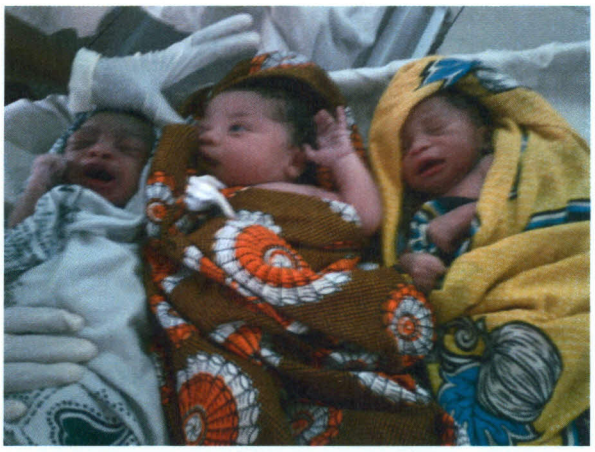
# REPORT ON THE FEASIBILITY APPRAISAL

# FOR

# THE INTRODUCTION OF THE REVISED WHO PMTCT AND INFANT FEEDING RECOMMENDATION IN TANZANIA



Source: Situation analysis of newborn in TZ: K.Manji

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## List of Abbreviations and Acronyms:

| | |
|---|---|
| AIDS | Acquired Immunodeficiency Syndrome |
| AFASS | Affordable, Feasible, Available, Sustainable and Safe |
| ART | Antiretroviral Therapy |
| ARV | Antiretrovirals |
| AZT | zidovudine |
| sd NVP | single dose Nevirapine |
| 3TC | Lamivudine |
| BMC, | Bugando Medical Centre |
| CHAI | Clinton HIV&AIDS Initiative Foundation |
| CTC | Care and treatment Clinic |
| DBS | Dry Blood Sport |
| EFV | Efavirenz |
| EGPAF | Elizabeth Glazier Paediatric AIDS Foundation |
| FTC | Emtricitabine |
| FGD | Focused group discussion |
| GoT | Government of Tanzania |
| HIV | Human immunodeficiency virus |
| HAART | Highly Active Anti-Retroviral Therapy |
| Hb | Haemoglobin |
| KCMC | Kilimanjaro Christian Medical Centre |
| KII | Key Informant Interview |
| MNH | Muhimbili National Hospital |
| ,MRH | Mbeya Referral Hospital |
| MoH&SW | Ministry of Health and Social Welfare |
| NACP, | National AIDS Control Programme |
| NBS | National Bureau of Statistics |
| PLHAs | People Living with HIV and AIDS |
| PMTCT | Prevention of Mother-to-Child Transmission |
| (PSU) | Pharmaceutical and Supply Unit |
| PORALG) | Prime Minister's Office Regional Administration and Local Government |

| | |
|---|---|
| RCH | Reproductive and Child Health |
| THMIS | Tanzania HIV and Malaria Indicator Survey |
| TDF | Tenofovir |
| UN | United Nations |
| UNICEF | United Nations Children's fund |
| UNFPA | United Nations Population Fund |
| UNAIDS | Joint United Nations Program on HIV/AIDS |
| WHO | World Health Organization |

**Acknowledgement**

We would like to thank the Ministry of Health and Social Welfare through tne NACP–PMTCT unit for entrusting us with this task and facilitating our access to relevant documents and our visit to the selected health facilities.

We would also like to acknowledge the cooperation we received from the administration and health workers from the 27 health facilities we visited.. They gave the team their meager time and data with which we have been able to make decisions according to the ToR we were given. They are very busy people and the interviews were conducted under very stressful conditions which could not have been avoided since clients were waiting for services. We acknowledge the inputs made by the health workers from PMTCT clinics and Care and Treatment Clinics at, Regional, District, Heath Centres and Dispensaries. Lessons from their experience of working in this area were useful. Also, our acknowledgements to Dr. Mohamed Manji(MD) and Faheem Sheriff MD, for providing details of the references and citations.

This work would not be complete without the insightful cooperation of the pregnant women at the antenatal clinics including those living with HIV. They are the living evidence of the HIV&AIDS epidemic and are very conversant with the daily realities of the epidemic. To them we say thank you very much and together we shall fight the epidemic and eliminate HIV infection in children

## SUMMARY

HIV&AIDS is a major global health threat and sub-Saharan Africa bears the heaviest burden. Mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) remains the major mode of transmission of HIV in children. The plight of HIV/AIDS is having an overwhelming impact on the world's children. Globally, over 1500 unborn or newborn babies are infected every day. The 2008 WHO/UNAIDS report shows that there were 430000 new infections in children in 2007 despite interventions to Prevent Mother to Child Transmission of HIV. More than 90% of the infections in children occurred in sub-Saharan Africa, where HIV-1 acquisition through breast milk accounts for more than 40% of the infection. . The best approach to prevent such transmission would be to avoid breastfeeding for infants born to HIV infected mothers as is the case in well resourced countries. However, in Africa, breast-feeding is a cornerstone for child survival as many women cannot implement the AFASS criteria Exclusive breast feeding has been shown to lower the risk of MTCT of HIV through breasts milk compared to mixed feeding but the infant remains exposed to HIV infection. Emerging New evidence from research shows that use of antiretroviral treatment/ prophylaxis in breast-fed infants or lactating mothers further significantly decrease postnatal acquisition of HIV .by the infant. These new findings have been considered important information and at the end of November 2009 experts at the WHO conducted a review of the available scientific information and came up with some new advice for the prevention of mother-to-child HIV transmission and feeding of infants born to HIV-infected mothers in communities where breast feeding of children born to HIV infected mothers cannot be avoided. [45].

Key changes in the WHO recommendations for PMTCT include the following:

- HIV-infected pregnant women who are not already taking anti-HIV medications (antiretroviral, ARVs) for their own health but are required to do so they should start using anti-HIV medications when the CD4 cell count $\leq 350$ /mm$^3$ when they are 14 weeks pregnant rather than waiting until they are 28 weeks pregnant.

- For women who do not need anti-HIV medications for their own health but live in settings where breastfeeding is critical for infant survival and who choose to

breastfeed, the WHO now advises that prophylaxis start when they are 14 weeks pregnant rather than waiting until they are 28 weeks pregnant and. either the mother or the infant take anti-HIV medications throughout breastfeeding period for up to 12 months.

The updated WHO advice is being reviewed by Ministries of Health around the world, including the MOHSW in this country to determine incorporating the changes in the standard of care for PMTCT in this country and when and how these changes are to be put into practice. Hence the basis of this consultancy.

PMTCT activities in Tanzania started in 1996 in affiliation with the Petra PMTCT trial [5]. A 2 year pilot program was later initiated in 2000 following which it was finally incorporated as part of the Reproductive and Child Health services under the PMTCT unit at the Ministry of Health and Social Welfare (MoHSW). Many development partners are keenly involved in the program and their effort has been dedicated ever since.

Regarding the use of ARV's for PMTCT in Tanzania, firm recommendations have been set by the Ministry of Health and Social Welfare [14].as per 2007 PMTCT guidelines whereby, two programs are in place. The first concerns ARV treatment during pregnancy where HIV infected pregnant women when eligible, are offered combination ARV treatment. Women's eligibility for initiating ART is based on the following criteria: WHO stage IV disease regardless of CD4 count, WHO stage III disease and CD4 cells count ≤ 350 cells/$mm^3$ and all clients whose CD4 cell count is ≤ 200 cells/$mm^3$. The first line ARV treatment regimen for pregnant women in Tanzania is a combination of Zidovudine (300mg BD), Lamivudine (150mg BD) and Nevirapine (200 mg initiated as a once daily dose for two weeks before it can be given BD). All infants born to HIV-infected women receiving ARV treatment should receive prophylaxis as described in the ARV prophylaxis regimen below.

The second use of ARV's is in the prophylaxis for PMTCT among women not eligible for ARV treatment This is the short term use of ARV's to reduce HIV transmission from mother to infant. There are two recommended ARV prophylaxis regimens for PMTCT in Tanzania.

One is a combination regimen for use at all health facilities that have the capacity to initiate ARV treatment. Under this regimen women are given AZT (300mg BD) from 28 weeks gestation age or anytime thereafter, sdNVP (200mg) at the onset of labor plus AZT (300mg every 3 hourly) and 3TC (150mg every 12 hours). A postpartum dose of AZT and 3TC (300mg and 150mg respectively BD) for 7 days has to be administered to

the mother. The infant should receive sdNVP 2mg/kg as soon as possible after delivery and AZT syrup (4mg/kg BD) for 4 weeks or 1 week if the woman had received at least 4 weeks of AZT during ANC.

The second ARV prophylaxis regimen is the use of a single drug in PMTCT at sites that do not have the capacity to initiate ARV drugs under this regimen, a sdNVP (200mg) is dispensed at the 28 week visit or anytime thereafter. This sdNVP (200mg) is administered to the mother at the onset of labour. All infants receive sdNVP (2mg/kg) within 72 hours after delivery.

In the post natal period, the 2007nationalPMTCTguideline recommendations advise infected mothers to exclusively breastfeed their infants for the first 6 months of life followed by addition of complementary foods thereafter. However mothers who wish to reduce risk of transmitting HIV to the infant may opt for replacement feeding exclusively for the first 6 months when it is affordable, feasible, available, sustainable and safe.

The implementation of the new WHO suggested changes looks hopeful. The challenge ahead would be to incorporate and adjust these advancements into the existing PMTCT infrastructure as we extend our reach further in curbing this overwhelming situation.

