

Updates of Lifetime Costs of Care and Quality-of-Life Estimates for HIV-Infected Persons in the United States: Late Versus Early Diagnosis and Entry Into Care

Paul G. Farnham, PhD,* Chaitra Gopalappa, PhD,* Stephanie L. Sansom, PhD,*
 Angela B. Hutchinson, PhD,* John T. Brooks, MD,* Paul J. Weidle, PharmD,*
 Vincent C. Marconi, MD,†‡§ and David Rimland, MD†‡

Background: Lifetime costs of care and quality-of-life estimates for HIV-infected persons depend on the disease stage at which these persons are diagnosed, enter care, and start antiretroviral therapy. Updated estimates were used to analyze the effects of late versus early diagnosis/entry on US lifetime care costs, quality-of-life estimates, and HIV transmissions.

Methods: The Progression and Transmission of HIV/AIDS model was used to estimate discounted (3%) lifetime treatment costs (\$US 2011) and quality-of-life variables from time of infection for cohorts of 10,000 HIV-infected index patients in 4 categories of CD4 count at diagnosis: (I) ≤ 200 cells/ μL , (II) 201–350 cells/ μL , (III) 351–500 cells/ μL , and (IV) 501–900 cells/ μL . It is assumed that index patient diagnoses were uniformly distributed across the CD4 count range in each category and that patients entered care at the time of diagnosis, remained in care, and were eligible to initiate antiretroviral therapy at a CD4 count of 500 cells/ μL . Lifetime transmissions of the index patients were also estimated.

Results: Discounted average lifetime costs varied from \$253,000 for category I index patients to \$402,000 for category IV patients. Discounted quality-adjusted life years lost decreased from 7.95 to 4.45 across these categories, additional years of life expectancy increased from 30.8 to 38.1, and lifetime transmissions decreased from 1.40 to 0.72.

Conclusions: Early diagnosis and treatment of HIV infection increases lifetime costs but improves length and quality of life and reduces the number of new infections transmitted by nearly 50%.

Key Words: HIV lifetime costs of care, Timing of diagnosis, entry into care

(*J Acquir Immune Defic Syndr* 2013;64:183–189)

INTRODUCTION

The lifetime costs of care for HIV-infected persons are an important measure of the economic burden of the epidemic in the United States. Researchers use these estimates in economic evaluations of HIV prevention interventions to compare the cost of an intervention with the treatment costs saved from infections averted by the intervention.^{1–3} Lifetime costs have been estimated by incorporating different categories of treatment costs, extracted from hospital and clinic records of persons living with HIV,^{4–10} into simulations of HIV disease progression.^{11,12}

HIV lifetime costs of care depend on the disease stage at which HIV-infected persons are diagnosed, enter care, and start antiretroviral therapy (ART), and the extent to which they adhere to therapy and are retained in care.^{13,14} Early initiation (ie, at a higher CD4 count) of care and treatment confers benefits to the health of infected persons and significantly reduces the risk of onward transmission.^{15–18} Thus, HIV costs of care are linked with corresponding quality-of-life estimates for HIV-infected persons.¹⁹

Using a disease progression model, we updated estimates of lifetime costs of care for HIV-infected persons in the United States with recent health care utilization and ART costs, and we analyzed the effects of timing of diagnosis, entry into care, and ART initiation on these costs and associated quality-of-life variables from the time of infection.

METHODS

Model

We used a model developed by the Division of HIV/AIDS Prevention in the US Centers for Disease Control and Prevention, the Progression and Transmission of HIV/AIDS (PATH) model,²⁰ to estimate lifetime costs of care, quality-adjusted life years (QALYs), additional years of life expectancy, duration on ART regimens, and years until onset of AIDS for a cohort of 10,000 HIV-infected index patients under different scenarios for diagnosis and entry into care.

Received for publication January 8, 2013; accepted April 15, 2013.

From the *Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, GA; †Atlanta Veterans Affairs Medical Center, Atlanta, GA; ‡Emory University School of Medicine, Atlanta, GA; and §Emory University Rollins School of Public Health, Atlanta, GA.

Presented at the 34th Annual Meeting of the Society for Medical Decision Making, October 17–20, 2012, Phoenix, AZ.

The authors have no funding or conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jaids.com).

Correspondence to: Paul G. Farnham, PhD, Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, MS E-48, Atlanta, GA 30333 (e-mail: pgfl@cdc.gov).

