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Cost Effectiveness of HIV Screening in Patients Over 55 Years of Age

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Abstract

BACKGROUND—Although HIV infection is more prevalent in people <45, a significant number of infections occur in older individuals. Recent guidelines recommend HIV screening of patients aged 13–64. The cost-effectiveness of HIV screening patients aged 55–75 years is uncertain.

OBJECTIVE—To examine the costs and benefits of HIV screening in patients aged 55–75 years.

DESIGN—Markov model.

DATA—Derived from the literature.

TARGET POPULATION—Patients aged 55–75 with unknown HIV status.

TIME HORIZON—Lifetime.

PERSPECTIVE—Societal.

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INTERVENTIONS—HIV screening program for patients aged 55–75 years compared to current practice.

OUTCOME MEASURES—Life-years, quality-adjusted life-years (QALYs), costs, incremental cost-effectiveness.

RESULTS OF BASE-CASE ANALYSIS—For a 65-year-old patient, HIV screening using traditional counseling costs \$55,440/QALY compared with current practice when the prevalence of HIV was 0.5% and they did not have a sexual partner-at-risk. In sexually-active patients, the incremental cost-effectiveness ratio was \$30,020/QALY. At a prevalence of 0.1%, HIV screening cost <\$60,000/QALY for patients <75 years old with a partner-at-risk if less costly streamlined counseling is used.

RESULTS OF SENSITIVITY ANALYSES—Cost-effectiveness of HIV screening depended on HIV prevalence, age of the patient, counseling costs, and whether the patient was sexually active. Sensitivity analyses with other variables did not change our results substantially.

LIMITATIONS—Uncertainty regarding effects of age on HAART toxicity, efficacy, and AIDS mortality. Sensitivity analyses exploring these variables did not qualitatively affect our results.

CONCLUSIONS—If the tested population has a prevalence of 0.1%, HIV screening in individuals between 55–75 years old reaches conventional levels of cost-effectiveness when counseling is streamlined and if the screened patient has a partner at risk. HIV screening of patients with advanced age is economically attractive in many circumstances.

Keywords

HIV; Aged; Cost-Benefit Analysis; Mass Screening; Highly Active Antiretroviral Therapy; Transmission

INTRODUCTION

The Centers for Disease Control and Prevention's (CDC) recently revised human immunodeficiency virus (HIV) screening guidelines recommend that all patients age 13 to 64 in health care settings be tested (1). Previous work by our group (2) and others (3–5) has demonstrated that screening for HIV in younger patients is cost effective even in relatively low-prevalence settings. For example, we found screening 40-year old individuals to cost less than \$50,000 per quality-adjusted life year (QALY) when the prevalence of undiagnosed HIV infection is 0.05% (1 in 2000) or higher (2). Although screening is cost effective in younger age groups, approximately 19% of all people with AIDS in the U.S. were aged 50 or older at the time of their diagnosis (6). The cost effectiveness of screening older patients has not been evaluated and is uncertain.

There are several reasons that screening in patients over 55 years of age may be less cost effective than screening younger individuals. First, the prevalence of HIV, a major determinant of cost effectiveness, is lower in older compared to younger age groups (7). Second, treatment of HIV will be less cost effective in older individuals because the competing risk of death from other causes will diminish the absolute benefits of therapy. Third, if older patients have fewer sex partners, screening will be less economically attractive because reduction of HIV transmission is an important benefit of screening and hence, a determinant of cost effectiveness (2). Finally, neither the effectiveness nor toxicity of highly active antiretroviral therapy (HAART) in patients aged 55–75 years old have been well studied; both could be less favorable than in younger patients (8). To assess the importance of these factors, we modified our previous cost-effectiveness model to assess the cost effectiveness of HIV screening in individuals over 55 years of age.

METHODS

We estimated the health and economic effects of a program of voluntary HIV screening in patients between the ages of 55 and 75 using a decision model, following the recommendations of the Panel on Cost Effectiveness in Health and Medicine. We performed the analysis using a societal perspective on health benefits and costs and applying a 3% annual discount rate (9).

Decision Model

We adapted a Markov model (10, 11) developed to assess the cost effectiveness of voluntary HIV screening in healthcare settings (2) using Decision Maker software (version 2007.0.1 Pratt Medical Group). The model tracked a cohort of older patients over their lifetime. Patients were either screened through a one-time voluntary HIV screening program or were followed without routine screening. Each month, the model assessed the patients' HIV status, whether their HIV status was identified, the clinical course of HIV disease, the costs and consequences of HIV transmission, and the costs and consequences of HAART for patients identified with HIV and eligible for treatment (Figure 1). Individuals were also at risk for age- and gender-specific non-HIV related mortality. Probability estimates were based on high-quality published literature and expert clinical judgment (Table 1) (2, 9, 12–156).

Patient Population

We assessed the cost-effectiveness of screening patients between 55 and 75 years of age whose HIV status was unknown in populations with a prevalence of unidentified HIV infection that varied from 0.1% to 1% (157). We estimated the incidence of HIV in age- and sex-specific strata based on previous models (18, 19)

HIV Testing

Patients who were not tested through an HIV screening program or who tested negative through screening could be selected for future testing through symptom-based case finding. We assumed that such case finding occurred only in patients with a CD4 count of 0.350×10^9 cells/L or lower and that the probability of identifying and testing for HIV increased as the CD4 count fell. We incorporated standard HIV testing using a serum enzyme-linked immunosorbent assay followed by confirmatory Western blotting.

