SPECIAL ARTICLE

Cost-Effectiveness of Screening for HIV in the Era of Highly Active Antiretroviral Therapy

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ABSTRACT

BACKGROUND

The costs, benefits, and cost-effectiveness of screening for human immunodeficiency virus (HIV) in health care settings during the era of highly active antiretroviral therapy (HAART) have not been determined.

METHODS

We developed a Markov model of costs, quality of life, and survival associated with an HIV-screening program as compared with current practice. In both strategies, symptomatic patients were identified through symptom-based case finding. Identified patients started treatment when their CD4 count dropped to 350 cells per cubic millimeter. Disease progression was defined on the basis of CD4 levels and viral load. The likelihood of sexual transmission was based on viral load, knowledge of HIV status, and efficacy of counseling.

RESULTS

Given a 1 percent prevalence of unidentified HIV infection, screening increased life expectancy by 5.48 days, or 4.70 quality-adjusted days, at an estimated cost of $194 per screened patient, for a cost-effectiveness ratio of $15,078 per quality-adjusted life-year. Screening cost less than $50,000 per quality-adjusted life-year if the prevalence of unidentified HIV infection exceeded 0.05 percent. Excluding HIV transmission, the cost-effectiveness of screening was $41,736 per quality-adjusted life-year. Screening every five years, as compared with a one-time screening program, cost $57,138 per quality-adjusted life-year, but was more attractive in settings with a high incidence of infection. Our results were sensitive to the efficacy of behavior modification, the benefit of early identification and therapy, and the prevalence and incidence of HIV infection.

CONCLUSIONS

The cost-effectiveness of routine HIV screening in health care settings, even in relatively low-prevalence populations, is similar to that of commonly accepted interventions, and such programs should be expanded.

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Timely identification of human immunodeficiency virus (HIV) infection is critical from both clinical and public health perspectives. A delay in diagnosis until late in the course of HIV infection may be associated with irreversible immunologic damage and related complications. Early identification also provides the opportunity to reduce transmission of HIV through changes in risk behavior.[1-3] Treatment with highly active antiretroviral therapy (HAART) most likely reduces infectivity[4] and may therefore afford an additional public health benefit by further reducing transmission.

Despite these compelling reasons for early identification, the Centers for Disease Control and Prevention (CDC) estimate that up to 20,000 new HIV infections annually can be attributed to people who are unaware of their HIV-positive status. Such people represent up to 280,000 of the approximately 950,000 people infected with HIV in the United States.[5] CDC data indicate that in 41 percent of HIV-positive patients, the acquired immunodeficiency syndrome (AIDS) develops within a year after they received the diagnosis,[6] suggesting that opportunities for preventing adverse outcomes were missed.

A fundamental strategy of a new CDC initiative to promote early identification of HIV disease is to make voluntary HIV testing a routine part of medical care.[7,8] Although we and others previously evaluated the cost-effectiveness of screening,[9-12] these analyses were performed before HAART became available. Because both the costs and the benefits of screening have changed since these analyses were published, the current cost-effectiveness of screening and the settings in which screening is economically attractive remain uncertain. We sought to evaluate the cost-effectiveness of voluntary HIV screening in health care settings and to assess how incorporating the costs and benefits associated with reductions in HIV transmission would influence the cost-effectiveness of a screening program.

METHODS

We used a decision model to estimate the health benefits and expenditures of performing voluntary HIV screening in health care settings. We adhered to the recommendations of the Panel on Cost-Effectiveness in Health and Medicine for conducting and reporting a reference-case analysis.[13]

DECISION MODEL

We used Decision Maker software (version 2003.11.1, Pratt Medical Group) to develop a Markov model that followed a cohort of patients over their lifetime (details are provided in Figure 1 of the Supplementary Appendix, available with the full text of this article at www.nejm.org). Our model includes voluntary HIV screening of a population, the natural history of HIV and AIDS, the costs and health consequences of transmission of HIV, and the costs and health consequences of HAART for patients so identified. Whenever possible, we based our probability estimates on high-quality published studies[1-4,7-9,13-165] (Table 1).

PATIENT POPULATION

The target population for our analysis was patients in health care settings whose HIV status was unknown. Reflecting the average age of patients in health care settings, our base-case analysis considered a cohort of 43-year-old men and women.[14] In our base-case analysis we assumed a prevalence of unidentified HIV infection of 1 percent, a value consistent with the CDC recommendation for screening.[8] The age- and sex-specific incidence of HIV was estimated on the basis of work by Rosenberg (Fig. 3 of the Supplementary Appendix).[21]

