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The Cost-Effectiveness of Antiretroviral Therapy for Treating HIV Disease in the Caribbean

Lindsey L. Wolf, SB[*], **Paul Ricketts, MD, MSc, DLSHTM**[†], **Kenneth A. Freedberg, MD, MSc**[*,‡,§,||], **Hazel Williams-Roberts, MD**[¶], **Lisa R. Hirschhorn, MD, MPH**[‡], **Kathleen Allen-Ferdinand, MD**[¶], **William R. Rodriguez, MD**[‡], **Nomita Divi, MSc**[*], **Michael T. Wong, MD**[#], and **Elena Losina, PhD**[*,‡,§]

* *Division of General Medicine and the Partners AIDS Research Center, Massachusetts General Hospital, Boston, MA*

† *Ministry of Health, Roseau, Dominica*

‡ *Division of AIDS and Center for AIDS Research, Harvard Medical School, Boston, MA*

§ *Departments of Epidemiology and Biostatistics, Boston University School of Public Health, Boston, MA*

|| *Department of Health Policy and Management, Harvard School of Public Health, Boston, MA*

¶ *Ministry of Health, Basseterre, Saint Kitts and Nevis*

Division of Infectious Disease, Beth Israel Deaconess Medical Center, Boston, MA

Abstract

Background—Antiretroviral therapy (ART) recently became available in the Organization of Eastern Caribbean States (OECS). Survival benefits and budgetary implications associated with universal access to ART have not been examined in the Caribbean.

Methods—Using a state-transition simulation model of HIV with regional data, we projected survival, cost, and cost-effectiveness of treating an HIV-infected cohort. We examined 1 or 2 ART regimens and cotrimoxazole. In sensitivity analysis, we varied HIV natural history and ART efficacy, cost, and switching criteria.

Results—Without treatment, mean survival was 2.30 years (mean baseline CD4 count = 288 cells/μL). One ART regimen with cotrimoxazole when the CD4 count was <350 cells/μL provided an additional 5.86 years of survival benefit compared with no treatment; the incremental cost-effectiveness ratio was $690 per year of life saved (YLS). A second regimen added 1.04 years of survival benefit; the incremental cost-effectiveness ratio was $10,960 per YLS compared with 1 regimen. Results were highly dependent on second-line ART costs. Per-person lifetime costs decreased from $17,020 to $9290 if second-line ART costs decreased to those available internationally, yielding approximately $8 million total savings.

Conclusions—In the OECS, ART is cost-effective by international standards. Reducing second-line ART costs increases cost-effectiveness and affordability. Current funding supports implementing universal access regionally over the next year, but additional funding is required to sustain lifetime care for currently infected persons.

Correspondence to: Lindsey L. Wolf, SB, Division of General Medicine, Massachusetts General Hospital, 50 Staniford Street, 9th Floor, Boston, MA 02114 (e-mail: llwolf@partners.org).

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Keywords

antiretroviral therapy; Caribbean; cost-effectiveness; Organization of Eastern Caribbean States

The Organization of Eastern Caribbean States (OECS) includes 9 territories—Anguilla, Antigua and Barbuda, the British Virgin Islands, Dominica, Grenada, Montserrat, St. Kitts and Nevis, St. Lucia, and St. Vincent and the Grenadines—with a total regional population of 609,000; 5000 are estimated to be HIV-infected.[1] In 2006, fewer than 800 people were aware of their infection.[1] With substantial mobility between OECS nations, the rest of the Caribbean, and Europe and the Americas and economies dependent on tourism, the AIDS epidemic in the OECS may have an inordinate impact regionally. Funding has been awarded to 6 of the OECS territories (Antigua and Barbuda, Dominica, Grenada, St. Lucia, St. Kitts and Nevis, and St. Vincent and the Grenadines) by the Global Fund to Fight AIDS, Tuberculosis, and Malaria to work toward several HIV control measures in the region. Top priorities include the provision of universal access to care and treatment, voluntary counseling and testing services, locally available laboratory monitoring, and antiretroviral therapy (ART) at low cost.[1]

Beginning in 2004, ART became available through national programs in the OECS. Although first-line ART is currently available at discounted negotiated prices, second-line regimens remain much more expensive. Because ART became available only recently, and the number of patients receiving ART is relatively small (an estimated 266 persons in the OECS in August 2006), there has not yet been a large demand for second-line drugs.[2] With an estimated 250,000 persons currently living with HIV/AIDS in the Caribbean and nearly 3000 HIV-infected persons identified since the beginning of the epidemic in the OECS, however, this is likely to change in the near future.[2,3]

Provision of HIV care in the OECS is largely governed by recommendations from the Caribbean HIV/AIDS Regional Training Network. These recommendations, consistent with those from the World Health Organization (WHO), suggest that ART should be offered to all symptomatic patients and asymptomatic patients with CD4 counts <200 cells/μL.[4,5] They also suggest that ART should "generally be offered" to patients who are asymptomatic or have minor symptoms and a CD4 count between 200 and 350 cells/μL. Our objectives were to model the HIV care currently available in the OECS to evaluate clinical outcomes and cost-effectiveness and to assess the budgetary impact of providing universal access to HIV treatment in this region of the Caribbean.