In our base-case analysis, patients received comprehensive pre- and post-test counseling with HIV testing. We explored the effects of streamlined counseling (abbreviated pre-test counseling requirements) as recommended by the CDC (1) on HIV screening in sensitivity analyses. The benefits of testing and counseling accrued only to those patients who received their test results and entered care.

HIV Disease Progression and Treatment

We modeled HIV disease progression using HIV viral load copy number and CD4 count and drawing on natural-history data (Table 1) (52, 77, 84). We assumed treatment of HIV infection would adhere to published treatment guidelines, including appropriate prophylaxis and immunization (41, 42). HAART was assumed to be initiated when an identified HIV-infected patient's CD4 count fell to or below 0.35×10^9 cells/L. Once HAART was initiated, we modeled the possible rise in CD4 count, virologic suppression, treatment-related toxicity, and virologic rebound. We assumed that patients with drug-related adverse effects switched to a new regimen and had the same probability of achieving suppression on this new regimen as they did on the initial regimen. In contrast, we assumed that patients who experienced virologic failure and were identified through viral load testing were switched to

a new regimen with a reduced likelihood of achieving virologic suppression (Table 1). We assumed that after being treated with three successive antiretroviral regimens, a patient would only be able to achieve partial virologic suppression due to multi-drug resistance. We assessed varying assumptions about the efficacy of treatment of such patients in sensitivity analysis.

Effectiveness and Toxicity of HAART in the Patients Over 55

Substantial uncertainty exists regarding the effectiveness of HAART and the course of HIV infection in the older aged population. Although patients over 55 may have higher rates of virologic suppression (perhaps due to better adherence or altered pharmacodynamics), the evidence regarding immunologic effects in patients over 55 is inconsistent. While several studies have suggested older patients have a longer time to CD4 reconstitution after starting HAART (89–91, 94, 98), other studies have found no differences, or differences in the first year only (8, 92, 93, 95–97). Studies have similarly differed as to whether older age is an independent risk factor for disease progression (90, 158). The evidence regarding toxicity of antiretrovirals in older patients is even more limited. Although there are many reasons to suspect that older patients will tolerate antiretrovirals less well than younger patients (such as cardiovascular and hepatic events), the evidence for this assertion is still weak (8, 91, 94, 96).

We approached the modeling of HAART effectiveness and toxicity in patients over 55 recognizing that the evidence for age effects are generally based on observational studies that are often small and with considerable potential for residual confounding. To address the uncertainty around these age effects and explore their potential impact, our base-case model assumed no difference in antiretroviral efficacy for older patients, but we included specific scenarios in which we modeled three effects that may be related to older age: greater failure rates with HAART, greater treatment-limiting toxicities, and greater non-AIDS age-specific mortality.

Transmission of HIV

We included in our analysis the potential costs and health benefits associated with transmission of HIV from an infected individual to their sexual partners. Transmission depended on the infected patient's gender, type of sexual activity, number of sexual partners, knowledge of HIV status, and viral load (Table 1). We assumed that a sexually active patient aged 55–75 years old would have on average 1 partner at risk for infection and also tested the situation in which patients had no sexual partners or multiple partners (see Technical Appendix).

Quality of Life

The model incorporated adjustments for the quality of life associated with age-specific current health, HIV disease (asymptomatic HIV, symptomatic HIV, and AIDS), and HAART (Table 1). Utilities measure the patient's quality-of-life and were rated on a scale from 0 to 1, where 0 represents death and 1 ideal health. We multiplied utilities based on HIV-related health status and knowledge by age-specific utility weights derived from the Beaver Dam Health Outcomes Study (151).

Costs

Our analysis included the direct costs of medical care associated with HIV testing and counseling, follow-up, and treatment of patients identified with HIV infection through a screening program or through symptom-based case finding (Table 1). We included age-specific medical expenditures unrelated to HIV care (<http://www.bls.gov/cex/csxann05.pdf>)

and updated all costs to 2007 dollars using the gross domestic product (GDP) deflator (159). While the GDP deflator is considered a more robust estimate of inflation than the consumer price index by some economists, it generally yields similar or slightly more conservative estimates of current costs.

Sensitivity Analyses

We performed one-way and multi-way sensitivity analyses to account for important model assumptions and uncertainties. For clinical variables, our ranges for sensitivity analyses represent our judgment of the variation likely to be encountered in clinical practice on the basis of both the literature and discussion with experts.

To estimate the uncertainty in our findings we performed a probabilistic sensitivity analysis. We assigned distributions to eighteen variables which described the natural history of HIV and effectiveness of HAART in older patients (see Technical Appendix). We selected distributions appropriate to the type of variable (for example, we modeled probabilities using a beta distribution) and selected corresponding parameters using the method of moments. For variables which represented alternative scenarios rather than uncertain estimates, we sampled from discrete distributions reflecting our belief in the likelihood of each scenario being true. We performed a second-order Monte Carlo simulation with 1,000 iterations over the sampled distributions.

Model Calibration and Validation

Calibration and validation of the decision model and its outputs occurred as an iterative process throughout its development. To assess the output of the model, we compared our predicted time from infection until death for untreated patients (10.3 to 13.4 years) to published estimates (12.1 years) (103). To assess our long-term estimates of treatment efficacy, we compared the estimated proportion of patients with multi-drug resistant virus at 10 years (7.2%) to published estimates (9.2%, 95% CI 5.0% to 13.4%) (66). Finally, we compared our model's estimate of life expectancy of identified HIV infected patients on HAART (varying between 14.9 to 18.5 years) to other modeled estimates by King et al (160) and Paltiel et al (4).

