Published in final edited form as:

J Acquir Immune Defic Syndr. 2013 June 1; 63(2): . doi:10.1097/QAI.0b013e3182918875.

Lives Saved by Expanding HIV Treatment Availability in Resource-Limited Settings: The Example of Haiti

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Abstract

Background—Guidelines recommend antiretroviral treatment (ART) initiation at CD4 <350/ μ L for HIV-infected individuals in resource-limited settings. However, funding for treatment expansion remains uncertain. We forecast the mortality impact of ART expansion alternatives in Haiti.

Methods—We used data from Haiti to develop a country-specific model of HIV disease. The model projects the mortality, total number of HIV-infected individuals, and number and coverage (% of those eligible) on ART by simulating cohorts of HIV-infected individuals over 10 years. We assessed 5 ART expansion scenarios, ranging from fully expanded ART (best case) to no new ART (worst case).

Results—By 2010, the model predicts 103,500 individuals living with HIV in Haiti, of whom 27,300 were estimated to receive ART. Continuing ART initiation at current rates requires increasing the number on ART to 43,300 by 2020 (56% coverage), with 89,700 deaths estimated between 2010 and 2020. The number on ART could increase by 7,400 (+17.1%, best case) or decrease by 25,600 (−59.1%, worst case), resulting in 19,500 deaths averted and 9,900 fewer in care awaiting ART (best versus worst case). Results are sensitive to untreated disease progression and pre-ART loss from care. Increased HIV testing, linkage to care, and retention in care can avert additional deaths and achieve nearly 80% ART coverage with optimal policy improvements.

Conclusions—In resource-limited settings, continued improvements in HIV treatment access will save lives. Efforts to efficiently expand ART access should remain a global priority.

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Preliminary results for this manuscript were presented in part at the Conference on Retroviruses and Opportunistic Infections [abstract 655], March 5 – 8, 2012, Seattle, USA, and the 5th Annual Conference on the Science of Dissemination and Implementation [Session 1B], March 19 – 20, 2012, Bethesda, USA.

The authors declare no financial or personal conflicts of interest.

Ethics Committee Approval

Human subjects approval was obtained from GHESKIO (Port-au-Prince, Haiti) and Weill Cornell Medical College (New York, USA).

Keywords

HIV/AIDS; antiretroviral therapy; mortality; resource-limited settings; simulation

Introduction

Major donor initiatives to combat HIV along with increasing in-country commitments to curb the epidemic have facilitated rapid HIV treatment scale-up in low- and middle-income countries.¹ However, while a minority of countries have achieved universal antiretroviral therapy (ART) access or coverage targets of 80% or higher, these targets remain challenging in many settings.¹ The global economic crisis and waning international political commitment to HIV prevention and treatment efforts globally have contributed to declines in donor disbursements for ART provision and decreasing country-level budgets.^{2,3} Diminishing resources for HIV treatment occur against a backdrop of increased need for ART due to efforts to improve case identification and retention in care;⁴ demonstrated survival benefit among those receiving ART;^{5,6} revised World Health Organization (WHO) guidelines calling for earlier ART initiation;^{7,8} and new clinical evidence that ART decreases the risk of transmitting HIV.^{9,10}

Limited funding and health system and social service capacity to address the increasing demand for ART will require country-specific policy decisions at the national level. Haiti, a poor Caribbean country with a per capita income of about US \$650 annually,¹¹ has mounted a successful response to the HIV/AIDS epidemic with assistance from international donors, similar to other resource-limited settings. For example, evidence suggests HIV prevalence in Haiti has declined over the past decade,¹² with the percentage of Haitian adults aged 15–49 living with HIV currently at about 1.9%.¹³ WHO estimates that of those medically eligible for treatment according to current WHO guidelines,⁷ the number of HIV-infected individuals receiving antiretroviral therapy in Haiti has increased significantly, from 5% in 2004 to over 40% in 2009.¹⁴ Despite these gains, however, funding in Haiti and other low-income settings remains limited. For example, U.S. PEPFAR funds allocated to Haiti decreased from US\$164.1 million in fiscal year 2010 to US\$158.5 million in fiscal year 2011.¹⁵ Global Fund disbursements to Haiti remained relatively flat in 2011 and 2012 at approximately US\$15.5 million.¹⁶ Future availability of resources for expanded treatment according to current WHO guidelines (i.e., ART initiation at WHO stage III-IV or CD4 count <350 cells/μL) versus previous guidelines (i.e., ART initiation at WHO stage IV or CD4 count <200 cells/μL) is uncertain. In this context, our objective was to forecast the potential lives saved resulting from further ART expansion in Haiti, potential lives lost as a result of not continuing to expand ART availability, and fraction of those eligible receiving ART with and without further expansion.