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We estimated lifetime costs and all quality-of-life variables from the time of HIV infection to death, assuming all persons were infected at an average age of 35 years.²¹ We also estimated lifetime transmissions of the index patients. We present a summary of key input parameters in Table 1 and a complete list of parameter values in the Supplemental Digital Content (see <http://links.lww.com/QAI/A428>).

The PATH model is a Monte Carlo health-state transition simulation of HIV-infected persons (index patients) and the partners they infect, in which both the index patients and the infected partners are individually tracked from time of infection to death. The model generates events such as testing for HIV infection, initiation of treatment, and change of ART regimen. The model updates HIV-specific parameters, including CD4⁺ T-lymphocyte count (CD4 count), plasma HIV RNA viral load (viral load), opportunistic infection (OI) incidence, onset of AIDS, and HIV transmission to sexual or needle-sharing partners every calendar quarter year based on disease stage and treatment status. The model also estimates costs incurred during the quarter (eg, HIV diagnosis, treatment, health care utilization) and assigns QALY estimates based on the CD4 count during the quarter. Costs were estimated from the provider perspective.

Assuming the CD4 count at infection was between 750 and 900 cells/ μ L,²² we simulated 10,000 index patients in each of the following categories of CD4 count at diagnosis: (I) ≤ 200 cells/ μ L, (II) 201–350 cells/ μ L, (III) 351–500 cells/ μ L, and (IV) 501–900 cells/ μ L. We assumed that index patient diagnoses were uniformly distributed across the CD4 count range in each of these categories and that these patients all entered care at the time of diagnosis. We defined the first 2 categories (I and II) as late diagnosis/entry into care and the latter 2 (III and IV) as early diagnosis/entry. Treatment with ART was initiated when the index patient's CD4 count was at or below the eligibility criteria for initiation of treatment, for which guideline recommendations at the time we performed this analysis were strongest for a CD4 count of 500 cells/ μ L.¹⁸ Thus, we assumed that an index patient who was diagnosed and entered care at a CD4 count more than 500 cells/ μ L would not begin ART until his/her CD4 count decreased to 500 cells/ μ L. We also assumed that all index patients remained in care continuously once they were diagnosed and entered care. Our results, therefore, reflect optimal care for HIV-infected persons.

In the simulation, we applied HIV-related costs derived from Gebo et al¹⁰ supplemented with data from Schackman et al,¹¹ all updated to \$US 2011 (Table 2). We applied the costs of medications for conditions not directly related to treatment of HIV from the start of infection to death and the costs of OI prophylaxis, and inpatient, outpatient, and emergency department utilization from the time of diagnosis to death. We also included the costs of CD4 count (\$45) and viral load testing (\$107) each quarter and HIV genotype testing (\$452) at initiation of the first ART regimen and with every regimen change thereafter.¹⁰

Based on current guidelines¹⁸ and expert opinion, we assumed that HIV-infected patients in the model were treated with up to 3 ART regimens (Table 1) followed by salvage therapy after failure of the last ART regimen. We simulated

TABLE 1. Summary of Input Parameters

Variable	Values	Source
Natural disease progression		
CD4 cell count when infected (cells/ μ L)	750–900*	22
HIV viral load set point (log ₁₀ copies/mL)	4.0–5.0*	39,40
Cumulative quarterly probability of developing an opportunistic infection (%)	0.3–35.3†	41,42
ART regimens		
CD4 counts for ART initiation eligibility (cells/ μ L)	500	18
Suppressed HIV viral load level (log ₁₀ copies/mL)	1.0–2.7*	43
Rebound HIV viral load level (log ₁₀ copies/mL)	3.1–4.5*	44
Maximum number of ART regimens	3	‡
Probability of initial virologic suppression in ART regimens 1–3	0.77–0.84§	45,46
ART regimen costs per person per quarter (\$US 2011)		
I. EFV/TDF/FTC	3597	10
II. ATV/r + ABC/3TC	5006	10
III. RAL + TDF/FTC	4819	10
Salvage therapy	7628	11
Opportunistic infection treatment costs per episode (\$US 2011)		
<i>Pneumocystis pneumonia</i> (PCP)	9319	
<i>Mycobacterium avium</i> complex	3721	
Toxoplasmosis	21,890	
Cytomegalovirus	5792	
Fungal infection	6341	
Other	4247	
Annual rates of sexual transmission (no. events per year per person)		
Acute	0.733	Derived from ^{26,27}
Nonacute unaware	0.091	
Nonacute aware, not on ART/on ART, viral load not suppressed	0.039	
Nonacute aware, on ART, viral load suppressed	0.004	
Other variables		
Age at infection (yr)	30–40*	21
Discount rate for costs and QALYs	3%	24
Utility weights to estimate QALYs	0.935–0.702¶	25

*We assigned truncated normal distributions based on the ranges of these variables to reflect individual variability in disease progression.

