risk for breastfeeding regardless of individual and household resources.

Summary of findings

The findings of the studies in this thesis provide some evidence of the challenges of moving from efficacy to effectiveness in public health interventions. Paper I highlights the low coverage of this intervention under operational conditions and identifies some of the health systems constraints to optimal effectiveness. This evaluation also drew attention to the issue of infant feeding choices and emerging problems with the provision of free formula milk. The infant feeding issues were explored in further depth in the subsequent three papers. Paper II describes the experiences of HIV positive women in making and implementing infant feeding decisions and the various influences and pressures that they face. The influence of HIV on infant feeding in general is a key finding from this research which helps to explain the

difficulties in implementing infant feeding recommendations for HIV positive women. Paper III provides unique findings relating to maintaining exclusivity in infant feeding and highlights the importance of good quality counselling, support and disclosure. The socio-economic constraints to ensuring exclusive formula feeding were also identified and led to further exploration of the concept of appropriateness in infant feeding choices in paper IV. The final paper attempts to provide practical guidance to counsellors in assisting women to make appropriate infant feeding choices. The findings highlight the high levels of inappropriate choices being made in both directions, under routine conditions with poor quality counselling. Most importantly, the results show the dangers of formula usage under unsafe conditions. HIV and infant feeding is a critical public health issue that needs to be addressed within a broad framework of optimising child survival.

Discussion

General overview

The research presented in this thesis was undertaken to provide an assessment of the key operational challenges in the implementation of the PMTCT programme in South Africa. One of the greatest challenges in the prevention of mother to child transmission is achieving safe infant feeding practices to reduce postnatal HIV transmission. The first paper in this thesis highlights the low uptake and coverage of PMTCT interventions and the high rates of intentions to formula feed amongst HIV positive women, particularly in rural areas. The second paper describes the challenges faced by HIV positive women when making an infant feeding decision and attempting to implement it in an environment with high levels of stigma and low levels of HIV status disclosure. The third paper explores the infant feeding experiences of HIV positive women at critical stages in the early postnatal period and identifies key characteristics of women that achieved some success in maintaining exclusive infant feeding. The fourth paper addresses the question of how to define appropriateness with regard to infant feeding choices. The results show that women's home circumstances do not appear to influence their infant feeding decisions and that inappropriate infant feeding decisions are being made in both directions. Meeting criteria for appropriate choice impacted on the HIV-free survival of infants and suggests that counselling needs to take into consideration women's home circumstances when advising about infant feeding options. These findings, gathered from operational settings, provide important insights into a critical child health problem.

Methodological considerations

Paper I used routine health service data to evaluate a particular health system intervention, namely the PMTCT programme. There are limitations with using routine data for research purposes due to the fact that it is collected by health workers rather than independent researchers and could be incomplete or contain inaccuracies[108]. Therefore, a limitation of using this data is that the interpretations of the indicators are only as good as the data which are collected at facility level and collated at a district level. However, one of the anticipated benefits of assessing routine data in this manner is to make the

data more visible; to put the data under the spotlight in order to highlight problem areas so as to make future monitoring and evaluation more meaningful.

The use of routine data also brings to the fore the stark differences between efficacy and effectiveness of health service interventions. Moving from efficacy to effectiveness requires translating the capacity to reduce the problem in ideal conditions, into a fully effective, efficient and financially sustainable programme. To be effective a programme has to fulfill the following conditions[89]:

- Availability of key resources e.g. an uninterrupted supply of HIV testing kits, nevirapine and formula milk.
- Physical and financial accessibility e.g. women need to be able to afford to access the service.
- Service utilisation e.g. if use of antenatal services is low few women will benefit from HIV counselling and testing.
- Continuity of care e.g. provision of ongoing care during the postnatal period to women and their infants.
- Quality e.g. high quality compassionate and confidential counselling.

The indicators assessed during the PMTCT evaluation have highlighted key bottle-necks to programme effectiveness in many of the above areas and they provide a baseline from which to measure the impact of improvements in programme functioning.

A further limitation of using health services data for programme evaluation is that it only captures individuals attending health services, thus it does not give a complete picture of the full population coverage or of missed opportunities. A population-based survey would be a better approach for assessing full programme coverage but this might be better suited to a more established programme rather than a new programme. Population-based surveys are also subject to the problem of non-response bias which needs to be taken into consideration when using this approach.