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RESULTS

Benefit of Screening Due to Early Identification of HIV

We estimated the increase in survival that resulted from early identification of asymptomatic HIV and initiation of HAART through a screening program compared with identification on the basis of case finding. The benefit varied depending on age and decreased for older patients. For a 65-year old HIV-infected patient, early identification and treatment increased life expectancy by 0.58 years or 0.41 QALYs. For a 75-year old HIV-infected patient, the benefit was 0.30 years or 0.20 QALYs (Figure 2). In the Technical Appendix we demonstrate how such increases in life expectancy from a one-time HIV screening program in the current US population aged 55–64 could save over 120,000 life years attributed to

almost 170,000 individuals. In the 65–74 year cohort, an additional 40,000 life years would be gained by almost 92,000 individuals.

Cost Effectiveness of HIV Screening Program

The costs and benefits of voluntary one-time HIV screening for patients aged 55–75 years old depended on the prevalence of unidentified HIV, the age of the patient, and whether the patient has a sexual partner at risk of infection.

Benefit of HIV Screening to Patients with a Sexual Partner at Risk—If a patient has an uninfected partner at risk for infection and the prevalence of unidentified HIV was 0.5%, a voluntary one-time screening program improved life expectancy in 65-year old patients by 1.56 days or 1.31 quality-adjusted days at a cost of \$107 relative to current practice (incremental cost-effectiveness of \$30,020/QALY) (Figure 3a). For a 75-year old patient, the incremental cost was \$90, while incremental life expectancy was 0.95 days or 0.79 quality-adjusted days (incremental cost-effectiveness of \$41,520/QALY). At a lower HIV prevalence of 0.1%, the incremental cost-effectiveness of screening a 65-year old with a sexual partner at risk was \$91,410/QALY. At this prevalence, HIV screening exceeds \$100,000/QALY for patients 70 and older (Table 2 and Figure 3a) if traditional pre-test (estimated cost of \$35) and post-test counseling (estimated cost of \$10 for negative tests and \$35 for positive tests) is used.

Benefit of HIV Screening to Patients without a Partner at Risk—If a patient does not have a partner at risk for infection, HIV screening costs less than \$100,000 per quality-adjusted life year for all patients (< 80 years) if the prevalence of unidentified HIV is greater than 0.5% (Figure 3b). For a 65-year-old patient, HIV screening using traditional counseling costs \$55,440/QALY compared with current practice when the prevalence of HIV was 0.5%. At an HIV prevalence of 0.1% however, screening a patient (< 50 years) without a sexual partner increases costs more than \$100,000/QALY (Table 2 and Figure 3b) with traditional counseling.

Effect of Streamlined Counseling on Cost Effectiveness of HIV Screening

Current CDC guidelines for HIV screening recommend streamlined counseling, which reduces the time and costs associated with pre-test counseling and, for those who test negative, post-test counseling (1). Based on a recent time-costing analysis by the Veterans Affairs (VA) Quality Enhancement Research Initiative for HIV and Hepatitis (QUERI-HIV/HEP), in this analysis we assumed the pre-test counseling costs would be reduced, relative to comprehensive counseling, from \$35 to \$5, post-test counseling of patients who tested negative would be reduced from \$10 to \$2, and post-test counseling of patients who tested positive would remain unchanged (\$35). We further assumed streamlined counseling did not affect either adherence with screening or modification of risk behaviors. Under these assumptions, the incremental cost effectiveness of HIV screening was more economically attractive at all ages and prevalences of HIV (Figure 4). For patients with a sexual partner at risk, HIV screening incorporating streamlined counseling would cost less than \$60,000/QALY compared with current practice for patients up to 75 years of age, even if the prevalence of unidentified HIV was as low as 0.1% (Figure 4). For patients without a partner at risk, HIV screening incorporating streamlined counseling costs less than \$100,000/QALY for patients from populations where the HIV prevalence is 0.1% if patients were 75 or younger (Figure 4), and cost less than \$50,000/QALY at a prevalence of 0.5%.

Sensitivity Analyses

We evaluated scenarios in which HAART was less effective or more toxic in older patients. After assuming that the failure rate of HAART was increased by 20% in patients over 55, HIV screening with traditional counseling cost less than \$60,000 per QALY for patients of all ages if they had a sexual partner at risk and the unidentified HIV prevalence in the population was greater than 0.5%. If the unidentified prevalence of HIV was 0.1%, HIV screening cost less than \$65,000/QALY for patients aged 75 years and younger with streamlined counseling.

Assuming that HAART-related toxicity requiring treatment change increased by 25% in patients over 55 had minimal effects on the analysis and did not qualitatively change our results. It is also uncertain whether the non-AIDS age-specific mortality of HIV-positive patients is increased compared with uninfected patients. We therefore evaluated the effect of HIV screening if we assumed that HIV-positive patients had an age-specific mortality 25% greater than that of an uninfected cohort. Again, these assumptions did not qualitatively affect the results of our analysis. Finally, when we varied all three of these assumptions simultaneously for patients with a partner at risk, HIV screening with traditional counseling cost less than \$65,000 per QALY if the unidentified prevalence of HIV was 0.5% or greater. If the unidentified prevalence of HIV was 0.1%, HIV screening cost less than \$70,000/QALY for patients 75 years and younger with streamlined counseling.

We performed a probabilistic sensitivity analysis in which we simultaneously varied the values of variables defining the natural history of HIV and effectiveness of HAART in older patients. Assuming traditional counseling costs, for 65–74 year old patients with a sexual partner at risk from a population with the prevalence of unidentified HIV which ranged from 0.2 to 1.2%, the probabilistic sensitivity analysis estimated a median and mean incremental cost-effectiveness ratio of \$36,980/QALY and \$44,530/QALY respectively. A cost-effectiveness acceptability curve (Technical Appendix) demonstrated that, at a willingness-to-pay threshold of \$50,000/QALY, the probability that HIV screening in this population was cost-effective was 75%. The probability that HIV screening with traditional counseling costs was cost-effective with a willingness-to-pay threshold of \$100,000/QALY was 96%.