†The lower and upper bounds reflect probabilities for CD4 counts of >500 cells/ μ L and 0–50 cells/ μ L, respectively.

‡Expert opinion.

§Probabilities vary by CD4 count at antiretroviral therapy initiation.

||We derived a quarterly probability of HIV transmission per infected person from the annual transmission rates, and we assumed that the acute phase of infection lasted one quarter.

¶We applied the utility weights from Tengs and Lin²⁵ as follows: 0.935, asymptomatic, for CD4 count >350 cells/ μ L; 0.818, symptomatic, for CD4 count ≥ 200 , <350 cells/ μ L; 0.702, AIDS, for CD4 count <200 cells/ μ L or for presence of an opportunistic infection.

ABC/3TC, abacavir/lamivudine; ATV/r, atazanavir/ritonavir; EFV/TDF/FTC, efavirenz/tenofovir/emtricitabine; RAL, raltegravir.

time in each regimen using rates that collectively represented regimen changes resulting from treatment failure, toxicity, and tolerability issues. We derived drug cost estimates for the initial 3 regimens from Gebo et al¹⁰ and those for salvage

TABLE 2. Quarterly Per-Person Health Care Utilization Costs by CD4 Count Category (\$US 2011)

Cost Components	CD4 Count Category				
	<50 Cells/ μ L	51–200 Cells/ μ L	201–350 Cells/ μ L	351–500 Cells/ μ L	>500 Cells/ μ L
Non-HIV medication	601	584	539	549	612
Opportunistic infection prophylaxis	270	173	70	42	29
Inpatient utilization	5469	2257	983	616	482
Outpatient utilization	170	185	180	171	166
Emergency department utilization	297	134	77	57	41

Adapted from Gebo et al¹⁰ with costs updated to \$US 2011.

therapy from Schackman et al.¹¹ Costs of treating an OI, derived from Schackman et al,¹¹ were applied during any quarter the model predicted an occurrence. HIV testing costs, derived from the program cost per positive test in an emergency department scenario (\$2573),^{20,23} were applied at the time of diagnosis. We estimated both undiscounted costs and lifetime costs discounted at 3% to the time of infection.²⁴

The PATH model also tracked years until onset of AIDS, additional life expectancy, duration on ART regimens, and QALYs lost to infection for each index patient. We estimated QALYs lost by subtracting the sum of health utilities assigned every quarter of infection from the life expectancy of an uninfected person, assuming a utility value of 1 when not infected. Utility values for HIV infection were based on the index patient’s CD4 count and OI occurrence, as adapted from Tengs and Lin.²⁵

We estimated quarterly transmission probabilities on the basis of a model first developed by Pinkerton,²⁶ updated by Prabhu et al,²⁷ and then applied to HIV screening.²⁰ We derived transmission probabilities for patients acutely infected and unaware of their infection, for patients nonacutely infected and unaware, for patients nonacutely infected who were aware and were not taking an ART regimen, and for patients taking an ART regimen whose viral load was not suppressed or who had a suppressed viral load. We used separate rates for sexual and injection drug use (IDU) transmission, and we assumed that 12.9% of the index patients would transmit through IDU.²⁸ We evaluated secondary transmissions for a single generation of transmissions, that is, transmission of HIV from index patients to their partners.

To reflect individual variability in disease progression, we assigned truncated normal distributions based on ranges in the literature to input variables, which included age at infection, CD4 count at infection, viral load set point, and the viral load values associated with the acute phase of infection, suppression while taking ART, rebound when ART failed, and salvage therapy, and finally the rate of decline in CD4 count in specific viral load strata and health care utilization costs (inpatient, outpatient, emergency department,

and costs for conditions not directly related to treatment of HIV). Ranges for these variables are presented in the Supplemental Digital Content (see <http://links.lww.com/QAI/A428>).

Cost and Outcome Measures

For each CD4 count diagnosis/entry category (I–IV), we estimated average values of lifetime costs (undiscounted/discounted) and discounted health care utilization, drug regimen, and OI treatment costs from the time of infection for the 10,000 simulated index patients who we assumed were continuously retained in care. We also estimated average discounted QALYs lost, additional life expectancy, duration on ART, years to onset of AIDS, and lifetime transmissions. To represent individual variability for each outcome measure, we estimated the mean and standard deviation of the outcomes of the 10,000 index patients. Assuming each measure followed a normal distribution, we used its estimated mean and standard deviation to estimate 95% confidence intervals.

