Commentary

Early antiretroviral therapy for HIV infection in sub-Saharan Africa, a challenging new step

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Abstract Recent changes in guidelines (World Health Organization (WHO), USA, and likely Europe soon) all move towards earlier initiation of antiretroviral therapy in asymptomatic patients infected with human immunodeficiency virus (HIV). Sonia Menon appropriately questions the feasibility and consequences at both individual and community levels of the early initiation of antiretroviral therapy in sub-Saharan Africa as likely effects will be both positive and negative. Local context should drive the uptake process in every country. Money, national and international, will be essential for the successful implementation of the new WHO recommendation. Leaders at both levels must take their responsibilities and mobilize the necessary resources, for example, doubling those for the Global Fund to Fight AIDS, Tuberculosis and Malaria from $10 billion to $20 billion USD for 2011–2013.

Journal of Public Health Policy (2010) **31,** 401–406. doi:10.1057/jphp.2010.36

Keywords: Africa; antiretroviral therapy; guidelines; HIV; WHO

Since November 2009, the World Health Organization (WHO) guidelines recommend that low-income countries initiate antiretroviral therapy in asymptomatic or mildly symptomatic patients infected with human immunodeficiency virus (HIV) earlier than was previously recommended, specifically when the CD4 count is less than 350 cells per μL instead of less than 200 cells per μL (also in all symptomatic patients classified at *WHO clinical stage 3 or 4* irrespective of the CD4 count).[1,2] In the last few months, the United States altered its guidelines, increasing the CD4 threshold at which antiretroviral therapy should be initiated (500 cells per μL versus 350 cells per μL previously).[3,4] European guidelines still recommend a threshold of 350 cells per μL (but they have not yet been updated from 2008).[5,6]

Sonia Menon, in this issue of *Journal of Public Health Policy*, questions the feasibility and consequences at both individual and community levels of the early initiation of antiretroviral therapy in sub-Saharan Africa.[7] Her questions are appropriate from several points of view. First, sub-Saharan Africa is the continent by far most affected. It has 22.4 million people living with HIV (out of 33.4 million worldwide), 1.9 million new infections annually (out of 2.7 million worldwide), and 1.4 million annual deaths (out of 2.0 million worldwide).[8] Second, antiretroviral therapy coverage remains low (roughly a third of the 10 million patients in need) despite a major increase in the last few years (100 000 patients treated in 2003) and far from the objective of universal access.[9] New HIV infections each year remain twice as frequent as treatment initiations.[10] Third, most African antiretroviral therapy programs adopt the WHO recommendations. Fourth, health system capacities are limited (HIV infection diagnoses occur late, access to CD4 testing is limited, and severe shortages of health workers), especially in the rural settings to which antiretroviral therapy is now decentralized and where most people live.[11,12] Fifth, the antiretroviral drugs that are available remain limited and most are from the first generation. Last but not least, most African programs are dependent on foreign financial support, with consequent uncertainty about future funding.

The new WHO recommendation was guided by recent data from clinical trials, cohort studies, and mathematical models in high- and low-income countries. They suggest that antiretroviral therapy started at a CD4 count of 350 cells per μL improves survival, delays disease progression and HIV-related morbidity, and is cost-effective.[13–16] Earlier initiation of antiretroviral therapy is, moreover, expected to reduce HIV transmission by increasing the number of patients with undetectable or low plasma HIV viral load – the main determinant of heterosexual transmission, the predominant type in Africa.

Importantly, the new WHO recommendation should be distinguished from the '*treatment as prevention*' strategy (also called '*test and treat*' strategy). The latter has been based on universal, voluntary, frequently repeated, HIV testing and immediate initiation of antiretroviral therapy in all infected people irrespective of the immunological and clinical status.[17] Only the '*treatment as*

prevention' strategy can be expected to reduce dramatically HIV incidence and, in theory, to drive the HIV epidemic towards elimination. The positive impact on HIV prevention of initiating antiretroviral therapy at a CD4 threshold of 350 cells per μL would be much smaller, although appreciable. On the other hand, its negative impact on the health systems would, in the short term, also be smaller.

As described by Menon, the potential negative impact of initiating antiretroviral therapy at a CD4 threshold of 350 cells per μL should not be underestimated, especially in terms of human, financial, and logistic resources required, and subsequent risks associated with resources diversion, especially from prevention and care of the sickest patients. The impact will reflect the number of additional patients attending treatment centers – those asymptomatic or mildly symptomatic with a CD4 count between 200 and 350 cells per μL. This additional patient load will, however, be highly dependent on the successful expansion of both HIV testing (through client-initiated and provider-initiated testing) and CD4 testing.[18,19] Currently, most African patients have a CD4 count below 200 cells per μL and/or are symptomatic at the time they are diagnosed with HIV and are therefore immediately eligible for antiretroviral therapy using the previous WHO guidelines.[20]

CD4 testing is not routine because of infrastructure and financial limitations, especially in rural settings.[21] Where CD4 testing is not feasible, only symptomatic patients will be treated. Thus WHO's recommendation for early antiretroviral therapy should be considered together with other current recommendations. In the case of the risk of long-term drug toxicity and dissemination of viral resistances, negative impacts of the new WHO recommendation can be expected to be lower when use of second generation, more potent and less toxic antiretroviral drugs (for example, tenofovir substituted for stavudine) expands. In many programs that use nevirapine in first-line regimens, an alternative should be made available because this drug is not recommended in women with a CD4 count above 250 cells per μL.

Of course, money will be a cornerstone of the successful implementation of the new WHO recommendation. Additional funds must be mobilized at both international and national levels. The Global Fund to Fight AIDS, Tuberculosis and Malaria, for

instance, on which many African programs rely will need twice the funds for the 2011–2013 period, compared to 2008–2010 (US$ 20 billion versus US$ 10 billion).[22] National funds (from households and governments) devoted to HIV/AIDS control contribute only half; more public resources should be allocated to HIV/AIDS (and to the health sector, in general).[23] In contrast, free access to antiretroviral therapy at the point of delivery should be expanded, as it favors adherence, effectiveness, and equity.[24] Clearly, these considerable efforts are particularly difficult during the present global economic crisis and will require both political will and innovative solutions.

National AIDS programs managers face a fundamental programmatic challenge: how to adapt and implement the CD4 threshold of 350 cells per μL as recommended by WHO? They must take into account:

- health system capacity (including human and logistic resources);
- number of patients in need of treatment who can be diagnosed and provided care;
- essential activities that must not be penalized as a consequence (for example, prevention, expansion of HIV screening and linkage to care, adherence support, earlier diagnosis, and treatment of HIV-related illnesses);
- other recommendations (for example, availability of CD4 testing, viral load assays, second-line regimens, and newer, more potent and better tolerated antiretroviral drugs; dissemination of viral resistance assessment tools);
- ethical issues (for example, equitable access to care); and
- the level and sustainability of financial resources.

Of particular importance, treatment should not be denied to patients with low CD4 counts (that is, at highest risk of death) because of exceeded capacity.

In conclusion, early initiation of antiretroviral therapy in sub-Saharan Africa represents a new public health challenge. In each country, the local context should drive the process. Most programs, undoubtedly, will need time to adapt. From now on, international and national political leaders must take on their responsibilities and mobilize the necessary resources.

About the Author

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