

Country adaptation of the 2010 World Health Organization recommendations for the prevention of mother-to-child transmission of HIV

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Abstract The World Health Organization (WHO) revised its global recommendations on treating pregnant women infected with the human immunodeficiency virus (HIV) with antiretrovirals and preventing mother-to-child transmission (PMTCT) of HIV. Initial draft recommendations issued in November 2009 were followed by a full revised guideline in July 2010. The 2010 recommendations on PMTCT have important implications in terms of planning, human capacity and resources. Ministries of health therefore had to adapt their national guidelines to reflect the 2010 PMTCT recommendations, and the Elizabeth Glaser Pediatric AIDS Foundation tracked the adaptation process in the 14 countries where it provides technical support. In doing so it sought to understand common issues, challenges, and the decisions reached and to properly target its technical assistance.

In 2010, countries revised their national guidelines in accordance with WHO's most recent PMTCT recommendations faster than in 2006; all 14 countries included in this analysis formally conducted the revision within 15 months of the 2010 PMTCT recommendations' release. Governments used various processes and fora to make decisions throughout the adaptation process; they considered factors such as feasibility, health delivery infrastructure, compatibility with 2006 WHO guidelines, equity and cost. Challenges arose; in some cases the new recommendations were implemented before being formally adapted into national guidelines and no direct guidance was available in various technical areas. As future PMTCT guidelines are developed, WHO, implementing partners and other stakeholders can use the information in this paper to plan their support to ministries of health.

Abstracts in **عربي**, **中文**, **Français**, **Русский** and **Español** at the end of each article.

Introduction

Considerable progress has been made by programmes for the prevention of mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV), as evidenced by the drop in the estimated annual number of children born to HIV-positive (HIV+) mothers from 570 000 in 2003 to 330 000 in 2011.¹ These gains are mostly attributed to increases in PMTCT service coverage. In low- and middle-income countries, the percentage of HIV+ pregnant women receiving antiretroviral therapy (ART) for PMTCT has increased from 15% in 2005 to 57% in 2011.¹ The Joint United Nations Programme on HIV/AIDS has now called for the "elimination" of mother-to-child transmission of HIV by 2015.² Elimination necessitates lowering the risk of transmission of HIV from mother to child to less than 5% and reducing the infection rate among young children by at least 90%.³ To attain these goals, an increase in PMTCT programme coverage and a scale-up in the use of the more efficacious ART regimens currently available are needed.⁴

The World Health Organization (WHO) revised its global guidance on the use of ART to treat HIV+ pregnant women and prevent HIV infection in infants (herein referred to as the 2010 PMTCT recommendations) with initial draft recommendations released in November 2009⁴ and final guidelines launched in July 2010.⁵ Key changes reflected in the 2010 PMTCT recommendations are summarized in **Box 1**.⁵

Implementation of the new guidelines in developing countries would allow PMTCT programmes to attain rates of mother-to-child HIV transmission comparable to those in developed countries.⁶ Yet putting the new recommendations into operation, especially in resource-limited settings, is

complex, costly and involves significant planning, human capacity and resources. In addition, the new guidelines call for longer patient follow-up than previous guidelines. Ministries of health (MOH) therefore faced a series of challenging decisions as they revised national guidelines to make them consistent with the 2010 PMTCT recommendations and at the same time appropriate for local contexts (herein referred to as the adaptation process).

The revision of international health guidelines is a dynamic process informed by emerging scientific evidence and practical programmatic experience. This article explores perspectives on the collective adaptation process, common issues, key themes and challenges and the decisions reached in relation to adaptation of the 2010 PMTCT recommendations in the 14 African countries where the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) works. This information is being provided to inform subsequent adaptation processes in response to future guideline revisions.

Since 2000, EGPAF has provided comprehensive technical support for the delivery of PMTCT and HIV care and treatment services to more than 13.6 million women in over 5900 health-care facilities in 16 countries, 14 in sub-Saharan Africa and 2 in Asia (data from EGPAF database, available from corresponding author). Of the 16 countries where EGPAF works, 15 are among the 22 countries with the highest estimated numbers of pregnant women living with HIV. This analysis focuses on experiences in 14 EGPAF-supported countries in sub-Saharan Africa (**Table 1**).

EGPAF staff work closely with ministries of health in supporting programme implementation, policy and advocacy, and research. Many of EGPAF's country-based

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Box 1. Summary of key changes in the 2010 PMTCT recommendations issued by the World Health Organization

Expand access to CD4+ lymphocyte testing for all HIV+ pregnant women.

Raise the recommended CD4+ lymphocyte threshold for eligibility for treatment to < 350 cells/mm³ from the previous threshold of 200 cells/mm³, irrespective of WHO stage, and provide ART to all women in WHO stages III and IV.

Provide ART to eligible HIV+ pregnant women consistent with national standard first-line treatment guidelines for adults. First-line treatment should be either AZT or a TDF-based regimen; d4t-based regimens should be phased out. Recommended regimens for pregnant women are:

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

EFV, only after the first month of pregnancy, should replace NVP if this is not tolerated or is contraindicated.

