Published in final edited form as:
AIDS. 2012 July 31; 26(0 1): . doi:10.1097/QAD.0b013e3283558526.

The impact of antiretroviral treatment on the age composition of the HIV epidemic in sub-Saharan Africa

Jan AC Hontelez[1,2,3], **Sake J de Vlas**[1], **Rob Baltussen**[2], **Marie-Louise Newell**[3], **Roel Bakker**[2], **Frank Tanser**[3], **Mark Lurie**[4], and **Till Bärnighausen**[3,5]

[1]Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands [2]Nijmegen International Center for Health System Analysis and Education, Department of Primary and Community Care, Radboud University Nijmegen Medical Centre, Netherlands [3]Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Somkhele, South Africa [4]Department of Epidemiology and the International Health Institute, Warren Alpert Medical School, Brown University, Providence, RI, USA [5]Department of Global Health and Population, Harvard School of Public Health, Boston, MA, USA

Abstract

Introduction—Antiretroviral treatment (ART) coverage is rapidly expanding in sub-Saharan Africa (SSA). Based on the effect of ART on survival of HIV-infected people and HIV transmission the age composition of the HIV epidemic in the region is expected to change in the coming decades. We quantify the change of the age composition of HIV-infected people in all countries in SSA.

Methods—We used STDSIM, a stochastic microsimulation model, and developed an approach to represent HIV prevalence and treatment coverage in 43 countries in SSA, using publicly available data. We predict future trends in HIV prevalence and total number of infections among the populations aged 15-49 and 50 years and older (50+) for different ART coverage levels.

Results—We show that, if treatment coverage continues to increase at present rates, the total number of HIV-infected patients aged 50+ will nearly triple over the coming years: from 3.1 million in 2011 to 9.1 million in 2040, dramatically changing the age composition of the HIV epidemic in SSA. In 2011, about 1 in 7 HIV-infected people was aged 50 years or older; in 2040, this ratio will be larger than 1 in 4.

Conclusion—The HIV epidemic in SSA is rapidly ageing, implying changing needs and demands in many social sectors, including health, social care, and old-age pension systems. Health policymakers need to anticipate the impact of the changing HIV age composition in their planning for future capacity in these systems.

Keywords

HIV; Antiretroviral therapy; Ageing; Mathematical model; Epidemiological trends

Introduction

The rapid and large scale-up of antiretroviral treatment (ART) for HIV in sub-Saharan Africa (SSA) constitutes an unprecedented global public health effort, resulting in great

Corresponding Author: Jan A. C. Hontelez. Department of Public Health, Erasmus MC, University Medical Center Rotterdam, P.O. Box 2040, 3000 CA, Rotterdam. j.hontelez@erasmusmc.nl, Tel: +31 30 704 46 32.

improvements in length and quality of life of those infected. The expansion of ART coverage since the early 2000s has led to a substantial increase in the number of HIV-infected patients on ART, with nearly 4 million people initiated in SSA as of late 2009 [1]. In June 2011, the United Nations General Assembly High Level Meeting on AIDS renewed its commitment to achieving universal ART coverage, calling for a doubling in scale-up efforts to initiate another 10 million people, to achieve universal coverage of those in need by 2015 [2]. Yet, while "[t]he UN meeting was tasked with charting the future course of the global HIV response, … [it] failed to mention the ageing of the pandemic" [3].

Effective ART increases survival [4-6] and can decrease HIV transmission probabilities [7-10]. Mills and colleagues estimated that life-expectancy of HIV-infected patients in SSA can approach life-expectancy of the uninfected population if treatment is initiated early (at CD4 cell counts of >250 cells/μL) [5]. The results of the HIV Prevention Trials Network (HPTN) 052 trial show that HIV transmission rates can be reduced by as much as 96% in HIV-discordant stable partnerships [8], and results from observational studies show reductions of about 90% in transmission rates [7,9]. Thus, as with expanding ART coverage HIV-infected people will live into older ages, and HIV incidence in the young and middle aged population is likely to decrease, a shift of the age composition of the HIV epidemic towards older ages might be expected. Such a shift has already occurred in developed countries. About 29% of HIV-infected patients in the United States was aged over 50 years in 2008, while this proportion was only 17% in 2001 [11]. A previous study quantified the ageing of the HIV epidemic for the South African province of KwaZulu-Natal, estimating that the number of HIV-infected adults aged 50 and older (50+) will double from 2004 to 2025 [12]. Similar projections for other parts of SSA are currently missing, and it is unlikely that the South African results can be generalized to countries with different demographic and behavioural characteristics as well as distinct HIV treatment and prevention efforts. Already, an estimated 3 million people aged 50+ live with HIV in SSA [13], and with a further 7 million HIV-infected people in SSA eligible for HIV treatment [14], there is a large pool of currently untreated HIV-infected adults that will be able to survive to older ages as treatment coverage expands.

Here, we predict age-specific HIV prevalence trends in 43 countries in SSA under different trajectories of ART coverage expansion. We used STDSIM, a stochastic microsimulation model that simulates individuals in a dynamic network of sexual contacts [15-17]. We developed an approach that can be applied to quantify all national HIV epidemics in 43 sub Saharan African countries in the period 2000-2009 by using country-specific data on demographic composition [18-20], data on country-specific ART coverage [1], and country specific circumcision prevalence rates [14,21], as well as epidemic specific sexual behaviour profiles.

Methods

Model

In the model, HIV is represented by 4 consecutive stages: early infection (0.25 years); asymptomatic infection (5.5 years); symptomatic infection (4 years); and AIDS (0.7 years). Median survival of an untreated HIV infection is about 10 years (95% confidence interval: 5 - 19 years) [22]. People on ART are assumed to have a 90% reduction in infectiousness [7,9], and their life-expectancy at the moment of treatment initiation is four times the remaining untreated life-expectancy (figure S1) [6]. More details about the model structure can be found in the supplementary material and in three previous publications [15,23,24].

Model quantification

Demographics—Background mortality rates (mortality in the absence of HIV) were calculated using country-specific life tables [19], and burden of disease estimates published by the World Health Organization (WHO) [20]. For each country, we first calculated the proportion of deaths attributed to HIV through comparison of the age- and sex-specific burden of disease estimates [20], and the all-cause mortality rates in the WHO life tables [19]. We then used the ratio between these two mortality estimates (HIV-specific and all-cause) to compute background mortality rates for all causes except for HIV. Figure S2A and S2B present the country-specific HIV-corrected background mortality rates for men and women, respectively. Age- and period-specific fertility rates for each country were obtained from the 2008 United Nations (UN) World Fertility Data [18]. We assumed that fertility rates remained constant after 2011.

ART scale-up—We fitted antiretroviral treatment coverage until 2009 to the coverage levels reported by WHO [1], using two sub-models. The first sub-model represents an individual's demand for ART as a function of HIV-disease stage; the second sub-model describes the capacity of the health system to meet this demand. ART coverage in our model is the ART demand met by the capacity of the health system. To fit the modelled ART coverage to the annual coverage data reported by WHO (for the period 2004-2009) [1], we used a quadratic (αx^2), linear (αx), or square-root ($\alpha x^{1/2}$) of scale-up of ART capacity in the health system, while assuming the ART demand function to be the same as previously estimated for South Africa [15]. For each of the three scale-up functions, we calculated the annual ART coverage of those eligible (at CD4 counts of $\leq$200 cells/μL) for all countries in SSA using the country-specific starting years of the ART scale-up (the scale-up started in all countries in the period 2001 - 2005). We choose the multiplication factors (α) in the different functions to maximize the model fit by minimizing the Mean Squared Error (MSE) of the model predictions compared to the country-specific ART coverage estimates reported by WHO [1].

