

PREVENTING MOTHER-TO-CHILD TRANSMISSION OF HIV

A STRATEGIC FRAMEWORK

This work was supported by the United States Agency for International Development (USAID) as part of Family Health International's (FHI) Implementing AIDS Prevention and Care (IMPACT) Project (Cooperative Agreement HRN-A-00-97-0017-00) and does not necessarily reflect the views of USAID or FHI.

FHI implements the USAID IMPACT Project in partnership with the Institute of Tropical Medicine, Management Sciences for Health, Population Services International, Program for Appropriate Technology in Health and the University of North Carolina at Chapel Hill.

© June 2004
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Table of Contents

I. INTRODUCTION	1
II. STATE-OF-THE-ART	1
Preventing Primary HIV Infection.....	2
Preventing Unintended Pregnancies Among HIV-Infected Women	4
Preventing HIV Transmission from Infected Women to Their Children	4
Improving Availability, Quality and Use of Maternal and Child Health (MCH) Services	5
HIV Counseling and Testing in the Context of PMTCT Services.....	5
Antiretroviral Chemoprophylaxis for PMTCT.....	7
Infant-Feeding Counseling and Support	8
Safer Obstetric Practices	10
Providing Care to HIV-Infected Mothers and Their Infants and Families (MTCT-Plus)	10
III. FHI GOALS AND OBJECTIVES	11
IV. FHI'S TECHNICAL AND PROGRAMMATIC APPROACHES	11
Guiding Principles	11
FHI's Approaches	12
Programmatic Approach	13
Global and Regional Activities.....	13
National Level	14
Implementation Level: MCH/PMTCT Services.....	15
Technical Approach.....	15
Counseling and Testing in ANC Settings.....	15
Antiretroviral Chemoprophylaxis and Therapy.....	17
Infant-Feeding Counseling and Support	16
Stigma and Discrimination	16
Research and Evaluation.....	16
V. ILLUSTRATIVE ACTIVITIES	17
Fund and Provide Technical Assistance to Implement PMTCT in Kenya	17
Fund and Provide Technical Support to Implement PMTCT Sites in Rwanda	17
Fund and Provide Technical Assistance to Implement PMTCT in Guyana.....	17
Provide Technical Assistance to Implement PMTCT in Nigeria.....	17
Provide Technical Assistance to PMTCT Sites Funded by the Elizabeth Glaser Pediatric AIDS Foundation.....	18
VI. INTERVENTION-LINKED RESEARCH	18
VII. COST AND COST-EFFECTIVENESS	18
VIII. MONITORING AND EVALUATION	19
IX. LINKAGES AND PARTNERSHIPS.....	20
ANNEX I	21
X. REFERENCES	27
XI. FURTHER READING.....	30

I. INTRODUCTION

Mother-to-child transmission (MTCT) of HIV accounts for over 90 percent of HIV infections among young children. In the absence of interventions to prevent MTCT, 30 percent of infants born to HIV-infected women will become infected during pregnancy, labor and delivery, or through breastfeeding. In 2003 alone, there were an estimated 700,000 new infections and 500,000 HIV-related deaths among children under 15 years of age (1).

Reported rates of mother-to-child HIV transmission in the absence of any intervention are higher in developing countries (25-45 percent) than in industrialized countries (15-25 percent) (2). Offering HIV testing as part of routine antenatal care, combination antiretroviral drug regimens, and elective cesarean section and advising complete avoidance of breastfeeding has cut MTCT transmission of HIV to below 2 percent among the limited number of HIV-infected women in developed countries. However, in the developing nations where the vast majority of HIV-infected women of childbearing age reside, MTCT rates remain high due to lack of access to feasible, affordable prevention interventions and are compounded by the nearly universal practice of breastfeeding for prolonged periods of time.

Implementing prevention of mother-to-child transmission (PMTCT) interventions poses significant challenges in resource-poor settings. However, lessons from such diverse countries as Thailand and Uganda, where simpler but effective MTCT interventions have been tested and quickly adapted into national programs, provide evidence that services can be made available to mothers in other middle- and low-income countries.

With close to 2,000 new pediatric HIV infections daily and PMTCT coverage rates as low as 1 percent in some of the countries most affected by HIV/AIDS, the rapid scale-up of PMTCT interventions must be considered an emergency effort. In June 2001, the United Nations General Assembly Special Session on HIV/AIDS (UNGASS) declared its commitment to reducing the proportion of HIV-infected infants by 20 percent by 2005 and by 50 percent by 2010. Global commitment to increase access to care and treatment for persons infected with HIV, including the U.S. government's Presidential Emergency Plan for AIDS Relief (PEPFAR) and the World Health Organization's "3 by 5" initiative, is growing, and PMTCT is a critical point of entry to care, particularly for HIV-infected women and their families.

This paper outlines Family Health International's (FHI) evidence-based strategy and its efforts to rapidly scale-up PMTCT interventions in resource-constrained countries.

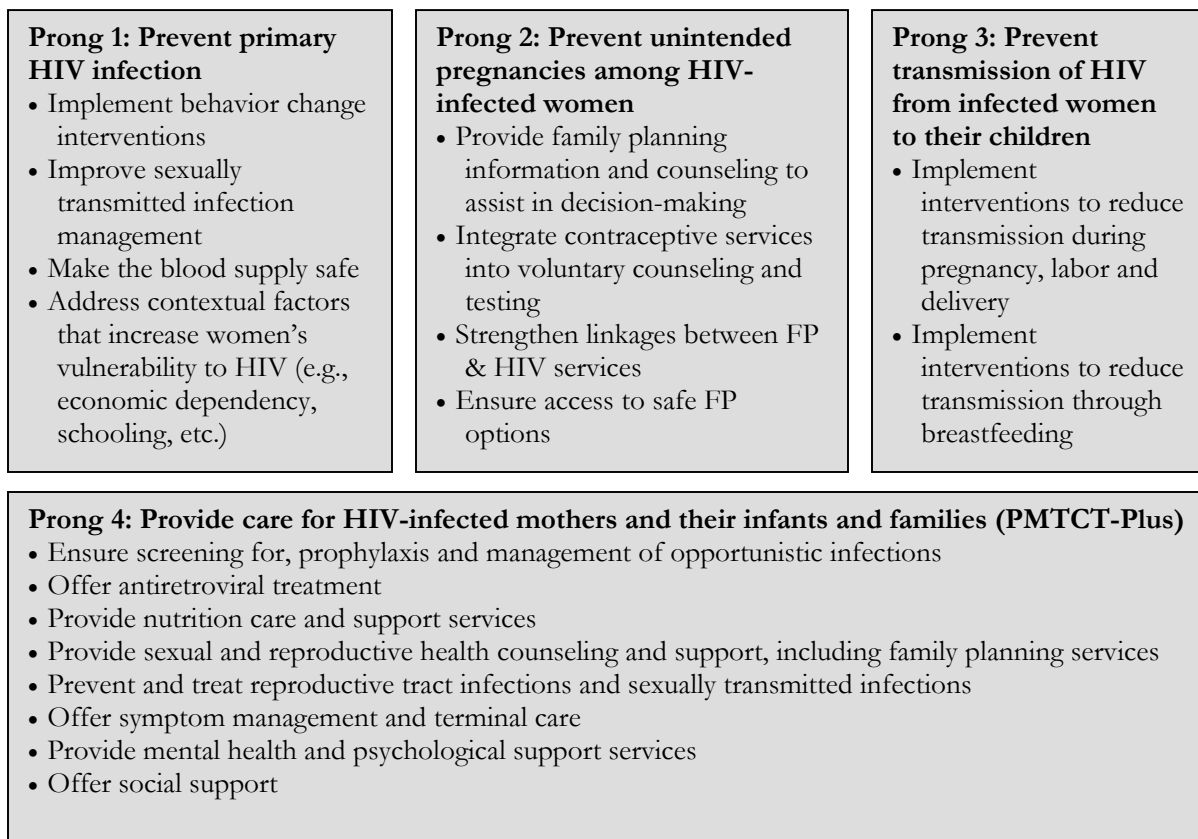
II. STATE-OF-THE-ART PMTCT INTERVENTIONS

Scientific progress in understanding MTCT, the availability of specific interventions to prevent MTCT and collective international experience over the last decade have provided better opportunities to reduce the number of children born with HIV worldwide. To significantly impact the pediatric HIV epidemic, the World Health Organization (WHO) and the United Nations (UN) have articulated a comprehensive, four-pronged strategic framework for preventing mother-to-child transmission of HIV:

1. Prevent primary HIV infections
2. Prevent unintended pregnancies among HIV-infected women
3. Prevent transmission of HIV from infected women to their children
4. Provide care for HIV-infected mothers and their infants and families (known as PMTCT-Plus) (3)

The simultaneous implementation of all four “prongs” of PMTCT at all levels in an environment that challenges and works to combat stigma and discrimination provides the only real hope for achieving international goals for PMTCT. Figure 1 below shows the four prongs and some examples of specific strategies for each.

Figure 1: The Four Prongs of a Comprehensive Program to Prevent MTCT



1. Preventing Primary HIV Infection

Preventing HIV in women, particularly young women, and their partners is the best way to ensure that secondary transmission to infants does not occur. The majority of HIV infections around the world are among young people age 10 to 24. Girls and young women account for most new infections among this age group, and the majority of women attending MCH clinics for pregnancy-related care are 15-to-24 years old. During these years, youth learn, explore and make decisions that will affect the rest of their lives. Without the information, skills and services they need to make informed choices, young people are more

likely to engage in risky behaviors that result in high rates of sexually transmitted infections (STIs), including HIV, and early and unintended pregnancies. By recognizing that youth are a complex group requiring segmenting based on age, gender, geographic setting, family, school and civil status, and special needs, interventions have enormous potential to turn the tide of HIV infections among youth, and ultimately to reduce mother-to-child transmission. A range of HIV prevention and broader community development initiatives—including behavior change communication (BCC) programs such as peer education targeting in-school and out-of-school youth—are underway in many countries. Other strategies include providing information through channels that young people enjoy—the media, theater, live arts and technology—and through anonymous sources such as hotlines and the internet. Enrolling and keeping girls in school also has been directly linked to delaying the start of sexual activity and preventing HIV infection.

Another approach to preventing primary HIV infections is through large-scale STI interventions. STIs are linked to HIV since similar behavior puts people at risk for both. Thailand reduced the incidence of curable STIs by more than 80 percent in less than five years through a comprehensive effort that included improved STI treatment and targeted promotion of condom use among sex workers. At the same time, HIV prevalence, which had been increasing rapidly, began to fall. FHI advocates strategies that strengthen the public health response to STIs, improve the quality of STI preventive and curative services, extend effective and appropriate interventions to groups with the highest STI exposure, and selectively implement focused measures to rapidly reduce the prevalence of specific STIs. Examples relevant to PMTCT include globally implemented, improved case management of genital ulcer disease and strengthened antenatal services to screen and treat pregnant women for latent syphilis infection using existing affordable technology. It is programmatically easier to integrate PMTCT interventions into MCH settings where essential services such as syphilis screening, treatment and partner notification are already in place. Conversely, adding PMTCT interventions presents an opportunity to improve and strengthen essential MCH services, including syphilis screening and treatment. Syphilis screening and treatment directly benefit women and their partners regardless of their HIV status, reduce perinatal morbidity and mortality, and prevent HIV. However, present approaches to managing vaginal discharge syndromes are less accurate, and better combinations of syndromic and laboratory diagnosis and screening are needed. Addressing men is also a key component of STI—and HIV—control.

Several observational studies have found a relationship between HIV voluntary counseling and testing services and reductions in risky sexual behaviors and increases in condom use. A multi-center randomized controlled study conducted by FHI, UNAIDS and WHO confirmed these findings (4). With the increasing availability and use of VCT and PMTCT services, a growing number of young people, couples, women and men know their HIV status. This presents an enormous opportunity to provide individually tailored risk-reduction counseling.

FHI recognizes that girls' and women's vulnerability to HIV infection is multi-faceted and requires strategies beyond BCC, youth-targeted services, access to education opportunities and comprehensive STI control programs. Strategies are needed to address power relations between men and women, access to economic resources and other assets, and ingrained cultural and social practices that increase women's vulnerability. Legal and human rights

frameworks that protect the interests of women and children and other marginalized population groups are also needed.

The ABC approach (**A**bstinence, **B**e faithful and use **C**ondoms consistently) and STI treatment, joined with a policy environment that encourages open community-level dialogue about sexuality and HIV/AIDS across all sectors and groups, have already helped control HIV in Cambodia, Senegal, Thailand, Uganda and Zambia.

2. Preventing Unintended Pregnancies Among HIV-Infected Women

PMTCT efforts have focused almost exclusively on preventing transmission after an HIV-positive woman is already pregnant. This approach neglects contraceptives' potential contribution to reducing MTCT by preventing unintended pregnancies among HIV-positive women. Because unintended pregnancies account for more than 50 percent of all births in some countries, contraception has the potential to prevent thousands of vertical HIV transmissions.

Similarly, VCT clients of reproductive age may need contraception. Women who come for VCT usually are not pregnant and not using contraception. VCT client studies report that while contraceptive use is low among this group, condoms are rarely offered as a contraceptive method, and referrals to family planning services are low and ineffective (5). Integrating FP and PMTCT services to increase contraceptive use among HIV-positive women who do not want to get pregnant or who are pregnant but want to begin using a method after delivery could potentially double the effectiveness of PMTCT programs. A USAID-funded analysis that examined the costs and benefits of adding family planning services to PMTCT programs found that family planning can enhance the cost effectiveness of PMTCT interventions by decreasing child infections, child deaths and, ultimately, the number of orphans (6).

Integrating family planning into VCT services is also acceptable and feasible. In Haiti (7) and Uganda (8), integrated FP/VCT services resulted in increased use of contraceptives among VCT clients.

Integrated FP/PMTCT programs will require a reorientation of routine consultations to cover protection against the dual risks of unintended pregnancies and HIV infection (9). Currently, there is only limited experience with such integrated models of care.

3. Preventing HIV Transmission from Infected Women to Their Children

A growing body of research and experience has identified safe, feasible and effective interventions to reduce HIV transmission from HIV-infected pregnant women to their infants, including:

- Antiretroviral chemoprophylaxis
- Safer obstetric practices
- Infant-feeding counseling and support

However, for a woman to benefit from these interventions, she must come for antenatal care (ANC) and/or maternity services, and she must access counseling and testing services.

Improving Availability, Quality and Use of Maternal and Child Health (MCH) Services

Most developing countries can provide only limited maternal and child health (MCH) services, as they face managerial, financial and human resource constraints. Even where services are available, potential beneficiaries do not fully use them. In many such countries, the majority of women will seek only one antenatal care (ANC) visit during a given pregnancy and report for ANC care late in pregnancy. Fewer than half of births occur inside MCH settings. Improving the availability, quality and use of MCH services is critical in reaching women who may benefit from PMTCT interventions.