Offer two antiretroviral prophylactic regimen options for pregnant women not eligible for treatment and provide antiretrovirals for prophylaxis starting at 14 weeks' gestation (most likely at diagnosis) and to mother or infant during breastfeeding:

- Option A: Maternal prophylaxis includes provision of AZT from 14 weeks gestation, single-dose NVP at the onset of labour and AZT + 3TC during labour and delivery, and AZT + 3TC for 7 days post-delivery. For infants who are breastfeeding, Option A includes provision of NVP from birth until one week after cessation of breastfeeding and for non-breastfeeding infants, provision of AZT or NVP until 4–6 weeks of age.
- Option B: Maternal prophylaxis includes provision of a three-drug regimen from 14 weeks' gestation until one week after the infant's exposure to breast milk has ended. Infant prophylaxis includes provision of AZT or NVP until 4–6 weeks of age to all HIV-exposed infants.

ART, antiretroviral therapy; AZT, zidovudine; d4t, stavudine; EFV, efavirenz; FTC, emtricitabine; HIV, human immunodeficiency virus; HIV+, HIV-positive; NVP, nevirapine; PMTCT, prevention of mother-to-child transmission; TDF, tenofovir; 3TC, lamivudine; WHO, World Health Organization.

technical staff actively participate in national PMTCT technical working groups, where they provide technical assistance on national policy related to PMTCT and HIV care and treatment. Thus, they have first-hand knowledge of country experiences in adapting the 2010 PMTCT recommendations.

Tracking of adaptation process

In anticipation of the release of the 2010 PMTCT recommendations, EGPAF launched an organized effort to help ministries of health incorporate the new recommendations at the national policy level. In 2009 EGPAF formed a technical advisory group to build the capacity of its staff in light of this objective. Specific interventions are outlined in [Box 2](#).

To understand common issues and to provide targeted support during this effort, EGPAF tracked the adaptation progress in 14 African countries. EGPAF headquarters staff gathered data from in-country technical staff from January 2010 to July 2011 through bimonthly queries, an online discussion forum,

and three international meetings attended by representatives from the 14 countries and EGPAF headquarters. [Box 3](#) contains the tool used to gather information on the adaptation progress from country teams.

Country experiences with adaptation

Timing

Of the 14 countries whose progress EGPAF tracked, 12 began the adaptation process before or immediately after WHO issued its rapid advice on the use of ART for treating HIV+ pregnant women and preventing HIV infection in infants, on the eve of World AIDS Day in 2009.⁴ The early release of the rapid advice and the speed with which countries responded allowed for faster adaptation of the guidelines. The total time needed for adaptation, as well as the time to implementation, varied across countries, but all 14 countries had officially revised their national guidelines within 15 months of the release of the new recommendations.

In most countries, the guideline adaptation process was quicker in 2010

than in 2006. For example, Lesotho and Uganda had just completed tools for implementing the 2006 guidelines when WHO's rapid advice was released in 2009. By contrast, their adaptation process for the 2010 guidelines was faster, more organized and participatory due to the support of partners such as the Centers for Disease Control and Prevention, the Clinton Health Access Initiative and EGPAF. Zambia noted that in 2006 its adaptation process took over a year, whereas in 2010 it took less than half that time. The Democratic Republic of the Congo noted that in the years between the release of the 2006 and 2010 guidelines, PMTCT had become more attractive to donors and ministries of health as a strategy for tackling HIV infection and acquired immunodeficiency syndrome (AIDS). For example, the Global Fund Round 10 guidelines for proposals focused on PMTCT, and the Democratic Republic of the Congo's application included the country's updated PMTCT guidelines in its Round 10 application. The timing of adaptation was affected by the type of process followed in each country and by lengthy discussions and debates surrounding the choice of prophylactic ART regimen (Option A or Option B, [Box 1](#)).

Decision-making process

Before making decisions, ministries of health consulted with stakeholders (e.g. implementation and technical assistance partners, multilateral organizations, research bodies and other groups working on HIV infection control) using a variety of methods. Kenya, Lesotho, Mozambique, Rwanda, Swaziland and Zambia gathered input through standing national PMTCT technical working groups, whereas Uganda convened participants for consultations specifically for the purpose of revising its PMTCT guidelines. Côte d'Ivoire, the Democratic Republic of the Congo and Kenya held workshops with stakeholders for several days; other countries held similar meetings over several months.

The decision-making process often involved intense lobbying to ministries of health and support from partners and donors. Although these partners expressed their preferred approach to PMTCT, ministries of health made final decisions based on what they

Table 1. **Context of prevention of mother-to-child transmission (PMTCT) of HIV in countries supported by the Elizabeth Glaser Pediatric AIDS Foundation, 2010**

Country	Pregnant women tested for HIV (%)	HIV+ pregnant women needing ART for PMTCT (No.)	HIV+ pregnant women on ART as per WHO's 2010 PMTCT guidelines (%)	Infants born to HIV+ women on ART for PMTCT (%)
Cameroon	41	30 000	53	27
Côte d'Ivoire	59	18 000	66	44
Democratic Republic of the Congo	11	50 000	1	6
Kenya	83	87 000	43	57
Lesotho	57	14 000	89	76
Malawi	66	57 000–76 000	23–31	35–46
Mozambique	87	100 000	52	42
Rwanda	68	12 000	78 ^a	74 ^a
South Africa	> 95	260 000	> 95	54
Swaziland	83	9 100	> 95	89
Uganda	63	94 000	42	22
United Republic of Tanzania ^a	51	84 000	70	51
Zambia	94	79 000	75	57
Zimbabwe	90	79 000	46	77

ART, antiretroviral therapy; HIV, human immunodeficiency virus.