With streamlined counseling, the probabilistic sensitivity analysis predicted a median and mean incremental cost-effectiveness ratio of \$22,460/QALY and \$24,420/QALY respectively. The cost-effectiveness acceptability curve (Technical Appendix) with streamlined counseling demonstrates that, at a willingness-to-pay threshold of \$50,000/QALY, the probability that HIV screening in this population with streamlined counseling is cost effective was 97%.

Results of additional sensitivity analyses are included in the technical appendix. Sensitivity analyses with other model variables (Table 1) did not change our results substantially.

DISCUSSION

We found that the cost effectiveness of screening in patients between 55–75 years compares favorably to that of other interventions that are accepted as good uses of resources, particularly if providers implement screening with streamlined counseling and if the person being screened has a sexual partner at risk. Under these circumstances, screening cost less than \$60,000 per QALY gained, even with an unidentified prevalence as low as 0.1%. Screening at age 64 years, as recommended by the CDC, cost about \$41,000 per QALY gained with streamlined counseling and a partner at risk. Screening is more expensive in patients who do not have a partner at risk, or if traditional counseling is used.

Although evidence about the prevalence of HIV in the older age groups is sparse, the limited available data suggest that the prevalence is sufficiently high for screening to be cost effective. In a blinded serologic survey we performed of 8627 inpatients and outpatients at six Department of Veterans Affairs Health Care Systems, we found the prevalence of undocumented HIV infection was 0.7% (95% confidence interval [CI] 0.2% to 1.7%) in outpatients aged 55 to 64 years, 0.5% (95% CI, 0.2% to 1.2%) in outpatients aged 65 to 74, and 0.1% (0.0% to 0.06%) in outpatients aged 75 and older (157). Because the VA population differs from that in other health care settings, evidence about the prevalence of undocumented HIV in the over 55 age groups from other populations would be useful to help guide screening decisions. We note however, that among outpatients aged 65 to 74, the prevalence in other settings could be only one-fifth as high as we found and screening with streamlined counseling would still be cost effective for patients who are sexually active.

As noted, an important determinant of the cost effectiveness of screening is whether the screened person has a sexual partner or partners at risk. A recent study used a probability sample of 3005 U.S. adults and found that 73% of people who were 57 to 64 years of age were sexually active, as were 53% of people 65 to 74 years of age, and 26% of people 75 to 85 years of age (161). The National Health and Social Science Survey in 1992 studied 3,492 members of the US general population and found that 84% of individuals between age 50–54 and 69% of those aged 55–59 had at least one sexual partner in the past year. The National AIDS Behavioral Surveys administered in 1991–1992 estimated that the prevalence of having at least one risk factor for HIV infection was approximately 10% among individuals aged 50 years or older. In addition, a small percentage of those individuals with a known risk for HIV infection used condoms during sex, or had undergone testing and were much less likely to have adopted these prevention strategies than younger individuals who engaged in the same behavioral risks (162). These studies suggest that a significant number of people over age 50 have risk factors for HIV and that majority of individuals up to age 75 have a partner at risk for infection.

Based on the results of our cost-effectiveness analyses, the data available on prevalence and the relatively high rates of sexual activity in people over age 55, we recommend one-time voluntary HIV screening with streamlined counseling on a routine basis for all persons aged 55–64 and one-time screening on a targeted basis to sexually active persons aged 65–74, if the HIV prevalence is $> 0.1\%$. For people aged 65 to 74 who do not have a partner at risk, screening costs between \$50,000/QALY and \$100,000/QALY gained with prevalence between 0.1% and 0.5%. Thus, screening is more expensive if the person is not sexually active, but is still a reasonable option, particularly if prevalence approaches 0.5%.

One approach that providers can use to estimate the prevalence of HIV is to begin a screening program, and assess the number of positive tests in the screened population. If approximately 4000 individuals are screened without a positive test, a prevalence of 0.1% can be excluded with 95% confidence, and the population would fall outside the prevalence threshold (0.1%) recommended for screening by the CDC (1).

The cost effectiveness of screening remained favorable if HAART were modestly less effective, or led to modestly higher rates of adverse events than in younger patients. An increase in age-specific mortality of 25% in infected patients did not substantively change the cost effectiveness of screening. This finding would not hold for patients whose life expectancy was substantially shortened by diseases with high mortality such as cancer or congestive heart failure. In general, however, our findings support the usefulness of screening older individuals who do not have high-mortality comorbidities if the prevalence of HIV is above 0.1% to 0.5%. Our analysis included three suppressive antiviral regimens before the start of nonsuppressive therapy. With the approval of new antiretrovirals, a fourth

suppressive regimen may be feasible, thus we may have underestimated the benefit from antiretroviral therapy in the elderly.

In conclusion, we found that routine HIV screening is cost effective in the age range (up to age 64) and prevalence (greater than 0.1%) recommended by the CDC. If the screened population has an unidentified prevalence of 0.1% or greater, HIV screening in older individuals aged 65 to 75 can also reach conventional levels of cost effectiveness if screening can be done inexpensively, such as by using streamlined counseling. Our analyses suggest that screening decisions in patients over 64 years of age should consider whether there are partners at risk, the expense of screening, and whether there are life-threatening comorbid conditions. Advanced age alone should not preclude screening for HIV. Rather, for many people in this age group, the cost effectiveness of screening falls within the range of other accepted interventions.

