Current Knowledge and Future Research on Infant Feeding in the Context of HIV: Basic, Clinical, Behavioral, and Programmatic Perspectives[1,2]

Sera L. Young,[3,4]* Mduduzi N. N. Mbuya,[5] Caroline J. Chantry,[6] Eveline P. Geubbels,[7] Kiersten Israel-Ballard,[8] Deborah Cohan,[3] Stephen A. Vosti,[9] and Michael C. Latham[4]

[3]Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, CA 94110; [4]Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853; [5]Zvitambo Project, Harare, Zimbabwe; [6]Department of Pediatrics, University of California Davis Medical Center, Sacramento, CA, 95817; [7]Ifakara Health Institute, Dar es Salaam, Tanzania; [8]PATH, Seattle, WA, 98109; and [9]Department of Agricultural and Resource Economics, University of California, Davis, CA 95616

ABSTRACT

In 2008, between 129,000 and 194,000 of the 430,000 pediatric HIV infections worldwide were attributable to breastfeeding. Yet in many settings, the health, economic, and social consequences of not breastfeeding would have dire consequences for many more children. In the first part of this review we provide an overview of current knowledge about infant feeding in the context of HIV. Namely, we describe the benefits and risks of breastmilk, the evolution of recommended infant feeding modalities in high-income and low-income countries in the last two decades, and contextualize the recently revised guidelines for infant feeding in the context of HIV current knowledge. In the second section, we suggest areas for future research on the postnatal prevention of mother-to-child transmission of HIV (PMTCT) in developing and industrialized countries. We suggest two shifts in perspective. The first is to evaluate PMTCT interventions more holistically, to include the psychosocial and economic consequences as well as the biomedical ones. The second shift in perspective should be one that contextualizes postnatal PMTCT efforts in the cascade of maternal health services. We conclude by discussing basic, clinical, behavioral, and programmatic research questions pertaining to a number of PMTCT efforts, including extended postnatal ARV prophylaxis, exclusive breastfeeding promotion, counseling, breast milk pasteurization, breast milk banking, novel techniques for making breast milk safer, and optimal breastfeeding practices. We believe the research efforts outlined here will maximize the number of healthy, thriving, HIV-free children around the world. *Adv. Nutr. 2: 225–243, 2011.*

Introduction

Breastfeeding is a pillar of child survival; it reduces morbidity and mortality in children worldwide (1). However, since the early 1980s when it was discovered that HIV could be transmitted to infants through human milk, the healthfulness of breastfeeding has been questioned, because of the risk of mother-to-child transmission of HIV (MTCT).[10] [A note on terminology: The International AIDS Society has been advised, in particular by networks of women living with HIV, that the term "prevention of vertical transmission" should be used instead of "preventing mother-to-child transmission (PMTCT)" (3). The concern is that "PMTCT" can sound stigmatizing in that it assigns blame to the mother. When the term PMTCT is used by UN agencies, it is understood to describe 4 pillars of preventing vertical transmission (3). In this paper, we use the terms PMTCT and MTCT in this broad sense of prevention and without any implication of culpability]. Indeed, scientists, policymakers, and program managers have spent the last several decades struggling to characterize the proportion of risk of MTCT attributable to breast milk and to develop appropriate and feasible guidelines on infant feeding in settings where HIV is present (4,5). For this reason, it has been said that the HIV pandemic has threatened to "knock breastfeeding off its pedestal as a pillar of child survival" (6).

The aim of this paper is to present an overview of current knowledge of infant feeding in the context of HIV and to

[1] Supported by NIH/National Institutes of Allergies and Infectious Diseases 5T32AI065388-04 to S.L.Y. M.N.N.M. was supported by UK Department for International Development/Zimbabwe grant no. AG 201 854-101.

[2] Author disclosures: S. L. Young, M. N. N. Mbuya, C. J. Chantry, E. P. Geubbels, K. Israel-Ballard, D. Cohan, S. A. Vosti, and M. C. Latham, no conflicts of interest.

[10] Abbreviations used: AFASS, acceptable, feasible, affordable, sustainable, and safe; ARV, antiretroviral; EBF, exclusive breastfeeding, exclusively breastfed; HAART, highly activated antiretroviral therapy; MTCT, mother-to-child transmission of HIV; PMTCT, prevention of mother-to-child transmission of HIV; sdNVP, single-dose nevirapine.

* To whom correspondence should be addressed. E-mail: sly3@cornell.edu.

highlight areas in which research is most urgently needed. Such a review is timely given the WHO's recent revision of the guidelines on infant feeding and HIV (7). We first present a discussion of the health benefits and risks of breast milk, followed by a short, chronological review of the history of infant feeding modalities that have been recommended in the context of HIV in the past several decades. We then contextualize the 2010 recommendations by discussing biomedical, social, and economic issues surrounding their current implementation. In the second part of this paper, we suggest areas for future research in infant feeding and related prevention of MTCT (PMTCT), recommendations that we think could have the biggest effect on improving the health of HIV-exposed infants. Basic, clinical, behavioral, and programmatic research questions are outlined for each area. It should not be forgotten, however, that infant feeding behaviors are only one aspect of vertical transmission and that the prevention of vertical transmission, in turn, is only 1 of the 4 components of the WHO's comprehensive strategic approach to the prevention of HIV infection in infants and young children (8). Eradication of vertical transmission of HIV must include the prevention of infection among women of reproductive age, prevention of unintended pregnancies among HIV-infected women, and provision of adequate treatment, care, and support to HIV-infected women and their families. In this review, however, we limit our discussion to PMTCT issues, with a particular emphasis on postnatal PMTCT strategies.

Current knowledge and recommendations

Risks and benefits of breast milk

Beneficial components of human milk. The short-term and long-term benefits of breastfeeding have been well documented for both the mother and her infant. In the short-term, breastfeeding decreases postpartum blood loss and promotes bonding between mother and child (6,9). Longer term, for women, it is associated with reduction in risks of breast and ovarian cancers, retained gestational weight gain, type 2 diabetes, myocardial infarction, and metabolic syndrome as well as delayed resumption of menses (lactational amenorrhea), which is important for birth spacing (9–11). For infants, breastfeeding is unequalled in its role in reducing morbidities and improving child growth, development, and survival in developing (12–14) and industrialized (10,15) countries. In addition to the well-established role of breast milk in preventing infectious diseases in infants, it reduces the risks of childhood obesity, type 1 and type 2 diabetes, leukemia, and sudden infant death syndrome (15).

The protective effects of human milk are due in part to its optimal nutritional composition (16). Breast milk typically provides most of the protein and energy needs of infants even in the latter part of the first year of life as well as a majority of several critical micronutrients such as vitamins A, C, and B-12 and folate and copper (17). These nutrients are not easily replaced by complementary feeding in the best of circumstances and less so in low-income populations (18).

Human milk is also beneficial because of its important and myriad immunological and antiinfective factors (19). They include, among many others, proteins with antimicrobial properties such as secretory IgA, lysozyme, and lactoferrin; lactoferrin provides immune-modulating properties in addition to its better-known antiinfective properties. Oligosaccharides in breast milk inhibit bacterial adhesion, further protecting against pathogens, and white blood cells provide passive immune protection. Nucleotides and cytokines also assist with T-cell maturation and immune system modulation, evidenced by, e.g., the more robust immune response that breast-fed infants exhibit after vaccination (20). Breast milk also promotes healthful gastrointestinal microbiota (21,22).

Health risks of breast milk: HIV transmission. Because lactation is a metabolically expensive process, there was initial concern that breastfeeding could be deleterious to HIV-infected mothers' health (23). Several studies have since been unable to demonstrate any adverse consequences for maternal health (24–27). Furthermore, a meta-analysis conducted by the Breastfeeding and HIV International Transmission Study Group indicated that mothers' mortality during the 18-mo period after delivery did not differ significantly according to children's feeding modality (ever vs. never breast-fed) (28). The apparent mortality and other health risks in HIV-infected breastfeeding women were explained by confounding. That is, HIV-infected women with lower CD4 counts were less likely to initiate breastfeeding and healthier women were able to breastfeed longer. However, because greater fat loss (29) and micronutrient deficiencies (30) have been observed during lactation among HIV-infected compared to uninfected women, some concerns remain about potentially unmet nutritional requirements of lactating HIV-infected women. However, in general, the major risk of breastfeeding is vertical transmission of HIV and not adverse health effects for the mother.

In 2008, ~430,000 (240,000–610,000) children became infected with HIV; 90% of these were due to vertical transmission (31). Vertical transmission can take place during pregnancy, labor, and delivery, as well as postpartum, through breastfeeding. The risk of transmission depends on many factors, including the timing of maternal infection, maternal viral load, immune function, nutritional status of both the woman and baby, antiretroviral (ARV) use, breast health (nipple pathology, mastitis), type of breastfeeding (exclusive, mixed, or replacement feeding) (**Table 1**), duration of any breastfeeding, and presence of oral lesions in the infant (32–37).

In the absence of interventions to prevent transmission, 5–10% of infants born to HIV-positive mothers become infected with HIV during pregnancy and 10–20% become infected around the time of delivery (31,33). Estimates of the risks of HIV infection via breast milk have varied due to the multifactorial nature of risk of transmission, including the difficulty of quantifying the instantaneous hazard rate of infection (38). In 1999, De Cock et al. (33) calculated that between 5 and 20% of infants would become infected if breastfed beyond 18 mo. A meta-analysis by the Breastfeeding

Table 1. Explanation of use of infant feeding terms[1]

Infant feeding terms
EBF is defined as the receipt of only breast milk (either directly from the breast or expressed); only oral rehydration solution, drops, and syrups (vitamins, minerals, or medicines) are permitted (207).
Mixed feeding is the receipt of both breast milk and other solids or liquids, including water and nonhuman milks, before 6 mo of age (208). Mixed feeding in the setting of HIV is often used interchangeably with non-EBF and even complementary feeding.
Complementary feeding is used prescriptively to mean the appropriate addition of other solids, semisolids, and liquids to a breastfeeding infant's diet at ~6 mo of age and thereafter (206).
Replacement feeding indicates that the infant receives no breast milk but is fed with formula or other breast milk substitutes (56).
"Human milk" is a more specific term than breast milk, as milk from all species is produced by the breast (3). We use "human milk" and "breast milk" interchangeably, noting that "human milk" is more accurate whereas "breast milk" is more conventional.

[1] There are many terms used in the field of infant feeding, some of which have been used interchangeably or inconsistently (209). We have made explicit our use of the most common infant feeding terms in this manuscript; however, debate remains about what terms should and do mean.

and HIV International Transmission Study Group found that 42% of infections were attributable to breast milk (32). Kourtis et al. (39) calculated that without any intervention, ~6% of HIV-negative but exposed infants would become infected via breastfeeding if they were exclusively breastfed (EBF) for 6 mo and rapidly weaned, 11% would become infected if they were mixed fed for 6 mo then rapidly weaned, and 15% of infants would become infected if they were breastfed for 2 y.

With currently implemented prenatal and perinatal interventions, one-third to one-half of all MTCT is estimated to occur in the postpartum period, i.e. through breastfeeding (40). Although the proportion of postnatal transmission attributable to breastfeeding is not known exactly, it is likely steadily increasing as prenatal and peripartum ARV prophylaxis continues to have increased availability and use in sub-Saharan Africa (39,41).

Health risks of not breastfeeding: increased morbidity and mortality. In general pediatric populations, i.e. those not specifically HIV exposed, replacement of breastfeeding with formula milks, animal milks, and other foods is attended by increased mortality, morbidity, poor growth, and development in both developing (1,14) and industrialized (42,43) countries. Pooled analyses of data from developing countries demonstrated that breastfeeding was strongly protective against mortality from infectious disease (13). The OR of survival among breast-fed infants 0–1 mo old was 5.8 (CI 3.4–9.8), 4.1 for 2–3 mo old (CI 2.7–6.4), 2.5 for 4–5 mo (CI 1.6–3.9), and 1.8 for 6–8 mo (CI 1.2–2.8). For second-year deaths, the pooled OR ranged between 1.6 and 2.1. The protective effects of breastfeeding are most striking in developing countries, but they are clear in industrialized settings as well. Pooled analyses of mortality by breastfeeding modality in industrialized countries is not available, but postneonatal infant mortality rates in the United States were 21% lower among ever breast-fed infants (44).

Specifically among HIV-exposed children, multiple studies in low-income settings have documented increased morbidity and mortality associated with earlier cessation of breastfeeding compared to continued breastfeeding. In Uganda, a mean duration of any breastfeeding of 4.0 mo compared to 9.3 mo in a later trial was associated with higher rates of severe gastroenteritis (8.0 vs. 3.1 episodes/1000 child-months; $P < 0.001$) (45). Similarly, cessation of breastfeeding by 6 mo of age compared to prolonged breastfeeding in Malawi resulted in greater rates of hospitalization for gastroenteritis (2.9 vs. 0.1% at 7–9 mo and 1.6 vs. 0.2% at 10–12 mo; $P < 0.001$) and higher gastroenteritis related mortality (19 vs. 7/1000 infants at 9 mo and 24 vs. 12/1000 infants at 12 mo; $P = 0.0002$) (46). In Zambia, a significantly greater decrease in weight-for-age Z-scores between 4 and 16 mo was reported among HIV-exposed, uninfected infants who stopped breastfeeding at 4 mo compared to those who continued (47). In Zimbabwe, infants whose mothers opted to cease breastfeeding at 9 mo after receipt of an HIV-PCR-negative result were fed grossly inadequate diets compared to those who continued to receive breast milk (48). During an outbreak of diarrhea in Botswana in 2006, HIV-exposed infants who were receiving formula provided free of charge were at much greater risk of death than their breast-fed peers (49,50). In summary, not breastfeeding increases morbidity and mortality in HIV-exposed and unexposed children in developing and industrialized countries.

HIV-free survival. Given that on one hand, breast milk can be a vector for HIV, but on the other hand, infants, particularly those in low-income settings, are at increased risk of malnutrition, diarrhea, acute respiratory infection, and death if they are not breastfed, any treatment of the issue of infant feeding and HIV must necessarily address the concept of balanced risks. The concept of HIV-free survival is one that captures the risks of both outcomes and is therefore a more balanced metric of success (safety) of an infant feeding modality. In using this concept, it is important to emphasize, however, that it reflects the desired outcome of a baby staying HIV-negative and alive. It does not imply that an HIV infection is equivalent to a death (38). One disadvantage to using this measurement is that it can "stack the deck in favor of interventions that prevent HIV transmission and neglect the range of other nonfatal, but potentially serious, adverse outcomes associated with limiting breastfeeding" (38). Studies typically report HIV-free survival to 18 mo (7; Annex 2), with some reporting up to 24 mo of age (51).