Methods

Analytic overview

We developed a multi-cohort mathematical model of untreated and treated HIV disease in Haiti. The model assesses two policy-relevant eras of HIV/AIDS treatment: (1) antiretroviral scale-up between 2004 and 2009, and (2) 10-year policy projections beginning in 2010, reflecting a period of funding uncertainty for HIV treatment. Model inputs were estimated from 30 years of well-characterized natural history cohort data, ART cohort data, and a randomized trial of early versus delayed ART all collected from the GHESKIO clinic in Port-au-Prince, Haiti.^{8,17–22} Additional model inputs came from a model verification process informed by country-level reports from Haiti on ART scale-up between 2004 and 2009.¹³ We evaluated the performance of alternative ART expansion scenarios at the

population level, including the total number of deaths and HIV-infected individuals alive, the number receiving ART, and ART coverage, defined as the fraction of those eligible to receive antiretroviral therapy who receive it. We conducted sensitivity analyses to assess the impact of uncertain model input parameters and policy-related variables on our results. The model is implemented in Microsoft Excel 2010 (Redmond, Washington, USA).

Scenarios

We evaluated five ART initiation scenarios: 1) No New ART initiation (worst case), 2) Restricted ART capacity to current treatment levels (Fixed Capacity), 3) Current Rates of ART initiation for patients with CD4 counts <200 cells/ μ L and CD4 counts 200–350 cells/ μ L (status quo), 4) Limited Expansion, increasing rates of ART initiation for patients with CD4 counts 200–350 cells/ μ L to implement the change from previous to current WHO guidelines,^{13,27} and 5) Full Expansion, increasing rates of ART initiation for all patients with CD4 counts <350 cells/ μ L (best case) (Table 1). Scenarios with limited treatment capacity, as occurs with the No New ART and Fixed Capacity scenarios, are designed to reflect treatment capacity constraints that may face Haiti's health sector and other similar health sectors in the current funding climate. In each of the scenarios, individuals eligible to initiate ART face competing risks for other events — including loss from care and AIDS- and non-AIDS-related death — that can precede ART initiation despite eligibility. To evaluate the number of deaths averted during the scale-up period (i.e., 2004 – 2009), we also evaluate a No ART scenario, in which we assumed no antiretroviral therapy was available for HIV-infected individuals in Haiti.

The scenarios were defined to reflect the current situation in Haiti and other resource-poor countries with constrained budgets in several ways. First, in accordance with international guidelines and clinical practice in Haiti, individuals are treated with up to two sequential ART regimens, receive semiannual CD4 tests, and have quarterly clinic visits unless otherwise clinically indicated.⁷ Second, disease progression in individuals receiving ART varies based on when in the course of disease ART is initiated, with ART initiation earlier in the course of disease (e.g., at CD4 count <350 cells/ μ L) associated with less rapid disease progression and improved health outcomes.⁸ Third, detection of ART failure and switching to second-line therapy occurs based on clinical and immunologic monitoring of treatment response in HIV-infected patients.⁷ In addition, individuals who are in care but not receiving ART have a decreased risk of disease progression and mortality compared to those who are not in care, including those who are lost.^{23,24} Finally, once an HIV-infected individual is lost from treatment and/or care, the individual is not eligible to return and is assumed to follow natural history disease progression until death. While this assumption may be a simplification, the literature suggests a high risk of mortality among patients lost from ART programs in resource-limited settings.²⁵

Model structure

We developed a state-transition Markov model for multiple cohorts of treated and untreated HIV-infected individuals.^{8,13,17–21} The model is defined by a set of 12 mutually exclusive and collectively exhaustive health states. Movement between health states occurs probabilistically through a series of possible events within an annual model cycle.^{26,27} For each cohort, the model simulates strategy-specific clinical disease progression and mortality that varies depending on engagement with clinical care over time. Cohorts of hypothetical prevalent and newly HIV-infected patients progress through mutually exclusive stages of untreated disease (Figure 1): CD4 count >350 cells/ μ L (i.e., asymptomatic HIV disease), CD4 count 200–350 cells/ μ L (i.e., Intermediate HIV disease with and without symptoms), and CD4 count <200 cells/ μ L (i.e., AIDS). Within each stage, the model is structured such that individuals may remain out of care, enter into care, initiate ART, become lost from

treatment or care, or die, representing 12 main health states; death was modeled as an absorbing state. The model applies transition probabilities to govern the fraction of each cohort moving among the health states. Those individuals eligible for ART can be in care and receive either 1st- or 2nd-line ART. Individuals may die of AIDS- or non-AIDS-related causes; mortality risk varies based on both disease stage and clinical engagement.

