

Cost-Effectiveness of HIV Testing and Treatment in the United States

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In September 2006, the US Centers for Disease Control and Prevention (CDC) released new guidelines calling for routine, voluntary human immunodeficiency virus (HIV) testing for all persons aged 13–64 years in health care settings. These guidelines were motivated, in part, by mounting evidence that the traditional approach of using risk factors to identify candidates for HIV testing is inadequate. Of the 1.0–1.2 million people in the United States thought to be infected with HIV, ~25% remain unaware of their infection, and nearly half of all infected patients develop acquired immunodeficiency syndrome ≤ 1 year after testing positive for HIV. Also contributing to the change in testing guidelines was recent evidence that routine HIV testing is cost-effective. Cost-effectiveness analysis, a method of assessing health care interventions in terms of the value they confer, reports results in terms of the resources that are required for the intervention to produce an additional unit of change in health effectiveness; more economically efficient programs are those with lower cost-effectiveness ratios. This article reviews the methods and results of cost-effectiveness studies in the United States and articulates why routine, voluntary HIV testing is not only of crucial public health importance but also economically justified.

Since 1993, Centers for Disease Control and Prevention (CDC) guidelines have recommended routine, voluntary HIV counseling, testing, and referral for all patients in hospitals where the prevalence of HIV infection is $\geq 1\%$ and in settings serving populations known to be at increased risk for HIV infection [1]. These guidelines were revised but largely unchanged in 2001 [2]. The 2001 guidelines included no discussion of the cost or cost-effectiveness of implementing the recommendations, but in fact there had been no economic evaluations of HIV testing published since the antiretroviral therapy (ART) era began [3, 4]. As the AIDS epidemic has matured in the United States, the incidence rate of

HIV infection has remained stable, with ~40,000 new infections reported yearly since 1992 [5]. Despite great clinical progress in the treatment of HIV infection, patients are still being identified far too late in the disease process: 40% of patients develop AIDS ≤ 1 year after learning that they are infected with HIV [6]. Only with earlier case identification and linkage to medical care will patients have the opportunity for timely receipt of ART, which can decrease the morbidity and mortality caused by the disease [7]. To promote the identification and treatment of HIV-infected individuals, the CDC revised its HIV testing guidelines in September 2006, recommending that all persons aged 13–64 years be tested for HIV infection as a matter of routine care—without regard to risk factors—in all health care settings in the United States; annual testing was recommended for persons known to be at high risk for HIV infection [8]. These recommendations have generated both enthusiasm and debate. One notable concern stems from the cost required to embark on testing efforts of this magnitude. Is routine HIV testing worth the cost? Is it cost-effective?

Presented in part: Opportunities for Improving HIV Diagnosis, Prevention & Access to Care in the U.S., Washington, D.C., 29–30 November 2006.

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Clinical Infectious Diseases 2007;45:S248–54

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1058-4838/2007/4512S4-0009\$15.00
DOI: 10.1086/522546

METHODS OF COST-EFFECTIVENESS ANALYSIS

Cost-effectiveness analysis is conducted according to well-established methods that have been described by national panels and journal editors [9–12]. A program is cost-effective if the additional resources needed to implement it result in health gains that are sufficient to justify using the resources in that program. Asserting that a health care screening or treatment program is cost-effective does not imply that it is cost saving nor does it mean that it is simply medically effective.

Cost-effectiveness ratio. In cost-effectiveness analysis, the measure of value is the incremental cost-effectiveness ratio. The numerator of the ratio, the incremental cost, is the difference between the cost of a primary program (i.e., program A) and the cost of an alternative program (i.e., program B). The denominator, the incremental health effectiveness, is a measurement of the health improvement associated with program A relative to that associated with program B. Program B may denote a less intensive variant of program A or the absence of any program. The cost-effectiveness of program A relative to program B is expressed as the following ratio: [cost of program A – cost of program B]/[health improvement produced by program A – health improvement produced by program B]. Because cost-effectiveness ratios are expressed in terms of resource use per unit of benefit conferred, programs that are more economically efficient have lower cost-effectiveness ratios.

