SPECIAL ARTICLE

Expanded Screening for HIV in the United States — An Analysis of Cost-Effectiveness

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ABSTRACT

BACKGROUND

Although the Centers for Disease Control and Prevention (CDC) recommend routine HIV counseling, testing, and referral (HIVCTR) in settings with at least a 1 percent prevalence of HIV, roughly 280,000 Americans are unaware of their human immunodeficiency virus (HIV) infection. The effect of expanded screening for HIV is unknown in the era of effective antiretroviral therapy.

METHODS

We developed a computer simulation model of HIV screening and treatment to compare routine, voluntary HIVCTR with current practice in three target populations: "high-risk" (3.0 percent prevalence of undiagnosed HIV infection; 1.2 percent annual incidence); "CDC threshold" (1.0 percent and 0.12 percent, respectively); and "U.S. general" (0.1 percent and 0.01 percent). Input data were derived from clinical trials and observational cohorts. Outcomes included quality-adjusted survival, cost, and cost-effectiveness.

RESULTS

In the high-risk population, the addition of one-time screening for HIV antibodies with an enzyme-linked immunosorbent assay (ELISA) to current practice was associated with earlier diagnosis of HIV (mean CD4 cell count at diagnosis, 210 vs. 154 per cubic millimeter). One-time screening also improved average survival time among HIV-infected patients (quality-adjusted survival, 220.7 months vs. 219.8 months). The incremental cost-effectiveness was $36,000 per quality-adjusted life-year gained. Testing every five years cost $50,000 per quality-adjusted life-year gained, and testing every three years cost $63,000 per quality-adjusted life-year gained. In the CDC threshold population, the cost-effectiveness ratio for one-time screening with ELISA was $38,000 per quality-adjusted life-year gained, whereas testing every five years cost $71,000 per quality-adjusted life-year gained, and testing every three years cost $85,000 per quality-adjusted life-year gained. In the U.S. general population, one-time screening cost $113,000 per quality-adjusted life-year gained.

CONCLUSIONS

In all but the lowest-risk populations, routine, voluntary screening for HIV once every three to five years is justified on both clinical and cost-effectiveness grounds. One-time screening in the general population may also be cost-effective.

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Of the estimated 900,000 Americans currently infected with human immunodeficiency virus (HIV), roughly 280,000 are unaware of their infection.[1] These people receive neither demonstrated life-prolonging care nor counseling to prevent further transmission.[2,3] Borne disproportionately by the most vulnerable communities,[4] the burden of undetected HIV persists despite the availability of technology for accurate and efficient detection.[5] Although studies have assessed the cost-effectiveness of increased screening for HIV among specific high-risk populations (e.g., pregnant women[6] and attendees at clinics for patients with sexually transmitted diseases[7]), the value of routine, population-based HIV counseling, testing, and referral (HIVCTR) in the era of effective antiretroviral therapy is unknown.

In the 2001 revised guidelines for HIV counseling, testing, and referral,[8] the Centers for Disease Control and Prevention (CDC) issued specific recommendations regarding one-time, hospital-based, inpatient HIV-antibody testing. However, the CDC offered little guidance with regard to choice in the outpatient setting, in which decision makers face a host of possible target populations, competing methods for screening, uncertain follow-up and linkage to care, alternative test frequencies, and the ongoing interaction of the prevalence and incidence of HIV. In subsequent policy statements (including the 2003 guidelines for incorporating prevention into the medical care of persons living with HIV[9] and the recently announced "new initiative" for HIV prevention[10]), the CDC urges decision makers to weigh the evidence on risks, benefits, and costs in determining whether to expand HIV-testing services in the outpatient setting. However, the CDC offers little practical advice on how these competing tradeoffs might be managed. Our objectives were to address these issues by estimating the clinical consequences of delayed HIV detection, assessing the cost-effectiveness of the guidelines for expanded HIVCTR in populations with different risks of HIV, and illustrating how publicly available data could be marshaled to address questions of value for money (e.g., what works, in what settings, with which patients, and at what cost) in HIVCTR.