The model begins in 2004, the beginning of antiretroviral scale-up in Haiti, with the prevalent cohort distributed across health stages and clinical care events based on population-level data. Successive cohorts of newly HIV-infected individuals enter the model annually in each of the following 15 years. The model predicts treated and untreated disease progression, mortality, and engagement with clinical care for each cohort between 2004 and 2009 (the ART scale-up period in Haiti), with inputs adjusted such that outcomes approximate the historical data available from Haiti during this timeframe.²⁸ The model then forecasts scenario-specific outcomes for the policy projection period, 2010 – 2020. Annual outcomes are summed across the cohorts in terms of mortality, number of individuals on ART, and ART coverage for each of the HIV treatment expansions scenarios.

Model input parameter estimation

We used patient-level data from three Haitian observational cohorts and a randomized controlled trial conducted in Haiti to derive model inputs — in the form of transition probabilities — for treated and untreated disease progression of individual cohorts (Table 2).^{8,17–22} Patient-level natural history data came from a prospective longitudinal cohort of 436 patients, including 40 seroconverters, recruited by the clinic of the Haitian Study Group for Kaposi's Sarcoma and Opportunistic Infections (GHESKIO) in Port-au-Prince, Haiti, between September 1985 and September 1998.^{17,18,20} To derive model inputs for HIV-infected individuals initiating ART with CD4 200–350 cells/μL, we used prospective longitudinal cohort data on 910 HIV-infected adults collected by GHESKIO between March 2003 and May 2009.^{19,21,22} To derive model inputs for individuals initiating ART with AIDS, patient-level data came from 408 patients in the early treatment group of the CIPRA HT-001 randomized, controlled trial of early versus delayed ART conducted at GHESKIO.⁸

To derive the model inputs, we performed incidence density analysis of the patient-level data and estimated event rates. Event rates were calculated by summing the total number of events (e.g., the number lost from ART conditional on ART initiation at CD4 count <200 cells/μL, the number of untreated individuals with CD4 count 200 – 350 cells/μL progressing to AIDS), relative to the total person-time at risk for the event. In deriving the event rates from the patient-level data, subjects who were event-free were right-censored at death, the end of the study, or the last documented clinic visit if lost from care or transferred to another care facility.²⁹ Following typical practice, censoring was considered independent and non-informative, such that individuals who were fully followed (and therefore not censored) during the study period were similar to those who were not fully followed (or censored). The patient-level data were analyzed using STATA software, release 11 (StataCorp, College Station, TX, USA). We calculated annual event rates to correspond with the model's annual cycle length. We assumed that the number of events from the patient-level data occurred in a Poisson process (i.e., continuously, independently, and at a constant rate) with time between events having an exponential distribution, allowing conversion of the event rates to probabilities for use as inputs in the model.³⁰

Additional model inputs were derived from a model verification process involving calibration of the model to population-level data from Haiti.²⁸ We first identified uncertain model inputs, including the number of newly HIV-infected individuals annually and their engagement with clinical care (i.e., probabilities of linkage to care, pre-ART retention in care, and ART enrollment). Next, multiple uncertain model input parameters were

systematically and simultaneously varied. We then identified those input values resulting in model estimates of the number on ART annually that minimized the percentage deviation between model predictions and historical data on the number receiving ART annually in Haiti. At the time this analysis was conducted, national data on the number receiving ART annually were available for 2004 – 2009.¹³ Finally, the mean of the input values represented in the best-fitting parameter sets were used as model inputs for policy projections beginning in 2010. The model allowed the number newly infected annually to vary between 2005 and 2009; however, in the base case, this parameter was held constant at 2009 levels of 8,600 per year over the 10-year policy projection period.

Analysis

One-way sensitivity analyses were conducted to evaluate the impact on results of uncertainty in model input parameters and in policy-related variables, including natural history disease progression, antiretroviral effectiveness, and HIV incidence (Table 2). Ranges were defined by the 95% confidence intervals derived from the patient-level primary data, estimated bounds for both population-level inputs and parameters derived during the model verification process, or by $\pm 25\%$ for the adjusted disease progression parameters.^{8,14,17–21,28}

We also conducted several targeted sensitivity analyses to reflect clinically and policy relevant concerns that may affect health outcomes and be important to decision makers. First, we varied the time of detection of first-line antiretroviral failure and switching to second-line ART and, in turn, mortality risk on second-line ART, reflecting potential earlier detection by using new HIV RNA monitoring technologies (HIV RNA Monitoring for Earlier ART Failure Detection, Table 2).³¹ Second, we considered the effects of antiretroviral therapy on HIV transmission^{9,10} by linearly decreasing the number of newly HIV-infected annually between 1% and 20% annually. Finally, we assessed the impact of simultaneous policies that increased HIV testing and linkage to care and retention in treatment and care (Optimal Policy Improvement, Table 2).

