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Malawi: Testing Infant for HIV

TECHNICAL BRIEF

Prevention of Mother-to-Child Transmission of HIV

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Introduction

The purpose of this brief is to summarize the latest evidence on the Prevention of Mother-to-Child Transmission (PMTCT) of HIV in an accessible format for policy makers and to inform the discussions of SADC member states with the ultimate aim of improving prevention policies, programs, and interventions.

In June 2011, the global community committed to accelerating progress in PMTCT through an initiative called the Global Plan to Eliminate New HIV Infections in Children by 2015 and Keeping Their Mothers Alive. The Plan has two global targets:

- 1) Reduce the number of children newly infected with HIV by 90% by 2015; and
- 2) Reduce the number of HIV-associated deaths in women during pregnancy, childbirth or puerperium by 50% by 2015.

While most SADC countries have PMTCT policies and have seen progress, full PMTCT coverage has not yet been achieved despite substantial efforts and the availability of resources dedicated to decreasing Mother-to Child Transmission (MTCT).

In general, HIV transmission through MTCT remains unacceptably high in the SADC region. Important steps have to be taken in the majority of countries to achieve the targets.

The 2011 Global Plan identifies 22 priority countries for scale up of PMTCT and the elimination of MTCT, of which 21 are in Sub-Saharan Africa and 12 are in the SADC region. Botswana, South Africa, and Swaziland have achieved up to 90% PMTCT coverage with a variety of strategies using dual- and triple-antiretroviral therapy (ART) regimens. Namibia, Zambia, and Zimbabwe appear to be on track to achieving this coverage rate.¹

The 2012 UNAIDS Progress Report on the Global Plan projects that: 1) Namibia, South Africa, Swaziland, Zambia, and Zimbabwe will achieve the 2015 target of reducing the number of children newly infected with HIV if the 2009–2011 decline of 30% or more continues through 2015; 2) Botswana, Lesotho, and Malawi will achieve the target if the 2009–2011 decline of 20% to 30% is accelerated; and 3) Angola, Democratic Republic of Congo, Mozambique, and Tanzania are in danger of not reaching the target as these countries saw a decline in 2009–2011 of less than 20%.²

¹ Joint United Nations Programme on HIV/AIDS, "A progress report on the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive," (2012), 10.

² Ibid, 5.

Rationale for PMTCT

PMTCT is the broad term for HIV prevention strategies that reduce vertical transmission from HIV-infected women to their children. It includes the following four components:

- 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 a woman living with HIV to her infant
- 4) Providing appropriate treatment, care, and support to mothers living with HIV and their children and families.³

MTCT of HIV can occur during pregnancy, labor, delivery, and breastfeeding, especially when mixed methods of infant feeding are used. The risk of transmission increases when the mother has a higher viral load (i.e., when she is newly infected with HIV or is in an advanced stage of the disease), or if the baby is highly exposed to the mother's infected body fluids during birth. Without intervention, the risk of MTCT ranges from 20% to 45%. With specific interventions in non-breastfeeding populations, the risk of MTCT can be reduced to less than 2%, and to 5% or less in breastfeeding populations.⁴ HIV transmission to children can be prevented by providing antiretroviral (ARV) medicines to HIV-positive mothers, implementing safe delivery practices, providing prophylactic ARVs to the new born/infant, and ensuring that mothers practice correct and safe breastfeeding (exclusive breastfeeding).

Global Policy Guidance

In 2010, WHO released PMTCT Guidelines: *"Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants"*⁵ recommend that all HIV-infected pregnant women with a CD4 count of less than 350 cells/mm³ should start lifelong antiretroviral treatment, regardless of WHO clinical staging and all immediately enrolling HIV-infected women in WHO clinical stage 3 or 4 should in ART, irrespective of their CD4 count. For women with CD4 counts of more than 350cells/mm³ there are two options, both of which should start as early as 14 weeks of pregnancy. The two options provide for a significant reduction in MTCT with equal efficacy (refer to the table on page...:

The effectiveness of ARVs to reduce transmission through breastfeeding resulted in two major changes from previous guidelines. The 2010 WHO Guidelines on HIV and infant feeding⁶ state:

National health authorities should decide whether health services will counsel and support HIV-positive mothers to either breastfeed and receive ARV interventions, or avoid all breastfeeding, as the strategy that will most likely give infants the greatest chance of HIV-free survival.