We assumed all countries to provide ART at CD4 counts of $\leq$200 cells/μL up to 2009, with three exceptions: (i) Botswana offered ART at CD4 counts of $\leq$250 cells/μL for all HIV-infected individuals since the start of its ART scale-up in 2003 [25]; (ii) Rwanda switched to ART at CD4 counts of $\leq$350 cells/μL for all HIV-infected individuals in 2007 [26]; and (iii) Namibia has offered lifelong ART at CD4 counts of $\leq$350 cells/μL for all pregnant women since 2007 (about 20% of all HIV-infected women aged 15-49 and with CD4 cell counts of 200-350 cells/μL seeking care) [27]. We assumed a baseline annual rate of stopping treatment of 5% [28], and that people who stopped will never re-initiate treatment. Since, retention in care varies with the capacity of the health system to deliver ART [29], we assumed that the annual rate of stopping treatment is reduced to 2.5% when the health-systems capacity to provide ART reaches 80%, and to further reduce to 1% when the capacity is 100%.

HIV epidemic and sexual-behaviour profiles—To represent to the HIV epidemics in SSA, we defined five sexual-behaviour profiles that differ in their age- and sex-specific rates of forming – and condom use during – three different types of sexual partnerships (table S1): stable relationships (lasting on average 25 years); casual relationship (lasting on average 6 months); and commercial sex (a once-off contact) [23,24].

We named the sexual behaviour profiles according to the epidemics they have produced: (i) *concentrated risk profile* (high risk of HIV among commercial sex workers (CSWs) and clients; low risk in the general population); (ii) *mixed risk profile* (high risk of HIV among CSWs and clients; medium risk in the general population), and (iii) *generalized risk profile*

(high risk in the general population). Three of the four parameter settings of the 'four cities study' fitted these three profiles, and were chosen accordingly: Cotonou, Benin (*concentrated risk profile*); Yaoundé, Cameroon (*mixed risk profile*); and Kisumu, Kenya (*generalized risk profile*) [24]. High levels of condom use among CSWs introduced in the early nineties in the *concentrated risk profile* and *mixed risk profile* resulted in declining HIV prevalence. To capture this distinction, we added two extra profiles: (iv) *concentrated risk profile* (*low condom use*) and (v) *mixed risk profile* (*low condom use*), both with reduced condom use rates during commercial sex.

In the 'four cities study' [24] sexual behaviour parameters for the population aged 15-49 were stratified by 5-year age groups and fitted to represent age-specific reported numbers of sex partners from behavioural surveys from the original 'four cities study' [30]. In order to derive parameter values for sexual behaviour for the age group 50+, for which measured data was not available in the study, we assumed that partner change rates and CSW-visiting behaviour remained the same for all age groups 45+. Within each partnership we assumed a 25% reduction in the frequency of sexual contacts in the age group 50+ relative to the age group 45-49. This assumption fitted closely to the data from a HIV and sexual behaviour surveillance in the population aged 50+ in KwaZulu-Natal, South Africa [12,31].

For each country, we ran the model with all five sexual-behaviour profiles and the country-specific circumcision prevalence [14,21], and ART scale-up function (see above). We then selected the profile that best described the HIV epidemic in a given county in the period 2000-2009. In order to do so, we constructed a 'fit score' that captures the development of the HIV prevalence over time. The score is the sum of the MSE of HIV prevalence predictions over 2000-2009 (for fitting prevalence levels), and the squared error (SE) over the difference between prevalence in 2000 to 2004, and 2005 to 2009 to fit the observed trend in HIV prevalence. We used UNAIDS estimates of the country-specific HIV prevalence in adults aged 15-49 over the period 2000-2009 in order to assess fit [14].

Finally, we fine-tuned the model quantifications for each country by choosing the best-fitting combination of overall partner change rates (range +/- 25%; see table S1) and year of HIV introduction that produced the lowest MSE on the HIV prevalence estimates in adults aged 15-49, as compared to UNAIDS estimates for the period 2000-2009. For the *concentrated risk* and *mixed risk profiles* we allowed for a maximum of 25% reduction in CSW visit rates to further fine-tune predicted HIV epidemics, because the epidemics produced by these profiles are largely driven by commercial sex.

Simulations

We predicted trends in HIV prevalence in the population aged 15-49 and 50+ over the period 2011 - 2040 in 43 countries in SSA. In our baseline estimate, we assumed ART to be scaled-up continuously after 2009 according to the country-specific scale-up function of the health system capacity (see above), until capacity reaches 100%. By October 2010, 7 countries in SSA had adopted the 2010 WHO treatment guidelines that recommend ART initiation at CD4 counts of ≤350 cells/μL into their national policy (Kenya, Lesotho, Malawi, Rwanda, Tanzania, Zambia, and Zimbabwe) [1], while South Africa adopted the guidelines in August 2011 [32]. We assumed that all other countries will have adopted the new guidelines by January 2013.

We calculated country-specific trends in HIV prevalence and total number of HIV infections in the population aged 15-49 and 50+. We assumed three alternative scenarios of scale-up of health-systems capacity to provide ART: (i) *decline* (reduction in capacity by 20% in 2012 and constant capacity levels thereafter); (ii) *no further scale-up* (capacity remains constant at 2011 levels); (iii) *rapid scale-up* (capacity increase to 100% for all countries by 2015).

Results

Using five predefined sexual-behaviour profiles (figure 1), our model was able to accurately replicate the ART coverage scale-up (figure 2A) and HIV epidemics (figure 2B and 2C) of all 43 sub-Saharan African countries. For only 9 countries, HIV prevalence projections differed more than 10% compared to UNAIDS estimates at some point during the period 2000-2009. The absolute number of HIV infections in older adults (2.6 million) and the population aged 15-49 (17.8 million) in 2007 are very similar to the estimates that Negin *et al* derived using a different methodological approach (2.9 million and 17.9 million, respectively) [13]. In addition, our model predictions regarding population growth over the period 2000 - 2040 are very similar to those provided by the United Nations Population Prospects (figure S3) [33]. A detailed description of the parameters for individual countries can be found in Table S2.

Figure 3 shows the HIV prevalence in the population aged 15-49 and 50+ for the years 2011, 2025, and 2040 under the baseline scenario of continued scale-up of ART. Overall, prevalence in the population aged 15-49 will decline from 5% in 2011 to 3% in 2040, while prevalence in the population aged 50+ will increase from 3% to 4% over the same period. The number of countries with an HIV prevalence of <1% in the population aged 15-49 will increase from 6 in 2011 to 17 in 2040, while the number of countries in this prevalence category for the population aged 50+ will halve in the same period, from 12 to 6. HIV prevalence in older adults will be 2% or higher in 22 countries in SSA in 2040, while this is the case for only 11 countries regarding adult HIV prevalence. In countries with currently very high HIV prevalence rates in both younger and older adults, HIV prevalence in the population aged 50+ will increase dramatically (table 1). For instance, in Botswana, HIV prevalence in the population aged 50+ was 15% in 2011, and will increase to 24% in 2040. Similar trends are predicted for South Africa (an increase of HIV prevalence in the population aged 50+ from 10% to 16%), Swaziland (15% to 27%) and Lesotho (13% to 25%) (figure 3).

