The impact and cost of the 2013 WHO recommendations on eligibility for antiretroviral therapy

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Objectives: The present study presents estimates of the number of people who would become newly eligible for antiretroviral therapy if all countries adopted the 2013 WHO treatment guidelines. It also shows the cost and impact that would result if coverage expanded to 80% of those eligible.

Methods: The AIDS Impact Model (AIM) and the Goals model within the Spectrum modelling system were used for these estimates. Projections of costs and AIDS deaths are based on estimates for 116 low-income and middle-income countries. Projections of impact on HIV incidence are based on simulation modelling for 24 high burden countries, with the results scaled up to represent all low-income and middle-income countries.

Results: If the 2013 guidelines were adopted universally, the number eligible for treatment would rise to 28.6 million in 2013. Achieving 80% coverage would mean 28 million on antiretroviral therapy by 2025, and would avert 2.9 million deaths and 3.9 million new infections from 2013 to 2025 compared with the 2010 guidelines.

Conclusion: The 2013 guidelines significantly expand the number eligible for treatment. Reaching those newly eligible will require additional resources, but is likely to produce significant benefits.

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Background

In 2013, WHO released new treatment recommendations that expand the number of people eligible for treatment [1,2]. The groups newly eligible for treatment include the following: all HIV-infected pregnant women, HIV-infected adults with hepatitis B infection and severe liver disease, serodiscordant couples, adults with $CD4^+$ T-cell counts between 350 and 500 cells/μl, all HIV-infected children between the ages of 2 and 5 years, and those age 5 years and above with $CD4^+$ T-cell counts between 350 and 500 cells/μl. If all countries adopt these new guidelines, the number of people eligible for treatment in low-income and middle-income countries will increase from about 16 million to over 28 million [3]. Not all of these newly eligible people will start treatment immediately. Some, such as pregnant women who visit antenatal clinics, will be more readily identified as HIV-infected than others who may have fewer opportunities for testing.

The purpose of this article is to examine the cost of providing treatment to these newly eligible populations and the impact of that expansion on the number of deaths and new infections.

Methods

This analysis uses two modules in the Spectrum software: the AIDS Impact Model (AIM) and Goals. AIM is used to estimate the number of people eligible for treatment and the impact of antiretroviral therapy (ART) on

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HIV-related deaths. The Goals model is used to estimate the impact of ART on new infections.

The AIM model tracks the HIV-infected adult population by age, sex, and $CD4^+$ T-cell count. There are seven $CD4^+$ T-cell count categories: less than 50, 50–99, 100–199, 200–249, 250–349, 350–500, and more than 500 cells/μl. The majority (55–64%) of new infections are assumed to be in the more than 500 category with the rest starting in the 350–500 category. Each year people can remain in the same $CD4^+$ T-cell category, move to the next lower category, die from HIV-related causes, die from non-HIV causes, or initiate ART. The parameters for these transitions were derived by fitting to cohort data from the Analyzing Longitudinal Population-based HIV/AIDS data on Africa network [4]. Mortality for those who initiate ART is dependent on their $CD4^+$ T-cell count at the time of initiation, as well as the duration on treatment (0–6, 7–12, greater than 12 months), sex, and age. Mortality rates while on ART are based on data and analysis from the IeDEA Consortium [5]. HIV-infected women who give birth have a chance of passing the infection to their newborn children at birth or later through breastfeeding, depending on whether or not they receive prevention of mother-to-child transmission services [6]. Infected children are also tracked by age and $CD4^+$ T-cell count. Their mortality depends on when they became infected (at birth or through breastfeeding 0–6, 7–12 or greater than 12 months after birth) and whether or not they receive ART and/or cotrimoxazole. The structure of the AIM model is described elsewhere [4]. The full set of parameter values used in this analysis is provided in the appendix, http://links.lww.com/QAD/A492.

In global analyses coordinated by UNAIDS, the AIM model is used by nearly all low-income and middle-income countries to estimate HIV epidemic levels and trends. The output from these country models is aggregated to produce global totals. We used these country files standardized to WHO guidelines to estimate the effects of changing guidelines in each country on the number of people eligible for treatment and then aggregated the result to estimate the global impact in all low-income and middle-income countries.