In settings where national authorities recommend HIV-positive mothers to breastfeed and provide ARVs to prevent transmission, mothers should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter, and should continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

Although many low- and middle-income countries are still in early stages of implementing the WHO 2010 PMTCT guidelines, recent experiences led the WHO to reassess current clinical guidance regarding the provision of ARVs for HIV-infected pregnant women who do not yet require treatment for their own health. The Ministry of Health (MOH) in Malawi recognized that the country does not have the laboratory or infrastructure capacity required to successfully implement either Option A or B. Therefore, a modified Option B (so-called "Option B+") has been introduced under which all HIV-infected pregnant and breastfeeding women are provided with lifelong ART regardless of CD4 count or clinical stage. In addition to eliminating the barrier of access to CD4 cell count analysis, Option B+ has the potential to reduce maternal postpartum mortality, facilitate access to PMTCT and ART, reduce HIV transmission risk for uninfected male partners, and provide protection against HIV transmission in future pregnancies.

The WHO programmatic update, *"Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants"*⁷, released in April 2012 provides information on key changes and considerations arising since publication of the 2010 PMTCT guidelines at a time when a number of countries are preparing to adopt Option B+. For example, as a result of Malawi's experience, both Namibia and Uganda have received MOH approval and are working on implementation plans to implement Option B+ in their National Plans for elimination of MTCT, while four other countries (Kenya, Mozambique, South Africa, and Zambia) are engaged in high level MOH discussions for transition to Option B+.

Current WHO guidance on ARV use in HIV-infected pregnant women is presented in the table that follows. The table also provides information on advantages and disadvantages of each option taken from the UNAIDS' 2012 progress report on the Global Plan, WHO's programmatic update mentioned above, and a 2011 article in the Lancet by Schouten et al.^{8,9,10}

3 World Health Organization, "PMTCT Strategic Vision 2010-2015, Preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals," (Geneva: WHO Press, 2010), 6.

4 Ibid.

5 Available at: http://whqlibdoc.who.int/publications/2010/9789241599818_eng.pdf

6 Guidelines on HIV and infant feeding, 2010. Principles and recommendations for infant feeding in the context of HIV and a summary of evidence.

7 Available at: http://www.who.int/hiv/pub/mtct/programmatic_update2012/en/index.html

8 World Health Organization, "Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants, Programmatic update," (Geneva: WHO Press, 2012), page 3.

9 Erik J. Schouten et al., "Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach", Lancet 378, No. 9787 (2011) 282-83.

10 Joint United Nations Programme on HIV/AIDS, "A progress report on the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive," (2012), 12.



Three Options for PMTCT Programs

Option A

| Woman receives: | | Infant receives: | Advantages: |
|---|--|--|--|
| Treatment (CD4 count \leq 350 cells/mm ³ or WHO clinical stage 3 or 4) | Prophylaxis (CD4 count >350 cells/mm ³) | | |
| ART starting as soon as possible irrespective of gestational age, and continued during pregnancy, delivery, and thereafter (lifelong) | <p><i>Antepartum:</i> AZT (twice daily) starting as early as 14 weeks pregnancy</p> <p><i>Intrapartum:</i> at onset of labor, sd-NVP and first dose of AZT/3TC</p> <p><i>Postpartum:</i> daily AZT/3TC (twice daily) through 7 days postpartum</p> | Daily NVP from birth through 1 week beyond complete cessation of breastfeeding; or, if not breastfeeding or if mother is on ART, through age 4-6 weeks | <p>Advantages:</p> <ul style="list-style-type: none"> • Successfully implemented in a number of HIV high-burden countries. Many high-burden countries initially chose Option A because of limited PMTCT program support; challenges of scale-up; lower drug costs; ease of adapting existing PMTCT approaches and, therefore, the associated training; and limited capacity to provide triple ARVs in maternal/child health (MCH) settings. <p>Disadvantages:</p> <ul style="list-style-type: none"> • CD4 testing is required to identify women who should initiate ART for their own health, which may delay ART enrollment in areas there are limited access to reliable CD4 testing. • The regimen does not address the HIV infection of the mother (higher TB incidence in women with CD4 count <500; higher postnatal maternal mortality in women with CD4 counts as high as 600). • The regimen does not reduce the risk of HIV infection to discordant sexual partners. • The regimen is less effective than Option B in stopping transmission from mother to child when mothers are at advanced stages of HIV disease. • Practical issues related to the long duration of infants on ARVs (for the whole breastfeeding period, which in some countries is up to 2 years of age). |