Results

Verification of model performance: ART scale-up in Haiti, 2004 – 2009

Model estimates of the number on ART in Haiti between 2004 and 2009 are within 7% for each year of the reported data and within 1% on average for the entire period.^{14,28} Model-based antiretroviral coverage estimates between 2004 and 2009 fall within the confidence intervals of other published estimates,¹⁴ with the model predicting 36.4% of those eligible for ART at a CD4 count <350 cells/ μ L receiving it in 2009.

By 2010, the model estimates 11,500 deaths averted since the beginning of ART scale-up in 2004 and of the estimated 103,500 individuals living with HIV, 27,300 are receiving ART. The model predicts that ART coverage increases to 57.4% and 40.3% for medical ART eligibility thresholds defined by CD4 count <200 cells/ μ L and <350 cells/ μ L, respectively. Approximately 15,600 individuals are estimated to be in care but off ART, with approximately three-quarters of those individuals eligible to receive treatment according to current WHO guidelines.

Base-case policy projections, 2010 – 2020

If ART initiation continues at current (i.e., 2010) rates, the number on ART will increase to 43,300 (+58.6% over 10 years) by 2020, with 89,700 deaths estimated between 2010 and 2020 (Table 3, **Panel A** and Figure 2). Compared to ART initiation at current rates, limited ART expansion (i.e., an increased rate of ART initiation for patients with CD4 counts 200 –

350 cells/ μ L in order to implement the change from the previous to current WHO guidelines^{7,32}) will increase the number on ART by 5,400 (+12.9%) and avert 3,000 deaths (−3.3%) by 2020. The Full Expansion scenario will increase the number on ART by 7,400 (+17.1%) and avert 4,300 deaths (−4.8%) by 2020. Restricting ART initiation to achieve constant ART capacity will reduce the number on ART by 15,700 (−36.3%) and result in 10,200 (+11.4%) additional cumulative deaths, while no new ART initiation will reduce the number on ART by 25,600 (−59.1%) and increase cumulative deaths by 15,200 (+16.9%).

By 2020, ART coverage according to current guidelines will reach 62.1% with Full Expansion, compared to 56.0% with expansion at current rates and 28.7% in the No New ART scenario. The number of HIV-infected individuals in care and eligible for, but not receiving ART, will fall to 6,500 with Full Expansion compared to 8,600 at current rates and 16,200 in the No New ART scenario. With predicted cumulative deaths ranging from 85,400 (best case) to 104,900 (worst case), the model estimates as many as 19,500 lives could be saved through ART expansion over the next decade. This is equivalent to nearly 20% of the number of individuals estimated to be living with HIV in Haiti in 2010.

Sensitivity analysis

When univariate sensitivity analyses were conducted to assess the impact of uncertainty in the model parameters, results are most sensitive to HIV incidence, untreated HIV disease progression, and the probability of pre-ART loss from care (Supplementary Digital Content, Figure S3). Variation in these parameters had a greater impact on treatment-related outcomes (e.g., ART coverage) than survival. For example, given the range of estimates for the number newly infected annually, ART coverage estimates vary from −12.8% to +4.4% (i.e., ART coverage 25% to 65%) for the No New ART (worst case) and Full Expansion (best case) scenarios, respectively. In contrast, estimated deaths vary from −5.4% to 6.4% (i.e., 4,600 to 6,700 cumulative deaths) for the worst and best scenarios. Results are less sensitive to disease progression on antiretroviral therapy and HIV testing and linkage to care.

We also conducted targeted sensitivity analyses to reflect specific concerns important to decision makers. We found that results are not sensitive to assumptions regarding earlier detection of antiretroviral failure and switching to second-line ART and lower mortality on second-line ART, resulting from HIV RNA treatment monitoring for patient management. For example, cumulative deaths over 10 years decreased by 900 to 104,000 (−0.9%) for the No New ART scenario and by 1,100 to 84,300 (−1.3%) for the Full Expansion scenario. Decreasing HIV incidence over time to reflect the prevention benefit of ART reduces cumulative deaths across all strategies over the analytic time horizon. The mortality difference between the Full Expansion and No New ART scenarios declines from 19,500 (base case) to 19,400 (1% decrease in the number newly infected annually) to 17,600 (20% annually) cumulative deaths averted over 10 years. ART coverage for all scenarios increases as the annual percent decrease in HIV incidence increases.

