

**Prevention of Mother-to-Child Transmission of HIV: Expert Panel Report and  
Recommendations to the U.S. Congress and U.S. Global AIDS Coordinator**

**January 2010**

**The independent Expert Panel issuing this report was established by Section 309 of the Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act of 2008 (“the Act”), P.L. 110-293. The Panel was also established in accordance with the provisions of the Federal Advisory Committee Act (FACA), as amended, codified in 5 U.S.C. App.**

According to the Act, the objectives and the scope of the activities of the Expert Panel are to **“provide an objective review of activities to prevent mother-to-child transmission of HIV” (human immunodeficiency virus, the pathogen that causes Acquired Immune Deficiency Syndrome (AIDS); and to “provide recommendations to the Global AIDS Coordinator and to the appropriate congressional committees for scale-up of prevention of mother-to-child transmission prevention services under this Act in order to achieve the target established” in the Act.** The target is statutorily defined in Section 307 of the Act as “a target for the prevention and treatment of mother-to-child transmission of HIV that, by 2013, will reach at least 80 percent of pregnant women in those countries most affected by HIV/AIDS in which the United States has HIV/AIDS programs.”

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## Acronyms

AIDS	Acquired immunodeficiency disease
AED	Academy for Educational Development
AFASS	Affordable, feasible, appropriate, safe, sustainable
ANC	Antenatal care
ARV	Antiretroviral drug
ART	Antiretroviral therapy
AZT	Azidothymidine/ zidovidine
CDC	US Centers for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
CMMD	Catholic Medical Mission Board
CTX	Co-trimoxazole
DHHS	Department of Health and Human Services
DNA	Deoxyribonucleic acid
EGPAF	Elizabeth Glaser Pediatric AIDS Foundation
EID	Early infant HIV diagnosis
ESTHER	Ensemble pour une Solidarité Thérapeutique Hospitalière en Réseau
FHI	Family Health International
FP	Family planning
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
HAART	Highly-active antiretroviral therapy
HBC	Home-based care
HBD	Home-based deliveries
HIV	Human immunodeficiency virus
HCW	Health Care Worker
IATT	Inter-agency PMTCT Task Team
ICRH	International Center for Reproductive Health
IEC	Information, education and communication
IF	Infant Feeding
M&E	Monitoring and evaluation
MCH	Maternal and child health
MNCH	Maternal, neonatal and child health
MOH	Ministry of health
MTCT	Mother to Child Transmission
NGO	Non-governmental organization
NVP	Nevirapine
OB/GYN	Obstetrician/ Gynecologist
OGAC	Office of the Global AIDS Coordinator
OR	Operational Research
OVC	Orphans and vulnerable children
PBF	Performance-based financing
PCR	Polymerase chain reaction
PEPFAR	President's Emergency Plan for AIDS Relief
PHE	Public Health Evaluation
PITC	Provider Initiated Counseling and Testing

PMTCT	Prevention of mother to child HIV transmission
PNC	Postnatal care
QI	Quality improvement
RFA	Request for application
RH	Reproductive health
sdNVP	Single-dose nevirapine
SI	Strategic Information
STI	Sexually transmitted infection
TB	Tuberculosis
TBA	Traditional birth attendant
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
USG	United States Government
WHO	The World Health Organization

## Executive Summary

### Objectives

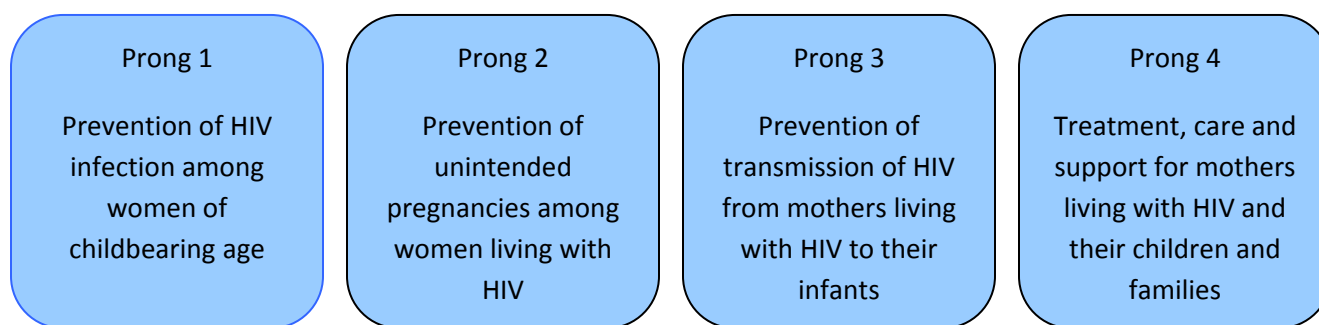
The independent Expert Panel issuing this report was established by Section 309 of the Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act of 2008 (“the Act”), P.L. 110-293. The Panel was also established in accordance with the provisions of the Federal Advisory Committee Act (FACA), as amended, codified in 5 U.S.C. App.

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### Introduction

According to the recently released joint World Health Organization (WHO), Joint United Nations Programme on HIV/AIDS (UNAIDS) and United Nations Children’s Fund (UNICEF) Universal Access report, 33.4 million people are estimated to be living with HIV worldwide; 15.7 million of these are women and 2 million are children younger than 15 years of age (UNAIDS, WHO, UNICEF 2009). **HIV is the leading cause of mortality among women of reproductive age worldwide and is a major contributor to maternal, infant and child morbidity and mortality (WHO 2009; UNAIDS 2009).** Without treatment, one third of children living with HIV die before they reach one year of age and over 50% die by the second year of life (Newell 2004). In 2008, an estimated 1.4 million pregnant women living with HIV in low- and middle-income countries gave birth, 91% of whom reside in sub-Saharan Africa (UNAIDS, 2009).

Without intervention, 25-40% of infants born to HIV-positive mothers will become infected. With current interventions, this risk can be reduced to less than 5%. **Therefore, transmission of HIV from a pregnant woman to her infant is preventable. Effective provision of Prevention of Mother-to-Child Transmission of HIV (PMTCT) interventions improves maternal health and infant HIV-free survival.** PMTCT is a key component of overall HIV prevention efforts and represents a critical opportunity for stemming the tide of the HIV epidemic. Comprehensive PMTCT consists of a 4-pronged approach:



When comprehensively implemented, PMTCT holds the potential to:

- substantially reduce new pediatric HIV infections, as has been accomplished in developed countries
- dramatically improve adult, maternal, infant and child health, particularly when well integrated into maternal, newborn and child health (MNCH) settings and in those countries where HIV contributes significantly to morbidity and mortality
- increase awareness of infection status for women and their partners and facilitate access to comprehensive care, support and treatment services
- identify children of HIV-positive women who also need to be tested and, if necessary, access HIV care, support and treatment services
- prevent new HIV infections in women and their male partners through prevention approaches targeted to the infection status of an individual woman and her partner
- prevent unintended pregnancies among HIV-positive women
- promote appropriate reproductive health services including family planning for those HIV-positive women who do not desire future pregnancies, and HIV transmission prevention interventions for those who wish to become pregnant
- contribute to reductions in HIV-related stigma and discrimination through partner, family and community education and awareness efforts
- help mitigate the disproportionate impact of HIV upon women and girls
- strengthen linkages between adult and pediatric treatment services available and PMTCT services
- build capacity for HIV, MNCH and reproductive health systems through education and training of health workers, improved laboratory and data systems, infrastructural improvements of antenatal clinics and labor and delivery wards, and strengthened systems for monitoring and evaluation

To successfully reduce mother-to-child transmission of HIV, population-level efforts to prevent HIV infection among women of childbearing age must be realized. For the individual woman, a comprehensive, coordinated continuum of services must be provided beginning with increased access to counseling, testing, and primary prevention services, as well as reproductive health choices enabling either the prevention of unintended pregnancies or appropriate planning for intended future pregnancies for women living with HIV. For HIV-positive women who become pregnant, access to and follow through on effective interventions to prevent transmission to the infant and to provide treatment for the woman herself and her child if infected must be provided

to maximize maternal health and infant HIV-free survival. This continuum of services is often referred to as the PMTCT cascade and includes:

1. Antenatal care attendance
2. HIV counseling and testing with same day return of results to the woman
3. Determination of eligibility for HIV treatment through CD4 count assessment (or less optimally, through clinical staging) with rapid return of results to the woman and her provider
4. Provision of antiretroviral therapy for women who require therapy for their own health and antiretroviral prophylaxis to prevent mother-to-child transmission to women who do not yet require therapy
5. Adherence to HIV treatment or prophylactic regimens as medically appropriate
6. Safe labor and delivery services
7. Timely provision of HIV prophylactic regimens and cotrimoxazole for the infant
8. Safe feeding practices for the infant
9. Early follow-up HIV testing for the infant with rapid initiation of antiretroviral treatment for those who are infected, and testing to determine final HIV status in breastfed infants.
10. Ongoing, clinical, psychological and social care, support and monitoring for the mother, infant and family

For optimal results, these services should be embedded within high-quality general maternal, newborn, infant and child health services and supported by national and local government commitment and funding, community sensitization and mobilization, male partner and other family involvement, strengthening of health systems to promote comprehensive care and treatment, accurate data collection, monitoring and evaluation, reliable supply of necessary equipment and supplies and well-trained, patient-friendly health care workers.

### **Progress to Date**

PMTCT has been a high priority for the international HIV/AIDS response as evidenced in the Declaration of Commitment on HIV/AIDS adopted at the United Nations General Assembly Special Session on HIV/AIDS in 2001 (United Nations 2001), the Abuja Call to Action Towards an HIV-free and AIDS-free Generation in 2005 (High Level Global Partners, 2005), the Political Declaration of the United Nations General Assembly High-Level Meeting on AIDS to work towards universal access to HIV prevention, treatment, care and support in 2006 (UNGA 2006), and numerous other high-level statements by multilateral organizations.

The United States Government (USG) has played a sustained and critical role in worldwide PMTCT research and program efforts, including funding research that identified key PMTCT interventions followed by spearheading global program scale-up of these interventions under the 2002 U.S. Mother and Child HIV Prevention Initiative and during the first 5 years of PEPFAR. The PEPFAR reauthorization bill has brought a renewed emphasis to the urgent need for scale-up of PMTCT services. Specifically, the bill calls for the establishment of a comprehensive, integrated, 5-year strategy for PEPFAR, which must include a plan to help partner countries in the effort to achieve goals of at least 80% access to counseling, testing, and treatment to prevent the transmission of HIV from mother-to-child, emphasizing a continuum of care model, and increase support for prevention of mother-to-child transmission. The PEPFAR Five-Year



Strategy, released in December 2009, outlines plans to ensure that every partner country with a generalized epidemic has both at least 80% coverage of testing for pregnant women at the national level, and 85% coverage of antiretroviral drug prophylaxis and treatment, as indicated, of women found to be HIV-infected (PEPFAR 2009). The policy also recognizes the work that PEPFAR is doing to expand access to PMTCT to at-risk populations in countries with concentrated epidemics. To help the children of these mothers, PEPFAR supports the expansion of early infant diagnosis to reach 65% coverage, along with comprehensive care and treatment of exposed infants.

Successful scale-up of PMTCT services is also well-aligned with the Obama administration's strong support for the empowerment of women and improving the health of women, children and families through the Global Health Initiative (GHI), and contributes to Millennium Development Goals 4 (Reduce Child Mortality), 5 (Improve Maternal Health) and 6 (Combat HIV/AIDS, Malaria and Other Diseases).

Countries have realized significant achievements in PMTCT. According to the 2009 Universal Access Report, 70 of 123 reporting low- and middle- income countries have established a national PMTCT scale-up plan that includes population-based targets, up from 34 in 2005 (UNAIDS, WHO, UNICEF 2009). Due in part to increased implementation of provider-initiated ('opt out') HIV testing in antenatal care (ANC) settings, rates of HIV counseling and testing for pregnant women have improved. In six of the ten countries estimated to have the largest numbers of pregnant women living with HIV (Kenya, Malawi, Mozambique, South Africa, Tanzania and Zambia), rates of counseling and testing for pregnant women have risen to 60–80%. Progress has also been made in providing antiretroviral medications for PMTCT to those women who test positive. In 2008, 45% of pregnant women living with HIV in low- and middle-income countries received antiretroviral drugs to prevent HIV transmission to their infants, including antiretroviral therapy for their own health, an increase from 35% in 2006. However, half of countries with a generalized HIV epidemic have an unmet need for family planning among married women age 15-49 years of over 25%.

In a supportive role for country-level leadership, PEPFAR has contributed significantly to many of these achievements. Specifically, three of the fifteen original PEPFAR focus countries (Botswana, Guyana, and South Africa) have achieved 80% coverage of HIV counseling and testing among pregnant women with PEPFAR support, with several others close behind (Figure 1). Nigeria, in contrast, is behind and requires special intervention given its size, poverty and gaps in health system capacity.

**Figure 1: Percentage of pregnant women who received HIV counseling and testing with USG support, 2004 and 2008**  
(Source: 2009 PEPFAR Annual Report)

Country	Estimated coverage of pregnant women receiving HIV counseling and testing Percent coverage	
	FY2004	FY2008
Botswana <sup>1</sup>	58%	86%
Côte d'Ivoire	3%	23%
Ethiopia	0.2%	6%
Guyana	32%	87%
Haiti	8%	53%
Kenya	19%	69%
Mozambique	4%	56%
Namibia	12%	76%
Nigeria	0.4%	12%
Rwanda	11%	59%
South Africa	46%	85%
Tanzania	2%	53%
Uganda	8%	55%
Vietnam <sup>2</sup>	0.1%	17%
Zambia <sup>2</sup>	11%	59%
<b>Total</b>	<b>6%</b>	<b>32%</b>

**Notes:**

Numbers may be adjusted as attribution criteria and reporting systems are refined.

This indicator was revised beginning in FY2005. FY2004 results include an adjustment accounting for pregnant women who were counseled, tested, and received their test results.

Coverage rates were calculated by dividing PEPFAR program (upstream and downstream) results by the estimated population eligible for the service. Eligible populations were based on the estimated number of births for each year provided by the International Database of the U.S. Census Bureau. Coverage estimates for FY2004 were revised from estimates provided in the PEPFAR Third Annual Report to Congress, using eligible populations from the U.S. Census Bureau. This methodology provides a standardized comparison across all countries and the reported rates may differ from those reported by countries.

**Footnotes:**

<sup>1</sup> Botswana results are attributed to the National HIV Program. Beginning FY2005, USG downstream contributions in Botswana are embedded in the upstream numbers, following a consensus reached between the USG and the Government of Botswana to report single upstream figures for each relevant indicator.

<sup>2</sup> An error occurred in reporting coverage rates in the PEPFAR Third Annual Report to Congress. FY2004 results for Vietnam and Zambia were reversed. The correct estimates are now reported in this table.

In 2008, three countries (Botswana, Guyana and Rwanda) achieved at least 80% antiretroviral drug (ARV) provision among known HIV-positive pregnant women with PEPFAR support (Figure 2). Sustaining these achievements and assisting the remaining countries to increase coverage to at least 80% (regardless of antenatal care attendance), is essential for successfully meeting the PMTCT goals outlined in the next phase of PEPFAR. It should also be noted that PMTCT programs can contribute significantly to each of the PEPFAR goals of directly supporting more than 4 million people on treatment, preventing 12 million new infections and enrolling 12 million HIV-infected persons in care and support.

**Figure 2: Estimated Coverage of HIV-positive pregnant women receiving ARV prophylaxis with PEPFAR support, FY2008**

Country	Number of HIV+ pregnant women receiving ARV prophylaxis in FY 2008	Estimated number of pregnant women living with HIV needing antiretrovirals for PMTCT based on UNAIDS/WHO methods 2008 <sup>1</sup>	Estimated coverage of HIV+ pregnant women receiving ARV prophylaxis FY2008 <sup>2</sup>
Botswana	10,900	12,000	91%
Côte d'Ivoire	5,800	22,000	26%
Ethiopia	5,300	36,000	15%
Guyana	200	<200	100%
Haiti	1,400	5,500	25%
Kenya	61,100	110,000	56%
Mozambique	39,900	110,000	36%
Namibia	6,500	8,200	79%
Nigeria	29,800	210,000	14%
Rwanda	9,800	10,000	98%
South Africa	129,600	200,000	65%
Tanzania	37,100	86,000 <sup>3</sup>	43%
Uganda	41,600	82,000	51%
Vietnam	900	3,300	27%
Zambia	42,900	70,000	61%
<b>Total</b>	<b>422,800</b>	<b>879,000</b>	<b>48%</b>
<b>Footnotes:</b>			
<sup>1</sup> Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector, Progress Report, 2009.			
<sup>2</sup> Coverage rates were calculated by dividing PEPFAR program (upstream and downstream) results by the estimated number of HIV+ pregnant women needing antiretrovirals for PMTCT based on WHO/UNAIDS methods.			
<sup>3</sup> This is a preliminary estimate, currently being reviewed and will be adjusted, as appropriate, based on ongoing data collection and analysis.			

## Challenges

Despite the successes realized thus far, significant challenges remain to achieving at least 80% coverage of counseling and testing for pregnant women and 80% coverage of ARV provision for HIV-positive pregnant women. Comprehensive provision of PMTCT is a complex intervention that involves multiple services delivered to different individuals at different points in time and in a variety of different settings. For example, for any intervention to be provided, a woman's HIV status must first be determined. This would ideally happen in an ANC setting; however, many women do not attend ANC services and those who do are unlikely to complete the WHO recommended 4 visits throughout a pregnancy. Thus, expansion of testing to other settings where women access services (eg. maternity wards, family planning clinics, immunization clinics and other pediatric services, community health centers, etc.) will help to achieve this goal and contribute to broader strengthening of women's health. Women who test negative remain at risk for acquiring HIV during pregnancy or lactation; thus engagement of their sexual partner in

preventive services is an important target. Transmission of HIV to the infant is very high when a woman acquires a new HIV infection during these time periods. Thus, women who test negative who are in high HIV prevalence and/or high-risk settings need ongoing prevention interventions and repeat testing during pregnancy. Women who test positive must be assessed for treatment eligibility by CD4 test and clinical exam. Increased availability of CD4 tests in antenatal settings is critically needed. The majority of pregnant women are clinically well, but as many as 50% are likely to be eligible for treatment for their own health based on low CD4 count. Women who receive a CD4 test typically wait 2 weeks or more for the results to return, necessitating a return visit which can result in losing the woman to follow-up.

As pregnancy is only for a limited time, urgent intervention to provide treatment or prophylaxis as quickly as possible is essential, or the window of opportunity to prevent HIV infection in the infant may close. However, clinics providing antiretroviral therapy and ongoing management for HIV-positive patients are not always located in the same place where the woman receives her ANC and labor and delivery care. This is due to multiple factors including limited numbers of health care workers trained in provision of such services, lack of appropriate infrastructure and facilities and potentially long distances between health care sites and the individual woman's home. Thus, following up with these services may be extremely difficult. PMTCT services must also be provided during labor and delivery. As many women deliver at home rather than in a health facility, ensuring women and their babies have access to and take the needed antiretroviral at the time of labor and delivery is very difficult. After delivery, the woman and infant need ongoing monitoring, care and support and potentially treatment which poses yet another challenge for reasons similar to those described above.

Moreover, risk of mother-to-child transmission of HIV does not end at birth but continues for as long as the infant is breastfeeding. Women may not be able to reliably access appropriate infant formula or the clean water needed to prepare it. Even if this can be accomplished, breastfeeding is often the cultural norm, and formula feeding may draw scrutiny from friends and family, potentially exposing the woman to stigma and discrimination, and leading to formula feeding in private and breastfeeding in public. This 'mixed' feeding of part breast milk and part formula has been shown to present the greatest risk for HIV transmission. Additionally, if formula feeding is interrupted due to inadequate supply of formula or compromised by use of unsafe water for preparation, infants are at extremely high risk for morbidity and mortality from other causes, such as diarrhea and malnutrition, thus defeating the ultimate goal of HIV-free infant survival. For these reasons, WHO infant feeding guidelines for HIV-positive women have recommended exclusive breastfeeding for all women unless specific criteria for formula feeding can be met - specifically formula feeding must be 'AFASS' (affordable, feasible, acceptable, safe and sustainable). This conditional approach has been extremely difficult to implement and has resulted in tremendous confusion among health care workers and mothers and likely contributed to ongoing transmission during breastfeeding. Given recent clinical trial results demonstrating that provision of antiretroviral drugs to the breastfeeding infant or lactating mother can significantly decrease breast milk transmission, WHO now recommends that countries develop a national plan for feeding guidance for all infants of HIV-positive women that should include a comprehensive approach to health care access. If breastfeeding is chosen for national guidelines, exclusive breastfeeding for 6 months followed by continued breastfeeding with appropriate

complementary feeding through age 12 months accompanied by antiretroviral prophylaxis of the infant or mother to prevent breast milk HIV transmission is recommended.

Even if all of the programmatic challenges of making services available are met, agreeing to testing, accepting a positive diagnosis and following through on the recommended interventions places a tremendous burden on the individual woman especially given the weakness of health systems and the impact of social barriers for women's health, including stigma. Disclosure of HIV infection to a partner, family or community member can be extremely daunting, and in some cases even dangerous, for a woman who culturally may have very little decision-making power and limited ability to provide for the needs of herself and her children. Stigma and discrimination combined with very little male involvement in issues related to pregnancy and childbirth and underlying cultural systems that disempower women create a situation that makes it extremely challenging to follow through on essential PMTCT interventions.

An additional challenge has been ambiguity around the definition of PEPFAR targets and whether the goals are PEPFAR program specific or whether they reflect national population level coverage. Finally, provision of adequate PMTCT services is dependent upon sufficient funding. As the USG, country governments and other donors face the reality of the current economic crisis, availability of resources to support PMTCT programs is limited. Although PEPFAR has recently allocated an additional one-time \$100 million for strategic acceleration of PMTCT scale-up in 6 countries in FY2010 (Malawi, Mozambique, Nigeria, Tanzania, South Africa, and Zambia), PEPFAR resources overall have not increased as substantially in 2009 or 2010 as in the program's earliest years. As these additional funds are currently provided on a one-time basis, it is difficult to strategize and plan for the scale-up of coverage on a long-term basis. While scale-up of PMTCT services requires additional initial investments, and a broadened strategic framework, the long-term savings, both in terms of improving maternal health, thus helping to ensure a stable caregiver for children and a potential contributor to economic development, political stabilization and in prevention of infections in infants who would otherwise go on to require a lifetime of treatment, must be considered.

### **PEPFAR Expert PMTCT Panel Recommendations**

The following recommendations of the PEPFAR Expert PMTCT Panel are directed to Members of the U.S. Congress, the U.S. Global AIDS Coordinator and PEPFAR field programs and headquarters staff. The Panel has summarized their recommendations below and organized them by the following categories: 1) Service Delivery; 2) Health Workforce; 3) Health Information Systems, Targets, and Monitoring and Evaluation; 4) Research and Innovation; 5) Financing; 6) Leadership and Governance; and 7) Collaboration and Coordination, in order to demonstrate the multisectoral approach needed to develop successful PMTCT programs, and to highlight the ways in which PMTCT has wider impacts on country health systems.

#### **A. Service Delivery:**

1. The first two prongs of PMTCT (prevention of HIV infection and unintended pregnancies) are often neglected but are crucial to the success of PMTCT and overall HIV and global health efforts. PEPFAR should support and fund comprehensive programs that include prevention of adult HIV infection, particularly for those women found to be HIV-negative in PMTCT settings, provision of accurate family planning

advice and safe contraception for all women of childbearing age living with HIV, and access to advanced health services if HIV-infected to prevent death of the mother and child.

2. Routine, provider-initiated, opt-out HIV screening during pregnancy, delivery and the postpartum period is essential to reduce the stigma of accessing the test, enabling women to know their infection status and access treatment and care and PEPFAR should support country efforts to make this standard policy and practice.
3. Given the dual benefits of improving maternal health and preventing new pediatric HIV infections and in light of USG efforts to provide woman- and family-centered services, PEPFAR should support policies that prioritize pregnant and lactating women for HIV care and treatment services and work with governments to improve their longitudinal care systems for PMTCT and linkages with care and treatment programs that aim to maximize the health and survival of mothers and infants.
4. PEPFAR should support policies and practices that ensure that:
  - a. Pregnant women found to be HIV-positive are urgently assessed, preferably with a CD4 cell count drawn on the day of diagnosis, to determine their need for antiretroviral therapy for their own health, with the added benefit of dramatically reducing transmission to the baby, and CD4 count assays need to be readily available in the antenatal setting.
  - b. All HIV-positive pregnant women should be integrated into ongoing care and those who are medically eligible for antiretroviral treatment for their own health initiated on ART as soon as possible and continued on this therapy for life, along with ongoing management of clinical, psychological and social issues.
  - c. Pregnant women not yet medically eligible for antiretroviral treatment for their own health are integrated into ongoing medical monitoring and care and, urgently started on a highly efficacious prophylactic ARV regimen to prevent *in utero*, peripartum, and postpartum breast milk transmission to the baby, and are linked to long-term follow up care to evaluate need for antiretroviral treatment and other interventions in the future. This also facilitates monitoring of their exposed infant for treatment services if infected and strengthens linkages for childhood vaccination and other child health initiatives.
5. PEPFAR must contribute to putting programs in place that ensure all infants born to mothers living with HIV are enrolled in ongoing care and support services and actively followed to ensure clinical HIV-related and general pediatric management, early and repeat HIV testing, developmentally appropriate psychological and social support, provision of cotrimoxazole, appropriate infant feeding and, if indicated, ongoing antiretroviral prophylaxis to further reduce the likelihood of transmission. These programs should ensure that infants who are determined to be HIV-infected are initiated on antiretroviral treatment given the high morbidity in untreated HIV-infected infants and children.
6. PEPFAR and the broader GHI should strongly promote country-level integration and coordination of PMTCT, HIV care and treatment programs, MNCH and family planning programs to maximize the benefits of these investments.
7. PEPFAR should promote nutrition counseling and support with linkages to food security programs as an integral component of PMTCT programs as pregnant women are under

increased nutritional and metabolic demands, and often suffer from preventable nutritional deficits, which are worsened by the additional burden of HIV infection.

8. PEPFAR programs and the wider GHI must focus additional resources to increase demand for antenatal care services and outreach services for women who deliver at home to increase the reach of PMTCT programs and potentially reduce stigma and loss to follow-up.
9. PEPFAR should promote policies and programs that prioritize the inclusion of male partners and other family members in PMTCT service delivery, as this has been shown to improve test acceptance by women and reduce the stigma of positive test results. Increased community and male partner knowledge, understanding, and participation in PMTCT services as well as the provision of psychosocial support services to women are critical in helping HIV-infected women successfully complete the PMTCT cascade, and can lead to improvements in men's health.

#### **B. Health Workforce:**

1. Improved and ongoing training, mentoring, supervision and appropriate compensation of both professional and lay health care workers are needed to ensure quality services are provided. Strengthening of local academic and technical educational institutions including new curriculum and certification programs in the area of maternal and child health and HIV are needed to achieve long-term sustainability. Training of health care workers to provide PMTCT and related pediatric HIV treatment services should be included in PEPFAR's goal of training 140,000 new health care workers.
2. PEPFAR should use Partnership Frameworks to encourage country governments to allow task-shifting, including non-physician health care worker initiation of antiretroviral treatment for pregnant women, infants and children and the use of trained counselors to provide HIV counseling and testing. Efforts should be made to utilize and compensate HIV-positive women who have been through PMTCT services as counselors and educators for new patients as their services have been successfully utilized in numerous PEPFAR-funded programs. PEPFAR should allow for "topping-up" of salaries for public health sector employees and incentivize productivity through performance-based financing.
3. Fear of stigmatizing behaviors from health care workers is a barrier to service uptake. PEPFAR should promote programs that focus on improving the counselor-patient interaction and including formal training for staff on the reduction of stigmatizing behaviors. They should address imbalances in quality of services offered at hospitals, health centers and maternities by improving training of staff and infrastructure at all venues.

#### **C. Health Information Systems, Targets, and Monitoring and Evaluation:**

1. The PEPFAR goals established in the Reauthorization and PEPFAR Five-Year Strategy as related to target set for PMTCT counseling and testing, provision of prophylaxis, early infant diagnosis, infants born HIV-free and pediatric testing and treatment must be better defined to enable a clear strategy toward achieving them. PEPFAR leadership should:
  - a. Convene an interagency USG group to rapidly assess methodologies and gain consensus on the definition of these targets for the next phase of PEPFAR.

- b. Use national figures for all denominators used in PEPFAR reporting, and include all women, regardless of antenatal care attendance.
  - c. Work with national monitoring and evaluation staff to promote disaggregation of data provided to OGAC on the ARV regimens provided in their programs, as a means of encouraging utilization of more efficacious regimens.
  - d. Define and measure targets that focus on providing HIV treatment to pregnant women who need it for their own health, including documentation of clinical and/or laboratory staging of HIV disease and engagement in care and/or treatment services for all women identified as HIV-positive.
  - e. Strongly encourage establishment of reporting systems that provide an indicator of linkage of HIV-infected women to treatment and care programs.
  - f. Establish indicators for and define program success in terms of PMTCT impact, such as infant HIV-free survival.
2. Promote ownership of the PMTCT program through feedback of program results to clinical sites and support of quality assurance (QA) and quality improvement (QI) activities that allow for local identification of problems and generation of potential solutions to improve program quality.
  3. Conduct public health evaluation studies to identify the barriers to treatment and care and the degree to which these barriers also negatively impact the completion of the PMTCT cascade.
  4. PEPFAR must support country-led efforts to move toward one monitoring and evaluation system and international efforts to harmonize targets and indicators.

#### **D. Research and Innovation:**

1. Operational research is urgently needed to determine optimal strategies for implementation of the PMTCT cascade. Research is particularly needed to ascertain program models that facilitate integration of MNCH, PMTCT, and comprehensive care and treatment services in a comprehensive, longitudinal, synergistic way to optimize maternal, infant and child health and survival. A recent meeting convened by UNICEF and the Elizabeth Glaser Pediatric AIDS Foundation, and attended by PMTCT and pediatric HIV experts from the USG, international agencies and implementing partners produced a list of 20 priority Operational Research questions reached by consensus among all attendees. PEPFAR is in a position to rapidly facilitate answering these questions and should fund, prioritize and fast track research in these areas through Public Health Evaluations and other research and evaluation mechanisms.
2. As increasing numbers of HIV-infected pregnant women receive antiretroviral drugs during pregnancy, surveillance for the effect of such treatments on maternal health, pregnancy outcome, including birth defects, and the short- and long-term effects of *in utero* antiretroviral drug exposure on their infants (including HIV-exposed but uninfected infants) is critical. PEPFAR support of pharmacovigilance programs to monitor for such effects is important.
3. PEPFAR should take a proactive approach to new interventions and development of new technologies, including funding pilot projects to evaluate innovative and cost-effective methodologies, such as point-of-care CD4 instruments and comprehensive provision of PMTCT to promote women's health and empower women to access services.



**E. Financing:**

1. Within PEPFAR, PMTCT should be prioritized for funding because it is one of the most effective and cost-effective forms of HIV prevention and contributes to multiple PEPFAR goals related to prevention, treatment, care and support, health care workforce and health system strengthening and embodies a woman- and family-centered approach to programming and foreign assistance funding.
2. PEPFAR should lead efforts to identify and implement cost-effective practices and reduce inefficiencies at multiple levels, including within USG agencies, implementing partners, country governments, and PEPFAR coordination with other donors.

**F. Leadership and Governance:**

1. PEPFAR should use the Partnership Framework as a means of improving country government engagement and should take a proactive role in working effectively with all stakeholders through effective national and international coordinating bodies. Strong country government leadership that translates throughout the leadership to the local level, prioritization of and commitment to PMTCT in the national HIV/AIDS plan and other critical national HIV/AIDS activities and strategies such as Global Fund applications and general health sector plans are required for rapid and comprehensive scale-up and ongoing sustainability of PMTCT services. National coordination among relevant country ministries (Health, Finance, Social Welfare, etc), USG agencies, implementing partners, international agencies and faith-based organizations is required for the most effective and efficient service provision.
2. Given staffing and capacity challenges often faced by national-level Ministries of Health, PEPFAR programs should also emphasize staffing up and supporting Provincial and District Health Offices as an effective method of promoting decentralization of country leadership around PMTCT activities.
3. PEPFAR programs should work with host country governments to focus on concrete efforts to reduce stigma and increase population-level understanding and acceptance of PMTCT interventions.
4. PEPFAR policies should protect people living with HIV/AIDS (PLWHA) and engage PLWHA in the development of country operational plans, Partnership Frameworks and other key documents and planning.

**G. Collaboration and Coordination:**

1. PEPFAR leadership and technical experts should work closely with those responsible for developing GHI strategy. There are tremendous opportunities for synergies and joint efforts toward achieving common health and development goals related to PMTCT and maternal, newborn, infant and child health. However, the approach must be developed and implemented in harmony so as to reduce redundancy, achieve common goals, capitalize on existing achievements and platforms and maximize sustainability. Comprehensive implementation of PMTCT achieves the woman- and family-centered approach articulated as a priority for USG initiatives.
2. In order to facilitate achievement of PMTCT goals, PEPFAR must:
  - a. Continue and expand coordination with international/multilateral organizations within the framework of the “three ones” (one national HIV/AIDS action framework, one national HIV/AIDS coordinating authority, one national

monitoring and evaluation system) based on the core competencies of the different stakeholders to ensure clear and unified information is provided to Ministries of Health and Finance.

- b. Actively engage international/multilateral organizations in the PEPFAR Partnership Framework process and coordinate where possible with the Global Fund National Strategy Application process.
- c. Provide support to improve capacity of international/multilateral organizations.
- d. Continue to fully engage with the UNICEF/WHO co-convened Interagency Task Team on PMTCT as the primary forum for coordination at headquarters level and emphasize strong coordination at country level to avoid duplication and gaps.
- e. Strengthen local governments and non-governmental organizations directly involved in implementing best practices in order to translate PEPFAR's successes into long-term sustainable programs that are part of the fabric of health care provided to women and children.

## **Conclusions**

The members of the Expert Panel emphasize the importance of maximizing the extent to which PMTCT, one of the most effective and cost-effective tools for the prevention of HIV, is funded and scaled-up. If PEPFAR is able to reach its stated goals over the next 5 years, it will have the effect of dramatically reducing new HIV infections and reducing the long-term costs of care and treatment costs for infected children, and improving the health of women. These investments and efforts should also be leveraged through the Administration's GHI to achieve broader MNCH and reproductive health goals through a woman-centered approach. Thank you for this opportunity to share our insights and recommendations.

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The Panel is thankful to the following individuals for their important contributions to the report: Charles Holmes, Andrea Swartzendruber, Funmi Adesanya and Alison Conforto.

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## **Chapter 1. Global Burden of HIV among Women and Children, Introduction to Prevention of Mother to Child HIV Transmission (PMTCT), and Expert Panel Objectives**

### **I. Introduction**

The burden of HIV disease among women and children worldwide is staggering. It is the most common cause of death among adult women worldwide, a leading cause of death among children in low and middle-income countries, and has caused widespread suffering and reversal of development advances in the hardest hit areas (UNAIDS, WHO, UNICEF 2009).

Comprehensive programs to combat vertical HIV transmission result in benefits for mothers, children and families and are well-aligned with US Government (USG) development goals of family and woman-centered initiatives.

### **II. Objectives**

**This chapter's objectives are:**

- To describe the global burden of HIV among women and children
- To present risk factors for mother to child HIV transmission
- To present the components of comprehensive Prevention of Mother to Child Transmission (PMTCT) programs
- Introduce the objectives and members of the Expert Panel

### **III. Global Burden of HIV among Women and Children, Introduction to PMTCT Services and Programs, and Expert Panel Objectives**

#### **Global Burden of HIV among Women and Children**

HIV/AIDS continues to be the leading cause of illness and death among women and their children, particularly in sub-Saharan Africa where HIV prevalence is highest. UNAIDS estimates that 33.4 million people worldwide were living with HIV in 2008, including 15.7 million (47%) women (UNAIDS, 2009). Women in sub-Saharan Africa are disproportionately affected; 60% of people living with HIV in sub-Saharan Africa are women (UNAIDS/WHO 2009). Globally, HIV prevalence varies substantially, ranging from <0.1% in places such as Bosnia and Herzegovina and the Republic of Korea to 26.1% in Swaziland. Madagascar has the lowest HIV prevalence in sub-Saharan Africa (0.1%), but seven other countries in that region have prevalence ratios >10% (Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia) (Sweat 2004).

An estimated 1.5 million of the 115 million annual births in low- and middle-income countries are born to HIV-infected mothers (Newell 2004). Ninety percent of HIV-infected pregnant women in need of ARVs for prophylaxis or treatment reside in twenty countries (Table 2). It is estimated that 1,000 children under 15 years become infected with HIV every day; 90% of them through mother-to-child HIV transmission and of that, 2 million children (6% of the 33 million people living with HIV) are living with HIV (UNAIDS, WHO, UNICEF 2009). The majority of these children (90%) live in sub-Saharan Africa, the most impacted and underserved region. HIV infection in children is extremely aggressive and, unattended, will kill over 50% of children before their second birthday (Newell 2004). In 2008, an estimated 280,000 children died of AIDS (UNAIDS 2009).