METHODS

Analytic Overview

We conducted a model-based analysis incorporating data from the best available sources from different sites in the Caribbean, including OECS countries, Barbados, and Jamaica. We examined 4 main strategies: (1) no treatment (for comparison purposes), (2) treatment with cotrimoxazole prophylaxis alone when the CD4 count was <200 cells/μL, (3) treatment with ART alone (CD4 count <350 cells/μL), and (4) treatment with ART (CD4 count <350 cells/μL) plus cotrimoxazole (CD4 count <200 cells/μL). For strategies that included ART, we considered 2 different cases: only 1 available regimen (or "line") of ART and the availability of a second-line regimen for use after immunologic (CD4 cell count) or clinical (opportunistic disease diagnosis) failure of first-line therapy. Treatment with ART was initiated at a CD4 count <350 cells/μL in accordance with the recommendations of the Caribbean HIV/AIDS Regional Training Network.[4] Cotrimoxazole prophylaxis was initiated at a CD4 count <200 cells/μL based on local practice.[6] Although the WHO recommends initiating cotrimoxazole

prophylaxis when the CD4 count is<350 cells/μL, this recommendation is targeted at settings with high prevalences of malaria and bacterial infections, which the OECS lacks.[7]

We assumed that CD4 cell count testing was available for clinical decision making, in addition to clinical diagnoses but that HIV RNA testing was not available, according to the current standard of care in the OECS.[4] Clinical assessments occurred every 3 months, and CD4 cell counts were tested every 6 months.[4] As recommended by the WHO, first-line therapy was switched to second-line therapy, if available, when the CD4 cell count decreased by 50% from the peak value on treatment or a severe opportunistic disease was observed at least 6 months after ART initiation.[5] The last available ART regimen for each patient was continued until death.[5] Different strategies for switching and stopping therapy were examined in sensitivity analyses, including using only immunologic information, only clinical information, or both.

The incremental cost-effectiveness ratio—the difference in cost divided by the difference in survival between a given strategy and the "next best" (less expensive but less effective) strategy—was calculated for each strategy. Strategies that were "dominated" by strong dominance (more expensive and less effective than another strategy) or weak dominance (less expensive, less effective, but less cost-effective than another strategy) were excluded.[8] We adopted a modified societal perspective, excluding patient time and travel costs, and discounted costs and life years by 3% per year.[9]

The WHO-sponsored Commission on Macroeconomics and Health has proposed that "cost-effectiveness" be defined in relation to an individual country's per capita gross domestic product (GDP).[10] Health interventions with incremental cost-effectiveness ratios <3 times a country's annual GDP would be considered "cost-effective," and interventions with ratios less than the annual GDP would be "very cost-effective." In the OECS, annual per capita GDP ranges from $3800 (St. Vincent and the Grenadines) to $11,200 (Antigua and Barbuda).

Model

The Cost-Effectiveness of Preventing AIDS Complications (CEPAC) international model, an adaptation of the published CEPAC US model,[11–13] is a state-transition model of HIV disease in resource-limited settings.[14–16] In a first-order Monte Carlo simulation, a cohort of patients proceeded through the model, with each patient making monthly transitions among different health states, including chronic HIV, acute complications from an opportunistic disease, and death. These health states were stratified by current CD4 cell count, current HIV RNA level, and history of opportunistic diseases. Opportunistic diseases were divided into 6 groups: *Pneumocystis jirovecii* pneumonia, *Mycobacterium avium* complex, toxoplasmosis, cytomegalovirus, fungal infections, and other severe diseases. Death in the model was attributed to chronic HIV, an acute opportunistic disease, or non–HIV-related causes. Other specifications of the model have been previously published (available at: http://content.nejm.org/cgi/data/355/11/1141/DC1/1).[14–16]