Sensitivity Analysis

We performed sensitivity analyses on the cost of drugs used in the ART regimens. We first switched the drugs used for the first and third regimens (Table 1) to examine the impact of substitute regimens with different drug combinations and costs on discounted lifetime costs and drug costs, assuming that this change would not impact the effect of the drugs on disease progression.^{29,30} All these are Department of Health and Human Service–preferred regimens.¹⁸ Second, we substituted ART regimen costs based on the average wholesale price (AWP), which were reported by the Panel on Antiretroviral Guidelines for Adults and Adolescents in March 2012,¹⁸ for the base case regimen costs, which were estimates of the average manufacturer’s price (AMP) from Gebo et al.¹⁰

RESULTS

Assuming that an index patient initiated ART at a CD4 count of 500 cells/ μ L or below, average per-person discounted lifetime costs from time of infection increased from \$253,000 for index patients with a CD4 count less than 200 cells/ μ L at diagnosis/entry into care (category I) to \$402,000 with diagnosis/entry at a CD4 count of 501–900 cells/ μ L (category IV) (Table 3). Average discounted health care utilization costs exhibited a similar pattern, increasing from category I (\$80,000) to category IV (\$113,000), as did average discounted drug regimen costs (\$157,000 in category I to \$272,000 in category IV). Average costs of OI treatment increased for those who were diagnosed and entered care late, particularly when their CD4 count was less than 200 cells/ μ L (\$8100 in category I compared with \$2400 in category IV).

Patients entering care at high CD4 counts lost significantly fewer discounted QALYs compared with patients entering at low CD4 counts, ranging from 4.45 in category IV (501–900 cells/ μ L) to 7.95 in category I (\leq 200 cells/ μ L). Additional life expectancy from time of infection and the average number of years from infection until the onset of AIDS (defined as either a CD4 count <200 cells/ μ L or the diagnosis of an OI) increased significantly from the late

TABLE 3. Average Per-Person Lifetime Costs and Outcome Measures (With 95% Confidence Interval) by CD4 Count at Diagnosis/Entry to Care: Assume ART Initiation Eligibility Criteria Set at CD4 Count of 500 Cells/ μ L (Costs in \$US 2011)

Index Patient		CD4 Count at Diagnosis/Entry to Care (cells/ μ L)		Undiscounted Lifetime Costs	Discounted Lifetime Costs	Discounted Health Care Utilization Costs	Discounted Drug Regimen Costs
I	≤ 200	496,784 (490,354 to 503,214)	253,222 (250,308 to 256,137)	80,277 (79,551 to 81,003)	157,290 (155,199 to 159,380)		
II	201–350	642,088 (636,376 to 647,801)	326,705 (324,118 to 329,292)	93,726 (93,100 to 94,351)	219,386 (217,489 to 221,283)		
III	351–500	714,822 (709,139 to 720,504)	372,344 (369,701 to 374,987)	101,266 (100,641 to 101,892)	256,430 (254,468 to 258,392)		
IV	501–900	750,452 (744,776 to 756,128)	402,238 (399,571 to 404,904)	112,554 (111,910 to 113,198)	272,408 (270,432 to 274,383)		

Index Patient		Discounted OI Treatment Costs	Discounted QALYs Lost	Additional Life Expectancy (yr)	Onset of AIDS (yr)	Duration on ART Regimens (yr)	Lifetime Transmissions
I	8092 (7927 to 8257)	7.95 (7.82 to 8.07)	30.73 (30.45 to 31.01)	9.42 (9.38 to 9.46)	18.87 (18.60 to 19.14)	1.40 (1.38 to 1.43)	
II	3006 (2916 to 3095)	5.15 (5.03 to 5.27)	36.57 (36.31 to 36.83)	16.30 (16.07 to 16.54)	26.89 (26.65 to 27.14)	1.19 (1.17 to 1.22)	
III	2436 (2359 to 2513)	4.52 (4.41 to 4.63)	37.94 (37.69 to 38.20)	19.20 (18.95 to 19.46)	31.21 (30.97 to 31.45)	0.99 (0.97 to 1.01)	
IV	2369 (2292 to 2446)	4.45 (4.34 to 4.47)	38.08 (37.83 to 38.33)	19.50 (19.25 to 19.75)	32.33 (32.09 to 32.57)	0.72 (0.70 to 0.73)	

diagnosis to early diagnosis/entry categories: 30.8 (category I) to 38.1 (category IV) years of added life expectancy and 9.4 (category I) to 19.5 (category IV) years until onset of AIDS. The average duration for ART increased from 18.9 years in category I to 32.3 years in category IV. Lifetime transmissions, which were significantly different for index patients in each category, decreased from the late diagnosis to the early diagnosis/entry categories (1.40 in category I to 0.72 in category IV).