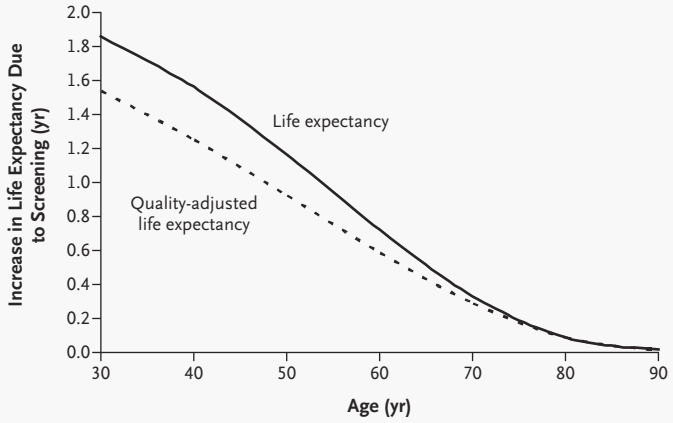

Figure 1. Effect of Early Identification of HIV Infection on Life Expectancy.
The solid line represents the effect on life expectancy of identifying asymptomatic HIV infection, as compared with symptom-based case finding. The dashed line represents the effect on quality-adjusted life expectancy.

Table 1. Variables and Sources.*

Variable	Base-Case Value	Range	Source
Demographic variables			
Age of patients in screening program (yr)	43	20–80	Kozak et al.[14]
Prevalence of unidentified HIV infection among patients (%)	1.0	0–15	CDC,[8] Janssen et al.[15]
Asymptomatic infection (%)	75	50–100	Estimate based on CDC,[7] Lemp et al.,[16] Sinclair et al.,[17] Bindman et al.,[18] Bozzette et al.,[19] Zingmond et al.[20]
Symptomatic infection (%)	15	0–30	
AIDS (%)	10	0–20	
Annual incidence (%)	0.03	1×–3× baseline	Fig. 3 of Supplementary Appendix; Rosenberg,[21] Karon et al.[22]
Proportion of uninfected population who are women (%)	60	50–70	Kozak et al.[14]
HIV-infected population (%)			
Men	75	50–90	HIV/AIDS surveillance report[23]
Men who have sex with men	50	25–75	HIV/AIDS surveillance report[23]
Natural-history variables (cells/mm³)			
CD4 count when infected with HIV	900	750–900	Turner et al.[24]
CD4 count at onset of symptoms	350	250–500	Turner et al.[24]
Case-finding variables			
CD4 count at which maximal case-finding rate is reached (cells/mm³)	50	0–350	Assumed
Maximal annual symptom-based case-finding rate (%)	80	50–100	Assumed
HIV testing variables			
Adherence to HIV-screening program (%)	100	50–100	Harris et al.,[25] Irwin et al.,[26] Kelen et al.[27]
Sensitivity of screening test (%)			
First 3 mo after infection	60	11–83	Owens et al.,[9] Schwartz et al.,[28] Mylonakis et al.[29]
Established disease	99.5	98.0–99.9	Owens et al.,[9] Mylonakis et al.,[29] CDC[30]
Specificity of entire sequence of screening tests (%)	99.9994	99–100	Owens et al.,[9] Mylonakis et al.,[29] MacDonald et al.[31]
Probability that patient returns to receive HIV test results (%)	80	70–100	Irwin et al.,[26] Kelen et al.[32] Kassler et al.,[33] Holman et al.,[34] CDC,[35,37,38] Erickson et al.,[36] Hightow et al.,[39] Sullivan et al.[40]
Months before false positive HIV diagnosis is discovered	2	0–12	Assumed
Frequency of CD4 testing without HAART (mo)	Every 3	Every 3–6	Panel on Clinical Practices[41]
Frequency of HIV testing (mo)	One time	Every 12–108	Assumed
Treatment variables			
CD4 count triggering HAART (cells/mm³)	350	—	Panel on Clinical Practices,[41] Yeni et al.,[42] AVANTI,[43] Erb et al.,[44] Mocroft et al.,[45] Rhone et al.[46]
Viral load triggering HAART (log copies/ml)	4.6	—	
Frequency of CD4 and viral-load testing during HAART treatment (mo)	Every 3	Every 2–6	

Table 1. (Continued.)