Effective PMTCT program implementation requires upgrading existing MCH services, for example, by enhancing physical infrastructure; ensuring that essential pregnancy, maternity and postnatal services are provided; and preparing staff to undertake expanded or new roles. Where human resources pose a serious challenge to the delivery of counseling and testing services, scale-up can utilize professional staff for complex tasks while attracting less-skilled staff for less complex tasks. The success of Thailand's national PMTCT program, one of the first in the developing world, is partly due to very its robust public and MCH clinic services—over 70 percent of all births occur in health facilities, and 95-98 percent of women delivering at health facilities report for prior ANC visits (10, 11). Many PMTCT programs around the world have produced improvements in existing MCH services and in their use by women.

HIV Counseling and Testing in the Context of PMTCT Services

Offering counseling and testing (C&T) services to women seeking ANC services helps identify HIV-infected women and provides an opportunity to empower HIV-positive women to make crucial decisions regarding specific MTCT-related issues such as antiretrovirals (ARV), infant feeding, and sexual and reproductive health. However, introducing and integrating C&T services into MCH settings requires significant planning and reorganization. This includes, but is not limited to, creating a private space for counseling, redesigning client flow, providing orientation and training, and occasionally hiring additional service providers. Because introducing and maintaining these services, particularly in crowded and understaffed ANC clinics, can limit scale up of PMTCT interventions, multiple approaches to C&T in MCH settings have evolved.

Two major approaches to C&T in ANC settings exist: opt-in and opt-out. The approach chosen has an impact on the uptake of PMTCT interventions. In the first approach, opt-in, HIV testing is offered to pregnant women as a separate intervention from routine ANC services, and women must provide explicit consent to receive testing. Interested women are given individual pre-test counseling, after which they decide whether or not to take the test. In the second approach, opt-out, HIV testing is presented and promoted as part and parcel of routine ANC services and will be conducted unless a woman expressly refuses.

Achieving a time-efficient, non-labor intensive, simplified package that increases C&T uptake without compromising quality or individual rights is the major challenge in

determining appropriate ANC/MCH C&T models. Table 1 below shows some advantages and disadvantages of the opt-in and opt-out approaches.

Table 1: ANC Counseling and Testing Approaches

OPT-IN	OPT-OUT
<ul style="list-style-type: none"> • The HIV test is not part of routine ANC tests for pregnant women. • A woman is either offered the choice of participating in C&T or she has to explicitly request services. • Offering and/or requesting C&T services may be based on risk-perception. • Opting-in for testing is based on informed consent and an explicit request for the test. The woman signs an informed consent form before being tested. • Opt-in is based on the <i>voluntary</i> model of providing tests to those who want to know their status. 	<ul style="list-style-type: none"> • In this model, pregnant women are notified that an HIV test will be included in the standard battery of prenatal tests and procedures and that they may refuse testing. • Women are told that they have the right to refuse an HIV test, but are not explicitly asked to consent to an HIV test. • All women are tested for HIV unless they specifically refuse. • The counseling focus is on post-test counseling for those who test positive. • Opt-out is based on a <i>public health</i> model. • Opt-out is based on the premise that because HIV testing for pregnant women is beneficial both to the individual woman and as a public health policy, it should be systematically and routinely implemented.
<p>Advantage of opt-in:</p> <ul style="list-style-type: none"> • Greater assurance that women will be tested only with their knowledge and consent 	<p>Advantages of opt-out:</p> <ul style="list-style-type: none"> • Testing is seen as routine and, therefore, may be less threatening. • Can achieve higher uptake of HIV counseling and testing, which facilitates access to other HIV-related interventions
<p>Disadvantage of opt-in:</p> <ul style="list-style-type: none"> • Lower uptake of HIV testing, which limits access to other HIV-related interventions 	<p>Disadvantage of opt-out:</p> <ul style="list-style-type: none"> • Probability is greater that women will be tested without knowledge and consent

Adapted from *Canadian Medical Association Journal* 2003 and *MMWR* 1999 (12, 13)

In practice, there are many variations of these two major approaches. For example, in some settings implementing an ‘opt-out’ approach, women still have the opportunity to provide explicit consent to HIV testing.

The opt-out approach has been successfully used in North America and in many countries and programs around the world, and it has contributed to the normalization and high uptake of HIV testing, even in very busy, understaffed MCH settings (14).

PMTCT interventions have their greatest impact when women are encouraged to take an HIV test regardless of when they present for services, whether during pregnancy or labor and delivery. However, counseling and testing women in labor presents different considerations and implications. In many resource-poor settings where women may come for only one ANC visit, labor and delivery might present the only opportunity for a woman to access HIV testing. C&T in labor is feasible with the following considerations: it should

be supplementary to, and should not in any way replace the ANC C&T component; it should not jeopardize the other activities of the labor ward; it should be encouraged in the early stage of labor in clinically stable women; and post-test counseling and referral for continuing care should be given to all women before discharge, with a special focus on HIV-positive mothers. The availability of rapid testing technology is a prerequisite for C&T during labor.

Antiretroviral Chemoprophylaxis for PMTCT

The administration of antiretroviral (ARV) drugs to the mother during pregnancy, labor and delivery and to the infant after delivery has been proven to significantly reduce the risk of MTCT. In 1994, the Pediatric AIDS Clinical Trials Group (PACTG) Protocol 076 demonstrated that zidovudine (ZDV) administered to the mother from 14-34 weeks of gestation and continued throughout pregnancy, followed by intravenous ZDV during labor and oral administration of ZDV to the infant for six weeks after delivery, reduced MTCT by two-thirds (15).

Over the last decade since this landmark study, two major developments in the use of antiretroviral therapy (ART) for PMTCT have occurred, and both are relevant to resource-constrained settings. Simplified versions of the PACTG 076 protocol and other ARVs in combined or single drug regimens have been and continue to be evaluated in middle- and low-income countries among both breastfeeding and non-breastfeeding populations. Substantial advances in the understanding of the pathogenesis of perinatal HIV-1 transmission and in the treatment of persons infected with HIV have led to recommendations that standard antiretroviral therapy (with ZDV incorporated) be discussed with and offered to HIV-infected pregnant women in North America (16) and, when feasible, in developing countries (17).

The least complex, most widely used regimes in resource-constrained settings currently are short course ZDV and single dose nevirapine. In studies conducted in Thailand (among a non-breastfeeding population), Cote d'Ivoire (the RETRO-CI trial) and in Cote D'Ivoire and Burkina Faso (the DITRAME trial), women were administered oral ZDV during the last four weeks of gestation with no ARVs provided to the infant. These regimens achieved transmission rates of 9 percent at 6 weeks, 16.5 percent at 3 months and 12.8 percent at 6 weeks, respectively. In some variations of this protocol, infants are also given ZDV for one week after delivery.

A second commonly used regimen is one modeled on the HIVNET 012 protocol (Uganda) (18). In this regimen, a single 200 mg oral dose of nevirapine (NVP) is given to the woman at the onset of labor, and a single 2 mg/kg oral dose is given to the infant 48-72 hours after birth. This regimen reduced transmission by nearly 50 percent compared to a very short regimen of ZDV given orally to the mother during labor and to the infant for 1 week after birth.

Increasingly, countries are using various combinations of the ZDV- and NVP-based regimens. Ongoing studies in Thailand and Cote D'Ivoire have demonstrated additional efficacy when short course ZDV is combined with single-dose intrapartum and neonatal NVP following the HIVNET 012 protocol (19, 20). Based on evidence of greater efficacy,

some countries using the short-course ZDV regimens are beginning to provide the drug earlier in pregnancy and add longer infant postpartum regimens.