**Table 2.** Twenty low- and middle-income countries with the highest estimated numbers of pregnant women living with HIV in need of antiretrovirals to prevent mother-to-child transmission of HIV and numbers of children in need of antiretroviral therapy (UNAIDS, WHO, UNICEF 2009)

Rank by number of pregnant women living with HIV	Country	Estimated number of pregnant women in need of antiretrovirals in 2008 [range]	% of the total in low- and middle-income countries	Estimated number of children in need of antiretroviral therapy in 2008 [range]	% of the total in low- and middle-income countries
1	Nigeria	210 000 [110 000-300 000]	15%	110 000 [57 000-160 000]	15%
2	South Africa	200 000 [120 000-280 000]	14%	94 000 [53 000-130 000]	13%
3	Mozambique	110 000 [50 000-180 000]	8%	45 000 [24 000-67 000]	6%
4	Kenya	110 000 [53 000-160 000]	8%	49 000 [25 000-71 000]	7%
5	United Republic of Tanzania*	— [40 000-130 000]	6%	40 000 [20 000-66 000]	5%
6	Uganda	82 000 [44 000-120 000]	6%	42 000 [23 000-60 000]	6%
7	Zambia	70 000 [38 000-96 000]	5%	34 000 [18 000-47 000]	5%
8	Malawi*	— [32 000-82 000]	4%	— [17 000-45 000]	4%
9	Zimbabwe	53 000 [29 000-73 000]	4%	37 000 [22 000-50 000]	5%
10	India	49 000 [25 000-80 000]	4%	30 000 [16 000-46 000]	4%
11	Ethiopia	36 000 [18 000-54 000]	3%	23 000 [12 000-33 000]	3%
12	Cameroon	36 000 [19 000-52 000]	3%	18 000 [10 000-26 000]	2%
13	Democratic Republic of the Congo	32 000 [17 000-48 000]	2%	16 000 [9 900-22 000]	2%
14	Côte d'Ivoire	22 000 [11 000-34 000]	2%	14 000 [6 900-21 000]	2%
15	Burundi	16 000 [7 200-24 000]	1%	8 000 [4 400-11 000]	1%
16	Angola	16 000 [8 000-24 000]	1%	7 400 [3 900-12 000]	1%
17	Chad	15 000 [7 700-23 000]	1%	7 300 [3 700-11 000]	1%
18	Lesotho	14 000 [8 600-19 000]	1%	7 300 [4 300-9 700]	1%
19	Ghana	13 000 [6 400-19 000]	1%	5 900 [2 600-9 200]	1%
20	Botswana	12 000 [7 500-16 000]	1%	7 900 [4 900-10 000]	1%

\* No point estimate is provided as the estimated number of pregnant women living with HIV in need of antiretrovirals (in the United Republic of Tanzania and Malawi) and the estimated number of children living with HIV in need of antiretroviral therapy (in Malawi) are currently being reviewed and will be adjusted, as appropriate, based on ongoing data collection and analysis.

## Risk Factors for Mother to Child HIV Transmission

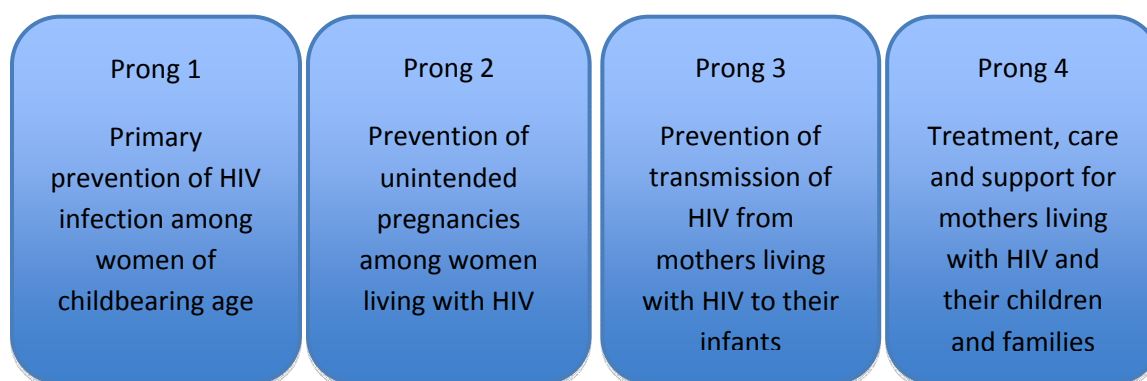
While viral maternal and infant factors all influence the risk of vertical transmission, the most important factor is the mother's HIV viral load (the amount of virus in the mother's blood). The chances of transmission are higher when maternal viral load is high, as during new infection or with advanced disease. Table 3 presents maternal factors that increase the risk of mother to child HIV transmission during pregnancy, labor and delivery and breastfeeding.

Table 3. Factors that may increase the risk of HIV transmission		
Pregnancy	Labor and Delivery	Breastfeeding
<ul style="list-style-type: none"> <li>High maternal plasma viral load (new infection or advanced AIDS)</li> <li>Viral, bacterial, or parasitic placental infection (eg, malaria)</li> <li>Sexually transmitted infections (STIs)</li> </ul>	<ul style="list-style-type: none"> <li>High maternal plasma and/or genital viral load (new infection or advanced AIDS)</li> <li>Rupture of membranes more than 4 hours before labor begins</li> <li>Vaginal delivery</li> <li>Invasive delivery procedures that increase contact with mother's infected blood or body fluids (eg, episiotomy, fetal scalp monitoring)</li> <li>First infant in multiple birth</li> <li>Chorioamnionitis (from untreated STI or other infection)</li> </ul>	<ul style="list-style-type: none"> <li>High maternal plasma and/or breast milk viral load (new infection or advanced AIDS)</li> <li>Duration of breastfeeding</li> <li>Early mixed feeding (eg, food or fluids in addition to breastmilk)</li> <li>Breast abscesses, nipple fissures, mastitis</li> <li>Oral disease in the baby (eg, thrush or sores)</li> </ul>

Source: WHO/HHS-CDC PMTCT Generic Training Package

### Introduction to PMTCT

Without intervention, 25-40% of infants born to HIV-positive mothers will become infected. With current interventions, this risk can be reduced to less than 5%. Ensuring provision of maternal antiretroviral therapy for pregnant women who require treatment for their own health and effective provision of PMTCT interventions improves maternal health and infant HIV free survival and can substantially reduce pediatric HIV over time. PMTCT is a key component of overall HIV prevention efforts and represents a critical opportunity for stemming the tide of the HIV epidemic. Comprehensive PMTCT consists of a 4-pronged approach:



When comprehensively implemented, PMTCT holds the potential to:

- substantially reduce new pediatric HIV infections, as has been accomplished in developed countries
- dramatically improve adult, maternal, infant and child health, particularly when well integrated into maternal, newborn and child health (MNCH) settings and in those countries where HIV contributes significantly to morbidity and mortality
- increase awareness of infection status for women and their partners and facilitate access to comprehensive care, support and treatment services
- identify children of HIV-positive women who also need to be tested and, if necessary, access HIV care, support and treatment services
- prevent new HIV infections in women and their male partners through prevention approaches targeted to the infection status of an individual woman and her partner
- prevent unintended pregnancies among HIV-positive women
- promote appropriate reproductive health services including family planning for those HIV-positive women who do not desire future pregnancies, and HIV transmission prevention interventions for those who wish to become pregnant
- contribute to reductions in HIV-related stigma and discrimination through partner, family and community education and awareness efforts
- help mitigate the disproportionate impact of HIV upon women and girls
- strengthen linkages between adult and pediatric treatment services available and PMTCT services
- build capacity for HIV, MNCH and reproductive health systems through education and training of health workers, improved laboratory and data systems, infrastructural improvements of antenatal clinics and labor and delivery wards, and strengthened systems for monitoring and evaluation

To successfully reduce mother-to-child transmission of HIV, population-level efforts to prevent HIV infection among women of childbearing age must be realized. For the individual woman, a comprehensive, coordinated continuum of services must be provided beginning with increased access to counseling, testing, and primary prevention services, as well as reproductive health choices enabling either the prevention of unintended pregnancies or appropriate planning for intended future pregnancies for women living with HIV. For HIV-positive women who become pregnant, access to and follow through on effective interventions to prevent transmission to the infant and to provide treatment for the woman herself and her child if infected must be provided to maximize maternal health and infant HIV-free survival. This continuum of services is often referred to as the PMTCT cascade and includes:

11. Antenatal care attendance
12. HIV counseling and testing with same day return of results to the woman
13. Determination of eligibility for HIV treatment through CD4 count assessment (or less optimally, through clinical staging) with rapid return of results to the woman and her provider
14. Provision of antiretroviral therapy for women who require therapy for their own health and antiretroviral prophylaxis to prevent mother-to-child transmission to women who do not yet require therapy
15. Adherence to HIV treatment or prophylactic regimens as medically appropriate
16. Safe labor and delivery services

17. Timely provision of HIV prophylactic regimens and cotrimoxazole for the infant
18. Safe feeding practices for the infant
19. Early follow-up HIV testing for the infant with rapid initiation of antiretroviral treatment for those who are infected, and testing to determine final HIV status in breastfed infants.
20. Ongoing, clinical, psychological and social care, support and monitoring for the mother, infant and family

**Expert Panel Objectives:**

The Panel was established by Section 309 of the Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act of 2008 (“the Act”), P.L. 110-293. The Panel was also established in accordance with the provisions of the Federal Advisory Committee Act (FACA), as amended, codified in 5 U.S.C. App.

According to the Act, the objectives and the scope of the activities of the Panel are to “provide an objective review of activities to prevent mother-to-child transmission of HIV” (human immunodeficiency virus, the pathogen that causes Acquired Immune Deficiency Syndrome (AIDS); and to “provide recommendations to the Global AIDS Coordinator and to the appropriate congressional committees for scale-up of prevention of mother-to-child transmission prevention services under this Act in order to achieve the target established” in the Act. The target is statutorily defined in Section 307 of the Act as “a target for the prevention and treatment of mother-to-child transmission of HIV that, by 2013, will reach at least 80 percent of pregnant women in those countries most affected by HIV/AIDS in which the United States has HIV/AIDS programs.” The Panel was asked to perform the following duties:

1. Assess the effectiveness of current activities in reaching the target for prevention of mother-to-child transmission established in the Act;
2. Review scientific evidence related to the provision of mother-to-child transmission prevention services, including programmatic data and data from clinical trials;
3. Review and assess ways in which the Office of the United States Global AIDS Coordinator collaborates with international and multilateral entities on efforts to prevent mother-to-child transmission of HIV in affected countries;
4. Identify barriers and challenges to increasing access to mother-to-child transmission prevention services and evaluate potential mechanisms to alleviate those barriers and challenges;
5. Identify the extent to which stigma has hindered pregnant women from obtaining HIV counseling and testing or returning for results, and provide recommendations to address such stigma and its effects;
6. Identify opportunities to improve linkages between mother-to-child transmission prevention services and care and treatment programs; and
7. Recommend specific activities to facilitate reaching the target established in the Act.

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## Chapter 2. Prevention of Mother to Child HIV Transmission (PMTCT): Scientific Evidence

### I. Introduction

While great progress has been achieved in preventing mother to child HIV transmission (MTCT) in resource-rich countries, the perinatal HIV epidemic continues generally unabated in resource-limited settings. Although much is known about preventing transmission from HIV-infected mothers to their children, implementation of international guidelines and scientific advances in resource-limited settings has been slow. As the state of the science in this field evolves rapidly, this chapter aims to summarize the current evidence on interventions for HIV-infected women to prevent HIV infection in children and key research activities.

### II. Objectives

This chapter's objectives are to:

- Summarize what is known about interventions for HIV-infected women to prevent HIV infection in children
- Identify gaps in knowledge and key ongoing research activities

### III. Prevention of Mother to Child HIV Transmission: Scientific Evidence

In resource-rich countries like the United States, there has been dramatic progress in reducing MTCT since 1994, when the Pediatric AIDS Clinical Trials Group (PACTG) 076 clinical trial demonstrated that a regimen of zidovudine (AZT) given during pregnancy, labor and to the newborn reduced transmission by 67% (Connor 1994). In these countries, early identification of HIV infection among pregnant women through routine, opt-out antenatal HIV testing and provision of antiretroviral treatment to HIV-infected pregnant women when needed for their own health or combination antiretroviral prophylaxis if therapy is not yet required has substantially reduced the risk of infants becoming infected during pregnancy and delivery. When combined with elective caesarean delivery and avoidance of all breastfeeding, these interventions have reduced the risk of HIV transmission to infants in the U.S., Europe and other countries with well-resourced health systems to approximately 1-2% (Townsend AIDS 2008).

However, in resource-limited countries, the perinatal HIV epidemic has been much more difficult to control. Clinical trials have identified simple, effective, and relatively inexpensive antiretroviral prophylaxis regimens capable of being implemented in resource-limited settings. The 2006 World Health Organization (WHO) guidelines on use of antiretroviral drugs for treating pregnant women living with HIV infection and preventing HIV infections in infants stress the importance of providing antiretroviral therapy (ART) for women who require it for their own health and the use of regimens such as AZT plus single-dose intrapartum/newborn nevirapine (sdNVP) for prevention of MTCT (PMTCT) in women who don't require therapy for their own health (WHO Antiretroviral Drugs 2006). However, implementation has been slow. Low rates of HIV testing among pregnant women, lack of availability and access to antenatal and PMTCT services, and difficulties integrating PMTCT interventions within existing antiretroviral treatment and maternal and child health (MCH) services, compounded by human resource constraints, have contributed to the slow pace of expansion of PMTCT coverage. In addition, postnatal transmission of HIV through breastfeeding remains a significant challenge.

### Comprehensive PMTCT Strategy

To optimize PMTCT program effectiveness and achieve the overall goal of improving maternal and child health in the context of HIV infection, implementation of all four components of the comprehensive PMTCT strategy is needed, including:

1. Primary prevention of HIV infection among women of childbearing age;
2. Preventing unintended pregnancies among women living with HIV;
3. Preventing HIV transmission from women living with HIV to their infants, and
4. Providing appropriate treatment, care and support to mothers living with HIV and their children and families.

Each new HIV-infected child represents a missed opportunity for prevention: failure to prevent HIV infection in women/girls; failure to prevent unintended pregnancy in HIV-infected women; and failure to initiate PMTCT interventions for a pregnant HIV-infected woman. To optimize survival of the mother and her infant, provision of care, treatment and support for the HIV-infected mother, her infant, and her family, is needed after delivery.

This comprehensive approach is built around the routine offer of HIV testing and counseling to all pregnant women, antiretroviral treatment for HIV-infected women who require treatment and antiretroviral prophylaxis for PMTCT for those not yet needing treatment, counseling and support for infant feeding, and continued provision of care, treatment, and support for women living with HIV. Special attention to primary prevention services for women, safe infant delivery, and strengthening linkages to other sexual/reproductive health services, particularly family planning, is an important part of this strategy.

### **Primary Prevention of HIV in Women and Prevention of Unintended Pregnancy**

Prevention of HIV infection in women of childbearing age and prevention of unintended pregnancies among those women who are infected with HIV are among the most cost-effective ways to prevent HIV infection in children. While the purpose of this report is to discuss what is known about interventions in HIV-infected pregnant women to prevent transmission, a brief discussion of primary prevention of HIV, focused on prevention during pregnancy, and avoidance of unintended pregnancy is provided below.

#### ***Primary Prevention of HIV in Pregnant Women***

Although a critical focus of attention for prevention of MTCT is on the HIV-infected pregnant woman, primary prevention for pregnant women found to be uninfected is also important. While one study in Zimbabwe did not find pregnancy to be associated with increased risk of HIV infection, in a large study in Rakai, Uganda, women had nearly twice the risk of acquiring HIV while pregnant compared with non-pregnant women, irrespective of their sexual behaviors or their partners' plasma viral load (Morrison 2007, Gray Lancet 2005). Increased risk of HIV acquisition during pregnancy, coupled with initial high levels of viral replication during acute infection, including in genital secretions, could make pregnancy itself a mechanism for efficient transmission of HIV from male sexual partners to pregnant women and subsequently to their infants. In resource-rich countries, a significant proportion of the remaining MTCT may be among women having acquiring HIV infection during pregnancy (Patterson 2007). Thus, it remains very important for antenatal programs and postnatal programs to stress the need for condom use to protect both mother and baby from HIV infection during the perinatal period and during lactation if breastfeeding. There is also a critical need to involve the partners of pregnant women in risk reduction strategies.

### ***Avoidance of Unintended Pregnancy***

Globally, approximately 80 million (38%) of the 211 million pregnancies each year are unintended (WHO Reproductive Health 2004, WHO Progress 2009). Sub-Saharan Africa has the lowest levels of contraceptive use, with only 22% of women of reproductive age who are married or in a union using any modern family planning method. Unintended pregnancies account for 14-58% of all births in countries where the burden of HIV is greatest (Reynolds Sex Trans Inf 2008). Several studies suggest that the rates of unintended pregnancy among HIV-infected women may be higher than in the general population. In a study in South Africa, 84% of pregnancies were reported to be unplanned; in Uganda, more than 90% of pregnancies among women enrolled in an antiretroviral treatment program were unintended; and a study in Cote d'Ivoire following 149 women diagnosed with HIV during a previous pregnancy found 37 had repeat pregnancies, of which 51% were unintended (Rochat 2006, Desgrees-du-Lou 2002, Homsy PLoS One 2009). A cross-sectional study of 1,092 HIV-infected men and women attending an AIDS support organization in Jinja, Uganda, found that 42% of participants were sexually active; 33% practiced pregnancy risk behavior, defined as having sex without contraceptive or condom use; and 73% of those sexually active did not want more children and were at high risk for unwanted pregnancies (Nakaviwa 2006). Meeting the contraceptive needs of HIV-infected women will greatly reinforce efforts to reduce the number of HIV-infected children. It is estimated that if all women in sub-Saharan Africa who did not wish to get pregnant accessed contraceptive services, as many as an additional 160,000 new infant HIV infections could be averted every year (Reynolds Sex Trans Inf 2005).

### **HIV Testing and Counseling**

Effective PMTCT requires a range of services. Since access to most interventions to reduce MTCT requires knowledge of maternal HIV serostatus, access to voluntary HIV testing and confidential counseling is critical. However, recent data from WHO suggest that only 21% of women who became pregnant in low- and middle-income countries in 2008 received HIV testing (WHO Progress 2009). While this represents an increase from 10% in 2004, it remains far too low to allow a population response to impact the pediatric HIV epidemic in resource-limited countries. HIV testing coverage among pregnant women in Africa in 2008 varied from 16% in Western and Central Africa to 28% in sub-Saharan Africa and 43% in Eastern and Southern Africa (WHO progress 2009).

High uptake of testing can be achieved with routine provider-initiated HIV testing and counseling combined with use of rapid tests offering same day results in antenatal and delivery settings. Studies have demonstrated that rapid point-of-care HIV tests have high diagnostic performance (Pai 2007). In Botswana, a shift from patient-initiated testing to provider-initiated routine testing increased the proportion of antenatal clients who accepted HIV testing from 76% to 95%; in urban Zimbabwe HIV testing rates increased from 65% to 99% when an opt-out provider-initiated testing program was implemented (Creek 2007, Chandisarewa 2007). The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has provided PMTCT services using opt-out testing to more than 2.6 million women in EGPAF programs in resource-limited settings. Overall, 92.9% of women who received antenatal care or were seen in labor have been counseled, and 82.8% accepted testing.

In the absence of provider-initiated testing and counseling in antenatal clinics, testing rates remain low, even where antenatal care attendance rates are high. While this is primarily due to lack of offering of the test, other factors are also involved including lack of test kits, inadequate counseling, need to discuss with male partner before making decision, and fear of stigma (Medley 2004).

Provision of couple counseling and testing has been shown to increase acceptance of HIV testing by pregnant women in a number of studies from Burkina Faso, Cambodia, Kenya, Tanzania, and Uganda (Kakimoto 2007, Msuya 2008, Kizito 2007, Sarker 2007, Homsy JAIDS 2007, Farquhar 2004). However, even in family-focused programs with free access to antiretroviral therapy such as the MTCT-Plus program in Cote d'Ivoire, only 53% of 568 women indicated that they had disclosed their HIV status to their male partner, with reasons for non-disclosure including fear of accusations of infidelity, abandonment, discrimination and violence (Tonwe-Gold 2009). Further research surrounding the issue of disclosure and involvement of male partners is needed.

Additionally, there are many countries where antenatal attendance and facility-based delivery rates are very low (e.g., Ethiopia, Nigeria), making identification of HIV-infected pregnant women and provision of antiretroviral interventions quite challenging. Innovative approaches and programs to provide PMTCT and HIV services to such populations are needed.

## Use of Antiretroviral Drugs by Pregnant Women for Treatment and to Prevent MTCT

### *How Do Antiretroviral Drugs Reduce Mother to Child HIV Transmission?*

Antiretroviral drugs are believed to reduce *in utero* and intrapartum MTCT through a number of different mechanisms. These include a) administration of antiretroviral drugs to the mother during pregnancy, with direct drug effects on maternal viral replication, thereby decreasing viral load in maternal blood and genital secretions; b) provision of fetal/newborn pre-exposure prophylaxis through transplacental passage of drug given to the mother during labor, resulting in systemic drug levels in the infant at a time of intensive exposure of the infant's skin and mucus membranes to HIV in the mother's genital tract during labor and passage delivery; and c) provision of post-exposure prophylaxis through administration of drug to the infant after birth to protect against cell-free or - associated virus that entered the circulation or had direct contact with the mucosa of the infant during delivery.

Efficacy is likely multifactorial. In women with high viral loads, it is likely that lowering the viral load by antenatal antiretroviral therapy is a critical component of protection. However, antiretroviral drugs have been shown to reduce the risk of transmission even among women with HIV RNA levels <1,000 copies/mL (Ioannidis 2001). Additionally, the level of HIV RNA at delivery and use of antenatal antiretroviral therapy are each independently associated with the risk of transmission, suggesting that antiretroviral prophylaxis does not work solely through reduction in viral load (Cooper 2000).

### *Lessons from Early Clinical Trials*

The AZT regimen used in PACTG 076 was complex and expensive, involving administration of the drug during 3 time periods – orally from 14 weeks gestation, intravenously during labor, and to the infant for 6 weeks (Connor 1994). Following the results of the PACTG 076 trial in 1994, initial trials in resource-limited settings were designed to find effective but shorter and less expensive antiretroviral interventions to reduce antepartum and intrapartum HIV transmission. Table 2 summarizes the results of the major early clinical trials of antiretroviral interventions for PMTCT. These trials have built sequentially on each other and have identified a number of simple and effective regimens. Direct comparison between trials must be done with caution, as patient populations differ considerably. For example, patients enrolled in Asian studies may be infected with different viral subtypes than those found in sub-Saharan Africa, and may have very different breastfeeding practices. In addition, study procedures, such as control interventions and the infant

age at which efficacy was determined may differ. However, some general conclusions can be drawn.

Efficacy has been demonstrated for short regimens with AZT alone; AZT plus lamivudine (3TC); sdNVP; and more recently, combining sdNVP with either short-course AZT or AZT/3TC (Shaffer 1999, Dabis Lancet 1999, Leroy 2002, Wiktor 1999, PETRA 2002, Jackson 2003, Moodley 2003, Lallemand 2000, Lallemand 2004, Dabis AIDS 2005). Combination regimens, such as short-course AZT plus sdNVP, are more effective than single-drug regimens in reducing MTCT (Lallemand 2004). Almost all trials have studied an oral (rather than intravenous) intrapartum prophylaxis component, with varying durations of maternal antenatal and/or infant (and sometimes maternal) postpartum prophylaxis. Regimens that include giving drugs during all 3 time periods - antepartum, intrapartum and postpartum - appear to have greater efficacy than regimens given only during 1 or 2 time periods (e.g., antepartum and intrapartum; intrapartum only; or intrapartum and postpartum). Regimens with antenatal components starting as late as 36 weeks gestation can significantly reduce the risk of transmission, even if they lack an infant prophylaxis component. However, to maximize effectiveness in prevention of *in utero* infection (i.e., virus detected in the infant at birth), interventions need to start earlier in pregnancy. For example, a trial in Thailand found that longer duration of antenatal AZT prophylaxis (starting at 28 weeks gestation) was more effective than a shorter duration (starting at 36 weeks gestation) in preventing *in utero* infection (*in utero* infection rates of 1.6 vs 5.1%, respectively) (Lallemand 2000). More prolonged post-exposure prophylaxis of the infant (which targets intrapartum infection) does not substitute for longer duration of maternal therapy (which targets *in utero* infection) (Lallemand 2000).

Although regimens that include antenatal prophylaxis are optimal, many women do not present to the health care system until late in pregnancy or at delivery. Regimens that include only intrapartum and postpartum drug administration are also effective in reducing MTCT (PETRA 2002, Jackson 2003, Moodley 2003). The PETRA study demonstrated that intrapartum pre-exposure prophylaxis alone, without continued post-exposure prophylaxis of the infant, is not effective (Petra 2002). The SAINT trial demonstrated that the two proven effective intrapartum/postpartum regimens (AZT/3TC or sdNVP) are similar in efficacy and safety (Moodley 2003).

Administration of prophylaxis solely to the infant can also reduce MTCT, although less effectively than when antepartum and/or intrapartum prophylaxis is also given. In the NVAZ trial of infant-only prophylaxis in Malawi, the addition of one week of AZT therapy to infant sdNVP reduced the risk of transmission by 36% compared to infant sdNVP alone when maternal intrapartum NVP was not received (Taha Lancet 2003). However, if maternal intrapartum sdNVP was received (thereby providing pre-exposure prophylaxis in addition to post-exposure prophylaxis), the addition of AZT to the infant sdNVP did not appear to add any incremental benefit (Taha JAMA 2004). In a study in breastfeeding and formula feeding infants in South Africa, transmission rates were similar in infants uninfected at birth who received sdNVP compared to those who received 6 weeks of AZT; however, sdNVP was more effective than AZT in breastfeeding infants (Gray AIDS 2005).

In an attempt to improve the efficacy of short-course regimens but retain a regimen that remains appropriate to the cost limitations existing in resource-limited countries, researchers evaluated whether the addition of a potent intrapartum intervention – the sdNVP regimen – to short-course AZT or AZT/3TC regimens might increase efficacy. The PHPT-2 study in non-breastfeeding women in Thailand, the Mashi study in Botswana (in the formula-fed but not the breastfed infants),

and the DITRAME studies in a partly breastfeeding population in the Ivory Coast, demonstrated that the addition of sdNVP did significantly increase efficacy (Table 1) (Lallemant 2004, Shapiro AIDS 2006, Dabis AIDS 2005). In the PHPT-2 study, transmission rates of 1.1% were observed with short course AZT combined with sdNVP (Lallemant 2004), similar to what is observed with triple drug prophylaxis regimens in resource-rich countries.

The relative importance of the maternal and infant components of sdNVP in the context of short-course AZT regimens remains unclear. The Thailand PHPT-2 study compared short course AZT plus intrapartum/neonatal NVP to AZT plus intrapartum NVP only; the infant NVP dose at day 2 of life did not appear to provide significant additional efficacy compared to the maternal intrapartum NVP dose alone (Lallemant 2004). However, the Botswana Mashi study compared short course AZT plus intrapartum/neonatal NVP to AZT plus infant NVP at birth only; in this study the maternal intrapartum dose did not appear to provide significant additional efficacy compared with infant NVP given at birth alone (Shapiro 2006). A direct comparison of maternal intrapartum only NVP to infant only NVP is now underway in Thailand (PHPT-5) but results will not be available for several years (Table 7). The advantage to eliminating the maternal intrapartum NVP dose is avoidance of the potential development of viral NVP resistance in the mother, which may affect her future treatment options. However, in some implementation studies of programs using the single-dose intrapartum/neonatal NVP regimen, significantly lower adherence to the infant than the maternal intrapartum NVP dose has been observed (Urban 2004, Stringer 2003, Delvaux 2009; Spensley 2009); administration of the infant dose has been particularly problematic when delivery occurs at home.

Although the short-course regimens identified as effective in non-breastfeeding populations are also effective in breastfeeding populations, their overall impact on the long-term risk of infant infection can be severely diminished by the continued risk of transmission during the breastfeeding period. (Dabis 1999, Leroy 2002, Wiktor 1999, PETRA 2003, Jackson 2003). The reduction in efficacy seems greatest with AZT or AZT/3TC short-course regimens, and less with sdNVP. This is likely attributable to the prolonged half-life of NVP in pregnant women in labor and neonates (Cressey 2005); drug levels can persist in the mother and infant for 2 weeks or longer following a single dose, thereby providing a much longer period of prophylaxis than AZT and 3TC, which have much shorter half-lives. Several ongoing and planned trials assess the effect of antiretroviral prophylaxis provided to the mother during lactation or provided to the breastfeeding infant, that will be discussed later (Table 7).

### ***ARV Drug Resistance following Single-Dose Nevirapine Prophylaxis***

Selection of non-nucleoside reverse transcriptase inhibitor (NNRTI)-resistance mutations following the use of sdNVP for PMTCT in women, and in infants who become infected despite prophylaxis, has been documented (Tables 3 and 4). The long half-life of NVP means that detectable drug levels may persist for some time in the face of active viral replication following a single maternal dose. This fact, coupled with the drug's low genetic barrier to resistance (only a single mutation in the viral reverse transcriptase gene is needed to confer drug resistance) means that many women who use sdNVP will develop at least transient drug resistance. The risk of resistance is affected by maternal CD4 count and viral load at the time of exposure and by viral subtype. In a meta-analysis of 10 studies, the prevalence of NVP resistance 4 to 8 weeks following sdNVP was 35.7% (95% confidence interval 23-51%) and in infants who became infected despite prophylaxis was 52.6% (95% confidence interval 37-67%) (Arrive 2007). Tables 3 and 4 summarize available data on rates of nevirapine resistance among women and infants in various studies; for both women and infants,

there is wide range in the proportion with drug resistance detected, varying by viral subtype, the timing of testing following sdNVP exposure, whether other antiretroviral drugs were given in addition to sdNVP, the type of resistance assay used, and for infants, whether the mother received sdNVP in addition to the infant.

While detection of resistance is frequent in the first few weeks following exposure, the likelihood of detection decreases over time. In most women, resistant virus can no longer be detected 6 to 12 months after exposure using standard population genotyping methods. However, low levels of viral resistance can persist for longer periods and in some cases can remain present in latently infected cells (Flys JID 2007, Wind-Rotolo 2009). The long-term relevance of the selection of NNRTI resistance for response to future antiretroviral therapy in both women and infected children is under study; data suggest that women starting NNRTI-based therapy within 6-24 months of sdNVP exposure have higher rates of viral failure than those without sdNVP exposure (Coovadia CID 2009, Lockman 2007, Chi 2007, Lockman 2009).

However, administration of antiretroviral drugs for a period of time following to sdNVP (a so-called “tail” regimen) can reduce the development of resistance to very low levels (Tables 3 and 4). Regimens studied for prevention of resistance include administration of AZT/3TC for 4 to 7 days following sdNVP; tenofovir/emtricitabine (TDF/FTC) as a single-dose during labor only or for 7 days postpartum; administration of AZT/didanosine (ddI)/lopinavir-ritonavir for 7 or 30 days; and administration of AZT/ddI for 30 days (Table 3) (McIntyre 2009, Chi 2007, van Dyke 2009, Farr 2009, Lallemand 2009, TeMAA 2009). NNRTI resistance rates of 0% to 7% at 2 to 6 weeks postpartum using ultrasensitive assays have been reported with use of various tail regimens. Thus, use of a minimum of 7 days of a tail regimen following use of sdNVP is currently recommended to reduce the risk of selecting NNRTI resistance mutations in women.

Selection of resistant virus among infants who become infected despite sdNVP can also be reduced by the addition of a short course of antiretrovirals; rates of resistance are lower among infants who received 3 to 7 days of AZT or AZT/3TC following sdNVP (Table 4).

### ***Antiretroviral Drugs for Maternal Treatment vs Prophylaxis of MTCT***

Clinical trials of PMTCT interventions have largely focused on prevention of HIV infection (as opposed to maternal health). At the time the early clinical trials were conducted, antiretroviral drugs were not widely available for treatment in many resource-limited countries. Given the inextricable link between maternal and infant survival, interventions that address maternal health as well as PMTCT are likely to provide maximal benefit. Antiretroviral drugs are now increasingly available in resource-limited countries, and there is consensus that women who require treatment for their own health should receive triple antiretroviral drugs for treatment (ART) during pregnancy. Women who meet criteria for treatment have lower CD4 counts and high viral loads than those who do not meet treatment criteria, and thus are those at highest risk of MTCT. In such cases, the benefit of reversing maternal disease progression and improving survival with maternal ART outweighs any theoretical risks of *in utero* exposure of the infant to multiple drugs. Additionally, the use of ART will reduce mother to child transmission (Cooper 2000).

A key issue in decisions related to what antiretroviral regimens to choose for an HIV-infected pregnant woman is whether the antiretroviral drugs are being provided for treatment (in which case ART should be provided) or for PMTCT (in which case shorter, less intensive regimens may be equally as effective). Treatment in this context means that antiretroviral drugs are started during



pregnancy and for continued life, even after no further MTCT risk exists; in contrast, antiretroviral drugs given solely for prophylaxis would presumably stop when the risk of MTCT is no longer present. The 2006 WHO guidelines on when to treat pregnant women recommend treating all women with WHO clinical stage 4; for women with WHO clinical stage 3, starting when CD4 cell count is <350 cells/uL; but for women with WHO clinical stage 1 or 2, which constitute the vast majority of pregnant women, therapy is only recommended if CD4 count is <200 cells/uL (WHO Antiretroviral drugs 2006).

Guidelines from the United States, United Kingdom and International AIDS Society all recommended initiation of treatment in all HIV-infected adults with a history of AIDS-defining illness or if mild or no symptoms, with CD4 cell count <350 cells/uL (Panel 2008). The dilemma for resource-limited countries is that if the higher threshold of CD4 <350 cells/uL were adopted, many more people would require immediate therapy, with a subsequent burden for the health care system, monitoring, and higher costs.

Data from Zambia indicate that about 84% of maternal deaths and 82% of postnatal infections occur among women whose CD4 cell count is <350 cells/uL; by contrast, only 55% of maternal deaths and 47% of postnatal infections occur among women whose CD4 is <200 cells/uL (Louise Kuhn, personal communication). Therefore, it is likely that a CD4 count threshold of <350 cells/uL is a much more effective threshold for starting treatment in pregnant women, as it has the potential to prevent substantially more maternal deaths and infant infections. After review of more recent data, in December 2009 WHO revised its guidelines for initiation of treatment of HIV-infected adults, including pregnant women, to a threshold of <350 cell/uL (WHO Rapid Advice Adult 2009, WHO Rapid Advice Pregnancy 2009)

It is therefore critical that programs that provide care for pregnant women, HIV testing and PMTCT also have available CD4 lymphocyte assays to determine the need for therapy and provide treatment to women who require it for their own health. However, many PMTCT programs are located within antenatal clinics that are generally not equipped to provide either CD4 testing or HIV treatment, which tend to be provided in stand-alone clinics that the women would have to be referred to, creating a significant barrier to provision of treatment to pregnant women who need it.

### ***Why not give Triple Drug Prophylaxis to all Pregnant Women Regardless of Need for Treatment?***

In resource-rich countries, triple drug prophylaxis regimens are also often used for PMTCT in women who do not yet require treatment for their own health. However, in the United Kingdom, women with CD4 >350 cells/uL and HIV RNA levels <10,000 copies/mL may receive AZT alone during pregnancy combined with elective cesarean delivery, rather than receiving three drugs. In an analysis of data from 2000-2006 from the United Kingdom and Ireland, the rate of transmission in 464 women who received only AZT during pregnancy and elective cesarean delivery was 0%; the rate of transmission among women receiving triple drug prophylaxis with and without elective cesarean delivery was 0.7% (Townsend AIDS 2008). Thus, for women with high CD4 count who do not require treatment for their own health, low transmission rates may be seen even with use of AZT alone (with elective cesarean delivery) in selected populations of women. However, in resource-limited countries, elective cesarean delivery for HIV-infected women may not be feasible or safe.

While there is evidence that triple drug prophylaxis is more effective than other PMTCT prophylaxis regimens in preventing transmission among women with more advanced disease, it is currently not known whether triple drug prophylaxis is more effective than the current WHO recommended short course regimen among women who do not require treatment for their own health. When drugs are not being administered for maternal treatment but rather to prevent MTCT, the risks of maternal drug toxicities, treatment interruption (presuming treatment stops after there is no further MTCT risk), and of fetal exposure to multiple drugs, need to be weighed against the incremental benefit for PMTCT of triple drug prophylaxis compared to less complex regimens in this population.

In resource-rich countries, when triple drug prophylaxis is used for PMTCT, protease inhibitor-based regimens are typically used for women with CD4 >350 cell/uL. In resource-limited countries, the choice of drugs for triple drug prophylaxis in women with CD4 >350 cells/uL can be problematic. The recommended first line therapy in such settings is NNRTI-based regimens. However, an increased risk of symptomatic and fatal acute hepatic events and of hepatic toxicity has been reported when NVP is used in women with higher CD4 cell counts. Recent data from Thailand demonstrated that hepatic adverse events and rash were more common among pregnant than non-pregnant women and among women receiving ARV for prophylaxis (high CD4 count) than those receiving ARV for treatment (low CD4 count) (Phanuaphak2007). The alternative NNRTI, efavirenz, is associated with teratogenicity in primates, and several cases of central nervous system defects with first trimester efavirenz exposure in humans have been reported in the Antiretroviral Pregnancy Registry (APR 2008). There are published reports on the use of efavirenz in resource-limited countries without finding congenital defects, but the reports include relatively small numbers of women receiving efavirenz in the first trimester. Given a rate of neural tube defects in the general population of 0.1%, over 800 cases with first trimester exposure would be required to rule out a relatively high, five-fold increase in risk (Watts 2007) The alternative use of protease inhibitor-based triple drug prophylaxis used solely for PMTCT is limited by the expense of protease inhibitors.