^a Only 2009 date were available.

Note: Data were obtained from reference ⁷ for all countries except the United Republic of Tanzania, for which the data source was reference ⁸.

Box 2. **EGPAF support to country programmes for the 2010 PMTCT recommendations' adaptation process**

- Coordination and communication fora, such as an internal e-mail discussion group (i.e. listserv) and a web site housing a database of country progress and resources to facilitate information synthesis and sharing across country programmes
- Three toolkits to support national level adaptation, implementation, and monitoring and evaluation of the revised guidelines
- Knowledge and capacity building of EGPAF staff, including trainings, technical assistance, and regularly scheduled discussions highlighting key issues and offering a venue for sharing early implementation experiences
- EGPAF staff travel to country programmes in need of technical assistance and/or advocacy during the adaptation process.
- Technical exchange calls among country staff to allow countries at a later stage in the adaptation process to provide assistance to those at an earlier stage
- Documentation support, including production of externally disseminated documents outlining promising practices and lessons learnt

EGPAF, Elizabeth Glaser Pediatric AIDS Foundation; PMTCT, prevention of mother-to-child transmission.

felt was most appropriate for their countries. Technical partners actively supported the decision-making process. For example, EGPAF developed a toolkit for its in-country staff and ministry of health partners that contained an overview of the revised guidelines and guidance on effective planning for implementation and monitoring of the revised guidelines and documentation of programme experiences.

Simultaneous revision of various guidelines

Most ministries of health decided to revise other guidelines concurrently released by the WHO, such as those for adult and paediatric ART and the feeding of infants and young children in the context of HIV, while revising their PMTCT guidelines due to the overlap between guidelines.^{9–11} Where

this occurred, it was observed that the PMTCT guideline adaptation process moved more quickly; as of July 2011, 13 of 14 MOHs had completed the revision of PMTCT guidelines, while only 11 and 12 finalized adult and paediatric HIV treatment guidelines, respectively.

Guidelines on the feeding of infants and young children in the context of HIV were sometimes incorporated into the national PMTCT guidelines or paediatric HIV care and treatment guidelines. This happened in Cameroon, the Democratic Republic of the Congo, Kenya, Mozambique, Rwanda, the United Republic of Tanzania and Zambia. However, in all other countries they exist separately.

In most of the 14 countries, activities for the prevention of HIV infection and HIV care and treatment are managed by different bodies within the health ministry, with separate national technical working groups for each area. This required additional coordination, yet countries did not report major difficulties and welcomed the opportunity to have different technical working groups collaborate among themselves and make joint decisions. In countries such as the Democratic Republic of the Congo, Kenya and Lesotho, these working groups jointly revised both sets of guidelines, whereas in the United Republic of Tanzania, PMTCT guidelines were revised first and then incorporated into adult guidelines after these were revised. In Swaziland, the technical working groups worked separately at first and then successfully harmonized their efforts through meetings. Challenges arose in Uganda and Zambia, where the technical working groups had chosen different adult first-line ART regimens. However, they were able to reconcile their differences and agree on a consistent approach.

Prophylactic regimen options

As of July 2011, 11 of the 14 countries (Cameroon, Democratic Republic of the Congo, Kenya, Lesotho, Mozambique, South Africa, Swaziland, United Republic of Tanzania, Uganda, Zambia and Zimbabwe) had officially chosen Option A for their national guidelines and 3 (Côte d'Ivoire, Malawi and Rwanda) had chosen Option B or modifications thereof. Malawi chose Option B+, which entailed initiating all HIV+ pregnant women on lifelong

Box 3. Tool used to gather information from countries on their progress in the 2010 PMTCT recommendations adaptation process

1. What is the current status of adaptation and implementation of the revised guidelines? Have there been any developments or progress since we last spoke?
2. Which aspects of this process are going well or represent successes?
3. Which aspects of this process are challenging?
4. Please provide feedback on the status of the following:
 - a) Revision of national PMTCT guidelines
 - b) Selection of maternal prophylaxis regimen
 - c) Roll-out of trainings
 - d) Distribution of revised tools and job-aids to facilities
 - e) Forecasting of drugs in accordance with revised guidelines
 - f) Revision of national indicators
 - g) Revision of registers and national reporting forms
 - h) Status of implementation roll-out

PMTCT, prevention of mother-to-child transmission.

ART. Uganda decided to remain flexible: it adopted Option A as standard policy while allowing facilities with sufficient resources to offer Option B. Kenya, Mozambique and Zambia chose Option A for their national policies but allowed some implementing partners to pilot Option B for future consideration in case resources became available to pursue this option.

Discussion

Choice of prophylactic regimen

The decision between Option A and B proved to be contentious in many countries. Although the 2010 PMTCT recommendations provide scientific evidence that both options are equally efficacious,⁵ many stakeholders still believed that Option B was more effective. Disagreements about the best way forward led to vigorous debate and discussions between stakeholders. This prolonged the revision process and left little time to address other critical issues, such as the logistical complexities of initiating all eligible HIV+ pregnant women on ART (e.g. limited access to CD4+ lymphocyte testing to determine treatment eligibility). [Table 2](#) and [Table 3](#) provide details of the decision-making processes in Lesotho (Option A) and Malawi (Option B+).