Input Data

Cohort Characteristics—Regionally, the most robust data clinically and demographically consistent with HIV-infected patients in the OECS were from Jamaica. We simulated a cohort of HIV-infected adults using characteristics reported in the Jamaican Ministry of Health HIV/AIDS Tracking System (HATS), a national surveillance database, with a mean age of 36 years and gender distribution 58% male.[17] Because CD4 cell counts were not available for patients in the HATS, a baseline CD4 cell count distribution was estimated by matching reported disease stages from the HATS data set (asymptomatic HIV, symptomatic HIV, and AIDS) with CD4 cell count distributions for corresponding WHO stages (stages II, III, and IV) reported from a clinical trial in a resource-limited setting.[18] An average of the mean stage-specific CD4 cell

counts, weighted by the percentage of patients in each disease stage in the HATS, gave a baseline CD4 count distribution with a mean of 288 cells/μL (SD = 130 cells/μL). We assumed the cohort had an HIV RNA distribution taken from a clinical trial in a similar setting (Table 1).[19]

Survival Data: Calibration to a National Surveillance Data Set—The best available region-specific survival data from the Caribbean were also from the Jamaican HATS data set.[17] We calibrated to obtain baseline estimates for the monthly probability of AIDS-related death in the model, varying the monthly probability of AIDS-related death while keeping all other parameters constant, to match the natural history (untreated) survival output from the model with the observed HATS survival at 1 year (~80%). This calibration yielded baseline values for the monthly probability of AIDS-related death, stratified by disease stage, that were 7.75 times the values observed in the United States Multicenter AIDS Cohort Study (MACS; see Table 1). Mortality during a month with an opportunistic disease was characterized separately and was assumed to be similar to the rates seen in the MACS.[20] Background mortality, stratified by age and gender, was applied from WHO estimates for Jamaica.[21] These assumptions were all tested in sensitivity analyses.

Natural History of Disease—Other estimates for the natural history of disease were taken from the MACS (see Table 1).[20,21a] These data were chosen because the spectrum of opportunistic diseases in the OECS is more similar to that seen in the United States than in many other resource-limited settings.[22] Specifically, there is a lower incidence of tuberculosis in the OECS than in other nearby resource-limited settings, such as Haiti.[23]

Prophylaxis and ART Efficacy—Estimates for cotrimoxazole prophylaxis efficacy were from a published meta-analysis.[24] Efficacy of first-line ART was from a cohort study in Barbados, with 80% of patients achieving virologic suppression after 12 months with a non-nucleoside reverse transcriptase inhibitor (NNRTI)–based regimen.[25,26] Efficacy of second-line therapy was from a lopinavir/ritonavir-based regimen in treatment-experienced patients with no protease inhibitor mutations at baseline (62% suppression at 12 months).[27,28] An additional ART benefit, on top of CD4 cell count increase, was a reduction in morbidity and mortality, as previously reported (see Table 1).[29]

Costs—Costs for ART and cotrimoxazole were from the regional OECS Pharmaceutical Procurement Service and represent the cost of publicly available treatment (F. Burnett, personal communication, September 2006; see Table 1). Standard-of-care first-line therapy includes zidovudine, lamivudine, and nevirapine throughout the OECS.[2,4] If available, the most commonly used second-line regimen includes didanosine, abacavir, and lopinavir/ritonavir.[2] In sensitivity analyses incorporating the currently available international cost of generic second-line drugs, costs were from the 2006 Médecins Sans Frontières drug pricing report.[30] Cost estimates for hospital and outpatient care were from the WHO CHOosing Interventions that are Cost Effective (CHOICE) study, which modeled costs of care in the OECS countries.[31,32] Mean regional costs for an inpatient day and outpatient visit were calculated from these data. Because regional estimates for utilization of inpatient and outpatient HIV medical care were not available, published health care utilization rates reported in the United States through the HIV Research Network study were used.[33,34] These values were varied widely in sensitivity analyses to assess any potential impact on the results. Cost per opportunistic disease was calculated by multiplying the utilization of outpatient visits by the cost of an outpatient visit and adding the result to the product of number of days of inpatient utilization and cost of an inpatient day (see Table 1). All costs were converted to and reported in 2006 US dollars using country-specific GDP deflators and the fixed exchange rate between the Eastern Caribbean dollar and the US dollar.[35,36]

Budgetary Analysis

Using the CEPAC international model, we calculated national and regional expenditures that would be required to treat currently identified HIV-infected persons in each of the OECS countries and the whole region. Average cost per person for treatment and care was modeled for 1 year and over a lifetime. These costs were multiplied by the estimated number of HIV-infected persons currently identified in the countries to obtain 1-year and lifetime cost estimates for the cohort of currently HIV-infected persons.