Quality-adjusted life-years (QALYs). Incremental cost can readily be measured in dollars, but to compare programs having diverse health consequences, the health outcomes must be measured in broadly applicable units. In cost-effectiveness analysis, health outcomes are most commonly measured in terms that capture not only increases in survival but also improvements in clinical health that are weighted according to a preference-based measure of well-being. The QALY is one such outcome unit [9].

A QALY is a measure of time spent in a given state of health that would be preferentially equal to 1 year of life spent in perfect health. To obtain the quality-adjusted life expectancy, each possible health state is assigned a numerical weight between 0 (representing a health state equivalent to death) and 1 (denoting perfect health). The scored weights of each health state are subjective and may be based on community surveys of health-state preferences (for policy decisions) or on patient preferences (for individual clinical decisions). As most cost-effectiveness analyses are conducted for the purposes of societal resource allocation, quality-adjustment scores are generally intended to reflect community preferences [9]. The expected duration of time spent in each possible health state is determined, often by means of a mathematical model to extrapolate durations reported in clinical studies with short-

term end points. Quality-adjusted life expectancy (measured in QALYs) is obtained by multiplying each health state's quality weight by the duration of time spent in that health state and then summing over all of the health states. For example, a patient with an expected survival of 8 years, with 4 years of perfect health (utility = 1.0), 1 year in the hospital (utility = 0.5), and 3 years in a nursing home (utility = 0.6), would have a quality-adjusted life expectancy of 6.3 QALYs (i.e., $[4 \times 1.0] + [1 \times 0.5] + [3 \times 0.6]$).

Discounting. Discounting, or adjusting for the timing of costs and health outcomes, is used in economic analysis to account for the time-specific value of costs and benefits. In general, people prefer to receive health gains sooner and to pay costs later. Discounting quantitatively incorporates these preferences into economic analyses by weighing costs and health outcomes less heavily the further into the future they occur; thus, a health gain in the future is weighted less than an equal immediate gain, and a cost in the future does not weigh as heavily as an immediate cost. As recommended by the Panel on Cost-Effectiveness in Health and Medicine, both the numerator (i.e., costs) and the denominator (i.e., effectiveness) should be discounted at the same rate (generally 3% per year) in all cost-effectiveness analyses [9]. When making health economic decisions for expenditures to be spent over the next 10 years, the question to ask is, what is the present value of all of those expenditures today? For example, at a 3% discount rate, a decision maker would consider \$100,000 in 10 years as equivalent to \$74,400 today [9]. Discounting is necessary even after all costs have been corrected for price inflation. Before discounting, all costs must be expressed in a single unit of currency at a point in time (e.g., 2006 US dollars).

COST-EFFECTIVENESS OF HIV TESTING

Several interventions in HIV treatment have been analyzed for cost-effectiveness (table 1). Routine HIV testing in the inpatient setting (\$38,600 per QALY gained) and for high-risk patients in the outpatient setting every 5 years (\$50,000 per QALY gained), although effective, is less cost-effective than several interventions routinely recommended as the standard of HIV clinical care in the United States. These include prophylaxis for *Pneumocystis jirovecii* pneumonia (PCP) (\$2,800 per QALY gained), treatment with ART (\$11,700 per QALY gained), and genotype testing after initiation of the first ART regimen (\$17,900 per QALY gained) [13–16, 18]. However, routine HIV testing is as or more cost-effective than use of enfuvirtide as salvage ART (\$69,500 per QALY gained), prophylaxis against cytomegalovirus infection (\$59,000 per QALY gained), or prophylaxis against fungal infection (\$240,000 per QALY gained) [19–21].

The cost-effectiveness of HIV testing compares favorably with

Table 1. Cost-effectiveness ratios for treatment of HIV infection.