Because of the limitations of the concept of HIV-free survival, the health of a population might better be measured in terms of HIV-free "thrival" (survival + thriving), which is a more comprehensive metric, because it captures not just if the child is alive, but how well she or he is doing. In this context, thriving could be operationalized as normal growth, i.e. no stunting or wasting. Thus, thrival measures some of the outcomes that may be associated with recurrent illnesses or malnutrition arising from early cessation of breastfeeding and is therefore not biased toward interventions that simply

prevent death or HIV infection, as is the concept "HIV-free survival".

Evolution of strategies for risk mitigation

Replacement feeding. The WHO has long championed the importance of breastfeeding. This is evidenced in numerous publications and consensus statements, e.g. the Innocenti Declaration, the Baby-Friendly Hospital Initiative, and the International Code of Marketing of Breastmilk Substitutes. In the early 1990s, great emphasis became placed on avoiding MTCT through breastfeeding. To that end, in 1998, WHO, UNICEF, and UNAIDS issued a series of documents stating that replacement-fed, HIV-exposed infants were less at risk of illness and death so long as they had "uninterrupted access to nutritionally adequate breast milk substitutes that are safely prepared and fed to them" (52). Although the importance of breastfeeding was underscored in the absence of satisfactory substitutes, these guidelines, together with the plans to conduct several trials of formula feeding among HIV-exposed infants, were perceived by many to be a major shift in WHO policy from the decades of promotion of "breast is best" (53,54).

The WHO introduced the acceptable, feasible, affordable, sustainable, and safe (AFASS) criteria into their infant feeding guidelines in 2001 (55). They recommended that all breastfeeding by HIV-infected mothers should be avoided when replacement feeding was considered to be AFASS. It was recommended that each mother, with appropriate counseling support, make the determination of whether the AFASS criteria were met (52). In the absence of AFASS, it was recommended that infants should be EBF "for the first months of life;" a time at which EBF or any breastfeeding should cease was not specified.

The 2010 recommendations did not use the AFASS language but instead defined in more detail the environmental (personal, household, and health service) conditions that make replacement feeding safer (7). They also shift decision-making away from counselors and mothers. They state that national health authorities should decide which infant feeding practice will be primarily promoted and supported by Maternal and Child Health services but that information about other practices should be made available.

Modified animal milk. At the time the 1998 recommendation was issued, the 2 main replacement milks were modified animal milks and commercial infant formula. Modified animal milk is typically powdered or fresh cow or buffalo milk to which water, sugar, and micronutrients are added (56). It is, however, no longer recommended for feeding infants < 6 mo because of insufficient macro- and micronutrient content, concerns about the safety of storage, and occult bleeding that nonhuman milks can cause (7,57). Indeed, data from the main study of replacement feeding with nonformula modified animal milks indicated that Indian infants who were primarily fed modified animal milks had a greatly increased rate of hospital admission than those who were breastfed, mainly due to gastroenteritis with dehydration (58).

Commercial infant formula. Commercial infant formula has been the most frequently discussed and provisioned replacement milk. It has been made available to HIV-positive mothers for free as part of government PMTCT policy [e.g. South Africa (59), Botswana (60)], through nongovernmental organizations [e.g. Partners in Health programs in Haiti, Rwanda, Lesotho; UNICEF in 8 African countries (61)] and as part of numerous research studies.

In industrialized countries, replacement feeding has been AFASS for most HIV-positive women, and it is now standard practice for women there to feed their infants formula. Indeed, in the United States, the CDC has recommended since 1985 that HIV-positive women not breastfeed (62), which they reiterated in 2010 (63). Replacement feeding, together with ARV medicines and other intensive obstetric prevention strategies for infected mothers, has undoubtedly contributed to the very low rates of PMTCT in high-income countries (64,65). Replacement feeding in low- and middle-income countries, however, has not yielded the same positive health outcomes as it has in high-income countries.

Indeed, replacement feeding ensures that HIV is not transmitted to the infant via breast milk and an initial study suggested that HIV-free survival was improved with replacement feeding (66). However, the analytical strategy was problematic, including the assignment of mixed feeders to the breastfeeding group (67,68) and the results have not been replicated since.

More recent data from 9 studies in sub-Saharan Africa suggest that reductions in HIV transmission achieved with formula feeding are offset by increases in HIV-unrelated mortality (Table 1 in 69). In short, current data suggests there is no net benefit of replacement feeding with formula to HIV-free survival in sub-Saharan Africa, even when formula is provided for free.

Furthermore, the promotion of replacement feeding can have negative health consequences for infants who are not at risk of vertical transmission. Because there is no (further) risk of vertical transmission, HIV-positive babies should not be fed replacement milks. However, the promotion of replacement feeding to HIV-positive mothers can result in HIV-infected infants not receiving breast milk (38). As for HIV-unexposed infants, the promotion of replacement feeding has led some women who do not know their status to opt not to breastfeed for fear of infecting their infant (70); this has been termed the spillover effect (71; M. Latham and P. Kisanga, unpublished data).

In addition to detrimental health consequences, replacement feeding has had negative economic, social, and reproductive consequences for some infants and mothers. A major burden of replacement feeding is the expense. In 2009, a 6-mo supply of formula had an estimated cost of $174; this figure does not include the cost of clean, safe water or the time to prepare it (7; Annex 8). This expense is beyond the reach of the many individuals and governments in the areas where the majority of MTCT occurs, namely sub-Saharan Africa.

The social consequences of replacement feeding have also been staggering. In places where breastfeeding is common

and expected, a woman's use of other feeding modalities frequently flags her as HIV-positive to both family members and the community at large (72–74). This can have serious consequences for the mother-infant dyad, e.g. divorce, ostracization, and abandonment of the child. All of these potential consequences, in turn, can dramatically change the economic calculus associated with decisions related to child feeding and care, e.g. ostracized women may lose traditional employment options or their asset bases and hence may choose not to participate in PMTCT programs, perhaps to safeguard the futures of children not affected by HIV. Replacement feeding has also had unintended reproductive consequences, because the absence of lactational amenorrhea can lead to unintended pregnancies (9,11,43) and consequently an increased number of HIV-exposed infants (60,75).

In conclusion, formula feeding in low-income settings often leads to serious negative health, economic, and social consequences for both child and mother and when formula has been provided in real-world conditions, HIV-free survival rates have generally been worse (38).

Breastfeeding. **EBF.** In 1999, Coutsoudis et al. (76) reported the striking finding that the risk of MTCT transmission with EBF was significantly lower than that associated with mixed feeding. In 2001 they reported that cumulative probability of HIV detection in infants was similar for babies never breastfed and those EBF (0.194), whereas the risk of HIV infection in infants fed breast milk and other foods was much higher (0.261) (77). The greatly elevated risk of MTCT associated with mixed feeding and the protective benefits of EBF were subsequently demonstrated in other studies (35,51,78–80). Furthermore, lower non-HIV morbidity and mortality rates are observed among HIV-exposed, EBF infants compared to their mixed fed counterparts (79,81).

The mechanisms by which EBF is associated with lower MTCT are not fully understood. They are likely numerous and have been described at length elsewhere (35,82). Briefly, EBF may promote maintenance of the integrity of the infant's gastrointestinal barrier, which is thought to be the primary mode of infection. The immunological factors in breast milk likely reduce viral activity in human milk. Additionally, EBF maintains the integrity of the mammary epithelial lining and promotes overall breast health. For all these reasons, the 2010 Guidelines recommend 6 mo of EBF in the absence of AFASS replacement feeding.

Abrupt cessation of breastfeeding. Because of the relatively low risk of HIV transmission during EBF compared to mixed feeding, it was thought that abrupt cessation of breastfeeding might offer infants the maximum health benefit with minimum risk. However, the sole randomized trial to investigate the effects of abrupt weaning (defined as "as soon as possible;" 68.8% weaned within 2 d) indicated that the health risks of rapid weaning (e.g. higher viral load in milk with abrupt weaning, inadequate nutritional intake thereafter, death) outweighed the health benefits of PMTCT (51,83,84). Data from a number of other studies also support these findings (45,46). Women are now advised to stop breastfeeding gradually within a month (7).

Another change in the 2010 guidelines is the recommended duration of breastfeeding in the absence of AFASS conditions. The recommended duration of breastfeeding for HIV-exposed infants is slowly approaching that for the general population. Women are now encouraged to breastfeed for a minimum of 12 mo and breastfeeding "should then only stop once a nutritionally adequate and safe diet without breastmilk can be provided" (85). Although the risk of HIV transmission continues for as long as breastfeeding continues (32), HIV-free survival of HIV-exposed infants who breastfed beyond 6 mo was similar to that of infants who received no breast milk after 6 mo (86,87). Infants given replacement foods after a period of breastfeeding also suffered increased serious infections, including diarrhea and pneumonia, growth faltering, and death (45–47,50,51,58). The importance placed on maximizing an infant's continued access to breast milk in the 2010 recommendations reflects the immunological benefits of breast milk as well as the importance of breast milk in providing adequate nutrition to infants > 6 mo of age.

Wet nurses. Previous iterations of infant feeding guidelines have discussed 3 modalities by which HIV-exposed infants may be fed HIV-free breast milk: wet nurses, milk banks, and mother's own expressed, heat-treated breast milk (88). Although wet nursing can ensure that an infant receives fresh breast milk, it presents challenges of its own, including making certain that the wet nurse remains HIV-negative and is available to feed the infant on demand. Presumptively, because of these challenges, wet nurses are not discussed in the 2010 guidelines. Wet nurses are extremely rare (89) and there is little evidence of HIV-positive women using them in high- or low-income countries.

Human milk banks. Human milk banks have provided donor milk for infants for over 100 y; the first milk bank was established in Vienna in 1909 (90). Milk banks have long been an important source of safe breast milk for vulnerable infants, such as those who are preterm, low birth weight, severely malnourished, orphaned, or born to HIV-positive mothers (91). When HIV was discovered in breast milk in the early 1980s, the safety and acceptability of human milk banking was questioned (92). However, human milk banks use Holder pasteurization (62.5°C for 30 min) to eliminate viral and bacteriological contaminants (93) such that there is little risk of HIV infection from banked milk. Indeed, the health benefits and long-term cost effectiveness of providing donor milk for vulnerable infants have been well characterized (94,95).

The WHO endorsement of human milk banking has remained consistently positive (96): "Where it is not possible for the biological mother to breastfeed, the first alternative, if available, should be the use of human breastmilk from other sources. Human milk banks, therefore, should be made available in appropriate situations." And in 1992, the WHO included donor milk as an acceptable feeding alternative for HIV-positive mothers (97,98).

Milk banking is not very common in general and it is extremely limited in most low-income countries. There is one exception: Brazil. Human milk banking began there in 1943 and has grown to become the widest breast milk bank network in the world. The Brazilian National Network of Human Milk Banks has 192 banks and is organized from the national to the local level, even including firemen who collect milk from donors' homes (99–102). Recognized internationally as a model system, the WHO awarded the Brazilian National Network of Human Milk Banks the Sasakawa Health Award in 2001 for making important contributions toward improving their nation's health and reducing infant mortality rates.

In high-income countries, some HIV-positive mothers feed their infants with banked human milk. Although banked human milk is more expensive than formula [e.g. ~$3/oz (29.5 mL) in the US], some insurance companies, including public insurance plans for low-income women, cover the cost if there is a maternal or infant indication. Several Web sites also offer breast milk of unverified safety and origin for sale or donation. The number of HIV-positive mothers feeding their infants human milk from either source is not known.

Breast milk pasteurization. Because of the importance of breast milk to young children and the lack of alternatives in low-income settings, efforts have been shifting toward mitigating the risk of MTCT by making a mother's own breast milk safer. There are 2 methods for doing so that are currently implementable; one is breast milk pasteurization, the second is extended ARV use (discussed in the next section).

Pasteurization can occur through a variety of techniques. Holder pasteurization (62.5°C for 30 min), the pasteurization technique used by most milk banks, is not possible in most homes, although a single-bottle Holder pasteurizer has been developed (103). Several other pasteurization methods have been suggested for in-home use. These include outright boiling of expressed breast milk (104), Pretoria pasteurization (a jar of expressed breast milk is placed in water that has been brought to a boil immediately after removal from the heat source) (105), and Flash-heat (a jar of expressed breast milk is heated in a pan of water until the water boils and then the jar is removed from the water and heat source) (106). Research has demonstrated that these heat-treatment techniques inactivate HIV and bacteria in breast milk (107,108) while retaining the majority of its nutritional, immunological, and antimicrobial properties (108–110). Pretoria and Flash-heat pasteurization preserve nutritional and immunological properties of milk better than breast milk boiling does, and the Flash-heat technique may be superior to the Pretoria method at inactivating viral activity (106).

In the 2001 WHO guidelines, heat treatment of expressed breast milk was one of the main options (along with EBF and replacement feeding) to be explained in counseling sessions with HIV-infected women. It is worth noting that the guidelines were never explicit about which technique to use for heat treatment. After 2006, heat-treated breast milk was no longer considered a main feeding option but rather one that may only be AFASS for a select group of women. This recommendation was likely made based on the unavailability of population-level studies of the methods. The 2010 guidelines listed feeding expressed, heat-treated breast milk as a possible "interim strategy" in 4 situations: *1*) for low-birth weight or sick infants unable to suckle; *2*) for mothers temporarily unable to breastfeed due to illness or mastitis; *3*) to assist mothers to stop breastfeeding; and *4*) in situations in which ARV are temporarily not available (the age of infant is not specified, i.e. it is not clear if heat-treated breast milk was recommended during EBF or only once complementary feeding had begun). Home pasteurization was not recommended for extended replacement feeding.

Of the 4 situations listed in the 2010 WHO recommendations during which heat-treated breast milk can be a possible interim strategy, the most is known about its use during the period of transition from EBF to complementary feeding. Field research from South Africa (111), Tanzania (112,113), and Zimbabwe (114) has indicated that Flash-heating breast milk is feasible, i.e. it can be accomplished by women in low-income households in rural sub-Saharan Africa during the transition from EBF to complementary feeding.