The number of HIV-infected persons currently alive and identified in each OECS country was estimated based on the cumulative total of HIV-infected persons reported by the OECS HIV/AIDS Project Unit in 2006.[2] We estimated the percent of patients who had died based on cumulative surveillance data from the United States before treatment was available there (315,475 deaths/506,538 AIDS cases [62%]).[37] This percentage was applied to estimate that 1768 persons reported with HIV in the OECS had died since the beginning of the epidemic. Remaining persons were assumed to be alive and to represent the number currently identified.

Assuming that those persons identified in each country were similar to the simulated population at model entry, with some requiring treatment based on CD4 count criteria and some not yet requiring treatment, we performed an analysis for 2 different cases: (1) the best practice recommendation for care (2 lines of ARTwhen the CD4 count was <350 cells/μL, with cotrimoxazole when the CD4 count was <200 cells/μL) and (2) the best practice recommendation for care, as already reported, but with generic drug costs currently available in other countries for second-line ART.[30]

RESULTS

Base Case Analysis

With no treatment, starting with a mean (SD) CD4 count of 288 cells/μL (130 cells/μL) and mean age of 36 years, projected mean per-person survival was 2.30 years, with a lifetime cost of $1600 per person. When we assumed that only 1 line of ARTwas available, initiating ARTwhen the CD4 count was <350 cells/μL, combined with cotrimoxazole prophylaxis when the CD4 count was <200 cells/μL, mean per-person survival increased to 8.16 years with a lifetime cost of $5620 per person, for an incremental cost-effectiveness ratio of $690 per year of life saved (YLS) compared with no treatment. Compared with the per capita annual GDPs in the region, and using the WHO Commission on Macroeconomics and Health guidelines for cost-effectiveness, treatment using 1 ART regimen with cotrimoxazole may be considered very cost-effective (less than the GDP for all OECS countries; Fig. 1) compared with no treatment. When second-line ART was available, survival increased to 9.20 years at an additional cost of $11,400, and the cost-effectiveness ratio increased to $10,960 per YLS compared with 1 line of ART, which may be considered cost-effective (<3 times the GDP for all OECS countries; see Fig. 1) by international standards (Table 2). Although the cohort spent an average of 1.96 years, or 21% of survival time, on second-line therapy, 68% of lifetime costs were spent on second-line drugs, an average of $11,610 per patient. In contrast, only 12% of lifetime costs were spent on first-line drugs. The remaining 20% of costs were spent on routine medical care, inpatient stays, cotrimoxazole prophylaxis, adverse events, and CD4 cell counts.

Sensitivity Analyses

Baseline CD4 cell count, rate of CD4 cell decline off therapy, and ART efficacy had the greatest impact on survival outcomes, although because longer or shorter survival incurred greater or fewer costs, these parameters did not have a major influence on cost-effectiveness. Baseline CD4 count was varied from that of a cohort with WHO stage II disease (mean CD4 count = 408 cells/μL) to that of a cohort with stage IV disease (mean CD4 count = 132 cells/μL),

resulting in mean life expectancies with treatment with 2 lines of ART varying from 9.83 to 6.39 years. Varying the rate of CD4 cell decline from twice to one half of the base case rate gave life expectancies with 2 lines of ART ranging from 8.14 to 10.39 years. Finally, varying first-line ART efficacy in terms of viral suppression at 6 months from 46% to 94% gave life expectancies ranging from 7.21 to 9.85 years. To test the impact of calibrated mortality rates, we varied the probability of chronic AIDS death, stratified by CD4 cell count, from twice to one half of the base case, which yielded life expectancies ranging from 8.21 to 10.06 years.

The cost of second-line ART and the strategies used to switch therapy had the greatest impact on cost-effectiveness. Decreasing second-line ART cost yielded substantially lower cost-effectiveness ratios. When the cost of second-line ART was decreased to the generic prices recently reported by Médecins Sans Frontières ($172 per month from the base case of $515 per month),[30] the incremental cost-effectiveness ratio for 2 lines of ART initiated when the CD4 count was <350 cells/μL with cotrimoxazole decreased to $3530 per YLS (see Fig. 1). At the generic cost for second-line ART, total lifetime costs decreased from the base case result of $17,020 to $9290, with second-line ART costs representing 42% of the total cost of lifetime medical care. Switching from first- to second-line therapy only with an opportunistic disease (removing the criterion of CD4 cell count decrease by 50% from on-treatment peak) decreased survival to 8.17 years from the base case survival of 9.20 years, with a cost-effectiveness ratio of $70,800 per YLS (Table 3).