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Technical Appendix

Public Health Benefit of HIV Screening

To estimate the public health benefit of HIV screening within the current U.S. population, we used the results of a blinded serologic survey of HIV within the VA population (157), the effect of HIV screening and early identification on life expectancy (shown graphically in Figure 2), and the current population of the United States. These data were used to estimate the life expectancy gain in the current US population from early HIV identification through a one-time voluntary HIV screening program. As the table below demonstrates, under these assumptions, a one-time HIV screening program in the current US population aged 55–64 would save over 120,000 life years attributed to almost 170,000 individuals. In the 65–74 year cohort, an additional 40,000 life years would be gained by almost 92,000 individuals.

Variable	Age Cohort, years	
	55–64	65–74
U.S. population, N [*]	24,274,684	18,390,986
Prevalence of unidentified HIV, % (95% confidence interval) [†]	0.7 (0.2–1.7)	0.5 (0.2–1.2)
Estimated number of HIV-infected individuals unaware of their HIV Status, N (range)	169,923 (48,549–412,670)	91,955 (36,782–220,692)
Estimated life expectancy gain per individual from early HIV identification, years	0.7227	0.4391
Estimated life expectancy gain in current US population from early HIV identification, years (range)	122,805 (35,087–298,242)	40,374 (16,150–96,899)

^{*} Based on 2000 US Census Data

[†] Estimated from blinded serologic survey of 8627 inpatients and outpatients at six Department of Veterans Affairs Health Care Systems (157)

HIV Screening Frequency

In our main analyses we focused on the incremental cost-effectiveness of a one-time voluntary HIV screening program as compared with current practice. In sensitivity analyses however, we wanted to explore the incremental costs and benefits of a repeated HIV screening program – especially in populations where the incidence of HIV may be increased. The figure below demonstrates the effect of screening frequency on the incremental cost-effectiveness of screening at various HIV incidence rates assuming patients are 55-years old and the prevalence of HIV is 1% in the cohort. 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 is twice the baseline rate, and the dashed line represents the cost-effectiveness of recurrent screening when the incidence of HIV 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 3 years with screening every 5 years). Recurrent screening becomes more economically favorable as the incidence increased – yet one time screening appears to be the best use of limited healthcare resources in these older cohorts. Similar findings were found in older cohorts and at varying prevalences.

Efficacy of Non-Suppressive Therapy

To explore the effect of additional regimens or increased efficacy of non-suppressive therapy, we varied the decrement in viral load which patients received while on non-suppressive therapy. Under our base-case assumptions (1.0 log₁₀ copies/mL decrement with non-suppressive therapy) screening a 55-year old individual with a sexual partner-at-risk for HIV cost \$71,060/QALY compared with current practice if the prevalence of unidentified HIV was 0.1%. Under these same assumptions, screening a 75-year old individual for HIV cost \$143,060/QALY compared with current practice. If the decrement in viral load realized through non-suppressive therapy was increased to 2 log₁₀ copies/mL, the incremental cost-effectiveness of HIV screening became more favorable at \$56,250/QALY and \$118,480/QALY in the 55- and 75-year old individuals with a partner-at-risk. Similarly, if the decrement in viral load was increased to 4 log₁₀ copies/mL, the incremental cost-effectiveness ratios of HIV screening was further reduced to \$43,780/QALY and \$110,980/QALY in the 55- and 75-year old cohorts.

Cost and Efficacy of Streamlined Counseling

Because the cost and feasibility of streamlined counseling in elderly patients who have competing comorbid conditions and may not have been tested previously is uncertain, we explored the effect of a more expensive streamlined counseling scenario in sensitivity analyses. In this analysis we assumed that a pre-test counseling session cost \$15 dollars (base-case value = \$5 in our streamlined analysis), and that post-test counseling for a negative test result cost \$5 (base-case value = \$2 in our original streamlined analysis). In our original analysis, if the prevalence of unidentified HIV was 0.1%, then screening patients aged 75 who had a partner-at-risk cost \$83,680/QALY compared with current practice. Under our assumptions of a more costly streamlined counseling scenario, this incremental cost-effectiveness ratio increased marginally to \$88,120/QALY. Although the incremental cost-effectiveness ratio increased for all age and prevalence combinations, these increases did not change our qualitative results or our clinical recommendations.

We also explored a scenario where the efficacy of streamlined counseling was reduced. It is important to note that under streamlined counseling, patients who test positive for HIV infection receive the same counseling (both in terms of costs and efficacy) as those who receive traditional counseling and therefore the true reduction of streamlined counseling effects on behavior modification is small. If we assumed that streamlined counseling reduced the efficacy of counseling from our base-case value of 20% reduction in transmission to a 10% reduction, then the incremental cost-effectiveness of HIV screening increases to \$19,800/QALY, \$23,090/QALY, and \$45,550/QALY in a cohort of 65-year olds with prevalence of unidentified HIV of 1%, 0.5%, and 0.1% respectively. If we assumed that streamlined counseling completely eradicated any benefit from counseling on transmission then the incremental cost-effectiveness of screening increased although the effects again are minimal (\$23,050/QALY, \$26,700/QALY, and \$50,730/QALY in 65-year old cohort with 1%, 0.5%, and 0.1% prevalence of HIV respectively).