Intervention	Treatment(s)	Cost-effectiveness, US\$ per QALY gained	Reference
PCP-toxoplasmosis prophylaxis	TMP-SMX	2,800	[13]
Antiretroviral therapy	AZT, 3TC, EFV	11,700	[14]
Resistance testing	...	17,900	[15]
Inpatient HIV testing	...	38,600	[16]
MAC prophylaxis	AZM	43,300	[17]
HIV testing of high-risk outpatients every 5 years	...	50,000	[18]

NOTE. AZM, azithromycin; AZT, zidovudine; EFV, efavirenz; MAC, *Mycobacterium avium* complex; PCP, *Pneumocystis jirovecii* pneumonia; QALY, quality-adjusted life-year; TMP-SMX, trimethoprim-sulfamethoxazole; 3TC, lamivudine.

many recommended routine screening programs in the United States (table 2). For example, routine HIV testing in the inpatient setting and routine HIV testing of high-risk individuals every 5 years in the outpatient setting are both more cost-effective than recommended routine screening for breast cancer (\$57,500 per QALY gained), colon cancer (\$57,700 per QALY gained), and type 2 diabetes (\$70,000 per QALY gained). In addition, routine HIV testing becomes even more favorable when potential decreases in HIV transmission resulting from the HIV testing program are taken into account [16, 18, 22–26].

Cost-effectiveness of testing in the outpatient setting.

In February 2005, the *New England Journal of Medicine* published 2 reports on the cost-effectiveness of routine HIV testing [18, 25]. Although each study used an independently developed mathematical model that simulated the process of HIV testing and disease progression, as well as independently derived data for model inputs, the results were remarkably similar. Sanders et al. [25] reported that routine testing in a population with a prevalence of undiagnosed HIV infection of 1% produced a cost-effectiveness ratio of \$41,000 per QALY gained; the inclusion of transmission benefits decreased the ratio to \$15,000 per QALY gained [25]. In the study by Paltiel et al. [18], the cost-effectiveness ratio of routine HIV testing among outpatients was \$36,000 per QALY gained for a 3% prevalence of undiagnosed HIV infection, \$38,000 per QALY gained for a 1% prevalence, and \$113,000 per QALY gained for a 0.1% prevalence

[18]. Paltiel and colleagues recently updated this analysis to include the potential transmission effects of a routine HIV testing program [26]. Routine HIV testing remained cost-effective (less than \$50,000 per QALY gained) for a prevalence of undiagnosed HIV infection as low as 0.2%. The results of these 3 studies provide strong economic support for the 2006 CDC guidelines calling for routine HIV testing in the outpatient setting [8].

Optimal frequency of retesting. The challenges of examining the impact of routine HIV testing are compounded when one tries to address the optimal frequency of HIV testing. The best strategy for retesting depends on the incidence of HIV infection, which is difficult to determine. Such a strategy also depends on the likelihood that individuals whose HIV infection was not detected during an initial test will be detected on a subsequent test. This is driven by factors such as rates of consent to be tested, rates of receipt of test results, and rates of linkage to health care. Paltiel et al. [18] examined a range of retesting frequencies and noted that, in high-risk populations (defined as a population in which the annual incidence of HIV infection is 1.2%), testing every 5 years remained cost-effective at a ratio of \$50,000 per QALY gained; the ratio for annual testing was \$100,000 per QALY gained. In lower-risk populations with annual incidence rates ranging from 0.12% to 0.01%, the cost-effectiveness ratio of HIV testing every 5 years ranged from \$71,000 to \$169,000 per QALY gained and for annual testing

Table 2. Cost-effectiveness of various screening programs in the United States.

Condition, intervention	Patient age, years	Cost-effectiveness ratio, US\$ per QALY gained	Reference
HIV infection			
Testing of inpatients at presentation	Any	38,600	[16]
Testing of high-risk outpatients every 5 years	Any	50,000	[18]
Breast cancer, mammography every year	50–69	57,500	[22]
Colon cancer, FOBT and sigmoidoscopy every 5 years	50–85	57,700	[23]
Diabetes mellitus type 2, one-time opportunistic screening of fasting plasma glucose level	>25	70,000	[24]

NOTE. FOBT, fecal occult blood test; QALY, quality-adjusted life-year.