**The ToR in the consultancy were to**:

- Undertake a feasibility appraisal of the policy and programmatic implications for the national PMTCT programme in Tanzania in introducing the 2010 updated who guidelines for PMTCT, laboratory capacity to identify eligible mothers for ART, cost effective option for ARV prophylaxis, and early infant HIV diagnosis. .
- Produce a report based on the results of the appraisal that can be used to inform MoHSW on selecting the option for national PMTCT program

The methodology which was used in the feasibility appraisal for the introduction of the revised 2010 WHO PMTCT and infant feeding recommendations for adoption in Tanzania; involved the use of several steps. These included desk reviews as well as qualitative and quantitative data capture

Desk appraisal involved extensive literature review including relevant national documents related to the subject

The team visited 27 selected health facilities in 6 regions. These included dispensaries, health centres and District hospitals table 4. Most health facilities with RCH services have also established PMTCT services table 5. Uptake of testing and use of ARVS for

PMTCT is shown table 6. More of the findings and discussions are summarised in table9. All these show that it feasible to accommodate the new changes in our PMTCT program Estimating the number of patients requiring ARV prophylaxis after new WHO guidelines changes and costs of different options, assumptions were that all women with CD4 cell count ≤ 350 /$mm^3$ will receive ART in CTC(these have been taken care [54]). ARVs and laboratory costs for different options and scenarios for prophylaxis are shown in table 10 **a** and **b**

Considering that option **A** is similar to option **B** in terms of efficacy it is obvious that option A table 10 a is cheaper and more cost effective than any of the options B table10b provided it is implemented properly and effectively. For this option to have the impact the program should have the capacity to identify women eligible for ART and link them to CTC.

Despite the success of antiretroviral prophylactic regimen in reducing perinatal transmission, post natal transmission through human milk continues to remain a serious problem. Given the overwhelming benefits of breastfeeding, lack of safe alternatives to human milk in resource-limited countries, and the documented risk of HIV transmission via breastfeeding, [32] there is an urgent need to make breastfeeding by HIV infected women safer to prevent postnatal transmission of the HIV virus'

# 1.0: INTRODUCTION AND REVIEW OF LITERATURE

HIV&AIDS is a major global health threat and sub-Saharan Africa bears the heaviest burden. Mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) remains the major mode of transmission of HIV in children. The plight of HIV/AIDS is having an overwhelming impact on the world's children. Globally, over 1500 unborn or newborn babies are infected every day. The majority of these babies will die before they celebrate their fifth birthday. Worldwide, in 2003, there were an estimated 700,000 children under the age of 15 years who were newly infected, and 500,000 children died of AIDS [1]. The 2008 WHO/UNAIDS report estimated that in 2007, 430000 new infection in children occurred despite interventions to Prevent Mother to Child Transmission of HIV. Without any intervention, about one third of infants born to HIV-positive mothers will be infected during pregnancy (5%–10%), labour and birth (10%–20%), or breastfeeding (5%–20%) [2] More than 90% of the 430,000 HIV-1 infections in children each year occur in sub-Saharan Africa, where HIV-1 acquisition through breast milk accounts for more than 40% of the infection. The best approach to prevent such transmission would be to avoid breastfeeding for infants born to HIV infected mothers as is the case in well resourced countries. However, in Africa, breast-feeding is a cornerstone for child survival. Strong support for exclusive breastfeeding for 6 months in the era of HIV has been promoted in resource limited countries as this ensures adequate nutrition for infants where AFASS policy cannot be implemented. This has also, been shown by scientists that it lowers the risk of MTCT of HIV through breasts milk compared to mixed breastfeeding, but does not eradicate it. New evidence emerging from research shows that use of antiretroviral treatment/ prophylaxis in breast-fed infants or lactating mothers further significantly decrease postnatal acquisition of HIV .by the infant. So a combination of these strategies in communities where breastfeeding cannot be avoided, it should be possible to eliminate new perinatal HIV infections globally when antiretroviral therapy (ART) is provided to eligible women, for the mother's health, and by providing extended postpartum prophylaxis to antepartum and intrapartum prophylaxis

Tanzania, one of the hardest hit countries in the AIDS pandemic in sub-Saharan Africa, has an estimated HIV seroprevalence of 7% among adults aged 15-49 years. This

translates to an estimated 1.8 million people living with HIV/AIDS nationally. HIV has orphaned more than 1 million children in this country [3]. Among pregnant women attending antenatal clinics in Tanzania, HIV prevalence ranges from 3.5% in Kigoma region to 18.2% in Iringa region. As of 2005, the national seroprevalence of HIV among these women was reported to be 8.2% [4].

WHO recommendations for PMTCT

In an attempt to control this devastating pandemic, United Nations (UN) agencies [UNICEF, UNFPA, UNAIDS, World Health Organization ((WHO), and the World Bank] recommend a four-component strategy. The first component supports prevention of HIV infection in all people, especially young women. The second component focuses on the prevention of unintended pregnancy among HIV-infected women. The third component promotes reduction of HIV transmission from HIV-infected women to their infants (PMTCT) through such interventions as use of antiretroviral drugs to reduce perinatal transmission, safer delivery practices, and counselling and support for infant-feeding. The fourth component provides care, treatment, and support to HIV-infected women, their infants, and their families [6].

While a four-component approach has been advanced by the UN agencies, the third component, principally the use of antiretroviral drugs for HIV-infected pregnant women, has dominated the attention of development partners and researchers in the field of prevention of mother-to-child HIV transmission. In many high-income countries, such attention has been successful, as widespread application of antiretroviral prophylaxis/therapy, caesarean section delivery, and avoidance of breast-feeding have reduced the rate of HIV transmission from mother to child to1- 2% [7][8][9]. However, this highly effective multicomponent intervention has been deemed difficult to implement in most developing countries because of its high cost and the lack of health care infrastructure [10]. Modifications of these standard interventions have been advocated for resource-poor settings despite of their decreased efficacy [11].

In resource constrained settings the 2006 WHO PMTCT guidelines recommended HAART in pregnancy for women at highest risk of MTCT. These include women with WHO clinical category III and IV and or CD4 cell count ≤200 cells/mm [13]. For those women who do not require HAART for their own health different PMTCT regimens can be provided according to the respective national guidelines.

PMTCT in Tanzania

Regarding the use of ARV's for PMTCT in Tanzania, firm recommendations have been set by the Ministry of Health and Social Welfare [14].as per 2007 PMTCT guidelines According to these guidelines, two programs are in place. The first concerns ARV treatment during pregnancy where HIV infected pregnant women when eligible, are offered combination ARV treatment. Women's eligibility for initiating ART is based on the following criteria: WHO stage IV disease regardless of CD4 count, WHO stage III disease and CD4 cells count ≤ 350 cells/$mm^3$ and all clients whose CD4 cell count is ≤ 200 cells/$mm^3$. The first line ARV treatment regimen for pregnant women in Tanzania is a combination of Zidovudine (300mg BD), Lamivudine (150mg BD) and Nevirapine (200 mg initiated as a once daily dose for two weeks before it can be given BD). All infants born to HIV-infected women receiving ARV treatment should receive prophylaxis as described in the ARV prophylaxis regimen below.

The second use of ARVs is in the prophylaxis for PMTCT among women not eligible for ARV treatment. This is the short term use of ARVs to reduce HIV transmission from mother to infant. There are two recommended ARV prophylaxis regimens for PMTCT in Tanzania.

One is a combination regimen for use at all health facilities that have the capacity to initiate ARV treatment. Under this regimen women are given AZT (300mg BD) from 28 weeks gestation age or anytime thereafter, sdNVP (200mg) at the onset of labour plus AZT (300mg every 3 hourly) and 3TC (150mg every 12 hours). A postpartum dose of AZT and 3TC (300mg and 150mg respectively BD) for 7 days has to be administered to the mother. The infant should receive sdNVP 2mg/kg as soon as possible after delivery and AZT syrup (4mg/kg BD) for 4 weeks or 1 week if the woman had received at least 4 weeks of AZT during ANC.

The second ARV prophylaxis regimen is the use of a single drug in PMTCT at sites that do not have the capacity to initiate ARV drugs Under this regimen, a sdNVP (200mg) is dispensed at the 28 week visit or anytime thereafter. This sdNVP (200mg) is administered

to the mother at the onset of labour. All infants receive sdNVP (2mg/kg) within 72 hours after delivery.

In the post natal period, national PMTCT guideline recommendations advise infected mothers to exclusively breastfeed their infants for the first 6 months of life followed by addition of complementary foods thereafter. However mothers who wish to reduce risk of transmitting HIV to the infant may opt for replacement feeding exclusively for the first 6 months when it is affordable, feasible, available, sustainable and safe.

The breastfeeding period

It is estimated that breastfeeding increases the overall risk of MTCT by 14% for established maternal infection and by 29% for primary maternal infection during lactation [31]. Transmission can occur at any point during breastfeeding [32] with most human milk transmission occurring during the first few months after birth, with a lower but continued risk thereafter [33] [34]. In a study conducted in Kenya, breastfeeding accounted for 44% of all infant infections at age 2 years; 75% of risk difference in transmission between the breastfed and formula-fed groups had occurred by 6 months of age [33]. The exact biologic mechanisms for human milk HIV-1 transmission are not yet fully understood but risk factors for transmission include women sero-converting during lactation, bleeding or cracked nipples, subclinical and clinical mastitis, and breast abscesses [32].

Despite the success of antiretroviral prophylactic regimen in reducing perinatal transmission, post natal transmission through human milk continues to remain a serious problem. Given the overwhelming benefits of breastfeeding, lack of safe alternatives to human milk in resource-limited countries, and the documented risk of HIV transmission via breastfeeding, [32] there is an urgent need to make breastfeeding by HIV infected women safer to prevent postnatal transmission of the virus [35].

With these problems in mind, focus shifts to the use of antiretrovirals in the post partum period both by the mother or the baby to reduce transmission rates, and considering the many advantages of breastfeeding, possibly allowing unrestricted access of breast milk to the infant. Recent studies have shown promising results on both these fronts.

To quote an example, the MITRA study [38] of infant prophylaxis and the MITRA Plus study [39] of maternal prophylaxis were conducted sequentially in the same clinics in Dares- Salaam. Both provided some maternal antepartum antiretroviral prophylaxis and both provided the same duration of postnatal prophylaxis (6 months). The cumulative HIV transmission rates were similar (4.9% in the MITRA study and 5.0% with Mitra Plus) and the risk of late transmission (between 6 weeks and 6 months) was also similar (1.1% and 1.0% respectively). Many other observational and ranomized studies conducted in sub Saharan countries point towards a similar trend for both infant [40] [41] [42] and maternal prophylaxis [5] [42] [43] [44]. In light of the fact that breastfeeding significantly increases the overall risk of MTCT, these findings are indeed noteworthy.The scientific evidence form these studies led to updating the PMTCT guidelines

At the end of November 2009 experts at the WHO conducted a review and came up with some new advice for the prevention of mother-to-child HIV transmission and feeding of infants born to HIV-infected mothers. [45]

Key changes in the WHO recommendations for PMTCT (now 2010WHO PMTCT guidelines)include the following:

- HIV-infected pregnant women who are not already taking anti-HIV medications (antiretrovirals, ARVs) for their own health should start using anti-HIV medications when they are 14 weeks pregnant rather than waiting until they are 28 weeks pregnant.