METHODS

STUDY DESIGN

We developed a mathematical simulation model of HIV disease to examine the incremental impact and cost-effectiveness of the addition of routine, voluntary HIVCTR to the current practice of HIV detection by means of either background testing or presentation with opportunistic infections. The analysis conformed to the reference-case recommendations of the U.S. Panel on Cost-Effectiveness in Health and Medicine.[11] Whenever possible, we used CDC guidelines[8-10] to specify input parameters. Outcome measures, including CD4 cell count at detection, life expectancy, life expectancy adjusted for the quality of life, and economic costs (in 2001 U.S. dollars[12]), were assessed from the societal perspective and are reported on a present-value basis with a 3 percent annual discount rate. We expressed comparative value in dollars per quality-adjusted life-year gained and evaluated the stability of the results with changes in model inputs, using multiway sensitivity analyses.

DISEASE MODEL

The Cost-Effectiveness of Preventing AIDS Complications (commonly known as CEPAC) model is a widely published computer simulation of HIV disease[13] (see the Supplementary Appendix, available with the full text of this article at www.nejm.org). It uses a Monte Carlo, state-transition framework to characterize disease progress as a sequence of monthly transitions between "health states" that summarize current status (CD4 cell count and HIV RNA level), relevant history, quality of life, and resource use. These health states predict further deterioration of the immune system, the development and relapse of opportunistic infections, toxic effects of medications, and mortality (Table A-1 in the Supplementary Appendix). The level of HIV RNA drives the decline of the CD4 cell count in this model, and the CD4 cell count determines the risk of opportunistic infections and mortality related to the acquired immunodeficiency syndrome (AIDS).[14] Each patient's clinical course is tracked from entry until death. Large numbers of individual simulations are aggregated to estimate population survival and cost.

SCREENING MODEL

The disease model simulates the course of HIV illness for all infected persons. However, only detected cases that are successfully linked to care are eligible for antiretroviral therapy and prophylaxis against opportunistic infections. The screening model conveys information about whether and when successful detection, follow-up, and linkage occur. Detection happens by means of one of the

following three mechanisms: expanded HIVCTR, nonroutine background screening (e.g., that which occurs in outpatient and inpatient settings and clinics for patients with sexually transmitted diseases), and clinical presentation with an AIDS-defining illness. Detection by means of the first two mechanisms is reported by the screening model to the disease model, with the use of a random-number generator to combine both literature-based estimates and user-specified assumptions regarding the accuracy and acceptance of HIV testing, background surveillance, and resource use (Table 1). The disease model compares the time of screen-based detection with the time of first opportunistic infection to determine actual detection time, as well as CD4 cell count and HIV RNA level at detection. These results are validated against CDC data from states that collect HIV reports (see the Supplementary Appendix).

SECONDARY TRANSMISSION

Recognizing that the preventive effects of expanded HIVCTR at the population level might exceed benefits to the individual patient, we estimated the probable number of secondary infections averted with alternative HIVCTR strategies. Published estimates of secondary transmission rates, stratified according to mechanism of detection, were obtained for a range of assumptions regarding the virologic and behavioral effects of antiretroviral therapy (see the Supplementary Appendix).

DATA ON DISEASE PROGRESSION

Data on disease progression were obtained from cohort studies, randomized clinical trials, and national resource-utilization surveys (see the Supplementary Appendix). Briefly, data about natural history (including the decline in the CD4 cell count, the incidence of opportunistic infections, and mortality) were derived from the Multicenter AIDS Cohort Study.[14,24] The efficacy of prophylaxis against complications (including *Pneumocystis jiroveci* pneumonia, toxoplasmosis, *Mycobacterium avium* complex infection, disseminated fungal infection, cytomegalovirus infection, and bacterial infections) was estimated from published sources (see Table A-1 of the Supplementary Appendix). Patient care was assumed to conform to national guidelines, including quarterly CD4 cell counts and HIV RNA laboratory tests, up to four sequential antiretroviral therapy regimens of decreasing efficacy,[25] and prophylaxis against opportunistic infections at appropriate CD4 thresholds.[26] The efficacy of antiretroviral therapy was estimated from trial data on viral suppression and changes in the CD4 cell count.[2,22,23] Data for estimating patient care costs and health-related quality-of-life weights were obtained from the national AIDS Cost and Services Utilization Survey[27] and the HIV Cost and Services Utilization Study.[28,29]