Option B

| Woman receives: | | Infant receives: | Advantages: |
|---|---|--|---|
| Treatment (CD4 count \leq 350 cells/mm ³ or WHO clinical stage 3 or 4) | Prophylaxis (CD4 count > 350 cells/mm ³) | | |
| ART starting as soon as possible irrespective of gestational age, and continued during pregnancy, delivery, and thereafter (lifelong) | Triple ARV prophylaxis starting from as early as 14 weeks of gestation and continued until delivery, or if breastfeeding, continued until 1 week after all infant exposure to breast milk has ended | Daily NVP or twice daily AZT from birth through ages 4-6 weeks regardless of infant feeding method | <p>Advantages:</p> <ul style="list-style-type: none"> • Use of the same regimen for PMTCT and for first-line ART considerably simplifies drug forecasting, procurement, supply to facilities, and drug stock monitoring, thereby reducing the risk of drug stock outs. • The regimen provides greater efficiency, very much in accord with the Treatment 2.0 Initiative, to simplify and optimize the use of ARVs and standardize the first-line treatment regimen. • The first-line regimen of tenofovir/lamivudine/efavirenz (TDF/3TC/EFV) is available as a single-pill fixed-dose combination. This has been recommended recently as the optimal regimen for first-line adult treatment, including for pregnant women. • Tenofovir and lamivudine are active against the hepatitis B virus. • The regimen addresses the HIV infection of the mother (higher TB incidence in women with CD4 count < 500; higher postnatal maternal mortality in women with CD4 counts as high as 600). • The regimen reduces the risk of HIV infection to discordant sexual partners. <p>Disadvantages:</p> <ul style="list-style-type: none"> • The cost of ARVs for Option B is considerably higher than that of Option A. • CD4 testing is required to identify women who should initiate ART for their own health, which may delay ART enrollment limited access to reliable CD4 testing. • Efavirenz is potentially harmful to the developing fetus in the first trimester, but the risk seems to be lower than previously thought. In the absence of conclusive evidence, women who desire pregnancy can be offered an alternative ART regimen in which nevirapine replaces efavirenz until the second trimester of pregnancy. |

Option B+

| Woman receives: | Infant receives: |
|--|--|
| <i>Same for treatment and prophylaxis</i> ART starting as soon as possible irrespective of gestational age, and continued during pregnancy, delivery, and thereafter (lifelong) | Daily NVP or twice daily AZT from birth through ages 4-6 weeks regardless of infant feeding method |

Advantages:

- Use of the same regimen for PMTCT and for first-line ART considerably simplifies drug forecasting, procurement, supply to facilities, and drug stock monitoring, thereby reducing the risk of drug stock outs.
- The regimen provides greater efficiency, very much in accord with the Treatment 2.0 Initiative, to simplify and optimize the use of ARVs and standardize the first-line treatment regimen.
- The first-line regimen of tenofovir/lamivudine/efavirenz (TDF/3TC/EFV) is available as a single-pill fixed-dose combination. This has been recommended recently as the optimal regimen for first-line adult treatment, including for pregnant women.
- Tenofovir and lamivudine are active against the hepatitis B virus.
- The regimen addresses the HIV infection of the mother (higher TB incidence in women with CD4 count <500; higher postnatal maternal mortality in women with CD4 counts as high as 600).
- The regimen reduces the risk of HIV infection to discordant sexual partners.
- Option B+ protects the infant from the start of pregnancy in the event of future pregnancies.
- PMTCT program requirements are further simplified. There is no need for CD4 testing to determine ART eligibility, as required in Option A or B, or whether ART should be stopped or continued after the risk of mother-to-child transmission has ceased, as in Option B.
- The regimen likely benefits women's health by allowing for earlier treatment and avoiding the risks of stopping and starting triple ARVs, especially in settings with high fertility.
- Option B+ allows for a simple message to be delivered to communities: once ART is started, it is taken for life.
- Prevention of maternal deaths has a striking effect on child survival, independent of any effect gained from the prevention of HIV transmission. By starting women on lifelong ART earlier, the risk for morbidity and mortality related to HIV is decreased, with positive benefits for the child, the family, and the community.
- The need for multiple guidelines and training are eliminated.

Disadvantages

- The cost of ARVs for Option B+ is considerably higher than Option A and moderately higher than Option B. (This depends on the average breastfeeding period and the average time interval between pregnancies.)
- Increased resources needed for continued treatment may be offset by simplified procedures, improved health outcomes for mothers and children, and additional benefits, such as preventing HIV transmission in discordant couples, and reducing the risk of developing resistant HIV strains as a consequence of treatment interruptions in women with multiple pregnancies.
- Option B+ needs to be evaluated in program and field settings, with community acceptability assessed and human rights protected.