The total number of HIV-infected patients aged 50+ in SSA will increase rapidly over the coming decades, from 3.1 million in 2011 to 9.1 million in 2040, an increase of 190% (figure 4, table 2). At the same time, the number of HIV infections among young adults (aged 15-34) will rapidly decline: from 12.1 million in 2011 to 9.1 million in 2030 (a 25% reduction). As prevalence levels stabilize in 2030, the total number of infections will increase again to 10.8 million in 2040. Overall, the total number of HIV-infected people aged 15 years and older (15+) will increase over the next three decades, from 22.4 million in 2011 to 32.4 million in 2040, an increase of 44%.

As a result of the dispro portionate increase in the number of HIV-infected older adults (figure 4), the age composition of the HIV-infected population will change (table 2). In 2011, about 13% of all HIV-infected people were aged 50+; by 2040 this proportion will have more than doubled, to 27% (table 2). In contrast, young adults (aged 15-34) will contribute decreasing proportions of infections to the total number, from 52% in 2011 to 33% in 2040 (figure 5). Countries that have both a high ART coverage and declining HIV prevalence among the population aged 15-49 will be faced with an especially dramatic shift in age composition of the HIV epidemic. The most extreme shift is observed in Zimbabwe, where the proportion of HIV-infected people being aged 50+ will increase from 16% in 2011 to 62% in 2040. Countries like Kenya (13% to 51%), Tanzania (14% to 48%), Namibia (12% to 38%), and South Africa (14% to 36%) show similar trends. In contrast, countries with low and slowly expanding ART coverage show less rapid changes in age composition. In Sierra Leone, the proportion of HIV-infected people being aged 50+ increases from 11% in 2011 to 18% in 2040, and similar trends are found in Democratic

Republic of Congo (13% to 15%), The Gambia (9% to 15%), Somalia (14% to 21%), and Burundi (16% to 22%) (table 2).

In the *decline* scenario, with 20% decrease in ART capacity in 2012, we predict that the number of HIV-infected older adults will reach 6.9 million in 2040, or 22% of all HIV-infected patients (figure 5). If, on the other hand, treatment capacity remained at the level of 2011 (i.e., in the *no further scale-up* scenario), the total number of HIV-infected older adults would be 7.4 million in 2040, which is 24% of all HIV-infected adults. Under the *rapid scale-up* scenario the number of HIV-infected older adults in 2040 would be 9.3 million in 2040, which is 28% of all HIV infections.

Discussion

We estimate that the total number of HIV-infected older adults (aged 50+) will nearly triple from about 3.1 million in 2011 to 9.1 million in 2040, assuming that ART scale-up continues at the current speed. In 2011, about 1 in 7 HIV-infected patients were aged 50 years or older in SSA, while in 2040 this ratio will be more than 1 in 4. Due to an overall increase in the number of people aged 50+ in SSA, the increase in prevalence is relatively modest, from 3% in 2011 to 4% in 2040. In contrast, HIV prevalence among the population aged 15-49 will decline over the coming decades, from 5% in 2011 to 3% in 2040.

This ageing of the HIV epidemic is likely to have broad and important consequences for the organization of health care services in SSA, as has been pointed out in a commentary on the results we present in this study [33]. Due to the increase in life-expectancy due to the ART scale-up, populations will age, “unmasking” the burden of non-communicable diseases (NCDs) previously hidden due to high rates of HIV-related mortality [34]. Already, NCDs are becoming more important in low- and middle income settings, where prevalence of risk factors is high and prevention efforts are limited [35-39]. In South Africa, 55% of all middle-aged women were found to be obese in a cross sectional survey [40,41]. Smoking prevalence in SSA is high and increasing, and meals generally contain high levels of calories and salt [40,41]. Consequently, hypertension and diabetes are becoming more common in SSA [42,43]. As the contribution of these risk factors to the overall risk of NCDs accumulates over age, they become particularly important as the HIV epidemic ages. In addition, HIV infections in older adults are often complicated by preexisting or developing non-AIDS related co-morbidities such as cardiovascular and metabolic diseases, which in turn might aggravate HIV disease progression [44]. Finally, HIV infection and ART are independent risk factors of many NCDs such as non-AIDS related malignancies, cardiovascular diseases (CVDs), kidney and liver failure, and osteoporosis [45-47]. Therefore, quantitative estimates on the impact of the ageing HIV epidemic on the overall disease burden in SSA are needed.

The predicted ageing of the HIV epidemic will also affect social sectors other than the health sector, in particular in countries where HIV prevalence in older adults will substantially increase over the coming decades. Currently, many countries in SSA have no, or very limited, pension programmes [48], and support for elderly generally falls under the responsibility of the family [49]. As the numbers of HIV-infected adults who live into old ages increases due to ART, the need for financial and social support of older adults will increase as well. Policy makers need to consider how this need can be met in the specific contexts of their countries' existing old-age pension and social care systems. At the same time, the increasing presence of older adults in the hyperendemic communities in SSA may bring important benefits to families and communities in the region, including improved child care and social cohesion, and greater flexibility of middle-aged family members to temporarily migrate in search for work opportunities. Future empirical research needs to

establish how the presence of older HIV-infected adults in sub-Saharan African households affects households' social and economic well-being, and which interventions can strengthen positive effects and mitigate negative ones.

Our results show that the total number of HIV-infected adults (aged 15+) will increase by 44% over the next three decades, creating a continuously growing need for financial and human resources to provide ART. Already, financial and human resources to provide ART in SSA are stretched [50,51], emphasizing the need for continued scale-up of cost-effective prevention interventions alongside treatment in order to reduce incidence and thus future treatment needs [52-54]. In addition, it might be necessary to more closely integrate the delivery of treatment and care for different chronic diseases, in order to reduce the financial and time burdens that older patients on ART bear in regularly utilizing healthcare for several conditions. Economies of scope might increase the efficiency of the healthcare delivery, and general health systems might be strengthened as vertical health systems structures are integrated [55].

Our study has several limitations. We modelled countries as a homogenous mix of people, assuming country averages to apply to the entire population. However, in reality there may be important differences in HIV epidemics within countries [56]. In addition, we assumed HIV survival and transmission probabilities to be universally applicable, while in reality there may be differences in these parameter by strains of HIV virus in different parts of Africa [57]. The HIV-2 virus, which is only prevalent in some Western-African countries, is known to have a lower virulence and transmission potential compared to the more common HIV-1 strain [57]. Also, our model does not include mother-to-child transmission of HIV. As HIV-infected children can be treated effectively with ART [58], they may now live into young adulthood, increasing the number of HIV-infected people in this age category.