In Zimbabwe, with weekly home visits from nurses, HIV-infected mothers of HIV-exposed, uninfected children 6–12 mo old could safely express and heat-treat breast milk for long periods of time (4.5 mo; range 1–11 mo). Children who consumed a higher proportion of energy from expressed and heat-treated milk compared with complementary foods showed more improvement in weight and length (114). In a study in Tanzania, more than one-half of HIV-infected mothers with HIV-uninfected children that were counseled by community health workers on the option of expressing and heat-treating their milk upon the introduction of complementary foods chose to do so at least once; the median volume of breast milk pasteurized was 300 mL/d for a median duration of 9.7 wk (1 d to 12 mo) (C. J. Chantry, S. L. Young, W. Rennie, M. Ngonyani, C. Mashio, K. Israel-Ballard, J. Peerson, M. Nyambo, M. Matee, D. Ash, K. Dewey, and P. Koniz-Booher, unpublished data). Furthermore, in Rwanda, a program supported by the Ministry of Health is underway to evaluate the inclusion of Flash-heat training and support within a comprehensive fortified complementary foods program for HIV-exposed infants (115). Preliminary results from this study suggest that integration of heat treatment counseling and support is possible at the PMTCT programmatic level.

Despite the promising laboratory and feasibility data, the WHO expert committee declined to recommend in-home breast milk pasteurization except as an interim strategy, citing the need for more data on scalability, sustainability, and health system requirements for supporting breast milk pasteurization.

ARV prophylaxis during breastfeeding. In low-income settings, ARV have been used to reduce the risk of prenatal and peripartum transmission for more than a decade (116). The mainstay of ARV prophylaxis for PMTCT in most countries

has been single-dose nevirapine (sdNVP), a regimen that consists of a maternal dose intrapartum and an infant dose within 72 h postpartum. Indeed, the testing, counseling, and ARV provided by these PMTCT programs are largely responsible for the steady decrease in the incidence of pediatric (<15 y old) HIV over the past decade from 800,000 in 2001 (117) to 430,000 in 2008 (31). The use of extended ARV in the postnatal period, however, is relatively new, and is an exciting area for discovery.

In the 2010 guidelines, the WHO recommended that all pregnant, HIV-1–infected women with CD4+ T-cell counts of ≤350 cells/mm^3 initiate lifelong, highly activated antiretroviral therapy (HAART) for their own health (118). These guidelines also recommended that ARV be administered prophylactically to pregnant women with CD4+ T-cell counts > 350 cells/mm^3; the recommended regimen is either a 2-drug regimen (antepartum azidothymidine (AZT) plus intrapartum nevirapine) or HAART, which is a combination of at least 3 ARV.

After delivery, it is recommended that women receiving HAART (either for their own health or to prevent HIV transmission) continue on ARV throughout the breastfeeding period and that their infants receive nevirapine for 6 wk. Those women on HAART for their own health should continue on ARV indefinitely. Those women on HAART as HIV-transmission prophylaxis should continue ARV until 1 wk after weaning. Those infants born to women who received antenatal AZT/intrapartum nevirapine should receive daily nevirapine until 1 wk after cessation of breastfeeding. The decision of who should receive the ARV (the mother or the child) is left to national governments.

At the time these recommendations were written, these recommendations are based on strong evidence from clinical trials that ARV interventions for infants and mothers significantly reduce HIV transmission through breastfeeding (119), with little evidence of diminished protection over time, no evidence of significant drug-related adverse events, and no increased adverse events with prolonged ARV intervention. Studies in Malawi (BAN, DREAM) (120), Mozambique (DREAM) (121), Tanzania (Mitra) (122), Kenya (Kesho Bora) (123), and Botswana (Mma Bana) (124) have all observed low rates (<5%) of HIV transmission (via all routes combined, i.e. intrauterine, intrapartum, and postpartum) in breastfeeding women receiving therapeutic regimens initiated during pregnancy and then continued thereafter in the context of a scientific study.

Data were available on the protective effects of maternal or infant prophylaxis up to 6 mo of age, but mathematical modeling suggested 12 mo of prophylaxis provides an optimal health risk:benefit ratio with regard to HIV-free survival, and thus the recommendation for duration of ARV provision was 12 mo (7). The 2 critical assumptions in making this recommendation are that the efficacy of ARV against transmission via breastfeeding continue beyond the first 6 mo of the child's life under "real life" conditions, and feasibility and adherence with ARV intervention are possible beyond the 6-mo period to which the clinical trials were limited.

Coverage of ARV prophylaxis. In 2009, 53% (40–79%) of pregnant women living with HIV in low- and middle-income countries received any ARV (either sdNVP or combination regimens) (125). This represents an increase in coverage of ARV from 45% (37–57%) in 2008 and 15% (12–18%) in 2005 (126). Prophylaxis coverage among the 1.4 million infants born to women with HIV has also increased between 2008 and 2009, but only slightly, from 32% (26–40%) to 35% (26–53%).

This steady increase in coverage represents real progress toward the reduction of MTCT, but clearly, universal access to ARV (defined as 80% coverage) is not available in countries with the highest rates of MTCT. Furthermore, coverage in these statistics included those women who received sdNVP, which, although much easier to implement in low-income settings, is not recommended because of problems with resistance and lower efficacy (125).

Extended regimens, such as those recommended during breastfeeding, will be difficult to make universally accessible given the substantial barriers to scaling up, including healthcare worker shortages and insufficient funding (127). The difficulties of universal coverage are just one of the many barriers to ARV prophylaxis during breastfeeding. Problems with consistent supplies, adherence, and acceptability of ARV use during breastfeeding mean that ARV must not be the only approach to postnatal PMTCT.

Next steps

Given the current knowledge about infant feeding and vertical transmission, most policy makers have felt it is safest for infants in industrialized countries to be replacement fed (63). In contrast, ARV prophylaxis while breastfeeding, 6 mo of EBF, and a minimum of 12 mo of any breastfeeding is currently considered the safest infant feeding modality in low-income settings (7). Although these recommendations are based on the results of several decades of enormous research efforts, the fact that 430,000 new cases of pediatric HIV occurred in 2008 suggests that there remains a great deal of work to be done by researchers working in the bench, clinical, behavioral, and implementation sciences. Below, we outline 2 perspectives, contextualization and holism, that should be applied to studies of infant feeding interventions for more informative evaluation and effective implementation. From this foundation, we describe a variety of basic, clinical, behavioral, and programmatic research topics that we expect will lead to a substantial reduction in postnatal MTCT in low-income settings.

Perspectives for future infant feeding interventions

Contextualizing infant feeding in the cascade of PMTCT events. The entire cascade of PMTCT events is relevant to those interested in infant feeding, because a woman who is unaware that she is infected will not have access to PMTCT services, including advice on prevention of postnatal MTCT. Therefore, efforts to reduce vertical transmission must begin well before an infant is born; they must start by maximizing the number of infected mothers who receive comprehensive

PMTCT services. PMTCT services involve many steps, each of which can become a stumbling block to the reduction of disease transmission (**Table 2**). Indeed, recent data has made clear that the number of women who receive adequate PMTCT care drops off substantially at each step (125,128).

HIV testing. The initial step in the cascade, learning one's HIV status, is a multi-faceted process that can fail at numerous points. A woman must attend a clinic that has PMTCT services available, be offered a test, agree to be tested, and then receive the results. PMTCT services are limited in coverage, although they are rapidly expanding. To increase the quantity and quality of PMTCT services, performance-based financing has been proposed. Performance-based financing involves offering financial incentives that have the potential to increase both the quantity and quality of the services that health-care providers deliver. Performance-based financing seems to improve HIV service delivery, though data are limited. For example, improved quantity and quality of HIV care, treatment and prevention were documented with performance-based financing in a pilot program supported by the Elizabeth Glaser Pediatric AIDS Foundation in Ivory Coast (129). Monetary factors are not the only obstacles to availability and quality of human resources for PMTCT; motivation is related to many aspects of the working environment (130). For this reason, human resource management tools like job design, supervision, recognition, continuing education, career planning, and accountability systems can effectively increase health worker motivation and performance. However, they are not used to their fullest potential (131,132). Research into the improvement in care given by the PMTCT cadre is an area that would likely have long-term beneficial effects on the entire health system, because PMTCT workers often care for HIV-unaffected segments of the population as well.

In many countries, HIV testing and subsequent ARV prophylaxis for PMTCT is provided as part of the Maternal and Newborn Child Health services and a woman thus must have at least one antenatal care visit or deliver in the hospital to enter PMTCT services. Although overall antenatal care attendance is high in most countries with the highest HIV burden, the poorer and more rural populations have less access to antenatal care, because they are unable to pay for transport and user fees or cannot afford to be away from the home for long periods (133). Interventions improving equity, accessibility, and acceptability of Maternal and Newborn Child Health services will therefore positively affect PMTCT as well.

With the shift from voluntary patient-initiated testing to routine ("opt-out"), provider-initiated testing and counseling in Maternal and Newborn Child Health clinics, the uptake of testing among pregnant women has been increasing (132). However, coverage remains far too low to prevent pediatric HIV infection (41). In 2009, only 26% of pregnant women in low- and middle-income countries received an HIV test (125). The rates of test coverage were higher in sub-Saharan Africa (35%), with 50% of women in southern and eastern Africa being tested compared to 21% in western and central Africa (125). These numbers do not indicate if results were received. Test results must be given to the woman in a timely manner, ideally the same day. The effort that is typically involved in returning to the clinic several days later means that some women never learn their status.

Prenatal and perinatal ARV use. Once a woman learns she is infected, a variety of factors influence if she is offered, accepts, and is adherent to an appropriate ARV regimen during pregnancy, delivery, and breastfeeding. First, a woman identified as HIV-infected needs to be evaluated to determine if she is eligible for ARV therapy for her own health. Women living with advanced HIV disease not only have an increased risk of dying, they also have progressively higher vertical and horizontal transmission rates than those with less advanced infection, because they have higher viral loads. A recent study calculated that women with CD4 counts < 200 cells/mm^3 (the previous WHO cutoff for ART eligibility) and between 200 and 350 cells/mm^3 (the current WHO cutoff) had MTCT rates of 44 and 28%, respectively, whereas MTCT rates among women with CD4 counts between 350 and 500 cells/mm^3 and >500 cells/mm^3 were only 13 and 10%, respectively (134). Therefore, whether a country applies the current or the previous WHO criteria, giving a treatment-eligible woman ARV prophylaxis instead of ARV therapy means missing an opportunity to reduce the likelihood of horizontal disease transmission.

Table 2. Potential barriers and motivators to the cascade of events of PMTCT care[1]

Event	Potential barriers and motivators
HIV testing	
Attend clinic	Accessibility, fear, and distrust of care received
Offered test	Stock-out of test supplies, broken machinery, reliable testing methods
Agree to test	Fear and distrust of clinic staff, fear of disclosure and discrimination by community, availability of efficacious treatment
Receive results	Accessibility (if necessary to return to clinic), availability and training of testing counselors
ARV use	
ARV offered to mother and baby	Accessibility (if necessary to return to clinic multiple times to collect infant medicines), availability of medicines
Medicines ingested by mother and baby	Accessibility (if necessary to return to clinic), fear, and distrust of their efficaciousness, potential for disclosure and subsequent discrimination, drug effectiveness and adherence, consistent availability of medicines
Safer feeding	Education about safest modality, local beliefs about optimal infant feeding practices, availability of safe replacement feeds, support of family to EBF
Infant tested	Accessibility (if necessary to return to clinic), clinic resources, maternal permission.

[1] Adapted with permission from (210).

Assessment of eligibility for ART is often impossible to conduct in a Maternal and Newborn Child Health clinic setting, either because CD4 count testing is not available or because staff are not trained to perform clinical staging. Even in health facilities in which both PMTCT and Care and Treatment services for HIV are offered, linkages between the 2 are often weak (135). These factors explain why only about one-half of the pregnant women who tested positive for HIV in low- and middle-income countries were assessed for ART eligibility (133). Stock-outs or expiration of ARV drugs may be other impediments to timely initiation of the prophylactic or therapeutic ARV regimen (136,137).

Uptake of the infant's ARV dose(s) is influenced by similar availability, accessibility, and acceptability factors as those affecting the uptake of the mother's dose(s), but with the added complication that in some countries only infants of mothers delivering in the facility or who are brought to the facility within 72 h after delivery get the postpartum sdNVP dose. Because institutional delivery rates are usually well below antenatal care attendance rates, and because returning to the health facility soon after homebirth may be uncomfortable and may also require money and careful planning, coverage of prophylaxis is much lower for infants than for mothers (125).

Holistic evaluations of PMTCT interventions. PMTCT interventions, postnatal and otherwise, will be better understood and therefore more effective if they are evaluated more holistically, i.e. in terms of their psychosocial and economic consequences as well as their biological ones. Much of the research on postnatal PMTCT to date has focused solely on the biomedical consequences of infant feeding modalities, primarily disease transmission and survival. Yet the spectrum of strategies for reducing MTCT has frequently come with a range of unintended and often unmeasured psychosocial ramifications, from unintended disclosure to physical abuse, rejection by partners, ostracization by families, and abandonment of infants. Thus, we recommend that regular feedback and open-ended evaluation by study or program participants and staff occurs throughout the course of the intervention to gauge psychosocial consequences. Moreover, these studies should also involve individuals who choose not to participate in PMTCT programs.

Similarly, the magnitude and timing of private costs (individual and household-level expenses), public sector costs (those paid for by the national government), and civil society costs (those paid for by international organizations, nongovernmental organizations, local volunteers, etc.) of interventions to HIV-affected persons is another component of PMTCT interventions that has frequently been overlooked. Individual costs include opportunity costs, such as income foregone while traveling far distances to clinics or waiting in long lines for care, as well as expenditures required to adhere to recommendations, e.g. to buy medicines, to pay for transportation to facilities, and to buy replacement milks for infants. The economic consequences of participating in PMTCT programs and adhering to prescribed recommendations have also received little attention. Families may sell assets to pay for care, HIV-positive women may engage in transactional sex to pay for formula for their infants, and governments may reappropriate funds from other programs to fund the purchase of formula and medicine or the training of health care workers. These consequences are not sufficiently documented in most analyses.