Feasibility

Common themes emerged during national-level discussions. Factors that influenced countries' choices included: feasibility, perceived complexity of implementing a given option, potential

health risks and health system capacity to incorporate the necessary changes. When WHO issued its 2010 guidelines, many countries were already offering pregnant women prophylaxis with zidovudine (AZT) at 28 weeks' gestation and health-care providers were familiar with the regimens that most resembled Option A. On the other hand, the choice of Option B required important policy changes. In many countries, nurses were not allowed to initiate a three-drug ART regimen and HIV+ pregnant women had limited access to clinics providing ART.

Where to locate follow-up services in the postpartum period under either option had to be decided. For Option A, discussions focused on how and where to follow up infants receiving extended PMTCT prophylaxis. For Option B, the follow-up of postpartum women on three-drug prophylaxis was perceived as problematic.

Health system capacity

Various factors were considered in determining the feasibility of implementing Option A or Option B. Cameroon, the Democratic Republic of the Congo and Mozambique were already facing antiretroviral stock-outs, and concerns were raised about having sufficient drug supplies, drug and commodity quantification capabilities and the adequacy of the supply chain management systems in place as new guidelines were implemented. Lesotho, Swaziland and Uganda experienced stock-outs of nevirapine (NVP) syrup following implementation of WHO 2010 PMTCT guidelines. Kenya

and Zimbabwe experienced stock-outs of AZT upon release of WHO's rapid advice, as patients and health-care providers demanded the use of certain antiretrovirals for first-line ART in accordance with the revised recommendations. Other countries, however, did not report stock-outs in connection with the revised guidelines.

Equity

The issue of equity surfaced during discussions surrounding the selection of ART regimens. Many countries debated whether pregnant women should be prioritized for ART over other eligible adults. Ministries of health in Côte d'Ivoire and Rwanda stressed that because Option B resembled the current standard of care in developed countries more closely than Option A, it should be the standard for their countries as well.

Costs

The cost of implementing either option was a critical consideration. Many countries weighed in the funding implications of adopting extended regimens for maternal and infant prophylaxis, initiating more HIV+ pregnant women on long-term ART, the scale-up of CD4+ lymphocyte testing, and the transition from older regimens containing stavudine (d4t) to newer ones based on tenofovir (TDF). After conducting various costing exercises, the ministries of health of Cameroon, the Democratic Republic of the Congo, Kenya, Lesotho, South Africa, Swaziland, the United Republic of Tanzania, Uganda, Zambia and Zimbabwe concluded that Option B would be considerably more expensive than Option A, so they chose the latter. Even governments that believed Option B to be superior saw the increased costs of adoption would be prohibitive. Uganda and Swaziland chose to implement Option A and transition to Option B later, upon resources becoming available.

Ministries of health in Cameroon, Côte d'Ivoire, Malawi and Zimbabwe were adapting their PMTCT national guidelines as they were preparing their Global Fund Round 10 proposals, anticipating that Global Fund resources would cover the increased costs associated with implementing WHO 2010 guidelines. In May 2009, the Global Fund launched an initiative to enable

Table 2. Elements of the decision-making process surrounding the choice of antiretroviral therapy (ART) regimen for the prevention of mother-to-child transmission (PMTCT) of HIV in Lesotho and Malawi

Element	Lesotho	Malawi
Context at time of decision-making	<ul style="list-style-type: none"> – Population: 1 800 000 – Prevalence of HIV infection: 27% – No. of HIV+ pregnant women: 13 000 – PMTCT coverage: 71% – Existing PMTCT prophylaxis regimen: combination regimens in accordance with 2006 PMTCT guidelines 	<ul style="list-style-type: none"> – Population: 13 000 000 – Prevalence of HIV infection: 12% – No. of HIV+ pregnant women: 1 560 000 – PMTCT coverage: 25–46% – Existing PMTCT prophylaxis regimen: single-dose NVP (70% of sites) and 2006 PMTCT guidelines (30% of sites)
Summary of national decision-making process ¹²	<ul style="list-style-type: none"> – Established an advisory committee to guide the process of adapting the PMTCT guidelines – Set up small team of volunteers from partner organizations, chaired by the health ministry, to examine the evidence – Analysed Option A and Option B in terms of WHO recommendations, efficacy, acceptability, cost, feasibility, health risks (including resistance) and future treatment options 	<ul style="list-style-type: none"> – PMTCT and ART TWGs invited all HIV partners to participate in discussions. – TWGs analysed the pros and cons of Option A and Option B – TWGs discussed the strengths and weaknesses of the PMTCT and ART programmes – A national HIV symposium was held to discuss the recommendations of the technical working groups – Presentations on the new policy recommendations were made to the Malawi HIV Partnership Forum and the CCM of the Global Fund to Fight AIDS, Tuberculosis and Malaria – The health ministry approved the revised national guidelines. – The CCM approved the revised national guidelines – PMTCT and ART TWGs invited all HIV partners to participate in discussions
Decision	Option A	Option B ^a
Basis for decision	<ul style="list-style-type: none"> – Easier to transition from 2006 guidelines – Easier to initiate by nurses – Initial take-up much cheaper – Easily integrated into maternal and child health setting in hospital 	<ul style="list-style-type: none"> – Strategy does not rely solely on CD4+ lymphocyte count, important in settings with minimal access to testing – High fertility rate (5–6 births per woman), combined with prolonged breastfeeding (median of 23 months) followed by a new pregnancy and with delayed antenatal care (50% initiation at 28 weeks' gestation), make interrupting ART until next pregnancy confusing, difficult to implement and risky – Where HIV transmission in couples significantly contributes to overall transmission rates, the use of ART reduces the risk of HIV transmission in serodiscordant couples – Allows for a simple message that is easily implemented at all health centres; three-drug therapy must be taken daily for life – Can be easily and rapidly rolled out to health centres – Increased access to ART – Reduction in postpartum mortality rates in HIV-infected women noted – Maternal ART reduces HIV transmission to infants and partners