The incidence used to determine the number of new infections is estimated using the Goals model [7]. This model divides the adult population aged 15 to 49 years by sex and risk group (not sexually active, low-risk stable couples, medium-risk people engaging in casual sex, sex workers and clients, men who have sex with men (MSM), and injecting drug users). The model calculates new HIV infections by sex and risk group as a function of behaviors and epidemiological factors such as prevalence among partners and stage of infection. The risk of transmission is determined by behaviors (number of partners, contacts per partners, condom use) and biomedical factors (ART use, male circumcision, prevalence of other sexually transmitted infections). Interventions can change any of these factors and, thus, affect the future course of the epidemic. We implemented the Goals model for 24 countries that together account for 80% of new adult infections in all low-income and middle-income countries (Table 1). Country-specific behavioral inputs are drawn from national surveys and fitted to match the national prevalence trends estimated with AIM. Epidemiological parameter values are based on reviews of international studies. Values and sources are given in the appendix, http://links.lww.com/QAD/A492. Results from these 24 countries were scaled up to represent totals for all low-income and middle-income countries.

Estimates of the effect of ART on incidence depend heavily on assumptions about the effect of ART on transmission. The HPTN 052 trial among serodiscordant couples in multiple countries found incidence was 96% lower in couples wherein the infected partner was initiated on ART at a $CD4^+$ T-cell count between 350 and 550 cells/μl compared with those who waited until $CD4^+$ T-cell counts had declined to below 250 cells/μl [8]. Donnell *et al.* [9] found a 92% reduction in the transmission of HIV among couples who initiated ART at $CD4^+$ T-cell counts above 250 cells/μl compared with those who did not. Tanser *et al.* [10] examined data from a large population-based cohort in rural South Africa and found that incidence was significantly lower in areas with high ART coverage (>30% of HIV-positive population) compared with areas of low coverage (<10%). An analysis of the effects of ART on transmission among serodiscordant couples in Yunnan Province in China found transmission was 66% lower in couples who initiated ART according to national guidelines (at $CD4^+$ T-cell counts below 350 cells/μl) compared with those who did not [11]. For the purposes of this study, we assumed that ART would reduce incidence by 80% under the assumption that about 80% of those on ART at any

Table 1. Countries that were examined in detail using the Goals model to estimate the impact of antiretroviral therapy on HIV incidence.

Sub-Saharan Africa	Latin America	Asia	Eastern Europe
Botswana	Brazil	Cambodia	Russia
Cameroon	Mexico	China	Ukraine
Côte d'Ivoire		India	
Ethiopia		Indonesia	
Kenya		Viet Nam	
Lesotho			
Mozambique			
Nigeria			
Rwanda			
South Africa			
Swaziland			
Tanzania			
Uganda			
Zambia			
Zimbabwe			

point in time would achieve viral suppression, given current patterns of rapid scale-up and adherence.

The costs per patient treated have declined substantially in the past few years. The median cost for recommended first-line drugs is now well below $200 per patient year [12] ($186 for a fixed dose combination of tenofovir+emtracitabine+efavirenz to as low as $112 for a two-pill regimen). Costs for second-line antiretrovirals are considerably higher, around $450 per patient year, and vary widely across countries. Additional costs for laboratory monitoring and service delivery can be higher than drug costs, averaging about $220 in President's Emergency Program for AIDS Response-supported programs and declining with site maturity [13]. Recent analyses by the Clinton Health Access Initiative found facility level costs to range from about $140 to $850. Additional costs above the facility may add approximately 40% to the total treatment costs. For the purposes of this analysis, we have used a total cost of $515 per patient (a weighted average median price in 2011 of $145 for first-line and second-line antiretrovirals, $222 for average service delivery and monitoring costs and an additional 40% for costs above the facility level for administration, logistics, training and planning), declining slowly to $445 by 2025.

We studied the effects of the new treatment guidelines by comparing two scenarios: 2010 guidelines that assumes high coverage of 2010 guidelines achieved by 2015 and remaining constant after that as shown in column 2 of Table 2 and 2013 guidelines (shown in the third column of Table 3 with different target coverage levels and target years for all groups eligible under the 2013 guidelines).