- For women who do not need anti-HIV medications for their own health but live in settings where breastfeeding is critical for infant survival and who choose to breastfeed, the WHO now advises that either the mother or the infant take anti-HIV medications throughout breastfeeding period for up to 12 months.

The updated WHO advice is being reviewed by Ministries of Health around the world, including the MOHSW in this country. Overtime, the MOHSW here hasl decided that these changes are to be incorporated in the standard of care for PMTCT in this country

but remains critical which option is best for the country to be put into practice. Several countries have started to implement these new guidelines, but many sub-Saharan African countries including Tanzania, Uganda and Zimbabwe are skeptical, because of the rapid changes in this science, and also because the previous guidelines have not even become fully rolled-out.

Nevertheless, even with the previous recommendations, it can unanimously be concluded that either approach significantly reduces transmission post partum. Until a time when exclusive replacement feeding becomes affordable, feasible, available, sustainable and safe, the implementation of these propositions looks hopeful. The challenge ahead would be to incorporate and adjust these advancements into existing PMTCT infrastructure as we extend our reach further in curbing this overwhelming situation.

**The Proposed WHO PMTCT Guideline changes**

Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants – 2010 version considers that in order to maximize prevention of HIV transmission, maternal and infant survival, is critical. To achieve this care of both the mother and the infant should be optimized. A key action to this is to make sure to provide **antiretroviral treatment to eligible woman and this treatment should be started soon after first trimester during pregnancy and should be for life** Where ARVs are given solely for prophylaxis they should be stopped when the risk of MTCT is no longer present. In both cases, effective linkages between PMTCT services and HIV care and treatment programmes are important.

Since the majorities of HIV-infected pregnant women are asymptomatic or have only mild symptoms, it is critical that services provide access to CD4 counts to determine which women should initiate lifelong ART. The 2010 revised PMTCT recommendations are based on two key approaches:

1. Lifelong ART for HIV-infected women in need of treatment for their own health, which is also safe and effective in reducing MTCT. In this case emphasis is put on shifting eligibility threshold for CD4 to $\leq$350 cells/mm$^3$.
2. ARV prophylaxis to prevent MTCT during pregnancy, delivery and breastfeeding for

HIV-infected women not in need of treatment. These revised recommendations emphasize the need to have a unified approach to preventing MTCT throughout pregnancy, labour and delivery, postpartum, and the breastfeeding period. The new recommendations allow ARV prophylaxis to either the mother or infant during breastfeeding, in areas where breastfeeding is judged to be the most appropriate choice of infant feeding. This is a major shift, allowing for extended postpartum interventions and breast feeding.

The 2010 Guidelines on Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants recommend.

1. To treat all HIV infected pregnant women with CD4 count ≤ 350 cells/$mm^3$, irrespective of WHO clinical stage.
2. To treat all patients with WHO HIV clinical stage 3 and 4, irrespective of CD4 cell count.
3. That all pregnant women with WHO Clinical Stage 1 and 2 should have access to regular CD4 testing to decide when to initiate treatment
4. ART or ARV prophylaxis to start as early as 14 weeks gestation or thereafter.

**Recommended regimens for initiating antiretroviral therapy in ART-naive pregnant women.**

- AZT+3TC+EFV
- AZT+3TC+NVP
- TDF+3TC or FTC+EFV
- TDF+3TC or FTC+NVP

**Table 1: Eligibility criteria for ART or ARV prophylaxis in HIV infected pregnant woman**

| **CD4 cell count available** | |
|---|---|
| CD4≤350 cells/$mm^3$ | CD4 >350 cells/$mm^3$ |
| ART<br>Regardless of clinical stage | ART<br>If symptomatic (Stage 3 or 4) |

| **WHO clinical stage** | |
|---|---|
| Stage 1 | ARV prophylaxis |
| Stage 2 | ARV prophylaxis |
| Stage 3 | ART |
| Stage 4 | ART |

**Recommendation for PMTCT prophylaxis:**

Two regimen options are recommended. All option should start at 14 weeks gestation or there after Table 2.

**Table 2 ARV REGIMEN FOR OPTIAN A AND B**

| Option A (**INFANT prophylaxis**) | Option B (**MATERNAL prophylaxis)** |
|---|---|
| Maternal AZT + infant ARV prophylaxis | Maternal triple ARV prophylaxis |
| Mother<br>Antepartum twice-daily AZT starting from as early as 14 weeks of gestation and continued during pregnancy. At onset of labour, sd-NVP and initiation of twice daily AZT + 3TC for 7 days postpartum.<br>(Note: If maternal AZT was provided for more than 4 weeks antenatally, omission of the sd-NVP and AZT + 3TC tail can be considered; in this case,)<br>continue maternal AZT during labour and stop at delivery | Mother<br>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<br>exposure to breast milk has ended.<br>Recommended regimens include:<br>AZT + 3TC + LPV/r or<br>AZT + 3TC + ABC or<br>AZT + 3TC + EFV or<br>TDF + 3TC (or FTC) + EFV |
| Infant<br>*For breastfeeding infants*<br>Daily NVP from birth for a minimum of 4 to 6 weeks and until 1 week after all exposure to breast milk has ended.<br>*Infants receiving replacement feeding only*<br>Daily NVP or sd-NVP + twice-daily AZT from birth until4 to 6 weeks of age | Infant<br>*Irrespective of mode of infant feeding*<br>Daily NVP or twice daily AZT from birth until 4 to 6<br>weeks of age. |

Laboratory monitoring for ART toxicity

- As a general principle, symptom-directed laboratory toxicity monitoring is recommended
- For patients receiving AZT-containing regimens, haemoglobin should be measured before initiation and then as directed by signs/symptoms. Patients receiving AZT-containing regimens and with low body weight and/or low CD4 cell counts are at greater risk for anaemia. Such patients should have routine Hb once per month after initiating AZT and then at least every 3 months of monitoring.

**Structure of National Health & Pharmaceutical system:**

The health system in Tanzania has two major components; the public and the private sector. The public share is 56%; while the private share is 44% (which includes 30% of Faith Based Organizations (FBOs) and 14% of private for profit). The health system works at four levels; first is the community where there are health posts,: second the ward where there are dispensaries and Health centres are found at the division level. Third level occur further up where there are district and regional hospitals and finally at the zonal and national level where there are the consultant/ referral and the national hospitals..

Currently in Tanzania there are a total of 5,379 health facilities geographically distributed so that 70% of the population is within 5 km of a facility and 90% is within 10 km. Of the 5379 health facilities only 4647 facilities offer RCH services. Administratively, the health system is largely decentralized. The MoH&SW has direct responsibility for the referral and regional hospitals, and regulatory function overall health facilities. The district facilities are independently run by the Prime Minister's Office Regional Administration and Local Government (PORALG).

Medicines Management at Health Facilities:

The Pharmaceutical and Supply Unit (PSU) is within the MoH&SW Directorate of Hospital Services. PSU is responsible for ensuring medicines availability and its proper use at public health facilities. At the same time, PSU is tasked with coordinating the selection of essential medicines according to the disease pattern for the public health facilities.

**HIV care and treatment service forecast:**

In its efforts to make ARV drugs accessible to its citizens who need them for ART or PMTCT, the government developed a National HIV&AIDS Care and Treatment plan (2003-2008) in early 2003 for a rapid scale up of ART.

In 2004,Tanzania started its HIV&AIDS care and treatment and support services offering HAART free of charge to eligible HIV patients.and by 2009, 700 CTCs had been established and cumulatively 447,209 patients were on care but actual cumulative 231,554 patients were on treatment, .

There has been significant reduction of HIV associated mortality and morbidity since the introduction of antiretroviral drugs (ARV). According to Tanzania National Guidelines for

the Management of HIV&AIDS, initiation of ARV is based on eligibility criteria which include: any HIV person with CD ≤200 cell/ul, stage III and CD 4+ between 200 – 350 cell/ul or WHO stage IV. The estimated reduction in mortality is projected to be up to 20% by 2015 if ART coverage is >85%. To achieve this WHO has proposed revision of ART guidelines for adults and adolescents to initiate ART at CD4+. ≤350/µl. Likewise the PMTCT guidelines have been revised and the threshold for initiation of HAART raised to CD4 cell count ≤350 cels/µl

**Performance of the Tanzanian PMTCT Program in**

PMTCT activities in Tanzania started in 1996 in affiliation with the Petra PMTCT trial [5]. A 2 year pilot program was later initiated in 2000 in 4 consultant hospitals (MNH,KCMC,BMC,MRH) and one regional hospital(Bukoba), following which it was finally incorporated as part of the Reproductive and Child Health services under the PMTCT unit at the Ministry of Health and Social Welfare (MoHSW). Many development partners are keenly involved in the program and their effort has been dedicated ever since.

Since then the program has been rolled out to other lower health facilities PMTCT services are now available throughout the country down to all the District hospitals and the health centres and majority of dispensaries. In 2009 of the 4647 health facilities with RCHC services in the country about 3626(78.6%) were providing PMTCT services (table3).