An optimal policy improvement in which HIV testing and linkage to care and retention in treatment and care are simultaneously improved results in 52,300 on ART by 2020 and 86,400 cumulative deaths over 10 years, if ART initiation continues at current rates (Table 3, Panel B). Further treatment expansion will increase the number on ART by 11,700 (+22.4%) and avert 6,800 deaths (−7.9%) by 2020. ART coverage by 2020 ranges from 30.0% (No New ART scenario) to 72.2% (Full Expansion scenario).

Discussion

Our results show that by 2020, treatment capacity at current ART enrollment rates in Haiti must increase by approximately 16,000 slots compared to treatment capacity in 2010, representing a 58.6% capacity increase over ten years. Near universal ART coverage, as defined by WHO's 80% coverage targets,¹ can begin to be realized in Haiti but requires taking additional, simultaneous steps to improve engagement with clinical care, including case identification and linkage to care, pre-ART retention in care, and retention on treatment, in addition to efforts to increase treatment expansion.

Findings from this analysis can inform country-level, HIV-related planning efforts in resource-limited settings. Enrolling new patients on ART at rates that reflect scale-up under the previous WHO HIV treatment guidelines³² (i.e., according to the Current Rates scenario) will require nearly 60% more treatment slots in 10 years. Implementing the current WHO HIV treatment guidelines⁷ at a level consistent with previous scale-up (i.e., the Limited Expansion scenario) will require over 75% more treatment slots in 10 years, while enrollment of all treatment-eligible individuals on ART will require approximately 85% more treatment slots at the end of this decade. Efficiency improvements in care delivery (e.g., integration of care across disease domains, task delegation), continued donor funding along with country-level financial sustainability plans, and human resource capacity building will need to be addressed simultaneously if treatment capacity increases are to continue.³³

In addition to continued treatment expansion, improvements in case identification and linkage to care, retention in pre-ART care, and retention on ART will all be required in order to increase ART coverage. This analysis suggests that these complementary efforts should focus in particular on retaining HIV-infected patients in care once identified and linked to care but prior to initiating ART. In the current analysis, along with a policy of full treatment expansion and efforts to improve case identification and treatment retention, increases in pre-ART retention of more than 70% were required to begin to achieve universal ART coverage. Similar opportunities for improvement regarding pre-ART retention in care exist in sub-Saharan African settings,³⁴ even though challenges remain to effectively retain newly diagnosed individuals in care. There may be a similar potential benefit from improved retention on treatment in settings other than Haiti.³⁵

We interpret our findings in the context of recent reports of the number on ART in Haiti. As of May 2012, 37,841 individuals were actively on ART in Haiti (personal communication), which is consistent with results from the increasing capacity and policy improvement scenarios considered in the current analysis. Treatment expansion and other policy improvements will not only increase the number on ART and ART coverage, but may also reduce tuberculosis (TB)-associated mortality and prevent new cases of TB, particularly when ART is initiated earlier in disease progression.³⁶ As data on these benefits continue to emerge, the model can be updated to provide additional insight into the health impact of treatment expansion.

Our analysis has several limitations. First, we assume that regimen-specific treatment effectiveness is fixed over the 10-year policy projection period. However, given the relatively short analytic time horizon, it is unlikely that improvements in ART effectiveness would have major impact on our policy conclusions that are driven by mortality among those who lack access to care. Second, the analysis does not consider changes in adherence to ART over time. While changes in adherence could affect mortality in this population,^{37,38} these effects would not be seen at the community level over the analysis period. Third, our projections reflected the adult HIV-infected population in Haiti and did not explicitly

include HIV-infected children. Finally, the current analysis does not explicitly account for population-level disease dynamics. Despite recent evidence indicating antiretroviral therapy may decrease the risk of HIV transmission at the patient-level,^{9,10} there was a relatively small impact on our results across strategies when we reduced the number of new HIV infections for the duration of our forecast.

This analysis suggests that expanding access to ART will save lives and that near universal access may be achievable. This will require a better understanding by HIV care providers and funders of how treatment-related resources can be more effectively and efficiently targeted to achieve these goals, including providing an adequate workforce, sufficient healthcare facilities, and necessary logistics support. Efforts to sustain international financing for ART must be coupled with strategies to improve health system efficiency in order to prevent avoidable deaths and increase access to ART.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are indebted to Heejung Bang, PhD, Ashley Eggman, MS, and Jared Leff, MS, for their assistance.

This work was supported in part by the Fogarty International Center (D43 TW000018, U2R TW006901), National Institute of Allergy and Infectious Diseases (K23 AI073190, K24 AI098627), and Robert Wood Johnson Foundation (63526). The funding sources played no role in the study, including study design; collection, analysis, and/or interpretation of data; the writing of the manuscript; and the decision to submit the manuscript for publication.