Results

The number of people eligible for treatment in 2013 is estimated to be 17.6 million under the 2010 guidelines and 28.6 million under the 2013 guidelines (Table 3). This table shows the number of adults and children actually on ART at the end of 2012 and the additional people who would be eligible under the two guidelines as estimated by the AIM model. The largest increases in the population eligible for treatment result from three groups that are newly eligible under the 2013 guidelines: HIV-infected adults with $CD4^+$ T-cell counts between 350 and 500 cells/μl (6.4 million), serodiscordant couples with $CD4^+$ T-cell counts more than 500 cells/μl (2.5 million), and children newly eligible, mostly those between the ages of 2 and 5 years who were not previously eligible (1.3 million). The number eligible in future years will depend on epidemic dynamics in each country and the rate of scale-up of patients on ART, but is expected to increase only slightly to 31–32 million by 2025 under the 2013 guidelines.

Implementing the 2013 guidelines for eligibility and achieving the coverage goals shown in Table 2 would result in 27 million on ART by 2020 and 28 million by 2025 compared with 24 million on ART in 2025 under the 2010 guidelines (Fig. 1). Scaling up ART under the 2010 guidelines would reduce the annual number of AIDS deaths in low-income and middle-income countries by 44% from 1.6 million in 2012 to 900 000 million by 2025. Implementation of the 2013 guidelines would lead to a 59% reduction in deaths to 650 000 by 2025 (Fig. 2). For the period 2013–2025, implementing the 2013 guidelines would avert 3.0 million deaths compared with the 2010 guidelines. One death would be averted for every 20 person-years of ART.

There would also be significant effects on new infections. Scale-up under the 2010 guidelines would contribute to a decline in the annual number of new infections from 2.2 million in 2012 to 1.0 million by 2025. Implementing the 2013 guidelines would further reduce new infections to 760 000 by 2025, 23% lower than the 2010 guidelines (Fig. 3). Implementing the 2013 guidelines would avert 3.1 million infections from 2013 to 2025 compared with the 2010 guidelines. Every 19 additional person-years of ART would avert one new infection.

Table 2. ART coverage of eligible populations in 2010 and 2013 WHO guidelines.

Eligible population	2010 Guidelines: coverage in 2015 (%)	2013 Guidelines: coverage in 2015/2025 (%)
Adults with $CD4^+$ T-cell counts <200 cells/μl	80	80/90
Adults with $CD4^+$ T-cell counts 200–249 cells/μl	70	80/90
Adults with $CD4^+$ T-cell counts 250–349 cells/μl	45	70/80
Adults with $CD4^+$ T-cell counts 350–500 cells/μl	5	30/80
HIV-positive children <2 years old	80	80/80
HIV-positive children 2–5 years old	80 with $CD4^+$ T-cell counts <750 cells/μl	80/80 of all HIV-positive children
HIV-positive children 5+ years old	80 with $CD4^+$ T-cell counts <350 cells/μl	80 with $CD4^+$ T-cell counts <500 cells/μl
Pregnant women with $CD4^+$ T-cell counts >500 cells/μl	0	80 by 2017
Serodiscordant couples with $CD4^+$ T-cell counts >500 cells/μl	0	80 by 2020
Adults coinfected with TB or severe HBV	0	80/80

HBV, hepatitis B virus; TB, tuberculosis.

Table 3. Number of people eligible for treatment in low-income and middle-income countries in 2013 (millions).

Population	Eligible under 2010 Guidelines	Eligible under 2013 Guidelines
Adults and children on ART	9.7	9.7
HIV-positive children (0–2 years) and those (2–14 years) eligible under 2010 guidelines but not on ART	1.9	1.9
Adults with $CD4^+$ T-cell counts <350 cell/μl not on ART	5.3	5.3
TB/HIV coinfected	0.6	0.6
HIV/HBV coinfected with serious liver disease	0.1	0.2
HIV-positive adults with $CD4^+$ T-cell counts 350–500 cells/μl not on ART		6.4
Additional children eligible under 2013 guidelines		1.3
Pregnant women with $CD4^+$ T-cell counts >500 cells/μl		0.7
Serodiscordant couples with $CD4^+$ T-cell counts >500 cells/μl		2.5
Total	17.6	28.6

ART, antiretroviral therapy.

