KEY MESSAGES

NEW WHO RECOMMENDATIONS:
Preventing mother-to-child transmission

The World Health Organization (WHO) is revising its guidelines on the use of antiretroviral (ARV) drugs for the prevention of mother-to-child transmission of HIV (PMTCT). Key recommendations of the new guidelines will be released on 30 November 2009 (see *Rapid advice* document). The full guidelines are expected in early 2010.

The new recommendations place increased emphasis on improving the mother's health while providing maximum protection against HIV infection in her child. They give countries guidance on how to reduce HIV transmission from mother to child through more effective treatment and prevention regimens.

WHO is also revising its guidelines on adult and adolescent antiretroviral therapy (ART) and infant feeding in the context of HIV. All three guidelines are being updated in a harmonized fashion.

Key 2009 recommendations: PMTCT

1. Earlier antiretroviral therapy (ART)[1] for a larger group of HIV-positive pregnant women to benefit both the health of the mother and prevent HIV transmission to her child during pregnancy.

2. Longer provision of antiretroviral (ARV) prophylaxis[2] for HIV-positive pregnant women with relatively strong immune systems who do not need ART for their own health. This would reduce the risk of HIV transmission from mother to child.

3. Provision of ARVs to the mother or child to reduce the risk of HIV transmission during the breastfeeding period. For the first time, there is enough evidence for WHO to recommend ARVs while breastfeeding.

The PMTCT recommendations refer to two key approaches:

1. *Lifelong ART for HIV-positive women in need of treatment.*
2. *Prophylaxis, or the short-term provision of ARVs, to prevent HIV transmission from mother to child.*

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BACKGROUND

WHO has a mandate to define global health norms and standards and to help countries adopt and adapt these recommendations according to their national circumstances.

The PMTCT ARV Guidelines, first issued in 2000, were revised in 2004 and again in 2006. They recommend the delivery of simple, standard and effective regimens at a large scale, even in resource-limited settings.

The 2006 guidelines represented a major advance from previous recommendations by emphasizing the importance of providing lifelong ART to eligible pregnant women in order to protect their own health and that of their children. They also moved from the provision of a single dose of the drug nevirapine to mother and newborn to a more effective combination of drugs for prophylaxis.

The 2006 guidelines have formed the technical backbone of the rapid scale-up in PMTCT services, especially in high burden countries in sub-Saharan Africa, where more than 90% of HIV-positive pregnant women reside. According to the 2009 *Towards universal access* progress report, published jointly by WHO, UNICEF and UNAIDS, an estimated 45% of HIV-positive pregnant women received some regimen of ARVs for PMTCT in 2008, up from 35% in 2007 and 10% in 2004.

In 2008, an estimated 1.4 million pregnant women in low- and middle-income countries were living with HIV. Much more needs to be done to accelerate the scale-up of HIV testing and counselling and PMTCT, and to integrate these services with strengthened maternal, newborn and child health programmes.

Globally, HIV/AIDS is the leading cause of mortality among women of reproductive age. Without treatment, one third of children living with HIV die before the age of one year and almost half by the second year.

NEED FOR UPDATED GUIDELINES

Significant evidence and experience have accumulated since the 2006 revision of the guidelines, especially with regard to:

- when women should receive treatment for their own health and to reduce the risk of HIV transmission;
- the benefits of starting ARV prophylaxis earlier during pregnancy with either one or three drugs;
- evidence that ARV prophylaxis for mothers or infants reduces significantly the risk of transmission through breastfeeding.

The 2009 recommendations represent a public health approach to best international clinical practice based on current evidence and will serve as a reference to help countries set their own national standards. Implementation of the recommendations and new country guidelines will depend on national circumstances, resources and priorities.

MAIN REVISIONS:

ELIGIBILITY FOR TREATMENT

The best method to determine when to start treatment is through CD4 testing, which measures the strength of the immune system.

The **2006 guidelines** recommended starting lifelong ART for pregnant women with a CD4 count at or below 200 cells/mm^3, usually the stage at which the immune system is no longer strong enough to prevent opportunistic diseases.	The **2009 recommendations** promote starting lifelong ART for all pregnant women with severe or advanced clinical disease, or with a CD4 count at or below 350 cells/mm^3, regardless of symptoms.

Clinical trials and additional data suggest that treating pregnant women with a CD4 count at or below 350 cells/mm^3 could prevent at least 75% of all mother-to-child transmission while also providing the best available treatment for the mother's health. ART will also provide protection during the breastfeeding period. These recommendations on ART for pregnant women are consistent with the new adult ART recommendations and offer great potential to improve both the mother's own health and protect the child from HIV infection.

ARV PROPHYLAXIS DURING PREGNANCY

HIV-positive pregnant women who are not eligible or are not receiving ART (lifelong treatment) should be given ARVs as prophylaxis to prevent transmission to their children.