Another important issue is whether the relatively healthy women who receive triple drug regimens solely for MTCT prophylaxis and then stop therapy face any significant long-term consequences. In the SMART study of 5,472 non-pregnant adults with CD4 cell counts >350 cells/uL at entry, there were more deaths, AIDS events, and serious non-AIDS events among patients randomized to stop treatment and re-start it when their CD4 cell count dropped to <250 cells/uL, compared to those who were randomized to continue treatment and never stop (SMART NEJM 2006). This result was observed regardless of CD4 count at treatment initiation and duration of prior therapy. Additionally, there was a continued elevated risk of opportunistic infections/death even after restarting continuous therapy in patients in the interruption arm (SMART Ann Int Med 2008).

There are long-term follow-up data on women who received AZT or placebo in PACTG 076 (where AZT was given from 14 weeks gestation to delivery and stopped after delivery), with a median of 4 years of follow-up. Temporary use of AZT during pregnancy as prophylaxis appeared to have no long-term effects with no difference in development of AIDS, drop in CD4 <200 cells/uL, death, viral load or resistance between the women who received AZT or placebo (Bardequez 2003). However, there are not yet long-term follow-up data in women stopping triple drug prophylaxis after pregnancy, although this will be evaluated in a clinical trial (PROMISE) that is due to start in 2009 (Table 7); results will not be available for several years.

There remains controversy about the association between maternal triple drug regimens during pregnancy and preterm delivery or low birth weight; some studies from Europe and a study from Miami in the U.S. suggest an increased risk of prematurity with triple drug regimens, while some other studies from the United States have not observed this (Townsend AIDS 2007, Cotter 2006, Tuomala 2002). There are also data from resource-limited countries that suggest maternal triple drug regimens may be associated with low birth weight. In a study of 696 pregnant women in Brazil, the risk of delivering a low birth weight infant was higher in women who were receiving triple drug regimens at the time they conceived compared to those who started during pregnancy (33% vs 17%) (Machado 2008). In a study of 326 women in Cote d'Ivoire, the risk of low birth weight (<2,500 grams) was significantly higher in women who received triple drug regimens (22%) compared to an earlier cohort of women who received a short course AZT or AZT/3TC regimen during pregnancy (12%;  $p=0.02$ ) (Ekouevi 2008). Further evaluation regarding the potential association of triple drug regimens with pregnancy outcome is critically needed in resource-limited countries, as use of antiretroviral drugs for treatment and/or prophylaxis of MTCT gets rolled out.

The long-term risks of fetal exposure of the infant to multiple antiretroviral drugs are not known. Short-term risks appear to be small, but there is currently less than 15 years experience with administration of multiple antiretroviral drugs during pregnancy. Long-term follow-up of antiretroviral-exposed but uninfected children in resource-limited countries is also important as triple drug regimens are increasingly used during pregnancy. Transient elevations in serum lactate (Giaquinto 2001), mild but persistent hematologic abnormalities (Le Chenadec 2003, Pacheco 2006), and rarely clinical symptoms of mitochondrial dysfunction have each been reported in uninfected children with *in utero* antiretroviral drug exposure (Barrett 2003). A recent modeling study suggested that the risk of mitochondrial toxicity due to use of triple drug regimens in pregnancy is at least an order of magnitude lower than the risk of HIV infection with use of less effective regimens (Ciarnello 2008).

Thus, for the subset of women with CD4 >350 cells/uL who do not meet treatment criteria for their own health, a critical question is the comparative prophylactic efficacy of less complex regimens compared to triple drug prophylactic regimens. Although there are some clinical trials that will directly address this question, results will likely not be available for several years (Table 7).

### ***Prevention of Antepartum/Intrapartum Transmission with Antiretroviral Drugs***

Stopping an antiretroviral regimen after the risk of MTCT is no longer present should be restricted to those women whose CD4 count is >350 cell/uL. Available data suggest that for these women, the WHO-recommended prophylaxis regimen of antepartum AZT starting in the second trimester plus intrapartum sdNVP and postpartum maternal administration of 7 days of AZT/3TC to prevent NVP resistance combined with infant prophylaxis with sdNVP around birth followed by 1 week of oral AZT (which will be referred to as “short course AZT/sdNVP”), may have comparable efficacy in preventing antepartum/intrapartum HIV transmission to maternal triple drug prophylaxis. In the PHPT-2 trial in Thailand, where the participants did not breastfeed, AZT from 28 weeks of pregnancy plus sdNVP resulted in MTCT rates of 1% in women with CD4 cell counts >200 cells/uL (Lallemant 2004).

In the Botswana national PMTCT program, HIV-infected pregnant women with CD4 cell counts >200 cells/uL receive the WHO-recommended prophylaxis regimen, while women with CD4 cell counts  $\leq$  200 cells/uL are given triple drug combination ART. In this program, PMTCT uptake stood at 90% in 2007; most HIV-infected women formula-feed their infants. Data on 10,516

children born to HIV-infected women from all health districts between October 2006 and November 2007 were analyzed and data were provided on MTCT rates at age 6 weeks by antiretroviral regimen (Tlale J 2008). In women receiving ART for treatment of maternal disease, MTCT rates were lower if treatment had been started prior to pregnancy than when started during pregnancy (0.7% vs 2.3%, respectively), likely because of prevention of early *in utero* infection. Comparing transmission from women who did not need treatment and received the WHO-recommended short course AZT/sdNVP regimen to those with CD4 <200 cells/uL who received ART during pregnancy for treatment demonstrated similar MTCT rates in this predominantly non-breastfeeding population (3.3% vs 2.3%, respectively).

Finally, the Kesho Bora trial (see Table 7) was a randomized trial in women with CD4 count between 200-500 cells/uL that compared short course AZT/sdNVP to maternal triple drug prophylaxis, both started between 28-26 weeks gestation; maternal triple drug prophylaxis was continued for 6 months postpartum if breastfeeding while the short course arm received no prophylaxis after 1 week during breastfeeding (deVincenzi 2009). Transmission rates at birth (indicating efficacy against *in utero* infection) were similar between the two arms, 1.8% (95% CI 0.8-3.7%) with the maternal triple drug regimen and 2.2% (95% CI 1.2-4.3%) with the short course regimen. Transmission rates at six weeks (indicating efficacy against intrapartum and early breastfeeding transmission) were also similar, 3.3% (95% CI 1.9-5.6%) with maternal triple drug prophylaxis and 4.8% (3.1-7.4%) with the short course regimen, despite the fact that the short course arm did not continue after 1 week of age while the maternal triple drug regimen was continued.

A clinical trial that will directly compare the prophylactic efficacy short course AZT/sdNVP to maternal triple drug prophylaxis to prevent MTCT in pregnant women with CD4 >350 cells/uL (PROMISE) will start in 2010 (Table 7).

### ***Prevention of Postnatal Transmission through Breastfeeding with Antiretroviral Drugs***

The only method known to completely eliminate the risk of breastfeeding-associated HIV transmission is not to breastfeed; this is recommended in settings in which infant replacement feeding is affordable and sustainable, clean water is widely available, hygiene and sanitation conditions are good, and deaths due to diarrhea and other infectious diseases are relatively uncommon. However, this approach is neither feasible nor safe in many resource-limited countries because of cost, inadequate replacement foods to meet the nutritional needs of the infant, unsafe water supply, and/or low acceptability due to stigma associated with not breastfeeding. In such resource-limited settings, infants of HIV-infected mothers who are not breastfed are at high risk for mortality and morbidity, which can outweigh the risk associated with HIV infection itself.

Thus, there has been a critical need to identify strategies to prevent HIV transmission by breastfeeding. Exclusive breastfeeding has been shown in observational studies to lower the risk of postnatal HIV transmission compared to mixed feeding, but does not eliminate risk (Coovadia Lancet 2007, Bland 2008). In resource-limited settings, the benefit of breastfeeding in terms of reducing infant mortality appears to be greatest in the first 6 months of life, although benefit is observed through age 1 year (WHO Collaborative Study Team 2000).

Two potential prevention strategies under study in resource-limited settings are provision of antiretroviral drugs to infants exposed to HIV during breastfeeding (Table 5) and provision of combination antiretroviral therapy to lactating women (Table 6). Both of these strategies have been

predicated on breastfeeding during the period of most benefit, followed by early weaning (e.g., at or before age 6 months).

There are a number of caveats to consider when comparing studies of maternal and infant prophylaxis of postnatal transmission:

- The numbers of patients studied in different reports differ tremendously;
- Reports often lack a 95% confidence interval to help understand the range of transmission encompassed by the intervention;
- There is sometimes a significant drop-off in the numbers of infants tested for HIV infection between early and later time periods (e.g., at 6 months) or the numbers tested at different periods may not be clearly specified;
- The populations studied are not necessarily comparable (e.g., baseline maternal CD4 cell count, different geographic regions);
- The administration and duration of antepartum antiretroviral treatment is clearly important in terms of prevention of *in utero* transmission, but differs between studies or is not specified (e.g., some studies give maternal antepartum drugs from 25 weeks gestation while other studies include late-presenting women who receive no antepartum drugs);
- The duration of postnatal prophylaxis differs among the studies;
- The duration of breastfeeding is clearly important in terms of the time at risk for postnatal transmission, but it is not specified in many studies;
- Rates of exclusive breastfeeding (which may lower postnatal transmission risk) differ; and
- Transmission rates at birth may not be provided, making it difficult to differentiate *in utero* transmission from intrapartum/early postpartum transmission and difficult to compare the incremental benefit of interventions during the breastfeeding period.

Given these caveats, the currently available data suggest that provision of antiretroviral drugs to the breastfeeding infant may have comparable efficacy to provision of maternal triple drug prophylaxis to the lactating mother. Tables 5 and 6 provide data on eight maternal prophylaxis studies and six infant antiretroviral prophylaxis studies to reduce postnatal transmission that have been published or presented at meetings as of August 2009, and includes data on the regimens used, numbers enrolled, maternal CD4 count, infant feeding and duration, and transmission rates at birth, 4-6 weeks and 6-7 months as well as the incremental risk of early (before 4-6 weeks) and late (between 4-6 weeks and 6-7 months) postnatal infection when available; and rates of HIV or death (HIV-free survival) when available (de Vincenzi 2009, Marazzi 2007, Palombi 2007, Thomas 2008, Kilewo 2009, Peltier 2009, Shapiro 2009, Chasela 2009, Thior 2006, Kilewo 2008, Vyankandondera 2003, SWEN 2008, Kumwenda 2008).

Because of differences among the studies in administration of maternal antepartum antiretroviral drugs, comparison of cumulative rates of transmission is misleading when trying to compare the effect of the interventions to reduce breast milk transmission. This is because the infection rate at birth, reflecting *in utero* infection, will be lower if the mother has received drugs during pregnancy than if she received no drugs, and further will be lower with longer than shorter duration of antepartum drug administration. Therefore, to compare the effect of the postpartum intervention, the better comparison is the rate of infection at 4-6 weeks or 6-7 months in infants who are uninfected at birth. However, many of the maternal prophylaxis studies do not provide information on infection rates at birth, therefore only the comparison of late postnatal infection occurring between 4-6 weeks and 6-7 months may be made between maternal and infant strategies. Another problem is that the duration of the actual postnatal intervention also differs between the studies,

with the two large infant prophylaxis studies providing 6 and 14 weeks of prophylaxis, while the maternal studies provide 6 months of prophylaxis. Thus, comparisons of late transmission may also be misleading.

In the four maternal prophylaxis and the four infant prophylaxis studies with adequate information for a meaningful comparison (has birth data to allow assessment of *in utero* infection and 4-6 week data to allow description of the increment in infection between birth and 4-6 weeks of age), the rate of postnatal infection at age 4-6 weeks in infants uninfected at birth with maternal prophylaxis was 0% in Mma Bana and Amata studies, 1.5% in the Kibs study, and 1.5% in the Kesho Bora study, and with infant prophylaxis was 0.8% in the SIMBA study, 1.3% in the Mashhi study, 1.7% in the PEPI-Malawi study and 2.5% in the SWEN study with infant prophylaxis (Table 5 and 6) (de Vincenzi 2009, Thomas 2008, Shapiro 2009, Thior 2006, Vyankandondera 2003, SWEN 2008, Kumwenda 2008). Thus, the early (<4-6 weeks) postnatal infection rates appear relatively similar with either maternal (range 0-1.5%) or infant (range 0.8-2.5%) interventions.

While the ability to evaluate late postnatal infection between 4-6 weeks and 6-7 months of age is possible in most of the studies, it is important to note that in some of the infant prophylaxis studies the intervention stops at 6-14 weeks. In the maternal prophylaxis studies, the rates of late postnatal infection are 0.4% (Mma Bana study), 0.5% (Amata study), 0.8% (Dream study), 1.0% (MITRA-Plus study), 1.5% (Dream study), 1.6% (Kesho Bora study), and 2.6% (Kibs study) (de Vincenzi 2009, Marazzi 2007, Palombi 2007, Thomas 2008, Kilewo 2009, Peltier 2009, Shapiro 2009). In the infant prophylaxis studies in which infant prophylaxis is given for six months as in the maternal studies allowing a comparison of prophylaxis over similar time periods, the rates of late postnatal infection are 0.8% (SIMBA study), 1.2% (MITRA study) and 4.4% (Mashhi study) (Thior 2006, Kilewo 2008, Vyankandondera 2003). Of note, the one infant prophylaxis study with the highest rate of late infection (4.4%) gave infant AZT prophylaxis while all the others used NVP or 3TC (Thior 2006). The late infection rate in the PEPI study, where infant prophylaxis stopped at 14 weeks, was 2.3% (Kumwenda 2008). The SWEN study only administered 6 weeks of infant prophylaxis and therefore no prophylaxis was being received during the period of late transmission risk (after age 6 weeks) (SWEN 2008). Thus, the late (4-6 weeks to 6 months) postnatal infection rates also appear relatively similar with either maternal (range 0.4-2.6%) or infant (range 0.8-4.4%) interventions. In studies that provided data on the endpoint of HIV or death, comparisons at age 6-7 months ranged from 4.7-8.6% in the maternal prophylaxis studies and 2.9-8.5% in infant prophylaxis studies.

Thus, taken together, the early and late postnatal infection rates appear relatively low and relatively similar with either maternal or infant interventions if being compared during similar periods of prophylaxis. The MITRA study of infant prophylaxis and MITRA-Plus study of maternal prophylaxis provide a non-randomized comparison of interventions as both were conducted sequentially in the same clinics, both provided some maternal antepartum antiretroviral prophylaxis, and both provided the same duration (6 months) of postnatal prophylaxis (Kilewo 2009, Kilewo 2008). The cumulative transmission risk at 6 months was 4.9% with infant prophylaxis in MITRA and 5.0% with maternal prophylaxis in MITRA-Plus, and the risk of late transmission between 6 weeks and 6 months was 1.2% with infant prophylaxis and 1.0% with maternal prophylaxis (Tables 5 and 6).

Data from a randomized comparison of maternal and infant interventions for prevention of postnatal transmission is available from the BAN study, which compared 6 months of maternal triple drug

prophylaxis or infant NVP prophylaxis to a control short course arm with no maternal or infant prophylaxis during breastfeeding (Table 7) (Chasela 2009). Transmission rates at age 7 months in infants uninfected at birth were 6.4% in the control arm, compared to 3.0% in the maternal triple drug prophylaxis arm ( $p=0.0032$  vs control) and 1.8% in the infant NVP arm ( $p<0.0001$  vs control). While the transmission rate in the infant NVP arm appeared lower than in the maternal triple drug prophylaxis arm, there was not a significant difference between the two experimental arms ( $p=0.12$ ), although the study was not powered to detect a difference between these two arms.

The data from these studies also indicate the importance of providing antiretroviral drugs during the antepartum period and that longer antepartum prophylaxis is better than shorter prophylaxis, as was already demonstrated in the early clinical trials discussed above. In the maternal prophylaxis studies where initiation of antiretroviral prophylaxis started at 25 to 34 weeks gestation, overall 6-7 month transmission rates were 1-5% (de Vincenzi 2009, Marazzi 2007, Palombi 2007, Thomas 2008, Kilewo 2009, Peltier 2009, Shapiro 2009, Chasela 2009). In the infant prophylaxis studies in which maternal antepartum prophylaxis was given but started significantly later, at 34-36 weeks gestation, overall 6-7 month transmission rates were 5-9% (Thior 2006, Kilewo 2008, Vyankandondera 2003), while in the infant prophylaxis studies where no maternal antepartum drugs were received, overall 6 month transmission rates were approximately 11-12% (SWEN 2008, Kumwenda 2008). Thus, for optimal prevention of mother to child transmission, it is critically important to identify HIV-infected women early in pregnancy and initiate prophylaxis by at least 28 weeks gestation, if not earlier.

#### ***Drug Resistance with Infant or Maternal Antiretroviral Prophylaxis of Postnatal Transmission***

There are concerns regarding potential drug resistance in infants infected postnatally despite either infant or maternal antiretroviral prophylaxis interventions, and further studies are needed to better define risk.

High rates of NVP resistance were seen in breastfed infants in the SWEN study of 6 weeks of infant NVP prophylaxis: 92% of infant who became infected during the first 6 weeks of life (i.e., during the period of NVP prophylaxis), had NVP resistance compared to 38% exposed to sdNVP only (Table 4) (Moorthy2009). However, the risk of NVP resistance among infants who became infected after prophylaxis had ceased (i.e., after 6 weeks of age) was similar, 15% between infants exposed to sdNVP and the extended 6 week NVP infant prophylaxis regimen. Whether the addition of AZT to the infant NVP prophylaxis regimen (as was used in the PEPI-Malawi study) will lead to lower NVP resistance among infants infected despite prophylaxis is not yet known but under study.

Antiretroviral drug resistance has also been observed in infants infected despite prophylaxis with maternal triple drug prophylaxis. Drug resistant virus was identified in 67% of the 24 infants infected postnatally in the KIBS study of maternal triple drug prophylaxis of postnatal transmission (Zeh2008).

It is known that some antiretroviral drugs enter breast milk, and that the concentration of drug in milk varies by drug. The drug 3TC appears to concentrate in breast milk, and is present at levels 3-5 times that in maternal plasma, while AZT appears to be present at levels similar to or somewhat less than maternal plasma (Mirochnick2009). NVP levels are only about 60-75% of maternal plasma, and the protease inhibitors that have been studied have had very limited entry into milk (Colebunders 2005). Thus, breastfeeding infants who become infected may be ingesting sub-therapeutic levels of antiretroviral drugs present in the breast milk of mothers receiving triple drug

regimens and therefore develop drug-resistant virus.

While the development of resistance in these infants is concerning, it should be noted that the proven efficacy of antiretroviral prophylaxis of the infant or mother to prevent postnatal MTCT make such regimens still an attractive choice overall. That is, even though a larger *proportion* of children who become infected while receiving prophylaxis will develop NNRTI resistance, the absolute *number* of children who develop resistance is small since the breastfeeding prophylaxis prevents a substantial number of infections.

### Infant Feeding

A number of studies from South Africa, Zimbabwe, and Cote d'Ivoire now provide strong evidence to support the finding that exclusive breastfeeding is associated with lower rates of postnatal transmission than mixed feeding (Coutsoudis 2001, Iliff 2005, Kuhn 2007, Becquet 2008).

Exclusive breastfeeding is associated with lower risk of diarrhea and pneumonia-related infant morbidity and mortality than mixed feeding (addition of other fluids and solids to breast milk) in infants of mothers without HIV infection and hence is recommended regardless of HIV infection status of the mother (Kuhn 2009). However, despite the clear benefits of exclusive breastfeeding for HIV-infected mothers, there has been difficulty in achieving good uptake of exclusive breastfeeding in many programs (Kuhn 2009).

Both maternal and infant antiretroviral interventions evaluated to date are predicated upon early weaning of the infant, generally at or prior to age 6 months. However, increasing data, including that from the infant and maternal prophylaxis trials, suggest that shortening the duration of breastfeeding may be associated with increased risk of malnutrition and infant mortality due to infectious diseases. Therefore, evaluation of the safety, additional efficacy and cost-effectiveness of more extended postnatal prophylaxis to allow for more prolonged breastfeeding is warranted. Several planned clinical trials are evaluating longer durations of infant prophylaxis, ranging from 9 to 18 months (ANRS PEP, PROMISE, ANRS 12200) (Table 7).

In the Zambia Exclusive Breastfeeding trial, early abrupt cessation of breastfeeding at 4 months by HIV-infected mothers in Zambia did not improve the rate of HIV-free survival among children born to HIV-infected mothers and was harmful to HIV-infected infants (Kuhn 2008). In the PEPI-Malawi infant prophylaxis study, where weaning at 6 months of age was recommended, there was a significantly higher incidence of gastroenteritis and infant mortality in the period immediately following breastfeeding cessation when compared to an historical control with continued breastfeeding (Kafulafula 2009). In the KiBS open-label study of maternal triple drug prophylaxis, an increase in serious gastroenteritis events, hospitalizations, and growth faltering were observed following early breastfeeding cessation around 6 months of age (Thomas 2008). Additionally, in the Mashi study, discontinuation of breastfeeding was the primary risk factor for serious infant morbidity (Thior 2006). Finally, in an outbreak of diarrheal disease associated with heavy rains in Botswana in 2006, a cross-sectional survey found that one-third of children less than age 5 years had diarrhea, which increased levels of acute malnutrition and mortality among children (Mach 2009). Breastfeeding was found to be protective, while age under 2 years and being HIV-exposed was a risk factor for diarrhea; this was particularly relevant because national policy in Botswana at that time was for HIV-infected mothers to formula-feed their infants (Mach 2009).

WHO guidelines in 2006 recommended for HIV-infected women that if replacement feeding was not acceptable, feasible, affordable, sustainable and safe (AFASS), HIV-infected mothers should



exclusively breastfeed their infant for the first 6 months of life (WHO 2006). At six months, if replacement feeding is still not AFASS, continuation of breastfeeding with additional complementary foods is recommended, while the mother and infant continue to be regularly assessed, and all breastfeeding should stop once a nutritionally adequate and safe diet without breastmilk can be provided. However, within program settings, the WHO/UNICEF guidelines were often not being implemented effectively, leading to inappropriate infant-feeding choices and consequent lower infant HIV-free survival (Doherty 2007).

Based in part on the data discussed above, in December 2009 WHO revised their infant feeding guidelines to recommend that national or subnational health authorities should decide whether health services will principally counsel and support HIV-infected mothers to either avoid all breastfeeding, or to breastfeed with infant or maternal antiretroviral prophylaxis (WHO Rapid Advice Infant Feeding 2009). If the approach chosen is to recommend breastfeeding, it is recommended that HIV-infected women exclusively breastfeed their infants for the first 6 months of life, and introduce complementary foods thereafter and while continuing breastfeeding for the first 12 months of life; breastfeeding should stop only once a nutritionally adequate and safe diet without breast milk can be provided. Gradual weaning over the course of one month is recommended, with infant or maternal antiretroviral prophylaxis continued until one week after breastfeeding is fully stopped.

Operational research to determine the optimal way to provide counseling of mothers and assessment of individual and environmental criteria to support appropriate infant-feeding choices is urgently needed.

#### **IV. Summary and Recommendations**

To maximize prevention of HIV transmission and maternal and infant survival, it is critical that care of both the mother and the infant is optimized. This begins with prevention of HIV infection among women and provision of safe contraception and other reproductive health services.

HIV screening during pregnancy is essential to enable women to know their infection status and make informed decisions regarding infant feeding. HIV -infected pregnant women need to be assessed to determine their need for therapy, and CD4 count assays need to be readily available in the antenatal setting. Women with advanced disease are more likely to transmit HIV to their infants (including during breastfeeding), develop resistance with use of sdNVP prophylaxis, and to have progression of disease and death; such women need to be started on ART as soon as possible and continue this therapy for life. To prevent *in utero* and peripartum transmission, women who do not require treatment (CD4 count >350 cells/uL) should receive at minimum an appropriate short-course antiretroviral intervention during pregnancy and intrapartum, and neonatal antiretroviral prophylaxis.

WHO currently recommends if HIV-infected women breastfeed, they exclusively breastfeed for the first 6 months of life and then continue to breastfeed with supplementary foods through age 12 months, and that breastfeeding should be accompanied by use of postnatal antiretroviral prophylaxis. Two interventions to reduce postnatal transmission have been identified as effective in both observational studies and randomized trials: infant antiretroviral prophylaxis and maternal triple drug prophylaxis during lactation. For women who require therapy for their own health, maternal triple drug regimens should be given during breastfeeding and continued after weaning. For women with CD4 >350 cells/uL who are breastfeeding, one of the proven effective

interventions (maternal or infant prophylaxis) should be provided; data are currently not adequate to determine whether one approach is superior to the other, and a number of factors need to be considered, including cost and feasibility.

While the optimal duration of postnatal prophylaxis during breastfeeding remains to be determined, studies have demonstrated that up to 6 months of either infant or maternal antiretroviral prophylaxis appears to be relatively safe and effective. The available data suggest that early weaning in many resource-limited settings may result in excess morbidity and mortality among infants who escape infection, resulting in no advantage of the intervention in overall HIV-free survival. Thus, evaluation of the safety, additional efficacy and cost-effectiveness of more extended postnatal prophylaxis to allow for more prolonged breastfeeding is warranted. The comparative efficacy, safety (for mother and infant), and cost-effectiveness of extended maternal vs infant prophylaxis during prolonged breastfeeding will be an important question to evaluate for HIV-infected women who don't require treatment for their own health.

As increasing numbers of HIV-infected pregnant women receive antiretroviral drugs during pregnancy, surveillance for the effect of such treatments on maternal health, pregnancy outcome, including birth defects, and the short- and long-term effects of *in utero* antiretroviral drug exposure on their infants (including HIV-exposed but uninfected infants) is critical. PEPFAR support of pharmacovigilance programs to monitor for such effects is important.

Finally, operational research is needed to determine the optimal ways to implement the cascade of steps needed for prevention of mother-to-child transmission. Research is particularly needed to ascertain program models that facilitate integration of maternal and child health services into a comprehensive, integrated and longitudinal program for prevention of mother to child HIV transmission. For example, programs for prevention of mother to child transmission need to include elements to ensure maternal health and survival by assuring that HIV-infected pregnant and/or lactating women are promptly assessed for their need for treatment for their own health, and provided rapid access treatment if needed. Programs must also provide access to early infant diagnostic testing to allow early identification and treatment of HIV-infected infants and must also address optimal infant feeding and nutrition counseling, as the goal of the prevention program is not just prevention of HIV infection but also to ensure survival of the uninfected infant.

**Table 1. Countries where 80% of the World's Children Living with HIV Infection Reside\***

Region	Countries
Africa	Botswana, Cote d'Ivoire, Democratic Republic of Congo, Botswana, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe
Asia and Pacific	China, India
Europe	Russia, Ukraine
Latin America	Brazil, Dominican Republic
Caribbean	Honduras, Haiti, Guatemala

\*Adapted from: Guidozzi F, Black V. The obstetric face and challenge of HIV/AIDS. Clin Obstet Gynecol 2009;52:270-84.

**Table 2. Results of Early Clinical Trials of Antiretroviral Prophylaxis to HIV Transmission from Mother to Infant**

Author, Year/ Study/Location/ Mode Infant Feeding	Drugs	Antepartum and Intrapartum	Postpartum	Mother to Child Transmission Rate and Efficacy
Connor, 1994 PACTG 076 United States, France Formula feeding	AZT vs placebo	Long (from 14 weeks); intravenous IP	Long (6 weeks), infant only	<ul style="list-style-type: none"> <li>8.3% in AZT arm vs 25.5% in placebo arm at 18 months (68% efficacy)</li> </ul>
Shaffer, 1999 CDC short-course AZT Thailand Formula feeding	AZT vs placebo	Short (from 36 weeks); oral IP	None	<ul style="list-style-type: none"> <li>9.4% in AZT arm vs 18.9% in placebo arm at 6 months (50% efficacy)</li> </ul>
Dabis, 1999; Leroy 2002 DITRAME (ANRS 049a) Côte d'Ivoire, Burkina Faso Breastfeeding	AZT vs placebo	Short (from 36 weeks); oral IP	Short (1 week), mother only	<ul style="list-style-type: none"> <li>18.0% in AZT arm, 27.5% in placebo arm at 6 months (38% efficacy); 21.5% vs 30.6% at 15 months (30% efficacy)</li> <li>22.5% in AZT arm vs 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy)</li> </ul>
Wiktor 1999; Leroy 2004 CDC short-course AZT Côte d'Ivoire Breastfeeding	AZT vs placebo	Short (from 36 weeks); oral IP	None	<ul style="list-style-type: none"> <li>16.5% in AZT arm vs 26.1% in placebo arm at 3 months (37% efficacy)</li> <li>22.5% in AZT arm vs 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy)</li> </ul>
PETRA, 2002 PETRA trial South Africa, Tanzania	Antenatal, IP/PP AZT + 3TC vs IP/PP AZT + 3TC vs IP- only AZT + 3TC vs	Short (from 36 weeks); oral IP	Short (1 week), mother and infant	<ul style="list-style-type: none"> <li>5.7% at 6 weeks for AP/IP/PP AZT + 3TC, 8.9% for IP/PP AZT + 3TC, 14.2% for IP-only AZT + 3TC and 15.3% for placebo (efficacy)</li> </ul>

and Uganda Breastfeeding and formula feeding	placebo			<p>compared with placebo: 63%, 42%, and 0%, respectively)</p> <ul style="list-style-type: none"> <li>14.9% at 18 months for AP/IP/PP AZT + 3TC, 18.1% for IP/PP AZT + 3TC, 20.0% for IP-only AZT + 3TC and 22.2% for placebo (efficacy compared with placebo: 34%, 18%, and 0%, respectively)</li> </ul>
Jackson, 2003 HIVNET 012 trial Uganda Breastfeeding	SD NVP vs. AZT	No AP ARV; oral IP: SD NVP vs oral AZT	SD NVP within 72 hours of birth (infant only) vs AZT (1 week), infant only	<ul style="list-style-type: none"> <li>11.8% in NVP arm vs 20.0% in AZT arm at 6 to 8 weeks (42% efficacy); 15.7% in NVP arm vs 25.8% in AZT arm at 18 months (41% efficacy)</li> </ul>
Moodley, 2003 SAINT trial South Africa Breastfeeding and formula feeding	SD NVP vs AZT + 3TC	No AP ARV; oral IP: SD NVP vs AZT + 3TC	SD NVP within 48 hours of birth (mother and infant) vs AZT + 3TC (1 week), mother and infant	<ul style="list-style-type: none"> <li>12.3% in SD NVP arm vs 9.3% in AZT + 3TC arm at 8 weeks (difference not statistically significant, <math>p=0.11</math>)</li> </ul>
Lallemant, 2000 Perinatal HIV Prevention Trial (PHPT-1) Thailand Formula feeding	Four AZT regimens with different durations of AP and infant PP administration, no placebo	Long (from 28 weeks), short (from 36 weeks); oral IP	Long (6 weeks), short (3 days), infant only	<ul style="list-style-type: none"> <li>Short-short arm stopped at interim analysis (10.5%); MTCT 6.5% in long-long arm vs 4.7% in long-short arm and 8.6% in the short-long arm at 6 months (no statistical difference); <i>in utero</i> transmission significantly higher with short vs long maternal therapy regimens (5.1% vs 1.6%)</li> </ul>
Dorenbaum, 2002 PACTG 316 trial Bahamas, Belgium, Brazil, France, Germany, Italy, Spain, Sweden, Switzerland, United Kingdom, United States	SD NVP vs placebo among women already receiving AZT alone (23%) or AZT + other ARV drugs (77% combination therapy)	Non-study ARV regimen; oral IP: placebo vs SD NVP + intravenous AZT	Placebo vs SD NVP within 72 hours of birth + non-study ARV drugs (AZT), infant only	<ul style="list-style-type: none"> <li>77% of women received dual or triple-combination ARV regimens during pregnancy</li> <li>Trial stopped early due to very low MTCT in both arms: 1.4% in SD NVP arm vs 1.6% in placebo arm (53% of MTCT was <i>in utero</i>)</li> </ul>

Formula feeding				
Lallemant, 2004 Perinatal HIV Prevention Trial (PHPT-2) Thailand Formula feeding	AZT alone vs AZT + maternal and infant SD NVP vs AZT + maternal SD NVP	AZT from 28 weeks; oral IP: AZT alone or AZT + SD NVP	AZT for 1 week with or without SD NVP, infant only	<ul style="list-style-type: none"> <li>AZT-alone arm was stopped due to higher MTCT than the NVP–NVP arm (6.3% vs 1.1%); in arms in which the mother received SD NVP, MTCT rate did not differ significantly between the infant receiving or not receiving SD NVP (2.0% vs 2.8%)</li> </ul>
Dabis, 2005 DITRAME Plus (ANRS 1201.0) Côte d'Ivoire Breastfeeding and formula feeding	Open label, AZT + SD NVP	AZT from 36 weeks; oral IP: AZT plus SD NVP	SD NVP + AZT for 1 week, infant only	<ul style="list-style-type: none"> <li>6.5% (95% CI 3.9–9.1%) at 6 weeks; historical control group receiving short AZT only had MTCT 12.8% (98% breastfed in historical control group)</li> </ul>
Dabis, 2005 DITRAME Plus (ANRS 1201.1) Côte d'Ivoire Breastfeeding and formula feeding	Open label, AZT + 3TC + SD NVP	AZT + 3TC from 32 weeks (stopped at 3 days PP); oral IP: AZT + 3TC + SD NVP	SD NVP + AZT for 1 week, infant only	<ul style="list-style-type: none"> <li>4.7% (95% CI 2.4–7.0%) at 6 weeks; historical control group receiving short AZT only had MTCT 12.8% (98% breastfed in historical control group)</li> </ul>

Taha, 2003 NVAZ trial Malawi Breastfeeding	Neonatal SD NVP vs SD NVP + AZT	No AP or IP ARV (latecomers)	SD NVP with or without AZT for 1 week, infant only	<ul style="list-style-type: none"> <li>15.3% in SD NVP + AZT arm and 20.9% in SD NVP only arm at 6 to 8 weeks; MTCT rate at 6 to 8 weeks among infants who were HIV-uninfected at birth 7.7% and 12.1%, respectively (36% efficacy)</li> </ul>
Taha, 2004 NVAZ Malawi Breastfeeding	Neonatal SD NVP vs SD NVP + AZT	No AP ARV; oral IP: SD NVP	SD NVP with or without AZT for 1 week, infant only	<ul style="list-style-type: none"> <li>16.3% in NVP + AZT arm and 14.1% in SD NVP-only arm at 6 to 8 weeks (difference not statistically significant); MTCT rate at 6 to 8 weeks among infants who were HIV-uninfected at birth 6.5% and 16.9%, respectively</li> </ul>
Gray, 2005 Post-exposure Infant Prophylaxis South Africa Breastfeeding and formula feeding	Neonatal SD NVP vs AZT for 6 weeks	No AP or IP ARV	SD NVP vs AZT for 6 weeks	<ul style="list-style-type: none"> <li>Formula-fed infants only, 14.3% in SD NVP arm and 14.1% in AZT arm at 6 weeks (not significant, <math>p=0.30</math>); breastfed infants only, 12.2% in SD NVP arm and 19.6% in AZT arm (<math>p=0.03</math>).</li> </ul>
Shapiro, 2006; Thior, 2006 MASHI Botswana Breastfeeding and formula feeding	<p>Initial: short-course AZT with/without maternal and infant SD NVP and with/without breastfeeding</p> <p>Revised: short-course AZT + infant SD NVP with/without maternal SD NVP and with/without breastfeeding; women with CD4 &lt;200 receive ART</p>	1 <sup>st</sup> randomization AZT from 34 weeks ; oral IP: AZT + either SD NVP vs. placebo	<p>2<sup>nd</sup> randomization Breastfeeding + AZT (infant) 6 months + SD NVP, infant only vs. Formula feeding + AZT (infant) 4 weeks + SD NVP, infant only</p>	<ul style="list-style-type: none"> <li>Initial design: In formula-feeding arm, MTCT at 1 month, 2.4% in maternal &amp; infant SD NVP arm and 8.3% in placebo arm (<math>p=0.05</math>); in breastfeeding + infant AZT arm, MTCT at 1 month 8.4% in SD NVP arm and 4.1% in placebo arm (difference not statistically significant)</li> <li>Revised design: MTCT at 1 month 4.3% in maternal + infant SD NVP arm and 3.7% in maternal placebo + infant SD NVP arm (no significant difference; no interaction with mode of infant feeding)</li> <li>MTCT at 7 months 9.1% in breastfeeding + AZT arm and 5.6%</li> </ul>

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in formula feeding arm; mortality at 7 months, 4.9% breastfeeding + AZT vs 9.3% formula feeding; HIV-free survival at 18 months 15.6% breastfeeding + AZT vs 14.2% formula feeding