The success of most of the protocols described above depends on a woman reporting early for pregnancy-related care. However, in many resource poor settings, women may make contact with MCH services for the first time when they are in labor. In addition to the HIVNET 012 protocol, one other identified regimen could be an effective intrapartum/postpartum intervention. This zidovudine with lamivudine (ZDV-3TC) regimen is modeled on the PETRA multi-country (Uganda, Tanzania and South Africa) trial. In the second arm of this trial (PETRA-B), mothers were given ZDV-3TC beginning in labor, and both women and their infants were given ZDV-3TC for one week, achieving a reduction in transmission of 42 percent at 6 weeks. Finally, in Malawi, a combination of single dose NVP with ZDV (NVP AZ) given to the infants of HIV-infected women who had received neither antenatal nor intrapartum drugs achieved an efficacy of 36.4 percent compared to NVP alone among infants who were uninfected at birth (21).

There is evidence that using single- and dual-drug antiretroviral prophylactic regimens (particularly NVP) results in a drug-resistant virus in exposed mothers and infants. The significance of this resistance phenomenon and its impact on future treatment outcomes for women and infants who develop HIV infection are not known.

NVP-based prophylactic regimens are the minimum that should be offered to HIV-infected women in urgent need of PMTCT services. As global commitment to providing resources and building capacity for HIV prevention, care and treatment grows, and as our understanding of the clinical significance of NVP-induced resistance increases, ARV options for PMTCT (including combination prophylactic regimens) will expand while preserving treatment options for women and children.

Infant-Feeding Counseling and Support

Postnatal HIV transmission through breast milk was first documented in 1985 and is of particular concern in resource-constrained settings where HIV is common, prolonged breastfeeding is almost universally practiced and alternatives to breastfeeding are frequently unavailable, unaffordable or culturally unacceptable. It is believed that among breastfeeding populations, 15-20 percent of MTCT occurs through breastfeeding, and this can jump to as high as 29 percent if maternal infection is recent (22). Thus, postnatal transmission is second only to transmission during labor and delivery as a source of pediatric HIV infection. As more women gain access to effective ARV regimens for the reduction of MTCT, breastmilk will constitute the most common source of infant HIV-infection among breastfeeding populations.

Most breastmilk transmission occurs in the first few months of life; however, the risk persists for as long as an infant is breastfed. A South African study suggests that exclusive breastfeeding¹ reduces the risk of postnatal infection. Infants in the study who were

¹ Exclusive breastfeeding means that the infant receives only breast milk from his/her mother or a wet nurse, or expressed breastmilk, and no other liquids or solids with the exception of drops or syrups consisting of vitamins, mineral supplements or medicines (WHO, 1991).

exclusively breastfed for at least three months had no excess risk of HIV infection at six months of age compared to those who were not breastfed (23).

Withholding breastmilk from infants born to HIV-infected mothers is the only way to fully prevent postnatal transmission of HIV. While this is the favored practice in developed countries and many middle-income countries, the situation is more complex in resource-poor countries where breastmilk is the primary—and sometimes only—source of nutrition for infants. The 2002 Global Strategy for Infant and Young Child Feeding adopted by the World Health Assembly and the United Nations Children's Fund (UNICEF) recommends that infants be exclusively breastfed for the first six months of life.

However, the strategy also recognizes that when the mother is HIV-positive, the need exists to reduce HIV transmission to the infant while at the same time avoiding increased risk of other morbidity and mortality. In these circumstances, the UN guidelines recommend that "when replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life" and should be discontinued as soon as conditions for replacement feeding are met (24).

Based on current knowledge and recommendations, an HIV-infected woman has two infant feeding options: replacement feeding² and modified exclusive breastfeeding. Modified exclusive breastfeeding means exclusive breastfeeding with early cessation or feeding with heat-treated expressed breastmilk (EBM).³ The implementation of replacement feeding with formula,⁴ exclusive breastfeeding (EBF) and, particularly, heat-treated EBM continues to present significant challenges in developing countries. Even in the rare cases where mothers can afford to safely and sustainably formula feed, not breastfeeding is a highly visible choice in communities where breastfeeding is the norm and can potentially identify a woman as having HIV. Given the beliefs and practices related to infant feeding in most developing countries, exclusive breastfeeding and early cessation are not easy choices. Because rapid, early cessation of breastfeeding can have negative consequences for the infant and mother, the mother must be adequately prepared and access to other nutritious food for the infant is necessary. Lastly, there is no documentation of the effects of long-term use of heat-treated EBM.

The efficacy of ARVs in reducing postnatal HIV transmission is not known. A recent open label study in Uganda and Rwanda (the SIMBA Study) evaluated the efficacy of postnatal prophylaxis with 3TC or NVP in infants during the first six months of breastfeeding. Early results indicate this strategy, coupled with counseling on breastfeeding practices, may reduce postnatal HIV transmission (25). Ongoing similar studies use different durations of infant prophylaxis or provide ARVs to the mother during the breastfeeding period. Results from a Kenyan study suggest that HIV-infected mothers who breastfeed experience higher mortality than those who do not (26). Although no other study has corroborated these

² Replacement feeding means feeding a child who is not receiving any breast milk with a diet that provides all of the nutrients the child needs. During the first six months, this should be with a suitable breast-milk substitute: either commercial formula or home-prepared formula with micronutrient supplements.

³ To heat-treat expressed breast milk at home, bring it a the boil, then cool it immediately. To pasteurize milk in hospital, heat it to 62.5 C for 30 minutes (the Holder pasteurization method).

⁴ As used in this document, formula feeding refers to use of either commercial or home-prepared formula.

findings, the results underscore that PMTCT should provide mothers with nutritional counseling and support that includes micronutrient supplementation and should at the same time care for mothers.

The outstanding challenges that remain for researchers, policy makers, practitioners, and affected women and communities include how to make breastfeeding safer for HIV-infected mothers and their infants and how to make formula feeding an acceptable, affordable, safe and sustainable option for more HIV-infected women, including those who initiate breastfeeding but cease early.

Safer Obstetric Practices

A number of obstetric interventions are believed or have been proven to reduce MTCT. These include elective cesarean section; vaginal cleansing; reducing the amount of time between rupture of membranes and delivery; avoiding unnecessary episiotomies, suction and other invasive procedures; and drying maternal secretions and blood off the newborn. Analysis of several studies from industrialized countries demonstrates that elective cesarean sections reduce HIV transmission, although this benefit is lost if the cesarean section is performed after labor starts (27). Cesarean section does not provide additional benefit for mothers with low viral loads (<1000) and high CD4 counts (>500) (28). While some countries such as Brazil and the Dominican Republic routinely perform cesarean sections on HIV-infected pregnant women, it nonetheless has very limited application in other resource-constrained settings due to lack of capacity, resources and infrastructure even for emergency obstetric indications. In these settings, cesarean sections are associated with increased rates of morbidity and mortality, especially among mothers with low CD4 counts and when the procedure is non-elective (29).

In a Malawian study, vaginal cleansing with chlorhexidine reduced MTCT only when there had been a prolonged rupture of membranes (more than four hours) (30). Vaginal disinfection has also been shown to reduce infant morbidity and mortality. Retrospective studies suggest that reducing the time from when membranes rupture to delivery reduces mother-to-child transmission.

4. Providing Care to HIV-Infected Mothers and Their Infants and Families (PMTCT-Plus)

Although groundbreaking progress in preventing mother-to-child transmission is being made, the absence of care for the mothers has been identified as a moral dilemma and a disincentive for women to participate in current PMTCT programs (31). Comprehensive care and support for the mother needs to be provided throughout pregnancy, after delivery and beyond. Maternal care should be fully coordinated with ongoing care and support for the children and family through fully integrated reproductive, maternal and child health services (32).

Because HIV is a family disease, behind each HIV-infected woman are potentially infected partner(s) and children. Experiences with family models of care with HIV-infected pregnant women as the index patients are beginning to emerge from the developing world, such as the

PMTCT-PLUS Initiative of the Mailman School of Public Health, Columbia University. Antiretroviral programs funded by USAID and implemented by FHI in Ghana, Kenya and Rwanda are also receiving referrals of HIV-infected women and children from spouses/parents in the ARV programs and from PMTCT programs.