Both acquired resistance (development of resistance within an individual on treatment) and transmitted resistance (spread of drug-resistant strains) may impact on the effectiveness of treatment programs, and consequently result in a less profound effect of the ART scale-up on the population age composition. Patients who develop resistance might fail to suppress viral replication while on treatment, resulting in shorter survival times and higher infectiousness. While second- or third-line therapies can be prescribed to treat those with resistance to first-line ART, many treatment programs in SSA are currently not well-equipped to deal with drug resistance, as both monitoring for treatment resistance and providing second- and third-line ART regimens is expensive and requires specialized expertise [59]. Therefore, if the prevalence of resistance increases, effective treatment coverage will decline. In our sensitivity analysis, we explore the effect of declining treatment coverage on the changes in age-composition. We find that the changes in age composition are similar but somewhat reduced in magnitude if effective coverage is reduced substantially (e.g., by one fifth compared to the baseline case). It is currently unclear, however, in how far the fears of rapidly spreading drug resistance expressed at the start of the ART scale-up [60] were justified. The prevalence of drug resistance remains low in most countries in SSA after nearly 10 years of scaling up ART [61,62]. In addition, adherence to treatment in SSA is comparable to many high income countries [63], and survival of patients on treatment in SSA approaches general life-expectancy [5], suggesting that resistance may not become a major problem in the region in the near future.

In this study, we assumed that risk behaviour remained the same after age 45. While detailed data on sexual risk taking in older age for SSA is lacking, it is plausible that the frequency of sexual activity declines to some extent in older adults [64]. On the other hand, there is evidence that older people are at increased risk for HIV through both biological mechanisms and increased increasing riskiness in behaviour during sex. Post-menopausal women might

be more susceptible to HIV because of the thinning of the vaginal wall [65], and data from the Demographic and Health Surveys (DHS) show that condom use and knowledge about condoms is particularly low in older adults [13]. In the United States, condom use among older adults with known risk factors for HIV was about six times lower compared to adults aged 15-49 [66]. Yet, despite the considerable and increasing burden of HIV in older adults in SSA, our understanding of sexual behaviour in this group remains limited. With increasing prevalence of HIV in older adults, HIV incidence in this age-group is also likely to increase, warranting the need for age-appropriate prevention interventions.

It is important to note that our model accurately replicated the HIV epidemic in all the 43 SSA countries (figure 2), suggesting that the theoretical limitations we describe above do not substantially matter for our estimations. This claim is further supported by comparison of our estimates of a total of 2.6 million HIV-infected older adults in 2007 to the number published by Negin *et al.* (which is 2.9 million) [13].

In conclusion, we show that the HIV epidemic in sub-Saharan Africa will rapidly age over the coming decades. This has important consequences for both the organization of health care services and the general organization of societies in the sub-continent, as older HIV-infected patients require specialized treatment and care, as well as social and financial support. In addition, expanded treatment coverage is likely to increase the burdens of other diseases in SSA, in particular NCDs. Health policymakers need to anticipate the impact of the ageing HIV epidemic in their planning for the future capacity of health systems to prevent and treat diseases of old age in HIV-infected individuals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This work is supported by the National Institute of Health [1R01MH083539-01 and R01 HD058482-01].

References

1. WHO. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector; progress report 2010. Geneva: World Health Organization; 2010.
2. UN. 2011 High level meeting on AIDS. New York: General Assembly - United Nations; 2011.
3. Negin J, Mills EJ, Albone R. Continued neglect of ageing of HIV epidemic at UN meeting. Lancet. 2011; 378:768. [PubMed: 21872745]
4. Herbst AJ, Cooke GS, Bärnighausen T, KanyKany A, Tanser F, Newell ML. Adult mortality and antiretroviral treatment roll-out in rural KwaZulu-Natal, South Africa. Bull World Health Organ. 2009; 87:754–762. [PubMed: 19876542]
5. Mills EJ, Bakanda C, Birungi J, Mwesigwa R, Chan K, Ford N, et al. Mortality by baseline CD4 cell count among HIV patients initiating antiretroviral therapy: evidence from a large cohort in Uganda. AIDS. 2011; 25:851–855. [PubMed: 21330903]
6. Mutevedzi PC, Lessells RJ, Rodger AJ, Newell ML. Association of age with mortality and virological and immunological response to antiretroviral therapy in rural South African adults. PLoS One. 2011; 6:e21795. [PubMed: 21747959]
7. Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. AIDS. 2009; 23:1397–1404. [PubMed: 19381076]
8. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365:493–505. [PubMed: 21767103]

9. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet. 2010; 375:2092–2098. [PubMed: 20537376]
10. Montaner JS, Lima VD, Barrios R, Yip B, Wood E, Kerr T, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet. 2010; 376:532–539. [PubMed: 20638713]
11. CDC (Published:June 2010) HIV/AIDS Surveillance Report. Vol. 20. Atlanta: Centers fo Disease Control and Prevention; 2008.
12. Hontelez JA, Lurie MN, Newell ML, Bakker R, Tanser F, Bärnighausen T, et al. Ageing with HIV in South Africa. AIDS. 2011; 25:1665–1667. [PubMed: 21681056]
13. Negin J, Cumming RG. HIV infection in older adults in sub-Saharan Africa: extrapolating prevalence from existing data. Bull World Health Organ. 2010; 88:847–853. [PubMed: 21076566]
14. UNAIDS. Report on the Global AIDS epidemic 2010. Geneva: UNAIDS; 2010.
15. Hontelez J, de Vlas S, Tanser F, Bakker R, Bärnighausen T, Newell M, et al. The Impact of the New WHO Antiretroviral Treatment Guidelines on HIV Epidemic Dynamics and Cost in South Africa. PLoS One. 2011; 6:e21919. [PubMed: 21799755]
16. Korenromp EL, Bakker R, Gray R, Wawer MJ, Serwadda D, Habbema JD. The effect of HIV, behavioural change, and STD syndromic management on STD epidemiology in sub-Saharan Africa: simulations of Uganda. Sex Transm Infect. 2002; 78(1):i55–63. [PubMed: 12083448]
17. van der Ploeg CPB, Van Vliet C, De Vlas SJ, Ndinya-Achola JO, Fransen L, van Oortmarssen GJ, et al. STDSIM: A Microsimulation Model for Decision Support in STD Control. Interfaces. 1998; 28:84–100.
18. UN. World Fertility Data 2008. Geneva: United Nations Population Division - Fertility and Family Planning Section; 2008.
19. WHO. Life tables for WHO member States. Geneva: World Health Organization; 2011.
20. WHO. The global burden of disease 2004; Update (2008). Geneva: World Health Organization; 2011.
21. Williams BG, Lloyd-Smith JO, Gouws E, Hankins C, Getz WM, Hargrove J, et al. The potential impact of male circumcision on HIV in Sub-Saharan Africa. PLoS Med. 2006; 3:e262. [PubMed: 16822094]
22. Ghys PD, Zaba B, Prins M. Survival and mortality of people infected with HIV in low and middle income countries: results from the extended ALPHA network. AIDS. 2007; 21(6):S1–4. [PubMed: 18032932]
23. Korenromp EL, Van Vliet C, Bakker R, De Vlas SJ, Habbema JD. HIV spread and partnership reduction for different patterns of sexual behavior – a study with the microsimulation model STDSIM. Math Pop Studies. 2000; 8:135–173.
24. Orroth KK, Freeman EE, Bakker R, Buve A, Glynn JR, Boily MC, et al. Understanding the differences between contrasting HIV epidemics in east and west Africa: results from a simulation model of the Four Cities Study. Sex Transm Infect. 2007; 83(1):i5–16. [PubMed: 17405781]
25. Steele KT, Steenhoff AP, Newcomb CW, Rantleru T, Nthobatsang R, Lesetedi G, et al. Early mortality and AIDS progression despite high initial antiretroviral therapy adherence and virologic suppression in Botswana. PLoS One. 2011; 6:e20010. [PubMed: 21698283]
26. Musiime S, Muhairwe F, Rutagengwa A, Mutimura E, Anastos K, Hoover DR, et al. Adherence to Highly Active Antiretroviral Treatment in HIV-Infected Rwandan Women. PLoS One. 2011; 6:e27832. [PubMed: 22114706]
27. Van der Veen F, Mugala-Mukungu F, Kangudi M, Feris A, Katjitae I, Colebunders R. Antiretroviral treatment in the private sector in Namibia. Int J STD AIDS. 2011; 22:577–580. [PubMed: 21998178]
28. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. PLoS Med. 2007; 4:e298. [PubMed: 17941716]
29. Mosoko JJ, Akam W, Weidle PJ, Brooks JT, Aweh AJ, Kinge TN, et al. Retention in an antiretroviral therapy programme during an era of decreasing drug cost in Limbe, Cameroon. J Int AIDS Soc. 2011; 14:32. [PubMed: 21679416]