DATA FOR SCREENING

Target Population

On the basis of the literature, we obtained estimates of the prevalence and incidence of HIV for three target populations (Table 1). The high-risk scenario (prevalence of undiagnosed HIV, 3.0 percent; annual incidence, 1.20 percent) represents a plausible but conservative view of a high-infection population.[15,16] The "CDC threshold" population (prevalence, 1.0 percent; annual incidence, 0.12 percent) meets the CDC's guideline for a prevalence of at least 1 percent.[8,15] We based the scenario of the U.S. general population (prevalence, 0.1 percent; annual incidence, 0.01 percent) on the widely cited estimate of 280,000 undetected, prevalent HIV infections and 40,000 infections annually in a population of roughly 290 million.[1,17]

Test Types and Frequencies

We defined two prototypical protocols for HIV testing: enzyme-linked immunosorbent assay (ELISA) and same-day antibody test (rapid testing).[5,18,19] For purposes of comparison, we distilled the distinctions between these protocols to differences in observed follow-up rates and cost (Table 1). All positive test results were confirmed by repeated duplicate tests and a Western blot analysis.[19,20] We assumed that patients receive ELISA results only after confirmation is complete. By contrast, results of rapid testing are communicated and referral to care is initiated before confirmation, yielding higher referral and follow-up rates. To account for a reduced quality of life while one awaits serologic refutation of initial results, we assigned a loss of 14 quality-adjusted days (sensitivity analysis range, 0 to 28 days) to HIV-uninfected persons who have false positive results on rapid testing. We considered testing frequencies ranging from a single test to screening every five years, three years, or one year.

Current Screening Practices

Reports that 57 percent of HIV-infected patients in large urban settings had CD4 cell counts below 350 per cubic millimeter at presentation (36 percent had cell counts below 200 per cubic millimeter) suggest average infection-to-detection times great-

Table 1. Summary of Input Parameters for the Model.*

Target Population	Undiagnosed HIV Prevalence	Annual HIV Incidence	Study
High-risk (%)	3.0	1.20	Seage et al.,[15] Webster et al.[16]
CDC threshold (%)	1.0	0.12	CDC,[8] Seage et al.[15]
U.S. general (%)	0.1	0.01	Fleming et al.,[1] CDC[17]
Test Protocols†	**ELISA**	**Rapid Testing**	
Sensitivity (%)			
Pre-seroconversion	2.5	2.5	Mylonakis et al.,[5] CDC,[18] Ekwueme et al.,[19] Farnham et al.[20]
Post-seroconversion	99.6	99.6	Mylonakis et al.,[5] CDC,[18] Ekwueme et al.,[19] Farnham et al.[20]
Specificity (%)			
Pre-seroconversion	97.5	97.5	Mylonakis et al.,[5] CDC,[18] Ekwueme et al.,[19] Farnham et al.[20]
Post-seroconversion	97.5	97.5	Mylonakis et al.,[5] CDC,[18] Ekwueme et al.,[19] Farnham et al.[20]
Test acceptance rate (%)	80 (67–100)	80 (67–100)	Ekwueme et al.[19]
Rate of HIV-infected return for test results and linkage to care (%)	75 (50–100)	97 (50–100)	CDC,[18,21] Ekwueme et al.[19]
HIV-negative return rate (%)	67 (50–100)	100 (50–100)	CDC,[18,21] Ekwueme et al.[19]
Test cost ($)	2 (1–20)	7 (1–100)	Ekwueme et al.,[19] Farnham et al.[20]
Confirmatory test cost ($)	34	40	Ekwueme et al.,[19] Farnham et al.[20]
Counseling and Linkage to Care			
Pre-test counseling cost ($)	25 (0–100)	25 (0–100)	Ekwueme et al.,[19] Farnham et al.[20]
Post-test linkage and counseling costs for patients who are HIV-positive ($)	38 (0–100)	24 (0–100)	Ekwueme et al.,[19] Farnham et al.[20]
Post-test counseling costs for patients who are HIV-negative ($)	29 (0–50)	13 (0–50)	Ekwueme et al.,[19] Farnham et al.[20]
Efficacy of Antiretroviral Therapy‡	**Variable**		
Starting criterion	CD4 cell count <200/mm³§		
Efficacy (%)			
First-line	70 (53–77)		Staszewski et al.[22]
Second-line	60 (45–66)		Hammer et al.[2]
Third-line	34 (26–37)		Baxter et al.[23]
Fourth-line	22 (17–24)		Baxter et al.[23]