AZT, zidovudine; CCM, country coordinating mechanism; HIV, human immunodeficiency virus; HIV+, HIV-positive; NVP, nevirapine; TWG, technical working group; US\$, United States dollars; WHO, World Health Organization.

^a For maternal prophylaxis, all HIV+ pregnant women to be put on lifelong ART; for infant prophylaxis, AZT or NVP until 4–6 weeks of age to all HIV-exposed infants.^{13,14}

grant recipients to “reprogramme” leftover funding from existing grants to procure drugs and other commodities as a way to facilitate switching from a single dose of NVP to more efficacious regimens for PMTCT.

Malawi and Zimbabwe's Global Fund proposals were rejected.¹⁵ As a result, Malawi's ministry of health had to postpone implementing the revised

adult treatment guidelines and to prioritize instead the guidelines for ART initiation in HIV+ pregnant and nursing women and in HIV+ individuals with tuberculosis.¹⁵ Similarly, Zimbabwe had to delay full implementation of revised adult ART treatment guidelines and to prioritize guidelines for the initiation of eligible pregnant women on newer, more effective ART regimens.¹⁶

Other issues

For the full intended impact of the 2010 PMTCT guidelines to be achieved, several issues identified during attempts to implement these guidelines must be more closely examined. They include the acceptability of the interventions to HIV+ pregnant women and their families; the implications of adherence

Table 3. **Factors considered by Lesotho and Malawi when selecting their antiretroviral therapy (ART) regimens for the prevention of mother-to-child transmission (PMTCT) of HIV**

Factor	Lesotho (Option A)		Malawi (Option B+ ^a)		Preferred
	Option A	Option B	Option A	Option B	
WHO recommendation	Strong	Strong	–	–	Equivalent
Efficacy of intervention	Comparable	Comparable	–	–	Equivalent
Acceptability	Similar to regimen already in use and familiar to mothers and providers	Unknown to mothers	–	–	Option A
	Can be initiated while awaiting CD4+ lymphocyte count	Providers less familiar with this approach	–	–	
		Can be initiated without CD4+ lymphocyte count	–	–	
Cost	US\$ 238 881	Option B EFV: US\$ 2 128 157	Drug regimen less expensive	Drug regimen more expensive; however, reductions in number of infections, morbidity and mortality in children and adults will lower costs in the long run	Option A
	Requires additional individual ARVs (AZT for mothers and NVP infants)	Requires additional ART (mothers) and NVP (infants)	Management costs for all options likely to be the same	Management costs for all options likely to be the same	
	Additional PCRs necessary during breastfeeding	Additional PCRs necessary during breastfeeding	–	–	
Feasibility	Additional laboratory monitoring necessary (mothers: Hb before delivery and infants: LFTs throughout breastfeeding)	Additional laboratory monitoring necessary (mothers: Hb, LFTs, Cr before delivery; mothers: Hb, LFTs, Cr throughout breastfeeding).	–	–	Option A
	Additional refresher training necessary	More extensive training necessary	More complicated than Option B, but not much different from the existing 2006 PMTCT guideline regimen	Would require extensive retraining, but could be easier in concept for both health care providers and mother/baby pairs once training takes place	
	ARVs already available in ANC facilities	Requires making ART available in antenatal clinics	Necessary to teach proper dosing of NVP	–	
		Requires increased laboratory capacity	–	–	

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Factor	Lesotho (Option A)		Malawi (Option B+ ^a)		Preferred
	Option A	Option B	Option A	Option B	
Health delivery infrastructure	–	–	CD4+ lymphocyte test needed to initiate and for early access to ART Necessary for follow up and support of mother/ baby pair for ongoing adherence Necessary to emphasize clinical review ± PCR for signs of infection Referral systems for infants who transmit – –	CD4+ lymphocyte test needed to know when to take off ART Necessary for laboratory monitoring of Hb levels Necessary for follow up and support of mother and infant for ongoing adherence Would require additional HAART classes at ANC Necessary to emphasize clinical review, with or without PCR, for signs of infection Referral systems for infants to whom HIV has been transmitted	–
Health risk	Risk of anaemia for mothers (AZT) Risk of hepatotoxicity in infants (NVP) Potential maternal resistance after delivery Potential infant resistance during breastfeeding (through exposure to infant NVP) Limits future ART options for HIV+ children	Risk of anaemia (AZT), hepatotoxicity (NVP) and elevated Cr (TDF) for mothers Risk of hepatotoxicity for infants (NVP) Potential maternal resistance when stopping ART Potential infant resistance during breastfeeding (through exposure to maternal ART) Limits future ART options for HIV+ children	Concern of drug adherence for infants No ongoing safety data for extended infant NVP beyond 1 year No indication of adverse effect on pregnancy outcome – –	Impact on maternal health of interrupted ART Side-effects of ART Concern over hepatotoxicity precludes use of NVP-based regimen Concern over EFV-based teratogenicity if mother gets pregnant while breastfeeding	Equivalent