Providing mothers with care and including partners and families nurtures and preserves the family unit, supports disclosure of HIV status and provides support for adherence to difficult infant feeding choices and ARV regimens. Access to care motivates women to participate in PMTCT interventions, ensures retention of mothers and infants in care, and thus can significantly improve the efficacy of interventions.

III. FHI GOALS AND OBJECTIVES

FHI's goal for its PMTCT programs is to prevent HIV transmission from mothers to their infants and to improve the well being of children, mothers and families. The specific objectives of FHI's PMTCT efforts are to:

- Complement ongoing HIV prevention and care activities
- Improve the quality of MCH services
- Improve and promote the availability and use of HIV C&T services in MCH settings
- Support the integration of HIV and MCH/FP planning services
- Improve and promote access to ARVs both for PMTCT and for treatment of HIV/AIDS
- Improve and promote safer obstetric practices
- Identify and promote locally appropriate infant feeding practices tailored to a woman's HIV serostatus (positive, negative or unknown)
- Improve access and referral to care and support services for mothers and their children and families.

IV. FHI'S TECHNICAL AND PROGRAMMATIC APPROACHES

Guiding Principles

FHI takes a *comprehensive approach* to preventing transmission of HIV from mother to child. It endorses the WHO and UN's four-pronged framework, which states that reducing pediatric HIV infections and disease requires action at the following levels:

1. Prevent primary HIV infections
2. Prevent unintended pregnancies among HIV-infected women
3. Prevent transmission of HIV from infected women to their children
4. Provide care for HIV-infected mothers and their infants and families (known as PMTCT-Plus)

For preventing MTCT among already-pregnant women, FHI's strategy is guided by the belief that prevention must go beyond specific PMTCT interventions (e.g., ARVs, safer

infant feeding and safer obstetric practices) and be placed within the context of a comprehensive HIV prevention, care and support program.

Because comprehensive care and support relies upon systems other than health care, **partnerships with traditional** (reproductive health, child survival) **and non-traditional** (private sector, legal bodies, etc.) **partners** are critical for successful interventions. Identifying and strengthening referral systems—both clinic- and community-based—to respond to the care and support needs of HIV-infected mothers and their children is key.

FHI recognizes and seeks to **build on and strengthen existing programs** to improve maternal health and newborn and child survival, such as Safe Motherhood, Saving Newborn Lives, the Baby Friendly Hospital Initiative (BFHI), the Global Strategy for Infant and Young Child Feeding, Integrated Management of Childhood Illnesses (IMCI) and PMTCT services.

PMTCT programs have demonstrated an unprecedented cascade of information from research to policy to practice, which will continue in the foreseeable future. The growing and rapidly changing scientific evidence, coupled with the urgent need to scale up services, requires that **programs remain flexible, open to incorporating lessons learned, innovative, and, particularly, abreast of current literature and learning.**

Continuous **capacity building** for the management, design, implementation, monitoring and evaluation of PMTCT programs is critical to mounting an effective emergency response on the scale that is needed to avert pediatric infections and provide HIV-infected women and their families with access to care and treatment.

In addition to providing care, treatment and support to families with HIV, PMTCT programs also focus on prevention in the care setting and link with ongoing community education and response initiatives—including those spearheaded by persons living with HIV/AIDS—to prevent HIV and combat stigma and discrimination. PMTCT, perhaps more than any other component of HIV programming, demonstrates the true synergy between care and prevention.

FHI's Approaches

To be effective, efforts to prevent MTCT must be:

- Based on a national policy and a comprehensive HIV strategic plan that are supported by committed leadership at the national, district and community levels
- Integrated and closely coordinated with MCH and FP services
- Closely coordinated with and linked to other HIV prevention, care, treatment and support efforts by clinics and the community
- Effective in reaching the intended beneficiaries

HIV infection will remain prevalent among women in countries where the disease is endemic for the foreseeable future. HIV threatens the survival of children in the worst affected countries, where it results in premature deaths, poor health and orphaning. Yet safe

and effective interventions are available to prevent this secondary epidemic. An urgent need exists to rapidly expand the coverage and accessibility of programs, as well as to improve the uptake of interventions aimed at reducing HIV transmission during pregnancy, labor, delivery and breastfeeding.

To meet the need for rapid scale up of PMTCT efforts, FHI:

- Advocates for and facilitates political will, leadership, understanding and support for PMTCT programs at the global, national, health facility and community level
- Builds the capacity of developing countries to design, implement and evaluate PMTCT programs
- Improves prenatal, maternity and postnatal care and environment in which the care is provided
- Makes family planning options available and accessible
- Makes HIV C&T available and accessible to women and their partners
- Ensures that MCH clinics meet the continuing needs of women and infants and link them to existing care, treatment and support programs in the community
- Reduces stigma and discrimination in the community, health facilities and elsewhere

Programmatic Approach

Programs for PMTCT are a relatively recent phenomenon in resource-constrained settings, having emerged over the last five years, and few countries have national programs. The urgent need for national programs requires simultaneous action on the global, regional, national, health facility and community levels and on the research, management, service delivery, monitoring and evaluation fronts.

Global and Regional Activities

- Through research and active collaboration with other international organizations, FHI manages clinical trials research for the HIV Prevention Trials Network, which supported the original research on the PMTCT use of nevirapine.
- Working with the Elizabeth Glaser Pediatric AIDS Foundation, FHI is providing technical assistance and helping to transfer lessons learned across the foundation's "Call to Action" projects in Africa, Asia and the Caribbean.
- FHI staff serve on global and regional expert task forces and help to develop technical guidance and policies in the areas of PMTCT and pediatric AIDS.
- With funding from WHO, FHI worked with several partners to produce a guidance document on norms and standards for HIV-related care, treatment and support for women and children in resource-constrained settings. PMTCT is a principal focus of this document (33).
- With funding from USAID's Bureau of Humanitarian Response, FHI is collaborating with the Child Survival Collaborations and Resources Group to develop and field-test PMTCT guidelines for frontline health workers.

National Level

FHI supports resource-constrained countries to increase their awareness of MTCT and to build their capacity to design and implement effective prevention programs. Support at the national level focuses on policy, advocacy, national PMTCT planning, behavior change communication, implementation and a monitoring and evaluation framework. For example, FHI:

- Supports the establishment of PMTCT working groups to provide technical leadership and oversight to national programs
- Supports policy formulation to enable smooth introduction of PMTCT services
- Promotes collaboration between MCH/FP departments and national AIDS control programs
- Supports the development of realistic national plans for PMTCT
- Supports the development and dissemination of appropriate standards, tools and guidelines for PMTCT design, implementation, monitoring and evaluation
- Ensures effective integration of PMTCT services into MCH and family planning services
- Builds capacity for the integration of PMTCT and other care and support services at all levels
- Advocates for increased access to enhanced HIV diagnostics and care and treatment options for mothers and infants. Appropriate infant diagnostics can improve infant feeding decisions in breastfeeding communities.