These costs will influence not only the willingness and ability of women to participate in PMTCT programs but also the amount of time they spend in programs and the degree to which they adhere to program recommendations. Therefore, we recommend that a household-level focus be adopted for economic analyses, that careful consideration be given to the economic and other risks to women and to their children (HIV-positive and other) of participating in MTCT programs, and that the likely inherent selectivity biases associated with studying only those women who participate in such programs be carefully addressed.

The measurement of programmatic costs (public sector and civil society) should include the cost of the purchase and distribution of medicines and foods and the burden to health care personnel that increased testing and counseling on HIV, optimal infant feeding, and ARV represents. Desmond et al.'s (138) work on infant feeding counseling in South Africa is exemplary and rare for its cost analyses. With data on these costs in hand, sound costing and cost-effectiveness calculations will be possible.

In addition to evaluating what are sometimes referred to as downstream factors or the outcomes of a program or intervention, i.e. the adoption of as well as adherence to recommended behaviors, PMTCT interventions must also pay attention to the delivery side, i.e. program coverage and the quality and consistency of implementation (139). It is important to ascertain the extent to which these interventions are delivered as intended, an endeavor that entails paying attention to and measuring factors such as training effectiveness, quality of supervision, motivational characteristics of frontline workers, and quality of contact between health care worker and client.

Finally, as promising interventions are developed, tested, become recommendations, and are rolled out, it is critical to bear in mind that the majority of MTCT occurs in sub-Saharan Africa. Indeed, in 2008, the majority (91%) of new infections among children occurred in sub-Saharan Africa, with the bulk of these occurring in southern and eastern Africa (31). It is also worth noting that transmission is disproportionately high, given that only 67% of people living with HIV worldwide live in sub-Saharan Africa (31). The unique agro-ecological and cultural circumstances of sub-Saharan Africa must be borne in mind as interventions are evaluated and as research priorities and public health policies are set. Although the enormous cultural diversity within sub-Saharan Africa must not be overlooked, it is fair to acknowledge the setting is distinct from middle-income countries or even other low-income regions of the world. These circumstances include particular environmental (e.g. poor access to adequate sanitation, limited availability of clean

water, reliance on subsistence farming), cultural (e.g. societal expectations to breastfeed, importance of extended family in raising infant), disease (e.g. high prevalence of malaria and intestinal parasites), and economic (e.g. cash-strapped public health programs, high prevalence of food insecurity) considerations, which must be taken into account when viable interventions are considered. Because of cultural and ecological variation, all interventions must include qualitative, formative research prior to implementation, such as that done in the BAN study in Malawi (140).

In summary, a holistic, contextualized understanding of the biological, psychosocial, and economic consequences of PMTCT strategies is critical for determining their real-world implementability, effectiveness, and sustainability. Furthermore, these consequences need to be considered not just for the mother or the health care system but in the context of the household and community in which the HIV-exposed infant is raised. For example, are community members supportive of EBF? And if not, why? How can mothers strategically navigate barriers to EBF? Is it culturally acceptable to give newborns nevirapine syrup for a prolonged period of time? Does the mother need to conceal this behavior? Can she enlist family member support, e.g. others reminding her to administer it or acquiring more from the clinic? Tonwe-Gold et al.'s (141) evaluation of family-focused HIV care in Cote d'Ivoire is exemplary in its consideration of the family as the unit for PMTCT.

Similarly, the presence and welfare of other children in the household must be considered. The literature to date has tended to focus very narrowly on the infant and his or her HIV-affected mother. Although this focus may be appropriate for single-child households, it is probably inappropriate for households with multiple children in which the welfare of siblings must be considered when making decisions about care sought by HIV-positive mothers and the infant feeding practices they adopt.

Given the need for a holistic evaluation, research on the prevention of postnatal HIV transmission is an endeavor that must engage and involve a multitude of international, government, private, programmatic, advocacy, and research groups. Large-scale international initiatives to prevent MTCT include the President's Emergency Plan for AIDS Relief, the MTCT-Plus Initiative (Columbia University), the Global Fund, the Call to Action project (Elizabeth Glaser Pediatric AIDS Foundation), the UN Interagency Task Team on MTCT, and the USAID flagship project on infant and young child nutrition (previously the LINKAGES project, currently IYCN). Donor support for multi-sectoral interventions, such as those that simultaneously address infant feeding and vertical transmission, could fuel some very effective partnerships. Currently, such alliances are limited in their appeal to funders. However, the Feed the Future and Global Health Initiatives, both of which have recently been launched by the U.S. government and aim to curb malnutrition and improve maternal and child health in a very comprehensive way, suggest that attitudes toward multidisciplinary interventions may be changing.

Infant feeding topics for future research

Future research into postnatal PMTCT is urgently needed in a number of domains: extended postnatal ARV prophylaxis, EBF, counseling, breast milk pasteurization, breast milk banking, novel techniques for making breast milk safer, and other optimal breastfeeding practices. There are basic, clinical, behavioral, and programmatic types of questions that need answers within each of these domains.

Extended postnatal ARV prophylaxis. The 2010 WHO recommendations for ARV to be used prophylactically to prevent MTCT during breastfeeding mean that research on their use is a pressing priority. Very little is known about the implementation or biological, economic, or social consequences of extended prophylactic ARV for PMTCT in real world settings; all data to date are from carefully conducted clinical trials.

At the time of writing, only a few countries (59) have determined their postnatal ARV policies in light of the 2010 recommendations, i.e. if ARV will be given to mothers or infants, and if it is to mothers, what that regimen will be and the duration of provision. Once the policies are implemented, it will be beneficial to describe the various implementation strategies. Will ARV support be integrated into general infant health programs? Or will it remain in PMTCT services? Will it be rolled out by peer counselors or by highly-trained medical staff? Will women be given the medicines they will require postnatally prior to delivery, e.g. the Mother-Baby pack (142)? An analysis of the strengths and weaknesses of the different implementation approaches from biomedical, psychosocial, and economic perspectives will help identify the most effective implementation strategies for prophylaxis during breastfeeding. Depending on the distribution of alternative policies that are adopted and the characteristics of programs and target populations, a natural experiment capable of clearly identifying the most effective and cost-effective approaches could present itself.

There is also much to learn about the biological consequences of extended ARV prophylaxis. For example, there are little available data on prophylaxis during 12 mo of breastfeeding. And although we have 15 y of data on ARV use in the prenatal and peripartum (to 6 wk postpartum) periods, we know very little about the safety of prolonged exposure to ARV early in life or of repeated courses of HAART in women not requiring the medicine for their own health (41). Also pressing are consequences for drug resistance (41,143). Other consequences to consider are those for lactogenesis; to our knowledge, there has been no study of the effect of ARV on the quality or quantity of breast milk production. It will also be useful to compare health outcomes for mothers and children in countries that have chosen maternal prophylaxis with those that have chosen infant prophylaxis. Given that available data suggest the efficaciousness of both regimens is comparable for rates of HIV-free survival, major differences in maternal health outcomes could influence subsequent recommendations.

The behavioral consequences of extended ARV prophylaxis are currently unknown. What will adherence be? Will it be higher in pregnant populations than in the general population? Will the heightened sense of smell and increase in nausea and vomiting (morning sickness) during pregnancy render ARV medicines intolerable? Will mothers understand the function of prophylactic ARV? In Malawi, e.g., some mothers thought that sdNVP protected their infant through 6 mo of breastfeeding, and others thought that co-trimoxazole prophylaxis (an antibiotic) prevented postnatal transmission of HIV (144). Will ARV prophylaxis make EBF seem less important with a concomitant increase in mixed feeding?

Even less is known about the social consequences of ARV during breastfeeding. ARV prophylaxis involves a higher number of pills being consumed more frequently, which has implications for voluntary and involuntary disclosure and subsequent stigma. It is also important to know if the use of ARV prophylaxis causes any other unanticipated stigma, e.g. HIV-exposed babies become regarded as HIV-positive ones.

Once they no longer qualify for prophylaxis or therapeutic treatment, how will mothers choose to feed their infants? Will they continue to breastfeed from the breast? Will they pasteurize their breast milk? What happens to the mother's health and her and her family's ability to care for her child (ren) after she stops ARV?

Finally, inadequate coverage remains a critical issue for ARV use. Given that in 2009, only 53% of pregnant women living with HIV in low- and middle-income countries received any ARV (either sdNVP or combination regimens) (125), there is a staggering amount of work to do. Both the number of women and infants who receive ARV as well as the duration for which they are now recommended to receive them has greatly increased without a commensurate increase in health care workers or funding.

The removal of barriers to EBF. Current rates of EBF are well below targeted levels in both HIV-affected and unaffected populations around the world. Increasing rates of EBF is one of the most powerful interventions to save child lives; the promotion of breastfeeding could prevent 13–15% of child deaths in low-income countries (1). Other benefits of the promotion of EBF include that it is also a healthful behavior for HIV-unexposed infants and their mothers, is helpful for birth spacing, requires minimal preparation, is not dependent upon outside materials, and breast milk does not need purchased. Additionally, the fact that breastfeeding is a common behavior means it is unlikely to flag the mother's HIV status.

Although there are many advantages of EBF, a woman's initial decision to EBF can be stymied by a range of societal, household, and individual factors. At the individual or household levels, poverty is a risk to EBF when women need to return to income-generating activities (145). Perceptions at the community level that breastfeeding always leads to HIV infection in the infant have dissuaded some women from EBF (146). At the macro-level, women from across the entire socioeconomic spectrum are thwarted in their efforts to EBF by well-meaning community members who insist that it is not appropriate. They may suggest that colostrum is harmful (147), that the infant is not getting all the nutrients and or liquid she needs from breast milk alone (148), or that formula is somehow superior (149). Women themselves may decide they are unable to EBF because of either perceived or actual (which is uncommon) insufficient milk production (148,150); in low-income settings this is frequently associated with perceived inadequate nutritional intake (151,152).

An additional barrier to EBF is misunderstanding what it is; women may think they EBF when in fact they do not. In Malawi, e.g., mothers did not understand that feeding warm water to infants was in conflict with EBF; it was done to prepare the infant gut "so that the intestines can open up" (144).

In summary, any efforts to increase EBF must first focus on local community expectations about infant feeding for all women as well as experienced and perceived barriers to EBF. They must also consider women's own perceptions of the consequences of breastfeeding when infected with HIV (144,153). Only once the reasons for not EBF are identified should approaches to increasing rates be implemented. There are a variety of interventions for improving rates of EBF, from education to cash transfers to mass media messages (154); the application of these to HIV-infected populations or general populations in countries with high HIV prevalence will be informative. Similarly, the evaluation of the high-priority strategies for protecting, promoting, and supporting EBF detailed in the *Global Strategy for Infant and Young Child Feeding* (155) would be useful in the context of HIV.

PMTCT counseling. So far, we have discussed both the enormous health benefits and the numerous potential barriers to both extended drug regimens and EBF. Serendipitously, the 2 practices share a proven way to increase them: counseling.

Although counseling has been proven effective, there is a dearth of high-quality infant feeding counseling material (156–159) and HIV counselors (for testing or for HAART) (160), in part because there are insufficient numbers of health care workers, especially in sub-Saharan Africa (160, 161). Indeed, the shortage of health care workers is a major obstacle to the scale-up of PMTCT services (127). For this reason, increases in coverage and quality of PMTCT services will likely require innovative staffing strategies among health care professionals, including shifting tasks from professional health workers to nonprofessionals (132). Studies of the cost-effectiveness of counseling-based strategies would also be welcome.

Peer counseling, i.e. counseling by community members who are not biomedically trained, has been demonstrated to be highly effective at increasing the rate of EBF in both HIV-negative (162–164) and HIV-positive (165) women through clinic-based and home-based counseling (166). Trained community-based treatment supporters have also increased

patient satisfaction and adherence in HIV and TB treatment programs (167–169). Unfortunately, the role of counseling has sometimes been overlooked as a strategy for PMTCT (170) and as such, far less research has been done evaluating its effectiveness in terms of health outcomes or cost than has gone into biomedical interventions.

Indeed, very little is known about the effect of using peer supporters, including mothers, grandmothers, traditional birth attendants, or other people living with HIV/AIDS in the prevention of vertical transmission. Futterman et al. (171) concluded that in a South African program deploying peer mentor mothers, medical follow-up visits to the PMTCT clinic increased as did knowledge about PMTCT. In India, the introduction of peer counselors resulted in a 6-fold increase in the percentage of HIV-positive women referred for care and more than doubled the institutional delivery rates (133). Additionally, promotion of infant feeding buddies, similar to ART adherence buddies, is currently being investigated in one South African PMTCT program as another mechanism of providing home- or community-based support for mothers to safely feed their infants. We do know that there is insufficient counseling in current PMTCT programs (136,172,173). Community supporters may be essential in helping mothers to access services and adhere to guidelines, especially because current PMTCT services and care are shown to be particularly poor in the postnatal period (174,175).

Even less is known about the role of peer counselors to support prophylactic ARV use. We do not know if women would welcome support to take (or administer) prophylactic ARV, and if they would, what the optimal messages and frequency of contact would be. Furthermore, because there have been no studies of the effect of peer counselors on prophylactic ARV adherence, we do not know the effect of such an intervention. Given recent efforts to respond to the 2010 guidelines, such a study would be extremely informative; the inclusion of cost-effectiveness evaluation would be invaluable for program planning.

Finally, it likely would be beneficial for all counselors to have standardized counseling materials, similar to what the Tanzanian Ministry of Health has adopted for infant feeding counseling in the context of HIV/AIDS (176). Such materials may help to mitigate some of the frustration, confusion, and misinformation that accompanies implementation of changes in guidelines (177).

The role of disclosure in adherence to PMTCT guidelines. A woman's social, economic, and cultural context may well be predictive of her acceptance of PMTCT care, including adherence to ARV and likely infant feeding behaviors. Many PMTCT counselors encourage women to disclose their HIV status to at least one person, usually a household member, because of its reported benefits of reduced anxiety, more social support, increased access to services, increased opportunities for prevention of transmission to sexual partners, increased ARV adherence, and better planning for the future (178,179). However, fear of stigma, discrimination, and blame by community or family members, partner violence, abandonment, and loss of personal or household assets or of economic opportunities may cause women to not want to know or disclose their status and shun PMTCT services (180–183). It stands to reason that disclosure may similarly affect her ability to adhere to recommended infant feeding practices, although currently very little is known about this (184). The consequences of disclosure to community members (i.e., those other than her partner) to achieve community support for adherence to ARV prophylaxis and infant feeding practices needs further exploring (185). Lastly, tools to identify women at higher risk for negative outcomes of disclosure need to be developed and tested (178).