ANC, antenatal care; ART, antiretroviral therapy; ARVs, antiretrovirals; AZT, zidovudine; Cr, creatinine; EFV, efavirenz; HAART, highly active antiretroviral therapy; Hb, haemoglobin; HIV, human immunodeficiency virus; HIV+, HIV-positive; LFT, liver function tests; NVP, nevirapine; PCR, polymerase chain reaction; TDF, tenofovir; US\$, United States dollars.

^a For maternal prophylaxis, all HIV+ pregnant women to be put on lifelong ART; for infant prophylaxis, AZT or NVP until 4–6 weeks of age to all HIV-exposed infants.^{13,14}
Note: Information in table obtained from reference.¹³

to prolonged drug regimens, and drug resistance among mothers and infants.

Early implementation and planning

In several countries health-care providers, patients seeking health care and members of the general public, cognizant of the key changes in the revised guidelines, advocated for their immediate implementation, before national guideline revision. In Kenya, many health-care providers began transitioning patients from d4t to AZT and TDF-based regimens and giving AZT for 28 weeks instead of 14 before national rollout of revised

national guidelines. This increased AZT consumption and caused stock-outs. In Zimbabwe, providers reported cases of patients refusing to accept d4t-containing regimens and demanding alternative regimens, even though these were not widely available.

Absence of direct guidance

Ministries of health grappled with several technical issues for which no definitive guidance was given in WHO 2010 PMTCT guidelines. Many were concerned about the potential for drug resistance resulting from the use of more prolonged regimens for maternal and infant prophylaxis and

about the effect such resistance might have on patients' long-term health and on future treatment options for women and infants. The provision of AZT monotherapy for women under Option A caused concern, since a growing body of evidence points to an increased risk of resistance to NVP in women who receive a single dose of the drug during labour.¹⁶ There were also reservations about the possible detrimental impact of Option B, given evidence from the Strategies for Management of Anti-Retroviral Therapy (SMART) trial to the effect that mortality and morbidity are greater among patients on therapy

causing intermittent suppression of HIV viraemia rather than continuous therapy.^{17,18}

In several countries where HIV seroconversion during pregnancy is an important concern, ministries of health sought guidance on protocols for ART prophylaxis in infants born to HIV-negative mothers in serodiscordant relationships and for ART prophylaxis administered to mothers who seroconvert while breastfeeding. In addition, countries struggled with defining appropriate protocols for mothers and infants with interrupted ART prophylaxis.

Many countries struggled to update national monitoring and evaluation tools and registers for tracking progress in implementing WHO 2010 revised guidelines because of difficulties in defining appropriate indicators. For both Option A and Option B, EGPAF developed a comprehensive list of such indicators. Although these were shared across EGPAF-supported country PMTCT programmes, guidance issued by WHO would have reached a wider audience. WHO did release a guide for adapting WHO normative guidelines for national PMTCT programmes,¹⁹ but this was not published until July 2011, one full year after its revised guidelines were released.

Limitations of this analysis

The collective experience summarized in this article stems from only 14 countries, located in sub-Saharan Africa. This limits the generalizability of the lessons learnt. Country experiences were gathered from in-country EGPAF technical staff working directly with ministries of health and supplemented by direct discussions with ministry of health programme managers in various fora. The information in this manuscript was also submitted for review and approval by health ministry staff in all countries included in this analysis.

Some informants may not have been aware of all aspects of the adaptation process and their feedback may reflect their own subjective views. The authors were not always able to obtain the same information across all countries, and some countries asked not to be mentioned in association with

certain data. Furthermore, it was not possible to objectively assess the main driving factor(s) behind national policy decisions or whether undue pressure from donors or other lobby groups may have been among them. The literature shows that Africa's health policies and priorities have been highly influenced, even distorted, by the international donor community, often because global health funding mechanisms prioritize vertical interventions over national health priorities.^{20,21} However, the potential impact of these influences within specific country adaptation processes was difficult to document and discern.

Conclusion

It is critical to explore country perspectives on the process of adapting national PMTCT guidelines in accordance with WHO revised 2010 recommendations. Knowledge of these country-level processes and the common factors that drive them can be used by WHO and other stakeholders to inform future international guideline revisions and to anticipate and address country needs during subsequent national adaptation processes.