The **2006 guidelines** proposed starting ARV prophylaxis in the third trimester (28 weeks) of pregnancy. They recommended a basic regimen of daily zidovudine (AZT) and single-dose nevirapine at labour and delivery, as well as infant prophylaxis for one week after birth.	The **2009 recommendations** include two options, both of which should start earlier in pregnancy, at 14 weeks or as soon as possible thereafter. 1. Daily AZT for the mother and infant prophylaxis for six weeks after birth. Infant prophylaxis should be continued until the end of the breast-feeding period. OR 2. A three-drug regimen for the mother taken during pregnancy and throughout the breastfeeding period, as well as infant prophylaxis for six weeks after birth.

ARV PROPHYLAXIS DURING BREASTFEEDING

In most developed countries, babies of HIV-positive mothers are given infant formula from birth in order to prevent postpartum transmission through breastfeeding. But in many countries, both health services and individual mothers have not been able to adequately support and provide safe replacement feeding. Mothers have faced the dilemma of either giving their babies all the benefits of breastfeeding but exposing them to the risk of HIV infection, or avoiding all breastfeeding and increasing the risk of death from diarrhoea and malnutrition.

At the time of the **2006 guidelines**, there were insufficient data supporting the use of ARVs to prevent HIV transmission from mother to baby during breastfeeding. Since then, several clinical trials have shown the efficacy and acceptability of prophylaxis either to the mother or to the infant during breastfeeding.

The **2009 recommendations** reflect this exciting breakthrough. They provide two alternative options for HIV-positive women who breastfeed and are not taking ART:

1. *If a woman received AZT during pregnancy*, daily nevirapine is recommended for her child from birth until the end of the breastfeeding period.

OR

2. *If a woman received a three-drug regimen during pregnancy*, a continued regimen of three-drug prophylaxis is recommended for the mother until the end of the breastfeeding period.

Recommendations on the infant feeding practices in the first 24 months of life, including the duration of breastfeeding, are provided in a separate, related guideline on HIV and infant feeding.

BENEFITS

PMTCT is one of the most powerful HIV prevention measures. It combines prevention with care and treatment for both mother and child. A growing number of countries now have national plans and are making significant progress in expanding more effective PMTCT services. WHO's new recommendations lay an important foundation for the scale up of quality programmes globally, including high-burden countries with limited resources.

The new recommendations have great potential to improve the mother's own health and to reduce mother-to-child HIV transmission risk to 5% or lower, from a background transmission risk of 35% (in the absence of any interventions and with continued breastfeeding).

The new recommendations offer the potential for all countries to virtually eliminate paediatric HIV. Combined with improved infant feeding practices, the recommendations can help to reduce both child mortality and new HIV infections.

An estimated 2.1 million children under the age of 15 were living with HIV in 2008, according to the latest available data, and there were some 430 000 new HIV infections in children. Nearly all of these new infections in children could have been prevented with effective PMTCT interventions.

PMTCT can also act as a gateway to improved reproductive, maternal and child health services at primary level and, in turn, bolster progress towards achieving the health-related Millennium Development Goals of reducing under-five mortality rates by two thirds, decreasing maternal mortality rates by three quarters, and halting and reversing the spread of HIV/AIDS by 2015.

CHALLENGES

The major challenges in scaling-up national PMTCT services and implementing the new recommendations are weak health infrastructure, limited human resources, limited management capacity, and limited funding and support for PMTCT. However there are many hopeful signs that PMTCT programmes now have greater priority both at the national and international level.

Successful implementation of the new guidelines will depend on:

- universal, voluntary HIV testing and counselling for pregnant women;
- availability of CD4 testing and ARVs at primary care level and antenatal facilities where most maternal-child health care takes place, and not just in specialized clinics;
- improved follow-up of pregnant women antenatally and of mothers and HIV-exposed infants after birth;
- ability to provide prophylaxis to the mother or baby throughout breastfeeding, as well as infant feeding counselling and support;
- appropriately trained staff.

THE REVIEW PROCESS

WHO has a guideline review committee which oversees the development, approval and updating of WHO recommendations, according to strict procedures specified by WHO's handbook for guideline development.

Summaries of the evidence for key recommendations reviewed by the guideline committee were produced by the University of California, San Francisco (Cochrane Collaboration Center for HIV) (USA), and in collaboration with the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the Centers for Disease Control and Prevention (CDC).

WHO is working with various partners on costing treatment and prophylaxis options and will conduct appraisals in high-burden countries to assess the cost and feasibility of the recommendations.

A multidisciplinary panel of experts, including civil society representatives, met 19–21 October 2009 to review, finalize and endorse the findings and recommendations; consider the balance of evidence for benefits and harms of these recommendations; and identify any uncertainties around the evidence, values and acceptability, as well as their implications.

The draft recommendations were subject to peer review from an additional group of international experts.

DISSEMINATION AND IMPLEMENTATION

The key recommendations will be published 30 November 2009 and the full guidelines are expected in early 2010. WHO, in collaboration with key partners, will provide technical support to all regions and additional support to high-burden countries to adapt and adopt the revised policy guidance. The full guidelines will be published in both English and French and will then be translated and published in at least three other languages.