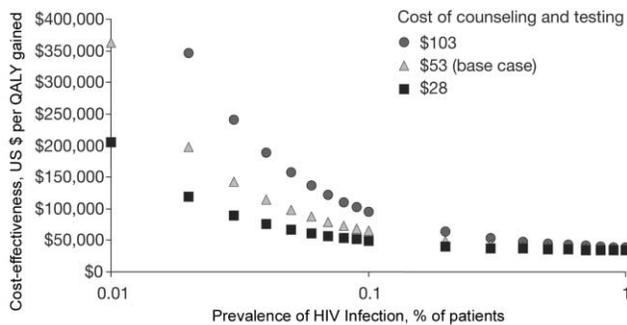


Figure 1. Sensitivity analysis examining the cost of HIV counseling and testing. When the prevalence of HIV infection is >1%, the lines reflecting cost-effectiveness ratios converge. Only at prevalences of <0.1% do the costs of counseling and testing drive the cost-effectiveness ratio. QALY, quality-adjusted life-year. Adapted from the following article with permission from Elsevier: Walensky RP, Weinstein MC, Kimmel AD, et al. Routine human immunodeficiency virus testing: an economic evaluation of current guidelines. *Am J Med* 2005;118:292–300.

ranged from \$165,000 to \$1,264,000 per QALY gained. In the absence of concrete data on the annual incidence of HIV infection, the current CDC testing guidelines recommend annual screening for persons presumed to be at high risk for HIV infection, including injection drug users, men who have sex with men, persons who exchange sex for money, and the sex partners of these people [8].

Cost-effectiveness of testing in the inpatient setting.

Because HIV disease is relatively asymptomatic for many years, infection in many infected individuals is only diagnosed after admission to an inpatient setting for treatment of a new opportunistic infection. A recent model-based analysis of inpatient HIV testing demonstrated that, without routine testing, a majority (53%) of newly diagnosed HIV infections are detected during presentation for an opportunistic infection; this is consistent with data from the CDC [16, 27]. The inclusion of routine testing among inpatients reduced the percentage of HIV infections identified with a new opportunistic infection from 53% to 36%.

As policy makers consider the costs of expanded routine HIV testing programs, the following point should be made clear: what determines the cost-effectiveness of any HIV testing program is not the cost of the HIV test itself—which, by nearly all standards, is inexpensive (\$1–\$100)—but rather the downstream (i.e., future) costs of HIV care for patients who are identified and then treated for their HIV infection (figure 1). The cost-effectiveness of routine inpatient HIV testing for a population in which the prevalence of HIV infection is 0.1%, ranges only from \$38,600 to \$86,800 per QALY gained, depending on the cost of the test. As the prevalence of HIV infection increases, the cost of the test becomes less critical; regardless of the test cost, the cost-effectiveness ratio of HIV

testing cannot decrease to less than \$36,000 per QALY gained. Routine testing will identify more individuals in settings where the prevalence of HIV infection is higher and should, therefore, be more cost-effective. However, the cost-effectiveness of screening cannot become more favorable than \$36,000 per QALY gained, because this is now the cost-effectiveness ratio for state-of-the-art HIV care in the United States [16]. This care includes antiretroviral therapy, opportunistic infection prophylaxis and treatment, outpatient care, inpatient care, and laboratory expenditures. It is therefore the care of identified HIV-infected patients that determines the cost, the survival, and the cost-effectiveness of a routine HIV testing program.

IMPORTANCE OF LINKAGE TO CARE FOR HIV-INFECTED PERSONS

Most discussions of HIV testing, both in the guidelines and in the literature, focus on the need for increased HIV testing, with little discussion of the value of linkage to medical care. Several studies of HIV testing document the challenges of linking infected patients to clinical care [28, 29]. The process of HIV testing should be viewed as a sequential pathway composed of at least 4 important steps: a health care professional offers the test, the patient agrees to undergo the test, the patient receives the test results, and the patient, if infected, is successfully linked to an appropriate care site. Failure of any one of these processes results in the overall failure of the testing system. If the objective is to maximize health benefits, the goal of the testing process lies not only in the detection of HIV-infected individuals but also in the linkage of HIV-infected patients to health care professionals who can care for them.