Although interventions for PMTCT are largely clinic based, effective programs rely on understanding a community's socio-cultural values and practices surrounding relationships between men and women, infant feeding and HIV/AIDS. FHI addresses these concerns through its behavior change communication strategy and PMTCT activities. For example, FHI supports:

- Communication activities to increase awareness, knowledge and mobilize around MTCT issues
- Advocacy with stakeholders to support PMTCT, MCH/FP, STI and HIV services
- Activities to improve health-seeking behaviors related to MCH/FP, STIs and HIV, specifically the acceptance of counseling and testing for HIV, the acceptance of antiretroviral prophylaxis for mothers and infants, and partner involvement
- Initiatives to promote optimal infant feeding practices for all women
- Initiatives to improve client/provider interactions
- Interventions aimed at improving the nature and extent of community, family and partner-to-partner discussion about HIV/AIDS, sexuality, reproductive health and other health-related topics
- Initiatives to support HIV prevention and care programs and to reduce the stigma associated with HIV

Implementation Level: MCH/PMTCT Services

FHI emphasizes participation of site staff in all activities, including the assessment, design and ongoing monitoring and evaluation of PMTCT programs. This helps to foster ownership of PMTCT by MCH staff, which is critical for the smooth functioning of a service that demands a great deal of staff time and energy. FHI:

- Assesses the availability, quality and use of existing MCH services, and identifies opportunities to integrate PMTCT interventions
- Supports appropriate MCH upgrades based on assessment results
- Develops training plans and provides appropriate training to MCH staff based on assessment results
- Supports the introduction and implementation of counseling and testing and PMTCT interventions in MCH services
- Builds the capacity of partners to deliver high quality PMTCT services
- Promotes male involvement using a variety of approaches, such as offering VCT services adjacent to or near antenatal clinics
- Supports referral linkages to care and support for the woman, her infant and family
- Provides technical assistance for monitoring and evaluation, including developing quality assurance measures for implementing sites

Technical Approach

Counseling and Testing in ANC Settings

Given that limited human and financial resources, limited space and a heavy workload in ANC clinics are the reality in most developing countries, FHI supports an approach that normalizes HIV testing and simplifies the counseling and testing process in ANC settings while ensuring that women are not tested against their will. For example, in ANC clinics with a heavy workload, interactive group discussions between a provider and a group of women have been successfully used to openly and positively facilitate decision-making about HIV testing. Variations of the opt-in and opt-out models of counseling are common. Approaches have evolved from one to the other with time and accumulated experience—typically from opt-in to opt-out—enabling better access, uptake and, ultimately, a greater program impact. Whichever approach is chosen, FHI recommends that post-test counseling of the highest quality always be provided.

Antiretroviral Chemoprophylaxis and Therapy

A range of safe and effective antiretroviral drug regimens—single, dual and highly active retroviral therapy (HAART)—are currently recommended for PMTCT. Whereas using antiretroviral regimens for PMTCT should be guided by their feasibility in a given setting, nevirapine-based regimes have been demonstrated in even the most rural health centers with the most basic infrastructure in Africa and India. While concerns exist about inducing resistance in mothers and infants exposed to NVP, it is the minimum that must be offered to all HIV-positive pregnant women when more complex regimes are not feasible or available. Systems to identify HIV-positive women and deliver single dose nevirapine regimens have created a foundation for the introduction of more complex regimens that

carry fewer risks of resistance. As more complex regimens for the management of chronic HIV disease are introduced, women should also be given access to chemoprophylactic regimens that are safe, effective and have less risk of inducing resistance.

Infant-Feeding Counseling and Support

Given the complexity of infant feeding issues in developing countries, FHI recommends a careful assessment of infant feeding practices and environmental and cultural factors in each setting to identify real infant feeding options for women rather than theoretical options. FHI suggests that each woman's circumstances be analyzed to provide practical guidance tailored to her. This will help determine whether formula/replacement feeding is acceptable, feasible, affordable, safe and sustainable in a particular woman's situation. The expectations and norms of the woman's culture, as well as a family's infant feeding practices—for example, if the mother is the only one responsible for feeding the infant—must also be considered.

Due to the realities of resource-poor settings, exclusive breastfeeding with early cessation is likely to be the most common option. It is therefore critical to identify ways to support mothers to sustain EBF and identify locally appropriate weaning foods. It is equally critical to find ways to get an early diagnosis for the infant (e.g., using viral detection tests such as PCR) because knowledge of the infant's HIV status can help tailor feeding decisions further and can motivate the mother to implement difficult decisions, such as to cease breastfeeding.

Stigma and Discrimination

Stigma and discrimination probably constitute the greatest barriers to preventing infections; providing adequate care, support and treatment; and alleviating the epidemic's impact. FHI's overall goal is to reduce the negative impact of AIDS-related stigma on the efficacy of STI and HIV/AIDS care and prevention, including PMTCT programs. FHI works toward this goal through clinic- and community-based interventions designed to improve health-seeking and care-providing behaviors. Emerging evidence is demonstrating that HIV-infected mothers can work to support newly diagnosed mothers through peer support groups and can initiate open dialogue about HIV and challenge stigma and discrimination in their communities.

Research and Evaluation

For a relatively new intervention like PMTCT, research and evaluation are critical and lessons learned must be applied to improve programming. FHI's approach is to:

- Provide technical assistance to enhance implementation, monitoring and evaluation of PMTCT interventions
- Expand the scale and depth of services based on program experience, particularly the transition of programs to include care and treatment for women, infants and their families (PMTCT-PLUS).
- Support the collection and dissemination of lessons learned

V. ILLUSTRATIVE ACTIVITIES

Below are some examples of FHI's ongoing or planned MTCT prevention activities.

Fund and Provide Technical Assistance to Implement PMTCT in Kenya

FHI's USAID-funded Implementing AIDS Prevention and Care (IMPACT) Project is supporting the integration of PMTCT into the MCH clinics of Kakamega Provincial Hospital and Busia District Hospital. This district-level approach involves upgrading MCH clinics, training MCH clinic staff, introducing HIV counseling and testing, offering nutritional counseling and support, providing NVP, identifying and operationalizing effective referral systems for mothers and their infants, and monitoring and evaluating the program. At the two sites, nearly 100 staff have been trained in PMTCT. Lessons learned are being used to expand PMTCT to other health facilities providing MCH services in the province and the district. In Mombasa, FHI is working with local hospitals and health centers to introduce antiretroviral therapy as a complement to ongoing VCT, PMTCT and community- and home-based care activities. USAID is providing funds and ARV drugs to this program through IMPACT.

Fund and Provide Technical Assistance to Implement PMTCT in Rwanda

With funding from the USAID mission in Rwanda, IMPACT is supporting the integration of PMTCT into MCH services at Biryogo Health Center in Kagali Ville, Kabgayi Health Center in Gitarama Province, Bungwe Health Center in Byumba Province and Ruli Hospital in Kagali Rural Province. There is a deliberate effort at each site to provide comprehensive service beyond HIV counseling and testing and nevirapine prophylaxis. With USAID assistance, FHI will integrate ARVs into its network of VCT clinics in Biryogo and Kabgayi districts. PMTCT is an integral component of this comprehensive program.

Fund and Provide Technical Assistance to Implement PMTCT in Guyana

With funding from the USAID mission in Guyana, FHI is supporting the expansion of PMTCT sites. Since September 2003, FHI has helped create 12 new PMTCT sites in both ANC clinics and local hospitals. Twenty more sites will open by May 2004. By providing PMTCT services, FHI hopes to reach 5,000-8,000 women and train 200-400 providers in PMTCT service delivery. This approach includes training health workers as counselors, introducing HIV C&T, enacting NVP prophylaxis, creating referral systems for mothers and their infants and monitoring and evaluating the program. Also with USAID assistance, FHI will expand counseling, testing and PMTCT services to women who present in labor at five Guyanese hospitals in 2004.

Provide Technical Assistance to Implement PMTCT in Nigeria

FHI is working with the USAID mission in Nigeria to assist in scaling up the President's PMTCT Initiative (PPI) to 25 satellite sites in United States government Centers of Excellence (COEs) in Kano, Anambra, Abuja and Edo states. The initiative's basic PMTCT package includes C&T, ARV prophylaxis, infant feeding counseling and support, and family planning. FHI's mandate in the PPI is to assist COEs and their satellites to establish counseling and testing as part of this intervention and to ensure that women attending ANC and their partners access these services. Appropriate linkages are being developed with

community care and support services to ensure that comprehensive care is provided to clients and their infants.