WHO has initiated a comprehensive revision of all HIV guidelines, including guidance on ARVs for pregnant women, which will be released in early 2013.



What Would Influence the Choice for Option B+?

There are a range of issues to consider if a country is contemplating the introduction of Option B+:

Availability of reliable CD4 count testing for all pregnant women

- In many counties in the SADC region, the availability of reliable CD4 count testing is not guaranteed everywhere in the country. The introduction of Option B+ in these areas will take away an important bottleneck for women to access effective PMTCT regimens and will help in the achievement of PMTCT targets.

Availability of adequate funding

- ARVs for Options B and B+ are more expensive than ARVs for Option A. The difference between the costs of Options B and B+ is most likely limited as only women who stop ART after the end of the breastfeeding period will influence the costs. The difference in drug costs is dependent on the average period of breastfeeding, average time interval between pregnancies, and disease progression. A proportion of women may become pregnant again or become eligible for ART because of disease progression.

As regards costs of the treatment, the WHO programmatic update states: The cost of ARV drugs was a major determinant in countries' choice of a PMTCT option. In 2009 the average ARV drug cost of Option B was three to five times higher than the cost of Option A (depending on regimen and assuming the provision of both ART and prophylaxis). However, by the end of 2011, this differential had diminished to two times higher. The annual cost of the TDF/3TC/EFV once-daily dose regimen costs approximately US\$180 per year. Further declines in the annual cost are anticipated.¹¹

¹¹ Ibid, 3.

Integration and harmonization of ART and PMTCT services

- The new WHO guidelines provides an opportunity to harmonize and integrate PMTCT and ART programs, as ART should be provided to all treatment-eligible women. In Option B and B+ triple regimens should be provided for either a limited period or for life. Uptake and retention are expected to improve when these services are provided as part of the antenatal care/maternal and child health (ANC/MCH) services that are already being used. This would mean, in practical terms, an upgrade of ANC/MCH services to provide ART.

Accreditation of lower level health facilities and staff in these facilities to prescribe/initiate ART

- Many women go for ANC services to health facilities that are close to where they live. In many countries the vast majority of women access these services in the lower tiers of the health system. Rolling out PMTCT services with access to triple ARV prophylaxis or ART from these health services depends on the level of "task shifting" of prescription of ART.

Regional Guidance and Promising Practices

In 2010, the Southern African Development Community issued Regional Minimum Standards for Harmonized Approaches to PMTCT in the SADC Region.

The guidelines are aligned with WHO guidance for PMTCT and include the following:

Minimum standards for prevention of HIV infection women and couples

- Health education and information on HIV prevention and care should include sexually transmitted infection screening, diagnosis, and treatment for women and couples; voluntary and provider counselling should be used to promote HIV testing and counseling (HTC) for couples and should include support for disclosure of HIV status to partners; provide for retesting for exposed individuals and promoting HIV counseling as part of routine health care.

Minimum standards for preventing unintended pregnancies in all women of reproductive age

- Family planning counseling and contraceptives must be provided at all opportunities. PITC must be offered during family planning services; PMTCT policies must include family planning. HIV positive women must be offered all available options for family planning and women must be given information and care to assist them in remaining healthy during pregnancy.

Minimum standards for preventing transmission of HIV from an infected woman to her infant

- Quality antenatal and postpartum care should be provided to all women, and include information on PMTCT, other sexual reproductive health services, safe obstetric practices, routine retesting in late pregnancy (in generalized epidemics) and support for infant feeding and counseling based on WHO recommendations.

Minimum standards for providing care and support for HIV infected women, their infants and families

- ART should be provided to all treatment-eligible pregnant women. ART and care must be extended to fathers and other family members. Member States must work towards cut-off point of 350 cell count for starting ART promote active participation of people living with HIV in planning service delivery, advocacy and community engagement, as well as tuberculosis (TB) screening for women and their families. Provide early diagnosis in infants, all HIV-exposed infants to start cotrimoxazole at 4-6 weeks after birth, all children suspected or known to have TB must be offered an HIV test, all HIV exposed children must have a confirmatory HIV antibody test around 18 months and all HIV infected children below 12 months must start ART.
- PMTCT must be integrated into other SRH and maternal and child health programs.

Promising Practices in the SADC Region

Option B+ in Malawi

Unable to ensure availability of CD4 testing for HIV-infected women, Malawi elected to combine ART with PMTCT in a new approach dubbed Option B+. The country saw a six-fold increase in ART uptake among HIV-infected women in its first year of implementation. Information on Option B+ and Malawi's experience to date is available from: Erik J. Schouten et al., "Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach", *Lancet* 378, No. 9787 (2011) 282–84 ([http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(10\)62303-3/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)62303-3/fulltext)).