Sensitivity Analysis

Results of the sensitivity analysis (Table 4) showed that reversing base case ART regimens I and III under current ART eligibility guidelines increased discounted drug regimen costs by 14%–21% and discounted lifetime costs by 9%–14% in the 4 diagnosis/entry categories. Substituting ART regimen costs based on AWP¹⁸ for costs based on AMP¹⁰ increased discounted drug regimen costs by 62%–67% and discounted lifetime costs by 39%–46% in the 4 diagnosis/entry categories.

DISCUSSION

Our updated estimates of lifetime HIV treatment costs and quality-of-life variables for the United States showed a

consistent pattern that HIV-infected patients who are diagnosed and enter care at an early stage of disease and who remain in care incur greater lifetime costs but experience substantial clinical benefits and reduce the number of new infections transmitted. Patients diagnosed and entering care at a CD4 count of 500 cells/ μ L or above incurred discounted lifetime costs of \$402,000 compared with \$253,000 for patients who were diagnosed and entered care at a CD4 count of ≤ 200 cells/ μ L.

Although the lifetime costs of early diagnosis and care exceeded the costs associated with late diagnosis and care by almost 60%, persons starting care earliest lost 44% fewer discounted QALYs to illness, experienced a 24% longer additional life expectancy, gained double the years on average until the onset of AIDS, and transmitted almost 50% fewer new infections. Persons diagnosed early were taking an ART regimen an average 13 years longer than those diagnosed late.

Our cost analysis showed that input drug prices have a major impact both on lifetime costs and drug regimen costs. Substituting AWP¹⁸ for AMP¹⁰ (all adjusted to \$US 2011) increased estimated discounted lifetime costs by more than 38% and drug regimen costs by more than 60%. With the wholesale prices, discounted lifetime costs ranged from

TABLE 4. Sensitivity Analysis: Assume ART Initiation Eligibility Criteria Set at CD4 Count of 500 Cells/ μ L (Costs in \$US 2011)

Category	CD4 Count at Diagnosis/Entry to Care (Cells/ μ L)	Base Case Discounted Lifetime Costs	Base Case Discounted Drug Regimen Costs	Reverse Base Case ART Regimens I and III*		Substitute 2012 Guidelines Prices for Base Case ART Regimen Prices†	
				Discounted Lifetime Costs (% Increase)	Discounted Drug Regimen Costs (% Increase)	Discounted Lifetime Costs (% Increase)	Discounted Drug Regimen Costs (% Increase)
I	≤ 200	253,222	157,290	275,224 (8.7)	179,147 (13.9)	350,583 (38.5)	254,159 (61.6)
II	201–350	326,705	219,386	364,182 (11.5)	257,702 (17.5)	468,019 (43.3)	361,036 (64.6)
III	351–500	372,344	256,430	426,006 (14.4)	308,853 (20.4)	544,526 (46.2)	427,454 (66.7)
IV	501–900	402,238	272,408	459,792 (14.3)	328,589 (20.6)	580,768 (44.4)	450,743 (65.5)

*See Table 1 for base case ART regimens and drug costs.

†Substitute prices from Appendix C, Table 1, Panel on Antiretroviral Guidelines for Adults and Adolescents¹⁸ for base case prices from Gebo et al.¹⁰

\$351,000 for late diagnosis/entry to \$581,000 for early diagnosis/entry. Thus, any future increases or decreases in antiretroviral drug prices will have a significant impact on lifetime HIV treatment costs. These changes will become increasingly important as current antiretrovirals go off patent and generic options become available.³¹ Future modeling will need to account for the complexities of generic drug pricing and the possible effects on patient adherence and antiretroviral efficacy from generic drugs.

Our results are similar to other published estimates. Our cost estimate of \$402,000 for early diagnosis/entry into care is slightly higher than that of Schackman et al,¹¹ who estimated a discounted lifetime cost from time of infection of approximately \$391,000 (\$US 2011). This difference probably results from the increased estimated life expectancy in our model. Sloan et al¹² estimated a discounted lifetime cost from entry into care of \$430,000 (\$US 2011) for a sample of patients in Northern France. (This estimate was derived using an average 2010 conversion rate of \$1.3 per Euro and a medical care consumer price index adjustment from 2010 to 2011). Differences among these analyses arise from variations in the cohorts used in the models, the average age at HIV infection, the number of drug regimens, and the prices of the drugs. As with our analysis, Sloan et al¹² estimated a greater life expectancy when patients presented to care early rather than late.