Finally, in our exploration of the effects of streamlined counseling, we assume that individuals who are sexually active have one partner-at-risk for transmitting their infection. In a sensitivity analysis, we varied this assumption to explore the effects on our results if individuals who were sexually active had 2 partners at risk. As expected, if individuals had a greater number of sexual partners-at-risk, this increased the benefits of HIV screening and early identification. As an example, if the prevalence of unidentified HIV in a population was 0.05%, HIV screening individuals aged 75 years who had one partner-at-risk would cost \$21,560/QALY if streamlined counseling was used. If however these individuals had two partners-at-risk, such HIV screening would become more favorable with an incremental cost-effectiveness ratio of \$10,100/QALY compared with current practice.

Probabilistic Sensitivity Analysis

To estimate the uncertainty in our findings we performed a probabilistic sensitivity analysis. We assigned distributions to twenty variables which described the natural history of HIV and effectiveness of HAART in older patients. For 15 variables, we used parametric distributions as described below:

Variable	Mean	SE	Selected Distribution
Prevalence of HIV, % *	0.5	0.27	BETA
Decrease in viral load during virologic rebound	0.5	0.5	GAMMA

Variable	Mean	SE	Selected Distribution
Decrease in viral load with nonsuppressive therapy	1	0.5	GAMMA
Increase in viral load after failed therapy (with AIDS)	1	0.5	GAMMA
Increase in viral load after failed therapy	0.8	0.4	GAMMA
Viral load during virologic suppression	1.3	0.6	GAMMA
Probability of not achieving virologic suppression during 1 st regimen	0.20	0.20	BETA
Probability of not achieving virologic suppression during 2 nd regimen	0.35	0.21	BETA
Probability of not achieving virologic suppression during 3 rd regimen	0.7	0.15	BETA
Probability of intolerance to HAART requiring discontinuation	0.25	0.13	BETA
Relative risk for discontinuation of HAART during 2 nd regimen	1.4	0.84	LOG NORMAL
Relative hazard of AIDS per increase in CD4 count	0.0154	0.12	LOG NORMAL
Relative hazard of AIDS per increase in viral load	0.43	1.25	LOG NORMAL
Relative hazard of death from AIDS per increase in CD4 count	0.118	1.43	LOG NORMAL
Relative hazard of death from AIDS per increase in viral load	0.64	0.92	LOG NORMAL

* The prevalence distribution was estimated from the blinded serologic survey of 8627 inpatients and outpatients at six Department of Veterans Affairs Health Care Systems (157).

For 5 variables, we sampled from discrete values, as defined below:

Variable	Discrete Values Sampled*
Age, years	65, 66, 67, 68, 69, 70, 71, 72, 73, 74 [†]
Multiplier on age-specific mortality for HIV infected patients over 55	1.0, 1.5
Relative risk of achieving suppression in patients over 55	0.5, 1.0
Relative risk of HAART discontinuation in patients over 55	1.0, 1.5
Relative risk for discontinuation of HAART during 3 rd regimen	1,2,3,4 [‡]

* Where not specified, the probability of each value was assumed to be equal

[†] The distributions of ages represented those of the US population based on US census data.

[‡] Corresponding probabilities are 0.5 (1); 0.25 (2); 0.25 (3); 0.25 (4)

We evaluated the incremental cost-effectiveness of HIV screening a 65–74 year old patient with a sexual partner in a population where the unidentified prevalence of HIV ranged from 0.2–1.2 %.

The following two figures show the results of our Monte Carlo simulation under assumptions of either traditional or streamlined counseling as an acceptability curve. Cost effectiveness acceptability curves allow decision makers to determine the probability that HIV screening in the given population is cost-effective at various willingness-to-pay thresholds (the highest incremental cost-effectiveness ratio that people would be willing to accept as reasonable value for their health care dollar).

Cost-Effectiveness Acceptability Curve of HIV Screening Assuming Traditional Counseling

Cost-Effectiveness Acceptability Curve of HIV Screening Assuming Streamlined Counseling

Figure 1. Schematic Representation of the Markov Model

The square node at the left represents the decision to screen for HIV or not. The patient's health thereafter is simulated by a Markov model shown on the right. Patients may enter the model with prevalent HIV infection (asymptomatic or symptomatic HIV or AIDS) or they may be uninfected. Each month, uninfected patients are at risk of developing HIV infection. Patients who have asymptomatic disease may progress to symptomatic HIV or remain in the asymptomatic health state. Patients that have symptomatic HIV infection may progress to an AIDS defining condition, or may remain with symptomatic HIV. Patients with AIDS may either die from their infection or remain with AIDS. Each month all patients may be identified either through a voluntary screening program in the HIV screen arm, or through symptom-based case finding in the symptomatic HIV and AIDS health states in both the HIV screen arm and the No Screening arm. Throughout the patients' lifetime, all patients are at risk for non-HIV related mortality. Health states are further characterized by viral load level, CD4 count, and antiretroviral treatment history (not shown).

Figure 2. Effect of Early Identification of HIV Infection on Life Expectancy

The effect on undiscounted life expectancy (solid line) and quality-adjusted life expectancy (dashed line) of identifying asymptomatic HIV infection, as compared with symptom-based case finding.

