



World Health Organization brief on antiretroviral treatment (ART) in HIV and TB prevention.

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This brief is intended as an introduction for WHO staff to the HIV and TB preventive benefit of antiretroviral treatment (ART). It is aimed at supporting WHO staff to facilitate discussions among stakeholders at the country level towards optimizing the preventive benefit of ART .

There is substantial evidence that ART reduces the transmission of HIV on an individual basis and a number of studies that show a community level impact. 1-5 The 2010 WHO ART guidelines recommend treatment for people ≤ 350 CD4 cells and all patients with TB irrespective of CD4 count. 6 Earlier treatment has a significant impact on reducing the incidence of TB for people living with HIV with likely reduction in TB transmission as well. 7,8 This is a rapidly evolving area of research and there are a number of planned and ongoing individual and community-level trials. Countries need to be prepared to consider how to best optimize the preventive benefit of ART as part of combination prevention (behavioural, biomedical, and structural strategies) and efforts to achieve universal ART coverage in line with 2010 WHO guidance to treat people living with HIV earlier than previously recommended (≤ 350 CD4 as opposed to ≤ 200).

The use of ARVs in HIV prevention and the case for optimizing the preventive impact of ART?

ARVs have been used to prevent HIV transmission for over 10 years—the best examples include the use of ARVs to prevent transmission of HIV as part of prevention of mother to child transmission (PMTCT), the use of ARVs for post exposure prophylaxis (PEP) after needle stick and/or sexual exposure and more recent studies that suggest that ARVs could be used as part of a microbicide. Results released in 2010 from the CAPRISA 004 vaginal microbicide trial, using a tenofovir-based vaginal gel, were promising with an ARV-based microbicide thought to be a few years

away from widespread use. 9 Pre-exposure prophylaxis (PrEP) is being assessed in at least 5 ongoing or planned international trials. 10 11 12 The first results, published in November 2010 from the I-PREX study in men who have sex with men, showed a 44% decrease in transmission in those who received a daily drug regimen of tenofovir and emtricitabine.¹³ While data showed that adherence to the medications was a major challenge for participants, for those participants who did adhere and had detectable drug levels, no infections were observed. Clinicians, public health experts and people living with HIV have also recognized the growing evidence base that earlier ART has immune restorative and prevention benefits.

Despite more than a 10-fold increase in access to ART between 2003 and 2009, the epidemic continues to outpace the HIV response. Globally, as of December 2009, an estimated 33.4 million people were living with HIV. By end-2009, while approximately 5.2 million people were accessing antiretroviral therapy in low- and middle income countries; that same year, over 9 million in immediate need of treatment could not access it. Although an additional 1.2 million people were added on treatment in 2009, over 2.7 million new infections occurred in 2008. Approximately 36% of those eligible under the 2010 WHO guidelines are on treatment. The “treatment gap”, which estimates the number of people with HIV eligible for ART against those with access to ART, decreased by end 2009 to around 64%. The bottom line is that current efforts to treat HIV are not keeping pace with all those who need therapy and without a dramatic reduction in new HIV infections this trend will continue. Clearly, without significant improvements in prevention, the likelihood of achieving the targets of the Millennium Development Goals for 2015 and Universal ART access appear increasingly remote for most countries.

Optimizing the HIV and TB preventive impact of ART should be considered a part of “combination prevention” and will not replace other prevention strategies. Multiple interventions are necessary to control HIV. ART will likely be most effective in preventing HIV and TB when used in combination with current HIV prevention interventions, including male and female condom use, treatment of sexually transmitted infections, reduction in number of concurrent sexual partners, risk-reduction counselling, harm reduction for injecting drug users, and male circumcision.

What is the evidence that ART has an HIV and TB preventive benefit?

There is a strong scientific evidence base supporting the fact that ART, by lowering a person's viral load and restoring the immune system, significantly reduces HIV transmission and TB. There are a number of studies and articles that support the preventive benefit of ART including 1) basic science on viral load and transmission, 2) a 2009 meta-analysis examining ART and HIV transmission among discordant couples, 3) a randomized trial in discordant couples, 4) cohort and randomized clinical trials on the impact of ART on TB and 5) community based studies on ART's role in HIV and TB prevention.¹⁴ Further evidence of the effect of ART on the prevention of HIV transmission is substantiated by the virtual elimination of paediatric HIV disease in high income countries by universal voluntary HIV testing of pregnant women and appropriate provision of ART. Research is ongoing and new studies are appearing in the literature regularly.