Variable	Base-Case Value	Range	Source
Increase in CD4 count at initiation of HAART (cells/mm³)	$110 + \frac{[535 \times (\text{initial CD4})^{0.98}]}{[(\text{initial CD4})^{0.98} + 260]}$†	—	Cohen Stuart et al.,[47] Hammer et al.,[48] Maher et al.,[49] Drusano and Stein,[50] Keita-Perse et al.[51]
Decline in CD4 count with detectable viral load (cells/mm³)	−79.2+33.5×log viral load	—	Mellors et al.,[52] Cook et al.[53]
Viral load (log copies/ml)‡			
Set point	4.6	3.0–6.0	Bindman et al.,[18] CDC[54]
During virologic suppression	1.3	1.0–2.7	Raboud et al.[55]
During virologic rebound	4.1	3.6–4.6	Le Moing et al.,[56] Deeks et al.[57]
Incremental rise above set point			
After suppressive therapy failed	0.8	0.0–1.5	CDC,[58] de Wolf et al.,[59] Mellors et al.,[60] Ioannidis et al.,[61] Keet et al.,[62] O'Brien et al.,[63] Spijkerman et al.,[64] Henrard et al.,[65] Sabin et al.[66,67]
After suppressive therapy failed and onset of AIDS	1.0	0.0–2.0	
Decrease with nonsuppressive therapy	1.0	0.0–2.0	Lucas et al.,[68] d'Arminio Monforte et al.,[69] Bonfanti et al.,[70] Valdez et al.,[71] Welch et al.[72]
Transition rate (events/100 patient-yr)			
From HIV to AIDS	6	2–12	Mellors et al.,[52] Vlahov et al.,[73] Hughes et al.[74]
From AIDS to death	3	1–10	Vlahov et al.[73]
Relative hazard of AIDS			
Per decline in plasma viral load of 1 log copy/ml	0.43	0.28–0.65	O'Brien et al.,[63,75,83,84] Henrard et al.,[65] Sabin et al.,[67] Vlahov et al.,[73] Hughes et al.,[74] Marschner et al.,[76] Brun-Vezinet et al.,[77] Coombs et al.,[78] Galetto-Lacour et al.,[79] Katzenstein et al.,[80] Mellors et al.,[81] Montaner et al.,[82] Pedersen et al.,[85] Phillips et al.,[86,87] Welles et al.,[88] Yerly et al.,[89] Chêne et al.,[90] Loveday and Hill[91]
Per increase in CD4 count of 1 log/mm³	0.0154	0.0002–1.0	
Relative hazard of death from AIDS			
Per decline in plasma viral load of 1 log copy/ml	0.64	0.55–0.75	
Per increase in CD4 count of 1 log/mm³	0.118	0.064–0.329	
Probability of virologic suppression (%)			Panel on Clinical Practices,[41] AVANTI,[43] Erb et al.,[44] Mocroft et al.,[45] Rhone et al.,[46] Cohen Stuart et al.,[47] Hammer et al.,[48] Maher et al.,[49] Raboud et al.,[55] Deeks et al.,[57] Lucas et al.,[68] Bonfanti et al.,[70,112] Valdez et al.,[71] Butcher et al.,[92] Guardiola et al.,[93] Casado et al.,[94] d'Arminio Monforte et al.,[95] Kirk et al.,[96] Roca et al.,[97,98] van Roon et al.,[99] Paredes et al.,[100] Kaufmann et al.,[101] Hogg et al.,[102] Fätkenheuer et al.,[103] Montaner et al.,[104] Zolopa et al.,[105] Shulman et al.,[106] Durant et al.,[107] Cohen et al.,[108] Baxter et al.,[109] Carpenter et al.,[110] Bernasconi et al.,[111] Gulick et al.,[113,114] Ledergerber et al.,[115] Moyle et al.,[116] Notermans et al.,[117] Paris et al.,[118] Powderly et al.,[119] Salzberger et al.,[120] Staszewski et al.,[121] Cameron et al.,[122] Clough et al.,[123] De Wit et al.,[124] Paredes et al.,[125] Kaufmann et al.,[126] Bellman,[127] Hall et al.[128]

Table 1. (Continued.)