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3TC: lamivudine; AP: antepartum; ARV: antiretroviral; ART: antiretroviral therapy; IP: intrapartum; MTCT: mother to child transmission; NVP: nevirapine; PP: postpartum; SD: single-dose; AZT: zidovudine



**Table 3. Studies of NNRTI Resistance in Women Following Single-Dose Nevirapine for Prevention of Mother to Child Transmission**

Study	Author/Year/ Country	No. women	HIV Subtype	Time of testing	Anteparutm/Intrapartum	Maternal Postpartum	% with resistant virus (standard assay)	% with resistant virus (sensitive assay)
NVAZ HIVNET 012	Eshleman 2006, Flys 2006 Malawi, Uganda	306	A, C, D	6-8 weeks	sdNVP	-	69% subtype C	70% subtype C
							36% subtype D	55% subtype D
							19% subtype A	42% subtype A
TOPS	McIntyre 2009/ South Africa	68	C	2-6 weeks	sdNVP (control arm)	-	57%	-
BAN	Farr 2009/ Malawi	66	C	6 weeks	sdNVP (control)	-	52%	-
South Africa	Loubser 2006/ South Africa	31	C	6 weeks	sdNVP	-	52%	87%
MASHI	Shapiro 2006/ Botswana	155	C	4 weeks	AZT/sdNVP	-	45%	-
PHPT-2	Jourdain 2004/ Thailand	209	CRF, B, C	10 days	AZT/sdNVP	-	32%	-
NCT 00204308	Chi 2007/ Zambia	166	C	6 weeks	AZT/sdNVP (control arm)	-	25%	-
RP Study	Flys 2008/ Uganda	91	A, C, D, CRF	6 weeks	sdNVP	-	-	23%
Western Cape	Van Zyl 2008/ South Africa	76	C	60 days	AZT/sdNVP	-	17%	
PACTG 316	Cunningham 2002/ US/France	217	B	6 weeks	70% combination ARV /sdNVP	-	15%	-
TOPS	McIntyre 2009/ South Africa	67	C	6 week	sdNVP + AZT/3TC	AZT/3TC x 4 d	13%	-
NCT 00204308	Chi 2007/ Zambia	173	C	6 weeks	sdNVP + sdTDF/FTC	-	12%	-
TOPS	McIntyre 2009/ South Africa	68	C	2-6 weeks	sdNVP + AZT/3TC	AZT/3TC x 7 d	9%	-
BAN	Farr 2009/ Malawi	123	C	6 weeks	sdNVP + AZT/3TC	AZT/3TC x 7 d	8%	-

**PMTCT: Scientific Evidence**

ANRS 12109	TEMAA study group 2009/Cote d'Ivoire, Cambodia, South Africa	38	CRF, A, C	28 days	AZT/sdNVP + sdTDF/FTC	TDF/FTC x 7 d	0%	-
ANRS 1201.1	Chaix 2006/ Cote d'Ivoire	88	CRF, A	4 weeks	AZT+3TC/sdNVP + 3TC	AZT/3TC x 3 d	1%	-
P1032	Van Dyke 2009/ Thailand	56	E,B	2-6 weeks	AZT/sdNVP + ddI/LPV	AZT/ddI/LPV x 7 d	0%	3.6%
P1032	Van Dyke 2009/ Thailand	56	E,B	2-6 weeks	AZT/sdNVP + ddI	AZT/ddI x 30 d	0%	7.1%
PHPT-4	Lallemant 2009/ Thailand	222	E, B	7-120 days	AZT/sdNVP + ddI	AZT/ddI x 30 d	0%	1.8%
P1032	Van Dyke 2009/ Thailand	57	E,B	2-6 weeks	AZT/sdNVP + ddI/LPV	AZT/ddI/LPV x 30 d	0%	5.3%

sdNVP: single-dose nevirapine; AZT: zidovudine; 3TC: lamivudine; ddI: didanosine; LPV: lopinavir/ritonavir; TDF: tenofovir; FTC: emtricitabine

AZTAZT

**Table 4. Studies of NNRTI Resistance in Infants Who Are Infected Despite Single-Dose Nevirapine for Prevention of Transmission**

Study	Country	No. infants	HIV Subtype	Time of testing	Mother Antepartum/Intrapartum	Infant Postpartum	% with resistant virus (standard assay)	% with resistant virus (sensitive assay)
SWEN	Moorthy 2009/ India	12	C	6 weeks	sdNVP	NVP x 6 weeks	92%	92%
NVAZ	Eshleman 2005/ Malawi	23	C	6-8 weeks	sdNVP	sdNVP	87%	-
SWEN	Church 2008/ Uganda	25	A, D	6 week	sdNVP	NVP x 6 week	84%	-
SWEN	Church 2008/ Uganda	24	A,D	6 weeks	sdNVP	sdNVP (control arm)	50%	-
HIVNET 012	Eshleman 2001/ Uganda	24	A, D	6-8 weeks	sdNVP	sdNVP	46%	-
India NACO	Kurle 2007/ India	13	C	8 weeks	sdNVP	sdNVP	46%	-
South Africa	Martinson 2007/ South Africa	42	C	12 weeks	sdNVP	sdNVP	45%	-
HIVNET 024	Nelson 2009/ Tanzania	16	A, C, D	4-6 weeks	sdNVP	sdNVP	44%	-
RP Study	Flys 2008/ Uganda	17	A, C, D, CRF	6 weeks	sdNVP	sdNVP	-	41%
SWEN	Moorthy 2009/ India	29	C	6 weeks	sdNVP	sdNVP (control arm)	38%	59%
NVAZ	Eshleman 2006/ Malawi	19	C	6-8 weeks	-	sdNVP	74%	-
NVAZ	Eshleman 2006/ Malawi	21	C	6-8 weeks	sdNVP	sdNVP + AZT x 7 days	57%	-
NVAZ	Eshleman 2006/ Malawi	15	C	6-8 weeks	-	sdNVP + AZT x 7 days	27%	-
TOPS	McIntyre 2009/ South Africa	9	C	2-6 weeks	sdNVP (control arm)	sdNVP	56%	-
TOPS	McIntyre 2009/ South Africa	8	C	6 week	sdNVP + AZT/3TC	sdNVP +AZT/3TC x 4 days	13%	-

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TOPS	McIntyre 2009/ South Africa	7	C	2-6 weeks	sdNVP + AZT/3TC	sdNVP +AZT/3TC x 7 days	14%	-
ANRS 1201.1	Chaix 2006/ Cote d'Ivoire	14	CRF, A	4 weeks	AZT+3TC/sdNVP + 3TC	AZT/3TC x 3 days	7%	-

sdNVP: single-dose nevirapine; AZT: zidovudine; 3TC: lamivudine

**Table 5. Published/Presented Studies of Maternal Triple Drug Prophylaxis to Prevent Postnatal HIV Transmission through Breast Milk**

Study	Timing of Maternal Triple Drug Administration	Number Infants	Median Maternal CD4 (cells/uL)	Infant Feeding	HIV Transmission at Birth and 4-6 Weeks % (95% CI)	HIV Transmission at 6-7 Months % (95% CI)	HIV or Death % (95% CI)
Dream/Mozambique Marazzi Eur J Ped 2007 Observational	Median 26.8 weeks gestation to 6 months postpartum if breastfeeding	985 mothers enrolled  707 infants tested at 1 month, 467 infants tested at 6 months  Did not specify % formula feeding vs breastfeeding	489	Formula and breastfeeding; breastfeeding duration not specified (counseled to wean at 6 months)	Birth: no data  Cumulative at 4 weeks: 3.8% (3.1-4.5)	Cumulative at 6 months: 5.3%  <u>Increment</u> between 4 weeks to 6 months: 1.5% (0.9-2.1)	Not specified
Dream/Mozambique Palombi AIDS Suppl 2007 Observational	25 weeks gestation to 6 months postpartum if breastfeeding	Formula feeding: 891 (data on 809 infants)  Breastfeeding: 341 infants tested at 1 month, 251 infants tested at 6 months	Not specified	Formula and breastfeeding; breastfeeding duration not specified (counseled to wean at 6 months)	Birth: no data  Cumulative at 4 weeks: 1.2% (4/341 breastfed)	Cumulative at 6 months: 2.2% (0.6-3.8) (6/266 breastfed)  <u>Increment</u> between 4 weeks to 6 months: 0.8% (0.1-2.8) (2/251 breastfed)	HIV or death not specified  Infant mortality at 6 months: 2.85 per 100 child-years
KiBS/Kenya Thomas CROI 2008 Open-label non-randomized trial	34 weeks gestation to 6 months postpartum	Breastfeeding: 497 infants	394 (24% ≤250)	Breastfeeding only, duration not specified (counseled to wean at 6 months)	Birth: 2.4% (95% CI 1.4-4.2%)  Cumulative at 6 weeks: 3.9% (2.5-6.0)  <u>Increment</u> between day 1 and 6 weeks: 1.5%	Cumulative at 6 months: 5.0% (3.4-6.3)  <u>Increment</u> between 1 week and 6 months: 2.6%	Not specified
MITRA-Plus/Tanzania Kilewo JAIDS 2009 Open-label non-randomized trial	34 weeks gestation to 6 months postpartum	501 mothers enrolled, 441 with data  Breastfeeding: 441 infants	415 (17.5% <200)	Breastfeeding only, median duration 24 weeks	Birth: no data  Cumulative at 6 weeks: 4.1% (18/423 infants) (2.2-6.0)	Cumulative at 6 months: 5.0% (22/397 infants) (2.9-7.1)  <u>Increment</u> between 6 weeks and 6 months: 1.0%	HIV or death: • 8.6% (6-11.2) at 6 months • 12.8% (9.6-16) at 12 months
AMATA/Rwanda Peltier 2009 Observational	28 weeks gestation to 7 months postpartum if breastfeeding	562 mothers enrolled, 551 delivered, 532 infants alive after 2 days  Breastfeeding: 227 infants	CD4 (mean) 498 (IQR 326-659)	Formula (57%) and breastfeeding (43%), breastfeeding duration not	Breastfeeding:  Birth: 1.3% (3/227)	Breastfeeding  Cumulative at 9 months: 1.8% (4/227 infants) (95% CI 0.7-	Breastfeeding:  HIV or death: • 4.9% (95% CI 3-9%)

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				specified (counseled to wean at 6 months)	Cumulative at 6 weeks: 1.3% (95% CI 0.4-4.1%)  <u>Increment</u> between birth and 6 weeks: 0%	4.8%)  <u>Increment</u> between 6 weeks and 6 months: 0.5% (1/227 breastfed)	(7/216) at 9 months
Mma Bana Study/Botswana Shapiro IAS 2009 Randomized comparative trial for CD4 >200 (see Table 7)	CD4 >200 randomized trial: 26-34 weeks gestation to 6 months postpartum  Median duration 11 weeks	Breastfeeding: 560 mothers enrolled, 553 infants with 6 month data	398-403	Breastfeeding only; 71% breastfed for ≥5 months but <1% after 6 months  93% reported EBF to weaning	Maternal triple drug arms combined:  Birth: 0.7% (4/553)  No 6 week data but no intrapartum transmission so <u>Increment</u> between birth and 4 weeks: 0%	Cumulative at 6 months: 1.1% (95% CI 0.5-2.0)  <u>Increment</u> between birth and 6 months: 0.4%	HIV or death not specified  Infant mortality at 6 months: 2.5%
Kesho Bora/Kenya, South Africa, Burkina Faso de Vincenzi IAS 2009 Randomized trial for CD4 200-500 (see Table 7)	CD4 200-500 randomized trial: 28-36 weeks gestation to 6.5 months postpartum	Breastfeeding: triple drug arm, 413 mothers enrolled, 402 live births	335	Formula (23%) and breastfeeding (77%), median duration 21.4 months  46% EBF at 3 months	Birth: 1.8% (0.8- 3.7%)  Cumulative at 6 weeks: 3.3 (95% CI 1.9-5.6)  <u>Increment</u> between birth and 6 weeks: 1.5%	Cumulative at 6 months: 4.9% (95% CI 3.1-7.5)  <u>Increment</u> between 6 weeks and 6 months: 1.6%	HIV or death:  Maternal triple drug arm: • 8.3% (6- 11.5) at 6 months • 10.4% (7.7- 13.9) at 12 months
BAN/Kenya Chasela IAS 2009 Randomized trial for CD4 >250 (see Table 7)	CD4 >250 Randomized trial: delivery to 6 months postpartum	Breastfeeding: triple drug arm, 851 mothers enrolled	428	Breastfeeding only; duration not specified (counseled to wean at 6 months)	Birth: enrolled at delivery, rates based on uninfected at 2 weeks  Cumulative at 6 weeks: Not specified	Cumulative at 7 months (uninfected at 2 weeks): 3.0%  <u>Increment</u> between 2 weeks and 6 months: 3.0%	HIV or death:  Maternal triple drug arm: • 4.7% at 7 months

95% CI: 95% confidence interval;; EBF: exclusive breastfeeding

**Table 6. Published/Presented Studies of Infant Antiretroviral Prophylaxis to Prevent Postnatal HIV Transmission through Breast Milk**

Study	Maternal Antepartum/ Infant Antiretroviral Prophylaxis	Number infants	Median Maternal CD4 (cells/uL)	Infant feeding	HIV transmission at 4-6 weeks	HIV transmission at 6-7 months	HIV or death
Mashi/Botswana Thior JAMA 2006 Randomized trial (see Table 2)	Mother: AZT 34 weeks to delivery (+- sdNVP)  Infant: AZT to 6 months if breastfeeding (+- sdNVP)	Formula feeding: 591 infants  Breastfeeding: 588 infants	372 (breastfeeding)	Formula and breastfeeding; median duration 5.9 months  51% EBF at 3 months	Birth: 3.3% (19/558 breastfed)  Cumulative at 4 weeks: 4.6% (27/557 breastfed)  <u>Increment</u> between day 1 and 4 weeks: 1.3%	Cumulative at 7 months: 9.0% (51/541 breastfed)  <u>Increment</u> between 4 weeks and 7 months: 4.4%	HIV or death: • 6.1% at 4 weeks • 12.9% at 12 months
Mitra/Tanzania Kilewo JAIDS 2008 Open-label non-randomized trial	Mother: AZT/3TC 36 weeks to 1 week postpartum  Infant: AZT/3TC x 1 week, then daily 3TC to 6 month	Breastfeeding: 398 infants	411 (15.4% <200)	Breastfeeding only, median duration 18 weeks	Birth: No data  Cumulative at 6 weeks: 3.8% (2.0-5.6)	Cumulative at 6 months: 4.9% (2.7-7.1%)  <u>Increment</u> between 6 weeks and 6 months: 1.2% (0-2.4)	HIV or death: • 4.5% (2.4-6.5) at 6 weeks • 8.5% (5.7-11.4) at 6 months
SIMBA/Uganda, Rwanda IAS 2002 Randomized trial	Mother: AZT/ddI 36 weeks to 1 week postpartum  Infant: randomized at birth to daily 3TC or NVP to 6 months	Breastfeeding: 397 infants  (199 randomized to 3TC, 198 to NVP; no difference between arms)	427	Breastfeeding only, median duration 100-107 days (~3.3 months)	Birth: 6.0% (24/397 infants)  Cumulative at 4 weeks: 6.8%  <u>Increment</u> from 1 week to 4 weeks: 0.8% (3/373 infants)	Cumulative at 6 months: 7.6% (30/397 infants) (5-14%)  <u>Increment</u> between 4 weeks and 6 months: 0.8% (3/358 infants)	Not specified
SWEN/Ethiopia, Uganda, India Swen Study Group Lancet 2008 Randomized trial (combined analysis 3 separate trials)	Mother: Late presenter, <u>no</u> antepartum antiretrovirals  Infant: sdNVP, and randomized to daily placebo vs extended NVP from day 8 to	Breastfeeding: 2074 infants (placebo 1047, extended NVP 977)  Uninfected at birth and data at 6 months: Placebo: 928 Extended NVP: 831	397	Breastfeeding only, most wean between 14 weeks (73% breastfeeding) and 6 months (31% breastfeeding)	Extended NVP arm:  Birth: 4.7%  Cumulative at 6 weeks: 7.2%  <u>Increment</u> from day 1 to 6 weeks: 2.5% extended	Cumulative at 6 months: 11.6%  <u>Increment</u> between 6 weeks and 6 months: 4.4%	HIV or death:  Extended NVP arm: • 3.7% at 6 weeks • 8.1% at 6 months

6 weeks			54% EBF at 14 weeks	NVP			
PEPI/Malawi Kumwenda NEJM 2008 Randomized trial	Mother: Late presenter, <u>no</u> antepartum antiretrovirals  Infant: sdNVP+1 week AZT, and randomized to daily placebo vs NVP vs NVP/AZT from day 7 to 14 weeks	Breastfeeding: 3016 infants (placebo 989, extended NVP 993, extended NVP/AZT 980)  Uninfected at birth and data at 9 months: Placebo: 788 Extended NVP: 800 Extended NVP/AZT: 801	379-401	Breastfeeding only, most wean between 6 months (90% breastfeeding) and 9 months (29-32% breastfeeding)  61-64% EBF at 6 months	Extended NVP or NVP/AZT:  Birth: 7.1% extended NVP and NVP/AZT  Cumulative at 6 weeks: 8.8% extended NVP and 8.7% NVP/AZT  <u>Increment</u> between day 1 and 6 weeks: 1.7% extended NVP and 1.6% NVP/AZT	Cumulative at 6 months: 11.1% extended NVP, 12.3% extended NVP/AZT  <u>Increment</u> between 6 weeks and 6 months: 2.3% extended NVP, 3.6% extended NVP/AZT	HIV or death:  Extended NVP arm: • 3.3% at 6 weeks • 6.6% at 6 months • 13.9% at 12 months  Extended NVP/AZT arm: • 1.8% at 6 weeks • 8.2% at 6 months • 15.0% at 12 months
BAN/Kenya Chasela IAS 2009 Randomized trial for CD4 >250, (see Table 7)	CD4 >250 Randomized trial: delivery to 6 months postpartum	Breastfeeding: infant NVP arm, 848 mothers enrolled	440	Breastfeeding only; duration not specified (counseled to wean at 6 months)	Birth: enrolled at delivery, rates based on uninfected at 2 weeks  Cumulative at 6 weeks: Not specified	Cumulative at 7 months (uninfected at 2 weeks): 1.8%  <u>Increment</u> between 2 weeks and 6 months: 1.8%	HIV or death (uninfected at 2 weeks):  Extended infant NVP arm, • 2.9% at 7 months

95% CI: 95% confidence interval; EBF: exclusive breastfeeding; NVP: nevirapine; AZT: zidovudine



**Table 7. Ongoing and Planned Studies on Prevention of Mother to Child HIV Transmission**

Study/Location/Design/ Infant Feeding/Enrolled	Antepartum Regimen	Intrapartum Regimen	Postpartum Mother Regimen	Postpartum Infant Regimen	Comments
<b><u>Breastfeeding, Antiretrovirals and Nutrition (BAN) Study</u></b>					
Malawi		<b>CD4 <math>\geq</math> 200 cells/uL:</b>			
<ul style="list-style-type: none"> <li>Intrapartum/postpartum intervention to reduce postnatal MTCT in women with CD4 <math>\geq</math> 200 cells/uL: Postpartum maternal triple drug vs infant NVP prophylaxis</li> <li>Includes randomization to maternal nutritional supplement or not for 6 months postpartum</li> <li>Breastfeeding</li> <li>N=2637 randomized</li> </ul>	No drugs, enrolls at delivery	<u>Arm 1: Control</u> sdNVP/AZT/3TC  <u>Arm 2: Maternal triple drug prophylaxis</u> sdNVP/AZT/3TC  <u>Arm 3: Infant prophylaxis</u> sdNVP/AZT/3TC	<u>Arm 1:</u> AZT/3TC x 1 week  <u>Arm 2:</u> AZT/3TC x 1 week; AZT/3TC/LVP-rtv day 7 to 6 months  <u>Arm 3:</u> AZT/3TC x 1 week	<u>Arm 1:</u> sdNVP + AZT/3TC x 1 week  <u>Arm 2:</u> sdNVP + AZT/3TC x 1 week  <u>Arm 3:</u> sdNVP + AZT/3TC x 1 week; then daily NVP day 7 to 6 months	<ul style="list-style-type: none"> <li>March 2008: DSMB recommended control Arm 1 close as at least 1 experimental arm superior (not powered to detect difference between Arms 2 and 3)</li> <li>7 month MTCT (in infants uninfected at 2 weeks):               <ul style="list-style-type: none"> <li>- Control: 6.4%</li> <li>- Maternal triple drug: 3.0%</li> <li>- Infant NVP: 1.8%</li> </ul> </li> <li>Maternal triple drug vs control, <math>p=0.0032</math>; infant NVP vs control, <math>p&lt;0.0001</math>; maternal triple drug vs infant NVP, <math>p=0.12</math></li> </ul>
<b><u>Kesho Bora Study</u></b>	Randomized trial:				
Kenya, South Africa, Burkina Faso	CD4 200-500 cells/uL: Starting at 34-36 wks				
<ul style="list-style-type: none"> <li>Antepartum/intrapartum/postpartum intervention to reduce MTCT in women with CD4 200-500 cells/uL: Maternal triple drug vs short course AZT/sdNVP</li> <li>Observational cohorts for women with CD4 &lt;200 cell/uL (receive NVP-based HAART) and <math>\geq</math>500 cells/uL (receive AZT/sdNVP)</li> <li>Breastfeeding (~ 50%) and formula feeding</li> </ul>	<u>Arm 1: Maternal triple drug prophylaxis</u> AZT/3TC/LPV-rtv  <u>Arm 2: Short course</u> AZT	<u>Arm 1:</u> AZT/3TC/LPV-rtv  <u>Arm 2:</u> AZT/sdNVP	<u>Arm 1:</u> AZT/3TC/LPV-rtv x 6 months  <u>Arm 2:</u> AZT/3TC x 1 week, then no drugs	<u>Arm 1:</u> sdNVP + AZT x 1 week  <u>Arm 2:</u> sdNVP + AZT x 1 week, then no drugs	<ul style="list-style-type: none"> <li>MTCT at birth (IU infection)               <ul style="list-style-type: none"> <li>- Maternal triple drug: 1.8% (0.8-3.7%)</li> <li>- Short course AZT: 2.2% (1.2-4.3%)</li> </ul> </li> <li>MTCT between birth-6 months (postpartum triple drug vs no prophylaxis)               <ul style="list-style-type: none"> <li>- Maternal triple drug: 3.1%</li> <li>- Short course AZT: 6.3%</li> </ul> </li> <li>Overall MTCT at 12 months               <ul style="list-style-type: none"> <li>- Maternal triple drug: 5.5% (3.6-8.4%)</li> <li>- Short course AZT: 9.5%</li> </ul> </li> </ul>

<ul style="list-style-type: none"> <li>N=824 randomized</li> <li>Observational: N=119 CD4 &lt;200; N=131 CD4 ≥500</li> </ul>					<ul style="list-style-type: none"> <li>(6.9-13.0%)</li> <li>Difference between maternal triple drug and short-course significant for strata of women with CD4 200-350 (p=0.044), but not for women with CD4 350-500 (p=0.33)</li> <li><i>Observational CD4 &lt;200</i>: MTCT at 12 months: 7.6%</li> <li><i>Observational CD4 ≥500</i>, MTCT at 12 months: 5.8%</li> </ul>
<u>Mma Bana Study</u> Botswana	Randomized trial: CD4 ≥200 cells/uL: Starting at 18-34 weeks:				<ul style="list-style-type: none"> <li>MTCT at birth: <ul style="list-style-type: none"> <li>AZT/3TC/ABC: 1.1%</li> <li>AZT/3TC/LPV-r: 0.4%</li> </ul> </li> <li>MTCT at 6 months (cumulative): <ul style="list-style-type: none"> <li>AZT/3TC/ABC: 1.8%</li> <li>AZT/3TC/LPV-r: 0.4%</li> </ul> </li> <li>No significant difference 6 months MTCT between triple drug regimens (p=0.53)</li> <li><i>Observational CD4 &lt;200</i>: MTCT at 6 months, 0.6%</li> </ul>
<ul style="list-style-type: none"> <li>Antepartum/intrapartum/pospartum intervention comparing 2 triple drug prophylaxis regimens to prevent postnatal MTCT in women with CD4 ≥200 cells/uL.</li> <li>Observational cohort for women with CD4 &lt;200 cell/uL (receive NVP-based HAART)</li> <li>Breastfeeding</li> <li>N=560 randomized, N=140 observational</li> </ul>	<u>Arm 1: Maternal triple drug prophylaxis</u> AZT/3TC/Abacavir  <u>Arm 2: Maternal triple drug prophylaxis</u> AZT/3TC/LPV-rtv	<u>Arm 1:</u> AZT/3TC/Abacavir  <u>Arm 2:</u> AZT/3TC/LPV-rtv	<u>Arm 1:</u> AZT/3TC/Abacavir x 6 months  <u>Arm 2:</u> AZT/3TC/LPV/rtv x 6 months	<u>Arm 1:</u> sdNVP + AZT x 4 weeks  <u>Arm 2:</u> sdNVP + AZT x 4 weeks	
<u>PHPT-5</u> Thailand	CD4 >250 cells/uL Starting at 28 weeks:				<ul style="list-style-type: none"> <li>Started spring 2009</li> </ul>
<ul style="list-style-type: none"> <li>Antepartum/intrapartum/pospartum intervention evaluating whether maternal NVP is needed for efficacy of sdNVP, and comparing short course AZT/sdNVP to short course AZT/protease</li> </ul>	<u>Arm 1:</u> AZT	<u>Arm 1:</u> sdNVP + AZT/3TC	<u>Arm 1:</u> AZT/3TC x 7 days	<u>Arm 1:</u> sdNVP birth and 48 hours + AZT x 1 week	

inhibitor	<u>Arm 2:</u>	<u>Arm 2</u>	<u>Arm 2:</u>	<u>Arm 2:</u>	
• Formula feeding	AZT	Placebo + AZT	Placebo x 7 days	sdNVP birth and 48 hours + AZT x 1 week	
• N=1,992					
	<u>Arm 3:</u>	<u>Arm 3:</u>	<u>Arm 3:</u>	<u>Arm 3:</u>	
	AZT/LPV-rtv	AZT/LPV-rtv	No drugs	AZT x 1 week	
<u>ANRS-PEP</u>	Infant enrolled postpartum	Infant enrolled postpartum	Infant enrolled postpartum		• In planning, to start spring 2009
Burkina Faso, South Africa, Uganda, Zambia				<u>Arm 1:</u> sdNVP at birth; 3TC from day 7 to 9 months	
• Postpartum intervention comparing infant prophylaxis during breastfeeding for 9 months to no prophylaxis				<u>Arm 2: s</u> sdNVP at birth; placebo from day 7 to 9 months	
• Breastfeeding					
• N=1,500 (in planning)					
<u>Promoting Maternal Infant Survival Everywhere (PROMISE-IMPAACT 1077)</u>	CD4 >350 cell/uL Starting at 28 weeks:		CD4 >350 cell/uL		• In planning, to start:
Multiple countries in Africa, Asia, South America, U.S.	<u>ANTEPARTUM RANDOMIZATION</u>		<u>NEW POSTPARTUM RANDOMIZATION AT DAY 7:</u>	<u>NEW POSTPARTUM RANDOMIZATION AT DAY 7:</u>	○ US/South America, fall 2009
• For women who do not require treatment for own health (CD4 >350), will address:					○ Resource-limited countries, late fall/early winter 2009
○ What is optimal antepartum regimen to prevent MTCT?	<u>Arm 1: Short-course</u> AZT	<u>Arm 1:</u> sdNVP + TDF/FTC ( and x 7 days postpartum)	<u>Arm 3: Infant prophylaxis</u> No ARV	<u>Arm 3:</u> sdNVP + AZT x 7 days; NVP from day 7 to cessation breastfeeding (up to 18 months)	
○ What is optimal postpartum regimen to prevent postnatal MTCT?	<u>Arm 2: Maternal triple drug prophylaxis</u> AZT/3TC/LPV-rtv	<u>Arm 2:</u> AZT/3TC/LPV-rtv (and x 7 days postpartum)	<u>Arm 4: Maternal triple drug prophylaxis</u> AZT/3TC/ LPV-rtv from day 7 to cessation breastfeeding (up to 18 months)	<u>Arm 4:</u> sdNVP + AZT x 7 days	
○ Is it safe for mothers to stop triple drug prophylaxis after receiving only for PMTCT?				<u>INFANT HEALTH RANDOMIZATION:</u>	

<ul style="list-style-type: none"> <li>○ How to maintain health of uninfected infants after weaning?</li> <li>• Resource-limited countries: Antepartum/intrapartum/postpartum intervention in women with CD4 &gt;350 cells/uL, undergo sequential randomizations</li> <li>• U.S./South America: Only participate in the Maternal Health randomization</li> <li>• Breastfeeding and formula feeding</li> <li>• Approximately 8,000 mother-infant pairs resource-limited, 2,000 U.S./South America</li> </ul>		<p><u>MATERNAL HEALTH RANDOMIZATION</u></p> <ul style="list-style-type: none"> <li>• Formula feeding and mother on triple drug prophylaxis(Arm 2), at day 7-12, CD4 &gt;350 cells/uL</li> <li>• Breastfeeding and mother on triple drug prophylaxis (Arm 4), at cessation of weaning, CD4 &gt;350 cells/uL</li> <li>• US/South America: Triple drug prophylaxis during pregnancy and CD4 &gt;400 cells/uL</li> </ul> <p>Arm 1: Stop triple drug regimen</p> <p>Arm 2: Continue triple drug regimen</p>		<ul style="list-style-type: none"> <li>• Breastfeeding, infant uninfected and &lt;12 months at time breastfeeding cessation</li> </ul> <p>Arm 1: Cotrimoxazole to 18 months</p> <p>Arm 2: Cotrimoxazole placebo to 18 months</p>
<p><u>ANRS 12200</u></p> <p>Cote d'Ivoire</p> <ul style="list-style-type: none"> <li>• Antepartum/intrapartum/postpartum intervention comparing 2 triple drug prophylaxis regimens to prevent MTCT</li> <li>• Randomized trial (non-inferiority design)</li> <li>• Breastfeeding and formula</li> </ul>	<p>Starting at 20 weeks</p> <p><u>Arm 1: Maternal triple drug prophylaxis</u></p> <p>TDF/FTC/EFV</p> <p><u>Arm 2: Maternal triple</u></p>	<p><u>Arm 1:</u></p> <p>TDF/FTC/EFV</p> <p><u>Arm 2:</u></p> <p>AZT/3TC/LPV-rtv</p>	<p>If breastfeeding, continue 6-9 months postpartum</p> <p><u>Arm 1:</u></p> <p>TDF/FTC/EFV</p> <p><u>Arm 2:</u></p> <p>AZT/3TC/LPV-rtv</p>	<ul style="list-style-type: none"> <li>• In planning, to start late 2009</li> </ul> <p><u>Arm 1:</u></p> <p>AZT x 1 week?</p> <p><u>Arm 2:</u></p> <p>AZT x 1 week?</p>

feeding	<u>drug prophylaxis</u>
• N=?	AZT/3TC/LPV-rtv

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AZT: zidovudine; 3TC: lamivudine; EFV: efavirenz; FTC: emtricitabine;; LPV-rtv: lopinavir-ritonavir; MTCT: mother to child transmission; NVP: nevirapine; sdNVP: single-dose NVP; TDF: tenfovir

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## Chapter 3. The Effectiveness of Current Activities in Reaching Targets

### I. Introduction

Although substantial progress has been made, PMTCT services are not reaching the majority of those in need and most programs are not on track to meet the ambitious goals that have been set. High coverage and impact of PMTCT services is achievable soon, but renewed focus and efforts are needed.

### II. Objectives

- To review PEPFAR and international targets and assess progress in reaching those goals
- To identify key strategies for and provide guidance to PEPFAR teams to accelerate the expansion of comprehensive PMTCT services
- To provide recommendations to the Global AIDS Coordinator and Congress in support of efforts to define and reach PMTCT targets

### III. The Effectiveness of Current Efforts in Reaching Targets

#### Global PMTCT Commitments, Goals and Targets

Numerous global commitments have been made to tackle PMTCT implementation in low and middle income countries:

- a) Through the 2000 Millennium Development Goals 4, 5, and 6, national governments have committed to reducing child mortality, improving maternal health, and combating HIV/AIDS, Malaria and other diseases by 2015 (United National Millennium Declaration 2000).
- b) In 2001, national governments through the Declaration of Commitment of the United Nations General Assembly Special Session on HIV/AIDS also committed to achieving reductions of 20% and 50% in the proportion of infants infected with HIV by 2005 and 2010 respectively by ensuring that 80% of pregnant women had 80% access to appropriate interventions (United National Millennium Declaration 2000).
- c) At the PMTCT High Level Global Partners Fora held in December 2005 in Abuja, Nigeria and in Johannesburg, South Africa in 2007, national governments and partners present, including PEPFAR, committed to virtual elimination of HIV infection in infants and children and global scale-up of PMTCT for an HIV-free and AIDS-free generation by 2015 (Abuja Call to Action 2005).
- d) In 2005, leaders of the G8 countries agreed to support development and implementation of a package for HIV prevention, treatment and care, with the aim of as close as possible to universal access to treatment for all those who need it by 2010. United Nations Member States endorsed this goal at the 2005 World Summit (High-level Plenary Meeting of the 60th Session of the United Nations General Assembly). At the June 2006 High-Level Meeting on AIDS, United Nations Member States agreed to work towards the broad goal of “universal access to comprehensive prevention programs, treatment, care and support” by 2010.

#### PEPFAR PMTCT Targets

The target outlined in the original PEPFAR legislation was to reach 80% of pregnant women in those countries most affected by HIV/AIDS where the U.S. supports HIV activities. The PEPFAR reauthorization established a target for PMTCT that, by 2013, PEPFAR-supported programs will reach at least 80% of pregnant women in countries receiving PEPFAR support.

Since neither target has been specific, there has been some ambiguity about the appropriate denominator for target calculations both for counseling and testing and for antiretroviral (ARV) coverage. For instance, for ARV coverage, the denominator varies greatly depending on whether it is defined as the estimated number of all HIV-infected pregnant women, the estimated number of HIV-infected women who attend at least one ANC visit, or the number of pregnant women who test HIV-positive. There has also been uncertainty as to whether the target is meant to be achieved in each country or across all PEPFAR-supported countries collectively. This overall lack of clarity may have hurt PEPFAR-wide momentum toward reaching PMTCT goals.

### **PEPFAR's PMTCT Support to Countries**

Beginning with the US President's Mother to Child HIV Prevention Initiative in 2002, and extending into PEPFAR in 2003, the USG has made substantial investments in preventing vertical transmission of HIV in countries with the highest burden of HIV. The fifteen original "PEPFAR focus countries" (Botswana, Cote d'Ivoire, Ethiopia, Guyana, Haiti, Kenya, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Tanzania, Uganda, Vietnam, Zambia) have received the bulk of PEPFAR support and are home to an estimated annual total of 1.3 million HIV-positive pregnant women, representing 89% of the 1.5 million HIV-positive women who deliver each year globally. Total planned 2009 PEPFAR budget support for PMTCT to the 15 original "focus countries" was \$210 million, with an additional \$14 million in 16 other countries. Funding for ARVs used in PMTCT programs was provided through a separate budget line making it difficult to account separately for the costs of those ARVs used for PMTCT.

### **Effectiveness of PEPFAR's Current Activities**

As described in Chapters 1 and 2, PEPFAR supports a multi-pronged strategic approach to scaling-up PMTCT services including primary prevention of HIV among pregnant women, prevention of unintended pregnancies among HIV-infected pregnant women, prevention of HIV transmission from HIV-infected women to their infants, and provision of treatment, care and support to HIV-infected mothers, their children and families. However, PEPFAR's indicators have focused on the collection of data on counseling and testing of pregnant women and provision of ARVs to HIV-infected pregnant women. PEPFAR has not systematically collected outcomes data on primary HIV prevention in pregnant women or prevention of unintended pregnancy and linking women and children to care, making progress on these interventions more difficult to judge.

#### **1. Primary Prevention**

Using modeling of available data, Sweat and colleagues were able to demonstrate that prevention of HIV infection in girls and women of childbearing age and of unintended pregnancies among those women infected with HIV are the most cost-effective methods to prevent HIV infection in infants (Lu 2008). A recent report from Botswana showed that with a scaled-up PMTCT program, up to 42% of new infections in children in Botswana are from women with newly acquired HIV infection (Seipone 2004). Implementation of primary prevention interventions has been challenging in most countries and evidence of effective interventions within the PMTCT

context remain very limited. The many women who test negative for HIV during their antenatal care (ANC) or other healthcare encounters represent an important group of women that have not been widely prioritized for targeted primary prevention interventions or other services within PEPFAR or other USG programs.

## **2. Prevention of Unintended Pregnancies among HIV-Infected Women**

A number of countries are integrating family planning with HIV testing and counselling in PMTCT services. However, there are limited systematic data either from national health information systems or population-based surveys to assess the access and uptake of family planning services among women living with HIV at the population level. Globally, an estimated 80 million (38%) of the 211 million pregnancies each year are unintended. Further, data from population-based surveys between 2006 and 2008 in countries with a generalized epidemic show a high unmet need for family planning among married women in several countries. Half the countries report more than 25% unmet need for family planning, with Togo and Uganda reporting the highest rates at 41%.