**Table 3: Tanzania PMTCT Coverage January – December 2009**

| Particular | National | PMTCT Coverage | Percent |
|---|---|---|---|
| No. of Regions | 21 | 21 | 100 |
| No. of Districts | 126 | 126 | 100 |
| Total No. of ANC facilities | 4647 | 3626 | 78.6 |
| Estimated New ANC 2009 | 1,611,870 | 1,223,964 | 76 |
| Tested for HIV | 1,611,870 | 1,125,185 | 70 |
| HIV Positive | 86000 | 70,423 | 5.8* |
| Received ARV prophylaxis /Estimates | 86,000 | 58,833 | 68 |
| Infants received Prophylaxis | 86,000 | 42,945 | 50 |

*prevalence

Derived from NACP spectrum analysis

## 2.0. Problem statement:

Parallel to updating the Adult and Adolescent treatment and care guidelines in 2010 WHO also updated the Guidelines on the Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. This was a result of adequate experience and significant new evidence that had accumulated on when to start ART in eligible pregnant women and the recommended regimens: and when to start ARV prophylaxis(including recommended prophylaxis drug regimens) in pregnant women who are not eligible for HAART This includes,: prophylaxis to newborn infants in the immediate postpartum, period and. extended post natal prophylaxis to breastfeeding-exposed infants beyond the immediate postpartum.

### 3.0. Rationale:

The purpose of the consultancy was 'to conduct a feasibility appraisal for the introduction of the revised 2010 WHO PMTCT and infant feeding recommendations for adoption in Tanzania.

Much as scientific evidence is accumulating towards eliminating MTCT of HIV and enhancing Child and Maternal survival the proposed WHO PMTC guidelines changes, will impact on the changes on health systems, equity, efficiency, responsiveness to affected population and public health outcomes (e.g. death, OI and TB rates, ARV toxicities and transmission of HIV) will be critical to the national HIV&AIDS programs. Therefore in developing or updating National PMTCT guidelines, WHO guidelines requires that both policy and programmatic implications in terms of: the , acceptability, **cost/financial implications and feasibility aspects** are clearly considered before introducing the change. Therefore, the MOHSW sponsored a feasibility appraisal in Tanzania to assess the likely impact of the proposed PMTCT guideline changes at the national programme level of the new WHO recommendations. The appraisal aimed at advising on the immediate impact likely to be felt by the national PMTCT programme if selected prophylaxis OPTION A or B recommendations are adopted. This has focused on what these guideline revisions would mean to Tanzania in terms of costs, staffing and service delivery requirements.

### 4.0. OBJECTIVES:

- Undertake a feasibility appraisal of the policy and programmatic implications for the national PMTCT programme in , Tanzania in introducing the 2010 updated who guidelines for PMTCT: laboratory capacity to identify eligible mothers for ART, cost effective option for ARV prophylaxis, and early infant HIV diagnosis. .
- Produce a report based on the results of the appraisal that can be used to inform MoHSW on selecting the option for national PMTCT PROGRAM.

## 5.0. METHODOLOGY:

The methodology which was used in the feasibility appraisal for the introduction of the revised 2010 WHO PMTCT and infant feeding recommendations for adoption in Tanzania; involved the use of several steps. These included desk reviews as well as qualitative and quantitative data capture. For each of these methodologies, specific details are given.

Desk appraisal involved extensive literature review of available relevant publications including some of them the following: documents: The Tanzania National Guidelines for the Management of HIV&AIDS NACP 2009, :Prevention of mother-to-child transmission of HIV. Tanzania National guidelines. 2007 (NACP)[14], Rapid advice use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infant(WHO.Nov 2009)[,48],National Scale up Plan for the Prevention of Mother to Child Transmission of HIV and Pediatric HIV Care and Treatment[46], HIV Early Infant diagnosis Guidelines for Tanzania and Antiretroviral (ARV) Price List(CHAI)[47], finally Published Research Articles on the subject. The desk review aimed at getting information on current performance of National HIV and the PMTCT programs and the existing treatment and the most recent operating PMTCT Guideline recommendations. It was also meant to collect information on financing issues when ARVs prophylaxis are to be offered at different scenarios in-order to project for the costs implications if recommended changes were adopted. Together with this laboratory costs were estimated to have a good picture the cost of the program in terms of ARVs + Laboratory costs It was also meant to collect information on the human resource implication if the recommendations are adopted Qualitative data was obtained through key Informant Interview (KII) and Focused group discussion (FGD) FGD interview guideline..

FGD targeted HIV infected women and non infected women found in the antenatal clinics with the aim of getting their views on

- Performance of the PMTCT under current criteria.
- Proposed changes in the ART and PMTCT guidelines
- Implications if guidelines were to change

KII was administered to technical groups, service providers and policy makers. Information sought was on their views with regard to:

- Current guideline and challenges in its implementation,
- Implications if Tanzania was to adopt proposed WHO guideline changes in terms of resources, coverage, quality of care, costs and financial sustainability and human resource

Data was also obtained from MoHSW recent draft documents (Report on the Rapid Feasibility Appraisal for the introduction of revised WHO ART recommendations: Tanzania country level inputs. December 2010[51 ] and, costing implications of adapting the new who recommendations[54 ]

Further, other sources of data was from the PMTCT UNIT of the Ministry of Health and Social Welfare (MoHSW), the National AIDS Control program (NACP),

Other type of data collected was on the following:

- ARV costs and funding projections
- Human resource issues
- Infrastructure including capacity for laboratory and minimum laboratory costs

**6.0: FINDINGS and DISCUSSIONS:**

The terms of reference (TOR) required that we visit Hospitals health centres and dispensaries in the following regions Mwanza Mbeya Dare s salaam, Kilimanjaro, Coast and Arusha. The team visited 28 health facilities in the 6 regions. These included dispensaries, health centres and District hospitals table 4. Most health facilities with RCH services have also established PMTCT services table 5. Uptake of testing and ARVS for PMTCT is shown table 6

**Table 4: Distribution of sites visited by level of care Health facilities visited**

| Name of facility | Level of facility | District | Region | Urban/Rural |
|---|---|---|---|---|
| Chekereni | Dispensary | Moshi Rural | Kilimanjaro | Rural |
| Geita | District hospital | Geita | Mwanza | Urba |
| Ikama | Dispensary | Kyela | Mbeya | Rural |
| Isansa | Dispensary | Mbozi | Mbeya | Rural |
| Ipinda | Healuth Centre | Kyela | Mbeya | Rural |
| Itumba | District Hospital | Ileje | Mbeya | Urba |
| Kahe | Dispensary | Moshi Rural | Kilimanjaro | Rural |
| Katunguru | Health Centre | Sengerema | Mwanza | Rural |
| Kilema | DD Hospital | Moshi Rural | Kilimanjaro | Rural |
| Longido | District Hospital | Longido | Arusha | Urba |
| Magu | District hospital | Magu | Mwanza | Urba |
| Makongoro | Healuth Centre | Nyamagana | Mwanza | Urba |
| Msia | Dispensary | Ileje | Mbeya | Rural |
| Mwasenkwa | Dispensary | Meya City | Mbeya | Rural |
| Ruanda | Healuth Centre | Meya City | Meya | Urba |
| Ukiluguru | Dispensary | Misungwi | Mwanza | Rural |
| Vwawa | District Hospital | Mbozi | Mbeya | Urba |
| Amana | District Hospital | DSM | DSM | Urban |
| Temeke | District Hospital | DSM | DSM | Urban |
| Mwananyamala | District Hospital | DSM | DSM | Urban |
| Sungwi | Dispensary | Kibaha | Coast | Rural |
| Mbagala RT | Dispensary | DSM | DSM | Urban |
| Buza | Dispensary | DSM | DSM | Urban |
| Kigamboni | Dispensary | DSM | DSM | Urban |
| Makangarawe | Dispensary | DSM | DSM | Urban |
| Maji matitu | Dispensary | DSM | DSM | Urban |
| Vijibweni | Dispensary | DSM | DSM | Urban |
| Zakiem | Dispensary | DSM | DSM | Urban |

**T able 5 District Health FACILITIES WITH PMTCT SERVICES AND CTCs**

| Name of District | RCH services | RCH with PMTCT services | CTC services | Facility Pmyct coverage % |
|---|---|---|---|---|
| Moshi Rural | 63 | 63 | 8 | 100 |
| Kyela | 34 | 34 | 7* | 100 |
| Mbozi | 37 | 37 | 4 | 100 |
| Ileje | 23 | 22 | 2 | 96 |
| Sengerema | 68 | 33 | 4** | 49 |
| Longido | 18 | 18 | 2 | 100 |
| Nyamagana | 37 | 32 | 19* | 86 |
| Meya City | 23 | 16 | 5 | 70 |
| Amana | 55 | 55 | 7 | 86 |
| Temeke | 64 | 64 | 6 | 100 |
| Mwananyamala | 58 | 58 | 12 | 98 |