The three sites where the Good Start study was undertaken were purposively selected and the infrastructural conditions differed greatly between them. They are however, representative of the main types of settings in South Africa, namely urban, peri-urban and rural. Generalisability or transferability in the case of the qualitative studies should be done with caution and limited to similar settings with similar HIV prevalence rates.

The criteria for appropriateness used in the analysis in Paper IV (piped water, fuel and HIV disclosure) should account for most of the infrastructural differences between sites, and allow for the sites to be pooled for this analysis; however, some residual confounding of the HIV transmission/death outcome as a result of not adjusting for site is possible.

The differences in appropriateness of choices between sites, especially the fact that only three women in the rural site who intended to formula feed met the three criteria, highlights the fact that not meeting the criteria can potentially result in different risks depending on the context in which women live. For women in Paarl and Umlazi who did not meet the criteria for piped water in their house or yard, all were able to access a public tap whereas for women in Rietvlei, not meeting the criteria meant accessing water from a river or well. All of the women who chose to formula feed in Paarl and Umlazi met the defined criteria for fuel, while women in Rietvlei who did not have electricity, gas or paraffin for cooking were using wood. The inability to present site specific estimates for the ever breastfeeding outcome is a limitation. Further operational research is needed with larger sample sizes, particularly in rural areas, to determine the risks of inappropriate choices in the different contexts found in African and other developing countries.

Paper IV used an intention to treat approach to determine the outcomes of infants based on their mother's feeding intentions and certain personal and environmental criteria. The actual feeding practices of these women did change over time from their intentions and the majority of women were practising mixed feeding. Adherence to exclusive formula feeding was taken into account as one of the outcomes and is a measure of actual feeding practices.

A potential limitation of the Good Start study was that the first test to determine infant HIV infection was at 3-4 weeks. This time point was chosen rather than 6 weeks, as has previously been used in similar studies, in order to separate as much as possible intrapartum transmission from postnatal transmission. A concern in regard to testing at 3-4 weeks is that we may have classified some cases of intrapartum HIV transmission as postnatal transmission because the testing was done so soon after delivery. However, a meta-analysis of published data from 271 infected children indicated that HIV DNA PCR was highly sensitive and that by 14 days after infection 93% (95% CI: 76% - 97%) of infected children were positive by PCR[109].

Reducing missed opportunities in PMTCT programmes

In the absence of interventions to prevent transmission, about 15-25% of infants of HIV-infected women will be infected during pregnancy or delivery, and an additional 5-20% may become infected during breastfeeding[3]. There is now overwhelming evidence for the efficacy of short course ARVs for prevention of mother to child transmission. For example, short course monotherapy regimes with either zidovudine from 36 weeks gestation or nevirapine (NVP) given as a single dose to mother during labour and once to the baby reduces transmission at six weeks by as much 50%[11,16].

Despite the introduction of PMTCT programmes and the availability of efficacious drug regimens, mortality in children, largely due to HIV, is rising in many of the worst affected countries[84]. This is due to the fact that less than 10% of pregnant women worldwide have access to interventions to prevent transmission of HIV to their infants. The majority of women receiving these interventions are in high-income countries, where HIV infection in infants and young children has been virtually eliminated with near zero transmission of infection. In contrast, in most sub-Saharan African countries where the epidemic is most intense, less than 5% of pregnant women receive any interventions to reduce transmission of the infection to their babies[110]. This research and others have found that even where PMTCT services are available in developing country settings with underlying weak health systems, the uptake has been low and is further reduced by large drop-offs in key programme steps.

In South Africa the PMTCT programme has been expanded across the country and is available in over 70% of facilities. Over 95% of pregnant women attend antenatal care (ANC) with an average of 4 visits per pregnancy [111]; however HIV testing of pregnant women remains low at 50%, and coverage of nevirapine amongst women identified to be HIV positive continues to be sub-optimal at 45%, [108] four years after implementation of the PMTCT programme. One reason for this low uptake is the fact that HIV counselling and testing has not been integrated as a routine component of antenatal care. The low uptake of PMTCT services in settings with a high HIV prevalence requires new approaches to HIV testing to prevent missed opportunities for access to care and treatment.

'Opt-out' testing models have recently been evaluated in several other countries in sub-Saharan Africa with encouraging results. An 'opt-out' approach to testing means that HIV testing is a recommended routine for all pregnant women but they have the right to refuse if they wish[112].