30. Buve A, Carael M, Hayes RJ, Auvert B, Ferry B, Robinson NJ, et al. Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: methods and prevalence of HIV infection. AIDS. 2001; 15(4):S5–14. [PubMed: 11686465]

31. Wallrauch C, Bärnighausen T, Newell ML. HIV prevalence and incidence in people 50 years and older in rural South Africa. S Afr Med J. 2010; 100:812–814. [PubMed: 21414272]

32. Statement on the meeting of the South African National AIDS Council (SANAC).

33. UN. World Population Prospects, the 2010 revision. Geneva: United Nations Population Division; 2010.

34. Bärnighausen T, Welz T, Hosegood V, Batzing-Feigenbaum J, Tanser F, Herbst K, et al. Hiding in the shadows of the HIV epidemic: obesity and hypertension in a rural population with very high HIV prevalence in South Africa. J Hum Hypertens. 2008; 22:236–239. [PubMed: 18046436]

35. Beaglehole R, Bonita R, Alleyne G, Horton R. NCDs: celebrating success, moving forward. Lancet. 2011; 378:1283–1284. [PubMed: 21982085]

36. Beaglehole R, Bonita R, Alleyne G, Horton R, Li L, Lincoln P, et al. UN High-Level Meeting on Non-Communicable Diseases: addressing four questions. Lancet. 2011; 378:449–455. [PubMed: 21665266]

37. Beaglehole R, Bonita R, Horton R, Adams C, Alleyne G, Asaria P, et al. Priority actions for the non-communicable disease crisis. Lancet. 2011; 377:1438–1447. [PubMed: 21474174]

38. Mbanya JC, Squire SB, Cazap E, Puska P. Mobilising the world for chronic NCDs. Lancet. 2011; 377:536–537. [PubMed: 21074252]

39. Dalal S, Beunza JJ, Volmink J, Adebamowo C, Bajunirwe F, Njelekela M, et al. Non-communicable diseases in sub-Saharan Africa: what we know now. Int J Epidemiol. 2011; 40:885–901. [PubMed: 21527446]

40. Thorogood M, Connor M, Tollman S, Lewando Hundt G, Fowkes G, Marsh J. A cross-sectional study of vascular risk factors in a rural South African population: data from the Southern African Stroke Prevention Initiative (SASPI). BMC Public Health. 2007; 7:326. [PubMed: 17999764]

41. Tibazarwa K, Ntyintyane L, Sliwa K, Gerntholtz T, Carrington M, Wilkinson D, et al. A time bomb of cardiovascular risk factors in South Africa: results from the Heart of Soweto Study "Heart Awareness Days". Int J Cardiol. 2009; 132:233–239. [PubMed: 18237791]

42. Tollman SM, Kahn K, Sartorius B, Collinson MA, Clark SJ, Garenne ML. Implications of mortality transition for primary health care in rural South Africa: a population-based surveillance study. Lancet. 2008; 372:893–901. [PubMed: 18790312]

43. Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review. BMC Public Health. 2011; 11:564. [PubMed: 21756350]

44. Kirk JB, Goetz MB. Human immunodeficiency virus in an aging population, a complication of success. J Am Geriatr Soc. 2009; 57:2129–2138. [PubMed: 19793157]

45. Kearney F, Moore AR, Donegan CF, Lambert J. The ageing of HIV: implications for geriatric medicine. Age Ageing. 2010; 39:536–541. [PubMed: 20685813]

46. Schmid GP, Williams BG, Garcia-Calleja JM, Miller C, Segar E, Southworth M, et al. The unexplored story of HIV and ageing. Bull World Health Organ. 2009; 87:162–162A. [PubMed: 19377704]

47. Justice AC. HIV and aging: time for a new paradigm. Curr HIV/AIDS Rep. 2010; 7:69–76. [PubMed: 20425560]

48. Stewart F, Yermo J. Pensions in Africa. OECD Working Papers on Insurance and Private Pensions. 2009

49. Kautz T, Bendavid E, Bhattacharya J, Miller G. AIDS and declining support for dependent elderly people in Africa: retrospective analysis using demographic and health surveys. Brit Med J. 2010; 340:c2841. [PubMed: 20554660]

50. Bärnighausen T, Bloom DE, Humair S. Universal antiretroviral treatment: the challenge of human resources. Bull World Health Organ. 2010; 88:951–952. [PubMed: 21124722]