**Table 6 HIV testing and counselling uptake(2010 qouarter3) and ARV regimen in use**

| FACILITY NAME | Facility level | New cases | Tested N | % | HIV +ve N | % | HIV+ve who had CD4 at CTC N | % | Prophylaxis regimen |
|---|---|---|---|---|---|---|---|---|---|
| Chekereni | Dispensary | 63 | 82 | **132** | 0 | **0** | 0 | **0** | NVP* |
| Geita | District Hospital | 1114 | 868 | **77.9** | 59 | **6.8** | 59 | **100** | ZVD |
| Ikama | Dispensary | 16 | 19 | **119** | 3 | **15,8** | 2 | **66.7** | NVP* |
| Isansa | Dispensary | 153 | 153 | **100** | 9 | **5.8** | 1 | 11.1 | NVP |
| Ipinda | Healuth Centre | 140 | 167 | **119.3** | 16 | **9.6** | 16 | **100** | ZVD |
| Itumba | District Hospital | 90 | 90 | **100** | 7 | **7,7** | 2 | **28.5** | ZVD |
| Kahe | Dispensary | 104 | 111 | **106.7** | 1 | **0.9** | 1 | **100** | NVP |
| Katunguru | Health Centre | 128 | 75 | **58.6** | 1 | **1.3** | 1 | **100** | NVP |
| Kilema | DD Hospital | 158 | 156 | **98.7** | 3 | **1,9** | 1 | **33.3** | ZVD |
| Longido | District Hospital | 114 | 114 | **100** | 2 | **1.8** | 2 | **100** | ZVD |
| Magu | District Hospital | 190 | 147 | **77.4** | 5 | **3.5** | 5 | **100** | ZVD |
| Msia | Dispensary | 34 | 23 | **67.6** | 2 | **8.6** | 0 | **0** | SdNVP* |
| Mwasenkwa | Dispensary | 36 | 35 | **97.2** | 3 | **8.6** | 3 | 100 | SdNVP* |
| Ruanda | Health Centre | 1397 | 852 | **62.8** | 79 | **9.3** | 30 | **37,9 (the others no reagent)** | ZVD |
| Ukiluguru | Dispensary | 95 | 75 | **78.9** | 5 | **6.5** | **all refered to district hospital** | | SdNVP* |
| Vwawa | District Hospital | 569 | 569 | **100** | 53 | **9.3** | 42 | **79.2** | ZVD |
| Amana * | DistrictHospital | 409 | 409 | **100** | 49 | **11.9** | 149 /160 | **93** | AZT, 3TC,NVP |
| Temeke * | District Hospital | 230 | 230 | **100** | 29 | **12.6** | 75/104 | **72** | AZT, 3TC,NVP |
| Mwananyamala | District Hospital | 460 | 460 | **100** | 52 | **11.3** | 171/223 | **76.7** | AZT, 3TC,NVP |
| Sungwi* * | Dispensary | - | - | | - | | - | | - |
| Mbagala Round Table | Dispensary | 1910 | 1131 | **59** | 122 | **10.7** | 61/840 | **7.2 ( no reagents, no CD4 facility , not functional machine)** | AZT, 3TC,NVP |
| Buza | Dispensary | 527 | 527 | **100** | 20 | **7.2** | 17/37 | **46** | AZT, NVP |
| Kigamboni | Dispensary | 689 | 397 | **57.6** | 19 | **4.8** | 19/29 | **65.5** | AZT,NVP |
| Makangarawe | Dispensary | 521 | 263 | **50.4** | 30 | **11.4** | 30/60 | **50** | AZT, ,NVP |
| Maji matitu | Dispensary | 979 | 572 | **58.4** | 13 | **2.3** | 13/288 | 4.5 **(done elsewhere)** | AZT, ,NVP |
| Vijibweni | Dispensary | 534 | 284 | **53** | 33 | 11.6 | 33/284 | **11.6( no reagents, no CD4** | AZT,NVP |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | facility , not functional machine) | | |
| Zakiem | Dispensary | 1999 | 931 | **46.5** | 22 | 2.4 | 81/103 | **78.6** | AZT, NVP |

Data from Yombo Vituka was not entred.
*These include those who have been referred from the catchment areas.
**On two occasions, there was no reliable staff available, and all the PMTCT charts and registers were under lock and key. There were only 2 patients seen in the centre.

There are 6 CTC in Temeke District RCH . (Temeke, Round table, Yombo, Rangi tatu, Makangarawe, Buza) . 2 CTC have no RCH centre: Vijibweni and Kigamboni. 1 new CTC expected to begin soon: Maji Matitu.

**Table 7: PMTCT implementing Partners in Areas Visited**

| Region | PMTCT Implementing partners |
|---|---|
| ARUSHA | Elizabeth Glaser Pediatric AIDS FoundatioN (EGPAF) |
| KILIMANJARO | Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) |
| MBEYA | Walter Reed |
| MWANZA | AIDS RELIEF |
| DSM | MDH |
| DSM | Clinton foundation |
| DSM | CDC |
| DSM | Paediatric Association of Tanzania |

**Table 8. Services available at visited sites**

| **Service** | Availability | Comment |
|---|---|---|
| **RCH** | Avilable up tp dispensary level | Most Dispensaries cannot measure Hb and. Bp measurement is sporadic. Staff available at this level are mainly Assistant Clinical Officer(ACO), Maternal Child Health Attendant (MCHA) and several medical attendants |
| **Booking Gestation** | Majority of pregnant women book between 16 – 24 weeks gestation | This provides opportunity to implement the new WHO recommendation of initiating the antepartum component of the treatment or prophylaxis. This will be early enough to allow for a minimum of more than 4 weeks of ARVs before labour and delivery With 94% |

| | | |
|---|---|---|
| | | of pregnant women making at liast one antenatal visit it is an opportunity to reach as many pregnant women as possible.(at least 80% the National target) |
| **PMTCT** | Available to dispensary level | Very few dispensaries that t have not established this services notably in Sengerema district. PMTCT services are offered routinely in RCH clinics. Each region is supported by a PMTCT development partner that oversee PMTCT operational activities, training of HCWs and ensure availability of supplies and adherence to standards as per national guidelines |
| **HIV testing and counseling** | PITC type | Almost all facilities are practicing PITC at the RCH clinics. Uptake of the programme is high in many facilities visited. This is so particularly in areas with low volume of clients(Dispensaries) as compared to clinics with high volume of clients (Health Centres-Makongoro and Ruanda health centers) see table 5 |
| **Male participation** | Very low | Disappointingly very low at every facility visited. Some health facilities have used a strategy by sending of invitation letters but this has not worked so far . Because of stigma, disclosure has been extremely low making PMTCT interventions mainly a female involment affair |
| **CD4 Testing** | Done at CTCs with testing capacity | Almost all the district hospitals and some health centres have the capacity to perform CD4 cell count.. CTCs without capacity blood is drown and send to CTCs with testing capacity. This challenge at dispensary level is more serious where the client has to travel to a CTC with testing capacity which in many cases is very far away. This demotivate mothers because of the distance and cost of the transport that may be incurred. Mobile outreach laboratory services should be considered |
| **Antiretroviral prophylaxis and treatment** | MECR, sdNVP | More efficacious regimen (MECR) AZT - starting from 28 weeks gestation is the current regimen used in many clinics. This has replaced sdNVP as far down as at health centre level. This will facilitate introduction of the New WHO recommendations because of the experience already accumulated. SdNVP is still being used at dispensary level by the time of the visit Found during this visit training had just finished at dispensary level and some dispensaries were given AZT but had not yet started using them. Their major concern was how can they monitor development of anemia when they cannot measure the level of Hb at that level |
| | HAART<br>&<br>CD4 count≤ 350//$mm^3$. | Women eligible for ART are referred to CTC for evaluation and initiation of ART. In all 6 regions ART for pregnant women is initiated at CD4 ≤ 350cells//$mm^3$/ cells/$mm^3$. No site was using HAART for PMTCT prophylaxis in non eligible HIV infected mothers |

| | | |
|---|---|---|
| **Linkage with CTC** | Referral via a referral form | At the ANC women who are found to be HIV positive are referred to CTC using a special form. When the CTC is within facility clients are escorted by counsellors, but when it is far clients have to travel alone and have to find their own transport to the CTC, This affects most of the women attending ANC at the dispensary level. |
| **Infant follow up** | At postnatal clinic and CTC | This works well when these clinics are within the same facility. The problem arises at dispensary level when the mother and infant have to travel to a CTCs which in many cases are far away. |
| **HEID** | Done at MNH,KCMC,BMC & MRH | This is done at the zonal consultant hospitals Average turn over time for results is 4 weeks, sometimes 8 to 10 weeks even more when they have stock out of reagents. This demotivate mothers from continuous follow up of results in general but in particular those at dispensary level. Results are sent by sms to CTCs . Children found infected are initiated treatment at the CTC where follow up is continued. . May clinics reported frequent stock out of DBS kits |
| **Infant feeding** | EBF for 6 mo and rapid weaning | Majority of women choose exclusive breast feeding for 6 months and are counselled for rapid weaning |
| **SUPPLIES** | Fair for ARVs but not for PCR reagents and DBS kits | Providers were satisfied with ARV drug supply , This is due to low demand. Major complaint from providers is erratic supply of DBS kits and out of stock of reagents for CD4 testing and PCR |
| **HR** | Fair | Shortage observed at all levels but more severe at dispensary level. Recommend comprehensive training of all staff at the facility considering that they all rotate in RCHC |

Estimating the number of patients requiring ARV prophylaxis after new WHO guidelines; ARVs and minimum Laboratory costs of different options

The quantitative data served as the basis for estimation of number of patients requiring ARV prophylaxis and its cost implications in different scenarios should Tanzania decide to adopt the WHO proposed PMTCT Guideline changes. By cross-tabulating WHO clinical staging and CD4+ categories the numbers of HIV patients eligible for ARV initiation can be projected as depicted the table 9 below. According to the Tanzania guidelines for management of HIV/AIDS, the number of HIV patients requiring treatment under the current criteria is equal to summation of A, B, C, D, G, and H. In view of the WHO proposed changes ,where the CD4 cell count threshold for initiating ART has been set at ≤ 350cells//$mm^3$/E+F+K will be additional load for ART .table 9. Costing for this group has been worked elsewhere (Costing Implications of Adapting the New WHO recommendations

in Tanzania[54]). Group **I+J** will need ARV prophylaxis for PMTCT only because this group is not eligible for maternal ART. We have projected for group I+J only which requires ARV for prophylaxes only if the New WHO Recommendations are adopted in Tanzania.