Studies from generalized epidemic settings in sub-Saharan Africa suggest that the rates of unintended pregnancy among women living with HIV may be higher than in the general population. Studies from Côte d'Ivoire, South Africa and Uganda have reported rates of unintended pregnancy that range from 51% to more than 90% in various populations of women living with HIV.

Although some programs are able to offer family planning as a “wraparound” service, this has not been implemented systematically throughout PEPFAR and certainly has not been widely monitored or evaluated. Given the infrastructure PEPFAR has built to support PMTCT activities, there exists a tremendous opportunity to integrate family planning into PEPFAR’s service delivery platforms.

## **3. Prevention of HIV Transmission from HIV-infected Women to their Infants**

Reducing HIV transmission from an infected pregnant woman to her infant requires implementation of a continuum of interventions, starting with HIV testing and counseling; CD4 screening to determine HIV disease status; provision of ART for women eligible by national guidelines; ARV prophylaxis for women with high CD4 count and their newborns; safer obstetric practices; and support for safer infant feeding practices. Many PEPFAR-supported countries have been successful in implementing most of these interventions. Some examples are highlighted below.

### **3A. HIV Testing and Counseling**

Increased access and use of PMTCT services in countries where PEPFAR is working have been facilitated by timely policy decisions to improve testing uptake through the introduction of routinely offered rapid HIV testing with-same day results in antenatal and delivery care settings—where providers offer HIV tests to all pregnant women and women are tested unless they specifically decline (Bolu 2007). Shifting from the earlier “opt-in” approach to the internationally-recommended policy of provider-initiated testing and counseling (PITC) has been shown to significantly increase the number of pregnant women who receive PMTCT services (both women who know their status and identification of HIV+ women so that they can receive

active PMTCT interventions). For example, testing rates went from 75% to 91% in Francistown Botswana and from 65% to 99% in Zimbabwe after PITC was introduced (Seipone 2004, Chandisarewa 2007). WHO and UNAIDS have issued new guidance on provider-initiated testing and counseling (PITC) in health facilities and PEPFAR has supported this approach.

According to the 2008 PEPFAR Annual Progress Report (APR), an average of 32% (range 6-86%) of pregnant women in the original PEPFAR “focus countries” received counseling and testing for HIV, up from 6% (range 0.1-58%) in 2004. Three countries have achieved at least 80% coverage of PMTCT counseling and testing, and Namibia is close to that level with 76% coverage of pregnant women (Figure 1). Ethiopia, Nigeria and Vietnam have all lagged substantially behind with counseling and testing coverage rates below 20% in 2008.

<b>Figure 1: Percentage of pregnant women who received HIV counseling and testing with USG support, 2004 and 2008</b> (Source: 2009 PEPFAR Annual Report)		
Country	Estimated coverage of pregnant women receiving HIV counseling and testing Percent coverage	
	FY2004	FY2008
Botswana <sup>1</sup>	58%	86%
Côte d'Ivoire	3%	23%
Ethiopia	0.2%	6%
Guyana	32%	87%
Haiti	8%	53%
Kenya	19%	69%
Mozambique	4%	56%
Namibia	12%	76%
Nigeria	0.4%	12%
Rwanda	11%	59%
South Africa	46%	85%
Tanzania	2%	53%
Uganda	8%	55%
Vietnam <sup>2</sup>	0.1%	17%
Zambia <sup>2</sup>	11%	59%
<b>Total</b>	<b>6%</b>	<b>32%</b>
<b>Notes:</b> Numbers may be adjusted as attribution criteria and reporting systems are refined. This indicator was revised beginning in FY2005. FY2004 results include an adjustment accounting for pregnant women who were counseled, tested, and received their test results. Coverage rates were calculated by dividing PEPFAR program (upstream and downstream) results by the estimated population eligible for the service. Eligible populations were based on the estimated number of births for each year provided by the International Database of the U.S. Census Bureau. Coverage estimates for FY2004 were revised from estimates provided in the PEPFAR Third Annual Report to Congress, using eligible populations from the U.S. Census Bureau. This methodology provides a standardized comparison across all countries and the reported rates may differ from those reported by countries. <b>Footnotes:</b> <sup>1</sup> Botswana results are attributed to the National HIV Program. Beginning FY2005, USG downstream contributions in Botswana are embedded in the upstream numbers, following a consensus reached between the USG and the Government of Botswana to report single upstream figures for each relevant indicator. <sup>2</sup> An error occurred in reporting coverage rates in the PEPFAR Third Annual Report to Congress. FY2004 results for Vietnam and Zambia were reversed. The correct estimates are now reported in this table.		

### 3B. Provision of Antiretroviral Therapy

Great advances have been made in increasing access to ARVs for HIV-infected pregnant women over the last five years. By September 2008, PEPFAR data demonstrated that an estimated 48%

of HIV-positive pregnant women in the 15 original “focus countries” received ARVs with PEPFAR support, up from an estimated 10% in 2004 (Figure 2). These interventions reached 422,800 HIV-infected pregnant women (361,300 direct PEPFAR targets), and averted an estimated 88,400 infant infections in 2008. However, this success has been mixed. Botswana, which was the first PEPFAR country to achieve national scale-up of ART, has also successfully scaled-up provision of highly effective PMTCT prophylaxis regimens and demonstrated a reduction of national MTC transmission levels to less than 5%. In addition, the MTC transmission rate decreased from 30.5% to 11.4% in Cambodia, and 30.5% to 8.9% in Rwanda (UNICEF/UNAIDS/WHO 2008). Namibia, Guyana, and Kenya are also close to achieving national PMTCT scale-up, whereas Cote d’Ivoire, Ethiopia, Mozambique, Nigeria, Tanzania and several other countries have a long way to go before achieving universal access.

Figure 2: Estimated Coverage of HIV-positive pregnant women receiving ARV prophylaxis with PEPFAR support, FY2008			
Country	Number of HIV+ pregnant women receiving ARV prophylaxis in FY 2008	Estimated number of pregnant women living with HIV needing antiretrovirals for PMTCT based on UNAIDS/WHO methods 2008 <sup>1</sup>	Estimated coverage of HIV+ pregnant women receiving ARV prophylaxis FY2008 <sup>2</sup>
Botswana	10,900	12,000	91%
Côte d’Ivoire	5,800	22,000	26%
Ethiopia	5,300	36,000	15%
Guyana	200	<200	100%
Haiti	1,400	5,500	25%
Kenya	61,100	110,000	56%
Mozambique	39,900	110,000	36%
Namibia	6,500	8,200	79%
Nigeria	29,800	210,000	14%
Rwanda	9,800	10,000	98%
South Africa	129,600	200,000	65%
Tanzania	37,100	86,000 <sup>3</sup>	43%
Uganda	41,600	82,000	51%
Vietnam	900	3,300	27%
Zambia	42,900	70,000	61%
<b>Total</b>	<b>422,800</b>	<b>879,000</b>	<b>48%</b>
<b>Footnotes:</b> <sup>1</sup> Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector, Progress Report, 2009. <sup>2</sup> Coverage rates were calculated by dividing PEPFAR program (upstream and downstream) results by the estimated number of HIV+ pregnant women needing antiretrovirals for PMTCT based on WHO/UNAIDS methods. <sup>3</sup> This is a preliminary estimate, currently being reviewed and will be adjusted, as appropriate, based on ongoing data collection and analysis.			

Following changes in WHO PMTCT guidelines in 2006, PEPFAR programs and governments have worked to provide the most effective regimens to pregnant women and have moved away from single-dose nevirapine (sdNVP), an intervention that may leave exposed women with drug resistance and does not provide protection during *in-utero* or breast-feeding periods. However, in countries reporting data on ARV regimen use in sub-Saharan Africa for 2008, 31% of women received only single-dose NVP, 26% received a two-drug regimen, 10% received ART for their own health (UNAIDS/WHO/UNICEF 2009). PEPFAR must move to recommend the implementation of full antiretroviral therapy (ART) for eligible women and for regimens more complex than single-dose NVP in order to provide the greatest benefits for mothers and their children. It is important to note that sites that have access to CD4 testing and staff with the ability to provide ARVs at the same location tend to have a larger proportion of women on ART.

### **3C. Support for Safer Infant Feeding Practices**

In industrialized countries, HIV-positive women are advised not to breastfeed their infants as a precaution against postnatal transmission of the virus. In most low- and middle-income countries, however, alternatives to breastfeeding are frequently unavailable or unaffordable and may increase child mortality. In some settings not breastfeeding may be culturally unacceptable.

There is a body of convincing evidence that exclusive breastfeeding carries a lower risk of HIV transmission than mixed feeding and that high rates of exclusive breastfeeding can be achieved with good quality counseling and support and consistent messages. PEPFAR's approach, outlined in its annual Technical Considerations document, has been to support countries' decisions to promote exclusive breastfeeding unless they meet WHO criteria suggesting that formula may be optimal if affordable, feasible, acceptable, safe and sustainable in a particular context. As detailed in Chapter 2, further data from a number of studies have suggested that the optimal approach may be to provide ART to pregnant women who qualify for treatment for their own health, which may also prevent the majority of postnatal transmission during the entire breastfeeding period. If ART is not available or if a woman does not qualify for ART based on her CD4 cell count, provision of infant nevirapine throughout the breastfeeding period appears to be a viable alternative.

### **4. Provision of Treatment, Care and Support to HIV-Infected Mothers, their Children and Families**

An estimated 25% of HIV-positive pregnant women are in need of antiretroviral therapy for their own health; however only 10% in low and middle income countries received it in 2008 (UNAIDS/WHO/UNICEF 2009). HIV-positive pregnant women must be assessed using CD4 screening for eligibility and those in need provided antiretroviral treatment to improve and maximize health outcomes.

PEPFAR support has also been instrumental in expanding the availability of early virological HIV testing for infants, linking children into care, and supporting mothers to optimally and safely feed their infants. Institutionalizing these interventions has been extremely challenging and the progress slow. Only 4% of children in low and middle income countries are getting early HIV virologic testing at four to six weeks of age based on unpublished programmatic estimates. The necessary capacity has been developed to rapidly increase the proportion of children receiving this service and quantitatively measure the effectiveness of PMTCT investments. More



importantly, monitoring and evaluation systems must be improved to enable tracking of mother-infant pairs and ensure 18 month HIV-free survival of exposed infants.

Investments in HIV programs can strengthen health systems if HIV interventions are appropriately integrated with other health services and aligned with national planning processes for the health sector as a whole. PEPFAR support has brought greater attention to integrating PMTCT services in maternal child health services within the continuum of care.

Other PEPFAR investments have included leadership and management support at the national level, and health systems support such as supporting supply chain forecasting and helping to strengthen national procurement and supply management systems to ensure uninterrupted access to antiretroviral drugs and other commodities, including laboratory supplies.

### IV. Conclusions

PEPFAR has made substantial contributions to scaling-up elements of the PMTCT cascade, with a focus on counseling and testing of pregnant women and provision of ARVs to women found to be HIV-positive. Much more could be done to expand programs for primary prevention of HIV among pregnant women, increase integration of family planning with PEPFAR programs, and improve linkages in service delivery for mother-baby pairs.

### V. Recommendations

Key recommendations are to:

- Prioritize pregnant women for HIV care and treatment services, and improve the capacity of PEPFAR programs and countries to build longitudinal care systems for PMTCT that aim to maximize the health and survival of mothers and infants;
- Better define the 80% reauthorization target. The Panel recommends:
  - Convening an interagency USG group to rapidly assess methodologies and gain consensus on the definition of these targets for the next phase of PEPFAR;
  - Using national figures for all denominators used in PEPFAR reporting, and including all women, regardless of antenatal care attendance;
- Expand family planning services to HIV-infected women as a priority;
- Define and measure targets that focus on providing HIV treatment to pregnant women who need it for their own health, including documentation of clinical and/or laboratory staging of HIV disease and engagement in care and/or treatment services for all women identified as HIV-positive.
- Define program success in terms of children's HIV-free survival.

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## Chapter 4. Barriers, Challenges and Potential Solutions for Optimizing PMTCT Services

### I. Introduction

The majority of countries have not reached population coverage of PMTCT services. This chapter focuses on barriers and challenges to increasing access to and uptake of PMTCT services and describes potential solutions. There is a paucity of implementation research in this area to provide a strong evidence base for many of these best practices; therefore, this chapter includes information gathered from published and unpublished program reports, data presented in meetings, and discussions with key stakeholders. While there are many challenges and obstacles to achieving widespread optimal PMTCT services, there has been incredible success in scaling up services over the last several years. Highly successful programs exist and demonstrate that it is possible to provide high-quality PMTCT and care and treatment services to women and their families in resource-limited settings when there is a strong commitment to do so.

### II. Objectives

- To identify key challenges in and barriers to the scale-up and utilization of PMTCT services
- To describe solutions that have been successful in overcoming these obstacles
- To make recommendations to improve the quality and reach of PEPFAR-supported PMTCT services

### III. Barriers, Challenges and Potential Solutions for Optimizing PMTCT Services

*“Researchers in the field of PMTCT all over the world have done, and continue to do, a remarkable job in acquiring new knowledge and developing new strategies to reduce mother-to-child transmission. The world can do much more in helping to translate these into practice”*

*-McIntyre J. and Lallemant M, 2008*

#### Service Delivery

As detailed in Chapter 3, the extraordinary scale-up of PMTCT services over the past five years has led to a dramatic decrease in the rate of vertical HIV transmission in countries with the most robust response, although there remains substantial unmet need over continuum of the PMTCT cascade. One of the critical challenges is that a comprehensive series of PMTCT services are delivered to HIV-infected women during pregnancy, delivery, and postpartum in a variety of settings, including ANC, labor and delivery, postnatal clinics and HIV care and treatment sites. Loss to follow-up at any step in the cascade threatens maternal outcomes and increases the likelihood of vertical transmission of HIV (Rispel 2009). Recent data from the PEARL study conducted in South Africa, Zambia, Cote D’Ivoire, and Cameroon demonstrated that the proportion of HIV-positive mothers delivering at study sites and their infants who successfully completed the full range of PMTCT services, including actually taking NVP, varied greatly by country and facility, ranging from a low of 17% to 69%, with an average of ~50% overall across sites (Coetzee 2009 abs). It is important to note that these analyses underestimate the true “failure” rate as they include only women who delivered at the health facility and not women who initiated PMTCT but did not deliver at the health centers. Identifying the factors associated with either success or failure to complete the full range of PMTCT services and adhere to the

ARV regimen will indicate areas where additional targeted interventions could improve the uptake of services (Bwirire 2008, Rispel 2009).

### ***PMTCT in ANC***

The majority of PMTCT services are facility-based in antenatal clinics, requiring women to attend ANC to access PMTCT services. One barrier to the PMTCT service delivery is lack of ANC attendance. Universal facility-based coverage does not translate to 100% population coverage if not all pregnant women attend ANC and access available services. Although in many settings the vast majority of women attend ANC at least once, the proportion varies and can be as low as 28% as is in Ethiopia for example (UNICEF children and AIDS fact sheet pg 48). A much smaller proportion of women complete the WHO-recommended 4 ANC visits during their pregnancy (State World Child 2009). Women often present to ANC late in gestation, preventing the early initiation of ARVs for either treatment or prophylaxis. Therefore, identifying mechanisms to encourage more pregnant women to attend ANC early and repeatedly and to reach those not attending ANC are critical gaps that must be addressed for the target of reaching 80% coverage of all pregnant women with PMTCT services to be achieved.

Some of the barriers to initial and ongoing ANC attendance include: high cost of transport for women in rural areas; user fees associated with institutional care and delivery services; poor quality of services (real or perceived); poor facility conditions; lack of organization and efficiency of services leading to overcrowding and long delays; and lack of privacy (Agyepong 1999, Chopra 2009, Doherty 2009, Bwirire 2008, Turan 2008). Use of HIV funds to address these areas also allows strengthening of broader health services. Negative or judgmental attitudes of health care workers (HCW) towards HIV-infected women and stigma have been cited as contributing to women's reluctance to return to ANC after the initial visit (see Chapter 5, Chopra 2009, Bwirire 2008, Turan 2008).

Practices that have successfully addressed some of these challenges include establishing PMTCT services wherever ANCs exist, reimbursement of transport costs, use of mobile outreach clinics linked to facility-based programs (Lesotho), facility rehabilitation or construction of facilities closer to the population, partitioning or constructing private counseling spaces within the antenatal/labor suite/postnatal clinics, hiring cleaning/maintenance personnel to maintain clean functioning facilities, and facility improvements as simple as providing a clean coat of paint (ICAP 2008). Close examination of the clinic flow, documentation requirements, placement of staff and other logistical improvements can maximize the efficiency of services, decrease women's waiting times and minimize staff time requirements (Barker 2007). Reorganizing services to enhance women's experiences at the facility can increase their willingness to return for additional services. Co-locating as many services as possible (lab, counseling, ARV, family planning, pharmacy, etc.) to decrease a woman's travel will maximize the likelihood of her receiving comprehensive services. Use of peer or lay counselors, "expert" patients, and task shifting to allow services to be dispersed across a wider number of personnel also contribute to smoother service provision (Shetty 2008, Zachariah 2009). Some programs have increased utilization of trained MCH personnel by offering staff the opportunity to work extra shifts during their off-duty times for overtime payment rather than working elsewhere to supplement their income (Chi 2005). Community mobilization and outreach for follow-up, training of traditional

birth attendants to follow-up on PMTCT services, and PMTCT “buddies” in the community have been reported to increase follow-up in PMTCT programs (Wanyu 2007, Bwirire 2008)

### ***HIV testing and counseling***

Early PMTCT programs were limited in their ability to provide HIV testing and counseling to all ANC attendees and testing uptake was limited (Creek 2007, Moses 2008). ANC clinics often did not have adequate staff to perform even basic ANC services, so the additional burden of HIV testing and counseling was problematic. This often occurred at the extremes of program size: large hospitals with extremely large volumes of ANC attendees had difficulty due to the sheer volume and extra time and space required to perform these activities and very small health centers often had only one midwife conducting all ANC, PNC, family planning, and immunization services and could not cope with added responsibilities.

Some solutions to these problems included the addition of specifically trained counselors or lay counselors/peers to support the ANC staff in these activities, performing pre-test counseling in groups so as to reserve time and personnel for the required individual post-test counseling, and improving clinic flow to maximize personnel time. In an attempt to make HIV testing a routine part of antenatal services, a change in counseling message to an “opt-out” strategy had a large impact on the uptake of HIV testing (Creek 2007, Moses 2008). In this system, HIV testing is presented as a routine ANC service performed for all ANC women; however, women are given the option of opting out of HIV testing if they choose. Preserving a woman’s right to decline testing without pressure is key so that women do not avoid ANC to avoid unwanted HIV testing (Bwirire 2008, Turan 2008). Many PMTCT programs have been able to counsel and offer HIV testing to >95% of client and achieve acceptance rates >95%. In facilities implementing opt-out HIV testing, most women who attend ANC at least once actually do receive HIV testing and counseling. Therefore, increasing facility coverage with PMTCT services goes a long way in increasing the number of women who access services (Welty 2005).

The change from HIV testing done in a laboratory to rapid testing done by clinic staff or counselors in ANC with same-day results has significantly increased the number of women who receive their results (Granade 2005, Sripipatana 2007). Previously, if a woman was tested on one day and then had to return to the ANC for a second visit sometime later to get her HIV test results, it was less likely that she would receive her results. Rapid testing does not require special equipment nor lab personnel, as lay personnel can easily be trained to provide high quality services. In some settings, testing is conducted in front of the woman, minimizing specimen errors and maximizing faith in the results. Rapid testing also facilitates outreach services, mobile testing, home and community testing since it can be done with whole blood and does not need electricity or equipment. As with all program components, quality assurance of HIV testing needs attention, however this is often overlooked.

### ***PMTCT ARV Regimens***

The mainstay of the majority of PMTCT programs in less-resourced settings has been the provision of sdNVP to women and their infants shortly after delivery (Univ Access Report 2009). This regimen is simple, low cost, and does not require special infrastructure. However, as discussed in Chapter 2, regimens that combine multiple drugs improve the efficacy of prevention and decrease the likelihood of selection of NVP-resistant virus, and have led WHO to

recommend use of combination regimens as much as possible for women not eligible for ART. While WHO and many country programs are moving away from use of sdNVP as an accepted regimen for PMTCT, some country guidelines still only use sdNVP due to concerns of feasibility, cost, and logistics of supporting combination regimens nationally.

*Combination PMTCT ARV Regimens for Women not Eligible for ART*

Challenges to the effective scale-up of combination prophylactic regimens for women not eligible for ART include lack of “buy-in” as to the urgency of the need to expand to these services, lack of HCW confidence in prescribing and overseeing the use of these regimens, variability in MOH regulations about who can prescribe ARVs, uncertainty about the need for laboratory toxicity monitoring, and unclear guidelines on criteria to use to determine whether the use of these regimens is “feasible.” Lack of appropriate training materials and tools and revised counseling messages around the use of these regimens hinder their rapid scale-up.

Some believe programs should first establish success using sdNVP before expanding to combination regimens. However, investing the time and resources needed to train healthcare workers and establish a system with one regimen and then to retrain and set up a different system with alternative regimens does not make sense. Therefore, when expanding services, combination regimens should be the mainstay, with very specific guidance as to the limited circumstances in which sdNVP is the only viable option. A clear timetable should be developed to focus existing programs’ attention on the urgent need to transition services to provide enhanced combination PMTCT regimens as soon as logistically feasible. Training and IEC materials about the importance of this transition at all levels of the MOH and service delivery sites are critical to making this transition a reality.

MOH leadership is critical to insure adequate drug supplies, both for therapeutic and prophylactic use in PMTCT programs. Programs in some countries have experienced difficulty in sharing drugs procured for care and treatment services with PMTCT programs even when procured centrally and present at the site. Clear procedures for initiating and monitoring combination PMTCT ARV regimens need to be in place. In particular, MOH guidelines need to specify whether routine laboratory monitoring for anemia is required when using AZT in pregnancy or whether clinical monitoring alone is acceptable (consistent with WHO recommendations). Equipment for hemoglobin measurement must be available if lab monitoring is required otherwise combination regimens may not be utilized.

Some countries have made considerable progress in transitioning from sdNVP to providing combination PMTCT ARV regimens to most women (Botswana, Swaziland, Lesotho, Rwanda). One creative method of insuring delivery of combination regimens to all women has been used in Lesotho. The MOH has determined that a “minimal package” of ARVs be used at all health facilities. This minimal package includes AZT from 28 weeks gestation, sdNVP at the onset of labor, and Combivir during labor and for 1 week after delivery as a “tail”. The package also includes sdNVP and one week of AZT/3TC for the infants. All the drugs, other than the AZT, are packaged together and given to the pregnant woman at the time of diagnosis of HIV infection so that she will have all the drugs needed for complete prophylaxis even if she does not attend additional antenatal visits. The exception has been the AZT, which is given for one month only and requires the woman to return to clinic for refills. As this requires repeat visits to ANC,

Lesotho is now piloting the inclusion of 3 months of AZT in the package. UNICEF and others are currently evaluating the Lesotho experience and are working on a comprehensive assessment of a “mother-baby pack” system that could be widely adopted.

Dispensing the maternal ARVs at first contact increases the number of women who have access to them. While having received the ARV in ANC does not guarantee that the medicine is taken, as the PEARL study has shown, at least women have access to it when they need it (Coetzee 2009 abs). Strict interpretation of the 2006 WHO guideline to start AZT at 28 weeks has caused women attending ANC early to miss out on receiving AZT, although they may receive sdNVP. If a woman comes later the AZT may be started, but if she does not return the AZT is never started and she is at greater risk for vertical transmission. This is a missed opportunity to begin ARV prophylaxis as soon as possible and could be improved by allowing dispensing of AZT along with the NVP at the first contact when diagnosed HIV-positive. Most PMTCT programs dispense AZT in one month supplies, requiring women to make several visits to the ANC. While some programs such as Zimbabwe have found that the use of combination regimens and the requirement for returns to clinic for additional drug have improved the retention of HIV-infected women in services and increased the likelihood for the facility delivery, other programs report anecdotal evidence of low rates of return for AZT refills. Good data on adherence to follow-up visits and PMTCT ARVs are severely lacking. Shorter duration of AZT therapy and lack of adherence to the daily dosing are likely to decrease the effectiveness of the PMTCT regimen. Data on adherence is critical, as the PEARL study documented that women who were taking AZT in combination with the sdNVP were less likely to swallow the NVP (Coetzee 2009). If women do not adhere regularly to AZT and do not take the NVP tablet, the use of the combined regimens may, in fact, be less effective than NVP alone. PMTCT monitoring and evaluation data generally are not sufficient to address adherence as they do not capture patient-level or follow-up data.

### HAART for eligible women

The most effective regimen for preventing mother-to-child transmission is the provision of ART to women who require it for their own health. Women with evidence of immune suppression and/or clinical AIDS have the highest risk of transmitting HIV to their infants during pregnancy, delivery, and for the duration of the breastfeeding period. These women are also at the highest risk of selecting for NVP resistance. Data from Zambia indicate that women with a CD4 cell count of  $\leq 350$  cells/mm<sup>3</sup> during pregnancy account for 82% of postnatal transmissions and 84% of maternal deaths (Kuhn personal communication). Providing ART before or during pregnancy to these women will substantially reduce the numbers of HIV-infected infants. Therefore, the adult treatment goal of reaching all women who require treatment with ARV services will also go a long way in achieving PMTCT goals. Redefining CD4 count criteria (by WHO and within countries) for therapy eligibility for pregnant women is essential in light of existing data.

There are still large gaps in access to HIV treatment services across the developing world. Prioritizing pregnant women for HIV treatment has the benefit of prolonging the life of an HIV-infected woman, which benefits the survival of all of her children, and also decreasing the chance that her infant will be infected. Currently there is no system requiring centers that provide ART services to reach out to PMTCT services in their catchment areas to provide ART to eligible pregnant women.

PMTCT and HIV treatment services are often implemented as vertical programs with no relation to each other. Often they are funded by different programs or partners, with different identification and monitoring systems and weak or non-existent referral mechanisms. There are multiple missed opportunities to provide the best quality PMTCT services due to lack of functional links between PMTCT and HIV care and treatment services. Often there are no systems to “fast track” pregnant women into HIV treatment services, with long waits and delays leading to failure to initiate HAART in a timely fashion to provide the best protection against vertical transmission (Killam 2009). The absence of ART services within MCH is a significant barrier. The MCH staff are usually not trained in ART, not permitted to dispense these medicines, and alternative efficient means of providing an appropriate “treater”, perhaps on a rotating basis, often do not exist. Therapy either needs to be brought to clinics where women receive antenatal care or efficient referral has to occur. Without well-functioning linkages, most women who need HAART do not receive it.

One common obstacle to providing HIV treatment is the lack of ability of MCH sites to identify pregnant and postpartum women who need HAART, either through the use of CD4 cell count lab monitoring or clinical determination of HIV disease stage (Universal Access 2009). Where CD4 monitoring is not available, challenges in the training and “comfort” of HCWs in determining need for HIV treatment based on clinical criteria, the limited number of physicians providing PMTCT services, and regulations against non-physicians determining and prescribing HAART, as well as the time required to adequately conduct clinical staging has lead to extremely low rates of treatment initiation in ANC based on clinical criteria (Zachariah 2009). More widespread access to CD4 testing, either on-site or through lab referral networks, is required to increase identification of treatment-eligible women.

### *Infant PMTCT ARV Regimens*

To maximally prevent mother to child HIV transmission, both the HIV-infected mother and her infant need to receive PMTCT ARVs. Currently, the numbers of infants receiving ARV prophylaxis are significantly lower than the numbers of HIV-exposed infants identified (Universal Access 2008, Spensley 2009). In many settings this reflects poor health system coverage of facility-based deliveries. In settings with high rates of institutional deliveries (Botswana, Swaziland), the maternal and infant dosing rates are similar. As described earlier, providing an infant take-home dose of NVP or other ARV at the time of maternal diagnosis, either alone or as part of a mother-baby pack, increases the numbers of infants who have access to the intervention (Spensley 2009). While there is no guarantee that a baby will actually receive the ARV just because the mother brings it home, we know that a large proportion of babies would definitely not receive any intervention if delivery in a health facility is required. Some MOH are concerned that providing the maternal and infant dosing in ANC will eliminate any need for the woman to either return to ANC or to deliver in the facility. A review of PMTCT and delivery data at Mulago hospital in Uganda before and after initiating the baby take-home dose of NVP failed to reveal any changes in either ANC attendance or facility-based deliveries, providing reassurance that mothers who come to ANC and delivery are not dissuaded from attending when given the infant ARV in advance (Yu personnel communication).

### *PMTCT in the Labor Ward*



While many PMTCT programs initially focused on ANC activities as the entry point into HIV services, greater emphasis in recent years on delivery services has made an impact. Although WHO recommendations in 2007 included routine testing in the labor ward, there remains a significant gap in the number of countries providing this PMTCT service (WHO 2007, Tonwe-Gold 2008). The introduction of HIV testing and counseling for pregnant women as part of routine delivery services allows women who were not HIV tested during pregnancy to be rapidly identified and provided sdNVP for themselves and their infants to decrease the chance of HIV infection. Women who present too late for HIV testing and ARV prophylaxis prior to delivery still benefit from testing after delivery, receipt of infant ARV prophylaxis, infant feeding (IF) counseling, and linkage to follow-up for herself and her infant. Improving delivery facilities to include private space for counseling and testing and having access to trained counselors to offer these services 24/7 in the labor ward are necessary for optimal provision of services (Turan 2008). Spouses are more likely to be present around labor and delivery than during ANC visits and often agree to participate in couple counseling and testing. However fear of HIV testing and inadvertent disclosure to partners may also serve as a disincentive for institutional delivery.

The importance of repeat testing of previously HIV-negative women either late in gestation or in maternity, particularly in generalized epidemic settings to identify women who seroconvert during pregnancy, should be stressed. This is important given the high risk of transmission to the infant during acute infection. A recent study in Swaziland found that an intervention of targeted training of labor ward staff around importance of addressing missed opportunities for prevention in the labor wards, including identifying HIV-infected women who were not tested in ANC, identifying women who became newly infected during pregnancy, and offering sdNVP to women who either refuse or do not have time for testing prior to delivery increased all these parameters compared to sites that did not receive the training (Kieffer 2009). Most concerning was the overall 4.4% seroconversion rate during pregnancy among women in this setting. In Botswana where there is high national PMTCT coverage and a 1.8% seroconversion rate during pregnancy, it has been calculated that lack of identification and provision of services to these women who seroconvert and their infants accounts for about 40% of infected children (Lu 2009). While recommended in most national PMTCT guidelines, retesting women who tested HIV-negative early in pregnancy is not commonly implemented. Optimal country specific re-testing strategies during pregnancy and the postpartum period need to be identified and implemented based on the population, background seroprevalence rate, and resources available for retesting.

### ***PMTCT in the Postnatal Clinic***

PMTCT services do not end with providing infant drugs after delivery, but continue through the postpartum period through the end of breastfeeding. In many less-resourced countries, the importance of postnatal follow-up has not been realized, adding a challenge to follow-up PMTCT services. The focus of postnatal care (PNC) has often been based exclusively on infant immunizations, which are often done without provision of services for postpartum woman including evaluation, family planning or cervical cancer screening. Often PNC for women is dependent upon women actively asking for postpartum evaluation or family planning services, rather than routinely providing them. This is another area of missed opportunity, not only for PMTCT services, but also for MCH services more broadly. Refocusing attention on the importance of comprehensive PNC services will also strengthen PMTCT follow-up. This includes providing family planning services, additional preventive HIV counseling to those

identified as HIV-negative, retesting of women who tested negative earlier to identify seroconverters, offering testing to women and infants who were not tested previously and providing ARV prophylaxis, infant feeding counseling and early infant diagnosis (EID). During ANC counseling, women should be assisted with developing a birth plan that includes postnatal follow-up for the woman and infant. This will be particularly critical as the revised WHO recommendations for ARV use for PMTCT that include postnatal prophylaxis for a year or more are rolled out.

One reason women do not return for PNC is the lack of services provided, often in poor quality facilities with insufficient staffing. If comprehensive services do not exist and infant immunization is the only activity, then women will attend immunization sites closer to home. The need for multiple PNC visits and different locations for HIV follow-up, maternal care, immunizations, family planning, and cervical cancer screening increases wait times and loss to follow-up (Bwirire 2008). Integrating comprehensive MCH services including family planning, PMTCT, and HIV care and treatment, if possible, in one location, would facilitate a woman's ability to access all of these services (Rispel 2009).

### ***Family Planning***

As noted in Chapter 2, broad implementation of PMTCT Prong 2 -- preventing unintended pregnancies among women living with HIV -- would significantly decrease the numbers of HIV-infected children. Despite the decades of work on promoting family planning, services are often limited and not integrated within other services. Lack of provider knowledge on family planning, particularly about newer methods and safety of use among HIV-infected women; lack of on-site provision of surgical contraception, Norplant, and intrauterine devices; and lack of availability of methods other than condoms has led to inadequate family planning services and high rates of unmet need, particularly among HIV-infected women (Rispel 2009). Family planning counseling should begin during pregnancy, a difficult concept since the woman is already pregnant, but important because she may not access health services after delivery. Integrated antenatal services should support advanced planning and discussion with partners about additional reproductive intent particularly if tubal ligation is considered at time of delivery. These messages should be repeated after delivery and consistently during PNC.

### ***Infant Feeding (IF)***

Preventing transmission during breastfeeding remains one of the biggest challenges in PMTCT. IF counseling starts in ANC with educating all women about the benefits of exclusive breastfeeding. For women identified as HIV-infected, there are risks and benefits of different IF options to consider during development of an IF plan. IF counseling and support should continue throughout the antenatal period and particularly around the time of delivery, when women start to feed their babies. Each woman should be provided guidance and support, to help her implement her chosen method. Infant feeding counseling and support must also continue through weaning and for the first few years of life.

IF issues at the implementation level remain complex and largely under-resourced. Over the last decade, the WHO recommendations on infant feeding in the context of HIV infection have changed considerably, leaving staff on the ground confused about what messages to deliver to women. The shift in recommendations initially from continued breastfeeding in high mortality

areas to a focus on replacement feeding or breastfeeding with early and rapid weaning, and then back to exclusive breastfeeding without early weaning has created uncertainty in the field. HCWs trained in PMTCT during different periods of time may not all be re-trained when guidelines are revised. MOH guidelines may lag behind WHO guidelines, so personnel may often receive mixed messages and then pass on confusing or contradictory information to women.

The complexities of understanding and then translating IF messages to women have not been adequately addressed in many settings (Rispel 2007). There is considerable concern about human resource shortages and work overload impacting the ability to provide adequate IF services. IF counseling is often provided only at the first visit when the pregnant woman is overwhelmed with receiving knowledge of her HIV-positive status and is not likely to absorb much of the IF information provided. This is done because many women make only one antenatal visit. It is critical that IF counseling is repeated in ANC, again after delivery and continually during the postnatal period (Piwoz 2005, Bland 2007). However, often there is no reorganization of facilities or roles/responsibilities to allow counselors sufficient time for these complex IF issues or for repeat counseling. HCWs may not understand the importance of IF issues for HIV-infected women, or may not believe in the guidance provided, thus limiting the attention given to IF issues or the accuracy of the information provided. Staff knowledge and attitudes often guide women's choices such that HCWs' lack of understanding, particularly about the risks of not breast feeding, and personal biases are reflected in the messages women are given and the choices that are made (Chopra 2009, Bwirire 2008, Rispel 2009). Some PMTCT programs rely heavily on external "peers" or lay counselors to supplement the existing MCH or PMTCT staff; however, the counseling they provide may be of variable quality (Rispel 2009). Limited mentoring or ongoing training and support to IF counselors leads to poor quality of services. One study found that while there were large numbers of staff trained in PMTCT including IF, there was a lack of understanding of the materials presented. A knowledge survey showed that there was no difference in correct responses between those staff who had IF training and those who never had IF training (Chopra 2008, Chopra 2009).

IF counseling and support are often designed and provided without involvement of nutrition personnel and the benefit of their expertise. While HCWs may have had IF training, they often lack specific guidance on how to operationalize the information presented to women. Some examples include: how to safely formula-feed; options for alternative feeding such as recipes for modified cow's milk; how and when to wean; specific definitions of AFASS criteria; what messages to give once infant status is known; and how to explain the apparent contradiction that mixed feeding early in infancy can be detrimental while complementary feeding after six months is required for adequate nutrition. There was little evidence of use of information collected on IF for decision making (such as use of AFASS checklists). The newly revised WHO IF guidelines have been designed to be simpler and clearer to reduce these challenges (WHO IF 2009).

The importance of IF issues on child survival and in HIV-infected families specifically, has produced varied MOH responses. Kenya used Global Fund money to hire nutritionists; Malawi utilized a large cadre of community-based health workers trained in IF and nutrition to provide support, ongoing counseling and infant follow-up in the community; and Rwanda implemented a program to provide counseling and nutritional supplements to support safer weaning by HIV-

infected women. Several programs are addressing these critical IF issues by supplementing PMTCT services with focused infant feeding support programs. There have been few evaluations of the impact of these IF services on infant health outcomes, but some are currently underway. Areas of food and nutrition, however, often do not get adequate emphasis or funding.

There has been a renewed focus on making long-term breastfeeding safer rather than avoiding breastfeeding for HIV-exposed infants. This includes ensuring that women who need therapy are started on ART early, ARV prophylaxis during breastfeeding through provision of ARV to either breastfeeding infants or to breastfeeding women, or, hopefully one day, through the use of a vaccine to prevent HIV infection. WHO guidelines recently have changed to include postnatal prevention for the duration of breastfeeding (WHO PMTCT 2009). It is essential that programs do not delay in implementing the new WHO guidelines with careful attention to counseling messages and training if we hope to make progress in the elimination of HIV infection in children. Work needs to be done to understand the feasibility and effectiveness of these postnatal interventions.