Variable	Base-Case Value	Range	Source
First regimen	80	30–98	
Second regimen	65	20–80	
Third regimen	30	5–40	
Rates of virologic rebound			
First rebound (% at 2 yr)	15	6–30	AVANTI,[43] Mocroft et al.,[45] Raboud et al.,[55,132] d'Arminio Monforte et al.,[69] Butcher et al.,[92] Paredes et al.,[100] Montaner et al.,[104] Gulick et al.,[114,131] Paris et al.,[118] Powderly et al.,[119] Salzberger et al.,[120] Pialoux et al.,[129] Havlir et al.,[130] Staszewski et al.,[133] D'Amato et al.,[134] Kempf et al.,[135] Tebas et al.[136]
Per subsequent regimen (relative hazard)	2.0	1.0–6.0	Kaufmann et al.,[101] Salzberger et al.,[120] Paredes et al.,[125] Havlir et al.[130]
Intolerance requiring discontinuation of first regimen (%)	25	5–40	AVANTI,[43] Lucas et al.,[68] d'Arminio Monforte et al.,[69,95] Bonfanti et al.,[70] Butcher et al.,[92] Guardiola et al.,[93] Casado et al.,[94] Kirk et al.,[96] Roca et al.,[97,98] van Roon et al.,[99] Paredes et al.,[100] Kaufmann et al.,[101] Gulick et al.,[131] Staszewski et al.,[133] Cameron et al.,[137] Sullivan et al.,[138] Safrin and Grunfeld,[139] Reijers et al.[140]
Relative risk of discontinuation of second regimen	1.0	1–4	
Relative risk of discontinuation of third regimen	1.4	1–4	
Transmission variables			
Age of patients' sexual partners (yr)	43	20–80	Assumed to be the same as the infected patient
No. of susceptible partners at risk			
Men who have sex with men	2	1–10	Michael et al.,[141] Laumann[142]
Heterosexual men	1	0.5–4.0	Michael et al.,[141] Laumann[142]
Heterosexual women	1	0.5–4.0	Michael et al.,[141] Laumann[142]
Annual probability of infecting a sexual partner (%)			
Men who have sex with men	4	1–5	Samuel et al.,[143] Keet et al.,[144] Caceres and van Griensven,[145] Buchbinder et al.[146]
Heterosexual men	3	0.5–5.0	Deschamps et al.,[147] de Vincenzi,[148] Padian et al.,[149] Operskalski et al.,[150] Musicco et al.[151]
Heterosexual women	1	0.5–4.0	Deschamps et al.,[147] de Vincenzi,[148] Padian et al.,[149] Operskalski et al.[150]
Relative risk of infectivity given change in viral load of 1 log copy/ml	2.45	1–3	Quinn et al.[4]
Effectiveness of testing and counseling in reducing the number of sexual transmissions (% reduction in infectivity)	20	0–50	NIMH,[1] Kamb et al.,[2] DiClemente and Wingood[3]

Table 1. (Continued.)

Variable	Base-Case Value	Range	Source
Cost variables (dollars)			
Negative HIV test	2.50	1–5	Cost of ELISA test at Palo Alto VA
Positive HIV test	64	45–80	Cost of ELISA and Western blot tests at Palo Alto VA
HIV-test counseling	45	25–100	Owens et al.[9]
Cost of measuring CD4 count per test	92	65–120	Freedberg et al.[152]
Cost of measuring viral load per test	122	90–200	Freedberg et al.[152]
Annual cost of HIV infection (CD4, >500 cells per cubic millimeter) with HAART§	2,978	2,228–3,723	Bozzette et al.[153]
Annual cost of HIV infection (CD4, 200–500 cells per cubic millimeter) with HAART§	5,096	3,821–6,369	
Annual cost of HIV infection (CD4, <200 cells per cubic millimeter) with HAART§	7,596	5,697–9,495	
Annual cost of AIDS with HAART§	10,998	8,251–13,748	
Cost of three-drug antiretroviral therapy	13,752	8,251–16,307	Panel on Clinical Practices,[41] Durant et al.,[107] Carpenter et al.,[110] Drugs for HIV Infection,[154] U.S. General Accounting Office[155]
Incremental cost of four-drug antiretroviral therapy	2,477	1,540–12,579	
Annual cost of salvage therapy	16,230	0–28,885	
Cost of HAART side effect per episode	148	98–733	Mole et al.,[156] Keiser et al.,[157] Gable et al.[158]
Quality-of-life variables‖			
Current health			Sex- and age-specific quality of life for current health from Fryback et al.[159]
Unknown asymptomatic HIV infection	0.91	0.85–1.00	Honiden et al.[160]
Diagnosed asymptomatic HIV infection			
First year	0.84	0.80–1.00	Honiden et al.[160]
Subsequent years	0.89	0.80–1.00	Honiden et al.[160]
Symptomatic (untreated) HIV infection	0.79	0.45–1.00	Honiden et al.,[160] Tsevat et al.,[161,162] Revicki et al.,[163] Tengs and Lin[164]
HIV infection during HAART	0.83	0.45–1.00	Honiden et al.,[160] Tsevat et al.,[161,162] Revicki et al.,[163] Tengs and Lin[164]
AIDS	0.73	0.24–0.80	Honiden et al.,[160] Tsevat et al.,[161,162] Revicki et al.,[163] Tengs and Lin[164]
Decrease in quality of life due to side effects of HAART (multiplier)	0.53	0.44–0.62	Keiser et al.,[157] Gable et al.,[158] Bayoumi and Redelmeier[165]
Other variables			
Discount rate (annual %)	3	0–5	Weinstein et al.[13]
Cycle length (mo)	1		Assumed

* All probabilities are annual unless otherwise noted. All costs are in 2004 U.S. dollars. NIMH denotes the National Institute of Mental Health, ELISA enzyme-linked immunosorbent assay, and VA Veterans Affairs.
† We assumed that all patients had an increase in the CD4 count of at least 60 cells per cubic millimeter.
‡ The maximal viral load was 6.0 log copies per milliliter.
§ Treatment costs do not include the cost of HAART.
‖ Quality-of-life variables represent a person's preference for a given state of health and are scaled from 0 to 1, with 1 equivalent to perfect health.