Provide Technical Assistance to PMTCT Sites Funded by the Elizabeth Glaser Pediatric AIDS Foundation

FHI provides technical assistance to more than 100 PMTCT sites in seventeen countries funded by the Elizabeth Glaser Pediatric AIDS Foundation as part of the Call to Action (CTA) Project. FHI helps the CTA sites improve the quality of their services and move towards scaling-up. Technical assistance includes national- and site-level monitoring, evaluation and implementation support with special assistance in the areas of C&T, family planning, ART and infant feeding.

VI. INTERVENTION-LINKED RESEARCH

Because existing interventions to prevent MTCT have not been fully implemented in most resource-constrained countries, many unanswered operational questions related to PMTCT remain. Intervention-linked research on current and future PMTCT efforts must be conducted to discern new opportunities to advance service delivery, to determine the effectiveness and cost-effectiveness of different interventions and to inform providers and policymakers.

Possible operational questions for intervention-linked research to be addressed by the global community include:

- What is the impact of the opt-out approach on testing in ANC settings?
- What is the acceptability and usefulness of counseling and testing in labor and delivery?
- What are the current infant feeding practices and their implications for programs to prevent MTCT?
- What is the feasibility of formula feeding, and what is its impact on infant morbidity and mortality?
- What impact does administering HAART after exposure to short-course ARV prophylactic regimens have on clinical, immunological and virological outcomes for women and infants?
- What is the natural history of HIV infection among infected children born to mothers exposed to ARV during pregnancy?
- What is the level of acceptability and willingness and ability to pay for C&T and/or ARV interventions among pregnant women in MCH settings?
- Do mothers understand the concept of the partial efficacy (e.g., 40 percent to 50 percent) of a given PMTCT intervention?
- What pregnancy prevention messages and HIV/FP integrated service delivery models are effective for HIV-positive women?

VII. COST AND COST-EFFECTIVENESS

FHI recognizes that cost information is necessary for the effective implementation, monitoring and evaluation of PMTCT programs. Cost data, together with other program data, provide strategic information needed to effectively plan for, implement and evaluate

PMTCT programs. FHI develops capacities among its partners to routinely collect cost data and other program data and to use these data for decision-making.

FHI provides guidance in using cost information to estimate a budget for introducing PMTCT programs and maintaining their annual operation. Start-up budgets include the cost of facility upgrades, provider training, technical assistance, and commodities and supplies that include HIV test kits, ARV drugs for mothers and infants, and client and provider information materials. Recurrent costs include refresher training, supervision, quality assurance and commodities.

FHI provides tools for tracking costs and outputs during program implementation so that the per-unit costs of PMTCT processes are computed and the implications analyzed. Indicators include cost per HIV-positive woman found and cost per provider trained. A key objective is to use these indicators to strengthen program accountability mechanisms and to minimize wastage of resources.

To evaluate PMTCT programs, FHI provides tools that measure their cost and effectiveness. FHI helps its partners compute cost-effectiveness ratios and analyze information to identify strategies that provide maximum program impact at minimum cost.

PMTCT efforts contribute to the overall improvement of care for the mother, child and family. Such an investment may also contribute to a reduction in the costs related to treating HIV-infected infants.

VIII. MONITORING AND EVALUATION

Monitoring and evaluation (M&E) is indispensable to the successful implementation of PMTCT interventions. Because PMTCT is relatively new in most resource-constrained countries, well-designed and well-conducted M&E identifies and corrects potential problems on a continuous basis and provides feedback to strengthen the planning, design and implementation of PMTCT programs.

Illustrative indicators include:

- The number of women who attend antenatal clinics with PMTCT services for a new pregnancy (mandatory USAID)
- The number of women with known HIV infection among those seen at antenatal clinics that offer PMTCT services (mandatory USAID)
- The number of women completing the testing and counseling process (attending at least one ANC visit, attending at least one ANC visit at a PMTCT site, accepting testing for HIV, receiving post-test counseling and receiving test results)
- The number of health facilities providing at least VCT, ARV prophylaxis and infant feeding counseling (mandatory USAID)
- The number of health workers newly trained in PMTCT services

Outcome/impact indicators include:

- The proportion of pregnant women testing positive for HIV who receive a complete course of ARV prophylaxis to reduce MTCT
- The proportion of babies born to HIV-positive mothers receiving ARV prophylaxis
- The percent of HIV-positive women referred for family planning services
- The number and percent of HIV-positive women referred to HIV care and support services from MCH site offering PMTCT services
- The percent of HIV-positive women having received PMTCT services who start preventive therapy for opportunistic infections
- The proportion of men and women ages 15 to 49 who are aware of MTCT
- Morbidity and mortality in infants with HIV-infected mothers
- Percent of HIV-infected infants born to HIV-infected mothers (UNGASS)
- Rates of MTCT among pregnant women receiving antiretroviral prophylaxis

FHI has produced *Baseline Assessment Tools for Preventing Mother-to-Child Transmission of HIV/AIDS*. This facility-level assessment tool is recommended for use at health facilities seeking to integrate PMTCT interventions, but it can equally be used early or later in the implementation process to inform improvements for successful interventions. The tool is comprised of seven independent parts: ANC, Maternity/Postnatal, Laboratory, Health Provider, Client, Inventory Checklist and Data Collection Records. The tool is available at www.fhi.org/en/HIVAIDS/Publications/manualsguidebooks/Baseline+Assessment+Tools+for+PMTCT.htm

FHI has also produced a monitoring and evaluation training guide that addresses all HIV care and treatment components, including PMTCT. It will soon be available at www.fhi.org

IX. LINKAGES AND PARTNERSHIPS

FHI understands the importance of linking its other prevention and care efforts and PMTCT-specific activities. Our prevention activities—for men and for women—help reduce HIV infection among women and thus also reduce MTCT. PMTCT activities at FHI are supported by efforts of the overall Care and Treatment Division and expertise from the Prevention and Mitigation Division. There is also close collaboration between the HIV Institute for HIV/AIDS and the HIV Prevention Trials Network, an NIH-funded research network also managed by FHI, to ensure better coordination between implementation and research efforts.

FHI links with groups and programs supporting PMTCT at the country level to ensure that proposed activities strengthen existing MCH services. In addition, FHI works with international organizations involved in PMTCT activities, such as WHO, the Centers for Disease Control and Prevention (CDC), the Elizabeth Glaser Pediatric AIDS Foundation, UNICEF and UNAIDS. FHI has existing formal collaboration arrangements with the Elizabeth Glaser Pediatric AIDS Foundation and is in the process of formalizing collaboration with organizations such as the CDC.