### ***Early Infant Diagnosis (EID)***

With high mortality for HIV-infected infants in the first year of life and increased survival with early ART, as reflected in the WHO recommendations to treat all infants, there is increased focus on making infant HIV diagnosis using PCR more broadly available. Many challenges remain in ensuring all HIV-exposed infants receive testing and all HIV-infected infants have access to HIV care and treatment. Poor postnatal MCH clinic attendance, as low as 15-20% in some settings, and inability to identify HIV-exposed infants result in missed opportunities for infant HIV testing and diagnosis. Counseling messages on the importance of EID and initiation of ART for the survival of HIV-infected children must begin in ANC and continue at delivery to encourage women to return for PNC. Several countries have succeeded in revising the hand held maternal and/or infant health cards to include maternal and infant HIV information to facilitate recognition of HIV exposed infants and record EID results.

DNA PCR is the test of choice for early infant diagnosis. Unfortunately DNA PCR testing is generally limited to a few higher level facilities (some district level hospitals & tertiary facilities). The ability to collect a filter paper blood spot specimen that is stable for long periods and can be easily transported to distant labs has expanded the ability to identify HIV-infected children. However, frequently there is a delay in receiving results from the referral facility, particularly if lab testing is done out of country (e.g. Swaziland and Lesotho). Once the facility receives results, there are additional challenges in providing results back to the infant's mother that also contribute to delays in providing care and treatment services to HIV-infected infants. This time delay is critical for infants given that the earlier ART is started in HIV-infected infants, the better the survival.

Several innovative programs have been set up to maximize the identification of HIV exposed and infected infants. Screening all infants who attend immunization and outpatient services initially with HIV antibody rapid tests to identify HIV-exposed children and then dried blood spot collection for PCR to identify infected children is being done in several settings (Rollins 2009, Chersich 2008, Barker 2007)). National immunization days that also offer similar services with infant antibody rapid testing and dried blood spot collection and national HIV testing days

specifically for children have been initiated in several countries as a means of identifying HIV-infected children and linking them with HIV care and treatment services. Diagnosing infection must lead to initiation of therapy as diagnosis alone will not improve outcome (Aledort 2006).

While PCR availability is being improved, WHO has supported the use of a clinical algorithm for diagnosis of presumptive HIV infection in infants less than 18 months of age (Horwood 2003, Horwood 2009). However, this process is done infrequently as staff often do not feel comfortable initiating treatment in an infant without a PCR result. Training on and implementation of the clinical evaluation is critical as many babies will die before reaching 18 months of age for the definitive antibody test.

### ***Quality Improvement (QI) Activities***

The quality of services remains a key to successful implementation of any program. PMTCT program performance has been linked to the overall quality of the health system; countries with strong health systems were able to more quickly scale-up quality PMTCT programs. The presence of high-quality MCH services is associated with more successful PMTCT services. One evaluation of several PMTCT programs found that most settings had resources, knowledge and training, but the programs failed to meet expectations due to lack of functional systems. Strengthening the health care delivery system, particularly in a decentralized district-type approach, with a strong quality monitoring and improvement system has led to significant improvements in program outcome (Chopra 2009, Doherty 2009, Rowe 2005, Perez 2004). Ownership of the health system by the district is required with district-led execution of system improvements. Building local capacity for QI activities and a very active QI system with solutions determined at “ground-level” can lead to substantial improvements (Doherty 2009, Barker 2007). Better data collection and reporting is critical and must include a feedback loop to the implementer so that performance on key outcomes can be measured and followed (Mate 2009, Rowe 2005). When using this district approach, other districts can be linked in a “learning network” so that each facility is not creating or reinventing systems but learning from those who have successfully implemented quality services (Barker 2007).

### **Health Workforce**

Inadequate human resources is a major limiting factor in the scale-up of all HIV services, including PMTCT in almost every country. This includes the quantity as well as the quality of service providers (Zachariah 2009, Doherty 2009, Barker 2007). Many countries face extreme HCW shortages within the ANC, labor ward, PNC, reproductive health, and family planning and in other areas (Chopra 2009, Miles 2006, Agyepong 1999). The increased workloads expected of already over-stretched staff due to the time and knowledge required for PMTCT and HIV care and treatment services make it exceedingly difficult to provide quality services integrated within existing services without additional resources. However, integration of these services within the existing antenatal and maternity services allows the ownership of the program and work responsibility to be shared by all staff (Doherty 2009). In some countries NGOs are able to hire and place personnel within facilities at the public sector rates with assurances from the MOH that these positions eventually will be transitioned to full government support (Druce 2007). In many countries, key cadres of personnel required for provision of PMTCT services, such as HIV counselors, do not exist within the MOH structure. This problem can be addressed by training a

cadre of lay counselors, by training the entire staff in ANC & maternity in counseling, and by task sharing (Shetty 2008, Zachariah 2009).

In many hospitals, personnel are routinely rotated to different areas of the hospital or health center. This creates a challenge to deliver quality PMTCT services due to the loss of experienced personnel and the continual need for resources to train new personnel (Chopra 2009). Frequently new, inexperienced personnel implement and manage PMTCT services. It can take quite a while to become comfortable with the complicated issues around PMTCT, ARV regimens, and IF guidance. New staff may miss out on comprehensive training yet be expected to provide these services as soon as they arrive. Similar challenges also arise due to high staff turnover, resulting from poor working conditions, increased workloads without increased compensation, or better paying positions elsewhere (Zachariah 2009). Poor working conditions include the often poor physical structure and appearance of the workplace, lack of adequate salary, lack of equipment, supplies and medicines needed to perform their job well, and too many patients (Agyepong 1999, Doherty 2009, Zachariah 2009, Rispel 2009). The additional data collection and reporting requirements, particularly in high volume sites, may contribute to poor performance, particularly if an understanding of the data and its use are not fed back to the site for program improvement.

Overall weak human resources management also contributes to HCW shortages. Lack of performance accountability with no reward for quality performance and no consequences for poor performance contributes to the poor motivation of staff (Agyepong 1999). Absenteeism or late arrival/early departure from duties contributes to the staff insufficiencies. For example, in one South African setting, it was found that adequate staffing was available when staff absenteeism was reduced by 20%.

Task shifting or sharing has been critical to successful PMTCT program implementation (Zachariah 2009). There are not enough physicians in many countries, particularly in the public sector, to conduct the traditional physician roles of clinical staging, laboratory ordering, and drug prescription (Doherty 2009, Zachariah 2009, Miles 2006). In most settings, nurses and nurse midwives are entrusted with the entire responsibility for antenatal clinic, maternity, and postnatal services with minimal physician participation. In some countries, there are union or legal provisions against non-physicians prescribing or physicians have found it difficult to accept giving up responsibility for these activities (Zachariah 2009). Restrictions on HIV management and ARV prescribing are increasingly recognized as a bottleneck in care of HIV-infected persons. Similar issues may also be found with laboratory testing, with rules or prejudices against nurses or counselors conducting HIV testing. Settings where nurses are allowed to prescribe ARVs, not only for PMTCT prophylaxis but also for treatment of women who need HIV treatment for their own health have been the most successful in scaling-up combination ARV regimens, including in ANC. However, the ability to prescribe ARVs must be accompanied with sufficient training and ongoing supervision (Miles 2006). Data have shown that nurse-run ARV programs have similar patient outcomes to those solely using physicians for all HIV care and treatment (Zachariah 2009). There must be adequate guidance on how to task shift/share with clear methods of evaluating the impact.

In many programs, non-medical personnel play an important role. This has allowed less technical activities to be carried out by lay staff, freeing up the nurses to concentrate on the provision of medical services (Zachariah 2009). These include lay counselors, peer counselors, and “expert patients.” Many programs now utilize these personnel and have documented the feasibility and acceptance of this method of supplementing clinic-based staff (Shetty 2008). However, there are limited data on the impact of these support staff on the overall effectiveness of PMTCT programs. Expert patients and psychosocial support groups are increasingly being used to provide ongoing support to HIV-infected women to improve adherence to the cascade, facilitate disclosure, and link PMTCT programs with ART services and the community. These additional personnel may have high turnover rates, may or may not cost the health care system additional money, and clearly require training to contribute appropriately. Defining the roles and responsibilities of non-medical personnel, with particular emphasis on the limitation of their activities, together with close supervision of their performance, is important for quality service provision (Zachariah 2009).

There has been less acceptance of the use of traditional birth attendants (TBAs) to provide PMTCT services. Traditionally, the medical community has not accepted TBAs due to their lack of training and provision of poor quality services that keep women from delivering with a trained medical provider. However, in many settings, TBAs are delivering a substantial portion of pregnant women in the community. Programs engaging TBAs in the community follow-up of women receiving PMTCT services in Malawi reported both some successes and challenges (Malawi IAS 2009 abs, Bwirire 2008). In Cameroon, trained birth attendants have been providing all health services including PMTCT in rural villages with considerable success under the guidance of nurses from the Cameroon Baptist Convention Health Board primary health care program (Wanyu 2007).

No matter what cadre of personnel or lay workers is used to provide PMTCT services, their training is critical. The type and quality of the training and more importantly, the oversight and ongoing mentoring provided after training, have the biggest impact on the quality of service delivery. Training is often provided as a short centralized training that takes staff away from workplace. Once the training is completed, staff are considered “trained” and sent back to their facilities to provide services; often without any assessment of their understanding of the information presented or skills learned (Rowe 2005, Agyepong 1999). With a rapidly changing field such as PMTCT, there must be ongoing training, skills/knowledge assessment, and follow-up mentoring and supervision to insure that quality service is being delivered (Zachariah 2009, Doherty 2009).

Surveys have indicated a perception (and reality, at times) of poor treatment and discrimination by HCW for HIV-infected women within ANC, labor and delivery, and MCH services. These negative attitudes drive women away from accessing services and discourage testing and adherence to the PMTCT program (Turan 2008). Enhanced training and sensitization to HCWs around these issues, HIV and stigma, and the impact of their attitudes on the health of their communities may improve the care that HIV-infected persons receive. Addressing HCW concerns about potential occupational exposure and infection as well as treatment for those HIC infected is also critical in improving HCW attitudes towards HIV-infected patients (Turan 2008).

In addition, supervision and better accountability to job performance may improve these activities (Agyepong 1999).

There is a perception that externally-supported HIV research and programs (including PEPFAR and other USG-supported activities) are contributing to internal “brain drain” (Larsson 2009, Serour 2009). These generally higher paying jobs take highly-skilled and -motivated HCW out of the field into management/technical assistance jobs, further contributing to the severe shortage of HCW providing care to HIV-infected patients. These programs can draw staff out of the public sector into more lucrative NGO or private-sector jobs. However, developing the local expertise to manage large programs and promoting personnel from within the country to leadership roles will advance the country’s capacity to develop sustainable health care infrastructure more than bringing in high-salaried expatriates to perform these technical and management jobs. In addition, the ability to remain in-country and receive a decent salary may, in fact, keep the in-country expertise from leaving for more lucrative jobs in other countries, or bring back to the country those local nationals who left to pursue more financially rewarding jobs elsewhere (ICAP 2008). Creative solutions to keeping highly-skilled personnel engaged in the public sector are necessary.

Some of the recommended ways to address these workforce challenges start with training. Detailed training on HIV, PMTCT, IF, and HIV care and treatment should be included in pre-service training for all health care workers (nurses, midwives, doctors, lab techs, medical assistants, pharmacists etc.) including rotations through clinics offering PMTCT and HIV care and treatment services (Agyepong 1999). This would decrease the challenge with continually rotating staff and allow subsequent trainings to be shorter and more targeted. Since there is evidence that current training activities may not be achieving desired outcomes, re-designing trainings to include more hands-on, practical training coupled with mentoring and on-site supervision to improve performance, with periodic skills assessment could improve this gap (Chopra 2009, Doherty 2009, Agyepong 1999, Rowe 2005). One potential mechanism might be a specific training curriculum with assessment that would lead to “certification” as an “authorized prescriber” (or other role) that would be viewed as attaining a higher job level and perhaps serve as an incentive for good work (Zachariah 2009). Creative use of training or travel as a reward for good quality performance may encourage better work output.

With task shifting or sharing, particularly when using lay or peer staff, it is also critical that there is ongoing training, mentoring, supervision and observation of skills. Clear definitions of roles and responsibilities are needed with indicators of adequate performance (Rispel 2009, Zachariah 2009). Physicians must embrace these shifts in nurse’s responsibility with respect and support their increased activities. Creating mechanisms for periodic refresher trainings and updates is particularly important in PMTCT, which regularly evolves and changes practices as new evidence becomes available. Sensitization and training of HCWs on the “customer care” model of attention to all patients, particularly PLWHA to improve the attitudes of HCWs would improve their performance but also encourage HIV-infected women to continue to access the health services. Similarly, improving health care facilities’ service delivery by increasing clients’ perception of quality of services and HCW satisfaction with their work environment is needed in some settings.



Improving client flow and efficiency of services may decrease the need for more staff and workload of existing staff. This includes decreasing any unnecessary reporting/documentation burdens so that HCWs have more time to provide better clinical care. Improved personnel management to address tardiness, absenteeism, and performance would optimize the work of existing staff. Providing incentives for staff to work in the public health system, such as performance-based incentives, voluntary overtime work with payment, support for training, and certification may help recruitment and retention (Zachariah 2009).

### **Health Information Systems**

Despite the millions of women and their infants receiving PMTCT services, there is a paucity of data documenting what works or does not work in maximizing program effectiveness. Facility-based coverage data are most commonly reported, yet these data do not reflect population coverage. Additionally, coverage does not reflect impact since significant loss to follow-up is documented using routinely collected process indicators (e.g. number tested, number given drugs). True outcome or impact indicators, such as the number of eligible women receiving ART or infant HIV-free survival, are more difficult to obtain and are not routinely collected.

Coordinating, collecting, and interpreting PMTCT data is a challenge (Mate 2009). Monitoring and evaluation systems are often more the “M” than the “E” and often are designed to satisfy donor reporting requirements rather than for program quality and evaluation. Few programs have a quality improvement system in place for data collection. Indicators should be standardized and simplified to reduce the workload, particularly with task shifting, and allow for consistency in training, recording, reporting, and data interpretation (Zachariah 2009). HCW often cite large data collection and reporting burdens as reasons for less than adequate performance (Risipel 2009)

Better data collection and reporting are critical for performance improvement (Forster 2008, Braitstein 2009, Mate 2009). One review of PMTCT data from three districts in South Africa found that data on six key elements evaluated were collected only 50.3% of the time and were accurate only 12.8% of the time, with considerable variation across districts (Mate 2009). Data were missing for 37% of the “HIV tested” indicator, 48% of the “CD4 tested” indicator, and 87% of the “infant PCR at six weeks” indicator. Overall, very few data points were considered either “reliable” or “acceptable.” There were large areas of over-counting and under-counting, making evaluating and improving services from the start difficult. Similar problems with accuracy of indicator reporting were seen in a pilot to scale-up PMTCT ARV combination regimens in Zimbabwe. Some examples of changes that led to data collection improvements included added checklists, revised registers, and regular reviews of program data. When gaps were identified, and ideas for improvement were generated from the clinics themselves, there was a substantial improvement in performance (Barker 2007, Doherty 2009). Key factors in improving PMTCT data quality include the importance of frontline staff belief in the value of the data collected for the delivery of health care to their patients, the site “ownership” of the data they collect, and the need for additional support for and oversight of clinic staff in data collection and management that may include allocation of dedicated well-trained data staff to focus on high-quality data collection and follow-through (Mate 2009, Risipel 2009).

In addition to the general problems described above, well-defined and widely used indicators assessing quality of IF counseling, IF outcomes, and family planning are non-existent or weak. Many national data collection tools indicate whether the mother and infant received ARV but with increasing use of combination regimens, these indicators do not accurately capture what ARV regimen was received. Drugs may be dispensed at several locations, and at several times during pregnancy such as NVP at diagnosis and AZT at 28 weeks, which then may appear as different regimens and be counted twice for the same woman. However, drugs dispensed may not reflect the drugs actually taken by the mother or baby. Adherence information is difficult to capture and is rarely included in M&E systems.

The common method of collecting aggregate data at service delivery points rather than individual-level data across service points leads to the inability to identify and capture data on HIV-infected mothers and HIV-infected or -exposed babies at all points in the health care system. Often there is no link between the mother's information and her baby's between sites, limiting the ability to determine the successful continuum of care from PMTCT to HIV care and treatment services and the true loss to follow-up rate. Inaccurate counting also results when one woman may be counted several times if her information is entered into separate registries multiple times as she re-enters the system at different time points or across different programs.

Most developing countries do not have a unique identifier system or a nationwide health information system that allows information collected from any site to be reconciled with that of other sites. Health information systems often do not “talk” to each other across service areas, facilities and programs or between and even within organizations, governments or programs (Forster 2008). Each donor/funder may have their own established system that is difficult to reconcile with other donors' or other programs. Government support and attention to monitoring and evaluation systems are critical, with a need to coordinate M&E reports and databases across disciplines and funders. National programs must invest appropriate resources into a coordinated M&E system both for reporting and program improvement. A few country programs have started to use electronic medical records or patient tracking systems that open the door to providing better patient care and improved data quality (Nucita 2009, Braitstein 2009, Forster 2008).

Several countries have implemented revised maternal and/or child health cards to include HIV-related information that allows all service delivery points to know whether a mother is HIV-infected and a child HIV-exposed, cotrimoxazole (CTX) use, ARV regimens prescribed, and results of lab testing (Barker 2007). While there was initial HCW reluctance to use cards with HIV indicators included for fear of “inadvertent HIV status disclosure” in some settings, these new tools have generally been well-accepted. Their use normalizes PMTCT services and reinforces them as part of general health services. Adequate input from multiple sectors on the design of such cards, piloting, and careful training prior to roll-out can improve their acceptance. These revised cards also enhance the ability to track mother-baby pairs.

### **Community and Cultural Issues**

Community and cultural issues impact the success of PMTCT programs at many levels, including broad cultural issues about gender and the place of women in society, economic insecurity, and access to health services (See chapter 5). Interpersonal issues within the family

and medical versus traditional beliefs often influence uptake of available services. These, coupled with lack of community awareness, education, and support, particularly around PMTCT, HIV-related stigma, and lack of disclosure to partners, often leave a woman negotiating the system alone. Determining the extent of the contribution of each of these areas to failure to access complete PMTCT and HIV services and identifying interventions to address them will maximize the program effectiveness.

In many settings, women lack empowerment around reproductive health and family planning decision-making (Medley 2004). Women may perceive the need to get “permission” from her partner to get tested, accept an intervention, or make infant feeding choices, which may delay or even prohibit uptake of PMTCT services. Fear of facing HIV testing and addressing potential HIV infection may keep women from accessing health services at all (Turan 2008). There may be a fear of death in hospitals, as they are seen as places where people go to die. Pregnant women may go to ANC to collect a registration card but do not plan to complete ANC or deliver in the facility. There may be a fear of delivery by cesarean section or a cultural belief in the need for delivery by a special type of person to protect baby from evil, which may limit facility deliveries. Additional cultural norms that may negatively impact PMTCT may include 40 days confinement for women after delivery, which limits the chance that an infant will be brought to receive ARV prophylaxis after home delivery or for early 1-2 week postpartum visits.

Cultural norms also play a significant role in the infant feeding choices of women, including those receiving PMTCT services, particularly if they have not disclosed their status to family members (Rispel 2009, Bwirire 2008). In one study examining cultural barriers to exclusive breastfeeding in Cameroon, they found that the primary reason for supplementing IF was pressure by village elders and families because of the tradition of providing additional food to infants (Kakute 2005). There was a belief that breast milk is an incomplete food and infants would not increase their weight sufficiently on breast milk alone. Also there was the belief that family members should benefit from food grown in the family plot/farm, and there was a taboo prohibiting sexual contact during exclusive breastfeeding. These types of strong cultural beliefs toward infant feeding methods and the potential stigma associated with avoidance of all breastfeeding may impact a woman’s feeding choice more than the IF counseling messages provided to her.

To empower women suggested activities include the addition of enhanced education/counseling around disclosure, gender issues, partner violence, health seeking behavior, and promotion of family planning as a routine part of all PMTCT programs (Deschamps 2009, Medley 2004). Use of peer support groups has been found to assist women with dealing with stigma and isolation, provide social support, and improve knowledge and positive living (Rispel 2009). Additional support groups for pregnant women, couples, discordant couples, and male partners may also provide more specific support tailored to the needs of the individual. However, low rates of utilization of these services have been reported even when they are available, requiring creative methods of making these services more accessible (Rispel 2009).

Low partner involvement in reproductive health and PMTCT services is a problem in most resource limited settings (Bwirire 2008, Tonwe-Gold 2008, Mbizvo 1996, Turan 2008, Medley 2004). Rwanda has addressed this issue by making couple attendance a requirement at ANC,

with a very high rate of partner involvement in ANC and PMTCT as a result (Mugwaneza 2009 abs). Disclosure and male participation in ANC/PMTCT services has been found to increase the likelihood of follow-up and completion of the PMTCT cascade (Alusio 2009 abs). While the majority of women who disclosed their positive status to their partners received supportive responses, 16.7-86% chose not to disclose their status (Medley 2004, Brou 2007). HIV-negative women are more likely to disclose their status than HIV-infected women. Most ANC, maternity wards, and PNC facilities are not male-friendly in design or time and thus discourage male participation.

Several methods have been used with varying levels of success to engage men in the PMTCT and general reproductive health of their pregnant partners. These include social marketing campaigns to promote male involvement, workplace education programs to reach men where they work, and community outreach and home visits to engage partners. The provision of personal written invitations to partners to attend ANC or special men's clinics has had some success in increasing male participation. Additional hours or separate entrances/places for couples to be seen together to make ANC a more "male-friendly" environment and moving couples who come to ANC together to the head of the line so as not to delay men from their work provide incentives to encourage couple counseling.

HIV and community education programs often are not well integrated with PMTCT. The HIV messages delivered may or may not include mention of PMTCT in sufficient detail to inform communities. There is still a huge knowledge gap around the fact that the majority of babies born to HIV-infected women are not infected and that we know how to prevent infection in babies (Rispel 2009, Bwirire 2008, Chopra 2008). This is true in the community, among the media, and even among HCWs. This leads to a somewhat fatalistic view that there is nothing that can be done to prevent infant HIV infections.

Health service utilization and health-seeking behavior is affected by knowledge about and acceptability of PMTCT services among pregnant women, their families, and key community figures (Medley 2004). Promotion of and community mobilization around PMTCT is needed to improve knowledge and awareness of PMTCT and the ability to prevent infection in infants (Bwirire 2008, Rispel 2009, Zachariah 2009). This includes focused methods of reaching partners, mothers-in-law, and key community and religious leaders. Bringing peer psychosocial support programs to the community, engaging networks of People living with HIV/AIDS (PLWHA) and women's groups to serve as advocates, and utilizing community leaders and HCWs to follow women in their homes have helped address these gaps (Zachariah 2009). Having community and individual support services in place once the technical services are in place has been found to improve program success. Use of community health workers can provide key linkages between facility personnel, the PMTCT participants, and the community to maximize sensitization, education, follow-up, support and improve program outcomes. Using home visitors or peer supporters to help women with IF and nutrition issues in the community should also be considered, particularly during important times such as weaning. Other activities that have been used successfully to disseminate information and identify women and infants who need PMTCT services include national PMTCT promotional days and mass media campaigns on PMTCT (Englesmann 2008).

## Medical Products and Technologies

Challenges around medical products and technologies in PMTCT are mainly concerned with the consistent availability of appropriate ARVs and HIV test kits and access to laboratory testing for CD4 and PCR for EID (Rispel 2009). Generally, there is more reliable access to these commodities and services where PMTCT programs are co-located or in close proximity to HIV care and treatment services. Access to pediatric ARV formulations for prophylaxis and EID may be particularly challenging in the absence of pediatric HIV care and treatment programs. These links are often lacking in lower-level facilities and clinics in rural or hard to reach places (Tonwe-Gold 2008, Bwirire 2008).

Moving from the sdNVP regimen to combination regimens, and more importantly to fully implementing the WHO guidelines including provision of ART to all eligible women, can only be achieved if these challenges are addressed (Tonwe-Gold 2008). Inadequate or intermittent use of combination regimens creates more problems than NVP alone, both for PMTCT and future treatment. Therefore, insuring an adequate drug supply is critical to scaling up more effective PMTCT regimens.

Some of the supply issue challenges include dependence on partner/donor systems rather than the existing MOH system if different systems are used for distribution for HIV-related drugs and supplies than for other commodities. These parallel systems are often set up when the national system does not have the capacity to reliably supply these commodities, but then it requires that personnel deal with two sets of paperwork (Druce 2007). Even if there is only one system, there is often the need to maintain buffer supplies of laboratory kits, reagents, or drugs when the national distribution system is inadequate. In addition, adequate supplies of protective gear (gloves, sharps containers, bleach) may also be a problem (Rispel 2009, Turan 2008). This may be due to inadequate forecasting, poor or tardy return of accountability data or supply requests from peripheral sites, or untrained staff responsible for procurement both locally and centrally. Poor stock management also leads to stockouts or loss of supplies due to kit or drug expiration. Basic training on procurements and small business skills may contribute to improving these areas.

Reports of PMTCT drug availability have been variable with some sites reporting regular stockouts (Rispel 2009). Tracking commodity use and ordering accurately to prevent stock-outs is complicated by the challenges in recording PMTCT drug use when drugs dispensed in ANC are recorded as being taken in maternity. Stockouts are reported most frequently with AZT alone since it is more commonly supplied in a fixed dose combination for HIV treatment. Rapid scale up of combination prophylaxis with AZT and NVP combined with expansion of PMTCT services to new sites may deplete MOH stores if adequate preparation is not made in advance. Sites have reported dispensing 1-2 week supplies of AZT when stocks are short, requiring women to come back frequently for drugs until more supplies are available. This has implications for adherence and potential gaps in AZT dosing when visits are missed for refills.

The biggest challenges as far as laboratory testing is concerned are the limited access to CD4 cell count and DNA PCR testing. Reliance on clinical criteria for the initiation of ART is challenging so measurement of CD4 cell counts remains the standard for determining ART eligibility in most countries. Expensive equipment for determining CD4 cell counts is often

lacking in peripheral sites and rural areas. Most CD4 testing is available in cities or facilities providing HIV care and treatment, and may be out of reach of many sites providing PMTCT services. Efforts to create “spoke and wheel” type systems to reach out from central labs to provide CD4 testing services in the periphery have been successful in some countries, including Kenya. However, central labs that support a wide catchment area with many PMTCT service delivery points report difficulties handling the large volume of specimens for CD4 testing, thus it is critical to provide additional capacity to handle the work load. Facilities report challenges in providing CD4 cell count testing to all women when, often, testing can only be done one day a week. CD4 cell counts must be run within 24 hours of collection using standard vacutainer tubes, restricting their utility in rural or remote programs with large distances to the test centers. Well-functioning transport systems for rapid delivery of specimens to the test center are required. More widespread use of specific stabilizer tubes that allow CD4 cell counts to be done up to 7 days after the blood draw would be a considerable improvement. Blood can be drawn whenever a woman appears in clinic and accurate results received even with increased time between collection and testing. This tube costs slightly more than a standard tube and requires the use of additional tubes for other tests such as hemoglobin.

Availability of point-of-care CD4 testing would be a major improvement in the ability to identify and provide ART to eligible women within PMTCT programs. CD4 cell count testing done in real time with rapid results in MCH clinics would allow eligible women to be started on ART immediately at the time of HIV diagnosis. Numerous point-of-care CD4 technologies are in currently in development or undergoing testing. It is hoped that these will be available soon for use in peripheral sites without the need for trained technicians and at a more reasonable price than current technology.

Point-of-care HIV diagnosis for infants is one of the highest priority needs for maximizing PMTCT program effectiveness and the linkage of infected infants into HIV care. While there has been some progress in this area, they are still far from being tested widely or generally available.

### **Health Financing**

Overall, PMTCT is under-funded. Scaling up current WHO guidelines including combination ARV prophylactic regimens and HIV treatment to eligible pregnant women will require a substantial increase in funding, but will reap cost benefits by decreasing the number of HIV-infected infants needing treatment and identifying women who need therapy earlier.

Significantly more resources are put into adult prevention services that are far less effective than PMTCT. PMTCT still remains the most effective HIV prevention method with broader maternal child survival benefits, yet it receives little attention with some countries and donors. HIV can be virtually eliminated in infants as it has already in the US and other developed countries, unlike HIV in adults. Increased advocacy at all levels is needed to ensure that pediatric HIV is eliminated worldwide. Requiring all HIV care and treatment programs to include targets for treatment of eligible pregnant women and to provide functional linkages to PMTCT services in their catchment areas is one method of addressing this gap. Including an active plan to expand and improve PMTCT services as a requirement for a country to receive funding from the Global Fund or other major donor HIV programs would also focus attention on the importance of PMTCT.

HIV, as a chronic disease requiring ever increasing health care resources in the absence of successful prevention programs, adds an unparalleled strain on the health care system. However, the cost of HIV care and treatment programs are more than recouped by the decrease in health care costs of treating HIV disease progression. Also, healthy HIV-infected persons continue to contribute meaningfully to the workforce. The initial investments in setting up the programs and ongoing costs of providing the treatment until the benefits are reaped are considerable. Few governments have kept their commitments in terms of the portion of the budgets spent on health care, particularly HIV programs. Therefore, the majority of programs for both PMTCT and HIV care and treatment are donor-supported. Poor donor coordination with different types or levels of support within a country leads to inefficiencies (Druce 2007, Tonwe-Gold 2008). Locally or regionally manufactured drugs or test kits may be used by the MOH but may not be accepted by donors. Bulk procurement by donors allows significant cost savings but leads to challenges in meeting individual country requirements or national algorithms. A health center receiving support for HIV testing services and PMTCT services from different donors may have completely different testing algorithms, supply chain services, and reporting mechanisms (Druce 2007).

The focus of many HIV care and treatment and PMTCT programs has been the public sector with the emphasis on provision of free services. Some programs, including PMTCT programs, have documented decreased visits and drug adherence in programs that include fees for service; however, this is not universal (ICAP 2008, Zimbabwe 2009). While many faith-based organizations (FBO) have been committed to the delivery of PMTCT services, the private sector is often not as engaged in providing these services to decrease the burden on the public sector. Corporate contributions to the HIV-related health care costs of their personnel have been underutilized as a cost-sharing mechanism. Private services may be able to provide better quality individualized care for those who are able to pay for it compared with the public health approach to HIV care used by government services.

### Cost-Effectiveness

In the next phase of PEPFAR there will be an increased emphasis on understanding the costs of services and cost-effectiveness. For individual partners and donors, it is often difficult to estimate the cost of PMTCT programs across and even within countries. The cost-per-patient may vary widely across countries supported by a single donor. Reconciling these costs may be a challenge when trying to optimize efficiencies, forecast costs of expansion, or make choices about where to invest resources. Costs are often calculated at the national or international level and may have little relevance to individual sites or for local decisions about site management or resource allocation. As new interventions are tested to improve the delivery of PMTCT services, they should be accompanied by a cost estimate to identify the interventions that have the biggest impact for the lowest cost. Providing updates and technical support to the MOH at all levels to assist in making decisions and negotiating pricing to maximize cost-effectiveness as new information is learned is an ongoing challenge.

### Performance-based financing

Some countries have implemented or are investigating innovative systems to address health financing issues, such as performance-based financing (PBF), using a district approach to

funding government services rather than through central MOH funding, and cost-sharing. Performance-based health care financing has been implemented throughout Rwanda with success and has been expanded to include HIV care and treatment and PMTCT services (ICAP 2008, Tonwe-Gold 2008, Druce 2007). PBF was implemented gradually from a pilot with an NGO to nation-wide implementation by the government and partners. PBF is a financing strategy that aims to increase the quantity and quality of health services by linking incentives to performance. Improved performance directly results in increased revenue for the health center and financial incentives for its staff. This approach provides an opportunity to motivate health staff to effectively address performance issues and strengthen service delivery. The core activity is to use PBF indicators to improve the quality of the program by identifying problems and working with the health center and district to address these problems. In the Rwanda setting, common indicators to measure quantity and quality of performance were established both for general service delivery and for HIV/AIDS at health centers and district hospitals. Each health center and district hospital reports monthly outputs, which are indexed by a quality score, measured quarterly through a standard supervisory checklist. Both quantity and quality of services are verified by PBF-trained supervisors from the district hospital and district partners. The payments motivate the underpaid health workers, who develop creative strategies to increase their outputs and quality score in order to improve their incentives. For example, some sites offered women “gifts” after delivery at the health center and some sites shared payment of a PBF indicator with community health care workers who successfully referred women for delivery at the health center.

A strong commitment from the MOH and integration of different levels of the health system and partners are critical to the success of this type of financial intervention. The fact that the incentive gained depends on the facility’s ability to record and report data offers the opportunity to improve that data recording and reporting. Well-reported indicators can then be used to identify gaps in program and service design and working with the health center and district to address these gaps.

Brazil implemented a system similar to PBF, but at the family rather than government or health sector level. Their poverty elimination-based program provided stipends to extremely poor families dependent on several factors, such as ANC attendance, children attending school, and completing immunizations, to encourage families to take care of themselves and their future.

Providing funding through a district approach supports the development of financial sustainability in each district, rather than relying on the central MOH program to provide resources and program management. Establishing district control over the budget, financial management, cost sharing, and procurement of equipment and supplies with the necessary capacity building and training to support it will not only contribute to PMTCT program improvement but overall functioning of the district and district leadership as well (EPGAF 2009). Management of donor funds at the district or more local level also improves the financial accountability on the best use of resources, particularly when there is strong district leadership and buy-in from the community about the importance of PMTCT services.

Whatever type of financial system is used, lack of financial accountability and lack of targets to be reached as a prerequisite for additional funding provides the opportunity for misuse or



inefficient use of funds. Mechanisms to tie funding to demonstrable outcomes may improve the performance and efficiencies of PMTCT programs.

### **Leadership and Governance**

Government and political commitment to PMTCT at the highest level is critical to the success of PMTCT services. A country's commitment to the elimination of pediatric HIV and willingness to prioritize this in country budgets, activities, and support can lead to a substantial decrease and eventual elimination of pediatric HIV (Druce 2007, Tonwe-Gold 2008, McIntyre 2008).

Prioritization of PMTCT in national strategic HIV plans and programs is critical. Working with the country to outline a budget and leverage both government and donor funding is important for country ownership of the program. Setting clear attainable targets for PMTCT within national AIDS programs is critical to pushing the PMTCT agenda. This has been accomplished in countries with limited resources as well as better resourced countries. Examples include Thailand, Botswana, and more recently Rwanda, Kenya, Namibia, and parts of South Africa. Some of the lessons that have been learned from the success in countries with high quality PMTCT services and nationwide scale-up include the presence of political commitment, a strong management system, national coordination of activities, and support from multiple partners (Tonwe-Gold 2008).

Clearly the limited health care infrastructure and government services described earlier contribute to the challenges. Governments must be willing to invest in strengthening health systems (human resources, supply chains, logistics, health information systems, etc.) as a base for any HIV-related programs including PMTCT (Barker 2007, Druce 2007). High quality MCH and RH services are required for high quality PMTCT services and vice versa. For successful and sustainable PMTCT services to be provided to the entire population of HIV-infected women and their infants, there must be ownership at all levels, local site level, community, district, and central (Doherty 2009, Barker 2007, Zakariah 2009). However, sometimes donor-driven programs offer PMTCT or HIV care and treatment services that are not well integrated within the existing government or hospital facilities, leading to lack of local ownership of the program. Leadership structures should ensure close collaboration between service areas and ensure that services are well-integrated and seen as part of the overall system rather than completely stand alone. When specialty clinics or services exist, they should be charged with elevating the overall level of health services provided, if not logistically or financially, at least through increased teaching, training and mentorship for all facility staff.

Service integration also can be challenging for governments. MOH departments for Reproductive Health (RH), MCH, HIV, sexually transmitted infections (STIs), nutrition, and tuberculosis (TB) may function as vertical programs with little integration of activities (Druce 2007). Funding "turf" battles may exist between well-funded externally supported HIV services and other less-well funded programs. Coordination may not exist even within different HIV services such as VCT, care and treatment, and PMTCT programs. These inefficiencies lead not only to more costly programs but also to problems in the quality of service provision.

Other areas where government leadership or policies may support or hinder scale-up of PMTCT service include MOH policies on task shifting/sharing as described earlier, ARV regimens for PMTCT or IF, dispensing maternal PMTCT regimens on first contact, and provision of infant

ARV doses during ANC. Policies must be in place to ensure that PMTCT services are present in the lowest level facilities providing ANC care to enable access by large populations of women living in rural or remote areas (Zakariah 2009). Decision makers' lack of education and knowledge about the importance of PMTCT or the impact of policies on the ability to deliver PMTCT services contribute to the problem. Improved advocacy and legislation on gender-based issues including violence against women, financial security, and legal rights of women are policy-related activities that are necessary to support HIV-infected women.