Disclosure of HIV status has generally been shown to be beneficial to mothers who choose to do so. Although couples counseling and facilitated disclosure has been shown to be feasible and scalable in selected areas (186,187), male involvement has been disappointing in others (186–188). Too little is known about what are optimal counseling scripts, who are the most effective counseling cadres, and what are the best places and times to assist women in disclosing to their partners or in improving partner involvement in PMTCT (189–192).

Breast milk pasteurization. Despite the promising laboratory and feasibility data, the WHO expert committee declined to recommend home-based breast milk pasteurization except for as an interim strategy, citing the need for more data on scalability, sustainability, and health system requirements (7). Even when ARV prophylaxis is successfully implemented for the first months of breastfeeding, MTCT can occur if breastfeeding continues after the cessation or during interruption of ARV (193). This suggests that methods to continue making breast milk safe will be needed when ARV are unavailable, refused, or interrupted, or for women who opt to breastfeed after prophylaxis is discontinued. As such, a large clinical study of the scalability and of the clinical and socioeconomic consequences of the method is overdue.

Breast milk banks. Breast milk banking is an underutilized strategy for the production of safe breast milk. Many industrialized countries have been able to provide donor milk through intensive commercial-grade pasteurization, but this has been limited in scope. For example, the United States Human Milk Bank Association of North America currently has only 14 functioning milk banks. There are far fewer milk banks in middle- and low-income countries (with the exception of Brazil) and the development and expansion of milk banking has remained a daunting challenge. Yet at the same time, milk banks may be most needed in low-income settings. For example, many children orphaned by HIV/AIDS are under the age of 5 y and at increased risk for negative health outcomes, including malnutrition (194). Such infants would benefit greatly from the rehabilitative and immunological properties of breast milk, such as that available from a breast milk bank. A community-based milk bank in South Africa was recently started to provide

donor milk to HIV-exposed infants in need (195). This model may be one that could work in other low-income settings; further research on the economic feasibility and sustainability of milk banks in such settings would be very useful, in part because such studies may shed light on the role of public policy in promoting and sustaining these institutions.

Other techniques for the reduction of vertical transmission. There are currently several types of research into novel techniques for making breast milk safer. One method involves chemical treatment of milk. There was some hope that the antiviral properties of chloroquine might reduce breast milk viral loads; this, however, has not been the case (196). A preliminary study of treating breast milk with a microbicide, SDS, has shown some promise in a laboratory setting (197). To our knowledge, there have been no field studies of this technique. Nipple shields with an insert that elutes microbicide or ARV are also under development. They are currently in prototype phase with considerable laboratory and field studies research remaining (198). A vaccine that could protect an infant from infection would make breast milk from an HIV-positive woman safer (199). Currently, there are several ongoing studies of vaccines in children [reviewed in (82)], but results are not yet available.

Another area of development is novel ARV delivery mechanisms. A number of international organizations have called for investment in innovative ARV delivery devices (3). These include dissolvable films, transdermal patches, microtablets, and injectable ARV. Other ideas are implantable devices in which ARV medicines are slowly released, akin to hormonal contraceptive implants. These alternative delivery systems may be more appropriate for pediatric formulations and for longer term prophylactic use and would likely be welcomed by those using ARV.

Breastfeeding in high-income settings. As additional data demonstrate the safety of breastfeeding with either maternal HAART or infant ARV prophylaxis, it is inevitable that HIV-infected women in high-income settings will express a desire to breastfeed their infants (200,201; D. Cohan, unpublished observations; C. Chantry, unpublished observations). Although HIV-infected mothers in such countries who choose to breastfeed may be prevented from doing so or even be charged with child endangerment if they persist (200), there is growing recognition that breastfeeding may be the only acceptable mode of infant feeding for some of these women (202). Clinicians will need to be prepared to help women make informed decisions about the relative risks of the variety of feeding modalities. Indeed, the UK Department of Health advises that "Under exceptional circumstances, and after seeking expert professional advice on reducing the risk of transmission of HIV through breastfeeding, a highly informed and motivated mother might be assisted to breastfeed" (202). Currently, there is minimal data on women in industrialized countries who feed infants their own breast milk [notable exceptions include (201,203)].

It is therefore informative to follow the health status of high-income, HIV-infected women who opt to breastfeed their infants, together with the health of their infants. It is also useful to characterize current infant feeding preferences among women in high-income settings and to track how these change as our understanding of PMTCT evolves. Such predictors of desired infant feeding modality could include, but should not be limited to: *1*) country of origin and time since immigration; *2*) HIV disclosure to partner/family members/community; *3*) time since HIV diagnosis; *4*) clinical disease progression; *5*) infant feeding experience with prior children; *6*) access to formula/human banked milk; *7*) self-perceived community standards/expectations; *8*) experience with ARV during pregnancy and/or the postpartum period; and *9*) socioeconomic characteristics of women and the households in which they live.

Other optimal breastfeeding practices. Although the 2010 guidelines recommend continued breastfeeding to 12 mo with extended ARV prophylaxis, the optimal duration of breastfeeding for HIV-exposed infants, i.e. one that balances the health risks of virus and ARV exposure with the nutritional and immunologic benefits of breastfeeding, is not yet clear. Environmental factors, such as inadequate sanitation and quality of complementary feeding (204,205), are sure to modify the risk:benefit ratio, but their effect size in HIV-exposed populations is currently unquantified. We also do not know what the relative risk:benefit ratio is for HIV-positive infants who have consumed nonbreast milk foods to initiate or resume breastfeeding from their HIV-infected mother. The differences in risk associated with vertical transmission during mixed feeding vs. complementary feeding have also not been made clear, because in much of the HIV literature, complementary feeding has not been differentiated from mixed feeding (Table 1). Elucidation of the basic science behind the mechanisms of transmission would be immensely useful in answering these questions.

When evaluating optimal duration of breastfeeding, it is worth considering that the 2010 recommendation of 12 mo of breastfeeding is contrary to the recommended duration of breastfeeding in HIV-unexposed infants, which is through the second year of life and beyond (206). The shorter recommended period of breastfeeding duration among HIV-positive compared to HIV-negative mothers may trigger another spillover effect, whereby uninfected mothers shorten the duration of breastfeeding.

Conclusion

The field of postnatal PMTCT-HIV is experiencing a number of exciting breakthroughs, which present important opportunities for research and programming to improve the welfare of HIV-affected women and their children. Recently developed interventions and methods with demonstrated effectiveness have the potential to prevent HIV infection and promote the growth of healthy infants more effectively than was previously possible. But much remains to be discovered about their biological, psychosocial, and economic consequences. We

therefore strongly suggest that future research focus on holistic evaluations of these practices in order to help policy makers choose the most feasible, cost-effective ways to reduce vertical transmission and promote the development and growth of children of HIV-positive mothers. Furthermore, prioritization of research that will increase the coverage of those interventions with the most promise, especially toward increasing rates of EBF, ARV coverage, and breast milk pasteurization, will certainly maximize the HIV-free thrival of the next generation of HIV-exposed infants.

Acknowledgments

This paper is dedicated to the memory and spirit of Prof. Michael Latham, whose intellectual and humanitarian commitment to the health of mothers and children will be carried forth by the many who knew and loved him. We thank Werner Schimana for his input during the formative stages of this manuscript, Anne Williams for sharing useful references, and Emily Wolfe-Roubatis for her comments on an earlier draft. S. Young conceived and cowrote all sections of the paper. M. Mbuya assisted with drafting the outline and cowrote the sections on program evaluation and breastmilk pasteurization. C. Chantry assisted with definitions of breastfeeding and cowrote the sections on benefits of breastfeeding, vertical transmission, breastmilk pasteurization, HIV-free thrival, and infant feeding in high- and low-income countries. E. Geubbels cowrote the sections on coverage of ARV prophylaxis and on the contextualization of infant feeding in the cascade of PMTCT events. K. Israel-Ballard cowrote the section on breastmilk pasteurization and human milk banking. D. Cohan cowrote sections on ARV prophylaxis and infant feeding in high-income countries. S. Vosti cowrote sections on costs, economic and otherwise, of infant feeding decisions. M. Latham cowrote the sections on the spillover effect and contributed significantly to the outline. S. Young had primary responsibility for final content. All authors read and approved the final manuscript.

Literature Cited

1. Jones G, Steketee R, Black R, Bhutta Z, Morris S. How many child deaths can we prevent this year? Lancet. 2003;362:65–71.
2. Gartner LM, Morton J, Lawrence RA, Naylor AJ, O'Hare D, Schanler RJ, Eidelman AI, American Academy of Pediatrics Section on Breastfeeding. Breastfeeding and the use of human milk. Pediatrics. 2005; 115:496–506.
3. WHO. Consensus statement: asking the right questions: advancing an HIV research agenda for women and children; 2010 [cited 2010 Nov]. Available from: http://www.who.int/hiv/pub/mtct/women_research_march_2010.pdf.
4. Preble E, Piwoz E. HIV and infant feeding: a chronology of research and policy advances and their implications for programs; 1998 [cited 2010 Nov 22]. Available from: http://www.linkagesproject.org/media/publications/Technical%20Reports/HIVIF.pdf.
5. Humphrey J, Iliff P. Is breast not best? Feeding babies born to HIV-positive mothers: bringing balance to a complex issue. Nutr Rev. 2001;59:119–27.
6. Coutsoudis A, Kwaan L, Thomson M. Prevention of vertical transmission of HIV-1 in resource-limited settings. Expert Rev Anti Infect Ther. 2010;8:1163–75.
7. WHO. Guidelines on HIV and infant feeding. Principles and recommendations for infant feeding in the context of HIV and a summary of evidence; 2010 [cited 2010 Nov]. Available from: http://www.who.int/child_adolescent_health/documents/9789241599535/en/index.html.
8. WHO. PMTCT strategic vision 2010–2015: preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals; 2010 [cited 2010 Nov]. Available from: http://www.who.int/hiv/pub/mtct/strategic_vision.pdf.
9. Labbok MH. Effects of breastfeeding on the mother. Pediatr Clin North Am. 2001;48:143–58.
10. Stuebe A. The risks of not breastfeeding for mothers and infants. Rev Obstet Gynecol. 2009;2:222–31.
11. Perez A, Labbok MH, Queenan JT. Clinical study of the lactational amenorrhoea method for family planning. Lancet. 1992;339:968–70.
12. Victora CG, Smith PG, Vaughan JP, Nobre LC, Lombardi C, Teixeira AM, Fuchs SM, Moreira LB, Gigante LP, et al. Evidence for protection by breast-feeding against infant deaths from infectious diseases in Brazil. Lancet. 1987;2:319–22.
13. WHO Collaborative Study Team. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. Lancet. 2000; 355:451–5.
14. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet. 2003;361:2226–34.
15. Ip S, Chung M, Raman G, Trikalinos TA, Lau J. A summary of the Agency for Healthcare Research and Quality's evidence report on breastfeeding in developed countries. Breastfeed Med. 2009;4 Suppl 1: S17–30.
16. Kramer MS, Chalmers B, Hodnett ED, Sevkovskaya Z, Dzikovich I, Shapiro S, Collet JP, Vanilovich I, Mezen I, et al. Promotion of Breastfeeding Intervention Trial (PROBIT): a randomized trial in the Republic of Belarus. JAMA. 2001;285:413–20.
17. Gibson RS, Ferguson EL, Lehrfeld J. Complementary foods for infant feeding in developing countries: their nutrient adequacy and improvement. Eur J Clin Nutr. 1998;52:764–70.
18. Brown K, Dewey K, Allen L. Complementary feeding of young children in developing countries: a review of current scientific knowledge; 1998 [cited 2010 Nov]. Available from: http://whqlibdoc.who.int/hq/1998/WHO_NUT_98.1.pdf.
19. Chirico G, Marzollo R, Cortinovis S, Fonte C, Gasparoni A. Antiinfective properties of human milk. J Nutr. 2008;138:S1801–6.
20. Pabst HF, Spady DW. Effect of breast-feeding on antibody response to conjugate vaccine. Lancet. 1990;336:269–70.
21. Mackie RI, Sghir A, Gaskins HR. Developmental microbial ecology of the neonatal gastrointestinal tract. Am J Clin Nutr. 1999;69:S1035–45.
22. Zivkovic AM, German JB, Lebrilla CB, Mills DA. Human milk glycobiome and its impact on the infant gastrointestinal microbiota. Proc Natl Acad Sci USA. Epub 2010 Aug 4.
23. Nduati R, Richardson BA, John G, Mbori-Ngacha D, Mwatha A, Ndinya-Achola J, Bwayo J, Onyango FE, Kreiss J. Effect of breastfeeding on mortality among HIV-1 infected women: a randomised trial. Lancet. 2001;357:1651–5.
24. Coutsoudis A, Coovadia H, Pillay K, Kuhn L. Are HIV-infected women who breastfeed at increased risk of mortality? AIDS. 2001; 15:653–5.
25. Kuhn L, Kasonde P, Sinkala M, Kankasa C, Semrau K, Vwalika C, Tsai WY, Aldrovandi GM, Thea DM. Prolonged breast-feeding and mortality up to two years post-partum among HIV-positive women in Zambia. AIDS. 2005;19:1677–81.
26. Sedgh G, Spiegelman D, Larsen U, Msamanga G, Fawzi WW. Breastfeeding and maternal HIV-1 disease progression and mortality. AIDS. 2004;18:1043–9.
27. Otieno PA, Brown ER, Mbori-Ngacha DA, Nduati RW, Farquhar C, Obimbo EM, Bosire RK, Emery S, Overbaugh J, et al. HIV-1 disease progression in breast-feeding and formula-feeding mothers: a prospective 2-year comparison of T cell subsets, HIV-1 RNA levels, and mortality. J Infect Dis. 2007;195:220–9.