HIV DISEASE PROGRESSION

The patients' viral load and CD4 levels together defined their risk of disease progression. We used natural-history data to estimate the rates of disease progression without therapy.[52,73,74] As the patients' viral load or CD4 count changed, so did their risk of AIDS or death. We estimated the relative hazard of AIDS or death for every change in the viral load of 1 log (on a base 10 scale) copy per milliliter and for every change in the CD4 count of 1 log per cubic millimeter (Table 1 and Fig. 4 of the Supplementary Appendix).

HIV TESTING

Each month, patients could be selected for testing through either an HIV-screening program or symptom-based case finding. We assumed that the frequency with which case finding occurred was constant and high below a CD4 count of 50 cells per cubic millimeter, linearly related to the CD4 count between 50 and 350 cells per cubic millimeter, and not relevant with a CD4 count of more than 350 cells per cubic millimeter, when patients were assumed to be asymptomatic (Fig. 4 of the Supplementary Appendix).

We assumed a standard testing strategy consisting of a serum enzyme-linked immunosorbent assay followed by confirmatory Western blotting (Table 1). The benefits of testing and counseling accrued only if patients received their test results and entered care. Our base-case assumption was that 80 percent of patients who screened positive for HIV would enter care and receive appropriate treatment.

TREATMENT OF HIV INFECTION

In accordance with published treatment guidelines, we assumed that HAART was started when the CD4 count of an identified HIV-infected patient was at or below 350 cells per cubic millimeter.[41,42] We estimated the viral load for such patients to be 4.6 log copies per milliliter, according to community-based populations of patients who had never received antiretroviral agents.[43-46]

After starting a HAART regimen, patients in whom virologic replication was suppressed also had an increase in their CD4 count (Table 1). Each month, patients with virologic suppression (defined as fewer than 500 copies per milliliter) could have treatment-related effects, virologic rebound, or continued virologic suppression (Supplementary Appendix). Patients who had drug-related adverse effects switched to a new antiretroviral regimen. Patients with incompletely suppressed viral loads owing to the development of resistance were identified when their viral load was determined at three-month intervals. When identified, these patients switched to a new antiretroviral regimen. We assumed that virologic suppression was less likely to be successful with each virologic rebound (Table 1).

If resistance developed to three successive antiretroviral regimens, we assumed that only partial virologic suppression was possible; such patients continued to receive HAART. We assumed that this partial suppression was sustained, reflecting the use of additional nonsuppressive regimens over time. All patients received prophylaxis against opportunistic infections when appropriate.

TRANSMISSION OF HIV

Transmission from an HIV-infected patient to his or her sexual partner depended on the infected patient's sex, type of sexual activity, number of sexual partners, knowledge of HIV status, and viral load (Table 1). On the basis of trials of counseling to prevent transmission of HIV by increasing condom use,[1-3] we assumed a 20 percent reduction in transmission for patients with identified HIV infection. We assumed that reductions in viral load further reduced transmission (Table 1).[4] Our assumptions and methods are in the Supplementary Appendix. In a sensitivity analysis, we included transmission from injection-drug users to their partners.

QUALITY OF LIFE

HIV infection and AIDS can markedly affect the quality of life. Accordingly, we incorporated adjustments for the quality of life in our analysis (Table 1 and Supplementary Appendix).

COSTS

Our analysis included the costs of testing and counseling, follow-up, and treatment for patients identified through screening or case finding (Table 1). We updated all costs to 2004 U.S. dollars (Supplementary Appendix).[166,167]

Costs for care of HIV-infected patients receiving HAART were separated into drug-related and non–drug-related costs (Table 1). The cost of multidrug HAART was estimated from published wholesale costs of recommended drug regimens. The non–drug-related annual cost of treating patients varied on the basis of the CD4 count and clinical status (Table 1).

Table 2. Lifetime Transmission Rates.*

Strategy	Men Who Have Sex with Men		Heterosexual Men		Heterosexual Women	
	No. of Lifetime Transmissions	Annual Transmission Rate	No. of Lifetime Transmissions	Annual Transmission Rate	No. of Lifetime Transmissions	Annual Transmission Rate
		%		%		%
Natural history	1.16	5.01	0.43	3.74	0.14	1.23
No screening	1.12	2.80	0.42	2.09	0.14	0.69
One-time screening	0.95	2.22	0.35	1.66	0.12	0.55
Recurrent screening	0.93	2.11	0.34	1.58	0.11	0.52

* The annual transmission rate is per partner at risk. These results represent the lifetime and annual transmissions of a patient infected with HIV at the age of 43 years. The base-case transmission rates found in Table 1 are reduced to those shown here through two mechanisms: when an HIV-infected patient is identified and undergoes behavior counseling he or she reduces risky behavior (base-case analysis, 20 percent reduction), and when an identified HIV-infected patient begins HIV-suppressive treatment and lowers his or her viral load, his or her infectivity is also reduced. The natural-history strategy represents a strategy in which HIV-infected patients are never identified and therefore do not receive treatment for their infection. Recurrent screening is every five years.