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Figure 1. Schematic of disease progression and engagement in clinical care for individual cohorts

For each cohort of HIV-infected individuals in the model, individuals may experience untreated disease progression in one of three mutually exclusive and collectively exhaustive stages of HIV disease (left-hand side). Within each disease stage, a fraction of the cohort may engage with clinical care (middle) through HIV case detection and linkage to care, ART initiation, or loss from treatment or care. Two sequential ART regimens are available among individuals initiating ART (right-hand side). Disease progression and movement through different clinical care-related events occurs according to transition probabilities, denoted by arrows. Dashed arrows indicate that transitions to or from a particular event can only arise among the fraction of the cohort that is eligible for or receiving antiretroviral therapy. Death can occur from HIV/AIDS- or non-HIV/AIDS-related causes. Abbreviations: ART = antiretroviral therapy; Lost = loss from treatment or care.

Figure 2. Number of HIV-infected individuals on ART and total alive beginning in 2011, by ART initiation scenario

Time, by year, is shown on the x-axis. On the y-axis is the number of HIV-infected on ART (Panel A) and the total number alive (Panel B). Continued antiretroviral expansion — as in the Current Rate (

), Expanded Current (

), and Expanded Current and Previous (

) scenarios — increases the number of HIV-infected individuals on ART and the total number alive over time. Capacity restrictions, as in the No New ART (

) scenario, decrease the number on ART by 33,000 and the number alive by 19,500 annually compared to expansion early and standard ART. “No New ART” indicates no HIV-infected individuals initiate ART beginning in 2011, although individuals on ART at this time remain on ART until loss from care or death. “Fixed Capacity” refers to a scenario in which treatment capacity is limited to 2010 levels. “Current Rate” refers to 2010 rates of early and

standard ART initiation. “Expanded Current” refers to increased rate of ART initiation according to 2010 WHO guidelines, while “Expanded Current and Previous” refers to increased rates of ART initiation according to 2010 and 2006 WHO guidelines.^{7,32}

Table 1

Scenarios for ART Expansion

Scenario	Capacity*	Description	Baseline Annual Probability	
			ART Initiation if CD4 Count 200–350 cells/μL	ART Initiation if CD4 Count <200 cells/μL
No new ART (worst case)	Decreased	No new ART initiation beginning in 2011	0	0
Fixed capacity	Flat	Number of individuals on ART remains fixed at 2010 levels	0.050	0.050
Current rates (status quo)	Increased	Probability of ART initiation remains fixed at 2010 levels [‡]	0.128	0.433
Limited expansion	Increased	Increased probability of ART initiation for patients with CD4 counts 200 – 350 cells/μL in order to implement the change from previous to current WHO guidelines ^{7,28} [‡]	0.400	0.433
Full expansion (best case)	Increased	All patients in care and eligible for treatment initiate ART ^{‡‡}	0.400	0.550

Abbreviations: ART = antiretroviral therapy; WHO = World Health Organization

* Capacity refers to the number of treatment slots, defined as the number of HIV-infected individuals receiving treatment annually, in a given year. The level of capacity (decreased, flat, or increased) is relative to estimated capacity in 2010.

[‡] In this scenario, individuals eligible to initiate ART with **Intermediate** HIV still face competing risks for other clinical events, including pre-ART loss from care, disease progression to AIDS prior to ART initiation, and AIDS- and non-AIDS-related mortality. Therefore, in this scenario, the upper bound of the increased annual probability of initiating ART with **Intermediate** HIV is estimated based on the annual probabilities of the competing risks.

^{‡‡} In this scenario, individuals eligible to initiate ART with **Intermediate** HIV or experiencing AIDS still face competing risks for other clinical events, including pre-ART loss from care, disease progression to AIDS prior to ART initiation, and AIDS- and non-AIDS-related mortality. Therefore, the annual probability of initiating ART when experiencing AIDS remains less than 1.