"

**Table 9: ASSUMMED distribution of patients by WHO clinical stage and CD4+**

| CD4+ | WHO Clinical Stage | | | |
|---|---|---|---|---|
| | I | II | III | IV |
| <200 | A | B | C | D |
| 200 – 350 | *E* | *F* | *G* | H |
| >350 | I | J | *K* | L |

**Assumptions used**

1. HIV epidemic will not change significantly
2. National PMTCT performance will reach target indicators each year
3. National pattern of CD4+/WHO clinical stage is constant but similar to that observed in the past

## Possible Scenarios based on adopting option A or B of the revised WHO PMTCT Recommendations

The following are estimated costs associated with adopting different options of the revised WHO recommendations, for pregnant women who are not eligible for ART. Estimates of costs for pregnant women eligible for ART including infants less than one year are included in the, Costing Implications of Adapting the New WHO Recommendations document[54]

Assumptions: **A: Pregnant Women for Prophylaxis for PMTCT of HIV**

Table 10

| | |
|---|---|
| Pregnant women (NBS 2010) | 1,823,780 |
| Proportion making 1 ANC visit 94% | 1713532 |
| HIV counselling and testing program reaches 80% | 1,370826 |
| ANC HIV prevalence rate(NACP Survey report No 4) | 7% |
| HIV+ women identified | 95958 |
| 80% reached with prophylactic intervention | 76766 |
| **Women to put on prophylaxis for PMTCT of HIV in old guidline(cd4 >200** | 61413 |
| Under old guidelines 20% CD4≤200 expected to be eligible for ART | 15353 |
| Under new guidelines 40% CD4≤350 expected to be eligible for ART | 30706 |
| **Women to put on prophylaxis for PMTCT of HIV** | **46060** |

Assumptions B: ***Infants < 1 year***

Table 11

| | |
|---|---|
| Pregnant women (NBS 2010) | 1,823,780 |
| Proportion making 1 ANC visit 94% | 1713532 |
| HIV counselling and testing program reaches 80% | 1,370826 |
| ANC HIV prevalence rate(NACP Surv report No 4) | 7% |
| HIV+ women identified | 95958 |
| Infants born infected | 3838 |
| EXPOSED INFANTS | 92120 |
| 80% reached with prophylactic intervention | 73696 |
| Under new guidelines 40% pregnant women expected to be eligible for ART so infant prophylaxis for 6 weeks only | 30706 |
| **INFANTS TO PUT ON PROPHYLAXIS FOR PMTCT** | **42990** |

### Laboratory Monitoring

Routine Laboratory monitoring costs for patients on treatment are estimated elsewhere(Costing Implications of Adapting the New WHO in Tanzania[54] )

Patients who are not yet eligible for ART should have CD4 count measurement (if available)every 6 months and more frequently as they approach the threshold to initiate ART

**Table 10 a: Estimated costs to reach 80% of all pregnant women for ARV prophylaxis:**

**1. Under current ARV drug regimens. (MECR-AZT from 28wks).**

**2. Under new WHO recommendations, OPTION A 2011-2015.**

**1. Estimated costs(usd) for prophylaxis Current regimen (MECR) Maternal AZT from 28 weeks where ART eligibility is CD4 ≤200**

| | 2011 | 2012 | 2013 | 2014 | 2015 | TOTAL |
|---|---|---|---|---|---|---|
| New Pregnant Women for ARV prophylaxis | 61413 | 61413 | 61413 | 61413 | 61413 | |
| ARV costs maternal/child/year usd | 26.8 | 26.8 | 26.8 | 26.8 | 26.8 | |
| **ARV costs National)** | **1645868.4** | **1645868.4** | **1645868.4** | **1645868.4** | **1645868.4** | **8229342** |
| **Lab cost maternal/child/year usd** | **49.67** | **49.67** | **49.67** | **49.67** | **49.67** | |
| **Lab costs National usd** | **3050383.7** | **3050383.7** | **3050383.7** | **3050383.7** | **3050383.7** | **15251918.5** |
| **Total ARV + Lab costs National** | **4696252.1** | **4696252.1** | **4696252.1** | **4696252.1** | **4696252.1** | **23481260.5** |
| **2. Estimated costs for New WHO Option A regimen prophylaxis Maternal AZT from 14 weeks where ART eligibility is CD4 ≤350** | | | | | | |
| New Pregnant Women for ARV prophylaxis | 46060 | 46060 | 46060 | 46060 | 46060 | |
| **a)**.ARV costs maternal/child/ 6mo usd | 55.25 | 55.25 | 55.25 | 55.25 | 55.25 | |
| **ARV costs National for 6 months post natal infant prophylaxis** | **2,544,815** | **2,544,815** | **2,544,815** | **2,544,815** | **2,544,815** | 12724075 |
| **Lab Costs maternal/child 6 mo** | **49.67** | **49.67** | **49.67** | **49.67** | **49.67** | |
| **Lab costs National** | **2287800.2** | **2287800.2** | **2287800.2** | **2287800.2** | **2287800.2** | 11439001 |
| **Total ARV + Lab costs National** | **4832615.2** | **4832615.2** | **4832615.2** | **4832615.2** | **4832615.2** | **24163076** |
| **b)**ARV costs maternal/child/ 12 mo usd | 57 | 57 | 57 | 57 | 57 | |
| **ARV costs National for 12 months post natal infant prophylaxis** | **2,625,420** | **2,625,420** | **2,625,420** | **2,625,420** | **2,625,420** | 13127100 |
| **Lab Costs maternal/child 12 mo usd** | **100** | **100** | **100** | **100** | **100** | |
| **Lab Costs National 12 mo us** | **4606000** | **4606000** | **4606000** | **4606000** | **4606000** | 23030000 |
| **Total ARV + Lab cost National** | 7231420 | 7231420 | 7231420 | 7231420 | 7231420 | **36157100** |

**Table10b: Estimated ARV& Laboratory Costs to reach 80% of pregnant women based on New WHO prophylaxis Recommendation Option B regimen from 14 weeks where ART eligibility is CD4 ≤350 Recommended regimens scenarios of Option B (Maternal) 2011-2015.**

| | 2011 | 2012 | 2013 | 2014 | 2015 | |
|---|---|---|---|---|---|---|
| New preg women for ARV prophylaxis | 46060 | 46060 | 46060 | 46060 | 46060 | |
| OPTION B1: AZT + 3TC + LPV/r + NVP syrup for the new born up to 6 wks | | | | | | |
| i). ARV cost M/C pair from 14wks to 6 mo postnatal usd | 565.5 | 565.5 | 565.5 | **565.5** | **565.5** | |
| ARV costs National | 26046930. | 26046930. | 26046930. | 26046930. | 26046930. | 130234 |
| Lab costs M/C pair for 6mo | 100 | 100 | 100 | 100 | 100 | |
| Lab costs National usd | 4606000 | 4606000 | 4606000 | 4606000 | 4606000 | 230300 |
| **Total ARV+Lab cost National** | 30652930 | 30652930 | 30652930 | 30652930 | 30652930 1 | **153264** |
| ii) ) ARV cost M/C pair from 14 wks to 12mo postnatal | 848 | 848 | 848 | 848 | 848 | |
| ARV costs National | 39058880 | 39058880 | 39058880 | 39058880 | 39058880 | 195294 |
| Lab costs M/C pair for 12mo | 150 | 150 | 150 | 150 | 150 | |
| Lab costs Nation usd | 6909000 | 6909000 | 6909000 | 6909000 | 6909000 | 345450 |
| **Total ARV + Lab cost National** | 45967880 | 45967880 | 45967880 | 45967880 | 45967880 | **229839** |
| OPTION B2: AZT + 3TC + ABC + NVP syrup 6 wks | | | | | | |
| 1)ARV cost M/C pair from 14w to 6 mo postnatal usd usd | 347.5 | 347.5 | 347.5 | 347.5 | 347.5 | |
| ARV costs National | 16005850 | 16005850 | 16005850 | 16005850 | 16005850 | 8002925 |
| Lab costs National usd | 4606000 | 4606000 | 4606000 | 4606000 | 4606000 | 2303000 |
| **Total ARV+Lab cost National** | 20611850 | 20611850 | 20611850 | 20611850 | 20611850 | **1030592** |
| ii) ) ARV cost M/C pair from 14 wks to 12mo postnatal | 521 | 521 | 521 | 521 | 521 | |
| ARV costs National usd | 23997260 | 23997260 | 23997260 | 23997260 | 23997260 | 1199863 |
| **Lab costs Nation usd** | **6900900** | **6900900** | **6900900** | **6900900** | **6900900** | 3454500 |
| Total ARV + Lab cost National | **30898160** | **30898160** | **30898160** | **30898160** | **30898160** | **1544908** |
| OPTION B3: AZT + 3TC + EFV + NVP syrup for the neonate up to 6 wks | | | | | | |
| 1)ARV cost M/C pair from 14w to 6 mo postnatal usd | 200.5 | 200.5 | 200.5 | 200.5 | 200.5 | |
| ARV costs National usd | 9235030 | 9235030 | 9235030 | 9235030 | 9235030 | |
| Lab costs Nation usd | 6909000 | 6909000 | 6909000 | 6909000 | 6909000 | |
| **Total ARV + Lab cost National** | 16144030 | 16144030 | 16144030 | 16144030 | 16144030 | 8072015 |
| Ii))ARV cost M/C pair from 14 wks to 12mo postnatal | 300.5 | 700.5 | 300.5 | 300,5 | 300.5 | |
| ARV costs National 300. | 13841030 | 13841030 | 13841030 | 13841030 | 13841030 | 6920515 |
| Lab costs Nation usd | 6909000''' | 6909000''' | 6909000''' | 6909000''' | 6909000''' | 3454500 |
| **Total ARV + Lab cost National** | 20750030 | 20750030 | 20750030 | 20750030 | 20750030 | **1037501** |

| OPTION B4: TDF + 3TC (or FTC) + EFV + NVP syrup for the neonate up to 6 wks | | | | | | |
|---|---|---|---|---|---|---|
| i)ARV cost M/C pair from 14w to 6 mo postnatal usd usd | 194.5 | 194.5 | 194.5 | 194.5 | 194.5 | |
| ARV Costs National usd | 8958670 | 8958670 | 8958670 | 8958670 | 8958670 | 4479335 |
| Lab costs Nation usd | 4606000 | 4606000 | 4606000 | 4606000 | 4606000 | 2303000 |
| **Total ARV + Lab cost National** | 13564670 | 13564670 | 13564670 | 13564670 | 13564670 | **6782335** |
| ii) ) ARV cost M/C pair from 14 wks to 12mo postnatal usd | 291.5 | 291.5 | 291.5 | 291.5 | 291.5 | |
| ARV costs National usd | 13426490 | 13426490 | 13426490 | 13426490 | 13426490 | 6713245 |
| Lab costs Nation usd | 6909000' | 6909000' | 6909000' | 6909000' | 6909000' | 3454500 |
| **Total ARV + Lab cost National** | 20335490 | 20335490 | 20335490 | 20335490 | 20335490 | **1016774** |

Considering that option A is similar to option B in terms of efficacy it is obvious that option A table 10 a is cheaper and more cost effective than any of the options B table10b above provided it is implemented effectively. For this option to have the impact the program should have the capacity to identify women eligible for ART and link r them to CTC Though option A is cheaper than any of option B, it may not be all that the easiest to implement when you consider that;