There have been some concerns that routine testing will discourage women from attending antenatal care; however, a study in Zimbabwe[113] that assessed the acceptability of routine testing found that 79% of women would accept HIV testing if 'opt-out' testing were introduced. In Uganda[114], an 'opt-out' testing policy was introduced at a rural hospital seven months following implementation of the PMTCT programme. The percentage of women discharged from the labour ward with documented HIV status increased from 39% to 88%. Results from paper I also show that where HIV testing is considered a routine part of antenatal care, as in the KwaZulu-Natal province of South Africa, higher rates of HIV testing uptake can be achieved.

In Botswana, PMTCT interventions have been offered in all antenatal clinics since 2001. HIV testing was performed after individual pre-test counselling with patients choosing whether to be tested ('opt-in'). In 2003, only 52% of pregnant women receiving antenatal care knew their HIV status. In 2004, to increase use of PMTCT and ARV programmes, Botswana introduced routine, non-compulsory ('opt-out') HIV testing in antenatal and other health care settings. To assess the early impact of routine testing on HIV test acceptance, the CDC Global AIDS Program evaluated routine antenatal testing at four clinics in Francistown[115]. Results showed that HIV testing increased from 75% to 91% following the change in strategy.

Changes to the testing policy in Botswana had an impact at an international level with WHO/UNAIDS[116] changing their policy in the same year, and recommending routine HIV testing in certain circumstances including pregnancy, in patients presenting with sexually transmitted infections and asymptomatic patients presenting to clinics where ARV treatment is available.

HIV testing is the entry point into the PMTCT programme and is the most critical stage to ensure optimal coverage. This research found that low coverage also occurred in subsequent stages of the programme, particularly uptake of nevirapine and mother-infant follow up. Poor postnatal follow up means that infants exposed to HIV, who are a high risk group, do not receive appropriate medical care that would enable monitoring of infant feeding practices and general health status.

The findings in relation to the infant feeding intentions of HIV positive women are cause for concern and suggest that counselling of women does not take home circumstances into account. It also prompts a re-consideration of the policy to provide free formula milk in South Africa with the understanding that in some settings, with the current poor quality of counselling[117], it could be reinforcing inappropriate infant feeding choices.

Achieving appropriate infant feeding practices

Of all the challenges in reducing mother to child transmission, the one most poorly met thus far is to find ways to make feeding safer for infants of HIV positive mothers. Improving infant feeding practices will require at the very least good quality counselling in all health facilities, ideally backed up by similar actions and messages both at the national policy level and at the community level.

This research and others have found that the counselling of mothers on infant feeding practices is sub-optimal. Results from paper I show a high rate of intentions to formula feed in rural areas where access to safe water and sustainable sources of fuel is difficult. A UNICEF review[118] of the experiences with free formula milk also found very high uptake of formula amongst HIV positive women with rates around 60% in Uganda and Zambia and 87% in Rwanda.

The qualitative studies reported in this thesis confirm that confusion and uncertainty regarding the competing risks of HIV transmission through breastfeeding and mortality caused by not breastfeeding increases women's reliance on the advice provided by health workers, who in the context of HIV have a greater influence on mothers' feeding decisions.

It is not surprising that health workers are generally unsure of how to guide HIV positive mothers in making feeding choices. Providing full information to achieve empowered decision-making in this context requires skilled counselling and additional time, which is often not available in busy health facilities. Poor quality infant feeding counselling has also been found in other studies. For example one observational study[117] across three facilities in SA found that only 9% of women were asked about access to clean water, fuel and a fridge before deciding upon a feeding option. For women who opted to formula feed there was no discussion about how the mother would explain to others the lack of breastfeeding. For women who chose to breastfeed, only 17% were asked if they understood the practice of exclusive breastfeeding and no one was asked if they thought it was feasible.

Consequently, as was found in paper IV, many HIV positive mothers are making inappropriate choices, such as choosing to avoid breastfeeding when the safety of replacement feeding cannot be assured and choosing to breastfeed when conditions for safe formula feeding are present.

A key finding of this research is the limited postpartum support available to HIV positive women and the enormous pressures they face from family members to introduce other liquids and foods from an early stage. Social

pressures experienced by HIV positive women have been reported in an ethnographic study in a rural area of South Africa[119]. In this study, social stigma was a strong influence on HIV positive women's feeding choices with some women expressing reluctance to opt for formula feeding in hospital to avoid disclosing their status to health workers.

