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The Clinical Impact and Cost-Effectiveness of Routine, Voluntary HIV Screening in South Africa

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Abstract

Background—Although 900,000 HIV-infected South Africans receive antiretroviral therapy (ART), the majority of South Africans with HIV remain undiagnosed.

Methods—We use a published simulation model of HIV case detection and treatment to examine three HIV screening scenarios, in addition to current practice: 1) one-time; 2) every five years; and 3) annually. South African model input data include: 16.9% HIV prevalence, 1.3% annual incidence, 49% test acceptance rate, HIV testing costs of $6.49/patient, and a 47% linkage-to-care rate (including two sequential ART regimens) for identified cases. Outcomes include life expectancy, direct medical costs, and incremental cost-effectiveness.

Results—HIV screening one-time, every five years, and annually increase HIV-infected quality-adjusted life expectancy (mean age 33 years) from 180.6 months (current practice) to 184.9, 187.6 and 197.2 months. The incremental cost-effectiveness of one-time screening is dominated by screening every five years. Screening every five years and annually each have incremental cost-effectiveness ratios of $1,570/quality-adjusted life year (QALY) and $1,720/QALY. Screening annually is very cost-effective even in settings with the lowest incidence/prevalence, with test acceptance and linkage rates both as low as 20%, or when accounting for a stigma impact at least four-fold that of the base case.

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Conclusions—In South Africa, annual voluntary HIV screening offers substantial clinical benefit and is very cost-effective, even with highly constrained access to care and treatment.

Keywords

HIV; screening; cost-effectiveness; South Africa

INTRODUCTION

In 2007, the World Health Organization (WHO) recommended routine HIV testing of all persons in countries, like South Africa, with generalized epidemics -- a recommendation still far from implementation.1 Of the five million South Africans currently living with HIV, over three million remain unaware of their infection and unable to access lifesaving care and counseling.2, 3 Although there are over 4,000 HIV voluntary, counseling and testing (VCT) centers throughout South Africa, only 47% of South Africans report ever having been tested for HIV infection and only an estimated 34% of all HIV-infected individuals (1.9 million patients) are receiving HIV care.4, 5

Obstacles to implementing the WHO recommendations for testing include cost, limited capacity for HIV care, and stigma.[4, 6–9] Soon after the release of the WHO recommendations, the South African province of Free State suspended antiretroviral treatment admissions due to financial constraints.[6] Such action implies an inability to pay for the care of persons with HIV already detected and in need of treatment, let alone to cover the costs of expanded testing and care of newly detected cases. Further, despite the tremendous progress that has been made in shifting cultural norms, both HIV testing and living with known HIV infection remain highly stigmatized.[4, 7–9]

Implementation of the WHO HIV testing recommendations in South Africa will inevitably be hampered by insufficient treatment resources, inadequate linkage to care and persistent stigma. Our objective was to take these challenges into explicit consideration – adopting a deliberately conservative approach with regard to the availability of funds, rates of program uptake, access to care, and not incorporating the benefits of preventing HIV transmission – to provide decision makers with a realistic assessment of the clinical impact and cost-effectiveness of HIV screening in South Africa.

METHODS

Analytic Overview

We use the Cost-Effectiveness of Preventing AIDS Complications (CEPAC)-International model to examine three HIV screening strategies (outside the context of pre-natal HIV screening), in addition to current practice: one-time screening at age 33 years, screening every five years, and annual screening (see Technical Appendix).10–13 We choose the every five years screening strategy as an intermediately aggressive and more immediately achievable approach compared to annual testing. For each strategy, we project mean quality-adjusted life expectancy, and mean per person lifetime costs (in 2006 US$) for both HIV-infected individuals and the general population. Outcome measures are assessed from a societal perspective (excluding patient travel time and lost wages), and quality-adjusted life expectancy and costs are discounted at 3% annually.14 Cost-effectiveness ratios, calculated by comparing each strategy to the next least costly, non-dominated strategy, are expressed in incremental cost per quality-adjusted life-year (QALY). Guided by recommendations from the WHO, we consider strategies with cost-effectiveness ratios less than the Gross Domestic Product (GDP) *per capita* – one measure of a nation's ability to pay – in South Africa ($5,400) to be "very cost-effective."[15, 16] Sensitivity analyses examine uncertainties in

model parameters, as well as criticisms of expanded routine testing, notably, limited test acceptance, incomplete ART availability, stigma, and cost.

Disease Model

The CEPAC-International model is a state-transition model of HIV disease and treatment in resource-limited settings (see Technical Appendix).[10–13] In the model, a hypothetical patient's health state (defined by CD4 count and HIV RNA) in any given monthly cycle predicts progression of HIV disease; in the absence of effective ART, HIV RNA level determines the monthly decline in CD4 cell count, resulting in increased risks of opportunistic disease and chronic HIV-related mortality.[17, 18] Mortality risks accrue from opportunistic diseases, chronic-HIV-related causes, and non-HIV-related causes.[18, 19]

In accordance with South African treatment standards, patients with diagnosed HIV infection who are successfully linked to care attend quarterly clinic visits and receive bi-annual CD4 counts.[20] When treatment criteria are met (either CD4 <350/μl or WHO Stage 4 disease), ART is initiated.[20, 21] According to South African treatment guidelines, we assume all patients receive the same first-line (tenofovir/lamivudine/efavirenz) and second-line (zidovudine/lamivudine/lopinavir/ritonovir) regimens.[20] Successful HIV RNA suppression leads to increased CD4 count and a concomitant reduction in the risk of opportunistic disease and death.[18, 22, 23] Patients experiencing virologic suppression on these regimens have an ongoing risk of treatment failure, resulting in virologic rebound and CD4 count decline. In the absence of HIV RNA monitoring, detection of treatment failure, based on observation of a 30% CD4 decline from peak or a severe opportunistic disease while receiving ART, triggers a switch to the second (and final) available ART regimen, on which the patient remains until death.[24]