RESULTS

BENEFIT OF SCREENING DUE TO EARLY IDENTIFICATION OF HIV

We used our model to estimate the increase in the length of life that resulted from the initiation of HAART at a CD4 count of 350 cells per cubic millimeter as compared with the initiation of HAART on the basis of case finding (associated with an average CD4 count of 175 cells per cubic millimeter). In our base-case analysis, early identification and treatment resulted in an increase in life expectancy of the HIV-infected patient of 1.52 years; the benefit decreased for older patients (Fig. 1).

BENEFIT OF SCREENING FROM REDUCED TRANSMISSION OF HIV

Without screening, we estimated that HIV-infected men who have sex with men transmit the virus to 1.12 sexual partners over their lifetime and that heterosexual men and women transmit the virus to 0.42 and 0.14 partner, respectively (Table 2). If a one-time screening program is implemented, the lifetime numbers of transmissions are reduced to 0.95, 0.35, and 0.12 partner among men who have sex with men, heterosexual men, and heterosexual women, respectively. At our base-case incidence, recurrent screening (every five years) had little additional effect on the lifetime numbers of transmissions (Table 2). These lifetime transmissions reflected a 44 percent reduction in the annual transmission rate in the absence of screening, as compared with the natural history of the disease (without any case finding), and a reduction in the annual transmission rate of approximately 21 percent with the use of a screening strategy, as compared with the absence of screening.

ONE-TIME SCREENING

We assessed the cost-effectiveness of screening both with and without considering the benefit to sexual partners. When we considered only the benefit to the identified patient, we found that with an unidentified HIV prevalence of 1 percent, a one-time screening program increased life expectancy by 3.92 days, or 2.92 quality-adjusted days, at a cost of $333 relative to current practice, for an incremental cost-effectiveness of $41,736 per quality-adjusted life-year (Table 3). Incorporating costs and benefits to partners, we estimated that one-time screening cost $194 more than the cost of current practice, while increasing life expectancy by 5.48 days, or 4.70 quality-adjusted days, for an incremental cost-effectiveness of $15,078 per quality-adjusted life-year (Table 3). As Figure 2A demonstrates, the prevalence of unidentified HIV can be as low as 0.5 percent and still have a cost-effectiveness ratio of less than $50,000 per quality-adjusted life-year, excluding the benefits to partners. Including the costs and benefits to partners, the prevalence of unidentified HIV can be as low as 0.05 percent before it costs $50,000 per quality-adjusted life-year gained.

Table 3. Health and Economic Outcomes.*

Strategy	Cost	Incremental Cost	Life Expectancy	Incremental Life Expectancy	Incremental Cost-Effectiveness	Quality-Adjusted Life Expectancy	Incremental Quality-Adjusted Life Expectancy	Incremental Cost-Effectiveness
	$	*$*	*years*	*days*	*$/LY*	*QALY*	*QALD*	*$/QALY*
Index patient only (transmission to partners excluded)								
No screening	51,517		21.063			18.626		
One-time screening	51,850	333	21.073	3.92	31,084	18.634	2.92	41,736
Recurrent screening†	52,086	236	21.076	0.97	88,328	18.636	0.70	123,614
Index patient and sexual partners (transmission to partners included)								
No screening	52,623		21.015			18.576		
One-time screening	52,816	194	21.030	5.48	12,919	18.589	4.70	15,078
Recurrent screening†	53,022	206	21.034	1.52	49,509	18.592	1.31	57,138

* The analysis was based on a 1 percent prevalence of underdiagnosed HIV infection. LY denotes years of life, QALY quality-adjusted years of life, and QALD quality-adjusted days of life.
† Recurrent screening is every five years.

RECURRENT SCREENING

At our base-case annual incidence of 0.03 percent, screening every five years relative to one-time screening cost $57,138 per quality-adjusted life-year gained, when we included the benefit to partners (Table 3). Because the incidence of HIV infection in health care settings varies, we evaluated the cost-effectiveness of screening when the incidence was increased by a factor of 2 or 3 (Fig. 2B). Recurrent screening became more cost-effective as the incidence increased. For example, if the incidence increased by a factor of 3, screening every five years cost $29,900 per quality-adjusted life-year gained, as compared with one-time screening.

SENSITIVITY ANALYSES

The reduction in HIV transmission that occurred with screening depended on the effectiveness of counseling, the degree to which HAART reduced infectivity, and the baseline viral levels at the time of transmission. If a 1-log decrease in viral load reduced transmission by a factor of 1.5, screening cost $24,800 per quality-adjusted life-year, as compared with no screening. If counseling resulted in a reduction in risk behavior of only 10 percent, screening cost $20,500 per quality-adjusted life-year. If men who have sex with men had only 1 partner at risk and heterosexuals had only 0.5 partner at risk, screening cost $25,300 per quality-adjusted life-year, as compared with no screening.