While exploring country experiences in implementing their revised national guidelines is beyond the scope of this paper, recent publications have highlighted some of the challenges associated with implementing Option A in Uganda,²² Zambia^{23,24} and Zimbabwe,²⁵ particularly with regard to extended infant NVP prophylaxis. Hence, continued monitoring of these challenges is essential. Future research should explore in greater depth the national policy adaptation process in the broader context of donor aid and development.

At the time of writing, the executive team of the Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and their Children had initiated meetings to discuss the next changes to WHO's new PMTCT guidelines, which will most likely favour Option B or B+. In light of these imminent changes, understanding the lessons learnt so far and the challenges faced when adapting international guidelines to national contexts is especially critical. ■

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ملخص

التكيف القطري لتوصيات منظمة الصحة العالمية لعام 2010 للوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل قامت منظمة الصحة العالمية بتنقيح توصياتها العالمية بشأن معالجة السيدات الحوامل المصابات بعدوى فيروس العوز المناعي البشري بمضادات الفيروسات القهقرية والوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل. وتلى المسودة الأولية للتوصيات الصادرة في تشرين الثاني/نوفمبر 2009 دليلاً إرشادياً منقحاً بالكامل في تموز/يوليو 2010. وكان لتوصيات عام 2010 المعنية بالوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل آثاراً مهمة من حيث التخطيط والقدرة البشرية والموارد. ولذلك، كان على وزارات الصحة تكيف أدلتها الإرشادية الوطنية لكي تعكس توصيات عام 2010 المعنية بالوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل وقامت مؤسسة إيزابيث غلاسر لرعاية الأطفال المصابين بفيروس العوز المناعي البشري (الإيدز) بتتبع عملية التكيف في الأربعة عشر بلداً التي تقدم فيها الدعم التقني. وفي سبيل ذلك، حرصت على فهم القضايا المشتركة والتحديات والقرارات التي تم التوصل إليها وعلى توجيه مساعدتها التقنية بالشكل المناسب. في عام 2010، قامت البلدان بتنقيح أدلتها الإرشادية الوطنية طبقاً لأحدث التوصيات المعنية بالوقاية من انتقال فيروس العوز

摘要

2010 年世界卫生组织预防艾滋病母婴传播建议的国家适应

世界卫生组织 (WHO) 修订了其有关使用抗逆转录病毒药物治疗感染艾滋病毒 (HIV) 的孕妇和预防母婴艾滋病毒传播 (PMTCT) 的全球建议。2009 年 11 月发布初步建议草案，随后于 2010 年 7 月发布完整的修订指导方针。2010 年对 PMTCT 的建议在规划、人力和资源方面具有重要的意义。因此，各国卫生部必须调适其本国的指导方针，以反映 2010 年的 PMTCT 建议，伊丽莎白格拉泽儿童艾滋病基金会也对其提供技术支持的 14 个国家展开适应过程的跟踪。这样做的目的是了解共同的问题、挑战和所达成的决定，并确定其技术援助的合适目标。

较之 2006 年，2010 年各个国家根据 WHO 最新 PMTCT 建议修订全国性指导方针的速度更快；在此次分析中包括的所有 14 个国家在发布 2010 年 PMTCT 建议的 15 个月内都正式进行了修订。在整个适应过程中，政府使用各种程序和论坛作出决定；它们将可行性、医疗卫生服务的基础设施、与 2006 年 WHO 指导方针的适应性、公平性和成本等因素考虑在内。产生新的挑战；在某些情况下，在被正式调适至国家的指导方针当中之前，新的建议就得以实施，在各个技术领域并没有直接的指南可循。随着今后 PMTCT 指导方针的制定，世卫组织、实施合作方和其他利益相关者可以使用本文中的信息来规划其对卫生部的支持。

Résumé

Adaptation nationale de la version 2010 des recommandations de l'OMS relatives à la prévention de la transmission de la mère à l'enfant du VIH

L'Organisation mondiale de la Santé (OMS) a révisé ses recommandations mondiales relatives au traitement des femmes enceintes infectées par le virus de l'immunodéficience humaine (VIH) avec des antirétroviraux, ainsi qu'à la prévention de la transmission de la mère à l'enfant (PTME) du VIH. Le projet initial des recommandations, publié en novembre 2009, a été suivi de lignes directrices entièrement révisées en juillet 2010. La version 2010 des recommandations relatives à la PTME a des implications importantes en termes de planification, de moyens humains et financiers. Les ministères de la Santé ont donc dû adapter leurs lignes directrices nationales pour refléter la version 2010 des recommandations relatives à la PTME, et la Elizabeth Glaser Pediatric AIDS Foundation a suivi le processus d'adaptation dans les 14 pays où elle fournit un appui technique. Ce faisant, elle a cherché à comprendre les problèmes communs, les défis rencontrés et les décisions prises de manière à correctement cibler son assistance technique.