The additional costs of implementing the 2013 guidelines would be US$1.8 billion in 2015 and US$3.3 billion in 2020 after which they would decline to US$ 1.71 by 2025. When future costs and benefits are discounted at 3% per year, the cost per infection averted from 2013 to 2025 of implementing the 2013 guidelines is $9000 and the cost per death averted is $9600. The cost per quality life year gained (QALY) would be just $350 well below the cost–effectiveness threshold recommended by the Commission on Macroeconomics and Health [14]. (QALYs are calculated with disability weights of 0.453 for HIV-infected population with $CD4^+$ T-cell counts less than 200 cells/μl, 0.779 for HIV-positive population with $CD4^+$ T-cell counts more than 200, 0.947 for those on ART, and 1.0 for the uninfected population [15].)

Discussion

The new 2013 treatment guidelines from WHO recommend expanding eligibility to include several new groups of people living with HIV, notably all HIV-infected adults with $CD4^+$ T-cell counts between 350 and 500 cells/μl, all pregnant women and serodiscordant couples regardless of $CD4^+$ T-cell count, and all HIV-positive children up the age of 5 years. If all counties were to adopt these guidelines in the coming years, the number of people on treatment would almost triple from 9.7 million in 2012 to 28 million by 2025. The benefits would be substantial, 3.9 million infections averted and 2.9 million deaths averted. Such a program would require additional resources, but would be a very cost-effective use of health resources.

There would be several challenges associated with achieving a doubling in the number of people on treatment, including mobilizing additional resources; expanding facilities, personnel, and drug supply chains; and identifying HIV-infected people at higher $CD4^+$ T-cell counts and those in serodiscordant partnerships. Identifying those eligible with higher $CD4^+$ T-cell counts will require expanding testing opportunities for apparently healthy populations and building demand for testing. With such a large amount of resources devoted to treatment, there will be pressure to continue to reduce the

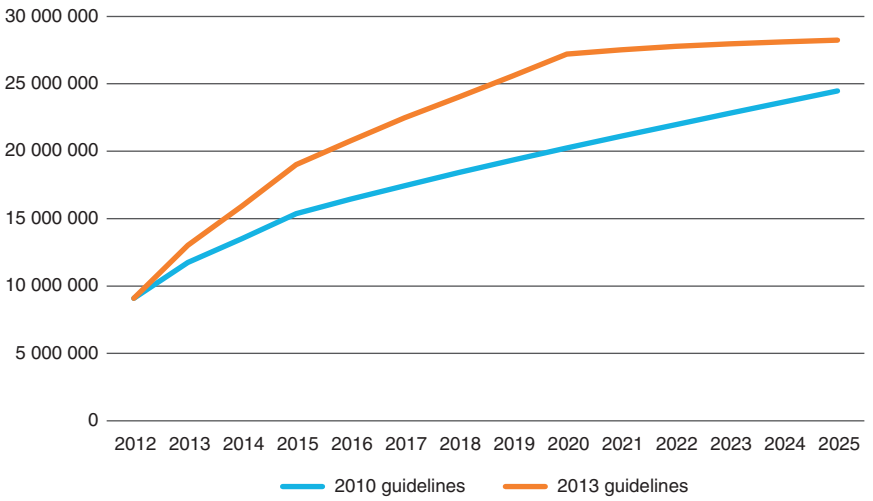

Fig. 1. Number of people receiving antiretroviral therapy by scenario.