Our estimates of life expectancy have increased compared with earlier published estimates. Schackman et al¹¹ estimated a life expectancy of 24.2 years from time of entry into care and 32.1 years from time of infection. Our estimate of 38.1 years from time of infection at an average age of 35 years, for those entering care early and initiating ART at a CD4 count of 500 cells/ μ L, reflects improvements in ART efficacy and increased length of treatment since the time of the analysis by Schackman et al¹¹. Sloan et al¹² estimated a 26.5-year life expectancy from time of entry into care. Adding the approximate 8-year delay from infection until entry into care gives a life expectancy from infection of 34.5 years.

In their disease progression model of 30-year old men who have sex with men, Nakagawa et al³² estimated a life expectancy (from birth) of 75.0 years for men diagnosed early and 71.5 years for men diagnosed late. These estimates are close to our overall life expectancies. The North American AIDS Cohort Collaboration on Research and Design has estimated that life expectancy for a 20-year-old HIV-infected person in North America is an additional 52.3 years, which is also consistent with our results.³³

Our conclusions regarding the effect of late diagnosis versus early diagnosis/entry into care on HIV treatment costs differ from the conclusions of earlier studies that directly estimated HIV treatment costs from cohorts of infected patients.^{8,9,34} Those studies, which concluded that costs associated with late entry into care were greater than those of early entry, were based on cohorts of patients followed for 8–15 years. This period is insufficient to observe the entire range of costs incurred by HIV-infected patients over their lifetime. Sloan et al¹² noted that, although lifetime costs and life expectancy were lowest for patients presenting with advanced disease, delayed entry into care resulted in higher immediate costs

after treatment initiation. Although these higher immediate costs for late entry compared with early entry may persist for up to 15 years,⁹ lifetime costs are greater for those who enter care early rather than later.

In contrast to many previous studies, our study also estimated gains in QALYs, life expectancy, and years until onset of AIDS, as well as the reduction in lifetime transmissions associated with early diagnosis and entry into care of HIV-infected patients. These beneficial changes from treatment with ART for patients with HIV infection must always be considered when comparing cost estimates of late versus early treatment. Previous analysis has shown that screening HIV-infected persons in settings where these persons were diagnosed earlier in the course of their infection was cost-saving compared with settings with later diagnosis when the effects of reduced transmissions were included.²⁰

Our results were derived from a model-based analysis where we assumed that all HIV-infected patients entered the model with a CD4 count between 750 and 900 cells/ μ L and were diagnosed, entered care, and started ART according to the assumptions in the analysis. We assumed that all patients entered care at the time of diagnosis, began ART at a CD4 count of 500 cells/ μ L, and remained in care throughout their lives. Thus, similar to Schackman et al,¹¹ our costs and quality-of-life measures are associated with optimal care.

Our results may differ from studies that begin their analyses with a cohort of HIV-infected patients drawn from clinical studies who differ with each other in their CD4 counts at the time of entry into the study and who may not have remained in care continuously.¹² Given that our model assumes optimal care for HIV-infected patients, our results do not represent the costs associated with all HIV-infected persons in the United States. Recent data suggest that approximately 82% of these infected persons are diagnosed, 66% are linked to care, 37% are retained in care, 33% have been prescribed ART, and 25% have suppressed viral load.^{35–37}

We included the costs of comorbidities in HIV-infected patients only as they were measured in the data sources used in our analysis.^{10,11} Analyzing the influence of other chronic diseases and non-HIV conditions on treatment costs and length and quality of life of HIV-infected patients is a major goal of future research. Better data on the impact of ART initiation at CD4 counts \geq 500 cells/ μ L on survival time and quality-of-life indicators for HIV-infected persons are also needed.

The PATH model contains numerous assumptions and data drawn from many sources, both of which need to be monitored and updated as HIV clinical events change. For example, we included only a single generation of transmissions from index patients to their partners. The percent of transmissions through IDU has also decreased slightly in recent years.^{21,38} However, the model can be used to project costs, other variables measuring length and quality of life of HIV-infected patients, and the number of transmissions from these patients over many years into the future, something that cannot be accomplished with existing cohorts of patients whose disease patterns are followed over shorter periods.