Routine Testing and PMTCT Scale Up in Botswana

Botswana introduced a PMTCT program in 1999, piloting it in two districts. In 2001, when the HIV prevalence rate in pregnant women was 36.2%, the country rolled out PMTCT to all public health facilities. Botswana reduced the rate of MTCT from approximately 40% to just 3 % in 2008. Its PMTCT program is now one of the most effective in the developing world, reaching 95% of all women and HIV-exposed infants in need¹². Various factors have contributed to the success of Botswana's PMTCT program: the introduction of routine/opt-out HIV counseling and testing, and ART at all facilities; the establishment of a "peer mother" program; provision of formula feeding for a year; integration of PMTCT and sexual reproductive health services; community mobilization to support the uptake of PMTCT services; and visible leadership at the national level. The scale up of PMTCT has also been supported by community mobilization campaigns using a mix of communication strategies to promote male involvement.

12 Tracy L. Creek, et al., "Successful Introduction of Routine Opt-Out HIV Testing in Antenatal Care in Botswana," *Journal of Acquired Immune Deficiency Syndrome* 45, no. 1 (2007), 104.





Recommendations

Scaling up PMTCT remains an urgent priority in the SADC region. Despite significant progress in the initiation of PMTCT in the region, there is still a need to ensure universal coverage, increase access and efficiency, and decrease vertical transmission. There are three options for PMTCT available and all have their unique advantages and disadvantages. Option B+ developed in Malawi has practical advantages, especially in areas with weak health systems and where, for most women, alternatives for breastfeeding up to 24 months are not feasible.

WHO confirms that Option B+ offers important programmatic and operational advantages that could accelerate progress towards eliminating new pediatric infections. If Option B+ is supported, funded, and effectively scaled up and sustained at the primary care level, it will provide the best protection for the mother's health and it offers a promising new approach to preventing sexual transmission and new HIV infections in the general population.¹³

Universal, lifelong ART for HIV-infected pregnant women will achieve maximum coverage and has the potential to contribute significantly to the elimination of pediatric HIV/AIDS. There are also other important health benefits.

HIV positive women in Zimbabwe, even those with CD4 cell counts higher than 350 cells per μL had a risk of death around six times higher than that in non-infected women within 24 months postpartum, and early ART could reduce mortality by 50–90%.

Prevention of maternal deaths has a striking effect on child survival, independent of any effect gained from the prevention of HIV transmission. The risk of developing tuberculosis increases with declining CD4 cell counts, from 500 cells per μL ; the majority of pregnant women have CD4 cell counts in this range.

Early initiation of ART, therefore, reduces the risk of tuberculosis. Observational cohort studies in the United States and Europe also suggest that the early start of ART significantly lowers mortality related to HIV infection and AIDS. In addition, HIV transmission in couples is an important contributor to overall transmission rates, and the use of ART greatly reduces the risk of HIV-transmission to non-HIV infected partners.

As regards specific guidelines for breastfeeding, with HIV-positive mothers it is important to consider the context of breastfeeding; its avoidance may not be appropriate and might even be dangerous. The cost of infant formula is often beyond the means of poor families, when it is widely available. Lack of access to safe and clean water for replacement feeding may cause infections, malnutrition, and infant death. In cultures where breastfeeding is the norm, the very fact that a mother chooses not to breastfeed may draw attention to her HIV status and invite discrimination, or even violence and abandonment by her family and community¹⁴.

The broad conclusions drawn from analyses of PMTCT for HIV prevention requires that any form of PMTCT services, including ART, safe infant feeding practices, or the use of contraception to prevent unwanted pregnancies, needs to be conducted in conjunction with other HIV prevention activities to ensure sustainability and effectiveness of the intervention.

This includes: implementing PMTCT; educating the community about the risk of MTCT and the availability of PMTCT services; addressing stigma; engaging key stakeholders and traditional leadership; assuring partner disclosure; increasing infant testing and diagnosis; addressing safe sexual behaviors; and committing to safe infant feeding practices. National bodies must ensure that key essential HIV services, including HTC, PMTCT, and ART, are integrated with other sexual and reproductive health services.

¹⁴ Centre for AIDS Development, Research and Evaluation, "Strengthening PMTCT Through Communication: A Review of Literature," 2009.

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¹³ World Health Organization, "Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants, Programmatic update," (Geneva: WHO Press, 2012), 4.