* Baseline estimates used in the analysis are reported, with ranges used for sensitivity analysis, when applicable, in parentheses. Costs are in 2001 U.S. dollars.
† ELISA denotes enzyme-linked immunosorbent assay, and rapid testing is antibody testing with results within 30 minutes.
‡ Antiretroviral efficacy is defined in terms of the rate of suppression of HIV RNA below 400 copies per milliliter at 48 weeks. When trials did not report 48-week data, we extrapolated for modeling purposes.[13]
§ Sensitivity analysis was conducted on all model outputs with the use of a starting criterion for antiretroviral therapy of less than 350 cells per mm³.

er than five years.[30] We therefore made the conservative assumption that current practice includes a monthly probability of ELISA of 1 in 60, implying that, on average, the time to HIV detection is five years, even in the absence of expanded HIVCTR. In sensitivity analyses, we considered average frequencies ranging from three years (i.e., a monthly probability of ELISA of 1 in 36) to never.

RESULTS

HIGH-RISK POPULATION

With current practices of HIV detection in the high-risk population, 29 percent of all HIV-infected persons remained undetected until their first opportunistic infection (Table 2). CD4 cell counts at detection averaged 154 per cubic millimeter for prevalent cases (in persons infected before entry into simulation) and 347 per cubic millimeter for incident cases (in persons infected after entry). Discounted life expectancy was 228.03 months among HIV-infected persons (377.54 months undiscounted) and 254.41 months for the overall population (446.38 months undiscounted). The lifetime costs for the population averaged $32,700 per person.

Adding a one-time screening with ELISA was associated with earlier diagnosis of HIV, so that the mean CD4 cell count at detection was 210 rather

Table 2. Performance of Alternative ELISA Protocols in the High-Risk Population Scenario.*

Variable	Current Practice	Current Practice and Single ELISA	Current Practice and ELISA Every 5 Years	Current Practice and ELISA Every 3 Years	Current Practice and Annual ELISA
Mechanism of HIV detection (%)					
Background testing	63	61	44	36	19
Screening program	0	3	34	47	73
Opportunistic infection	29	27	16	12	6
Never detected†	8	8	5	4	2
Mean CD4 cell count at detection (cells/mm³)					
Prevalent cases‡	154	210	210	213	227
Incident cases	347	347	397	422	473
Mean survival (mo)					
HIV-infected persons only	228.03	229.18	232.26	233.42	235.22
Population	254.41	254.88	256.17	256.66	257.41
Mean quality-adjusted survival (quality-adjusted life-month)					
HIV-infected persons only	219.84	220.74	222.78	223.46	224.29
Population	250.89	251.26	252.11	252.40	252.75
Mean lifetime costs per person ($)					
HIV-infected persons only	78,100	80,700	89,000	92,500	98,600
Population	32,700	33,800	37,300	38,900	41,700
Cost-effectiveness ($ per quality-adjusted life-year gained)§	—	36,000	50,000	63,000	100,000

* For the high-risk population, the prevalence of undiagnosed HIV was 3 percent and the annual incidence of HIV was 1.2 percent. ELISA denotes enzyme-linked immunosorbent assay. All survival, cost, and cost-effectiveness outcomes are reported on a present-value basis with an annual discount rate of 3 percent. Because of rounding, not all percentages total 100.

† Infected persons were labeled "never detected" if they were not tested before death or if they were tested but never received their test results.

‡ CD4 cell count at detection in prevalent cases increases slightly with higher test frequencies because of the rate of refusal of testing at any one time.

§ Cost-effectiveness is the difference in cost divided by the difference in quality-adjusted life expectancy for each strategy as compared with the next least costly strategy. The dash represents the convention of not reporting the cost-effectiveness ratio for the least costly strategy.[11] Because of rounding, reported ratios do not precisely equal the ratios of reported costs and effects.

than 154 per cubic millimeter. When repeated testing was introduced, further gains were observed, especially among incident cases. For example, expanding from a single test to screening every five years raised CD4 cell counts at detection among incident cases from 347 to 397 per cubic millimeter and reduced from 27 percent to 16 percent the proportion of cases that were not detected until the patient presented with an opportunistic infection.