Observational data have shown reduced HIV transmission in serodiscordant heterosexual couples after the introduction of combination ART, and programmatic data support reduction in HIV transmission at the population level.^{1,14,15} A 2009 meta-analysis including 11 cohorts (5021 heterosexual couples) found zero risk of sexual transmission in patients treated with ART and with viral load below 400 copies per ml (upper confidence limit of 1.27 per 100 years).¹ A recent randomized controlled study of genital herpes simplex virus (HSV) treatment among long-term, HIV-serodiscordant heterosexual couples in Africa found that transmission reduced by at least 90% if the HIV-positive partner is on antiretroviral therapy.¹⁶ The proportion of couples who had unprotected sex actually decreased when the HIV-positive partner started treatment, allaying fears about behaviour change.¹⁶ There is also growing evidence of the impact of ART on community-level HIV transmission. In British Columbia a decrease in community plasma HIV RNA concentrations and HIV incidence among injecting drug users was associated with HAART use.¹⁷ Between 2004 and 2008, the number of HIV diagnoses in San Francisco fell by 45%, the average viral load among the HIV-positive population by 40%, and the actual HIV incidence fell by one-third between 2006 and 2008.³ In Taiwan a 53% reduction in new HIV cases was associated with free access to HAART.⁴ Research is ongoing and/or in planning and we expect new scientific data to be forthcoming on a regular basis.

Current state of the research

There are a number of ongoing and planned studies exploring the preventive impact of ART. WHO and its collaborators are engaged in

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further modeling on the impact of ART on TB, the relative importance of drug resistance and other assumptions, the effect of combination PrEP and ART coverage scenarios, effects of ART on maternal to child or partner transmission, an in-depth economic analysis of the various strategies, and a review of different models of providing testing and counseling. NIH HPTN 052 began in 2005 and will examine ART in 1,750 discordant couples in Botswana, Brazil, India, Malawi, South Africa, Thailand and Zimbabwe and the results are expected in 2012 or 2013.¹ There are a number of planned field trials and analyses including ongoing and planned work in Washington, District of Columbia and the Bronx in New York City,^{18,19} Vancouver, British Columbia,⁵ San Francisco California,³ Botswana²¹ and Kwa-Zulu Natal, South Africa.²¹

What are the possible implementation challenges?

The challenges involved in optimizing the preventive benefit of ART and the challenges involved in achieving universal access to ART for everyone who needs it are one and the same. HIV testing and counseling must be dramatically expanded within a framework of protecting human rights. Drug regimens must be optimized to be robust, with minimal toxicities, and in formulations, preferably one pill per day, that optimize adherence. Point of care CD4 and/or viral load diagnostic tests could greatly simplify monitoring. Delivery systems need to be decentralized to further advance simplification of treatment, to better integrate combination prevention approaches with treatment and to link treatment more effectively, depending on the local epidemiological context, with primary care, TB, maternal and child health, and sexual and reproductive health services, as well as harm reduction and other substance use services for people who use drugs. Communities must be mobilized to stimulate greater demand for treatment and to support simplified delivery. Across the board, costs must be reduced and efficiency greatly improved. The **Treatment 2.0** initiative aims to accelerate the further simplification of quality ART towards achieving sustained universal access and achieving the greatest preventive impact of treatment. WHO and UNAIDS are working together to advance **Treatment 2.0**.

What is the role of WHO globally, regionally and in country offices

WHO regularly monitors and reviews the results of ongoing research in the area of ART in prevention, identifies evidence gaps, and advocates for further research to address the gaps identified. In addition, WHO ensures that the evidence for preventive impact of ART is included in its ongoing guidance development process to support countries to scale up treatment and care for people living with HIV.

Technical assistance to support countries to adapt and implement global guidance on HIV treatment is provided primarily through WHO's regional and country offices. This technical assistance is focused on supporting national policy to scale up HIV treatment in line with WHO guidance. As countries progress towards universal access to treatment for all people who are eligible, operations research will be crucial to help guide service delivery to maximize the HIV and TB preventive benefits of ART, in line with the *Treatment 2.0* initiative.

For further clarification or questions, please contact:
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Helpful reading

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