51. Voelker R. HIV/AIDS funding dropped by 10% in 2010. J Am Med Assoc. 2011; 306:1642–1643.

52. Schwartlander B, Stover J, Hallett T, Atun R, Avila C, Gouws E, et al. Towards an improved investment approach for an effective response to HIV/AIDS. Lancet. 2011; 377:2031–2041. [PubMed: 21641026]
53. Hontelez JA, Nagelkerke N, Bärnighausen T, Bakker R, Tanser F, Newell ML, et al. The potential impact of RV144-like vaccines in rural South Africa: a study using the STDSIM microsimulation model. Vaccine. 2011; 29:6100–6106. [PubMed: 21703321]
54. Padian NS, McCoy SI, Balkus JE, Wasserheit JN. Weighing the gold in the gold standard: challenges in HIV prevention research. AIDS. 2010; 24:621–635. [PubMed: 20179575]
55. Bärnighausen T, Bloom DE, Humair S. Going horizontal--shifts in funding of global health interventions. N Engl J Med. 2011; 364:2181–2183. [PubMed: 21651390]
56. Napierala Mavedzenge S, Olson R, Doyle AM, Changalucha J, Ross DA. The Epidemiology of HIV Among Young People in Sub-Saharan Africa: Know Your Local Epidemic and Its Implications for Prevention. J Adolesc Health. 2011; 49:559–567. [PubMed: 22098766]
57. Tebit DM, Arts EJ. Tracking a century of global expansion and evolution of HIV to drive understanding and to combat disease. Lancet Infect Dis. 2011; 11:45–56. [PubMed: 21126914]
58. Fatti G, Bock P, Eley B, Mothibi E, Grimwood A. Temporal trends in baseline characteristics and treatment outcomes of children starting antiretroviral treatment: an analysis in four provinces in South Africa, 2004-2009. J Acquir Immune Defic Syndr. 2011; 58:e60–67. [PubMed: 21857355]
59. Boyd M, Emery S, Cooper DA. Antiretroviral roll-out: the problem of second-line therapy. Lancet. 2009; 374:185–186. [PubMed: 19616706]
60. Nagelkerke NJ, Jha P, de Vlas SJ, Korenromp EL, Moses S, Blanchard JF, et al. Modelling HIV/AIDS epidemics in Botswana and India: impact of interventions to prevent transmission. Bull World Health Organ. 2002; 80:89–96. [PubMed: 11953786]
61. Hamers RL, Wallis CL, Kityo C, Siwale M, Mandaliya K, Conradie F, et al. HIV-1 drug resistance in antiretroviral-naive individuals in sub-Saharan Africa after rollout of antiretroviral therapy: a multicentre observational study. Lancet Infect Dis. 2011; 11:750–759. [PubMed: 21802367]
62. Manasa J, Katzenstein D, Cassol S, Newell ML, de Oliveira T. Primary drug resistance in South Africa - data from 10 years of surveys. AIDS Res Hum Retroviruses. 2012
63. Nachega JB, Mills EJ, Schechter M. Antiretroviral therapy adherence and retention in care in middle-income and low-income countries: current status of knowledge and research priorities. Curr Opin HIV AIDS. 2010; 5:70–77. [PubMed: 20046150]
64. Palacios-Cena D, Carrasco-Garrido P, Hernandez-Barrera V, Alonso-Blanco C, Jimenez-Garcia R, Fernandez-de-Las-Penas C. Sexual Behaviors among Older Adults in Spain: Results from a Population-Based National Sexual Health Survey. J Sex Med. 2011
65. Drew O, Sherrard J. Sexually transmitted infections in the older woman. Menopause Int. 2008; 14:134–135. [PubMed: 18714080]
66. Mack KA, Ory MG. AIDS and older Americans at the end of the Twentieth Century. J Acquir Immune Defic Syndr. 2003; 33(2):S68–75. [PubMed: 12853855]

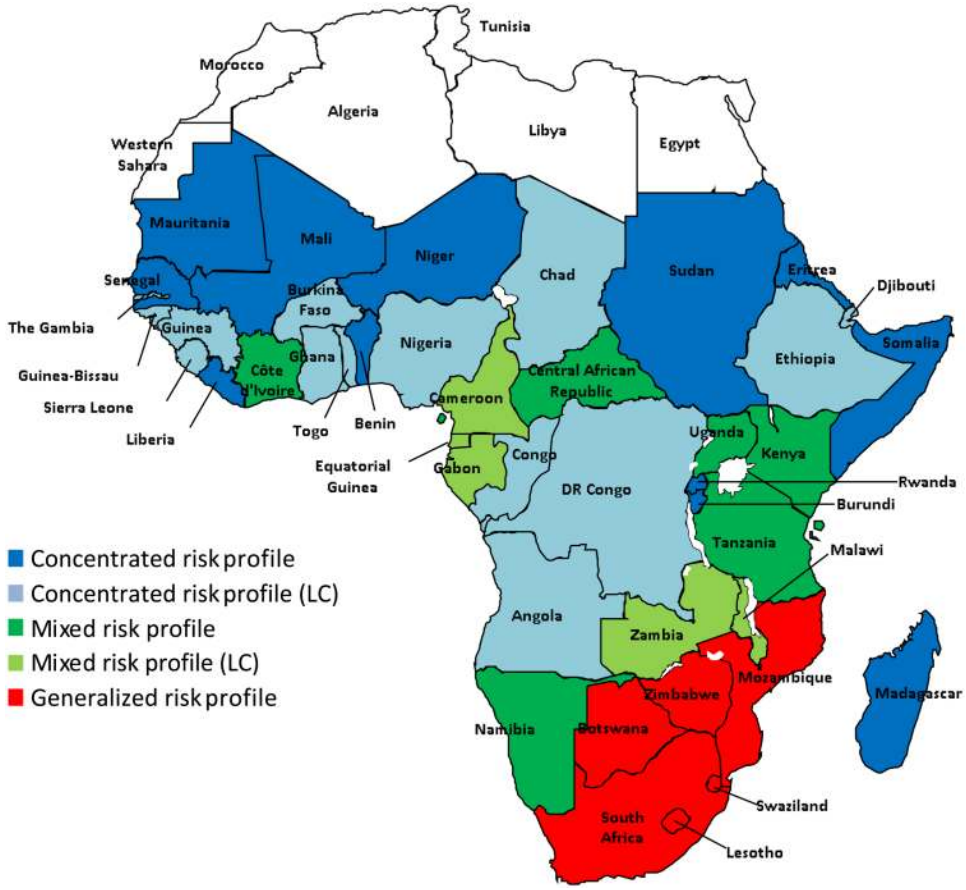

Figure 1. Geographical distribution of sexual-behaviour profiles

The colour of each country represents the best fitting sexual-behaviour profile given country-specific circumcision levels (table S2) and ART roll out (figure 2A). A detailed description of the profiles is given in table S1.

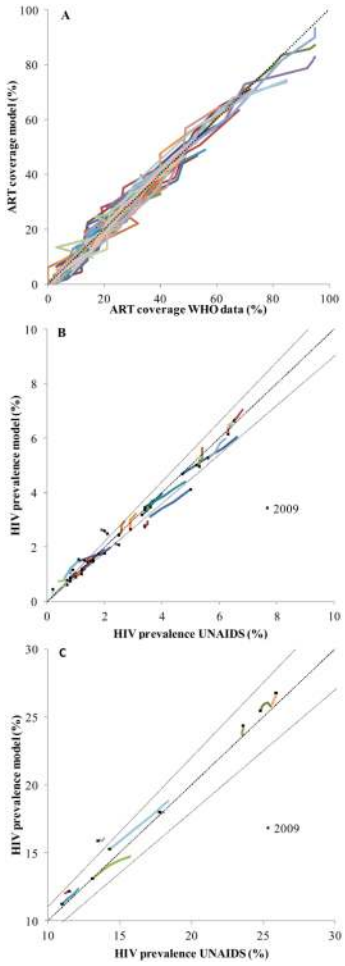

Figure 2. Model fit compared to data

A. Predicted ART coverage of those eligible at ≤200 cells/μL in the model compared to WHO data over the period 2004-2009. The dashed line represents a perfect fit (ie predicted coverage in model = WHO data). **B.** Predicted HIV prevalence for low and medium endemic countries in the model compared to UNAIDS prevalence estimates over the period 2004-2009. The dashed line represents a perfect fit (eg predicted prevalence in the model = UNAIDS data), the dotted line represents a 10% difference between model predictions and data. **C.** Predicted HIV prevalence for high endemic countries in the model compared to UNAIDS prevalence estimates over the period 2004-2009. The dashed line represents a perfect fit (eg predicted prevalence in the model = UNAIDS data), the dotted line represents a 10% difference between model predictions and data. Full country-specific parameter settings are given in table S2.