Table 2

Selected Model Input Parameters

Parameter	Value *	Range *	Source(s)
Prevalent HIV-infected Cohort (2004)			
Total HIV-infected population (number)	110,000		UNAIDS ¹³
Number on ART (number)	3,000		UNAIDS ¹³
Fraction unaware of serostatus	0.750		DHS 2006 ³⁹
Initial health stage distribution			
Asymptomatic	0.452		Model verification [†]
Intermediate	0.303		Model verification [†]
AIDS	0.245		Model verification [†]
Incident Cohorts (2010+)[‡]			
Newly infected annually (number)	8,600	6,500 – 11,000	Model verification [†]
Disease Progression			
Untreated			
Progression to Intermediate if Asymptomatic	0.200	0.150 – 0.250 [§]	Model verification [†]
Progression to AIDS if Intermediate (not lost)	0.300	0.225 – 0.375 [§]	Model verification [†]
Progression to AIDS if Intermediate (lost)	0.240	0.180 – 0.300 [§]	Model verification [†]
Death if Asymptomatic	0.017	0.009 – 0.031	Deschamps et al., ¹⁷ Pape et al., ²⁰ Fitzgerald et al. ¹⁸
Death if Intermediate	0.026	0.010 – 0.068	Deschamps et al., ¹⁷ Pape et al., ²⁰ Fitzgerald et al. ¹⁸
Death if AIDS	0.385	0.315 – 0.466	Deschamps et al., ¹⁷ Pape et al., ²⁰ Fitzgerald et al. ¹⁸
Death (multiplier), not in care	1.066	1.005 – 1.176	Model verification [†]
Treated			
2 nd -line ART if Intermediate 1 st -line ART Initiation	0.009	0.004 – 0.014	Severe et al. ⁸
2 nd -line ART if AIDS 1 st -line ART Initiation	0.031	0.025 – 0.038	Severe et al., ²¹ Leger et al. ¹⁹
Death if Intermediate 1 st -line Initiation or 2 nd line ART	0.005	0.002 – 0.010	Severe et al. ⁸
Death if AIDS 1 st -line ART Initiation 12 mo	0.148	0.126 – 0.174	Severe et al., ²¹ Leger et al. ¹⁹
Death if AIDS 1 st -line ART Initiation >12 mo	0.026	0.021 – 0.032	Severe et al., ²¹ Leger et al. ¹⁹
Death if AIDS 2 nd -line ART	0.094	0.068 – 0.131	Charles et al. ²²
Linkage to Care and Treatment			
Testing and Linkage to from No Care to Care, No ART			
Linkage if Asymptomatic	0.074	0.058 – 0.089	Model verification [†]
Linkage if Intermediate	0.099	0.078 – 0.118	Model verification [†]
Linkage if AIDS	0.469	0.370 – 0.538	Model verification [†]
Linkage from Care to ART			
Linkage to ART if Intermediate	0.128	0.024 – 0.197	Model verification [†]
Linkage to ART if AIDS	0.433	0.150 – 0.550	Model verification [†]
Pre-ART Loss from Care			

Parameter	Value [*]	Range [*]	Source(s)
Loss if Asymptomatic	0.307	0.097 – 0.740	Model verification [†]
Loss if Intermediate	0.182	0.035 – 0.404	Model verification [†]
Loss if AIDS	0.059	0.005 – 0.155	Model verification [†]
Loss from ART			
Loss from 1 st - or 2 nd -line ART if Intermediate ART Initiation	0.014	0.008 – 0.021	Severe et al. ⁸
Loss from 1 st -line ART if AIDS ART Initiation and on ART 12 mo	0.032	0.022 – 0.047	Severe et al., ²¹ Leger et al. ¹⁹
Loss from 1 st -line ART if AIDS ART Initiation and on ART >12 mo	0.011	0.008 – 0.016	Severe et al., ²¹ Leger et al. ¹⁹
Loss from 2 nd -line ART if AIDS ART Initiation	0.027	0.014 – 0.052	Charles et al. ²²
Selected Sensitivity Analyses			
HIV RNA Monitoring for Earlier ART Failure Detection^{††}			
2 nd -line ART if AIDS 1 st -line ART Initiation	0.113		Kimmel et al., ³¹ Mellors et al. ⁴⁰
Death if AIDS ART Initiation and 2 nd -line ART	0.026		Assumption
Optimal Policy Improvement			
Testing and Linkage to Care if Asymptomatic	0.089		Model verification [†]
Testing and Linkage to Care if Intermediate	0.118		Model verification [†]
Testing and Linkage to Care if AIDS	0.538		Model verification [†]
Pre-ART loss if Asymptomatic	0.097		Model verification [†]
Pre-ART loss if Intermediate	0.035		Model verification [†]
Pre-ART loss if AIDS	0.020		Model verification [†]
Loss from 1 st - or 2 nd -line ART if Intermediate ART Initiation	0.008		Severe et al. ⁸
Loss from 1 st -line ART if AIDS ART Initiation and on ART 12 mo	0.022		Severe et al., ²¹ Leger et al. ¹⁹
Loss from 1 st -line ART if AIDS ART Initiation and on ART >12 mo	0.008		Severe et al., ²¹ Leger et al. ¹⁹
Loss from 2 nd -line ART if AIDS ART Initiation	0.014		Charles et al. ²²