To address some of these governance and leadership challenges, it is important to have high-level political engagement and strong advocacy for PMTCT from the international community (Tonwe-Gold 2007). Sometimes this can be accomplished by placing or supporting technical staff within the MOH, or supporting dedicated PMTCT staff within MOH peripheral facilities rather than adding PMTCT activities onto their otherwise overloaded set of responsibilities (Druce 2007, EGPAF 2009). This contributes to the increased capacity for program improvement, better data collection, ongoing training and mentoring, as well as providing a vehicle to disseminate best practices and to help inform the MOH.

To achieve PMTCT targets, it is important that regular implementer meetings are held between the government and all partners or donors in PMTCT and HIV care and treatment to coordinate efforts, link vertical programs, establish systems of referral, and evaluate progress in achieving these goals. There should be support for the formation of oversight bodies within the government to gauge and report on progress in PMTCT and keep it continuously on the agenda. Models of successful integration of PMTCT into primary care systems and at different levels of the health care system need to be shared with the governments and stakeholders so continual learning and evidence-based decisions can be made. It is important that there is an attempt to harmonize funding approaches, communication, and coordination for synergy and efficiencies, particularly in this difficult economic environment and as donors reach the limit of their available contribution to program scale-up. Joint collaboration and participation on working groups, global advocacy, cross sector activities, and overall primary health care system performance and strengthening need attention.

### *District –wide approach to HIV programs*

Using a district-wide approach that involves working through the districts to build district-level capacity to plan, implement, and monitor PMTCT activities provides a more sustainable, measurable, and integrated program (EGPAF 2009). Characteristics of the district-based approach include a focus on building technical capacity at the district level, emphasis on financial sustainability, and mechanisms for ongoing supportive supervision and monitoring. The added value of the district approach fosters greater ownership and sustainability that enables rapid scale-up of new PMTCT services through integration with existing structures and systems. A successful program requires that it is consistent with national policies and guidelines, support is customized to the local setting, services are integrated, it strengthens the general health system, and it is “close to the people.” The communities must be engaged in the process, understand and appreciate the importance of the program, and contribute to the overall successful outcomes. One of the first activities should include the establishment of district PMTCT training capacity, which can then be linked to the start-up of new sites. Supportive supervision of PMTCT services should be integrated into the district routine and should facilitate the exchange

of experiences and best practices between districts. District stakeholders should be involved in M&E, with frequent and routine feedback of results to facilities as well as the district and communities so that they can directly see the progress and outcomes of their efforts and suggest local solutions to the challenges or problems that are identified (EGPAF 2009, Zakariah 2009, Barker 2007, Doherty 2009). Linkages between PMTCT and other services such as HIV care and treatment, OVC programs, and support services will be easier when managed through the district rather than facility to facility. Local, site-specific, creative solutions can address challenges or gaps such as use of existing newspaper delivery systems to carry blood samples to testing centers in Kenya, use of horseback home-visiting in Lesotho, and development of PMTCT outreach services for hard to reach areas.

However, even district-based programs are faced with the same multiple constraints as within other areas of the HIV/AIDS services -limited manpower, limited rural coverage, service delivery bottlenecks, stigma, social issues, weak referral system (EGPAF 2009). For donors, one challenge is less direct control of program outcomes, with the quality and rate of service expansion often dependent on district leadership and existing capacity. Large variability in quality of services provided may result from differences in the quality and commitment of district leadership. Often there are communication, quality assurance, and logistic challenges of rapid expansion of services throughout a district. Clear parameters and goals must be set to determine when the districts are ready to operate independently; however this may be challenging.

### **PEPFAR-specific Issues**

PEPFAR has been hailed as one of the most successful international programs in addressing the HIV epidemic globally. Most acknowledge that overall PEPFAR funding has been a success and many PMTCT and HIV care and treatment programs would not exist if not for PEPFAR funding.

However, PMTCT is not as visible within PEPFAR as HIV care and treatment. PMTCT does not get the attention it needs and deserves as the most effective method of HIV prevention. While the PMTCT program funding initially ‘launched’ the PEPFAR program, it was quickly lost under the care and treatment focus. With only 6-7% of the entire PEPFAR budget going to PMTCT, it is not surprising that PMTCT programs have failed to attain their targets. PMTCT services do not get the resources needed when lumped with all other prevention efforts and hindered by prevention earmarks. Separated prevention, care and treatment money lead to inefficient systems and obstruct integrated service delivery. Partners could use resources more wisely if the integration of PMTCT and care and treatment services were required with equal responsibility for both.

There are some PEPFAR-specific challenges that have been identified by PEPFAR funding recipients and others. There are two frequently identified challenges. The first is related to the inability to provide supplemental pay to government personnel. The inability to supplement pay of government personnel particularly in very demanding and understaffed government programs leads key MOH staff to leave government programs for better paying NGO or consultant jobs. If PEPFAR programs were allowed to provide small “incentives” or supplements that would encourage MOH personnel to stay and work within the public sector, this may improve services. Alternatively, using resources to hire and second additional HCW to work within existing services

may improve services by decreasing the workload and improving the retention of public sector employees. Allowing greater flexibility to support local solutions to address workforce challenges would be an improvement. Allowing resources to provide educational or training opportunities, travel to present at national and international meetings, or other non-monetary incentives may also help.

The second challenge is the limitation on purchasing drugs or commodities. Programs are limited by restrictions on purchasing non-US sourced drugs, especially routine medications for common illnesses, drugs for opportunistic infections, HIV test kits, and family planning products. Lack of inclusion of commodities needed for FP in PMTCT or HIV care and treatment services leaves programs with few alternatives other than condoms and referrals as means of providing FP.

The DHHS (CDC) restriction on use of PEPFAR funds for construction or renovation that leads to increasing square footage of existing facilities is also seen as an obstacle to high quality service delivery. A critical challenge identified in many settings is the lack of sufficient space to provide services in crowded public facilities, particularly private counseling space and space for ongoing support such as for IF and FP. Poor facilities lead to poor patient follow-up and demotivated staff. Use of PEPFAR funds to support one-time infrastructure costs that the MOH may not be able to provide is an investment that will have long-term benefits not only to HIV/PMTCT programs but to improving the overall health care system.

Lack of communication, coordination or even competition between USG agencies in some countries have been cited as a major challenge. While some countries have well-coordinated and functioning USG teams, those that do not pose considerable challenges to the MOH and implementing partners. The basic regulations governing the use of funds differ between agencies. The knowledge and technical skills of in-country USG personnel at all levels with regards to PEPFAR programming in general and PMTCT more specifically may be quite variable.

One major obstacle noted is a lack of clarity on how decisions are made by the USG team in a country about how implementing partners are assigned activities in a region. Assignments may not be according to skills and technical expertise of the partner, thus there may be poor performance and poor linkages between PMTCT and Care and Treatment services.

Difficulties in managing large consortia of implementing partners, all with different areas of expertise, activities and reporting systems have been noted. Concern has been expressed about the long-term sustainability of PEPFAR programs given the large and ever increasing need and the current economic crisis. The bureaucracy governing receipt of USG funding and the delays in actually receiving funds once awarded create challenges in the continuity of funding. The gaps in funding between the end of one contract and the beginning of a new one are disruptive to services. There was considerable uncertainty around maintaining activities while awaiting new RFAs or changes in funding mechanisms or altered geographic locations of services.

Large and frequent PEPFAR reporting requirements in some cases hinder the ability of some partners to provide services. The PEPFAR PMTCT indicators are often seen as burdensome and

inadequate for providing and improving services. It was also noted that PEPFAR indicators should focus more on impact rather than process indicators. Refinement of indicators should continue with attention to the denominators used. There is often a lack of sufficient resources and time devoted to focusing on PMTCT information systems and local support for building monitoring and evaluation capacity. The focus on rapid-scale up has hindered the ability to focus on program quality and better program monitoring. Increased operations and implementation research is needed to establish an evaluation framework with feedback to facilities to improve quality of services.

PEPFAR should re-evaluate its focus to maximize program effectiveness. PEPFAR has the reputation that it “lags behind the new science.” Programs follow current national guidelines, so they do not have the flexibility to change quickly as new information emerges. Rather than being a leader in the field and pushing country programs to rapidly evaluate and implement state of the art programs, PEPFAR programs defer to the national MOH to make change their national policies. A much more pro-active approach to piloting new interventions for the MOH and gathering high quality implementation data to inform the MOH about cost and feasibility of scaling up new approaches would be an important PEPFAR contribution to eliminating pediatric HIV.

### Conclusions

Prevention remains the key to elimination of HIV and must be a priority for global HIV focus and funding. Collaboration and coordination between funders, implementing partners and country governments is critical. The primary barriers to the global scale-up of PMTCT are not related to a lack of scientific knowledge, but rather to failures in implementation. Data-driven best practices that can be shared to advance the goal of elimination of pediatric HIV and implementation research are needed. As programs, linkages, and regimens become more complex, there is a continual need for re-evaluating, expanding, and strengthening M&E systems. Evaluation of the actual impact of PMTCT programs should be a priority. If we are truly going to stem the tide of this pandemic, PEPFAR’s approach to prevention must change dramatically in this next phase. Specifically, proven effective prevention measures must be scaled up immediately. PMTCT is the most glaring example of this failure of prevention scale-up. Despite great progress, we all need to challenge ourselves to do better, to do more, to be creative and innovative in reaching the ambitious PEPFAR and international targets.

### V. Recommendations

- Prioritize pregnant women for HIV treatment (or ARV prophylaxis if not eligible for ART) because of the dual benefits of improving maternal health and preventing new HIV infections.
- Scale-up access to PMTCT programs at all levels of service delivery across countries to reach as many women as possible with the most efficacious regimen possible.
- Improve the follow-up of all pregnant women, including those that test HIV- negative, in order to ensure completion of the entire cascade of PMTCT services including retesting prior to birth in high prevalence settings.

- Provide more emphasis, training, and resources for the collection of adequate and accurate program data in order to improve data quality that can be used to develop evidence based approaches to also improving the quality of PMTCT programs.
- Local “ownership” of the PMTCT program with feedback of program results to the site in order to facilitate identification of the problems and generation of potential solutions to these problems by the site will increase the likelihood of program success. Development of specific tools to assist sites in evaluating their program to identify areas of weakness and target interventions to address them should be a priority activity to improve the quality of PMTCT programs.
- Incorporate family planning into PEPFAR’s PMTCT and care and treatment infrastructure to reduce the numbers of unintended pregnancies among HIV-positive women.
- PEPFAR and the broader GHI should strongly promote country-level integration and coordination of PMTCT, HIV care and treatment programs, MNCH and family planning programs to maximize the benefits of these investments.
- Improved and ongoing training, mentoring, supervision and appropriate compensation of both professional and lay health care workers are needed to ensure quality services are provided.
- Strong government leadership and prioritization of PMTCT in the country’s HIV/AIDS plan are required for rapid and comprehensive scale up of PMTCT services. National coordination among implementing partners, USG agencies, and other international agencies is required for the most effective and efficient service provision. PEPFAR country teams should use the Partnership Framework instrument as a means of improving Government engagement and coordination.
- PEPFAR should also use Partnership Frameworks to encourage Governments to change policies that prevent task-shifting, including initiation of treatment by non-physician health workers, and the use of trained counselors to provide HIV counseling and testing.
- Given staffing and capacity challenges often faced by national-level Ministries of Health, PEPFAR programs should also emphasize staffing up and supporting Provincial and District Health Offices as an effective method of promoting decentralization of country leadership around PMTCT activities.
- PEPFAR must support country-led efforts to move toward one monitoring and evaluation system and coordinated health information systems.
- Within PEPFAR, PMTCT should be prioritized for funding because it is one of the most effective and cost-effective forms of HIV prevention and contributes to multiple PEPFAR goals related to prevention, treatment, care and support, health care workforce and health system strengthening and embodies a woman- and family-centered approach to programming and foreign assistance funding.
- PEPFAR should take a proactive approach to new interventions and development of new technologies, including funding pilot projects to evaluate innovative and cost-effective methodologies, such as point-of-care CD4 instruments and comprehensive provision of PMTCT to promote women’s health and empower women to access services.
- Allow for “topping-up” of salaries for Ministry of Health and other public sector employees and incentivize productivity through performance-based financing schemes.

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## Chapter 5. Stigma as a barrier to PMTCT services

### I. Introduction

Stigma is a potential barrier to service uptake and achieving high coverage of PMTCT as well as other HIV services. Fear of stigma and discrimination (enacted stigma) can affect health care seeking behaviors and disclosure of one's HIV status. Lack of knowledge about HIV transmission, prevention and available interventions fuels stigma. Efforts to increase knowledge among the general population and provide support to HIV-positive pregnant women and their families through community-based efforts and support groups are key methods to prevent and reduce stigma. The organization and delivery of services and health care worker attitudes also influence stigma. Programs should implement known best practices to increase access to and uptake of PMTCT services. While stigma is a significant potential barrier, other issues, such as the quality of reproductive health services, gender, and whether services are comprehensive and integrated with other health services, likely reduce the effectiveness of PMTCT services to an even greater degree in most settings. This chapter focuses primarily on stigma associated with HIV testing, the first step of PMTCT services.

### II. Objectives

- To define stigma and its potential negative impact to achieving high coverage of PMTCT services
- To describe the extent to which stigma is a predominant factor to the rapid expansion of PMTCT services
- To identify and describe additional factors that reduce the effectiveness of PMTCT programs
- To present case studies illustrating stigma's influence on women's health-seeking behaviors and receipt of needed services
- To identify key strategies for and provide guidance to USG PEPFAR teams to address stigma in the settings in which they work
- To provide recommendations to the Global AIDS Coordinator and Congress to address stigma within the context of PMTCT in PEPFAR-supported countries

### III. Stigma as a Barrier to PMTCT Services

#### Background

Despite substantial progress over the last 5 years, PMTCT programs have been hindered by challenges, including the impact of stigma, fueled by myths, that prevent full uptake of these services (Peltzer 2007, Thorsen 2008, Murray 2009, Bwirire 2008). The prevalence of these myths, coupled with the association of HIV infection with disenfranchised groups, sometimes causes people to avoid being tested, fear disclosure to family and friends, and distrust health care systems.

As detailed in Chapter 4, barriers to PMTCT services are complex and partially derive from the plethora of procedures, locations and personnel that women must negotiate in some settings to access comprehensive services, each of which may involve challenges caused or exacerbated by stigma. At each step, lack of access, stigma and discrimination may play a role when best practices are not implemented. Where the PMTCT program itself is physically located,

transportation costs to the site, home visits that may characterize outreach services for HIV-positive mothers, and the reliance on exclusive breastfeeding or replacement feeding, which may challenge cultural or social taboos, can exacerbate stigma (Thorsen 2008, Peltzer 2007, Bwirire 2008).

The stigma affecting the uptake of PMTCT services is sometimes further embedded in a general context of antipathy among community members as well of health care workers towards people with HIV, the low value of women in many developing world societies and their lack of power, and inadequate knowledge of HIV transmission (Meiberg 2008). Concerted efforts to address the impact of stigma have, however, been lacking, due in part to the continuing lack of consensus on the actual role of stigma as a barrier to the uptake of PMTCT services (PEPFAR summary report 2009c).

### **Defining stigma and its potential negative impact as a barrier to PMTCT service delivery**

Link and Phelan (2001) conceptualize stigma as a process that involves labeling the differences between those who are acceptable from those who are not, ascribing negative characteristics to those differences, and, finally, separating the acceptable from non-acceptable persons.

Discrimination (or enacted stigma) is further described as the concrete acts that result from stigma and which result in unfair or biased treatment towards others based on external or behavioral characteristics of the person (USAID 2005). This process has a direct impact on access to care and treatment among women with HIV. Table 1 highlights the steps in accessing PMTCT services and the possible barriers, exacerbated by stigma, at each point when best practices are not necessarily implemented.

Table 1: Potential barriers to access/acceptance of PMTCT services when best practices are not necessarily implemented\*

<b>PMTCT process</b>	<b>How stigma will affect program uptake</b>
Access clinic	<ul style="list-style-type: none"> <li>• General population may not be tested due to perception that only “other” stigmatized groups can get HIV</li> <li>• Is PMTCT clinic located in separate, recognizable building that will indirectly inform others that woman is HIV-positive</li> </ul>
Offer test	<ul style="list-style-type: none"> <li>• Health care workers (HCW) may be selective about offering the test</li> </ul>
Agree to test	<ul style="list-style-type: none"> <li>• Women may fear being seen by others in clinic (anonymity of urban location appears related to higher levels of testing)</li> <li>• Women may know HCW personally</li> <li>• Women may fear outcome of test and responses of family/community</li> </ul>
Get results	<ul style="list-style-type: none"> <li>• Second visit to get results may alert others in family</li> <li>• Information on clinic cards may alert staff/other patients to HIV status</li> <li>• Inadequate or inappropriate counseling</li> <li>• Women may fear outcome and responses</li> </ul>

Offered drugs	<ul style="list-style-type: none"> <li>• HCW may not offer appropriate care to HIV-positive persons</li> </ul>
Accept drugs	<ul style="list-style-type: none"> <li>• Woman may fear being seen by others in clinic</li> <li>• Woman may know HCW personally</li> <li>• Woman may fear outcome and responses</li> </ul>
Take drugs pre-natal and during delivery	<ul style="list-style-type: none"> <li>• Judgment of community and family</li> <li>• Lack of support due to cultural, religious, other taboos against the practices prescribed by the PMTCT treatment</li> </ul>
Safer feeding & post-natal care, including drugs	<ul style="list-style-type: none"> <li>• Judgment of community and family</li> <li>• Post-natal care may not be the norm for non-infected babies – clinic visits may arouse suspicion</li> <li>• Stigma may prevent woman from seeking education and assistance for safer practices</li> </ul>
Continue taking drugs for longer term	<ul style="list-style-type: none"> <li>• Judgment of community and family</li> <li>• Husbands may be unwilling to get testing themselves and thus may force wives to share their own meds, leading to ineffective and possible drug-resistance for both</li> </ul>

\* Modified from Avert 2009 & UNAIDS 2005

USAID (2005) details four major domains that describe various aspects of stigma and its impact: fear of casual transmission; values, shame, blame and judgment; enacted stigma (discrimination); and disclosure. Fear of transmission sometimes causes people to refuse to have contact with people living with HIV. This fear often stems from inadequate or incorrect information regarding the transmission of HIV. For example, in Haiti, approximately 50% of a sample of over 4,000 believed that supernatural means and mosquitoes were possible transmission vectors of HIV (Devieux 2009). In another study of over 14,000 people in Ethiopia, the researchers reported that 75% of the respondents had misconceptions about HIV and its transmission (Kassie 2008). These studies highlight the importance of educating the general population about HIV transmission.

Shame, blame and judgment often characterize people's assumptions about those with HIV; particularly because the epidemic was first associated with homosexual behaviors and with populations, e.g., sex workers and drug users, who were already marginalized by society (Meiberg 2008). This compounded or layered stigma, in which HIV-related stigma combines with stigma towards already excluded or marginalized groups has made the stigma associated with HIV particularly difficult to address.

This shame-based judgment is often also associated with religion and its values. In a study in Tanzania (Zou 2009), respondents reported thinking that HIV was a punishment from God. As a result of this belief, 81% of church-goers in the sample believed that prayer could cure HIV. However, 94% said that they would utilize ARV drugs if they were HIV-positive, suggesting the positive impact of education. In an attempt to change attitudes in rural Haiti, review of an *accompagnateur* program, which involved full participation of the community in assisting HIV-positive individuals, noted a reduction in social stigma attached to HIV (Behforouz 2004). These findings suggest that value judgments are possibly open to change.

Enacted stigma or discrimination has many forms, levels and attributes. In a study in Puerto Rico (Norman 2009), individuals who were more knowledgeable about HIV transmission were more tolerant of those living with HIV, suggesting an important role for education to counteract myths and assumptions. Based on hypothetical scenarios, the sample reported greater acceptance of HIV-positive teachers, and HIV-positive children being allowed to go to school; however they were less accepting of HIV-positive nurses engaging in patient care.

The effects of felt and enacted stigma may be ameliorated by women's participation in self-help or psychosocial support groups (Nguyen 2009, Kabbash 2008). Research in Vietnam has shown that participation in self-help groups improved women's self-esteem, increased their knowledge about HIV, and reduced the effects of felt and enacted stigma from family members, health services and the community (Nguyen 2009).

The extent to which persons living with HIV disclose their status to family and friends is an indirect measure of a person's perception of the level of stigma and discrimination they face. Studies in Africa and Asia describe pregnant women avoiding disclosure to labor and delivery staff, even with the knowledge that neither they nor their infants will receive ARV as a result, due to fears of stigma and discrimination (Varga 2008, Brickley 2008). Studies have shown that higher levels of disclosure are associated with protective and/or health-seeking behaviors. For example, mathematical modeling suggests that disclosure may reduce the risk of HIV transmission by 18% - 41% compared to not disclosing (Pinkerton 2007), because disclosers are more likely to engage in protective behaviors.

Studies (Makin 2008) have also found different correlates for disclosure and care-seeking. Seeking care was positively related to having symptoms and negatively associated with denial of status. Being married, prior discussion about testing, having a partner with tertiary education and less experience of violence were associated with disclosing to partners prior to enrollment in a PMTCT program. On the other hand, disclosure to others was associated with having better housing, being less financially dependent on partners, and knowing someone with HIV (Fitzgerald 2004).

These studies serve to illustrate the point that efforts to address the effects of stigma will necessarily be challenging, however, they must be made because of the far-reaching effects as a barrier to uptake of treatment services. Many of the barriers that occur, and which increase the potential for stigma and discrimination, would be significantly reduced if best practices, e.g., opt-out testing and integrated services, were effectively implemented.

### **Health workforce**

Stigma and discrimination by health care workers is particularly harmful, as it affects patients' willingness to be involved with the health care system. For example, concern about poor treatment from health care workers in South Africa was shown to affect adherence to PMTCT recommendations (Varga 2008). A study in Belize (Andrewin 2008) found that nurses, more than doctors, gave different levels of care to patients, based on their HIV status. This study also found that female and religious health care workers exhibited more stigmatizing attitudes compared to male and non-religious health care workers. On the other hand, positive treatment



has been found to enhance program effectiveness. In South Africa, the relationship between client and counselor was found to be an important factor in whether HIV-positive teens participated in PMTCT programs (Varga 2008).

In Botswana, as mentioned previously, during the earlier years of the epidemic, even though the government offered free counseling, testing, ARV and infant formula, women were reluctant to participate in PMTCT programs (Creek 2009). Botswana represented a well-resourced country where 95% of women received antenatal care, yet only approximately 33% of women in the second largest city had been HIV tested. Researchers found that barriers to enrollment included fear of knowing their status, lack of support from their partners, stigma associated with the infant feeding distribution program and negative attitudes of health workers. Researchers concluded that stigma and discrimination were the major barrier to participation (Kebaabetswe 2007). In this program, utilizing lay counselors for pre-test counseling improved uptake of testing to 60% in 2003 (Creek 2009).

Supportive work environments influence the quality of services provided by health care workers as well as their commitment to their jobs. A study in five African countries found that perceived stigma (against HCWs themselves) was the strongest predictor of job satisfaction (Chirwa 2009). Recommendations were therefore made to address this issue to reduce turnover and burnout among staff, and increase quality of care. To address stigmatizing behaviors from staff to patients, research suggests that conducting formal HIV/AIDS trainings reduces enacted stigma (Andrewin 2008).

Utilizing non-health care workers may reduce the impact of stigma and also address staff shortages. The mother to mother program in South Africa utilizes HIV-positive mothers to counsel new mothers; this program has been successful in increasing participation (Khan 2007). In addition, traditional birth attendants could potentially be effectively utilized. With sufficient training, midwives might be able to provide other services such as HIV education, testing and counseling, and advice on infant feeding.

### **Information systems/ Measurement**

Because of the significant impact of stigma and discrimination, defining constructs, measuring the impact and the manner in which they affect help-seeking behaviors, is important. One of the best sources of measuring/quantifying indicators related to stigma is from a study in Tanzania (USAID 2005). The four key domains, as mentioned earlier, are: fear of casual transmission; values, shame, blame and judgment; enacted stigma (discrimination); and disclosure.

Because stigma is difficult to define, as its impact, characteristics and definition change across cultures, it would be a challenge to create measures applicable across nations and cultures. However, there are commonalities in the experience of women with stigma, for example, lack of power, availability of alternative sources of support, fear of family and community repercussion, and fear for their unborn children that indicate particular areas that should be assessed.

Measuring stigma faces several important challenges. Many potential respondents lack familiarity with the type of questioning involved, therefore it is vital that issues concerning language, adaptation of items, definition of terms, and explanations of unfamiliar concepts be

addressed (USAID 2005). Defining the sample is also an issue. The general population may be less willing to speak honestly about their fears and actual stigmatizing thoughts and behaviors; and HIV-positive persons may be reluctant to self-identify. In addition, key concepts/behaviors that may be common and known to locals, may be outside the realm of experience of researchers, hence the importance of involving and using to the extent possible, the local staff.

Other efforts have been made to develop questionnaires to measure stigma. The HASI-N, (the HIV AIDS stigma instrument) (AIDS care 2009; 21 (2) : 150- 9) for example, was developed by inductive methodology incorporating qualitative and quantitative techniques to measure nurses' stigmatization of patients and their being stigmatized as a result of their work with HIV-positive patients (Uys 2009). The research was conducted in five eastern and southern African countries and is perhaps the most extensive effort to assess stigma in this population on the continent.

We are unaware of formal efforts to develop measures of stigma specifically within the context of PMTCT. While initiation of these efforts is important, perhaps more significant would be the development of coordinated activities to adequately address the impact of stigma across countries.

### **Health systems financing**

In many of the PEPFAR countries, health care is under-resourced. Inadequate staffing and lack of sufficient materials and supplies often mean basic services are unavailable. In this context, specific financing directed towards the reduction of stigma, such as education programs, media campaigns, or other efforts are simply not possible, given the dearth of financing available to meet even basic needs.

Because in many instances there has not been a measurable association between funding anti-stigma and education campaigns and increases in the number of women who access PMTCT, there may be a reluctance to utilize valuable resources on these efforts. Planners should be aware however, that higher levels of information/education have been associated with lower levels of stigma (Norman 2009, Nguyen 2009). As stigma is reduced, there may be an expectation of higher levels of disclosure, which has been linked in the literature with increases in health-seeking behaviors (Pinkerton 2007). These associations therefore suggest the importance of campaigns targeting stigma reduction.

According to a recent informal PEPFAR survey (2009c), there may be a direct link between improving the quality of services, which necessarily entails higher levels of funding for services, and higher numbers of women who access services. The report notes that higher levels of funding are needed to improve physical infrastructure, and increase the number of women who have access to family planning, nutrition assistance and other services. The report also notes the need to place additional focus on the quality of primary health care.

### **Leadership and Governance**

The involvement of key leaders in the effort to promote an environment conducive to the reduction of barriers to care is important. The report suggests that involving community leaders and HCWs as advocates could increase the utilization of services and reduce the impact of stigma.

While leadership is often thought of primarily in terms of those at the community and higher levels, the recent PEPFAR report highlighted the important influence of mothers-in-law to acceptance of PMTCT services (PEPFAR 2009c). A key local intervention for the reduction of stigma may therefore be targeted messages to this group.

The government has an important role to initiate legal and policy reform (UNAIDS 2006). By helping to change social values, such as allowing people with HIV to work for government, and by advocating for and maintaining the right of persons living with HIV (London 2008), for example by upholding the rights of women, the impact of stigma and discrimination would potentially be reduced. Government should also provide leadership for policies that will have a direct impact on stigma reduction. Providing guidelines for service quality, recommending opt-out testing, and heightening awareness of stigma through the media, for example, will reduce its impact. PEPFAR can contribute to reducing stigma and improving service delivery through ensuring gender equity and other progressive policy reforms are a central feature of PEPFAR Partnership Frameworks with partner governments.

### **Related Barriers to Service Uptake**

#### ***Gender Issues***

Gender issues can serve as major barriers to accessing PMTCT services (2009c). However, a meta-study of 32 research reports conducted to understand the effect on stigma among HIV-positive women found that despite the samples being all-female, the issue of gender was rarely directly addressed (Sandelowski 2009). This is certainly an oversight, as the experience of stigma will necessarily be influenced by issues of gender, with the concomitant associations of lack of power, reduced economic resources, less education and reduced access to sources of information to address the experience of their illness.

In some settings, male relatives routinely make health care decisions for their wives, daughters or sisters, and there have been reports of HCWs informing the husband or nearest male relative first about the HIV status of a woman (UNFPA 2006). In these cultures where women lack power, there can be a strong disincentive for women to get HIV tested, due to lack of assurance of confidentiality.

The lack of power has also been associated with the issue of forced sex. The World Health Organization notes that up to one-third of adolescent girls worldwide reported forced sex during their first sexual experience (WHO 2002). Women and girls may be at heightened risk of HIV as a result. Data on street children in Africa and the Caribbean suggest that adolescent girls are two to three times more likely to be HIV- or syphilis-infected as compared to boys of the same age due to sex with older men; in addition, girls are younger at first sex, and have a greater number of partners (Pape 2004, Avert 2004, Kayembe 2008).

Another study among women in rural Haiti found that 54% reported forced sex (Smith Fawzi 2005). Forced sex was associated with having a relationship of longer duration, and having STD-related symptoms. Ortiz-Torres and colleagues (2000) found that in the Caribbean, traditional beliefs about the rights of men with regard to their definition of the boundaries of a relationship

may create barriers for more protective behaviors among women. These long-standing traditions are difficult to directly address, however, researchers recommend that if interventions are to be successful, culturally appropriate interventions that empower women and address stigma should be developed (Rogers 2006).

The effects of gender also have an impact on enacted stigma and disclosing behaviors. In one study, respondents who were older, male, less educated, and less likely to know someone with HIV reported more stigmatizing attitudes towards those who were HIV-positive (Visser 2009). Being female and poor has also been associated with reduced chances of notifying a partner of one's positive status (Fitzgerald 2004).

Stigma has some unforeseen effects, particularly on women. For example, some have noted that due to high levels of stigma associated with HIV, women may be forced to share their medication with their partners, because the partner fears facing the public shame of getting tested and getting his own medication. As a result of this sharing, both parties get ineffective levels of medication, possibly leading to the development of drug-resistant strains of the illness (Macklin 2004).

### ***Partner Support***

Lack of male partner support has been commonly noted as a barrier to participation in PMTCT. (Kebaabetswe 2007), and favorable reactions from husbands found important in increasing HIV test acceptance by women (Maedot 2007). Partner attendance at antenatal care visits is associated with higher utilization of nevirapine and greater likelihood of following infant feeding recommendations (Msuya 2008); however, having an unsupportive spouse has been shown to be a factor in women failing to receive comprehensive PMTCT services (Moth 2005). These findings strongly suggest the importance of including men in the efforts to reduce the impact of stigma on utilization of PMTCT services. To date, however, efforts at couples counseling and greater male involvement have not been highly successful in some settings, due in part to the reluctance of men to become involved with services they perceive as “for women only” (Msuya 2008, Brou 2007).

### ***Education and Lack of Knowledge about HIV and PMTCT***

Low educational levels and lack of knowledge have been significantly associated with lower uptake of PMTCT services and reduced adherence (Peltzer 2007). As mentioned earlier, a study in Zambia among church-goers found that even though a majority believed that HIV was a punishment from God, hypothetical refusal to take ARV was not correlated with their religious beliefs, but rather to their level of education and lack of knowledge about ARV (Zou 2009). In Nigeria, among pregnant women attending antenatal clinic, only 27% knew about mother to child HIV transmission and almost 70% of those who had heard about HIV did not know about the availability of testing and counseling (Adeneye 2006-7). In India, 48% of pregnant women knew that there was any means to prevent vertical HIV transmission (Rogers 2006). Further, the effects of traditional beliefs in the power of the supernatural should not be underestimated. Not seeking care and refusal to notify sexual partners have been related to the belief that HIV is transmitted by magic (Fitzgerald 2004). In contrast, studies have shown that higher levels of knowledge on transmission and higher levels of education are associated with testing and adherence to exclusive breastfeeding (Adeneye 2006-7, Murray 2009, Matovu 2008).

Women in the developing world often have less access to education as compared to men. Every effort should therefore be made to ensure that education sessions are conducted at a level that women can understand and over multiple sessions. One-time interventions are simply not enough. A comprehensive study in Uganda (Matovu 2008) showed that women who adhered to exclusive breastfeeding had attended at least four antenatal breastfeeding sessions and six post-natal counseling sessions. Another study in Kenya reported that even after counseling, knowledge of PMTCT was inadequate, as many could not remember what they had been taught in the session (Moth 2005). Multiple education sessions are not the norm in the developing world, as health care systems are overburdened, but these data suggest their importance to effective program implementation.

A major theme in refusing PMTCT services among a sample in Uganda was women's lack of understanding of the implications of having a chronic disease (Murray 2009). If women have had a more comprehensive understanding of the potential benefits of PMTCT for themselves and their families, it is possible that the refusal rate could have been reduced. Finally, while informal education on HIV testing and the need for services are vital, research suggests that formal education, most particularly for girls, reduces their risk of contracting HIV (Jukes 2008).

Efforts such as that of the radio drama programs in Botswana have proven quite successful in reducing stigma, increasing the intention to get an HIV test and to talk to partners about testing (Pappas-Deluca 2008). In addition, identifying with characters in PMTCT dramas was significantly associated with higher levels of testing during pregnancy (Sebert Kuhlmann 2008). These interventions suggest the importance of the media in increasing knowledge and influencing protective behaviors.

### ***Other Factors***

Though stigma plays an obvious role, some research suggests that in some locations, it may not be the primary barrier to PMTCT uptake (Creek 2009). In Botswana, where a survey was conducted to determine why HIV testing rates were so low, researchers concluded that stigma was not a primary reason. Those more likely to accept testing were in an urban site, had a high level of knowledge about PMTCT, knew someone else who was receiving PMTCT or ARV, and had a partner who had been tested. The main reasons reported for refusing testing were feeling they would not be able to cope with a positive test result and the fear of becoming ill or dying.

In other countries, such as Ethiopia (Maedot 2007), the strong impact of stigma is influenced by other factors which appear to be correlated with the uptake of testing services by women. These factors include a perception of being able to cope with a positive test result, favorable reaction from their husband and community, and their ability to get continuing medical care. In Ethiopia, Kenya, India, and Nigeria, studies have found that fear of their husband's negative reaction, fear of the stigma and discrimination resulting from a positive test result, and concern about confidentiality are related to not wanting to get tested (Maedot 2007, Rogers 2006, Moth 2005, Adeneye 2006-7).

It is important that evidence-based programs be implemented to increase the general population's knowledge about prevention, transmission, and the availability of treatment in order to reduce

stigmatizing behaviors (Visser 2009). These are extremely important for youth, as the next wave of potential patients. Targeted programs that take the social and economic context into account, and which provide realistic options are recommended (Jukes 2008).

### IV. Conclusions

Stigma plays a tremendously important role in limiting the uptake of PMTCT services in developing countries. It has an impact at all stages of the process, from attending clinics to accepting testing, receiving results, agreeing to and using prescribed medications and following recommended feeding practices. However, stigma is not an inherent component of the implementation of PMTCT services. It is important to recognize that many barriers to service arise because best practices, including integrated services, opt-out testing, and rapid testing with same-day results, are not consistently implemented and would significantly reduce the impact of stigma. There are some indications, however, that the effects of stigma are being reduced in the face of educational and outreach interventions, and wider accessibility to ARV.

It is noteworthy that during the course of researching this paper, it became evident that while stigma occupies a very high profile in the area of PMTCT, and there are a multitude of studies assessing it and trying to understand its impact, very few papers discuss concrete efforts to directly reduce stigma. This is an important deficit in the field.

Competing cultural frameworks, shaped by stigma, also affect the potential impact of PMTCT programs. For example, the seeming focus on the health of children versus that of their mothers, and the emphasis on details of program implementation, rather than the environmental context in which these women live, serves to highlight the areas for potential improvement in these programs. The focus on preventing transmission to the newborn infant, to the possible detriment of the health of the mother, represents a potential barrier to fuller uptake of PMTCT services (PEPFAR 2009c). The take-home message is that women need to feel that the programs are of benefit to themselves, not just to their infant. In the presence of continued availability and proven effectiveness of PMTCT programs, women may attend clinics in increasing numbers.

Besides the importance of addressing stigma directly by means of educational outreach and other activities, there are several major issues that should be kept in mind as researchers and practitioners move forward. First is the importance of addressing the quality and completeness of services for women. This includes a focus on ensuring that all of the components of the four-pronged PMTCT strategy be addressed, and that education not be a one-time intervention. Related to this point is the need to understand that HIV and PMTCT services are conducted in the context of dismayingly poor reproductive health services in the developing world. The UN (UNAIDS 2006) recommends that services for these women and their families encompass a full range of services, including prevention, access to antenatal care, treatment for HIV, integrating food and nutritional support, and eliminating inequalities related to gender, including abuse and violence. These efforts will require more coordination among implementing agencies.

Finally, the overwhelming impact of poverty, including poor nutrition, lack of education and reduced economic options, should be acknowledged. These factors cannot be addressed by any one entity or organization alone. More focused efforts should be made to coordinate educational,

poverty reduction, nutrition, reproductive health and other services to improve the chances of reaching ambitious PMTCT goals and targets.