The fact that neither exclusive breastfeeding nor exclusive formula feeding are normative practices within the South African context was also clearly evident in this research. Results from Paper III show that just under half of the women who initiated breastfeeding maintained exclusivity to twelve weeks. Low rates of exclusive feeding amongst HIV positive women have been reported from other studies. In Abidjan, Ivory Coast[120] women choosing to breastfeed were counselled to exclusively breastfeed for three months and then rapidly wean to replacement feeding. Results showed that the probability of practising exclusive breastfeeding from birth was 18% and 10% at 1 and 3 months of age respectively. Similar low rates of exclusive breastfeeding have been reported in Kenya[121], Tanzania and Uganda[122]. Whilst evidence exists on rates of exclusive breastfeeding, very little qualitative research has been undertaken to describe the socio-cultural influences on infant feeding practices and the enabling factors identified in women who are able to maintain exclusivity. The qualitative results in Papers II and III therefore provide a valuable contribution to the literature by exploring these issues in greater depth.

This research has also identified challenges associated with the use of formula milk in resource poor settings. There are few published reports of experiences with formula milk in PMTCT settings other than clinical trials. Results from this research highlight that even in the context of free formula milk provision, women bear other costs in terms of travel to health facilities to collect supplies, purchasing of cups or bottles and materials to clean them and a flask to store boiled water for easier night feeding. Unreliable formula supply at health facilities was also identified in both qualitative studies and is a reality of weak health systems with poor supply mechanisms. These very practical constraints to ensuring exclusive formula feeding have not been previously described and have implications for the ability of women to practise safe formula feeding.

The difficulties faced by HIV positive women in carrying out infant feeding recommendations highlights the importance of ongoing community-based support and strategies to change community norms about infant feeding and to reduce stigma. On an individual level, peer counselling has been found to be a cost-effective approach for changing behaviour. Several studies have also examined its impact on breastfeeding behaviour. Recent studies have shown that intensive counselling and support can increase the proportion of

women who breastfeed exclusively, although there are considerable variations on the type of counselling support provided. Haider et al[123] in Bangladesh in a trial randomised by community, Morrow et al[124] and Agrasada et al.[125] in trials randomised at the individual level, in Mexico and the Philippines, obtained substantial increases in exclusive breastfeeding with community-based counselling and support.

This research has highlighted the dynamic nature of infant feeding during the critical early postpartum period. Whilst antenatal counselling needs to prepare women for common challenges during the postpartum period, community home-based support is also critical to assist women with disclosure to their family members and with increasing levels of confidence and self-efficacy which could lead to a more sustained improvement in exclusive feeding practices.

On a policy level, this research has found that the translation of the WHO/UNICEF guidelines into operational settings is a challenge for health workers and counsellors as there is little guidance on what the terms 'acceptable', 'sustainable', 'safe' and 'feasible' mean in practice. The research presented in Paper IV is the first attempt that we know of to provide a practical definition for the WHO/UNICEF infant feeding guidelines for HIV positive women. Using three criteria of appropriateness for formula feeding, namely piped water, electricity, gas or paraffin for cooking fuel, and disclosure of HIV status, we found inappropriate choices being made in both directions. Almost a third of women who chose to breastfeed did have these three basic conditions suitable for formula use, and two thirds of women who chose to formula feed did not have these conditions for safe formula use. Both of these groups had a more than two and a half fold increased risk of HIV transmission or death compared to appropriate formula feeders.

Excess mortality risks from formula feeding have been described in research settings in Africa. In a cohort study of HIV infected infants in Nairobi[67], formula feeding was found to be a predictor of early infant mortality. The recently completed MASHI study[126] undertaken in Botswana also found increased mortality amongst infants who were formula fed in the context of free formula milk being provided. The 18 month HIV-free survival was similar in the breastfeeding and formula feeding groups suggesting that the gains in preventing postnatal HIV transmission from formula feeding were lost due to increased mortality from other causes.

Given the increasing burden of HIV with concomitant rising infant mortality rates, governments in high burden countries need to strive to improve HIV positive women's access to basic resources that would allow for appropriate formula feeding. This research suggests that infant HIV free survival could

be improved if HIV positive women who choose to formula feed have at least three criteria (piped water, fuel and have disclosed their HIV status) and that without these criteria a choice to exclusively breastfeed would be more appropriate. Greater investment is therefore needed in supporting the role of infant feeding counsellors through simplified, structured counselling tools to promote adequate individual assessment to determine appropriate infant feeding choices, with the ultimate aim of reducing avoidable infections and mortality.

Many countries in sub-Saharan Africa are experiencing increases in child mortality largely as a result of HIV. Strategies to reduce HIV transmission through breastfeeding need to take into consideration the context within which infant feeding decisions are made and the multiple influences on feeding practices. This is important to ensure that appropriate infant feeding decisions are made and supported.

