

The Strategic Use of Antiretrovirals to Prevent HIV Infection: A Converging Agenda

Rachel Baggaley, Meg Doherty, Andrew Ball, Nathan Ford, and Gottfried Hirsenschall

Department of HIV/AIDS, World Health Organization, Geneva, Switzerland

There is a clear convergence toward an overarching strategic use of antiretroviral drugs to prevent human immunodeficiency virus (HIV) infection. Four interventions—immediate antiretroviral therapy (ART) for the infected partner in a serodiscordant couple, preexposure prophylaxis (PrEP), prevention of mother-to-child transmission (PMTCT), and postexposure prophylaxis (PEP)—are all strongly recommended by the World Health Organization as effective ways to prevent HIV infection. For HIV-infected individuals, ART to protect an HIV-uninfected partner and PMTCT are both part of an expanding list of recommendations for starting ART immediately to both treat and prevent HIV infection. For HIV-uninfected individuals, PrEP and PEP are increasingly being seen as related interventions, and there are compelling reasons to consider the provision of PEP as a potential gateway to PrEP. The effectiveness of each of these interventions depends on overcoming barriers to seeking services, adequate community understanding and engagement, high levels of access and uptake of services including HIV testing and counselling, and high levels of adherence.

Keywords. antiretroviral therapy; HIV/AIDS; postexposure prophylaxis; preexposure prophylaxis; PMTCT.

Global efforts to scale up access to antiretroviral drugs have largely focused on the life-saving benefits of treatment, and over the last decade these efforts are estimated to have saved >4 million lives [1].

More recently, increased attention has been given to the use of antiretroviral drugs to prevent human immunodeficiency virus (HIV) infection, following the results of several large randomized trials providing clear evidence of reduced HIV transmission and acquisition when antiretroviral drugs are provided immediately to HIV-infected individuals in serodiscordant relationships [2], or when taken by HIV-uninfected individuals as pre-exposure prophylaxis (PrEP) [3, 4]. These interventions add to the well-established antiretroviral-based prevention interventions to prevent mother-to-child transmission of HIV (PMTCT) [5] and to prevent the establishment of HIV infection following occupational or nonoccupational exposure using postexposure prophylaxis (PEP) [6].

These 4 interventions—immediate ART for the infected partner in a serodiscordant couple, PrEP, PMTCT, and PEP—are all strongly recommended by the World Health Organization (WHO) as effective ways to prevent HIV infection; these ART-based interventions are recommended as part of a comprehensive HIV prevention package of evidence-based interventions that include male and female condoms, male medical circumcision, and needle and syringe programs [5–7]. In the formulation of global guidance, an important principle for WHO has been to harmonize, as far as possible, recommendations for treatment and prevention, to simplify procurement and prescribing and improve uptake. Consistent with this approach, the same 2 nucleoside reverse transcriptase inhibitor (NRTI) antiretroviral drugs—tenofovir combined with either lamivudine or emtricitabine—are recommended for all 4 interventions. For early treatment and for PMTCT, this 2-drug NRTI backbone is combined with a third antiretroviral drug, efavirenz, whereas for the revised PEP recommendation, this NRTI backbone is combined with lopinavir/ritonavir. For PrEP, trials thus far have used a single or dual antiretroviral regimen of tenofovir or tenofovir/emtricitabine, respectively, and WHO recommendations reflect this choice.

Correspondence: Rachel Baggaley, MBBS, Department of HIV/AIDS, World Health Organization, 20 Avenue Appia, 1211 Geneva, Switzerland (baggaley@who.int).

Clinical Infectious Diseases® 2015;60(S3):S159–60

© The Author 2015. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

DOI: 10.1093/cid/civ091

Traditionally, each of these 4 interventions has been considered separately, with recommendations provided in different guidelines and directed at different audiences. These distinctions have become less meaningful, and there is a clear convergence toward an overarching strategic use of antiretroviral drugs to both treat and prevent HIV infection. For HIV-infected individuals, ART to protect an HIV-uninfected partner and PMTCT are both part of an expanding list of recommendations for starting ART immediately to both treat and prevent HIV infection. In 2013, WHO recommended giving HIV-infected pregnant women ART for life irrespective of CD4 cell count, effectively bringing pregnant women alongside serodiscordant couples as populations considered eligible for immediate life-long ART [5]; several countries have moved to providing immediate ART irrespective of CD4 cell count to other populations according to their epidemic situation, and future WHO guidance will document and reflect these country experiences. For HIV-uninfected individuals, PrEP and PEP are increasingly being seen as related interventions, and there are compelling reasons to consider the provision of PEP as a potential gateway to PrEP [8].

Current WHO recommendations for immediate ART and PrEP are limited to those populations for whom high-quality evidence supports their use—serodiscordant couples in the case of early ART [2] and men who have sex with men for PrEP [3]. However, a number of ongoing studies are anticipated to inform future recommendations that may expand the range of options. In many settings, there are populations that remain disproportionately affected by HIV and in which incidence continues to be high, and a new focused effort is needed. This could include expanding access to HIV testing with the provision of ART for those testing positive, and offering a range of prevention choices, including PrEP, for those who test negative. The effectiveness of each of these interventions depends on overcoming barriers to seeking services, adequate community understanding and engagement, high levels of access and uptake of services including HIV testing and counseling, and high levels of adherence. These remain major challenges, albeit for different reasons [9–11]. The development of drugs with improved safety and robustness to drug resistance and long-acting formulations will help, but further work is also needed to identify models of service delivery to improve uptake and adherence.

As part of an overarching vision to promote the strategic use of antiretrovirals for both the treatment and prevention of HIV,

WHO remains committed to responding to new evidence with new recommendations, and supporting countries to translate recommendations into further declines in mortality due to HIV and incidence of new infections.

Notes

Financial support. This work was in part supported by funds from the Bill & Melinda Gates Foundation.

Supplement sponsorship. This article appears as part of the supplement “HIV Postexposure Prophylaxis,” sponsored by the World Health Organization.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. World Health Organization. Global update on HIV treatment 2013: results, impact and opportunities. Geneva, Switzerland: WHO, 2013.
2. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365:493–505.
3. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010; 363:2587–99.
4. Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2013; 381:2083–90.
5. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva, Switzerland: WHO, 2013.
6. World Health Organization. Guidelines on post exposure prophylaxis for HIV: recommendations for a public health approach. Geneva, Switzerland: WHO, 2014.
7. World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva, Switzerland: WHO, 2014.
8. Jain S, Krakower D, Mayer KH. The transition from postexposure prophylaxis to preexposure prophylaxis: an emerging opportunity for biobehavioral HIV prevention. *Clin Infect Dis* 2015; 60(suppl 3): S200–4.
9. Ford N, Irvine C, Shubber Z, et al. Adherence to HIV postexposure prophylaxis: a systematic review and meta-analysis. *AIDS* 2014; 28:2721–7.
10. Tweya H, Guga S, Hosseinipour M, et al. Understanding factors, outcomes and reasons for loss to follow-up among women in Option B+ PMTCT programme in Lilongwe, Malawi. *Trop Med Int Health* 2014; 19:1360–6.
11. Fox MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007–2009: systematic review. *Trop Med Int Health* 2010; 15(suppl 1):1–15.