Walensky et al. [30] attempted to dissect the HIV testing process into these individual steps. In an examination of 100 possible combinations of test acceptance and linkage rates, they found that pathways in which the same number of people were linked to medical care were not equally cost-effective. For example, a program in which 100% of patients were offered an HIV test, 100% took the test, 100% received their test results, and 30% who had positive test results were linked to medical care was less cost-effective than a program in which 100% of patients were offered the test, 30% took the test, 100% who were tested received their test results, and 100% who had positive test results were linked to care. The analysis demonstrated that, other things being equal, programs in which the rate of linkage to medical care is higher than the rate of test acceptance are more cost-effective. These results suggest that if HIV testing dollars are limited, funds should be devoted to ensuring that persons who test positive for HIV infection are effectively linked to care, before they are allocated toward initiating new testing efforts [30].

Lifetime cost of treatment for HIV infection. The cost and

Table 3. Per-person survival benefits, numbers of patients with AIDS entering care, and era-specific and cumulative survival benefits.

Year	Intervention	Mean survival benefit per person ^a	Patients with AIDS entering care, no.	Patients surviving to next treatment era, %	Infections averted, no.	Total survival benefit, years
HIV disease treatment						
1989–1992	PCP prophylaxis	3.1 months	158,370	33	...	40,912
1993–1995	PCP/MAC prophylaxis	24.4 months	226,458	39	...	460,465
1996–1997	PCP/MAC prophylaxis and ART 1	93.7 months	72,716	86	...	567,788
1998–1999	PCP/MAC prophylaxis and ART 2	132.6 months	52,702	93	...	582,359
2000–2002	PCP/MAC prophylaxis and ART 3	138.8 months	71,946	91	...	832,179
2003	PCP/MAC prophylaxis and ART 4	159.9 months	24,780	330,189
Subtotal						2,813,892
pMTCT						
1994–1999 (pMTCT-ZDV)	Child receives OI prophylaxis and ZDV monotherapy	60.5 years	223	51,646
1994–1999 (pMTCT-ZDV)	Child receives OI prophylaxis and combination ART	45.8 years	833	...
2000–2003 (pMTCT-cART)	Child receives OI prophylaxis and combination ART	46.7 years	1839	85,833
Subtotal						137,479
Total						2,951,371

NOTE. cART, combination antiretroviral therapy; MAC, *Mycobacterium avium* complex; OI, opportunistic infection; PCP, *Pneumocystis jirovecii*; pMTCT, prevention of mother-to-child transmission; ZDV, zidovudine. Adapted from [35].

^a Data are reported as weighted averages of the per-person survival benefit among individuals receiving care, derived from each year in the current treatment era, and reflect changes in both the life expectancy of HIV-positive patients and the general US population over time.

cost-effectiveness of routine HIV testing programs are heavily dependent on the cost of treating HIV-infected individuals. In a model-based analysis, Schackman et al. [31] recently projected the lifetime cost of current treatment for HIV infection in the United States. Model input data were derived from the HIV Research Network, a consortium of high-volume primary care sites specializing in the treatment of HIV infection [32, 33]. The analysis focused on a cohort of HIV-infected individuals with a mean CD4 cell count of 310 cells/mm³ and projected a mean survival of 24.2 years after cohort initiation. The discounted lifetime cost of comprehensive treatment per HIV-infected person was \$385,000 for this survival benefit (undiscounted cost, \$618,900). Antiretroviral therapy accounted for 73% of the total cost, inpatient care accounted for 13%, and outpatient care accounted for 9%.

Although the study by Schackman and colleagues included only the direct medical costs associated with treating HIV infection, another recent study included the cost of lost productivity [34]. Hutchinson et al. [34] projected the total cost associated with the estimated 40,000 new HIV infections expected to occur in the United States every year. The undiscounted total lifetime cost of illness was approximately \$53 billion. Medical care accounted for only \$8 billion of the total, whereas lost productivity accounted for the remaining \$45 billion.