ANNEX I

Table 1: Prophylactic ARV Regimens for MTCT Prevention (Summary of the Evidence) (34)

Study	Drugs	Antenatal/ Intrapartum	Postpartum	Median maternal CD4+ count by arm at enrolment	Mode of infant feeding	Vertical transmission rate (VTR) and efficacy
PACTG 076 / ANRS 024 Trial, USA, France	ZDV versus placebo	Long (from 14 wks), intravenous intrapartum	Long (6 weeks) (infant only)	538,560	Formula feeding	VTR 7.6 percent in intervention arm versus 22.6 percent in placebo arm at 18m (68 percent efficacy)
Bangkok CDC Short-Course ZDV Trial, Thailand	ZDV versus placebo	Short (from 36 weeks), oral intrapartum	None	411,427	Formula feeding	VTR 9.4 percent in intervention arm versus 18.9 percent in placebo at 6m (50.1 percent efficacy)
Thai Perinatal HIV Prevention Trial, Thailand	ZDV different regimens, no placebo	Long (from 28w), short (from 36 w)	Long (for 6w), short (for 3 days) (infant only)	350,380	Formula feeding	Short-short arm was stopped. VTR 6.5 percent in long-long arm versus 4.7 percent in long-short arm and 8.6 percent in the short-long arm at 6m (statistical equivalence) In utero transmission significantly higher with short compared to long maternal therapy regimens (5.1 percent versus 1.6 percent)

Study	Drugs	Antenatal/ Intrapartum	Postpartum	Median maternal CD4+ count by arm at enrolment	Mode of infant feeding	Vertical transmission rate (VTR) and efficacy
Ivory Coast CDC short- course ZDV Trial, Côte D'Ivoire	ZDV versus placebo	Short (from 36 weeks)	None	528,548	Breastfeeding	VTR 15.7 percent in intervention arm versus 24.9 percent in placebo at 3m (37 percent efficacy)
DITRAME / ANRS 049a Trial, Côte D'Ivoire, Burkina Faso	ZDV versus placebo	Short (from 36 weeks)	Short (1 week) (mother only)	535,568	Breastfeeding	VTR 18.0 percent in ZDV arm, 27.5 percent in placebo at 6m (38 percent efficacy); 21.5 percent versus 30.6 percent (30 percent efficacy) at 15m; 22.5 percent versus 30.2 percent (26 percent efficacy) in pooled analysis with other Ivory Coast trial at 24 m

Study	Drugs	Antenatal/ Intrapartum	Postpartum	Median maternal CD4+ count by arm at enrolment	Mode of infant feeding	Vertical transmission rate (VTR) and efficacy
PETRA Trial, South Africa, Tanzania and Uganda	ZDV+3TC in 3 regimens versus placebo	Short (from 36w)	Short (7 days) (mother and infant)	435,475	Breastfeeding	<p>VTR 5.7 percent at 6-8w for antenatal/intrapartum/neonatal ZDV+3TC, 8.9 percent for intrapartum/neonatal ZDV+3TC, 14.2 percent for intrapartum ZDV+3TC only, and 15.3 percent for placebo (efficacy compared to placebo: 63 percent, 42 percent and 0 percent, respectively)</p> <p>VTR 14.9 percent at 18m for antenatal/intrapartum/neonatal ZDV+3TC, 18.1 percent for intrapartum/neonatal ZDV+3TC, 20.0 percent for intrapartum ZDV+3TC only and 22.2 percent for placebo (efficacy compared to placebo is 34 percent, 18 percent and 0 percent, respectively)</p>

Study	Drugs	Antenatal/ Intrapartum	Postpartum	Median maternal CD4+ count by arm at enrolment	Mode of infant feeding	Vertical transmission rate (VTR) and efficacy
French AZT+3TC/ ANRS 075 Trial, France	Open label, non- randomised ZDV+3TC	From 32 weeks	3TC and ZDV for 6 weeks (infant only)	426	Formula feeding	VTR 1.6 percent; 5- fold lower than in historical controls receiving ZDV only
Thai ZDV+3TC Trial, Thailand	Open label, non randomised ZDV+3TC	Short (from 34w)	Long (ZDV 4 weeks) (infant only)	274	Formula feeding	VTR 2.8 percent at 18m
PACTG 316 Trial, USA, Europe, Brazil, Bahamas	NVP versus placebo in women already receiving ZDV or ZDV plus other ART	Non-study ART antenatal Intrapartum: single NVP dose 200mg plus ZDV continuous infusion intravenously	Single dose 2mg/kg within 72 hr of birth plus non-study ART including 6 w ZDV (infant only)	423,441	Formula feeding	77 percent of women received combination ARV during pregnancy. Trial stopped early due to very low VTR in both arms. VTR 1.4 percent in intervention arm versus 1.6 percent in placebo arm

Study	Drugs	Antenatal/ Intrapartum	Postpartum	Median maternal CD4+ count by arm at enrolment	Mode of infant feeding	Vertical transmission rate (VTR) and efficacy
HIVNET 012 trial Uganda	NVP versus ZDV	No antenatal ART Intrapartum: single dose NVP 200mg versus oral ZDV	Single dose NVP 2mg/kg within 72 hr of birth versus short ZDV (7 days) (infant only)	426,461	Breastfeeding	Placebo arm was stopped. VTR 13.1 percent in NVP arm versus 25.1 percent in ZDV arm (47 percent efficacy) at 14-16 w VTR 15.7 percent in NVP arm versus 25.8 percent in ZDV arm (41 percent efficacy) at 18 m
SAINT Trial, South Africa	NVP versus ZDV+3TC	No antenatal ART Intrapartum: single dose NVP 200mg versus ZDV+3TC	Single NVP dose within 48 hrs of birth (infant) versus short ZDV+3TC (7 days) (mother and infant)	384,404	Breastfeeding (42 percent) and formula feeding	VTR 12.3 percent in NVP arm versus 9.3 percent in ZDV+3TC arm at 8 weeks (not significantly different)
DITRAME Plus / ANRS 1201.0 Trial, Abidjan, Côte D'Ivoire	Open label, ZDV boosted by single dose NVP	ZDV from 36 weeks, NVP one dose at onset of labour	Single dose NVP, plus one week ZDV (infant only)	370	Breastfeeding (50 percent) and formula feeding	VTR at 6 weeks 6.4 percent
DITRAME Plus / ANRS 1201.1 Trial, Abidjan, Côte D'Ivoire	Open label, ZDV+3TC boosted by single dose NVP	ZDV+3TC from 32 weeks (stopped at day 3 postpartum), NVP one dose at onset of labour	Single dose NVP, plus one week ZDV (infant only)	439	Breastfeeding and formula feeding	VTR at 6 weeks 4.6 percent

Study	Drugs	Antenatal/ Intrapartum	Postpartum	Median maternal CD4+ count by arm at enrolment	Mode of infant feeding	Vertical transmission rate (VTR) and efficacy
Thai Perinatal HIV Prevention Trial, Thailand	ZDV alone versus ZDV plus mother/infant NVP versus ZDV plus mother NVP	ZDV from 28 weeks and intrapartum Intrapartum: ZDV alone or plus NVP one dose at onset of labor	One week ZDV with or without single-dose NVP (infant)		Formula feeding	ZDV alone arm was stopped due to higher transmission. In arms where mother got single-dose NVP, VTR not significantly different when infant received or did not receive single-dose NVP
SIMBA Trial, Rwanda, Uganda	NVP versus 3TC postnatally in neonates exposed antenatally and 1 wk postpartum to ZDV+ddI	ZDV+ ddI from 36 weeks and given intrapartum	ZDV+ ddI for 1 week (mother) NVP once then twice daily versus 3TC twice daily while breastfeeding (infant)	423,432	Breastfeeding (median 3.3-3.5 months, upper inter-quartile limit 4.9-5.3 months)	VTR at 6 months 5.3 percent (no difference between the two arms). Postnatal (day 4 - 6 months) transmission rate 2.4 percent (1.6 percent between day 4-28, 0.8 percent 1-6 mo; median duration breastfed, 3.5 mo)
NVAZ Trial, Malawi	Neonatal NVP versus NVP+ZDV	None (late comers)	Single dose NVP right after birth; ZDV twice daily for one week (infant only)	Not reported	Breastfeeding	Overall VTR at 6-8 weeks 15.3 percent in NVP+ZDV arm and 20.9 percent with ZDV only. VTR at 6-8 weeks in infants who were negative at birth 7.7 percent and 12.1 percent, respectively (36 percent efficacy)

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