### V. Recommendations

Key strategies for reducing the impact of stigma on the implementation of PMTCT services should recognize the resource-constrained settings in which these services are offered, while at the same time strive to attain the goals of best-practice. In developing countries, PMTCT services are often offered in the context of poverty, poor overall reproductive health services, and inadequate health infrastructure. These factors highlight the vital need for integration of PMTCT with specific programs to reduce the impact of these “external” factors. Stronger efforts should also be made to integrate services within the existing health structure, reducing the need for women to attend several different clinics, e.g., ARV, nutrition assistance programs, and family planning, to meet their health needs. These suggestions are components of PEPFAR’s policy reform recommendations (PEPFAR 2009b). Finally, the developed world is expending a great deal of resources on addressing the HIV epidemic. However, from a developing world perspective, there may be other, more important, health priorities that are being inadequately addressed. Because PEPFAR’s efforts are HIV-focused, there is limited ability to address other priorities; however, some attempt should be made to ensure that the priorities of these countries are somehow addressed by creating linkages with other funding sources. Without these efforts, programs will lack sustainability when external sources of support for these programs end.

Based on the findings of this report, the following specific recommendations are made:

- Routine, provider-initiated, opt-out HIV screening during pregnancy, delivery and the postpartum period is essential to reduce the stigma of accessing the test, enabling women to know their infection status and access treatment and care and PEPFAR should support country efforts to make this standard policy and practice.
- PEPFAR programs and the wider GHI must focus additional resources to increase demand for antenatal care services and outreach services for women who deliver at home to increase the reach of PMTCT programs and potentially reduce stigma and loss to follow-up.
- PEPFAR should promote nutrition counseling and support with linkages to food security programs as an integral component of PMTCT programs as pregnant women are under increased nutritional and metabolic demands, and often suffer from preventable nutritional deficits, which are worsened by the additional burden of HIV infection.
- PEPFAR should promote policies and programs that prioritize the inclusion of male partners and other family members in PMTCT service delivery, as this has been shown to improve test acceptance by women and reduce the stigma of positive test results. Increased community and male partner knowledge, understanding, and participation in PMTCT services as well as the provision of psychosocial support services to women are critical in helping HIV-infected women successfully complete the PMTCT cascade, and can lead to improvements in men’s health.
- Fear of stigmatizing behaviors from health care workers is a barrier to service uptake. PEPFAR should promote programs that focus on improving the counselor-patient interaction and including formal training for staff on the reduction of stigmatizing behaviors. They should address imbalances in quality of services offered at hospitals,

health centers and maternities by improving training of staff and infrastructure at all venues.

- In the context of under-resourced programs and overburdened staff, utilization of traditional birth attendants and/or lay counselors to provide needed services related to testing and counseling, and support and delivery of non-medical services should be considered.
- Knowing people who have HIV is associated with reduced levels of stigma and increased levels of test acceptance. Efforts should be made to utilize HIV-positive women who have utilized PMTCT services as counselors and educators for new patients; their services have been successfully utilized in programs such as the mothers to mothers program in South Africa.
- Significant progress has been made in measuring the impact of stigma, including in those areas that directly affect uptake of PMTCT services, including testing and acceptance of breastfeeding. However, more efforts should be made to design programs and deliver evidence-based interventions to reduce the impact of stigma.
- Efforts should be made to address the staff shortages that affect service delivery in the majority of developing countries. It is short-sighted to implement programs without adequate measures to address medium to long-term increased staffing needs.
- Targeted education and awareness campaigns are necessary to reduce stigma. PEPFAR programs should focus on concrete efforts/programs to reduce stigma itself. The general population and especially high risk populations, e.g., youth, military, pregnant women, and sex workers should be educated about transmission and the myths surrounding casual contact.
- PEPFAR should encourage inclusion and implementation of policies to protect persons living with HIV, through country programmatic plans and in Partnership Frameworks with partner governments.

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## **Chapter 6. Opportunities for Improved Linkages Between PMTCT, HIV Care and Treatment, and Related Services**

### **I. Introduction**

One of the biggest challenges of implementing the PMTCT cascade is to link HIV-positive women to treatment and care and their exposed children to diagnosis and treatment if positive. Losses to follow-up in the PMTCT cascade and the poor linkage of HIV-positive women and their exposed infants to diagnosis, treatment and care are inter-related and reflect social (lack of empowerment of women in health care choices, stigma), economic (poverty, the inability to pay transport costs and hospital fees), and structural (poor articulation between different tiers of the health care system and long distance to higher level facilities) challenges.

Substantial progress has been achieved in screening large numbers of women for HIV infection through PEPFAR, largely through rapid test-based opt-out strategies integrated into prenatal clinics at hospitals, community health centers and local maternities. The goal of effective PMTCT is to ensure that all HIV-positive women not only benefit their baby through effective implementation of ARV prophylaxis but also that they are fully engaged in HIV care and treatment. The degree to which this linkage of PMTCT to treatment and care is being achieved in PEPFAR is not quantified since record linkage and referral processes between facilities engaged in identifying HIV-positive pregnant women and treatment and care centers are poorly developed in most resource-limited settings. The extent of the problem is poorly understood because there is no reliable medical record-keeping system between facilities in most low-income countries and PEPFAR-supported strategic information systems do not routinely capture this information. At the patient level, the barriers to health care access for their HIV infection include lack of a clear imperative for local staff to refer patients to a treatment facility that may be some distance away, often with an oversubscribed clinic with long waiting periods, transportation costs, inadequate social structures to support care of other children, and social barriers related to women's health choices (Bland RM 2008).

Overarching this is the proposal under the evolving Global Health Initiative (GHI) for expanding services to integrate a broad range of women's health interventions for all pregnant women whether HIV-positive or negative. Such an approach benefits the health of mother and child through provision of needed services such as malaria prevention, pre-natal vitamins, safe water, family planning, childhood vaccinations and other services and destigmatizes HIV by embedding PMTCT and HIV treatment in an environment where all women are accessing similar services. By comprehensively bundling these services, there is not only a positive benefit to maternal and child health but also a benefit to addressing the breakdown in the PMTCT "cascade" so that every woman who is HIV-positive is positioned to receive ongoing HIV care and treatment when clinical or laboratory stage dictates. Thus PMTCT programs cannot be successful as a "stand-alone" interventions but must address the larger issues surrounding women, child and family health.

### **II. Objectives**

- To characterize the barriers to linking HIV-positive pregnant women to HIV care and treatment services



## Opportunities for Improved Linkages Between PMTCT and HIV Care and Treatment

- To identify key strategies for and provide guidance to USG PEPFAR teams to more effectively providing HIV care and treatment services to more HIV-infected women identified in PMTCT settings
- To provide recommendations to the Global AIDS Coordinator and Congress in support of efforts to reach PMTCT targets
- To recommend how PMTCT resources can be utilized to support a more holistic agenda that includes a broader range of women's health needs and health care access in the context of programs that "bundle" services for the woman, the child and the family.

### III. Opportunities for Improved Linkages between PMTCT and HIV Care and Treatment

#### 1. Background

As originally conceptualized and implemented, prevention of mother-to-child transmission (PMTCT) adopted a traditional public health model that promoted a simple, low-tech and self-limited intervention targeting a single outcome, the prevention of infection of a baby at the time of birth. Single dose nevirapine (sdNVP) was the ideal for such an intervention since it was easy to use, inexpensive, doesn't require a substantial supply chain, and little medical sophistication is needed for the program to be successful within the narrow parameters of this targeted outcome. From a health systems perspective PMTCT as originally formulated was a stand-alone program with a simple prevention target that had little need for linkages to more sophisticated medical care infrastructures. As such, the original guidelines from WHO were easy to adopt at the country level since little investment and infrastructure was required by the host government.

The current PMTCT landscape is much different because of an explosion of knowledge that documents safety issues linked to sdNVP's potential for drug resistance and the high rate of transmission during breastfeeding and especially mixed feeding. PMTCT is no longer a "simple public health intervention" since it now requires a more sophisticated longitudinal, continuity of care system to achieve even the most basic PMTCT services such as more complex antiretroviral combinations and interventions to counter breast milk transmission. Synchronous with the growing body of knowledge about the complexity of implementing "**highly-effective PMTCT**," is the new public health paradigm on care and treatment of HIV/AIDS that emerged in the context of PEPFAR. PEPFAR care and treatment scale-up challenges conventional public health approaches since the intervention targets a chronic incurable medical condition that is complex to manage and subject to ongoing modification as new knowledge challenges established policy. Thus PMTCT, historically a "stand-alone" public health intervention, has morphed into a complex medical intervention that must now become tightly linked to the PEPFAR treatment and care program. The bridge between PMTCT that reaches out to provide HIV prevention services at the community level through provision of antiretroviral prophylaxis to women who not only deliver in hospitals but also deliver their babies at community health centers, maternities or in the home, and PEPFAR treatment and care programs implemented mainly at hospitals or higher level health facilities, requires mutual proactive intervention that "reaches across" to support the health of mother and baby by ensuring ongoing continuity of care.

PEPFAR is in a unique position to impact treatment and care access for all HIV-infected women (and many HIV-uninfected women) in its programs, and their spouses and children, and in this process redefine how PMTCT integrates into a continuum of care and treatment. To produce

such an outcome, PEPFAR must promote diagonal integration of traditionally “siloe” programs and in the process employ innovative approaches to changing health care delivery in a broad range of settings. Prevention, care, and treatment can no longer be set into motion in isolation but must be tightly integrated by linking community to care, and by taking services from the hospital to the community. Maternal and child health cannot be only about PMTCT but must address the broader issues of integrating PMTCT into healthy mother and child programs.

### 2. Service Delivery

There is limited published data on the barriers between PMTCT and access to care and treatment, a reflection of the need to invest Public Health Evaluation and research funding in this topic area. Discussions as part of the process for developing this report identified several themes that are relevant to this issue.

***Silo Mentality:*** First is the acknowledgement by many experts engaged in PMTCT programs that a “silo” mentality surrounds PMTCT, partly because it is considered a prevention activity and thus subject to narrowly focused guidelines and limitations. Under the original PEPFAR implementation process, PMTCT was at the vanguard of expanded access and as a public health program was insulated from the mainstream of ARV scale-up at the center of PEPFAR’s “emergency response.” This early mindset of two separate tracks has contributed to the poor linkages between the programs despite their convergence in need for more sophisticated paradigms. The new reality is that every HIV-positive person identified, whether through HCT or PMTCT screening, should be integrated into a care system that provides ready access to all PEPFAR services and proactive follow up to accommodate the needs of PLWHA. There can no longer be parallel tracks for PMTCT and treatment and care access. There must be a new approach that capitalizes on the PEPFAR infrastructure to proactively link services and document through strategic information the degree to which this is being achieved and the barriers. To achieve that goal, new models of PEPFAR implementation need to be developed and include an emphasis on bundling women and family health services as a means of promoting sustained engagement of women by linkage between prenatal care, nutrition, immunization/well baby assessments, malaria prevention and other women’s health services. A woman-focused, family-oriented program has substantial potential for providing a strong platform for supporting continuity of care of the HIV-infected mother and infant.

***Accessibility:*** Given the high demand for HIV services in particular areas, it has been suggested by some implementers that a “fast track” could be created to allow women to be directly integrated into treatment and care programs. In one model, such a “fast track” would engage dedicated staff from the PMTCT/prenatal program who would serve as the advocate for the newly diagnosed HIV-positive woman. The first goal is to educate the client on the importance of ongoing care and the need for treatment staging and monitoring and to ensure that means for contacting the client are well-established. Given that a number of studies have demonstrated that disclosure of HIV status to spouse strengthens uptake of services and retention in care, counseling and support in engaging family members in the support of the client is a high priority (Flys 2006, 2007, 2008). The patient advocate facilitates scheduling of the client for an initial care and treatment visit that includes arranging for laboratory staging evaluation (e.g. CD4 and other laboratory testing). A clinic-based community outreach worker may be engaged to perform an initial home visit in conjunction with the patient advocate as a means of assessing

needs and providing a “bridge” to care and treatment. Accessibility to the care and treatment clinic also plays a role since distance from treatment and care facility is a major barrier to reliable treatment access (Giaquinto 2001, Goga 2009). Not only are the costs of transport significant, but personal circumstances such as lack of empowerment (husband’s permission to seek health care) and the need for child care and household responsibilities limit the time available for personal health seeking (Goga 2009). To respond to this need, innovative approaches such as mobile laboratory services or simple point of service tools for performing CD4 cell counts, a vital tool for treatment staging and decision making which would allow for treatment to be started in lower-level facilities, helping to “decongest” over-subscribed centers. Focusing on transitioning women who require treatment to the ARV clinic while maintaining ongoing longitudinal follow up at a community clinic near the client’s home where mobile or point of service CD4 testing and access to other supportive activities (breast milk substitute, malaria prevention, clean water, women’s health services, etc.) are provided, is a viable model for supporting continuity and longitudinal follow up. This community-centered approach that engages dedicated outreach staff to support clients in care, to facilitate transition to treatment and to encourage continued engagement as their treatment and care advocate provides a model for addressing sustainable engagement. Another common theme in the report and in the published literature is the “distance from services” is a significant barrier to treatment access, retention and adherence to medication. Some experts recommended that patient access be incentivized by covering transport and/or lost wages.

*Integration of Services:* One means of streamlining patient time is to integrate the PMTCT-treatment access interface into the larger public health structure that targets women’s health and health needs and the health needs of their babies. Bundling services into a mother-child friendly environment that provides a one stop shop for immunization of their child (and a chance for dry blood spot PCR-based pediatric diagnosis), nutritional interventions, acute care needs (e.g. malaria treatment), and HIV care and treatment services, improves efficiency for the program and for clients (regardless of HIV serostatus) and helps to reduce stigma. Such an approach has been suggested in a “family-centered” public health clinic approach that has been implemented successfully in some locales (Arrive 2007). An added benefit is the observation that when the husband is engaged in the health care needs of mother and child, that many markers of improved health are achieved and as is often the case; the husband can access his HIV care needs as well.

*Tuberculosis:* Because of their high risk for TB, all HIV-infected pregnant women should be evaluated for active or latent TB infection. However the same barriers that plague linking women to HIV treatment and care are also implicated in access to TB services. At the community level TB services are provided at community-based TB DOTS sites but the diagnostic facilities of these community-based centers are often limited. Emphasizing TB evaluation in the context of HIV treatment and care centers provides a more reliable platform for this evaluation but even within these treatment facilities, there may be barriers to access because TB services are separate from HIV programs and linkages between the programs often result in patients being lost to follow-up. This is a reflection of the fact that TB programs and HIV programs often exist in different silos. Even at WHO there is separation between these programs and this often translates to the Ministry level within country where issues of mission and territoriality threaten best practices.

To address this issue in the context of PMTCT, there are several approaches that can be implemented, including training maternity staff to systematically perform simple clinical evaluations for signs of TB, training HIV clinical staff at treatment and care centers to undertake structured TB clinical and laboratory evaluation and where appropriate employ a patient advocate to support pregnant women who require TB treatment to ensure they return to the HIV clinic for continued follow-up and treatment where indicated. Programs should look to the advances in TB and HIV program integration in Rwanda for ideas and guidance (Gasana 2008).

*Postnatal Integration:* An important component of PMTCT is the prevention of infant infection in the postnatal period through breast milk exposure, as described in Chapter 2 (Gray 2005, Homsy, 2009). There is a growing body of evidence that supports the provision of maternal or infant antiretroviral therapy for prolonged periods in the postnatal breastfeeding period and recent data supports the use of full antiretroviral therapy. This need emphasizes the importance of transitioning HIV-positive women into an environment where knowledgeable providers and clinical and laboratory infrastructure support staging and monitoring. Rather than attempting to implement such interventions in a community health center without sophisticated infrastructure such intervention is best implemented in a PEPFAR-supported ARV treatment center, perhaps engaging an obstetrical physician in the clinic to support this activity or as suggested above creating special women's clinics for HIV treatment.

*Early Infant Diagnosis:* Within the continuity of PMTCT services, early infant diagnosis is a critical outcome. In the current setting there is a dislinkage between pre- and peri-natal PMTCT interventions and follow-up of the exposed infant for HIV diagnosis. Better integration of all HIV-infected women into HIV treatment and care centers provides a useful pathway for reliably evaluating the HIV status of the infant and should be a major goal of transitioning all HIV-positive women from PMTCT into treatment and care. However for those women who do not become enrolled, the early infant dry blood spot testing program for pediatric infection is a useful avenue for “recapturing” women lost to PMTCT follow-up into treatment and care. A good venue for achieving this is in the routine childhood immunization clinics that are integral to most public health programs targeting women and child health. In this setting HIV-positive women should be recruited as described above into treatment and care to ensure their long-term engagement in care and treatment. The diagnosis of an infected infant in this setting provides another path for bringing the mother and infant into a full-fledged treatment and care program.

### **3. Health Workforce**

Outside of the hospital-based obstetrical environment, the majority of maternity services are delivered by community health workers, nurse midwives and traditional birth attendants at community-based venues such as local health centers and maternities or in the home.

*Capacity of Maternity Staff:* Obstetrical physicians are infrequently involved in the delivery and direct management of pregnant women in resource-limited settings including sub-Saharan Africa save for women with economic means or who are referred because of complex medical problems. Even when referred, poverty and distance from hospital site are barriers for accessing services provided by physicians. Therefore, the vast majority of women who are HIV-infected receive PMTCT services at local maternities staffed by nurses or other non-physician providers. The mindset of the traditional maternity worker is on ensuring at least one prenatal intervention

and a successful delivery within the local network. Upgrading the capacity of local health clinics to be effective partners in linking HIV-positive women into treatment and care involves several possible approaches. One approach develops and streamlines processes by which existing staff make appropriate patient referrals. Alternatively, the capacity of local clinics can be upgraded to undertake initial management of patients employing nurses as the primary provider to achieve initial staging of the patient and potentially care and support and even dispensing of ART for stable patients under the supervision of a trained provider analogous to the nurse practitioner model.

*Treatment Support Staff:* Limitations in number of staff available to support comprehensive PMTCT services is a major barrier to effectively managing the transition of HIV-positive pregnant women into treatment and care. Expanding the work force to include a cadre of staff dedicated to supporting transition of the HIV-infected mother into care provides a pathway for addressing both the delivery of ARV prophylaxis as well as the transition into care and treatment. Models that employ persons living with HIV and AIDS (PLWHA) who themselves are mothers in a “mother-to-mother” support network, is one approach. In this model, successful graduates of the PMTCT experience who themselves are integrated into care and treatment are a particularly effective advocacy group for continuity of care because they have “walked the walk” and can witness to the benefits. They are familiar with the challenges of stigma and can facilitate a “fast tracking” into care and treatment.

*Limitations of Training:* A frequent comment is the limitation of training among the work force that staff community-based health care venues. This issue has been exacerbated as PMTCT has evolved from a simple approach to an increasingly complex multidrug intervention with greater emphasis on longitudinal follow-up and the need to engage HIV-positive women into treatment and care. To address this training gap, a staged approach that builds capacity to assume greater autonomy in supporting treatment and care services is needed. Basic training targets capacity building for onsite real time HIV counseling and testing and management of ARV prophylaxis and the need to encourage all women to access care and treatment. The next level of training integrates capacity for implementing continuity of care and follow-up of HIV-positive women that ensures that they either access HIV staging services locally or have these services provided at a regional treatment center. As capacity grows local maternities and public health clinics with sufficient infrastructure have the potential to serve as satellite treatment venues linked through the hub and spoke model to a hospital-based treatment site. The main targets for such trainings are nurse midwives and community health workers. To optimize sustainability such health strengthening programs should engage academic and non-university schools to be supported in developing training and certification programs based on best practices.

*High Turnover of Staff:* Another challenge identified is the high turnover of trained workforce who as they acquire PMTCT training are more “marketable” leading to their transition to a new position outside of the front lines of PMTCT program delivery. A means of addressing this issue is to perform training of all members of the regional health care work force to engage as the point of entry of any HIV-positive women into a sustained long-term treatment program. Financial and performance-based compensation and work environment upgrades are needed if such highly trained nurse midwife/community health worker staff are to be retained in these frontline treatment and care settings.

#### 4. Health Information Systems

In many resource-limited settings, the health care delivery system model is structured for acute care and single encounter interventions, and as such medical record systems are not always geared for longitudinal follow-up. The lack of a unique national patient identifier in most countries and health systems that lack the ability to link patients between primary health care settings and subsequent care at facilities where ARV services are delivered make it very difficult to adequately account for the extent to which women and their infants identified through PMTCT screening access care and treatment. The development of health information systems that can adequately track patients such as creation of unique identifiers based on patient metrics such as were used for tracking HIV testing in the US in non-name reporting states might be a reasonable first step. Beyond this, there is often a temptation to “over-sophisticate” solutions and to move beyond solutions such as good paper-based systems in favor of electronic medical records systems that may not be well-matched to the infrastructure (unreliable electricity) and healthcare workers at the community level. Health information systems should emphasize collection of information relevant to “tracking” HIV-positive women for follow-up delivery of treatment and care services. This may include employing geo-positioning technologies, collecting cell phone numbers and providing reliable information for community outreach workers such as “mother-to-mother” support staff to contact the woman and her baby for ongoing retention or re-integration into the care paradigm. Additionally the health information system requires that data from laboratory testing be integrated into the medical information of the patient to support their treatment decision making.

#### 5. Medical Products and Technologies

There are some key technologies that could positively impact the capacity to link HIV-positive women identified in the PMTCT setting to care and treatment. The first is a simple technology for point-of-service CD4 testing that would have the ease of use of a rapid HIV test.

CD4 Testing for Staging for Treatment Eligibility: Reliance on clinical criteria for the initiation of ART is unreliable, so measurement of CD4 cell count is necessary to determine who requires immediate ARV treatment. Efforts to create “spoke and wheel” type systems to reach out from central labs to provide CD4 testing services in the periphery have been successful in some countries, including Kenya. However, central labs that support a wide catchment area with many PMTCT service delivery points report difficulties handling the large volume of specimens that require CD4 testing, thus it is critical to provide additional capacity to handle the work load. Measurement of CD4 cell counts must be run within 24 hours of collection using standard vacutainer tubes, restricting their utility in rural or remote programs with large distances to the test centers. Well-functioning transport systems to provide rapid delivery of specimens to the test center are required. More widespread use of specific stabilizer tubes that allows CD4 cell count testing to be done up to 7 days after the blood draw would improve this problem considerably, allowing the blood to be drawn any day the woman appears in clinic rather than only on certain testing days, and allowing for more time to elapse between acquisition and testing. This tube has been reported to cost slightly more than a standard tube and does require the use of additional tubes for other tests such as hemoglobin. Point-of-care CD4 testing, currently under development by several companies, would be a major improvement in the ability to perform PMTCT services. CD4 cell count testing done in real time with rapid results in MCH

clinics would allow women to be started on ART immediately at the time of HIV diagnosis or to target such women for immediate linkage to a “mother-to-mother” support staff to guide their treatment access process.

*Early Infant Diagnosis:* Even more complicated and technologically challenging are methods of detecting HIV infection in infants. As referenced in Chapter 4, DNA PCR is the test of choice, but it is currently available only in few sites in most countries, often leading to long turnaround times due to transport and other delays. Shortening the delay in reporting results is vital to infant survival given that the earlier HIV treatment is started in HIV-infected infants, the better the survival.

*Communication Technologies:* Simple technologies for maintaining patient contact, for example by employing secure and coded messaging through ubiquitous cell phone access is an important strategy for maintaining linkages between clients and providers. For privacy purposes especially given the issues of stigma and gender inequality, any communication with a client must provide a secure mechanism for maintaining privacy. So a technology challenge is to exploit existing technologies such as cell phones as a means of maintaining communication and for voluntary tracking of clients through GPS technology that is intrinsic to all cell phone systems. Translating these technologies into simple tracking tools to aid community outreach workers is an important technology challenge.

### **6. Health Systems Financing**

Meeting the financial challenges of engaging a “broken” health care system require creativity and careful investment of resources. First, integration of PMTCT into effective and bundled health service delivery system is cost-effective since the separation of PMTCT from other maternal and child services adds additional costs and contributes to the isolation of PMTCT from mainstream services. Second, investment in innovative systems for promoting care and treatment programs that provide local access is a high priority and thus mobile services and investments in local staff capacity-building are important. Ultimately, however, the sustainability of gains will depend on tight linkages of funding from all sources to a common and integrated structure for linking PMTCT to ARV services.

### **7. Leadership and Governance**

For sustainability, promoting alignment between PMTCT and care and treatment services requires clear policy at the national and international level since WHO policy substantially influences national policy which in turn percolates down to the state and local government level. This alignment has significant implications because of traditional silos of influence have contributed to the disconnect between PMTCT and care and treatment services and integration with TB services. PEPFAR is in a strong position at the country level to influence governmental structuring and coordination through country specific negotiations and alignment of Country Operational Plan and Partnership Framework goals to achieve improved integration of PMTCT and care and treatment. By strengthening Public Health Evaluation programs to assess best practices, PEPFAR can impact WHO policies by being a leader in contributing to the knowledge base that will guide improved linkages and best practices. PEPFAR must model this linkage through program planning and by setting clear milestone driven targets based on reliable and relevant and linked indicator data.

### Relevance to USG PEPFAR Country Programs

USG Country leadership teams are in a unique position to change the face of PMTCT and treatment and care linkages. While the impetus is to reformulate PEPFAR to rapidly transition to an indigenous model of service delivery, the push back comes from the fact that without the kind of leadership that has shown that the “impossible” public health scale-up can be done, the fundamental success of the PMTCT-treatment and care linkage will not be achieved. The USG Country Program leadership must take a bold position in advocating for “**highly effective PMTCT**” that requires that all HIV-positive women and their family members identified through PMTCT-based HCT be linked to care and treatment. PEPFAR is at a crossroads where its leadership holds in the balance the sustainability of a noble cause. Now is the time for evidence-guided action that will shape the policy to come. By boldly aligning PMTCT, treatment and care and a broader women’s health initiative into a holistic model with ongoing investment in innovative strategies as detailed above, country PEPFAR teams are in the position to be agents of change for the mothers and their infants whose lives depend on this leadership. A concern is that too rapid a transition of program capacity building to indigenous organizations not yet equipped to understand how to innovate rather than just implement threatens the kind of creative response that has been the hallmark of PEPFAR since its inception.

### IV. Conclusions

PEPFAR has defined a new paradigm of public health that is at the vanguard of changing the face of health in the developing world. This has been achieved by employing highly capable technical partners to create and implement innovative public health programs of large scale. As detailed above there are substantial challenges in integrating PMTCT into treatment and care. It is not sufficient that women and their children be referred “up” to treatment and care clinics. Rather, “**highly-effective PMTCT**” requires that multiple models are employed including bringing services to HIV-positive mothers and their infants in their communities and integrating these services into existing health services for women and children. Strengthening laboratory structures at the local level, employing mobile clinical and laboratory services, training a new cadre of health care workers, strengthening client support structures are but a few of the new approaches that must be developed. There is new knowledge that is challenging old paradigms and without bold leadership and continued investment in change that engages ongoing involvement of US implementing partners to consolidate gains, the successes achieved so far will be lost in the entropy of health care structures that are slow to change. “**Highly-effective PMTCT**” requires that sustainable in country training and certification programs be implemented. The barriers to linking HIV-positive women and their family members to treatment and care is emblematic of the challenges to sustainability that require PEPFAR to maintain its proactive role in transitioning success into sustainable and permanent change. Critical to this change is “**highly-effective PMTCT**” that focuses the PMTCT to treatment and care linkage in the broader context of women and child health that empowers clients to become agents of change for better health for women.

### V. Recommendations

1. Promote “**highly effective PMTCT**,” the development of innovative approaches to integrate PMTCT into a holistic program that promotes women’s health and empowers women to access prevention and treatment services.



## Opportunities for Improved Linkages Between PMTCT and HIV Care and Treatment

2. Encourage countries to implement policy initiatives that set a policy goal for PMTCT programs to enroll all HIV-positive women into treatment and care from the time of diagnosis. It was suggested by some that a “fast track” be created to allow women to be directly integrated into treatment and care programs.
3. Support countries to develop health care structures that link primary care and maternity venues that support access to treatment and care in their local community including hub and spoke models, mobile services and upgrading of facilities and staff training to extend through task shifting primary access of HIV-positive women identified through PMTCT to local service venues.
4. Support countries to develop proactive strategies such as engagement of mother-to-mother PLWHA outreach workers to promote recruitment of women identified through HIV testing in the PMTCT setting into adult and pediatric care and treatment programs.
5. Support countries to address imbalances in quality of services offered at hospitals versus primary health care centers and maternities by improving training of staff and infrastructure at these local venues.
6. Support countries to define and measure targets that focus on providing HIV treatment to pregnant women who need it for their own health, including documentation of clinical and/or laboratory staging of HIV disease and engagement in care and/or treatment services for all women identified as HIV-positive.
7. Conduct public health evaluation studies to identify the barriers to treatment and care and the degree to which these barriers also negatively impact the completion of the PMTCT cascade.

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## Chapter 7. PEPFAR Collaboration with International and Multilateral Entities on PMTCT

### I. Introduction

Several international and multilateral organizations have key global, regional, and country-level roles in providing resources, formulating strategies, and supporting PMTCT scale-up. In particular, the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) are key international/multilateral organizations collaborating actively in PMTCT. Within the UN system, WHO takes the lead in the global health sector response to HIV/AIDS, UNICEF takes the lead in procurement, supply chain, and care and support for persons living with HIV infection, orphans and vulnerable children, and together WHO and UNICEF lead in scaling up PMTCT programs. The GFATM is a global partnership dedicated to attracting and disbursing resources to prevent and treat HIV/AIDS, tuberculosis and malaria—as of 2008, 271,000 HIV+ pregnant women had been reached with prophylaxis for PMTCT by the Global Fund (Global Fund Press Release 2008). The GFATM recently reemphasized the importance of PMTCT by redirecting some grant funds to this area.

The various roles of international/multilateral organizations in PMTCT are both complementary and similar to PEPFAR's; as such, close communication, coordination and leveraging with these organizations is a critical component of PEPFAR's strategy. These objectives are achieved through fostering close working relationships, formal linkages on working groups, joint engagement in key activities, collaborative funding and technical exchanges

### II. Objectives

- To describe the collaborative relationship between PEPFAR and key international/multilateral organizations on PMTCT
- To provide recommendations for continued and improved collaboration

### III. Key Areas of Collaboration

**PEPFAR and its funded partners are actively engaged with the PMTCT Interagency Task Team.** The Inter-agency Task Team (IATT) on PMTCT was first established in 1998 among several UN organizations. In 2001, the Task Team was renamed the Interagency Task Team on Prevention of HIV Transmission in Pregnant Women, Mothers and their Children. The IATT now includes the WHO, the UNICEF, UNFPA, UNAIDS Secretariat, the World Bank (WB), GFATM, CDC and USAID, as well as prominent international nongovernmental organizations including EGPAF, the International Center for AIDS Care and Treatment Programs at Columbia University's Mailman School of Public Health, Family Health International (FHI), the Clinton Foundation HIV/AIDS Initiative (CHAI), Catholic Medical Mission Board (CMMB), the Academy for Educational Development (AED), Population Council, the International Center for Reproductive Health (ICRH), and Ensemble pour une Solidarité Thérapeutique Hospitalière en Réseau (ESTHER).

The purpose of the IATT is to contribute to improving and scaling up PMTCT programs to meet UNGASS goals through strategic planning, advocacy and mobilization, and coordinating

program implementation, monitoring, and evaluation. The IATT is the key forum for coordination of PMTCT implementation across global stakeholders. PEPFAR agency and implementing partner representation on the IATT has been active. PEPFAR also provides some funding to support the operations of the IATT.

**PEPFAR participates in IATT-coordinated technical assistance to country programs.** One of the major activities of the IATT has been a series of joint technical missions to countries to review and provide recommendations regarding the scale-up of national PMTCT and pediatric HIV programs. These joint missions provide a forum for coordinating technical assistance, recommendations, and other implementation support to the countries, based on the comparative advantages of the different participating IATT members, and using a government-led process in each country. PEPFAR headquarters and country-based staff and partners have participated and provided technical leadership in these joint IATT technical missions, allowing close coordination of PEPFAR's PMTCT program support with that of the Global Fund and other donors, in support of national PMTCT programs.

**PEPFAR actively contributes to developing normative global guidance on PMTCT with WHO/UNICEF.** WHO has developed and issued a series of recommendations for various aspects of PMTCT in response to scientific findings and programmatic experience. These include comprehensive guidelines for PMTCT in 2006 (MTCT 2006), an interim update from an expert consultation in 2008 (New and Emerging Evidence 2008), and new comprehensive PMTCT guidelines due in the first quarter of 2010 (4). In addition to these clinical guidelines, operational and scale-up guidelines for PMTCT programs have been issued (Operational Guide for National Programmes 2007, Guidance on Global Scale-Up 2007), as well as guidance on diagnosis, care, and treatment of HIV-infected children (Scale up of HIV-Related Prevention 2008). Guidance on monitoring and evaluation of PMTCT programs, including harmonization of PMTCT indicators, is expected to be disseminated soon.

PEPFAR staff, agencies, and implementing partners have contributed substantially to the development of these guidelines:

- PEPFAR's technical staff participate in technical working groups that develop the global guidance documents, and serve as leaders for some groups, such as laboratory.
- PEPFAR agencies' and partners' research and evaluation experience is used to inform global guidance.
- PEPFAR provides some funding to support the process for guidance development and dissemination.

**PEPFAR assists in translating global normative guidance and bases its implementation activities on global guidance.** PEPFAR works closely with WHO and UNICEF regional and national offices to support regional workshops to guide national program managers in understanding new WHO guidelines when they are issued. PEPFAR, WHO, and UNICEF, and other organizations provide technical assistance to national governments in adapting global guidance into national guidelines and strategic plans. PEPFAR's PMTCT Technical Considerations guidance is based on WHO global guidance, and PEPFAR funds implementation that is in line with national and WHO guidelines.

**PEPFAR collaborates with international/multilateral organizations to produce globally relevant tools to support PMTCT programs.** Two prominent examples of close collaboration between PEPFAR, WHO, and other organizations are the development of Testing and Counseling for PMTCT Support Tools, a set of educational materials, job aids, and training resources to support the integration of testing and counseling into antenatal care, labor and delivery, and post-delivery settings (Testing and Counseling 2005), and the Prevention of Mother-to-Child Transmission of HIV Generic Training Package, a comprehensive, evidence-based generic PMTCT training course (2009). PEPFAR contributed both financially and technically to these products.

**PEPFAR has engaged international/multilateral organizations in PEPFAR's Public Private Partnership effort on pediatric AIDS and PMTCT.** Through PEPFAR's Public Private Partnership initiatives, PEPFAR has worked closely with WHO, UNICEF, and other organizations to engage the private sector in developing key areas in Pediatric HIV treatment and in PMTCT (Building a New Public-Private Partnership 2009). These include collaborations on the innovative development of pediatric antiretroviral formulations, diagnostic technologies for the diagnosis of HIV infection in infants, incorporation of information technology solutions and development of a "mother-baby pack" of needed medicines.

**PEPFAR directly funds international/multilateral organizations in some countries for implementation activities.** To leverage core strengths and capacities of the national and regional offices of international/multi-lateral organizations, PEPFAR has provided direct country funding for such activities as purchase of commodities, provision of PMTCT services, and community engagement.

**PEPFAR has joined international/multilateral organizations in high-level advocacy meetings.** PEPFAR lent its support and advocacy for key global high-level PMTCT advocacy meetings in Abuja, Nigeria in 2005 and in Johannesburg, South Africa in 2007 (PMTCT High-Level Global Partners Forum 2007).

**PEPFAR joined with international/multilateral organizations in sponsoring the annual HIV Implementers Meetings.** These meetings allowed dissemination of information on PMTCT implementation to Ministries of Health and other organizations implementing PMTCT programs worldwide (HIV/AIDS Implementers' Meeting 2009).

#### **IV. Conclusions**

Collaborating closely with international and multilateral organizations has been a key part of PEPFAR's global strategy for support of national PMTCT scale-up. Through active coordination, joint planning, technical exchange, and targeted funding, PEPFAR's goals for PMTCT can be fully aligned with other global efforts. Concrete outcomes have been achieved already through these relationships, such as establishing an effective coordinating body, development of globally-useful implementation tools and products, and in collaborative efforts to develop, disseminate, and implement evidence-based guidance for PMTCT. To reach UNGASS and PEPFAR targets, continued and enhanced collaboration is essential.

#### **V. Recommendations**

- Continue and expand coordination with international/multilateral organizations within the framework of the “three ones” (one national HIV/AIDS action framework, one national HIV/AIDS coordinating authority, one national monitoring and evaluation system) based on the core competencies of the different stakeholders to ensure clear and unified information is provided to Ministries of Health and Finance.
- Actively engage international/multi-lateral organizations in the PEPFAR Partnership Framework (PEPFAR 2009) process and coordinate where possible with the GFATM National Strategy Application process (Global Fund NSA 2009).
- Provide support to improve capacity of international/multi-lateral organizations.
- Emphasize harmonization and collaboration with international/multi-lateral organizations, in support of the “three ones.”
  - In particular, emphasize need to harmonize monitoring and evaluation efforts.
  - Continue to fully engage with the UNICEF/WHO co-convened Interagency Task Team on PMTCT as the primary forum for coordination at headquarters level and emphasize strong coordination at country level to avoid duplication and gaps.
- Expand PEPFAR’s interface with international/multi-lateral organizations to begin to embrace broader maternal and child health, and reproductive health issues related to PMTCT, as well as a primary care model that can be applied to other emerging health concerns such as diabetes, high blood pressure, etc within the Global Health Initiative.

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