Years of life saved by comprehensive HIV care. Although these costs are considerable, one cannot examine the costs of

comprehensive medical care for HIV infection without examining the improvements in health and survival that these expenditures have produced. A recent analysis by Walensky et al. [35] found that >3 million years of life have been saved in the United States as a direct result of treatment of AIDS. In this analysis, they examined increases in per-person survival since 1989 and the number of people for whom HIV infection was diagnosed, the number who were receiving care, and the number eligible to benefit from increased survival (table 3). Advances in AIDS care were divided into 6 eras, including the pre-ART era, when only PCP and *Mycobacterium avium* complex prophylaxis were available, and 4 eras of ART. They also included increases in life expectancy associated with the prevention of mother-to-child transmission. For each era, per-person survival benefits for individuals receiving treatment for AIDS were compared with those for individuals whose disease went untreated. Per-person survival benefits ranged from 3.1 months during the era of PCP prophylaxis (in 1989) to 159.9 months during the era of comprehensive care and antiretroviral therapy (in 2003). With initiation of PCP prophylaxis in 1989, median survival for patients with AIDS and a mean CD4 cell count of 87 cells/mm³ was 1.7 years after cohort initiation; in 1996, receipt of first-generation ART boosted median survival to 7.4 years; and by 2003, receipt of fourth-generation ART led to a median per-person survival of 14.1 years. The study noted that these per-person survival gains are superior to those seen

for non-small cell lung cancer, node-positive breast cancer, 3-vessel coronary artery disease, and relapsed non-Hodgkin's lymphoma, as documented over the same period [35].

CONCLUSIONS

Survival gains among patients with HIV disease in the United States have increased dramatically over time. The full extent of these increases, however, is achievable only for patients who are identified with HIV infection and receive appropriate care. This review has summarized substantial data from the literature that document that routine, voluntary HIV testing, as recommended in the 2006 CDC guidelines, is a cost-effective intervention. HIV testing is relatively inexpensive and highly effective, and diagnosis of HIV infection can, when followed by prompt linkage to medical care, lead to a sequence of events, including initiation of ART, that yield substantial survival benefits. For this reason, efforts to implement routine HIV testing must be accompanied by a simultaneous clinical and public health commitment to link HIV-infected persons to medical care and to ensure that adequate funding for treatment of HIV infection is available.

Acknowledgments

We thank Neil Canavan, for assistance in preparing this manuscript, and Mariam Fofana, for technical assistance.

The "Opportunities for Improving HIV Diagnosis, Prevention & Access to Care in the U.S." conference was sponsored by the American Academy of HIV Medicine, amfAR, the Centers for Disease Control and Prevention, the Forum for Collaborative HIV Research, the HIV Medicine Association of the Infectious Diseases Society of America, and the National Institute of Allergy and Infectious Diseases. Funding for the conference was supplied through an unrestricted educational grant from Gilead Sciences, amfAR, GlaxoSmithKline, Pfizer, Abbott Virology, OraSure Technologies, Roche Diagnostics, and Trinity Biotech.

Financial support. The National Institute of Allergy and Infectious Diseases (R01 AI42006, K24 AI062476, and P30 AI060354), the National Institute of Mental Health (R01 MH65869 and R01 MH073445), the National Institute on Drug Abuse (R01 DA015612), and the Doris Duke Charitable Foundation (Clinical Scientist Development Award).

Supplement sponsorship. This article was published as part of a supplement entitled "Opportunities for Improving the Diagnosis of, Prevention of, and Access to Care for HIV Infection in the United States," sponsored by the American Academy of HIV Medicine, amfAR, the Centers for Disease Control and Prevention, the Forum for Collaborative HIV Research, the HIV Medicine Association of the Infectious Diseases Society of America, and the National Institute of Allergy and Infectious Diseases.

Potential conflicts of interest. All authors: no conflicts.

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