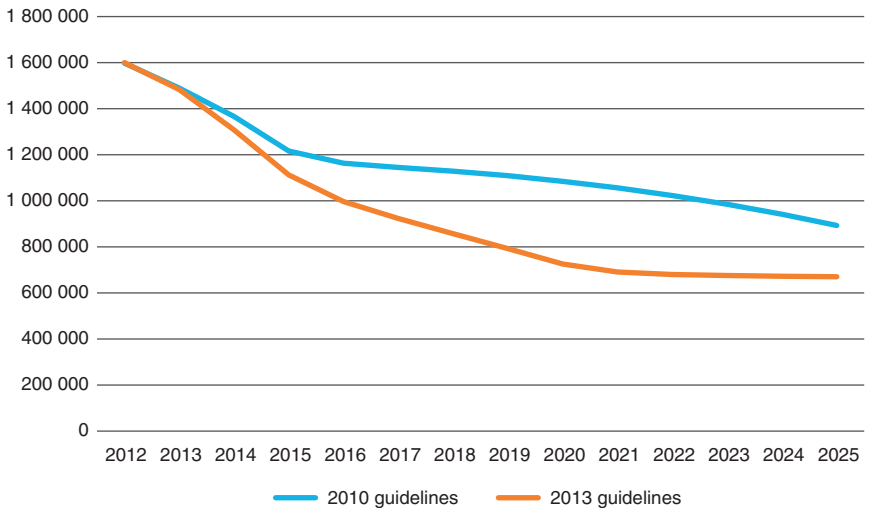

Fig. 2. Annual number of AIDS deaths in low-income and middle-income countries, 2012–2025.

costs of treatment. There may be opportunities to reduce costs through less frequent visits and testing, bulk purchases of drugs, use of new inexpensive point-of-care tests, and task shifting to lower level health workers and community workers. It will be a challenge to implement these changes without compromising the quality of care at the same time that the number of patients is increasing rapidly.

There is a high degree of uncertainty associated with these estimates. Need for ART among adults in 2012 is reported by UNAIDS as 14 million with a range of 13.1–15.2 million. Similar uncertainty bounds would apply to estimates of need under the 2013 guidelines. We have assumed that country reports of the numbers receiving ART are accurate, but there may be considerable errors associated with procedures to remove patients from the rolls when they drop out of treatment. There are also uncertainties that are difficult to quantify associated with the benefits of early treatment. WHO assesses this information using the GRADE method and has assigned different levels of evidence to the recommendations for each population group. For most population groups, the guidelines make a strong recommendation and assess the quality of evidence as moderate, except for those coinfected with HIV and tuberculosis or hepatitis B virus (low quality of evidence) and serodiscordant couples (high quality of evidence [1].)

The progress in expanding treatment programs from their beginnings shortly after 2000 to nearly 10 million on treatment in 2012 shows that remarkable achievement is possible when all are agreed on the need. The scale-up required to fully implement the 2013 guidelines represents a continuation of this effort. We expect significant benefits for those who are infected

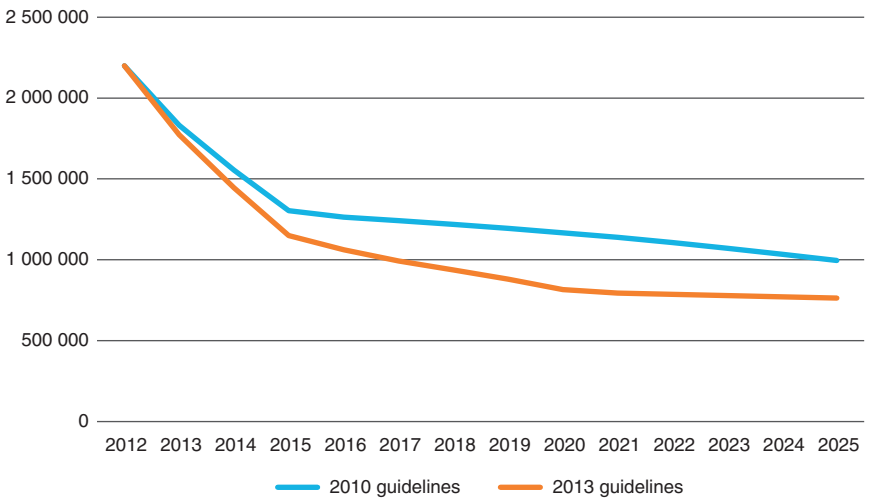

Fig. 3. Annual number of new adult HIV infections.

and the prevention of new infections in the coming years.

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All authors contributed to the writing of the article and approved the final version. J.S. and C.G. conducted the impact and cost modelling. M.M. and P.G. led the effort to prepare the country files for all low-income and middle-income countries. J.S., M.M., P.G., M.D., and P.E. prepared the estimates of the number of people eligible under the new guidelines. M.D. and P.E. contributed to the development of the new treatment guidelines.

Conflicts of interest

There are not conflicts of interest.

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