- Sero status disclosure in the family/communiyy is very low
- There must be capacity to monitor and prevent development of anemia
- Male participation in PMTCT is very low
- Infants are left with grandmas or baby minders and therefore this mayl affect treatment adherence and mode of infant feeding
- Babies are not good for long term medication program as this may end in vomiting medicine or refusing medicine. This will affect adherence

This area requires monitoring to see how effective this option impacts on PMTCT. It is very important to emphasise that

- Mothers in need of ART for their own health should get lifelong treatment
- Importance and critical need of CD4 for decision-making on ART eligibility
- Maximize effectiveness of interventions to reduce mother-child HIV transmission risk
- Effective postpartum antiretroviral-based interventions for women or children will allow safer breastfeeding practices
- Simple, to implement but cost effective programs should be one of the major reasons for the country to decide on the option recommended,

**Table 11: Reasons for Option A than B:**

| Sn | Option A | Option B |
|---|---|---|
| 1 | Low rates of adverse events in infants | Low rates of adverse events in infants |
| 2 | Low rates of maternal NVP resistance with use of AZT+3TC tail, (changing of regimen between ante and postpartum is not simple) | No change of maternal regimen between ante- and postpartum period |
| 3 | Long half life of NVP allows potential miss in daily dose (BF population) But dose adjusting is complex as the child grows. | May improve maternal health during the prophylactic period |
| 4 | No drastic change into the existing guidelines and M&E framework if adapted | Drastic changes in the guidelines and M&E framework if adapted |
| 5 | Short refresher training (minimal investment is required) | Might need longer refresher training ( much more resources will be required) |
| 6 | No change of policy is required to implement option A at all levels | Change of policy is required to implement option B at all levels |
| 7 | Strengthening of the existing model of care is required to implement option A at all levels | Change of model of care is required to implement option B at all levels (manning level, frequency of visits, enhanced competence to deal with triple therapy side effects) |
| 8 | Likelihood of NNRTI resistance in infected infants | Likelihood of multiple drug resistance in mothers and infected infants |
| 9 | Safety, effectiveness and feasibility of NVP beyond 6 months in infants is not known | Acceptability of prolonged triple ARV is not known |

**Table 12: Advantages and Disadvantages of Tanzania Adopting the New WHO Recommendations**

| Advantages | Disadvantages |
|---|---|
| • Pregnant women are an easily accessible population through RCH services, available in 4,647 health facilities<br>• PMTCT services already available in more than 4,000 health facilities throughout Tanzania, which would facilitate implementation of new recommendations<br>• Mother represents index patient for entire family (partner and other children); by putting mother on treatment you can simultaneously:<br>  ○ prevent infection in infants since pregnant women with/CD4 < 350 account for 80% of HIV transmission<br>  ○ save on costs for pediatric HIV services and eliminate additional and complicated drug regimens required<br>  ○ prevent infection of sexual partner (for discordant couples)<br>  ○ prevent re-infection (for positive sexual partners)<br>  ○ prevent transmission to infants in future pregnancies<br>  ○ prevent opportunistic infections in mothers<br>• Children need their mothers – when maternal deaths are averted there is a positive impact on under-5 mortality<br>• Pregnant women are relatively young which means there is an economic benefit of keeping them healthy (avoiding loss of productivity due to illness for mother and household)<br>• Global community is focused on PMTCT and interested in funding PMTCT programs<br>• PMTCT program has plan in place for Costing study/evaluation that will generate critical information on program cost that can be used for future planning<br>• Can easily integrate other programs (e.g. family planning) into PMTCT programs<br>• Strategic planning documents already approved and in place for scaling up PMTCT programs which can be adjusted for new WHO recommendations | • Women in this target group are relatively healthy (as evidenced by their pregnancy) – because they are not sick it may be more difficult to retain them on ART and this could have implications on:<br>  ○ their adherence to treatment and future health<br>  ○ drug resistance (due to poor adherence)<br>  ○ additional costs related to added support groups/adherence counselling<br>• Cost for this target group higher than others<br>• *Limitations of model*<br>  ○ *All women assumed to become pregnant only once (may be double counting)* |
| **Summary Recommendation:**<br>Based on the advantages of this program, particularly prevention of infection to infants and maternal survival we recommend Tanzania adopt this new WHO recommendation and evaluate its implementation over time. | |

## 7. CONCLUSION

Significant progress has been made in developed countries where transmission rates have fallen to less than 2%. However, it has not been easy to replicate the same feat in resource poor settings. Some of the challenges that we need to address include

1) Development of an effective drug delivery system that facilitates distribution of Combination antiretroviral for prophylaxis to all mothers and babies requiring it
2) How best to incorporate anti-retroviral drugs in post natal prophylaxis programs while Encouraging breastfeeding (in light of its many advantages) and
3) To overcome the challenges of drug resistance which emerges as a result of Prophylactic therapy and ascertain what influence it would have on potential commencement of HAART by the baby and the mother. Though PMTCT services are now available in almost 86% of health facilities these need strengthening for program effectiveness. However future efforts to prevent HIV transmission should focus on rapid scale-up and implementation of the current mother-to-child HIV prevention programs while incorporating positive changes that future research may unveil.
4) There is already a laid down ground to implement option A of the New WHO recommendations therefore it is much easier to adopt this without changing policy, there is already an accumulated experience. Dispensaries which will be starting the programme for the first time will benefit by starting with this option. However providers will need to be oriented on the changing dose of the drug for the infant during postnatal period
5) There is room to improve quality of services at all levels but much so at health centres and dispensaries.

## 8. Recommendations

- Adapt the new WHO PMTCT recommendations of starting ART or ARV prophylaxis as early as possible after the first trimester because this is feasible
- Because of the known advantages of initiation of ART at CD4 count threshold ≤ 350 this should be adopted, officially
- Health workers in RCH should make extra efforts to identify HIV infected pregnant women and evaluate them so that those eligible for HAART are provided for
- The program should urgently facilitate availability of Hemoglobin tests at dispensaries in light of use of AZT
- To motivate clients to adhere to the programme DBS kits should be available regularly and so is HEID results in time so that infected infants are initiated treatment as early as possible,
- In view of the functioning capacity which is in place now and the pace of scaling up and the cost in the programme Option A (INFANT PROPHYLAXIS) is recommended for the time being. provided the providers effectively are able to identify women who need ARV for their health However close monitoring to see that good adherence is followed otherwise we may not get the desired effect mainly because of poor adherence
- Primary health facilities should be assisted so that laboratory specimen are collected on site rather than referral to CTC sites which are very far away. Encourage outreach programmes especially laboratory services
- .Get more community health workers involved in the PMTCT programme
- There should be room for consultant hospitals to adopt option B because they have the required capacity. Data from these institutions can be useful learning experience

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**APPENDIX 1**

## Terms of Reference for Tanzania's adoption of 2009 WHO guidance for PMTCT of HIV.

### Background

In the deliberate efforts to reduce Mother to child transmission of HIV, the Government of Tanzania is rolling out the implementation of the national guidelines developed and approved in 2006. While the science of PMTCT of HIV is still going on intensively locally and world-wide, It has come to fore that the scientific findings obtained, compel us to use this new information in order to further reduce MTCT of HIV and improve quality of life among HIV exposed and infected children.

In December 2009, the WHO has provided new recommendation on PMTCT in the light of the most technically feasible and relatively safe infant feeding option, and that is Breast feeding. The recommendations provide guidance to countries on how to significantly reduce HIV transmission from mother-to-child. The recommendations represent significant shifts in current practice including; revision of CD4 threshold for initiation of ART; time for initiation and duration of prophylaxis for PMTCT as well as more effective treatment and prevention regimens, More over the new recommendations calls for extension of breastfeeding duration for women living with HIV. Therefore the Government has initiated the process of revising its National Guidelines to align with the WHO recommendations.

However, incorporating these new recommendations can be challenging and an overwhelming task, thus the country must be able to critically look at and support its health system in terms of feasibility, sustainability and access in adopting these recommendations.

### Objective

To conduct Rapid Assessment for the introduction of revised WHO PMTCT, and Pediatric ART and infant feeding recommendations, critically analyzing policy and programme implications of implementing the new recommendations and to examine different scenarios in which recommendations are to be adopted.

### Scope of work of consultancy:

1. Familiarize with the existing documents (PMTCT, HIV care and treatment including pediatric ART guidelines; Infant and young child nutrition guidelines in the context of HIV etc).

2. Conduct rapid assessment for the introduction of the revised WHO PMTCT, Pediatric ART and infant feeding recommendations.

a. Identify data sources; Ministry + other sources with representative data from at least 30 sites-6 hospitals,9 health centres and 15 dispensaries both public and private health

facilities in urban and rural settings( Consider health facilities with High volume in areas with high prevalence).

b. Develop simple data collection tool and share with the PMTCT Secretariat -MoHSW.

c. Collect data and conduct key interviews (these should include additional qualitative elements) and field visits to the identified sites including those that may be in the plan for expansion.

d. Develop estimates/inputs for data elements such as:

- Access and volume
  - What is the current status of the national programme in ensuring all pregnant women living with HIV receive more efficacious prophylaxis/ART as needed.
  - What are estimated numbers of pregnant women living with HIV who will be in need of ART yearly, over the next five years if the CD4 count threshold for starting long term ART is revised to 350?
  - What are estimated numbers of pregnant women living with HIV who will be in need of Prophylaxis yearly over the next five years?
  - What will be the impact on the numbers of infected children and the need for pediatric treatment following improved access to more efficacious ARV prophylaxis for prevention of mother-to-child transmission?

- Prophylaxis options
  - What are the expected benefits and constraints of using the chosen option for prophylaxis included in the 2009 WHO recommendations?
  - What is the cost effective way of ensuring HIV infected pregnant have access to CD4 testing and getting timely results (preferably within two weeks).
  - What would be the required adjustments to meet diagnostic requirements (CD4 & DBS samples) for the recommended changes in the guidelines
- Supply Chain
  - What volume and cost of the additional ARVs would be required?

- Sites
  - Given cost and constraints, what is a feasible rate at which scale-up of prophylaxis could take place under different scenarios of guideline adoption?
  - What would be the cost effective way of ensuring exposed infants have access to early infant diagnosis and those infected are linked to Care and Treatment services.
  - What would the priority sites be, based on need?
  - What are site storage and stock level implications?