Budgetary Analysis of Universal Access

To provide lifetime treatment and care to the currently identified 1070 HIV-infected persons living in the OECS with the best practice strategy (2 lines of ART when the CD4 count was <350 cells/μL with cotrimoxazole), $18.2 million would be required region-wide for medical care and drugs, or $2.0 million per year over the mean length of survival of 9.20 years (Table 4). Four percent of that amount (or $685,500) is required over the next year. If second-line drug prices in the OECS were reduced to those currently available for generic second-line drugs elsewhere, the regional estimate for lifetime care cost would decrease by 45%, to $9.9 million, with $678,800 required over the next year (see Table 4).

DISCUSSION

We used the best available Caribbean data and a published computer simulation model of HIV disease to estimate the survival, cost-effectiveness, and budgetary implications of different strategies for HIV care in the OECS. The most effective strategy included 2 sequential lines of ART, initiated when the CD4 count was <350 cells/μL, with cotrimoxazole when the CD4 count was <200 cells/μL; this strategy was cost-effective throughout the OECS and provided a mean survival gain of 6.90 years per person compared with no treatment. Although this strategy was cost-effective by international standards and consistent with current regional guidelines, the cost of second-line ART comprised 68% of total lifetime care costs, making the 2-line strategy much less affordable than a 1-line strategy. Early initiation of treatment with 1 line of ART provided 89% of the life expectancy achieved with 2 lines of ART at one third of the cost. Projected costs for the complete scale-up of universal lifetime access to treatment to currently identified patients in the OECS were $18.2 million over the next 9 years.

Although there are no published studies on the cost-effectiveness of ART from the Caribbean, several studies have examined the cost-effectiveness of ART in other resource-limited settings.[15,38–40] Goldie et al[15] reported cost-effectiveness for ART treatment in Côte d'Ivoire that ranged from very cost-effective (less than the GDP) to cost-effective (<3 times the GDP). Two studies from South Africa reported incremental cost-effectiveness ratios that ranged from cost-effective at current ART prices to cost saving at anticipated reduced ART prices.[38,39] Paton et al[40] reported cost-effectiveness for treatment in Singapore, finding that ART was cost-

effective across all stages of HIV infection. The results of the current analysis are consistent with these findings from Africa and Asia.

In March 2005, funding from the Global Fund to Fight AIDS, Tuberculosis, and Malaria began a 5-year effort to develop structure and capacity for treatment of HIV in the OECS, with a project budget of $8.9 million.[1,41] According to the current study, although the 1-year cost for providing medical care and drugs to all currently identified HIV-infected persons in the OECS is $685,500, the cost to provide services over the lifetimes of these persons is between $9.9 and $18.2 million over the next 9 years, depending on the price of second-line ART. These forecasted costs do not include costs required to achieve other regional aims, including the expansion of voluntary counseling and testing; capacity for local laboratory monitoring; and capacity building, including infrastructure, new systems, and personnel training or resources needed for newly identified patients through expanded testing. Therefore, this study suggests that although implementation of universal access to treatment for currently identified patients in the OECS may be initiated with current support from the Global Fund to Fight AIDS, Tuberculosis, and Malaria, additional funding is required to sustain lifetime care for currently infected persons. Reducing the cost of second-line ART to the region would substantially lower overall expenditures required to provide universal access to treatment in the OECS.

This analysis has several limitations. There remains a dearth of region-specific data from the Caribbean, especially on CD4 cell counts, HIV RNA levels, and other markers of HIV natural history. Therefore, data for this study were derived from multiple sources. Because of the lack of complete OECS data, including data on short-term mortality from opportunistic diseases and chronic mortality, we calibrated the chronic mortality rate in the model to Jamaican national surveillance data.[17] Although the calibrated chronic mortality is quite high compared with mortality in the MACS, this rate may include increased death from opportunistic diseases in the OECS as well as other AIDS-related deaths. Although better estimates for these parameters would give more specific projections for survival and cost-effectiveness, we dealt with the lack of primary data through calibration and sensitivity analyses, finding that the policy conclusions remained robust across a wide range of estimates. It was similarly difficult to find high-quality data on the prevalence of HIV infection in the region and the proportion of those infected who require treatment. The most recently reported results were used; however, as better estimates become available, the lifetime cost results of the current study can be applied to update the budgetary analysis for the region. Finally, the budgetary projections did not account for costs arising from the treatment and care of incident HIV cases, because the model used was not an epidemic model.