In conclusion, discounted lifetime costs for HIV-infected patients who are diagnosed and enter care at an early stage of disease and begin ART at 500 cells/ μ L are approximately

\$402,000 and may range as high as \$581,000 depending on antiretroviral drug prices. The corresponding lifetime costs for persons diagnosed and entering care very late are approximately \$253,000 and may range as high as \$351,000. The additional lifetime cost of earlier diagnosis and more immediate therapy produces an average per-person gain in life expectancy of 7 years, an additional 3.5 QALYs, and, perhaps most importantly, an approximate 50% reduction in new infections. As improvements are made in the continuum of diagnosis and treatment in the United States, costs to treat HIV infection with current drug prices will increase together with gains in the quality of life for HIV-infected persons and substantial reductions in transmission of HIV to uninfected persons.

REFERENCES

- Pinkerton SD, Holtgrave DR. A method for evaluating the economic efficiency of HIV behavioral risk reduction interventions. *AIDS Behav*. 1998;2:189–201.
- Pinkerton SD, Johnson-Masotti AP, Holtgrave DR, et al. Using cost-effectiveness league tables to compare interventions to prevent sexual transmission of HIV. *AIDS*. 2001;15:917–928.
- Hutchinson AB, Patel P, Sansom SL, et al. Cost-effectiveness of pooled nucleic acid amplification testing for acute HIV infection after third-generation HIV antibody screening and rapid testing in the United States: a comparison of three public health settings. *PLoS Med*. 2010;7:e1000342.
- Bozzette SA, Joyce G, McCaffrey DF, et al. Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. *N Engl J Med*. 2001;344:817–823.
- Gebo KA, Chaisson RE, Folkemer JG, et al. Costs of HIV medical care in the era of highly active antiretroviral therapy. *AIDS*. 1999;13:963–969.
- Chen RY, Accortt NA, Westfall AO, et al. Distribution of health care expenditures for HIV-infected patients. *Clin Infect Dis*. 2006;42:1003–1010.
- Krentz HB, Auld MC, Gill MJ. The high cost of medical care for patients who present late (CD4<200 cells/ μ L) with HIV infection. *HIV Med*. 2004;5:93–98.
- Krentz HB, Gill J. Despite CD4 cell count rebound the higher initial costs of medical care for HIV-infected patients persist 5 years after presentation with CD4 cell counts less than 350 μ L. *AIDS*. 2010;24:2750–2753.
- Krentz HB, Gill MJ. The direct medical costs of late presentation (<350/mm³) of HIV infection over a 15-year period. *AIDS Res Treat*. 2012; doi: 10.1155/2012/757135.
- Gebo KA, Fleishman JA, Conviser R, et al. Contemporary costs of HIV healthcare in the HAART era. *AIDS*. 2010;24:2705–2715.
- Schackman BR, Gebo KA, Walensky RP, et al. The lifetime cost of current human immunodeficiency virus care in the United States. *Med Care*. 2006;44:990–997.
- Sloan CE, Champenois K, Choisy P, et al. Newer drugs and earlier treatment: impact on lifetime cost of care for HIV-infected adults. *AIDS*. 2012;26:45–56.
- Hellinger FJ. Economic models of antiretroviral therapy: searching for the optimal strategy. *Pharmacoeconomics*. 2006;24:631–642.
- Farnham PG. Do reduced inpatient costs associated with highly active antiretroviral therapy (HAART) balance the overall cost for HIV treatment? *Appl Health Econ Health Policy*. 2010;8:75–88.
- Kitahata MM, Gange SJ, Abraham AG, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. *N Engl J Med*. 2009;360:1815–1826.
- When to Start Consortium. Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: a collaborative analysis of 18 HIV cohort studies. *Lancet*. 2009;373:1352–1363.
- Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365:493–505.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. March 27, 2012; 1–239. Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Accessed April 25, 2012.
- Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1997;16:54–62.
- Prabhu VS, Farnham PG, Hutchinson AB, et al. Cost-effectiveness of HIV screening in STD clinics, emergency departments, and inpatient units: a model-based analysis. *PLoS One*. 2011;6:e19936.
- Prejean J, Song R, Hernandez A, et al. Estimated HIV incidence in the United States, 2006–2009. *PLoS One*. 2011;6:e17502.