Expanded screening also increased rates of survival and costs. Among HIV-infected persons, discounted life expectancy across the range of frequencies for screening with ELISA rose from 228.03 to 235.22 months (from 377.54 to 392.60 undiscounted months), with concomitant increases in lifetime medical costs (from $78,100 to $98,600). Averaged over the entire population for purposes of a societal cost-effectiveness analysis, one-time ELISA screening cost $36,000 per quality-adjusted life-year gained, as compared with current detection. Incremental ratios for screening every five and three years were $50,000 and $63,000 per quality-adjusted life-year gained, respectively; annual screening cost $100,000 per quality-adjusted life-year gained.

CDC THRESHOLD POPULATION AND U.S. GENERAL POPULATION

Lifetime risks of HIV infection were 41.8 percent in the high-risk population (prevalence, 3.0 percent; annual incidence, 1.20 percent), 6.1 percent for the CDC threshold population (prevalence, 1.0 percent; annual incidence, 0.12 percent), and 0.7 percent for the U.S. general population (prevalence, 0.1 percent; annual incidence, 0.01 percent). In the CDC threshold population, we observed longer overall life expectancies and lower costs than in the high-risk population. Expanded HIVCTR remained an attractive investment but at reduced frequency. For example, the cost-effectiveness ratio for a single ELISA was $38,000 per quality-adjusted life-year gained; screening every five and three years cost $71,000 and $85,000 per quality-adjusted life-year gained, respectively (Table 3); annual screening cost $165,000 per quality-adjusted life-year gained.

In the population with the lowest incidence, the U.S. general population, one-time screening with the ELISA had an incremental cost-effectiveness ratio of $113,000 per quality-adjusted life-year gained. More frequent screening produced little incremental benefit, owing to the effect of false positives on health-related quality of life (Table 3).

SENSITIVITY ANALYSIS: ALTERNATIVE SCREENING PROTOCOLS

Figure 1 compares ELISA and rapid testing in the high-risk population. The proximity of the curves suggests roughly equivalent performance. Rapid testing, with its higher rates of linkage to care, maximized benefit at most frequencies. This advantage was eventually offset by diminishing yield as well as by the effect of false positive results on both quality of life and cost, causing the curves to cross. In the scenarios of the CDC threshold and U.S. general populations, these effects were more pronounced — the curve representing rapid testing eventually sloped downward. Higher specificity assumptions (99 percent) attenuated this effect.

ADDITIONAL SENSITIVITY ANALYSES

We reevaluated all findings for the three population scenarios using the data ranges specified in Table 1. In general, results were not sensitive to plausible changes in test characteristics, reduced quality of life due to false positives, or the efficacy of antiretroviral therapy. However, when we varied assumptions about background testing, adherence to antiretroviral therapy, and rates of linkage to care, results changed in informative ways. For example, reducing the average time to HIV detection by means of background testing from five to three years increased the incremental cost-effectiveness ratio of a single ELISA in the high-risk population from $36,000 to $43,000 per quality-adjusted life-year gained.

Varying the assumptions about the efficacy of antiretroviral therapy with the use of the ranges specified in Table 1 produced small, parallel changes in both cost and survival but had little effect on overall cost-effectiveness assessments. To reflect both incomplete availability and imperfect adherence to therapy in vulnerable populations, we explored in sensitivity analyses how results differed when we assumed that only 50 percent of patients diagnosed with HIV would receive antiretroviral therapy. The incremental cost-effectiveness ratio of screening with a single ELISA under this assumption increased from $36,000 to $48,000 per quality-adjusted life-year gained. When no patients received antiretroviral therapy, expanded HIVCTR produced higher costs and little or no health benefit.