Most patients in the Barbados cohort, from which we derived first-line ART efficacy, were initiated on an efavirenz-based regimen with 2 nucleoside reverse transcriptase inhibitors.[25,26] Although the current standard of care for first-line ART in the OECS is a nevirapine-based regimen, there is evidence of similar efficacy using either of these NNRTIs.[42] Therefore, we applied the efficacy estimate from Barbados, coupled with nevirapine cost, which is used in most cases in the OECS, for the base case. Further, the percentage of patients suppressed in the Barbados cohort was similar to that in other studies, including the Antiretroviral Therapy in Lower Income Countries Collaboration (ART-LINC), the Haitian Study Group for Kaposi's Sarcoma and Opportunistic Infections, and the Médecins Sans Frontières Khayelitsha, South Africa cohort.[23,43–45]

Much attention has been given to the HIV epidemic in the Caribbean, yet few epidemiologic and clinical research studies have been published from the region, and most of those are from Haiti.[23,46] Furthermore, there is a lack of operational and policy research to inform efficient regional HIV policy formation. The compilation of available region-specific data inputs for this analysis highlights the need for increased research in the Caribbean to understand better

the natural history of HIV disease, the efficacy of prophylaxis and ART, and the impact on quality of life of HIV disease and its treatment. This analysis shows that the current cost of second-line ART is extremely high and strongly influences the cost-effectiveness and total lifetime cost of adequate HIV care in the Caribbean. Even if currently reported generic drug prices could be obtained in the region, the cost of second-line drugs remains a major component of total costs and may ultimately limit access to effective treatment. Lower drug prices are needed for second-line therapy. At the same time, national programs should distribute less expensive first-line therapy to all who need it and work to increase total funding for treatment in the region, which is going to be required in the near future. The budgetary impact of second-line ART highlights the critical importance of adherence support programs, because maximizing the effectiveness of first-line ART regimens should contribute to sustainable HIV treatment programs. ART for HIV disease in the Caribbean is cost-effective and can be further optimized by obtaining lower cost second-line therapy to make the best use of available resources.

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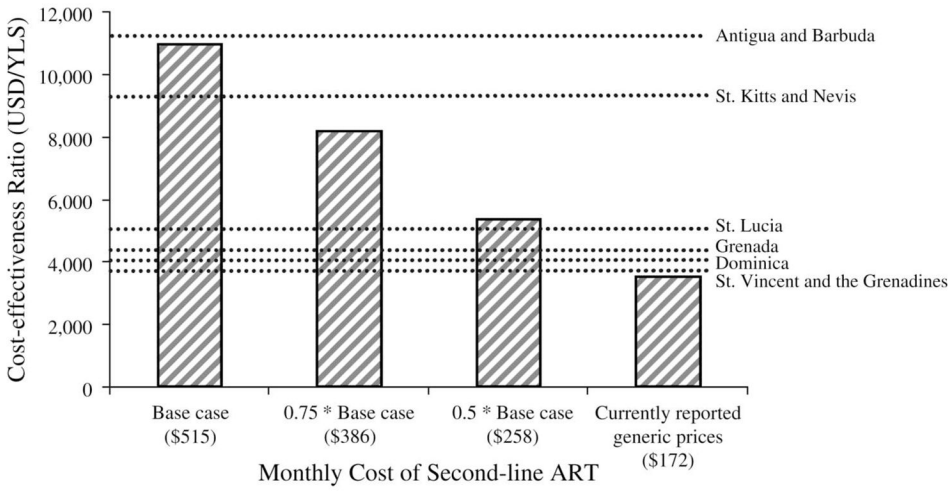

FIGURE 1.

Impact of the cost of second-line ART on the incremental cost-effectiveness of 2 lines of therapy initiated when CD4 count is <350 cells/μL, with cotrimoxazole when the CD4 count is <200 cells/μL, compared with 1 line of therapy initiated when the CD4 count is <350 cells/μL, with cotrimoxazole when the CD4 count is <200 cells/μL. The GDP per capita (constant 2006 US dollars [USD]) for each OECS country is indicated with a dotted horizontal line.