- Human Resources
  - What will be the costs for human resource capacity building needed to provide new prophylaxis to HIV infected pregnant women and exposed infants?
  - What is the most cost-effective way of building HR capacity to support introduction and scale up of the new recommendations without hampering the quality of services?

- Others
  - What other changes to follow up and monitoring requirements might be needed to implement the recommended regimen?
  - What would be the model of service provision needed at primary, secondary and tertiary levels of health facilities in order to provide new prophylaxis to HIV infected pregnant women and ART to eligible pregnant women in line with the new WHO guidelines

e. Consider the use of models to estimate and project ART/prophylaxis and other commodities needs under different scenarios

**Approach**

A team of three consultants will conduct the rapid appraisal for introduction of new WHO recommendations, among them one is appointed as a team leader.

The approach of conducting this consultancy will be as follows:

- Consultants will familiarize themselves with the existing documents
- Visit selected sites and conduct interviews with key people including PMTCT implementing partners
- Prepare the draft 0 report and share with the TWG in a one day meeting
- Incorporate the comments and prepare final report ready for submission

**Required Competencies and Qualifications**

- Minimum of MD/MPH or MSc/MMED
- Demonstrated extensive experience and knowledge in the areas of PMTCT, Paediatrics HIV care and treatment and infant feeding in the context of HIV.
- Demonstrated experience in the Tanzania health care system
- Excellent knowledge of international policy on PMTCT ,Pediatrics HIV and Infant feeding with regard to strategies of HIV prevention, care and treatment
- Must be capable to work in a team

**Deliverables**

The lead consultant will be responsible for reporting the following deliverables to the PMTCT Secretariat of the MOHSW:

1. Estimates from various data elements highlighted above
2. Comprehensive report on the feasibility, accessibility, sustainability and impact of incorporating these changes.
3. Detailed recommendations of strategies on how to build Human Resource capacity to support introduction and scale up of new recommendations.
4. Advise on model care depending on the level of facility
5. Recommend on immediate, intermediate and longterm measures of rolling out new guidelines basing on responsibilities at different health facility levels.
6. The final report will be submitted after incorporating comments from the TWG

**HPTN 046**

## Key Messages/Talking Points: Primary 6-Month Results

### Background

HPTN 046 is a Phase III, randomized, placebo-controlled clinical trial designed to determine the efficacy and safety of an extended regimen of nevirapine in infants born to HIV-infected women to prevent vertical HIV transmission during breastfeeding.

The study was conducted at sites in four African countries:

- Durban, South Africa: Prince Mshiyeni Hospital
- Dar es Salaam, Tanzania: Muhimbili Hospital
- Kampala, Uganda: MUJHU Clinic/Mulago Hospital
- Chitungwiza, Zimbabwe: Chitungwiza Clinics

All breastfeeding HIV-exposed infants received daily Nevirapine (NVP) from birth to age 6 weeks, at which point, those who were determined to be HIV-uninfected and otherwise eligible (n=1,522) were randomized to receive daily extended NVP (n=759) or placebo (n=763) through age 6 months or through cessation of breastfeeding, whichever was earliest.

- Randomization was stratified by maternal antiretroviral drug use (29% of mothers were receiving antiretroviral drugs for their own health at the time of randomization).
- HIV infection was defined as confirmed positive HIV DNA PCR.
- Time of infection was defined as the midpoint between the last negative and first positive test.
- Complete data for evaluation of the primary 6-month endpoint are available for all infants.
- Follow-up is ongoing. Infants are followed through 18 months of life; all randomized infants are expected to have reached that point by July 2011.

Prior to this trial, the incremental benefit of extending infant NVP prophylaxis from 6 weeks (as in SWEN) to 6 months (as in BAN) had not been directly evaluated.

### Findings

1. This trial had high retention rates: 97% retention at 6 months, with 99% complete data for the primary efficacy and safety endpoints among those retained.

2. Adherence to study drugs (defined as taking all scheduled doses of drug by self-report) was 88-96% through 6 months of age and balanced between the two study arms. 95% of women in each arm reported exclusively breastfeeding through 3 months and 85% at 5 months.

3. The study was balanced between study arms in maternal baseline characteristics and CD4+ cell count at randomization; use of antiretroviral drugs for one's own health at randomization and at 6 months; and breastfeeding duration.

a. Extended daily NVP was found to be safe and well-tolerated by infants through 6 months of age, with no significant difference in adverse events (including serious adverse events) between the two study arms. Adverse events were seen in 83% of infants in each arm and serious adverse events in 19% of extended NVP and 17% of placebo infants.

b. The study found that extending daily infant NVP from 6 weeks to 6 months lowers the risk of breast milk HIV transmission at age 6 months overall, and that extended infant NVP is most important for infants of mothers with high CD4+ cell counts (>350 cells/$mm^3$) who are not receiving antiretroviral therapy. Postnatal infection rates were low among breastfeeding infants of mothers receiving antiretroviral therapy for their own health and did not differ when infants were given 6 weeks vs. 6 months of NVP. Thus, this study supports the benefits and safety of extended infant NVP to prevent breast milk transmission in infants of HIV-infected mothers who do not yet require antiretroviral therapy for their own health (those with CD4 $\geq$ 350 cells/$mm^3$).

c. HIV infection risk after age 6 months (after the extended NVP intervention had ceased) accounted for 30% of all transmission and was similar between study arms.

d. Mortality risk was similar between study arms; however, two-thirds of deaths occurred after age 6 months, when the majority of mothers had reported cessation of breastfeeding. Only 12% of deaths occurred in infants known to be HIV-infected. Mortality was also similar in infants born to mothers receiving and not receiving antiretroviral therapy for their own health.

e. Continued follow-up of the children through age 18 months is ongoing and will be completed in July 2011. Resistance testing of infected infants is planned.

4. Messages relevant to current WHO guidelines:

- WHO recommends treatment of women with CD4 counts of <350 cells/$mm^3$ with antiretroviral drugs for their own health. HPTN 046 demonstrated low transmission rates in women who received antiretroviral drugs for their own health.
- Use of extended infant NVP in infants born to mothers with CD4 $\geq$ 350 cells/$mm^3$ who are not receiving antiretroviral drugs is relatively simple, inexpensive and highly effective in reducing postnatal infection after age 6 weeks during the period in which it is given.
- Once the intervention has stopped, the risk of postnatal infection recurs if continued breastfeeding occurs.
- To date, two-thirds of infant mortality occurred in infants between 6 and 12 months of age. This supports other studies which have shown increased mortality following cessation of breastfeeding at 6 months.
- These data support continued breastfeeding beyond 6 months with use of infant NVP to prevent breastfeeding transmission beyond 6 months in order to maximize infant survival and prevent HIV transmission.

3. The study was balanced between study arms in maternal baseline characteristics and CD4+ cell count at randomization; use of antiretroviral drugs for one's own health at randomization and at 6 months; and breastfeeding duration.

a. Extended daily NVP was found to be safe and well-tolerated by infants through 6 months of age, with no significant difference in adverse events (including serious adverse events) between the two study arms. Adverse events were seen in 83% of infants in each arm and serious adverse events in 19% of extended NVP and 17% of placebo infants.

b. The study found that extending daily infant NVP from 6 weeks to 6 months lowers the risk of breast milk HIV transmission at age 6 months overall, and that extended infant NVP is most important for infants of mothers with high CD4+ cell counts (>350 cells/$mm^3$) who are not receiving antiretroviral therapy. Postnatal infection rates were low among breastfeeding infants of mothers receiving antiretroviral therapy for their own health and did not differ when infants were given 6 weeks vs. 6 months of NVP. Thus, this study supports the benefits and safety of extended infant NVP to prevent breast milk transmission in infants of HIV-infected mothers who do not yet require antiretroviral therapy for their own health (those with CD4 $\geq$ 350 cells/$mm^3$).

c. HIV infection risk after age 6 months (after the extended NVP intervention had ceased) accounted for 30% of all transmission and was similar between study arms.

d. Mortality risk was similar between study arms; however, two-thirds of deaths occurred after age 6 months, when the majority of mothers had reported cessation of breastfeeding. Only 12% of deaths occurred in infants known to be HIV-infected. Mortality was also similar in infants born to mothers receiving and not receiving antiretroviral therapy for their own health.

e. Continued follow-up of the children through age 18 months is ongoing and will be completed in July 2011. Resistance testing of infected infants is planned.

4. Messages relevant to current WHO guidelines:

- WHO recommends treatment of women with CD4 counts of <350 cells/$mm^3$ with antiretroviral drugs for their own health. HPTN 046 demonstrated low transmission rates in women who received antiretroviral drugs for their own health.
- Use of extended infant NVP in infants born to mothers with CD4 $\geq$ 350 cells/$mm^3$ who are not receiving antiretroviral drugs is relatively simple, inexpensive and highly effective in reducing postnatal infection after age 6 weeks during the period in which it is given.
- Once the intervention has stopped, the risk of postnatal infection recurs if continued breastfeeding occurs.
- To date, two-thirds of infant mortality occurred in infants between 6 and 12 months of age. This supports other studies which have shown increased mortality following cessation of breastfeeding at 6 months.
- These data support continued breastfeeding beyond 6 months with use of infant NVP to prevent breastfeeding transmission beyond 6 months in order to maximize infant survival and prevent HIV transmission.

These results provide additional information to allow policy makers to make decisions about the use of extended NVP by breastfeeding infants born to targeted groups of HIV-infected women (those with CD4 $\geq$ 350 cells/mm$^3$ ).

**Additional Background**

The study was sponsored by the US National Institute of Allergy and Infectious Diseases (NIAID) and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH), initially through the HIV Prevention Trials Network (HPTN) and later through the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group.

Study products were provided free of charge by Boehringer Ingelheim Pharmaceuticals.

The study was originally initiated in February 2007; however, enrollment was halted in August 2007 when the results of the SWEN study became available. HPTN 046 was then re-designed to provide daily NVP to all infants through six weeks of age. The study was re-started under the current design in May 2008; enrollment was completed in January 2010. Complete data for the primary 6-month endpoints are available and were included in these analyses. Follow-up is ongoing.

Picture from UNAIDS annual report 2009