Table 3. Performance of ELISA in the CDC Threshold and U.S. General Population Scenarios.*

Scenario	Current Practice	Current Practice and Single ELISA	Current Practice and ELISA Every 5 Years	Current Practice and ELISA Every 3 Years	Current Practice and Annual ELISA
CDC threshold population					
Mean quality-adjusted survival (quality-adjusted life-month)					
HIV-infected persons only	213.12	215.28	216.93	217.60	218.76
Population	278.81	278.94	279.03	279.08	279.15
Mean lifetime costs per person ($)					
HIV-infected persons only	77,700	83,500	90,500	93,800	99,900
Population	4,700	5,100	5,700	6,000	6,900
Cost-effectiveness ($ per quality-adjusted life-year gained)†	—	38,000	71,000	85,000	165,000
U.S. general population					
Mean quality-adjusted survival (quality-adjusted life-month)					
HIV-infected persons only	219.05	220.81	222.73	222.87	224.23
Population	283.49	283.49	283.51	283.51	283.52
Mean lifetime costs per person ($)					
HIV-infected persons only	75,400	80,200	087,200	90,600	96,800
Population	549	624	830	980	1,600
Cost-effectiveness ($ per quality-adjusted life-year gained)†	—	113,000	169,000	1,002,000	1,264,000

* For the CDC threshold population, the prevalence of undiagnosed HIV was 1.0 percent and the annual incidence of HIV was 0.12 percent. ELISA denotes enzyme-linked immunosorbent assay. For the U.S. general population, the prevalence was 0.10 percent and the incidence was 0.01 percent. All survival, cost, and cost-effectiveness outcomes are reported on a present-value basis with an annual discount rate of 3 percent.

† Cost-effectiveness is the difference in cost divided by the difference in quality-adjusted life expectancy for each strategy as compared with the next least costly strategy. The dash represents the convention of not reporting the cost-effectiveness ratio for the least costly strategy.[11] Because of rounding, reported ratios do not precisely equal the ratios of reported costs and effects.

Finally, reduced rates of patient return for HIV-test results and linkage to care yielded lower survival and cost, but incremental cost-effectiveness ratios remained stable. Values above $50,000 per quality-adjusted life-year gained were not observed for single ELISA screening in the high-risk population until we assumed linkage-to-care rates below 25 percent.

SECONDARY TRANSMISSION BENEFITS

Under current screening practices in the high-risk population, we expect to observe 44,000 to 60,000 secondary transmissions per 100,000 participants in the screening program. A single ELISA could avert up to 300 of these secondary transmissions. Repeated testing every five years, three years, and one year could avert 2700, 3600, and 5100 infections, respectively. In the CDC threshold population, a single ELISA could avert more than 105 of the expected 6500 to 8700 secondary transmissions per 100,000. For the U.S. general population, a single ELISA could avert up to 10 of the 780 to 1050 expected secondary transmissions per 100,000. With the use of repeated testing every five years, there would be 420 fewer infections in the CDC threshold population and 49 fewer in the U.S. general population.

DISCUSSION

Although our analysis supports CDC recommendations for routine HIVCTR in populations with a prevalence greater than 1.0 percent,[8] we find that these recommendations are not strong enough. In

populations barely meeting the CDC's threshold of 1.0 percent prevalence, estimated gains in survival and cost-effectiveness for a single HIV test ($38,000 per quality-adjusted life-year gained) compare favorably with other recommended interventions in HIV patient care[13] and many commonly used screening interventions in chronic conditions, including breast cancer, colorectal cancer, diabetes, and hypertension.[31] Expansion of HIVCTR into settings with levels of HIV infection similar to those in the general population would cost $113,000 per quality-adjusted life-year gained and perhaps substantially less if population-wide transmission benefits can be demonstrated. Although an operational description of expanded HIVCTR services is beyond the scope of this article, recently reported results from the successful implementation of routine, voluntary HIVCTR for patients in urgent care settings support the feasibility of this approach.[32]

With regard to extending HIVCTR into the general population, our results should be interpreted with caution. This analysis is based on nationwide average costs, benefits, and data about prevalence and incidence that include high-risk and low-risk persons. The analysis cannot definitively address whether an existing HIVCTR program in the highest-risk populations should be expanded to include people at lower-than-average risk. It does, however, suggest that further study is warranted.

Our findings are less conclusive with regard to the choice of testing technology. Rapid testing is sensitive to assumptions regarding rates of return, linkage to care, and test specificity. Although sensitivity analysis suggests that the expected costs of false positive results and the reduced quality of life associated with waiting for serologic confirmation are small, a model-based assessment may not adequately capture the range of personal and social distress caused by false positives that could, in rare cases, take months to be recognized.