28. Breastfeeding and HIV International Transmission Study Group. Mortality among HIV-1-infected women according to children's feeding modality: an individual patient data meta-analysis. J Acquir Immune Defic Syndr. 2005;39:430–8.
29. Papathakis PC, Van Loan MD, Rollins NC, Chantry CJ, Bennish ML, Brown KH. Body composition changes during lactation in HIV-infected and HIV-uninfected South African women. J Acquir Immune Defic Syndr. 2006;43:467–74.
30. Papathakis PC, Rollins NC, Chantry CJ, Bennish ML, Brown KH. Micronutrient status during lactation in HIV-infected and HIV-uninfected South African women during the first 6 mo after delivery. Am J Clin Nutr. 2007;85:182–92.
31. UNAIDS, WHO. Report on global AIDS epidemic; 2009 [cited 2009 Nov]. Available from: http://data.unaids.org/pub/Report/2009/jc1700_epi_update_2009_en.pdf.
32. Coutsoudis A, Dabis F, Fawzi W, Gaillard P, Haverkamp G, Harris DR, Jackson JB, Leroy V, Meda N, et al. Late postnatal transmission of HIV-1 in breast-fed children: an individual patient data meta-analysis. J Infect Dis. 2004;189:2154–66.
33. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, Alnwick DJ, Rogers M, Shaffer N. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. JAMA. 2000;283:1175–82.
34. Embree JE, Njenga S, Datta P, Nagelkerke NJ, Ndinya-Achola JO, Mohammed Z, Ramdahin S, Bwayo JJ, Plummer FA. Risk factors for postnatal mother-child transmission of HIV-1. AIDS. 2000;14:2535–41.
35. Coovadia HM, Bland RM. Preserving breastfeeding practice through the HIV pandemic. Trop Med Int Health. 2007;12:1116–33.
36. Liang K, Gui X, Zhang YZ, Zhuang K, Meyers K, Ho DD. A case series of 104 women infected with HIV-1 via blood transfusion postnatally: high rate of HIV-1 transmission to infants through breast-feeding. J Infect Dis. 2009;200:682–6.
37. Lunney KM, Iliff P, Mutasa K, Ntozini R, Magder LS, Moulton LH, Humphrey JH. Associations between breast milk viral load, mastitis, exclusive breast-feeding, and postnatal transmission of HIV. Clin Infect Dis. 2010;50:762–9.
38. Kuhn L, Aldrovandi G. Survival and health benefits of breastfeeding versus artificial feeding in infants of HIV-infected women: developing versus developed world. Clin Perinatol. 2010;37:843–62.
39. Kourtis AP, Lee FK, Abrams EJ, Jamieson DJ, Bulterys M. Mother-to-child transmission of HIV-1: timing and implications for prevention. Lancet Infect Dis. 2006;6:726–32.
40. WHO, UNICEF, UNAIDS, UNFPA. HIV and infant feeding. Update. Based on the technical consultation held on behalf of the Inter-agency Task Team (IATT) on Prevention of HIV Infection in Pregnant Women, Mothers and their Infants; 2006 Oct 25–27; Geneva, Switzerland; 2007 [cited 2010 Nov]. Available from: http://whqlibdoc.who.int/publications/2007/9789241595964_eng.pdf.
41. Mofenson LM. Prevention in neglected subpopulations: prevention of mother-to-child transmission of HIV infection. Clin Infect Dis. 2010; 50 Suppl 3:S130–48.
42. Duijts L, Jaddoe VWV, Hofman A, Moll HA. Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. Pediatrics. 2010;126:e18–25.
43. McNiel ME, Labbok MH, Abrahams SW. What are the risks associated with formula feeding? A re-analysis and review. Birth. 2010;37:50–8.
44. Chen A, Rogan WJ. Breastfeeding and the risk of postneonatal death in the United States. Pediatrics. 2004;113:e435–9.
45. Onyango-Makumbi C, Bagenda D, Mwatha A, Omer SB, Musoke P, Mmiro F, Zwerski SL, Kateera BA, Musisi M, et al. Early weaning of HIV-exposed uninfected infants and risk of serious gastroenteritis: findings from two perinatal HIV prevention trials in Kampala, Uganda. J Acquir Immune Defic Syndr. Epub 2009 Sep 25.
46. Kafulafula G, Hoover DR, Taha TE, Thigpen M, Li Q, Fowler MG, Kumwenda NI, Nkanaunena K, Mipando L, et al. Frequency of gastroenteritis and gastroenteritis-associated mortality with early weaning in HIV-1-uninfected children born to HIV-infected women in Malawi. J Acquir Immune Defic Syndr. 2010;53:6–13.
47. Arpadi S, Fawzy A, Aldrovandi GM, Kankasa C, Sinkala M, Mwiya M, Thea DM, Kuhn L. Growth faltering due to breastfeeding cessation in uninfected children born to HIV-infected mothers in Zambia. Am J Clin Nutr. 2009;90:344–53.
48. Lunney KM, Jenkins AL, Tavengwa NV, Majo F, Chidhanguro D, Iliff P, Strickland GT, Piwoz E, Iannotti L, et al. HIV-positive poor women may stop breast-feeding early to protect their infants from HIV infection although available replacement diets are grossly inadequate. J Nutr. 2008;138:351–7.
49. Mach O, Lu L, Creek T, Bowen A, Arvelo W, Smit M, Masunge J, Brennan M, Handzel T. Population-based study of a widespread outbreak of diarrhea associated with increased mortality and malnutrition in Botswana, January-March, 2006. Am J Trop Med Hyg. 2009; 80:812–8.
50. Creek TL, Kim A, Lu L, Bowen A, Masunge J, Arvelo W, Smit M, Mach O, Legwaila K, et al. Hospitalization and mortality among primarily nonbreastfed children during a large outbreak of diarrhea and malnutrition in Botswana, 2006. J Acquir Immune Defic Syndr. 2010;53:14–9.
51. Kuhn L, Aldrovandi GM, Sinkala M, Kankasa C, Semrau K, Kasonde P, Mwiya M, Tsai WY, Thea DM. Differential effects of early weaning for HIV-free survival of children born to HIV-infected mothers by severity of maternal disease. PLoS ONE. 2009;4:e6059.
52. WHO. HIV and infant feeding. Guidelines for decision makers. Geneva: WHO; 1998.
53. Latham MC, Preble EA. Appropriate feeding methods for infants of HIV infected mothers in sub-Saharan Africa. BMJ. 2000;320:1656–60.
54. Latham MC, Greiner T. Breastfeeding versus formula feeding in HIV infection. Lancet. 1998;352:737.
55. WHO Technical Consultation. New data on the prevention of mother-to-child transmission of HIV and their policy implications; 2001 [cited 2010 Dec]. Available from: http://whqlibdoc.who.int/hq/2001/WHO_RHR_01.28.pdf.
56. WHO. UNICEF, UNAIDS. HIV and infant feeding counseling: a training course: participants' manual; 2000 [cited 2010 Nov]. Available from: http://whqlibdoc.who.int/hq/2000/WHO_FCH_CAH_00.3.pdf.
57. Papathakis PC, Rollins NC. Are WHO/UNAIDS/UNICEF-recommended replacement milks for infants of HIV-infected mothers appropriate in the South African context? Bull World Health Organ. 2004;82:164–71.
58. Phadke MA, Gadgil B, Bharucha KE, Shrotri AN, Sastry J, Gupte NA, Brookmeyer R, Paranjape RS, Bulakh PM, et al. Replacement-fed infants born to HIV-infected mothers in India have a high early postpartum rate of hospitalization. J Nutr. 2003;133:3153–7.
59. Doherty T, Sanders D, Goga A, Jackson D. Implications of the new WHO guidelines on HIV and infant feeding for child survival in South Africa. Bull World Health Organ. 2011;89:62–7.
60. Coutsoudis A, Goga AE, Rollins N, Coovadia HM. Free formula milk for infants of HIV-infected women: blessing or curse? Health Policy Plan. 2002;17:154–60.
61. de Wagt A, Clark D. A review of UNICEF experience with the distribution of free infant formula for infants of HIV-infected mothers in Africa. Presented at the LINKAGES Art and Science of Breastfeeding Presentation Series; 2004 [cited 2010 Nov]. Available from: http://www.linkagesproject.org/media/publications/Technical%20Reports/InfantFormula_UNICEF_Art&Science.pdf.
62. CDC. Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus and acquired immunodeficiency syndrome. Morb Mortal Wkly Rep. 1985;34:721–6, 31–2.
63. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States; 2010 [cited 2010 Dec]. Available from: http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf.
64. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000–2006. AIDS. 2008;22:973–81.

65. Paul ME, Chantry CJ, Read JS, Frederick MM, Lu M, Pitt J, Turpin DB, Cooper ER, Handelsman EL. Morbidity and mortality during the first two years of life among uninfected children born to human immunodeficiency virus type 1-infected women: the women and infants transmission study. Pediatr Infect Dis J. 2005;24:46–56.
66. Mbori-Ngacha D, Nduati R, John G, Reilly M, Richardson B, Mwatha A, Ndinya-Achola J, Bwayo J, Kreiss J. Morbidity and mortality in breastfed and formula-fed infants of HIV-1-infected women: a randomized clinical trial. JAMA. 2001;286:2413–20.
67. Kent G. Breastfeeding vs formula-feeding among HIV-infected women in resource-poor areas. JAMA. 2002;287:1110, author reply 2–3.
68. Eastman A, Tompson M, Brussel C, Buchanan P, Crowe D, Fram JL, Hathaway J, McClain VW, Morrison P, et al. Breastfeeding vs formula-feeding among HIV-infected women in resource-poor areas. JAMA. 2002;287:1111, author reply 2–3.
69. Kuhn L, Reitz C, Abrams EJ. Breastfeeding and AIDS in the developing world. Curr Opin Pediatr. 2009;21:83–93.
70. Program Review Team, PMTCT Advisory Group, Infant Feeding Study Group. Evaluation of a pilot programme and a follow-up study of infant feeding practices during the scaled-up programme in Botswana. Eval Program Plann. 2002;25:421–31.
71. UNICEF, UNAIDS, WHO, UNFPA. HIV and infant feeding: a guide for health-care managers and supervisors; 2003 [cited 2011 Jan]. Available from: http://whqlibdoc.who.int/hq/2003/9241591234.pdf.
72. 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." Bull World Health Organ. 2006;84:90–6.
73. Manuela de Paoli M, Manongi R, Klepp K-I. Are infant feeding options that are recommended for mothers with HIV acceptable, feasible, affordable, sustainable and safe? Pregnant women's perspectives. Public Health Nutr. 2004;7:611–9.
74. Cames C, Mouquet-Rivier C, Traoré T, Ayassou KA, Kabore C, Bruyeron O, Simondon KB. A sustainable food support for non-breastfed infants: implementation and acceptability within a WHO mother-to-child HIV transmission prevention trial in Burkina Faso. Public Health Nutr. 2010;13:779–86.
75. Reynolds HW, Janowitz B, Wilcher R, Cates W. Contraception to prevent HIV-positive births: current contribution and potential cost savings in PEPFAR countries. Sex Transm Infect. 2008;84 Suppl 2: ii49–53.
76. Coutsoudis A, Pillay K, Spooner E, Kuhn L, Coovadia H. Influence of infant-feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa: a prospective cohort study. South African Vitamin A Study Group. Lancet. 1999;354:471–6.
77. Coutsoudis A, Pillay K, Kuhn L, Spooner E, Tsai W, Coovadia H. Method of feeding and transmission of HIV-1 from mothers to children by 15 months of age: prospective cohort study from Durban, South Africa. AIDS. 2001;15:379–87.
78. Iliff PJ, Piwoz EG, Tavengwa NV, Zunguza CD, Marinda ET, Nathoo KJ, Moulton LH, Ward BJ, Humphrey JH. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. AIDS. 2005;19:699–708.
79. Piwoz EG, Humphrey JH, Tavengwa NV, Iliff PJ, Marinda ET, Zunguza CD, Nathoo KJ, Mutasa K, Moulton LH, et al. The impact of safer breastfeeding practices on postnatal HIV-1 transmission in Zimbabwe. Am J Public Health. 2007;97:1249–54.
80. Coovadia HM, Rollins NC, Bland RM, Little K, Coutsoudis A, Bennish ML, Newell M-L. Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. Lancet. 2007;369:1107–16.
81. Taha TE, Kumwenda NI, Hoover DR, Kafulafula G, Fiscus SA, Nkhoma C, Chen S, Broadhead RL. The impact of breastfeeding on the health of HIV-positive mothers and their children in sub-Saharan Africa. Bull World Health Organ. 2006;84:546–54.
82. Bulterys M, Ellington S, Kourtis AP. HIV-1 and breastfeeding: biology of transmission and advances in prevention. Clin Perinatol. 2010;37: 807–24.
83. Kuhn L, Aldrovandi GM, Sinkala M, Kankasa C, Semrau K, Mwiya M, Kasonde P, Scott N, Vwalika C, et al. Effects of early, abrupt weaning on HIV-free survival of children in Zambia. N Engl J Med. 2008; 359:130–41.
84. Thea DM, Aldrovandi G, Kankasa C, Kasonde P, Decker WD, Semrau K, Sinkala M, Kuhn L. Post-weaning breast milk HIV-1 viral load, blood prolactin levels and breast milk volume. AIDS. 2006;20:1539–47.
85. WHO. Infant feeding HIV new guidelines. Geneva: WHO; 2010.
86. Kagaayi J, Gray RH, Brahmbhatt H, Kigozi G, Nalugoda F, Wabwire-Mangen F, Serwadda D, Sewankambo N, Ddungu V, et al. Survival of infants born to HIV-positive mothers, by feeding modality, in Rakai, Uganda. PLoS ONE. 2008;3:e3877.
87. Thior I, Lockman S, Smeaton L, Shapiro R, Wester C, Heymann S, Gilbert P, Stevens L, Peter T, et al. Breastfeeding plus infant zidovudine prophylaxis for 6 months vs formula feeding plus infant zidovudine for 1 month to reduce mother-to-child HIV transmission in Botswana: a randomized trial: the Mashi Study. JAMA. 2006;296:794–805.
88. WHO. HIV and infant feeding counselling tools: orientation guide for trainers; 2005 [cited 2010 Dec]. Available from: http://whqlibdoc.who.int/publications/2008/9789241596534_eng.pdf.
89. Thorley V. Sharing breastmilk: wet nursing, cross feeding, and milk donations. Breastfeed Rev. 2008;16:25–9.
90. Golden J. From wet nurse directory to milk bank: the delivery of human milk in Boston, 1909–1927. Bull Hist Med. 1988;62:589–605.
91. Arnold L. Global health policies that support the use of banked donor human milk: a human rights issue. Int Breastfeed J. 2006;1:26.
92. Arnold LD. HIV and breastmilk: what it means for milk banks. J Hum Lact. 1993;9:47–8.
93. Tully DB, Jones F, Tully MR. Donor milk: what's in it and what's not. J Hum Lact. 2001;17:152–5.
94. Renfrew MJ, Craig D, Dyson L, McCormick F, Rice S, King SE, Misso K, Stenhouse E, Williams AF. Breastfeeding promotion for infants in neonatal units: a systematic review and economic analysis. Health Technol Assess. 2009;13:1–146.
95. Arnold LDW. The cost-effectiveness of using banked donor milk in the neonatal intensive care unit: prevention of necrotizing enterocolitis. J Hum Lact. 2002;18:172–7.
96. WHO/UNICEF meeting on infant and young child feeding. J Nurse Midwifery. 1980;25:31–9.
97. Tully MR. Is pasteurized mother's own or donor milk an answer to the HIV crisis? J Hum Lact. 1999;15:345–6.
98. Global programme on AIDS. Consensus statement from the WHO/UNICEF consultation on HIV transmission and breast-feeding. Wkly Epidemiol Rec. 1992;67:177–9.
99. Maia PR, Novak FR, Almeida JA, Silva DA. The management strategy of the Brazilian National Network of Human Milk Banks. Cad Saude Publica. 2004;20:1700–8.
100. Giugliani ERJ. National Network of Human Milk Banks in Brazil: first class technology. J Pediatr (Rio J). 2002;78:183–4.
101. Almeida SG, Dórea JG. Quality control of banked milk in Brasilia, Brazil. J Hum Lact. 2006;22:335–9.
102. Pimenteira Thomaz AC, Maia Loureiro LV, da Silva Oliveira T, Furtado Montenegro NC, Dantas Almeida Júnior E, Fernando Rodrigues Soriano C, Calado Cavalcante J. The human milk donation experience: motives, influencing factors, and regular donation. J Hum Lact. 2008;24:69–76.
103. ACE InterMed. [cited 2010 Dec]. Available from: www.ace-intermed.com/sbp.
104. Lawrence RA, Lawrence RM. Breastfeeding: a guide for the medical profession. St. Louis: Mosby; 2005.
105. Jeffery BS, Webber L, Mokhondo KR, Erasmus D. Determination of the effectiveness of inactivation of human immunodeficiency virus by Pretoria pasteurization. J Trop Pediatr. 2001;47:345–9.
106. Israel-Ballard K, Chantry C, Dewey K, Lonnerdal B, Sheppard H, Donovan R, Carlson J, Sage A, Abrams B. Viral, nutritional, and bacterial safety of flash-heated and Pretoria-pasteurized breast milk to prevent mother-to-child transmission of HIV in resource-poor countries: a pilot study. J Acquir Immune Defic Syndr. 2005;40:175–81.