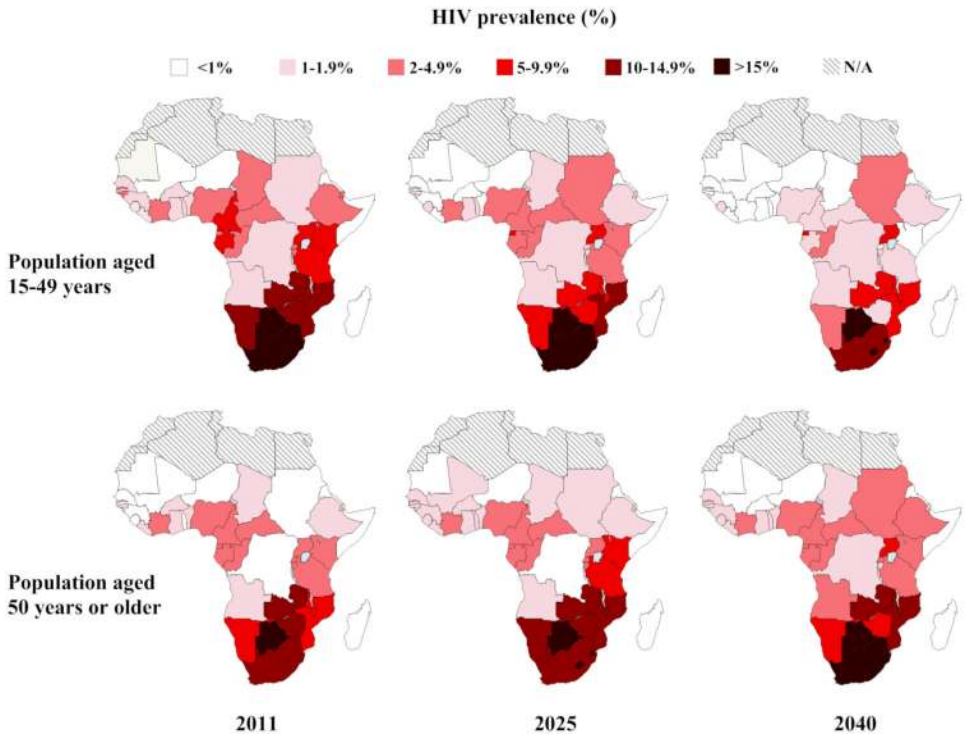

Figure 3. HIV prevalence in the population age 15-49 and 50+ in sub-Saharan Africa for the years 2011, 2025 and 2040, under continuous scale up of antiretroviral therapy
N/A = Not Applicable

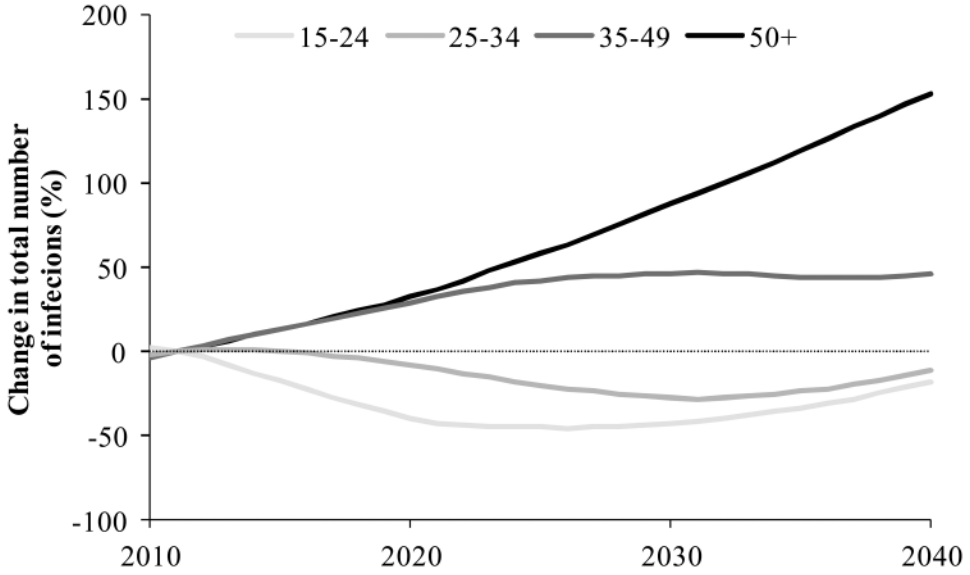

Figure 4. Projected trends of total number of infections and in sub-Saharan Africa over the period 2010-2040 under continuous scale up of antiretroviral therapy

The change is relative to the total number of HIV infected patients per age category in 2011.

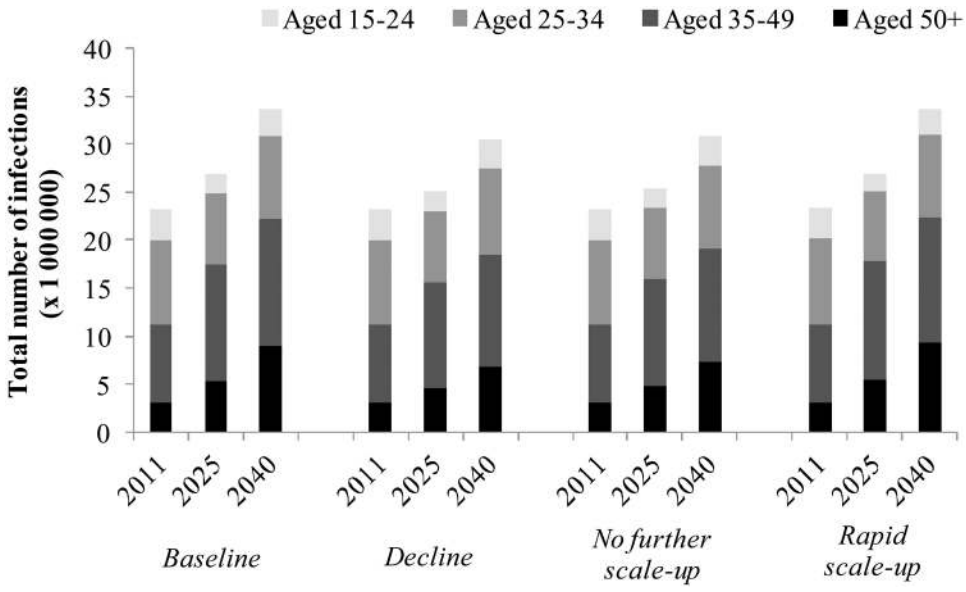

Figure 5. Predicted age composition of the HIV-infected population by ART scale-up scenario

Baseline = baseline scenario of continued scale-up of ART coverage; *decline* = scenario in which health-system capacity to deliver ART is reduced by 20% in 2012; *no further scale-up* = scenario in which health-system capacity to deliver ART remains at the same level as in 2011; *Rapid scale-up* = scenario in which health-system capacity to deliver ART is scaled-up to 100% for all countries by 2015.

Table 1

HIV prevalence in the population aged 15-49 and 50+ in 2011, 2025 and 2040, assuming continued scale-up of ART.