Sensitivity analyses identified three principal sources of uncertainty. First, the effect of expanded HIVCTR will be inversely related to the amount of background testing performed concurrently elsewhere (e.g., at clinics for patients with sexually transmitted diseases, at family planning centers, in inpatient settings, during prenatal screening, at primary care offices, for insurance applications, or in prisons). Limited data suggest current frequencies of testing ranging from never to as often as every two years.[33] However, indirect evidence of low CD4 cell counts at detection suggests that our baseline frequency assumption of five years probably understates the value of expanded HIVCTR.[30]

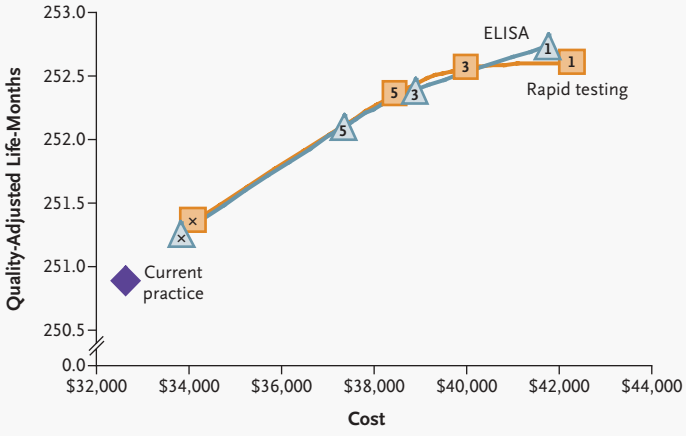

Figure 1. Cost-Effectiveness of HIVCTR Strategies in the High-Risk Population Scenario.

Net program costs are depicted on the horizontal axis and health benefits, measured in quality-adjusted life-months, on the vertical axis. The stand-alone diamond (◆) in the lower left represents the result of current practices for the detection of HIV by means of either background testing of patients or testing of patients who present with an opportunistic infection. The points depict cost and benefit outcomes for enzyme-linked immunosorbent assay (ELISA) and rapid testing at various frequencies: one time (denoted with an X) and every five years, three years, and one year. The slopes of the lines connecting these points represent incremental ratios of effectiveness to cost. The flattening of these lines illustrates the diminishing marginal returns with increased investment in higher-frequency testing.

Acceptance of testing and linkage to care represent a second area for study. Although failure to attract, retain, and treat participants in HIV testing is well documented,[34] the principal driver of both costs and benefits in HIVCTR is not the HIV test itself but the increased number of patients receiving expensive care as a result of improved case detection.

Finally, there is need for more study of the effect of HIVCTR on the secondary transmission of HIV. Our sensitivity analysis shows that even minimal therapy-related improvements in viral load and risk behaviors could reduce secondary infections and produce substantially more favorable cost-effectiveness ratios. By ignoring such effects, our base-case analysis represents a conservative appraisal of expanded HIVCTR. However, the effect of antiretroviral therapy on reducing the transmission of HIV could be dampened or reversed by an increase in risky behavior that some patients may engage in after a diagnosis of HIV. These issues merit further

investigation. We also acknowledge that our analysis does not consider stigma, a critical concern in shaping public perceptions of HIV. There is a paucity of data quantifying the extent to which stigma acts as a barrier to wider acceptance of HIV testing and linkage to care. The effect of stigma on a person's behavior — and the potentially beneficial effect of expanded HIVCTR in reducing negative perceptions of HIV illness — represents an important area for further study.

HIV infection meets all the U.S. Preventive Services Task Force criteria for targeted screening.[35] It is a severe disease that, left untreated, leads to substantial morbidity and death. It has a long preclinical phase and can be diagnosed with the use of effective, inexpensive tests. Most important, early detection speeds linkage to care and prevention. The scientific basis for effective treatment of patients with HIV has been successfully laid.[2,3] We find an equally solid body of evidence to support expanded HIVCTR. Specifically, our results justify a shift in focus away from targeted approaches that are based on provider assessments of individual risk factors. Routine voluntary screening for HIV every three to five years is effective and cost-effective by U.S. standards, except in populations with the lowest prevalence of HIV. One-time screening in the setting of the general population merits further investigation. Efforts to promote, finance, and expand existing national HIV-testing guidelines should be pursued aggressively.

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