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TABLE 1

Selected Baseline Model Inputs

Variable	Baseline Value (SD)						References
Cohort characteristics							
Age (y)	36 (11)						17
Gender distribution (% male)	58						17
Initial CD4 distribution (cells/μL)	288 (130)						17,18
Initial HIV RNA distribution (%)							19
>100,000 copies/mL	69.21						
30,001 to 100,000 copies/mL	22.27						
10,001 to 30,000 copies/mL	7.06						
3001 to 10,000 copies/mL	1.35						
500 to 3000 copies/mL	0.11						
<500 copies/mL	0.00						
Natural history							
Monthly AIDS-related death probability	With no OD history			With OD history			17,20*
CD4 count >500 cells/μL	0.00049			0.02325			
CD4 count 301 to 500 cells/μL	0.00073			0.13175			
CD4 count 201 to 300 cells/μL	0.00822			0.21305			
CD4 count 101 to 200 cells/μL	0.01155			0.16624			
CD4 count 51 to 100 cells/μL	0.06673			0.18073			
CD4 count ≤50 cells/μL	0.14361			0.75036			
Monthly CD4 count decline (cells/μL per month)							21a
HIV RNA >30,000 copies/mL	6.375 (5.064)						
HIV RNA 10,001 to 30,000 copies/mL	5.400 (4.327)						
HIV RNA 3001 to 10,000 copies/mL	4.600 (3.759)						
HIV RNA 501 to 3000 copies/mL	3.733 (3.832)						
HIV RNA ≤500 copies/mL	3.025 (2.725)						
Monthly OD probability, primary	PCP	MAC	Toxo	CMV	Fungal	Other†	20
CD4 count >500 cells/μL	0.000410	0.000059	0.000029	0.000059	0.000088	0.000470	
CD4 count 301 to 500 cells/μL	0.000850	0.000055	0.000092	0.000129	0.000276	0.000870	
CD4 count 201 to 300 cells/μL	0.003730	0.000220	0.000420	0.000580	0.000290	0.002240	
CD4 count 101 to 200 cells/μL	0.009600	0.001010	0.000670	0.002140	0.001350	0.007160	
CD4 count 51 to 100 cells/μL	0.031000	0.003750	0.001400	0.005230	0.005910	0.024600	
CD4 count ≤50 cells/μL	0.037000	0.012200	0.002700	0.018570	0.011230	0.039400	
Probability of death from OD event	0.063200	0.158500	0.178600	0.105300	0.056600	0.074900	20
ART							
Efficacy	Viral suppression at 12 months (% suppressed)			CD4 count increase at 12 months (cells/μL)			
First-line therapy	80			165			26
Second-line therapy	62			121			27,28‡
Percent reduction of morbidity and mortality on ART, independent of CD4 count	46%						29
Costs (2006 USD)							
Inpatient day, mean cost (range in OECS)	42.38 (24.89 to 68.19)						31,32
Outpatient visit, mean cost (range in OECS)	18.20 (4.58 to 24.30)						31,32
Cotrimoxazole prophylaxis, monthly cost	1.28						OECS PPS
First-line ART (AZT/3TC/NVP), monthly cost	24.22						OECS PPS
Second-line ART (ddI/ABC/LPV/r), monthly cost	515.08						OECS PPS§
CD4 count test	28.09						33,34‖
Utilization of medical care							

Variable	Baseline Value (SD)		References
Within 90 days of OD event	Inpatient days (days/OD)	Outpatient visits (visits/OD)	
PCP	6.26	2.19	
MAC	3.08	2.74	
Toxo	14.57	2.50	
CMV	4.57	2.54	
Fungal	4.77	2.67	
Other	3.29	2.77	
Routine, in absence of OD event	Inpatient days (days/month)	Outpatient visits (visits/month)	
CD4 count >500 cells/μL	0.08	0.58	
CD4 count 301 to 500 cells/μL	0.14	0.75	
CD4 count 201 to 300 cells/μL	0.17	0.83	
CD4 count 101 to 200 cells/μL	0.26	0.88	
CD4 count 51 to 100 cells/μL	0.44	0.96	
CD4 count ≤50 cells/μL	0.58	0.99	
In the month of death	16.14	0.71	

[*] Monthly probabilities for AIDS-related death were derived through calibration of data from the United States to the Jamaica HATS data set at 1 year (see Methods section for details).

[†] The “Other” opportunistic disease category included Kaposi sarcoma, cryptosporidiosis, isosporiasis, non-Hodgkin lymphoma, brain metastases, progressive multi-focal leukoencephalopathy, HIV dementia, disseminated tuberculosis, chronic mucocutaneous herpes simplex virus, salmonellosis, wasting syndrome, and pulmonary tuberculosis.

[‡] Estimates for the efficacy of protease inhibitor–based therapy after NNRTI-based therapy were extrapolated from the Bristol-Myers Squibb 045 trial, with viral suppression taken from the group of patients on lopinavir/ritonavir with no protease inhibitor mutations at baseline.[28]

[§] In the sensitivity analysis that applied generic second-line drug prices reported by Médecins Sans Frontières, 7% was added to the reported drug prices to account for current shipping and handling fees in the OECS (F. Burnett, personal communication, September 2006).[30]

[||] Billing Office, Joseph N. France General Hospital, Basseterre, St. Kitts, September 2006.