(a)

(b)

Figure 3. Incremental Cost Effectiveness of HIV Screening in Patients Over 55 Years of Age with Traditional Counseling

Each figure represents the incremental cost effectiveness of HIV screening (assuming traditional counseling) compared with current practice for patients of varying ages with differing underlying prevalence of unidentified HIV. The solid line represents an unidentified HIV prevalence of 0.1%, the black dashed line represents an HIV prevalence of 0.5%, and the grey line represents an HIV prevalence of 1%. In each figure the horizontal dashed lines indicate a cost effectiveness threshold of \$50,000 and \$100,000 per QALY. (a) Patients with a sexual partner at risk (b) Patients without a partner at risk. QALY = quality-adjusted life year, HIV = human immunodeficiency virus

Figure 4. Incremental Cost Effectiveness of Screening in Patients Over 55 Years of Age with Streamlined Counseling

The incremental cost effectiveness of HIV screening compared with current practice for patients of varying ages with differing underlying prevalence of unidentified HIV assuming implementation of streamlined counseling. The solid line represents an unidentified HIV prevalence of 0.1%, the black dashed line represents an HIV prevalence of 0.5%, and the grey line represents an HIV prevalence of 1%. The horizontal dashed lines indicate a cost effectiveness threshold of \$50,000 and \$100,000 per QALY or LY gained. (a) Patients with a sexual partner at risk (b) Patients without a partner at risk. QALY = quality-adjusted life year, LY = life year, HIV = human immunodeficiency virus

Table 1

Input Variables and Sources

Variable	Base-Case Value	Range	Source
Demographic Variables			
Age of patient in HIV screening program, years	55–75		
Prevalence of unidentified HIV among patients, %	0.1–1.0		
Proportion of prevalent unidentified HIV that are:			
Asymptomatic, %	75	50–100	Estimate based on (12–17)
Symptomatic, %	15	0–30	
AIDS, %	10	0–20	
Annual incidence, %	0.02–0.0003		(18, 19)
Proportion of uninfected population that is female, %	60	50–70	(20)
Proportion of HIV infected population that are men, %	75	50–90	(21)
Proportion of male HIV infected population that are men-who-have-sex-with-men, %	50	25–75	(21)
Relative risk of age specific mortality of infected patients over age 55	1.0	1.0–1.5	(22)
Natural History Variables			
CD4 count when infected with HIV	900		(23)
CD4 count (10^9 cells/L) at which symptoms start occurring	0.350	0.250–0.500	(23)
Case Finding Variables			
CD4 count (10^9 cells/L) at which maximum case finding rate is reached	0.050	0–0.350	Assumed
Maximum annual symptom-based case finding rate, %	80	50–100	Assumed
HIV Testing Variables			
Adherence with HIV screening program, %	100	50–100	(24–26)
Sensitivity of screening test, first 3 months after infection, %	60	11–83	(27–29)
Sensitivity of screening test, established disease, %	99.5	98–99.9	(27, 29, 30)
Specificity of entire sequence of screening tests, %	99.9994	99–100	(27, 29, 31)
Probability that a patient returns to receive HIV test results, %	80	70–100	(25, 32–40)
Months before false positive HIV diagnosis is discovered	2	0–12	Assumed
Frequency of CD4 testing when off HAART, months	3	3–6	(41)
Treatment Variables			
CD4 count at which HAART begins (10^9 cells/L)	0.350		(41–46)
Viral load at which HAART begins ($\log_{10}$ copies/mL)	4.6		
Frequency of CD4 and viral load testing during HAART treatment, months	3	2–6	
Increase in CD4 count when starting HAART	$110+535*(cdstart^{0.98}/(cdstart^{0.98}+260))^{1/3}$		(47–51)
Decline in CD4 count with detectable viral load	$-79.2+33.5*\log_{10}$ viral load		(52, 53)
Viral load ($\log_{10}$ copies/mL)			
Set point	4.6	3.0–6.0	(15, 54)
During virologic suppression	1.3	1.0–2.7	(55)
During virologic rebound	4.1	3.6–4.6	(56, 57)

Variable	Base-Case Value	Range	Source
Incremental rise above set point ^S			
After suppressive therapy failed	0.8	0–1.5	(58–66)
After suppressive therapy failed and AIDS	1.0	0–2.0	
Decrease with non-suppressive therapy	1.0	0–2.0	(67–71)
Relative hazard of AIDS per			
1 log ₁₀ copies/mL decline in plasma viral load	0.43	0.28–0.65	(63, 65, 66, 72–88)
1 log ₁₀ 10 ⁹ cells/L increase in CD4 count	0.0154	0.0002–1.0	
Relative hazard of death from AIDS per			
1 log ₁₀ copies/mL decline in plasma viral load	0.64	0.55–0.75	
1 log ₁₀ 10 ⁹ cells/L increase in CD4 count	0.118	0.064–0.329	
Probability of achieving virologic suppression, %			
1 st regimen	80	30–98	(12, 66–72, 77, 79, 90, 91, 108–144)
2 nd regimen	65	20–80	
3 rd regimen	30	5–40	
Relative risk of achieving suppression in patients over 55	1.0	0.5–1.0	(89–98)
Rates of virologic rebound			
1 st rebound, % at 2 years	15	6–30	(55, 68, 98–114)
Per subsequent regimen (relative hazard)	2.0	1.0–6.0	(100, 109, 115, 116)
Intolerance requiring discontinuation, 1 st regimen, %	25	5–40	(67–69, 98, 102, 103, 107, 111, 112, 115, 117–126)
Relative risk for discontinuation, 2 nd regimen	1.0	1–4	
Relative risk for discontinuation, 3 rd regimen	1.4	1–4	
Relative risk for discontinuation in patients over 55	1.0	1.0–1.50	(91, 94, 96)
Transition rate (events/100 patient years)			
From HIV to AIDS	6	2–12	(52, 77, 84)
From AIDS to death	3	1–10	(84)
Transmission Variables			
Age of patients' sexual partners, years	55–75		Assumed to be the same as the infected patient
Number of susceptible partners at risk	1	0–10	(127, 128)
Annual probability of infecting a sexual partner, men-who-have-sex-with-men, %	4	1–5	(103, 129–131)
Annual probability of infecting a sexual partner, heterosexual men, %	3	0.5–5	(132–136)
Annual probability of infecting a sexual partner, heterosexual women, %	1	0.5–4	(132–135)
Relative risk of infectivity given 1 log ₁₀ copies/mL change in viral load	2.45	1–3	(137)
Effectiveness of testing and counseling in reducing the number of sexual transmissions, % reduction in infectivity	20	0–50	(138–140)
Costs, 2007\$			
HIV test, negative result	12.41	1–20	Cost of ELISA test at Palo Alto VA based on Medicare pricing