- Turner BJ, Hecht FM, Ismail RB. CD4+ T-lymphocyte measures in the treatment of individuals infected with human immunodeficiency virus type 1: a review for clinical practitioners. *Arch Intern Med*. 1994;154:1561–1573.
- Farnham PG, Hutchinson AB, Sansom SL, et al. Comparing the costs of HIV screening strategies and technologies in health-care settings. *Public Health Rep*. 2008;123(suppl 3):51–62.
- Gold MR, Siegel JE, Russell LB, et al, eds. *Cost-effectiveness in Health and Medicine*. New York, NY: Oxford University Press; 1996.
- Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. *Med Decis Making*. 2002;22:475–481.
- Pinkerton SD. How many sexually-acquired HIV infections in the USA are due to acute-phase HIV transmission? *AIDS*. 2007;21:1625–1629.
- Prabhu VS, Hutchinson AB, Farnham PG, et al. Sexually-acquired HIV infections in the USA due to acute-phase HIV transmission: an update. *AIDS*. 2009;23:1792–1794.
- Hall HI, Song R, Rhodes P, et al. Estimation of HIV incidence in the United States. *JAMA*. 2008;300:520–529.
- Marconi VC, Grandits GA, Weintrob AC, et al. Outcomes of highly active antiretroviral therapy in the context of universal access to health-care: the U.S. Military HIV Natural History Study. *AIDS Res Ther*. 2010;7:14.
- Khanna N, Opravil M, Furrer H, et al. CD4+ T cell count recovery in HIV type 1-infected patients is independent of class of antiretroviral therapy. *Clin Infect Dis*. 2008;47:1093–1101.
- Walensky RP, Sax PE, Nakamura YM, et al. Economic savings versus health losses: the cost-effectiveness of generic antiretroviral therapy in the United States. *Ann Intern Med*. 2013;158:84–92.
- Nakagawa F, Lodwick RK, Smith CJ, et al. Projected life expectancy of people with HIV according to timing of diagnosis. *AIDS*. 2012;26:335–343.
- Hogg R, Samji H, Cescon A, et al. *Temporal Changes in Life Expectancy of HIV+ Individuals: North America*. Presented at CROI: 19th Conference on Retroviruses and Opportunistic Infections. Seattle, WA; March 5–8, 2012.
- Fleishman JA, Yehia BR, Moore RD, et al. The economic burden of late entry into medical care for patients with HIV infection. *Med Care*. 2010;48:1071–1079.
- Gardner EM, McLees MP, Steiner JF, et al. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis*. 2011;52:793–800.
- Centers for Disease Control and Prevention. Vital signs: HIV prevention through care and treatment—United States. *MMWR Morb Mortal Wkly Rep*. 2011;60:1618–1623.
- Centers for Disease Control and Prevention. CDC fact sheet: HIV in the United States: the stages of care. 2012. Available at: www.cdc.gov/nchhstp/newsroom/docs/2012/Stages-of-careFactSheet-508.pdf. Accessed September 10, 2012.
- Centers for Disease Control and Prevention. Estimated HIV incidence in the United States, 2007–2010. HIV Surveillance Supplemental Report. 2012;17(No. 4).
- Herbeck JT, Gottlieb GS, Li X, et al. Lack of evidence for changing virulence of HIV-1 in North America. *PLoS One*. 2008;2(1–8).
- Vo TTN, Ledergerber B, Keiser O, et al. Durability and outcome of initial antiretroviral treatments received during 2000–2005 by patients in the Swiss HIV Cohort Study. *J Infect Dis*. 2008;197:1685–1694.
- Weinstein MC, Goldie SJ, Losina E, et al. Use of genotypic resistance testing to guide HIV therapy: clinical impact and cost-effectiveness. *Ann Intern Med*. 2001;134:440–450.

42. Paltiel AD, Weinstein MC, Kimmel AD, et al. Expanded screening for HIV in the United States—an analysis of cost-effectiveness. *N Engl J Med*. 2005;352:586–595.
43. Raboud JM, Montaner JSG, Conway B, et al. Suppression of plasma viral load below 20 copies/ml is required to achieve a long-term response to therapy. *AIDS*. 1998;12:1619–1624.
44. The United Kingdom Collaborative HIV Cohort (CHIC) Study. Treatment switches after viral rebound in HIV-infected adults starting antiretroviral therapy: multicentre cohort study. *AIDS*. 2008;22:1943–1950.
45. Lennox JL, DeJesus E, Berger DS, et al. Raltegravir versus Efavirenz regimens in treatment-naive HIV-1-infected patients: 96-week efficacy, durability, subgroup, safety, and metabolic analyses. *JAIDS*. 2010;55:39–48. doi: 10.1097/QAI.1090b1013e3181da1287.
46. Lennox JL, DeJesus E, Lazzarin A, et al. Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naive patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial. *Lancet*. 2009;374:796–806.