	HIV prevalence					
	Population aged 15-49			Population aged 50+		
	2011	2025	2040	2011	2025	2040
Sub-Saharan Africa	**5%**	**3%**	**2%**	**3%**	**4%**	**4%**
Central Africa	***2%***	***2%***	***1%***	***2%***	***2%***	***2%***
Angola	2%	2%	2%	1%	2%	2%
Cameroon	5%	3%	1%	4%	4%	4%
Central African Rep.	5%	3%	1%	4%	4%	3%
Chad	3%	1%	1%	2%	2%	1%
Dem. Rep. Congo	1%	1%	1%	1%	1%	1%
The Congo	5%	3%	2%	4%	4%	4%
Equatorial Guinea	4%	8%	7%	3%	6%	7%
Gabon	3%	3%	2%	2%	4%	4%
Eastern Africa	***4%***	***3%***	***2%***	***3%***	***3%***	***3%***
Burundi	3%	1%	1%	3%	2%	2%
Djibouti	2%	1%	1%	2%	1%	1%
Eritrea	1%	<0.5%	<0.5%	1%	1%	1%
Ethiopia	2%	2%	2%	2%	2%	2%
Kenya	6%	3%	1%	5%	6%	4%
Madagascar	<0.5%	<0.5%	<0.5%	<0.5%	<0.5%	1%
Mozambique	12%	11%	9%	8%	12%	14%
Rwanda	3%	1%	1%	3%	3%	2%
Somalia	1%	1%	1%	1%	1%	1%
Sudan	1%	2%	2%	1%	2%	2%
Tanzania	5%	3%	1%	4%	5%	4%
Uganda	7%	5%	5%	4%	4%	6%
Southern Africa	***16%***	***12%***	***9%***	***10%***	***13%***	***13%***
Botswana	25%	18%	16%	17%	23%	25%
Lesotho	25%	24%	21%	14%	19%	25%

	HIV prevalence					
	Population aged 15-49			Population aged 50+		
	2011	2025	2040	2011	2025	2040
Malawi	11%	8%	8%	9%	10%	12%
Namibia	13%	8%	4%	10%	10%	9%
South Africa	18%	15%	11%	11%	14%	16%
Swaziland	25%	21%	20%	16%	23%	27%
Zambia	14%	8%	9%	8%	11%	12%
Zimbabwe	14%	6%	2%	12%	13%	8%
Western Africa	***2%***	***2%***	***1%***	***2%***	***2%***	***2%***
Benin	2%	1%	<0.5%	1%	1%	1%
Burkina Faso	1%	1%	<0.5%	1%	1%	1%
Côte D'Ivoire	4%	2%	1%	3%	3%	2%
The Gambia	2%	2%	2%	1%	2%	2%
Ghana	2%	1%	1%	1%	2%	2%
Guinea	2%	1%	1%	1%	1%	1%
Guinea-Bissau	2%	1%	1%	1%	2%	2%
Liberia	1%	1%	<0.5%	1%	1%	1%
Mali	1%	1%	<0.5%	1%	1%	1%
Mauritania	1%	1%	<0.5%	<0.5%	1%	1%
Niger	1%	<0.5%	<0.5%	1%	1%	1%
Nigeria	4%	2%	2%	2%	3%	3%
Senegal	1%	1%	1%	1%	1%	1%
Sierra Leone	1%	1%	1%	1%	1%	1%
Togo	2%	1%	1%	1%	1%	2%

Table 2

Impact of continued ART scale-up on absolute number of HIV infections and proportion of all HIV-infected patients aged 50+ in sub-Saharan Africa

	HIV infections in population aged 15-49			HIV infections in population aged 50+					
	Absolute number (× 1000)			Absolute number (× 1000)			As proportion of all infections		
	2011	2025	2040	2011	2025	2040	2011	2025	2040
Sub-Saharan Africa	***19 325***	***20 244***	***23 358***	***3 119***	***5 307***	***9 059***	***13%***	***20%***	***27%***
Central Africa	***1 308***	***1 450***	***1 774***	***211***	***349***	***547***	***14%***	***19%***	***23%***
Angola	150	205	339	21	40	82	12%	16%	20%
Cameroon	450	431	303	75	135	200	14%	24%	40%
Central African Rep.	110	82	46	21	31	37	16%	27%	44%
Chad	83	86	115	14	22	26	14%	20%	19%
Dem. Rep. Congo	378	500	792	55	86	141	13%	15%	15%
The Congo	54	65	97	9	16	33	14%	20%	25%
Equatorial Guinea	21	38	51	3	6	11	11%	14%	18%
Gabon	49	44	31	8	13	17	14%	23%	35%
Eastern Africa	***6 147***	***6 956***	***9 138***	***955***	***1 769***	***3 067***	***13%***	***20%***	***24%***
Burundi	115	95	133	22	26	38	16%	22%	22%
Djibouti	10	8	8	2	2	3	14%	22%	27%
Eritrea	21	19	20	3	7	11	14%	26%	34%
Ethiopia	817	1 234	2 016	135	263	583	14%	18%	22%
Kenya	1 101	728	341	172	319	357	13%	30%	51%
Madagascar	26	50	78	7	18	40	20%	27%	34%
Mozambique	1 533	1 888	2 366	215	397	752	12%	17%	24%
Rwanda	140	90	83	30	56	62	19%	38%	43%
Somalia	31	54	80	5	11	21	14%	17%	21%
Sudan	339	631	1 054	44	140	318	12%	18%	23%
Tanzania	1 126	846	458	189	342	426	14%	29%	48%
Uganda	751	1 314	2 501	84	188	456	10%	13%	15%
Southern Africa	***8 443***	***8 211***	***8 196***	***1 356***	***2 202***	***3 706***	***13%***	***19%***	***29%***
Botswana	286	310	425	43	91	175	15%	23%	29%

	HIV infections in population aged 15-49			HIV infections in population aged 50+					
	Absolute number (× 1000)			Absolute number (× 1000)			As proportion of all infections		
	2011	2025	2040	2011	2025	2040	2011	2025	2040
Lesotho	298	375	450	34	55	105	10%	13%	19%
Malawi	773	909	1 602	112	209	429	13%	19%	21%
Namibia	185	132	76	26	35	47	12%	21%	38%
South Africa	5 120	4 902	3 733	822	1 293	2 065	14%	21%	36%
Swaziland	147	201	289	20	43	84	12%	18%	22%
Zambia	692	763	1 326	89	185	361	11%	20%	21%
Zimbabwe	798	618	295	158	291	440	16%	32%	60%
Western Africa	***3 428***	***3 626***	***4 249***	***594***	***987***	***1 739***	***15%***	***21%***	***29%***
Benin	47	36	35	10	16	22	17%	31%	38%
Burkina Faso	74	61	62	14	22	27	16%	26%	30%
Côte D'Ivoire	370	288	176	77	122	170	17%	30%	49%
The Gambia	15	26	38	1	3	7	9%	12%	15%
Ghana	225	256	257	38	82	153	15%	24%	37%
Guinea	66	70	88	11	22	35	14%	24%	28%
Guinea-Bissau	11	13	16	2	4	7	15%	24%	29%
Liberia	24	18	17	5	7	11	16%	28%	39%
Mali	77	57	56	13	20	27	14%	26%	33%
Mauritania	12	12	11	2	5	8	15%	28%	41%
Niger	48	46	53	9	20	31	17%	30%	37%
Nigeria	2 299	2 542	3 188	373	620	1 158	14%	20%	27%
Senegal	54	76	100	7	18	35	12%	19%	26%
Sierra Leone	38	62	82	5	101	18	11%	14%	18%
Togo	47	62	69	7	15	31	13%	20%	31%