Variable	Base-Case Value	Range	Source
HIV test, positive result	51.87	40–60	Cost of ELISA and Western blot tests at Palo Alto VA based on Medicare pricing
HIV pre-test counseling	35	5–60	Estimate based on (2, 27) and VA time-cost analysis (unpublished data)
HIV post-test counseling post (negative test)	10	2–30	Estimate based on (2, 27) and VA time-cost analysis (unpublished data)
HIV post-test counseling post (positive test)	35	10–100	Estimate based on (2, 27) and VA time-cost analysis (unpublished data)
CD4 count, per test	96	65–120	(141)
Viral load, per test	127	90–200	(141)
Annual cost of HIV infection (CD4 > 0.500 10 ⁹ cells/L), on HAART*	3,112	2,228–5,000	(142, 143)
Annual cost of HIV infection (CD4 0.200–0.500 10 ⁹ cells/L), on HAART*	5,324	3,821–6,369	
Annual cost of HIV infection (CD4 < 0.200 10 ⁹ cells/L), on HAART*	7,937	5,697–12,000	
Annual cost of AIDS, on HAART*	11,491	8,251–25,000	
3-drug antiretroviral therapy	14,369	8,251–16,307	(41, 144–147)
Incremental cost of 4-drug antiretroviral therapy	2,588	1,540–12,579	
Annual cost of salvage therapy	16,957	0–28,885	
HAART side effect, per episode	155	98–733	(148–150)
Age-specific medical costs unrelated to HIV	2,672–4,210		Based on age-specific healthcare expenditures http://www.bls.gov/cex/csxann05.pdf
Quality of Life			
Current health			Gender and age-specific utilities for current health from (151)
Asymptomatic HIV infection (unknown)	0.91	0.85–1.0	(156)
Asymptomatic HIV infection, diagnosed			
First year	0.84	0.80–1.0	(156)
Subsequent years	0.89	0.80–1.0	(156)
Symptomatic (untreated) HIV	0.79	0.45–1.0	(152–156)
HIV infection on HAART	0.83	0.45–1.0	(152–156)
AIDS infection	0.73	0.24–0.80	(152–156)
Quality of life loss with HAART side effects (multiplier)	0.53	0.44–0.62	(2, 149, 150)
Other			
Discount rate, annual %	3	0–5	(9)
Cycle length, months	1		Assumed

All probabilities are annual unless otherwise noted. Monthly transition probabilities were estimated where needed based on annual probabilities using the relationship of $p=1-e^{-rt}$.

All costs are in 2007 U.S. dollars, ‡treatment costs are listed exclusive of HAART drug therapy cost

HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome; HAART = highly active antiretroviral therapy.

[†]cdstart denotes the initial CD4 count, we assumed all patients had an increase of at least 0.060×10^9 cells/L.

[§]maximum viral load was $6.0 \log_{10}$ copies/mL

Table 2

Health and Economic Outcomes with Traditional Counseling, Prevalence of HIV = 0.1%

Strategy and Age of Patient, Years	Cost, \$	Incr. Cost, \$	Life Expectancy, years	Incr. Life Expectancy, days	Incr. Cost Effectiveness, \$/LY	Quality-Adjusted Life Expectancy, QALYs	Incr. Quality-Adjusted Life Expectancy, QALDs	Incr. Cost Effectiveness, \$/QALY
Patients With Sexual Partner At Risk								
55 No Screening	47,646		16.847			14.276		
HIV Screening	47,716	70	16.846	0.44	59,230	14.277	0.36	71,060
60 No Screening	44,297		14.872			12.466		
HIV Screening	44,365	68	14.873	0.38	65,850	12.467	0.31	78,910
65 No Screening	40,242		12.857			10.607		
HIV Screening	40,308	66	12.858	0.33	76,570	10.608	0.26	91,410
70 No Screening	35,499		10.808			8.853		
HIV Screening	35,563	64	10.808	0.25	93,010	8.854	0.21	110,630
75 No Screening	30,344		8.815			7.135		
HIV Screening	30,406	62	8.816	0.18	119,820	7.135	0.16	143,060
Patients Without A Partner At Risk								
55 No Screening	47,561		16.851			14.280		
HIV Screening	47,640	79	16.852	0.37	81,200	14.281	0.26	112,180
60 No Screening	44,244		14.874			12.469		
HIV Screening	44,320	76	14.875	0.31	89,010	12.469	0.22	124,680
65 No Screening	40,212		12.858			10.608		
HIV Screening	40,285	72	12.859	0.26	101,240	10.609	0.18	142,700
70 No Screening	35,481		10.808			8.854		
HIV Screening	35,550	69	10.809	0.21	121,090	8.855	0.15	172,090
75 No Screening	30,333		8.816			7.135		
HIV Screening	30,398	65	8.816	0.15	154,880	7.136	0.11	222,920

Note: Costs and life expectancy estimates are discounted at 3% annually. LY = life years, QALY = quality-adjusted life years, QALD = quality-adjusted life days, HIV = human immunodeficiency virus