Abbreviations: ART = antiretroviral therapy; Asymptomatic = HIV-infected individuals with CD4 count >350 cells/ μ L; Intermediate = HIV-infected individuals with CD4 count 200–350 cells/ μ L; AIDS = HIV-infected individuals with CD4 count <200 cells/ μ L; Lost = loss from HIV treatment or care; mo = months

^{*} Values shown for disease progression, linkage to care and treatment, pre-ART loss from care, loss from treatment, and selected sensitivity analyses are annual probabilities. Ranges for the model inputs reflect the upper and lower bounds used in one-way sensitivity analyses, which assessed the impact of uncertainty in the parameters estimates on model results. Values used in the targeted sensitivity analyses, which are intended to reflect programmatic and policy decisions that may impact health outcomes and which are important to decision makers, are shown later in the table.

[†] Model input values and associated ranges were obtained from the model verification process, which was used to confirm that model projections correspond with historical data on ART scale-up in Haiti.¹³ The process involves systematically varying multiple, uncertain model input parameters and identifying the input values resulting in model outcomes that best approximate empirical data.²⁸ Additional information on this process is available in the Methods section.

^{††} Between 2005 and 2009, model predictions (versus the World Health Organization's estimated range) for the number of newly HIV-infected individuals annually were 11,000 (8,100 – 13,000); 10,100 (7,700 – 12,000); 10,200 (7,000 – 12,000); 9,200 (6,800 – 12,000); and 8,600 (6,500 – 11,000), respectively.

[§]The range for this input parameter represents +/-25% of the base case value.

[¶]In the HIV RNA monitoring sensitivity analysis, a 3.8-fold increase in the rate of 1st-line antiretroviral failure and switching to 2nd-line ART was applied to individuals receiving ART initiated at CD4 <200 cells/ μ L.³² The 2nd-line ART mortality risk among those initiating ART at CD4 <200 cells/ μ L was equivalent to the mortality risk of those on 1st-line ART >12 months.

The optimal policy improvement included: (a) HIV testing and linkage to care equal to the upper bound of the estimated bounds derived during the model verification process, regardless of disease stage; (b) pre-ART loss from care equal to the lower bound of the estimated bounds derived during the model verification process for all individuals in the Asymptomatic and Intermediate disease stages; and (c) loss from treatment equal to the lower bound of the estimated bounds derived during the model verification process, regardless of the disease stage in which they initiated ART. Pre-ART loss from care for individuals in the AIDS disease stage was assumed to be 0.02, which is within the range of the estimated bounds derived during model verification.

Main Results

Table 3

Scenario	Number in Care Off ART		Number on ART		Cumulative Deaths, Beginning in 2010		ART Coverage, * CD4 <350 cells/ μ L	
	2015	2020	2015	2020	2015	2020	2015	2020
Panel A. Base Case								
No new ART	20,300	19,500	22,000	17,700	55,600	104,900	0.328	0.287
Fixed capacity	17,200	16,300	27,600	27,600	54,200	99,900	0.403	0.411
Current rates	12,200	11,700	37,500	43,300	50,100	89,700	0.513	0.560
Limited expansion	10,400	10,000	41,000	48,900	49,200	86,700	0.554	0.609
Full expansion	9,900	9,600	42,200	50,700	48,500	85,400	0.565	0.621
Panel B. Optimal Policy Improvement [†]								
No new ART	30,500	31,300	22,600	18,700	55,800	105,300	0.333	0.301
Fixed capacity	26,900	26,500	27,500	28,400	54,800	101,000	0.397	0.423
Current rates	18,100	17,400	41,600	52,300	49,700	86,400	0.559	0.640
Limited expansion	14,700	14,200	46,400	59,800	48,500	82,400	0.613	0.697
Full expansion	13,300	12,800	49,300	64,000	47,200	79,600	0.640	0.722

Abbreviations: ART = antiretroviral therapy.

* ART coverage is defined as the fraction of those eligible for ART who actually receive it. Reported estimates assume ART eligibility at CD4 count <350 cells/ μ L.

[†]The optimal policy improvement included: (a) HIV testing and linkage to care equal to the upper bound of the estimated bounds derived during the model verification process, regardless of disease stage; (b) pre-ART loss from care equal to the lower bound of the estimated bounds derived during the model verification process for all individuals in the Asymptomatic and **Intermediate** disease stages; and (c) loss from treatment equal to the lower bound of the estimated bounds derived during the model verification process, regardless of the disease stage in which they initiated ART. Pre-ART loss from care for individuals in the AIDS disease stage was assumed to be 0.02, which is within the range of the estimated bounds derived during model verification. See Table 2 for details.