107. Israel-Ballard K, Donovan R, Chantry C, Coutsoudis A, Sheppard H, Sibeko L, Abrams B. Flash-heat inactivation of HIV-1 in human milk: a potential method to reduce postnatal transmission in developing countries. J Acquir Immune Defic Syndr. 2007;45:318–23.
108. Israel-Ballard K, Coutsoudis A, Chantry CJ, Sturm AW, Karim F, Sibeko L, Abrams B. Bacterial safety of flash-heated and unheated expressed breastmilk during storage. J Trop Pediatr. 2006;52:399–405.
109. Israel-Ballard KA, Abrams BF, Coutsoudis A, Sibeko LN, Cheryk LA, Chantry CJ. Vitamin content of breast milk from HIV-1-infected mothers before and after flash-heat treatment. J Acquir Immune Defic Syndr. 2008;48:444–9.
110. Chantry CJ, Israel-Ballard K, Moldoveanu Z, Peerson J, Coutsoudis A, Sibeko L, Abrams B. Effect of flash-heat treatment on immunoglobulins in breast milk. J Acquir Immune Defic Syndr. 2009;51:264–7.
111. Sibeko LN, Nzuza S, Coutsoudis A, Gray-Donald, K. Heat-treated expressed breast milk is a feasible feeding option for South African mothers living with HIV: a mixed methods approach. AIDS 2008 XVII International AIDS Conference; Mexico City. Abstract no. MOPE0507.
112. Young SL, Chantry CJ, Ngonyani MM, Israel-Ballard K, Ash DM, Nyambo MT. Flash-heating breastmilk is feasible in Dar es Salaam, Tanzania. FASEB J. 2009:LB443.
113. Chantry CJ, Young SL, Ngonyani M, Israel-Ballard K, Ash D, Nyambo M. Feasibility of Flash-heating breastmilk to reduce maternal to child transmission of HIV. Denver: American Public Health Association; 2010. p. 4198.0.
114. Mbuya MN, Humphrey JH, Majo F, Chasekwa B, Jenkins A, Israel-Ballard K, Muti M, Paul KH, Madzima RC, et al. Heat treatment of expressed breast milk is a feasible option for feeding HIV-exposed, uninfected children after 6 months of age in rural Zimbabwe. J Nutr. 2010;140:1481–8.
115. Pantazis A, Israel-Ballard KC, Van Zyl C, Mukandagano P, Kayumba J, Nyirahabineza A. Evaluating the implementation of flash-heating breast milk as part of the infant and young child feeding program in Rwanda. AIDS 2010 – XVIII International AIDS Conference: CD Abstract. Vienna; 2010.
116. Guay LA, Musoke P, Fleming T, Bagenda D, Allen M, Nakabiito C, Sherman J, Bakaki P, Ducar C, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. Lancet. 1999;354:795–802.
117. UNAIDS. Report on the global HIV/AIDS epidemic; 2002 [cited 2010 Dec]. Available from: http://data.unaids.org/pub/Report/2002/brglobal_aids_report_en_pdf_red_en.pdf.
118. WHO. Antiretroviral therapy for HIV infection in adults and adolescents; 2010 [cited 2010 Nov]. Available from: http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf.
119. Sturt AS, Dokubo EK, Sint TT. Antiretroviral therapy (ART) for treating HIV infection in ART-eligible pregnant women. Cochrane Database Syst Rev. 2010;CD008440.
120. Kumwenda NI, Hoover DR, Mofenson LM, Thigpen MC, Kafulafula G, Li Q, Mipando L, Nkanaunena K, Mebrahtu T, et al. Extended antiretroviral prophylaxis to reduce breast-milk HIV-1 transmission. N Engl J Med. 2008;359:119–29.
121. Marazzi MC, Liotta G, Nielsen-Saines K, Haswell J, Magid NA, Buonomo E, Scarcella P, Altan AMD, Mancinelli S, et al. Extended antenatal antiretroviral use correlates with improved infant outcomes throughout the first year of life. AIDS. 2010;24:2819–26.
122. Kilewo C, Karlsson K, Massawe A, Lyamuya E, Swai A, Mhalu F, Biberfeld G, Team MS. Prevention of mother-to-child transmission of HIV-1 through breast-feeding by treating infants prophylactically with lamivudine in Dar es Salaam, Tanzania: the Mitra Study. J Acquir Immune Defic Syndr. 2008;48:315–23.
123. Kesho Bora Study Group. Eighteen-month follow-up of HIV-1-infected mothers and their children enrolled in the Kesho Bora study observational cohorts. J Acquir Immune Defic Syndr. 2010;54:533–41.
124. Shapiro RL, Hughes MD, Ogwu A, Kitch D, Lockman S, Moffat C, Makhema J, Moyo S, Thior I, et al. Antiretroviral regimens in pregnancy and breast-feeding in Botswana. N Engl J Med. 2010;362:2282–94.
125. WHO. UNAIDS, UNICEF. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector; 2010 [cited 2010 Nov]. Available from: http://whqlibdoc.who.int/publications/2010/9789241500395_eng.pdf.
126. UNAIDS, WHO. Report on global AIDS epidemic; 2010 [cited 2010 Nov]. Available from: http://www.unaids.org/documents/20101123_GlobalReport_em.pdf.
127. Nakakeeto ON, Umaranayake L. The global strategy to eliminate HIV infection in infants and young children: a seven-country assessment of costs and feasibility. AIDS. 2009;23:987–95.
128. Stringer EM, Ekouevi DK, Coetzee D, Tih PM, Creek TL, Stinson K, Giganti MJ, Welty TK, Chintu N, et al. Coverage of nevirapine-based services to prevent mother-to-child HIV transmission in 4 African countries. JAMA. 2010;304:293–302.
129. Tanoh A. Performance based financing: an impact evaluation on prevention and care and treatment activities. HIV/AIDS Implementers' Meeting; 2009 June 10–14; Windhoek, Namibia. Abstract no. 1084.
130. Manongi RN, Marchant TC, Bygbjerg IC. Improving motivation among primary health care workers in Tanzania: a health worker perspective. Hum Resour Health. 2006;4:6.
131. Dieleman M. Triggering meaningful change. Human resources management and health worker performance in an AIDS-endemic setting. Amsterdam: Free University of Amsterdam; 2010.
132. Toure H, Audibert M, Dabis F. To what extent could performance-based schemes help increase the effectiveness of prevention of mother-to-child transmission of HIV (PMTCT) programs in resource-limited settings? A summary of the published evidence. BMC Public Health. 2010;10:702.
133. UNICEF. Children and AIDS. Fifth Stocktaking Report; 2010 [cited 2010 Dec 14]. Available from: http://www.unicef.org/media/files/Children_and_AIDS-Fifth_Stocktaking_Report_2010_111610.pdf.
134. Kuhn L, Aldrovandi GM, Sinkala M, Kankasa C, Mwiya M, Thea DM. Potential impact of new WHO criteria for antiretroviral treatment for prevention of mother-to- child HIV transmission. AIDS. 2010;24:1374–7.
135. Myer L, Rabkin M, Abrams EJ, Rosenfield A, El-Sadr WM. Focus on women: linking HIV care and treatment with reproductive health services in the MTCT-Plus Initiative. Reprod Health Matters. 2005;13:136–46.
136. Nkonki LL, Doherty TM, Hill Z, Chopra M, Schaay N, Kendall C. Missed opportunities for participation in prevention of mother to child transmission programmes: simplicity of nevirapine does not necessarily lead to optimal uptake, a qualitative study. AIDS Res Ther. 2007;4:27.
137. Muhamadi L, Nsabagasani X, Tumwesigye MN, Wabwire-Mangen F, Ekström A-M, Peterson S, Pariyo G. Inadequate pre-antiretroviral care, stock-out of antiretroviral drugs and stigma: policy challenges/bottlenecks to the new WHO recommendations for earlier initiation of antiretroviral therapy (CD<350 cells/microL) in eastern Uganda. Health Policy. 2010;97:187–94.
138. Desmond C, Bland R, Boyce G, Coovadia H, Coutsoudis A, Rollins N, Newell M. Scaling-up exclusive breastfeeding support programmes: the example of KwaZulu-Natal. PLoS ONE. 2008;3:e2454.
139. Menon P, Mbuya M, Habicht JP, Pelto G, Loechl CU, Ruel MT. Assessing supervisory and motivational factors in the context of a program evaluation in rural Haiti. J Nutr. 2008;138:634–7.
140. Corneli AL, Piwoz EG, Bentley ME, Moses A, Nkhoma JR, Tohill BC, Adair L, Mtimuni B, Ahmed Y, et al. Involving communities in the design of clinical trial protocols: the BAN Study in Lilongwe, Malawi. Contemp Clin Trials. 2007;28:59–67.
141. Tonwe-Gold B, Ekouevi DK, Bosse CA, Toure S, Koné M, Becquet R, Leroy V, Toro P, Dabis F, et al. Implementing family-focused HIV care and treatment: the first 2 years' experience of the mother-to-child transmission-plus program in Abidjan, Côte d'Ivoire. Trop Med Int Health. 2009;14:204–12.
142. UNICEF. Innovation for an HIV-free generation: The Mother-Baby Pack; 2010 [cited 2010 Dec]. Available from: http://www.unicef.org/