ABC indicates abacavir; AZT, zidovudine; CMV, cytomegalovirus; ddI, didanosine; LPV/r, lopinavir/ritonavir; MAC, *Mycobacterium avium* complex; NVP, nevirapine; OD, opportunistic disease; OECS PPS, Organization of Eastern Caribbean States Pharmaceutical Procurement Service; PCP, *Pneumocystis jirovecii* pneumonia; 3TC, lamivudine; Toxo, toxoplasmosis; USD, 2006 US dollars.

TABLE 2

Discounted Survival, Cost, and Cost-Effectiveness Outcomes for a Simulated Cohort of HIV-Infected Adults in the Caribbean

Strategy	Mean Cost (USD)	Mean Life Expectancy (y)	Incremental Cost-Effectiveness Ratio* (USD/YLS)
No treatment	1600	2.30	—
Cotrimoxazole alone, CD4 count <200 cells/μL†	1620	2.37	290
One line of ART, CD4 count <350 cells/μL	5520	8.04	690
One line of ART, CD4 count <350 cells/μL, with cotrimoxazole	5620	8.16	830
Two lines of ART, CD4 count <350 cells/μL, with cotrimoxazole‡	17,020§	9.20	10,960

*Incremental cost-effectiveness ratios were calculated from rounded values for mean cost and mean survival presented in this table and may differ slightly from ratios calculated from the nonrounded values.

†All strategies including cotrimoxazole prophylaxis began prophylaxis when the CD4 count was <200 cells/μL and discontinued prophylaxis if the CD4 count increased to >300 cells/μL.

‡A second-line of ART was initiated 2 months after failure of the first-line regimen was detected.

§For 2 lines of ART with cotrimoxazole, total costs included $40 for cotrimoxazole prophylaxis, $13,590 for ART drugs, and $3390 for medical care and monitoring.

USD indicates 2006 US dollars.

TABLE 3

Selected Sensitivity Analyses for a Strategy of Care Including 2 Lines of ART With Cotrimoxazole

Parameter	Range Varied	Mean Life Expectancy (y)	Incremental Cost-Effectiveness Ratio* (USD/YLS)
Baseline CD4 count, mean (cells/μL)	132 to 408	6.39 to 9.83	11,130 to 11,210
Monthly natural history CD4 count decline (cells/μL per month)	2 to 0.5 times the base case rates†	8.14 to 10.39	9990 to 12,970
Monthly probability of AIDS-related death	2 to 0.5 times the base case rates‡	8.21 to 10.06	10,400 to 11,950
Efficacy of first-line ART (% virologic suppression at 6 months)	46 to 94	7.21 to 9.85	10,420 to 11,320
Criteria to switch from first- to second-line ART	OD event only to OD event or 50% drop from on-treatment peak CD4 cell count	8.17 to 9.20	70,800 to 10,960
Monthly cost of second-line ART (USD per month)	172 to 515	No effect	3530 to 10,960

*Incremental cost-effectiveness ratios are compared with the next best strategy: 1 line of ART with cotrimoxazole.

†These rates are stratified by baseline HIV RNA level, as shown in Table 1.

‡These rates are stratified by current CD4 cell count, as shown in Table 1.

USD indicates 2006 US dollars.

TABLE 4

Budgetary Impact of Implementing ART for HIV Disease in the OECS: Projected 1-Year and Lifetime Costs for HIV Treatment and Care of Currently Infected Patients in Each OECS Country Using 2 Different Strategies of Care

Country	Number Currently Identified*	Cost of Care Using Best Practice Strategy† (USD)		Cost of Care Using Best Practice Strategy With Reported Generic Second-Line ART Prices† (USD)	
		1 Year	Lifetime	1 Year	Lifetime
Antigua and Barbuda	209	133,600	3,549,300	132,300	1,936,700
Dominica	115	73,900	1,964,000	73,200	1,071,700
Grenada	104	66,900	1,777,900	66,300	970,100
St. Kitts amd Nevis	95	60,900	1,617,400	60,300	882,600
St. Lucia	223	143,000	3,799,700	141,600	2,073,300
St. Vincent and the Grenadines	324	207,300	5,506,900	205,200	3,004,900
Total	1,070	685,500	18,215,200	678,800	9,939,400

*The number of cases identified in each country was estimated based on the cumulative total of HIV-infected persons reported by the OECS HIV/AIDS Project Unit in 2006 (see Methods section for details).[4]

†The best practice strategy was 2 lines of ART when the CD4 count was <350 cells/μL with cotrimoxazole when the CD4 count was <200 cells/μL.[30] In the last 2 columns, all costs represent the best practice strategy implemented with currently reported generic drug prices for second-line ART.

USD indicates 2006 US dollars.