In a sensitivity analysis, we evaluated the cost-effectiveness of screening when a proportion of HIV-positive patients were injection-drug users and accounted for additional transmission that could occur (Supplementary Appendix). In one-way sensitivity analyses, we changed our assumptions about infectivity (from a factor of 2 per 1-log decrease in viral load to no change), the proportion of injection-drug users among HIV-infected patients (from 25 percent to 35 percent), and the effectiveness of counseling in reducing high-risk injections (from 25 percent to 50 percent). The corresponding cost-effectiveness ratios were $15,900, $9,700, and $8,800 per quality-adjusted life-year, respectively.

Given the high specificity of HIV tests, the occurrence of false positive results was very rare. Even at a prevalence of HIV of 0.1 percent, for every 100,000 patients tested, only 0.48 patient would be falsely identified as infected with HIV. In the base-case analysis, we assumed that such persons would be identified as not having HIV within two months after the false positive result. Even if such identification took three years, the cost of screening would be less than $45,000 per quality-adjusted life-year gained at a prevalence of 0.1 percent.

If HAART was started at a lower CD4 count

(e.g., 300 cells per cubic millimeter), screening cost $14,200 per quality-adjusted life-year.

DISCUSSION

We evaluated the cost-effectiveness of routine screening for HIV infection in the era of HAART. Our analysis indicates that screening for HIV infection is cost-effective relative to other commonly accepted screening programs and medical treatments,[168] even when the prevalence of HIV infection is substantially lower than 1 percent, a prevalence that the CDC has used as general guidance for the initiation of routinely recommended as opposed to targeted screening.[8] This finding has potential public health implications in that screening for HIV infection is likely to be cost-effective in a much broader range of health care settings than has previously been recognized. Our analysis also highlights the importance of the public health benefit afforded by the identification of HIV infection. The identification of HIV infection can reduce transmission through two mechanisms: reductions in risk behavior and in infectivity from HAART. When we accounted for these important benefits, the cost-effectiveness of screening for HIV became favorable even at infection prevalences of less than 0.1 percent.

The main benefit of screening is that people identified as having HIV can begin lifesaving HAART before severe immunologic destruction has occurred. We assumed that, in patients in whom the infection was diagnosed early, HAART would begin when the CD4 count declined to 350 cells per cubic millimeter, the threshold recommended in current treatment guidelines. However, the best time to begin HAART is controversial.[44,169-176] The clinical benefit of starting therapy at various CD4 counts has not been evaluated directly in clinical trials. The ongoing Strategies for Management of Antiretroviral Therapy (SMART) study may help determine whether starting treatment when the CD4 count exceeds 350 cells per cubic millimeter and maintaining an undetectable viral load are more clinically beneficial than waiting to start treatment until the CD4 cell count reaches 350 cells per cubic millimeter.[177] Our model-based estimates indicate that identifying patients early and beginning therapy when the CD4 count was 350 cells per cubic millimeter, rather than through case finding and beginning therapy when the CD4 count was, on average, 175 cells per cubic millimeter, resulted in a survival advantage of about 1.5 years. This substantial survival advantage is the reason that screening reaches conventional levels of cost-effectiveness even when we did not consider the additional benefit from reduced transmission to sexual partners.