videoaudio/PDFs/UNICEF_Mother_Baby_Pack_one_pager_October_2010media.pdf.
143. MacLeod IJ, Rowley CF, Thior I, Wester C, Makhema J, Essex M, Lockman S. Minor resistant variants in nevirapine-exposed infants may predict virologic failure on nevirapine-containing ART. J Clin Virol. 2010;48:162–7.
144. Levy JM, Webb AL, Sellen DW. "On our own, we can't manage": experiences with infant feeding recommendations among Malawian mothers living with HIV. Int Breastfeed J. 2010;5:15.
145. Moland KMI, van Esterik P, Sellen DW, de Paoli MM, Leshabari SC, Blystad A. Ways ahead: protecting, promoting and supporting breastfeeding in the context of HIV. Int Breastfeed J. 2010;5:19.
146. Chopra M, Rollins N. Infant feeding in the time of HIV: rapid assessment of infant feeding policy and programmes in four African countries scaling up prevention of mother to child transmission programmes. Arch Dis Child. 2008;93:288–91.
147. Nankunda J, Tumwine JK, Nankabirwa V, Tylleskar T. Study Group P-E. "She would sit with me": mothers' experiences of individual peer support for exclusive breastfeeding in Uganda. Int Breastfeed J. 2010;5:16.
148. Obermeyer CM, Castle S. Back to nature? Historical and cross-cultural perspectives on barriers to optimal breastfeeding. Med Anthropol. 1996;17:39–63.
149. Thairu LN, Pelto GH, Rollins NC, Bland RM, Ntshangase N. Socio-cultural influences on infant feeding decisions among HIV-infected women in rural Kwa-Zulu Natal, South Africa. Matern Child Nutr. 2005;1:2–10.
150. Buskens I, Jaffe A, Mkhatshwa H. Infant feeding practices: realities and mind sets of mothers in Southern Africa. AIDS Care. 2007;19:1101–9.
151. Piwoz EG, Bentley ME. Women's voices, women's choices: the challenge of nutrition and HIV/AIDS. J Nutr. 2005;135:933–7.
152. Webb-Girard A, Cherobon A, Mbugua S, Kamau-Mbuthia E, Amin A, Sellen DW. Food insecurity is associated with attitudes towards exclusive breastfeeding among women in urban Kenya. Matern Child Nutr. Epub 2010 Sep 28.
153. Bentley ME, Corneli AL, Piwoz E, Moses A, Nkhoma J, Tohill BC, Ahmed Y, Adair L, Jamieson DJ, van der Horst C. Perceptions of the role of maternal nutrition in HIV-positive breast-feeding women in Malawi. J Nutr. 2005;135:945–9.
154. Quinn VJ, Guyon AB, Schubert JW, Stone-Jimenez M, Hainsworth MD, Martin LH. Improving breastfeeding practices on a broad scale at the community level: success stories from Africa and Latin America. J Hum Lact. 2005;21:345–54.
155. WHO. UNICEF. Global strategy for infant and young child feeding; 2003 [cited 2010 Dec]. Available from: http://whqlibdoc.who.int/publications/2003/9241562218.pdf.
156. de Paoli MM, Manongi R, Klepp KI. Counsellors' perspectives on antenatal HIV testing and infant feeding dilemmas facing women with HIV in northern Tanzania. Reprod Health Matters. 2002;10:144–56.
157. Orne-Gliemann J, Mukotekwa T, Miller A, Perez F, Glenshaw M, Nesara P, Dabis F. Community-based assessment of infant feeding practices within a programme for prevention of mother-to-child HIV transmission in rural Zimbabwe. Public Health Nutr. 2006;9:563–9.
158. Fadnes LT, Engebretsen IM, Wamani H, Wangisi J, Tumwine JK, Tylleskar T. Need to optimise infant feeding counselling: a cross-sectional survey among HIV-positive mothers in Eastern Uganda. BMC Pediatr. 2009;9:2.
159. Coutsoudis A. Infant feeding dilemmas created by HIV: South African experiences. J Nutr. 2005;135:956–9.
160. Frontières MS. Help wanted: confronting the health care worker crisis to expand access to HIV/AIDS treatment: MSF experience in southern Africa; 2007 [cited 2010 Dec]. Available from: http://www.doctorswithoutborders.org/publications/reports/2007/healthcare_worker_report_05–2007.pdf.
161. Connell J, Zurn P, Stilwell B, Awases M, Braichet JM. Sub-Saharan Africa: beyond the health worker migration crisis? Soc Sci Med. 2007;64:1876–91.
162. Haider R, Ashworth A, Kabir I, Huttly S. Effect of community-based peer counsellors on exclusive breastfeeding practices in Dhaka, Bangladesh: a randomised controlled trial. [see commments] Lancet. 2000;356:1643–7.
163. Morrow AL, Guerrero ML, Shults J, Calva JJ, Lutter C, Bravo J, Ruiz-Palacios G, Morrow RC, Butterfoss FD. Efficacy of home-based peer counselling to promote exclusive breastfeeding: a randomised controlled trial. Lancet. 1999;353:1226–31.
164. Leite AJ, Puccini RF, Atalah AN, Alves Da Cunha AL, Machado MT. Effectiveness of home-based peer counselling to promote breastfeeding in the northeast of Brazil: a randomized clinical trial. Acta Paediatr. 2005;94:741–6.
165. Bland RM, Little KE, Coovadia HM, Coutsoudis A, Rollins NC, Newell ML. Intervention to promote exclusive breast-feeding for the first 6 months of life in a high HIV prevalence area. AIDS. 2008;22:883–91.
166. WHO. Learning from large-scale community-based programmes to improve breastfeeding practices; 2008 [cited 2010 Dec]. Available from: http://whqlibdoc.who.int/publications/2008/9789241597371_eng.pdf.
167. Etienne M, Burrows L, Osotimehin B, Macharia T, Hossain B, Redfield RR, Amoroso A. Situational analysis of varying models of adherence support and loss to follow up rates; findings from 27 treatment facilities in eight resource limited countries. Trop Med Int Health. 2010;15 Suppl 1:76–81.
168. Abaasa AM, Todd J, Ekoru K, Kalyango JN, Levin J, Odeke E, Karamagi CA. Good adherence to HAART and improved survival in a community HIV/AIDS treatment and care programme: the experience of The AIDS Support Organization (TASO), Kampala, Uganda. BMC Health Serv Res. 2008;8:241.
169. Egwaga S, Mkopi A, Range N, Haag-Arbenz V, Baraka A, Grewal P, Cobelens F, Mshinda H, Lwilla F, van Leth F. Patient-centred tuberculosis treatment delivery under programmatic conditions in Tanzania: a cohort study. BMC Med. 2009;7:80.
170. Young SL, Chantry CJ, Vosti SA, Rennie WA. Infant feeding counseling: a neglected strategy for the reduction of mother-to-child transmission. AIDS. 2009;23:2543–4, author reply 4.
171. Futterman D, Shea J, Besser M, Stafford S, Desmond K, Comulada WS, Greco E. Mamekhaya: a pilot study combining a cognitive-behavioral intervention and mentor mothers with PMTCT services in South Africa. AIDS Care. 2010;22:1093–100.
172. Nguyen TA, Oosterhoff P, Ngoc YP, Wright P, Hardon A. Barriers to access prevention of mother-to-child transmission for HIV positive women in a well-resourced setting in Vietnam. AIDS Res Ther. 2008;5:7.
173. Falnes EF, Tylleskär T, de Paoli MM, Manongi R, Engebretsen IMS. Mothers' knowledge and utilization of prevention of mother to child transmission services in northern Tanzania. J Int AIDS Soc. 2010;13:36.
174. Horwood C, Haskins L, Vermaak K, Phakathi S, Subbaye R, Doherty T. Prevention of mother to child transmission of HIV (PMTCT) programme in KwaZulu-Natal, South Africa: an evaluation of PMTCT implementation and integration into routine maternal, child and women's health services. Trop Med Int Health. Epub 2010 Jun 17.
175. Nassali M, Nakanjako D, Kyabayinze D, Beyeza J, Okoth A, Mutyaba T. Access to HIV/AIDS care for mothers and children in sub-Saharan Africa: adherence to the postnatal PMTCT program. AIDS Care. 2009;21:1124–31.
176. Young SL, Israel-Ballard KA, Dantzer EA, Ngonyani MM, Nyambo MT, Ash DM, Chantry CJ. Infant feeding practices among HIV-positive women in Dar es Salaam, Tanzania, indicate a need for more intensive infant feeding counselling. Public Health Nutr. 2010;13:2027–33.
177. Leshabari SC, Blystad A, de Paoli M, Moland KM. HIV and infant feeding counselling: challenges faced by nurse-counsellors in northern Tanzania. Hum Resour Health. 2007;5:18.
178. Medley A, Garcia-Moreno C, McGill S, Maman S. Rates, barriers and outcomes of HIV serostatus disclosure among women in developing countries: implications for prevention of mother-to-child transmission programmes. Bull World Health Organ. 2004;82:299–307.

179. Delvaux T, Elul B, Ndagije F, Munyana E, Roberfroid D, Asiimwe A. Determinants of nonadherence to a single-dose nevirapine regimen for the prevention of mother-to-child HIV transmission in Rwanda. J Acquir Immune Defic Syndr. 2009;50:223–30.
180. Njunga J, Blystad A. 'The divorce program': gendered experiences of HIV positive mothers enrolled in PMTCT programs: the case of rural Malawi. Int Breastfeed J. 2010;5:14.
181. Bwirire LD, Fitzgerald M, Zachariah R, Chikafa V, Massaquoi M, Moens M, Kamoto K, Schouten EJ. Reasons for loss to follow-up among mothers registered in a prevention-of-mother-to-child transmission program in rural Malawi. Trans R Soc Trop Med Hyg. 2008;102: 1195–200.
182. Varga C, Brookes H. Factors influencing teen mothers' enrollment and participation in prevention of mother-to-child HIV transmission services in Limpopo Province, South Africa. Qual Health Res. 2008;18: 786–802.
183. Mbonye AK, Hansen KS, Wamono F, Magnussen P. Barriers to prevention of mother-to-child transmission of HIV services in Uganda. J Biosoc Sci. 2010;42:271–83.
184. Sibeko L, Coutsoudis A, Nzuza S, Gray-Donald K. Mothers' infant feeding experiences: constraints and supports for optimal feeding in an HIV-impacted urban community in South Africa. Public Health Nutr. 2009;12:1983–90.
185. O'Gorman DA, Nyirenda LJ, Theobald SJ. Prevention of mother-to-child transmission of HIV infection: views and perceptions about swallowing nevirapine in rural Lilongwe, Malawi. BMC Public Health. 2010;10:354.
186. Allen S, Karita E, Chomba E, Roth DL, Telfair J, Zulu I, Clark L, Kancheya N, Conkling M, et al. Promotion of couples' voluntary counselling and testing for HIV through influential networks in two African capital cities. BMC Public Health. 2007;7:349.
187. Kairania R, Gray RH, Kiwanuka N, Makumbi F, Sewankambo NK, Serwadda D, Nalugoda F, Kigozi G, Semanda J, Wawer MJ. Disclosure of HIV results among discordant couples in Rakai, Uganda: a facilitated couple counselling approach. AIDS Care. 2010;22:1041–51.
188. Auvinen J, Suominen T, Valimaki M. Male participation and prevention of human immunodeficiency virus (HIV) mother-to-child transmission in Africa. Psychol Health Med. 2010;15:288–313.
189. Msuya SE, Mbizvo EM, Hussain A, Uriyo J, Sam NE, Stray-Pedersen B. Low male partner participation in antenatal HIV counselling and testing in northern Tanzania: implications for preventive programs. AIDS Care. 2008;20:700–9.
190. Theuring S, Nchimbi P, Jordan-Harder B, Harms G. Partner involvement in perinatal care and PMTCT services in Mbeya Region, Tanzania: the providers' perspective. AIDS Care. 2010;22:1562–8.
191. Byamugisha R, Tumwine JK, Semiyaga N, Tylleskär T. Determinants of male involvement in the prevention of mother-to-child transmission of HIV programme in Eastern Uganda: a cross-sectional survey. Reprod Health. 2010;7:12.
192. Orne-Gliemann J, Tchendjou PT, Miric M, Gadgil M, Butsashvili M, Eboko F, Perez-Then E, Darak S, Kulkarni S, et al. Couple-oriented prenatal HIV counseling for HIV primary prevention: an acceptability study. BMC Public Health. 2010;10:197.
193. Taha TE, Kumwenda J, Cole SR, Hoover DR, Kafulafula G, Fowler MG, Thigpen MC, Li Q, Kumwenda NI, Mofenson L. Postnatal HIV-1 transmission after cessation of infant extended antiretroviral prophylaxis and effect of maternal highly active antiretroviral therapy. J Infect Dis. 2009;200:1490–7.
194. Lindblade KA, Odhiambo F, Rosen DH, DeCock KM. Health and nutritional status of orphans <6 years old cared for by relatives in western Kenya. Trop Med Int Health. 2003;8:67–72.
195. UNICEF. iThemba Lethu breast milk bank; 2009 [cited 2010 Dec 12]. Available from: http://www.unicef.org/southafrica/hiv_aids_809.html.
196. Luchters SM, Veldhuijzen NJ, Nsanzabera D, Kankindi B, Tuyizere S, Paxton WA, Nyaruhirira I, Leeuwen van R, Wit FW, et al. A phase I/II, randomized, placebo controlled study to evaluate chloroquine administration to reduce HIV-1 RNA in breast milk in an HIV-1 infected-breastfeeding population: The CHARGE study. International Conference on AIDS; 2004; Bangkok, Thailand. Abstract no. TuPeB4499; 2004.
197. Hartmann SU, Wigdahl B, Neely EB, Berlin CM, Schengrund C-L, Lin H-M, Howett MK. Biochemical analysis of human milk treated with sodium dodecyl sulfate, an alkyl sulfate microbicide that inactivates human immunodeficiency virus type 1. J Hum Lact. 2006;22:61–74.
198. Israel-Ballard K, Hart C, Thungu F, Joanis C, Baniecki M, Sokal D. Acceptability of a modified nipple shield device to reduce breast milk transmission of HIV in developing countries: a qualitative study. AIDS 2010 – XVIII International AIDS Conference; 2010; Vienna; 2010. Abstract MOPE0231.
199. Luzuriaga K, Newell M-L, Dabis F, Excler J-L, Sullivan JL. Vaccines to prevent transmission of HIV-1 via breastmilk: scientific and logistical priorities. Lancet. 2006;368:511–21.
200. Walls T, Palasanthiran P, Studdert J, Moran K, Ziegler JB. Breastfeeding in mothers with HIV. J Paediatr Child Health. 2010;46:349–52.
201. Giles M, Mijch A. Breast milk pasteurisation in developed countries to reduce HIV transmission. Do the benefits outweigh the risks? Infect Dis Obstet Gynecol. 2005;13:237–40.
202. UK Department of Health. HIV and infant feeding: guidance from the UK Chief Medical Offices' Expert Advisory Group on AIDS; 2004 [cited 2010 Dec 1]. Available from: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4089892.
203. Chantry CJ, Abrams BF, Donovan RM, Israel-Ballard KA, Sheppard HW. Breast milk pasteurization: appropriate assays to detect HIV inactivation. Infect Dis Obstet Gynecol. 2006;2006:95938.
204. Humphrey JH. Child undernutrition, tropical enteropathy, toilets, and handwashing. Lancet. 2009;374:1032–5.
205. Habicht JP, DaVanzo J, Butz WP. Mother's milk and sewage: their interactive effects on infant mortality. Pediatrics. 1988;81:456–61.
206. WHO. Complementary feeding. Report of the global consultation and summary of guiding principles; 2002 [cited 2010 Dec]. Available from: http://whqlibdoc.who.int/publications/2002/924154614X.pdf.
207. WHO. Indicators for assessing infant and young child feeding practices. Part 1: definitions. Conclusions of a consensus meeting held 6–8 November 2007 in Washington D.C.; 2008 [cited 2010 Nov]. Available from: http://whqlibdoc.who.int/publications/2008/9789241596664_eng.pdf.
208. UNICEF. Facts for life; 2010 [cited 2010 Dec]. Available from: http://www.factsforlifeglobal.org/resources/factsforlife-en-full.pdf.
209. Labbok M, Krasovec K. Toward consistency in breastfeeding definitions. Stud Fam Plann. 1990;21:226–30.
210. AVERT. Preventing mother to child transmission (PMTCT) in practice; 2010 [cited 2010 Dec]. Available from: http://www.avert.org/pmtct-hiv.htm.