En 2010, les pays ont adapté plus rapidement qu'en 2006 leurs lignes directrices nationales aux ultimes recommandations

de l'OMS relatives à la PTME; les 14 pays inclus dans cette analyse ayant formellement effectué la révision dans les 15 mois suivant la diffusion de la version 2010 des recommandations relatives à la PTME. Les gouvernements ont utilisé divers processus et instances pour prendre des décisions tout au long du processus d'adaptation. Ils ont considéré des facteurs tels que la faisabilité, l'infrastructure de la fourniture de soins, la compatibilité avec la version 2006 des lignes directrices de l'OMS, l'équité et le coût. Ils ont été confrontés à plusieurs défis. Dans certains cas, les nouvelles recommandations ont été mises en œuvre avant d'être officiellement adaptées sous la forme de lignes directrices nationales, et aucune indication directe n'était disponible dans différents domaines techniques. Lors du développement des futures lignes directrices relatives à la PTME, l'OMS, les partenaires en charge de l'exécution et les autres parties prenantes pourront utiliser les informations contenues dans cet article pour planifier leur soutien aux ministères de la Santé.

Резюме

Принятие странами рекомендаций Всемирной организации здравоохранения по профилактике передачи ВИЧ от матери к ребенку в редакции от 2010 г.

Всемирной организацией здравоохранения (ВОЗ) пересмотрены глобальные рекомендации по лечению беременных женщин, инфицированных вирусом иммунодефицита человека (ВИЧ), с применением антиретровирусных препаратов, а также меры по профилактике передачи ВИЧ от матери к ребенку (ППМР). Первоначальный проект рекомендаций, изданный в ноябре 2009 года, был заменен более полным и пересмотренным руководством в июле 2010 года. Рекомендации по ППМР, изданные в 2010 году, имеют важное значение с точки зрения планирования, человеческого потенциала и ресурсов. В связи с этим министерствам здравоохранения пришлось адаптировать свои национальные рекомендации таким образом, чтобы они отражали принципы рекомендаций по ППМР от 2010 года, а Фонд педиатрической помощи при СПИДе Элизабет Глейзер отслеживал процесс адаптации в 14 странах, где им обеспечивалась техническая поддержка. При этом Фонд ставил перед собой задачи понять общие проблемы, трудности и принятые решения для соответствующего направления своей технической помощи.

В 2010 году страны привели свои национальные рекомендации в соответствие с последними рекомендациями ВОЗ по ППМР быстрее, чем в 2006 году. Все 14 стран, включенных в этот анализ, согласно отчетам, провели ревизию в течение 15 месяцев после выхода в свет рекомендаций ППМР от 2010 года. Правительствами использованы различные процессы и форумы для принятия решений на протяжении всего процесса адаптации, учитывая такие факторы, как осуществимость, инфраструктура оказания медицинской помощи, соответствие рекомендациям ВОЗ от 2006 года, собственные средства и затраты. При этом возникли определенные проблемы – в некоторых случаях новые рекомендации были выполнены до того, как они были официально приняты в качестве национальных рекомендаций, и для различных технических областей прямых указаний еще не имелось. По мере разработки будущих рекомендаций по ППМР Всемирная организация здравоохранения, ее партнеры и другие заинтересованные стороны могут использовать информацию в данном докладе для планирования помощи, оказываемой министерствам здравоохранения.

Resumen

La adaptación a cada país de las recomendaciones de la Organización Mundial de la Salud del año 2012 para la prevención de la transmisión del VIH de madres a hijos

La Organización Mundial de la Salud (OMS) revisó sus recomendaciones globales sobre el tratamiento de mujeres embarazadas infectadas con el virus de la inmunodeficiencia humana (VIH) con antirretrovirales y la prevención de la transmisión del VIH de madres a hijos. A las recomendaciones del borrador inicial hecho público en noviembre del 2009 siguió en julio del 2010 una directriz completamente revisada. Las recomendaciones del año 2010 sobre la transmisión del VIH de madres a hijos presentan unas implicaciones importantes en cuanto a la planificación, la capacidad humana y los recursos. Los ministerios de salud tuvieron, por tanto, que adaptar sus directrices nacionales para reflejar las recomendaciones sobre la prevención de la transmisión del VIH de madres a hijos del año 2010, y la Elizabeth Glaser Pediatric AIDS Foundation (Fundación Elisabeth Glaser para el SIDA pediátrico) ha hecho un seguimiento del proceso de adaptación en los 14 países en los que proporciona apoyo técnico. Con ello, trató de entender los problemas comunes, los desafíos y las decisiones tomadas y dirigir su asistencia técnica de forma adecuada.

En el 2010, los países modificaron sus directrices nacionales de acuerdo con las recomendaciones actuales sobre la prevención

de la transmisión del VIH de madres a hijos de la OMS más rápidamente que en el año 2006. Los 14 países incluyeron en el presente análisis realizado oficialmente la modificación en un plazo de 15 meses desde que se dieran a conocer las recomendaciones sobre la prevención del VIH de madres a hijos del año 2010. Los gobiernos usaron diversos procesos y foros para tomar decisiones durante el proceso de adaptación, y tuvieron en cuenta factores tales como la viabilidad, la infraestructura asistencial, la compatibilidad con las directrices de la OMS del año 2006, la equidad y el coste. Surgieron desafíos, en algunos casos las recomendaciones nuevas se aplicaron antes de haberlas adaptado formalmente a las directrices nacionales y en numerosas áreas técnicas no hubo orientación directa disponible. Mientras se van desarrollando las directrices futuras sobre la prevención de la transmisión del VIH de madres a hijos, la OMS, los asociados encargados de la ejecución y las partes interesadas pueden emplear la información de este documento a fin de planificar su apoyo a los ministerios de salud.

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