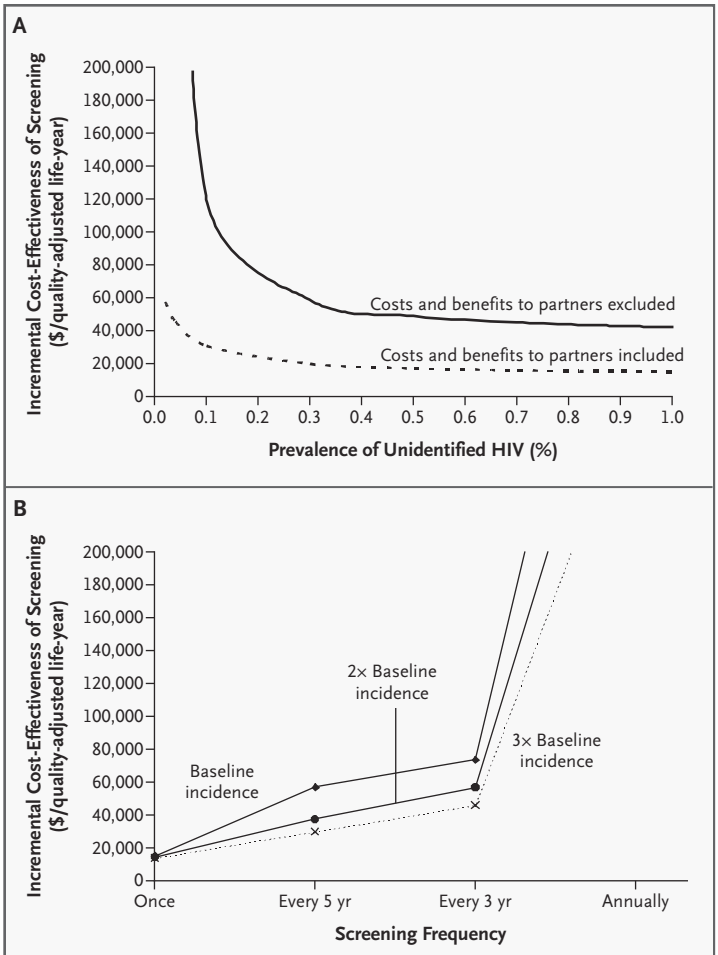

Figure 2. Sensitivity Analysis of the Effect of the Prevalence of Unidentified HIV on the Incremental Cost-Effectiveness of One-Time Screening, as Compared with Current Practice (Panel A), and the Effect of Screening Frequency on the Incremental Cost-Effectiveness of Screening at Various HIV Incidence Rates (Panel B).

In Panel B, the solid line marked with diamonds represents the baseline incidence, the solid line marked with circles represents the cost-effectiveness of recurrent screening when the incidence of HIV infection is twice the baseline rate, and the dashed line represents the cost-effectiveness of recurrent screening when the incidence of HIV infection is three times the baseline rate. The incremental cost-effectiveness ratio compares screening every A years with screening every B years, where B refers to the screening frequency directly to the left of A on the x axis (i.e., comparing screening every five years with one-time screening).

When we accounted for changes in risk behavior associated with counseling and the reduction in

transmission related to a decreased viral load during HAART, the rates of HIV transmission with the use of screening dropped by slightly more than 20 percent, as compared with no screening. Both changes in behavior and reduced viral load are important mediators of this benefit: HAART would reduce transmission even if patients who screened positive for HIV did not change their risk behavior (a reduction of 12 percent, as compared with no screening). However, the rate of transmission of HIV depends on many factors, including the number of sexual partners, the type and frequency of sex acts, the length of partnerships, the use or nonuse of condoms, and the viral load of the index patient. These factors will vary among populations that are screened, and there is uncertainty about each of them. Nonetheless, the benefit from reduced transmission remained important in our analyses under a broad range of assumptions.

The available evidence strongly indicates that current approaches to testing are inadequate. As noted, AIDS developed in 41 percent of the patients reported in CDC surveillance data within a year after they learned of their HIV-positive status.[6] In an ongoing cohort study of veterans, 20 percent of patients had an AIDS-defining illness at presentation for HIV care and 41 percent had a CD4 count of 200 cells per cubic millimeter or less (Justice AC: personal communication). Another study of veterans found that of almost 14,000 patients identified as at risk, only about one third to one half had documentation of HIV testing.[178] Together these studies indicate that many patients at risk are not tested at all and that of those who are identified, many have advanced disease.

Given the inadequacies of current testing, we believe the case for systematic voluntary HIV screening in health care settings is now compelling. When implementing screening, providers must decide whether to recommend routine screening for all patients or targeted screening based on risk-behavior assessment. The CDC recommends providers consider the type of setting, prevalence of HIV, and behavioral and clinical HIV risk of individual patients when they are deciding between targeted and routinely recommended screening.[8] The guideline suggests that a prevalence of 1 percent can be used as a general threshold for recommending routine (as compared with targeted) screening, but it also notes that routine screening may be recommended at lower prevalences depending on available resources and circumstances. Our findings suggest that routine screening would be cost-effective if the prevalence of undiagnosed HIV infection were as low as 0.05 percent. Although the prevalence of undiagnosed HIV infection is largely unknown, it is likely to reach 0.05 percent in many settings, including urgent care clinics, emergency departments, and some primary care clinics. For example, in a blinded serologic survey, we found that the prevalence of undiagnosed HIV infection ranged from 0.13 percent to 2.9 percent in unselected outpatients at six Department of Veterans Affairs health care systems.[179] Outpatient populations are rarely offered routine HIV screening. Because the prevalence of HIV infection in these populations is low, the HIV tests that are used should have very high specificity, ensuring low rates of false positive results.

Our analysis indicated that screening would be more effective than current practice and that the cost-effectiveness of screening is well within the range of that of other commonly accepted health care interventions. In addition, we demonstrated that screening is likely to be cost-effective at a substantially lower prevalence than previously recognized. This finding suggests that in many health care settings, HIV screening will provide important health benefits for a reasonable investment in health care resources.

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