The public health imperative to address mother to child transmission of HIV

The transmission of HIV through breastmilk is a critical public health problem that is complicated by the fact that breastfeeding is a cultural norm and that replacement feeding is known to lead to increased mortality risks, particularly in resource poor settings[37]. In attempting to address this issue there are several imperatives that require public health action. The first of these is that the promotion of exclusive breastfeeding as the optimal method of infant feeding for the general population should receive additional support both at the facility level, through initiatives such as the BFHI, and at the community level through information, education and communication campaigns and community-based health workers. This is especially important given the increasing evidence to support a lower HIV transmission risk through exclusive breastfeeding compared with mixed feeding. Promotion of exclusive breastfeeding in the general population and for HIV positive women in settings where replacement feeding is difficult to achieve, is one strategy to reduce postnatal HIV transmission whilst supporting exclusive breastfeeding as a infant feeding norm and strategy to improve child health outcomes for the majority of women who are HIV uninfected or do not know their HIV status.

The second imperative is to scale up access to HIV testing for pregnant women through approaches that incorporate testing as a routine component of antenatal care. This is vital to ensure that all pregnant women are aware of their HIV status and can access information to make appropriate infant feed-

ing choices and prophylaxis to reduce HIV transmission to their infants. The current coverage of PMTCT programmes in Africa is extremely low and this situation denies many women the opportunity to make decisions and implement behaviours that could minimize the risk of HIV transmission to their infants.

The third imperative is to invest in the training, supervision and support of infant feeding counsellors. This is critical to ensure that HIV positive women receive the required information to make truly informed choices. In addition, counsellors should be provided with job aids to guide them through a structured process and to ensure that all necessary topics are covered. Job aids have gained status in health promotion as a cost effective way to improve the performance of service providers such as nurses, and are often defined as tools that reduce guesswork, minimise reliance on memory, and promote compliance with standards. Decision aids, or client oriented job aids, are often used to guide patients through a series of steps, giving them personalised information and/or helping them clarify their values and risk exposure in the context of health related options[127]. Job aids should include practical assessment scores to determine appropriateness of formula milk selection based on research such as that described in this thesis.

The fourth imperative is for support to HIV positive women to extend into the postpartum period and for this to be integrated into routine primary level services. This research has highlighted the isolation experienced by HIV positive women and the limited support available to them following delivery. HIV positive women need support to assist with disclosure of their status to partners and family members, support to maintain exclusive infant feeding in the face of family and community pressures to mix feed, and ongoing care and support to monitor their disease progression and the health status of their infants. Strategies to address this should include links between PMTCT programmes and community-based support structures as well as improved strategies to identify HIV positive women through routine primary level services. HIV positive women and their infants are at high risk for morbidity and mortality due to HIV disease progression, opportunistic infections, and malnutrition, and regular follow up care is essential.

HIV poses an enormous threat to maternal and child health, with women bearing the greatest burden of infection in sub-Saharan Africa. Whilst drugs can contribute substantially to reducing early transmission, the greatest challenge remains to reduce postnatal transmission through breastfeeding whilst maintaining a focus on child survival. Addressing this challenge is critical to ensure that global commitments such as the millennium development goals are achieved.

Conclusions and implications

Enormous advances have been made in reducing in-utero and intrapartum HIV transmission from mothers to infants. However, relatively little progress has been made with reducing postnatal HIV transmission through breastfeeding. This is a significant challenge for health policy makers and health care workers who have to balance the desire to reduce HIV transmission in infants with the need to increase overall child survival. Implementation of the WHO/UNICEF guidelines[75]: "when replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended" is difficult for health workers who have to define terms such as acceptable and feasible on an operational level when counselling women.

This research has attempted to provide greater understanding of the challenges facing HIV positive women implementing infant feeding recommendations in real life settings. The findings have serious implications for the effectiveness of PMTCT programmes and highlight the enormous challenge of achieving safe infant feeding practices within contexts of high levels of stigma, inadequate counselling, limited postpartum support and community mixed feeding norms. Given these constraints, interventions to optimise infant feeding are more critical then ever for improving child survival.

This research has identified several strategies to improve optimal infant feeding practices amongst HIV positive women, namely improving the quality of antenatal counselling through clear messages and individual assessments of home circumstances, increasing HIV disclosure, and ensuring ongoing support to women during the postpartum period. These findings can guide local policy development on infant feeding recommendations. They can also inform the development of interventions to improve infant-feeding counselling and postpartum support to HIV positive women.

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