Screening Model

Entry into the disease model is regulated by a population-level model of HIV detection that captures HIV prevalence and incidence (see Technical Appendix).[25, 26] Briefly, this model allows users to define characteristics (age, sex, CD4 count, HIV RNA level, history of opportunistic disease) of patients who are already HIV-infected at the simulation outset. Given the demographic characteristics of the HIV-negative subpopulation and the user-defined incidence of HIV infection, the model determines if and when a new HIV infection occurs.

Undiagnosed cases of HIV infection may be detected by one of three mechanisms: 1) "background testing," as occurs currently in VCT sites, tuberculosis clinics, sexually transmitted infection centers, or antenatal clinics; 2) presentation with an AIDS-defining opportunistic disease; or 3) an expanded routine HIV screening program. In this study, "current practice" is defined as detection via mechanisms 1 and 2, but not 3. To be conservative with respect to the value of expanded screening, the model assumes that detection via either background testing or opportunistic disease development is completely accurate and always results in successful linkage to care. Expanded screening programs, in contrast, have "leakage" based on user-specified test acceptance and linkage-to-care rates. While all HIV-infected individuals enter the disease model, only those who are HIV-tested, diagnosed, linked to care, and meet eligibility criteria receive ART and opportunistic disease prophylaxis. Likewise, only patients with an HIV diagnosis who link to care accrue HIV-related costs. This is because costs captured in the model are intended to represent services that would only incur with an HIV diagnosis.

In an attempt to quantify the impact of stigma on psychosocial health, we first assign quality of life decrements to HIV testing itself ("test-associated stigma"), regardless of the HIV

serostatus of the individual tested. In the base case, we assign a high degree of test-associated stigma by basing the decrement on quality of life values associated with the anxiety of waiting for a confirmatory test result following a positive screen (Table 1).[27] The reported decrement in quality of life is 0.32, measured over the course of a single week. To spread this value evenly over the one-month cycle time used in the model, we used a monthly decrement of 0.32/4 = 0.08. The quality of life decrement associated with the HIV test applies only to those who are tested and only in the month of testing. Recognizing the scarcity of data on "test-associated stigma" either in the US or in South Africa, we consider in sensitivity analyses quality of life decrement values ranging from 0.0 to 1.0 in the month of testing.

We also consider the stigma associated with a known diagnosis of HIV infection ("diagnosis-associated stigma"). To account for potentially diminished psychosocial health, we apply a quality of life penalty -- derived from the decrement associated with a new diagnosis of asymptomatic HIV infection. The quality of life decrement associated with diagnosis-associated stigma is applied starting in the month when a patient receives an HIV diagnosis (Table 1); this monthly decrement is maintained until death.[28] This penalty is imposed regardless of whether the patient links to care or is initiated on antiretroviral therapy. The impact of diagnosis-associated stigma is also examined in sensitivity analyses.

We recognize that stigma is one of many factors that may diminish quality of life in HIV disease, including opportunistic infections and treatment-related toxicities. We sought to understand the magnitude of the potential stigma-related harms due to HIV testing. Accordingly, we portrayed both the test- and disease-associated stigma effects in an isolated and deliberately unfavorable light. We therefore considered the hypothetical case where all patients who have not been tested for HIV enjoy a quality of life equivalent to perfect health (i.e., the quality adjustment value assigned to all untested health states is 1.0). This is not to deny the reality that quality of life in HIV is influenced by a host of additional considerations, including opportunistic infections and treatment-related toxicities. Rather, it is to examine just how great an impact stigma alone might reasonably exert.

Input Parameters (Table 1)

Data on the population and clinical characteristics of the simulated cohort are derived from several South African studies, including the Cape Town AIDS Cohort (CTAC).[18] We first perform the simulation with 16.9% HIV prevalence and 1.3% annual incidence (adults aged 15–49 years) based on national estimates from the South Africa Human Sciences Research Council (base case).5, 29 We then repeat the analyses for province-specific prevalence and incidence estimates.5

Test acceptance (49%) and linkage-to-care rates (47%) for those identified are derived from ongoing South Africa testing programs and are, by design, lower than the 64–69% test acceptance rate found in a 2008 South African survey where voluntary HIV screening was routinely offered.5, 32, 39 The potential for accepting the offer of any given test is likely correlated with prior test acceptance behavior. Lacking any data on such conditional behavior, we assume average participation (49%) each time a test is offered and consider alternative values ranging from 0–100% in sensitivity analysis. We assume a point-of-care rapid HIV test, with 99.6% sensitivity and 98.0% specificity.37 Reactive results are confirmed via a second rapid test.32

Individuals enter the simulation with a mean age of 32.8 (± 9.2) years.[18] Patients with prevalent HIV infection have CD4 count and HIV RNA distribution parameters defined by South African cohorts (Table 1).[18, 35] We estimate the proportion of HIV-infected

individuals in the acute and chronic stages of disease based on published reports on the natural history of HIV-infected patients in South Africa.[40, 41]

The median CD4 cell count of chronically HIV-infected persons in the cohort is 288/μl (SD 331/μl). Data on natural history and on cotrimoxazole prophylaxis efficacy have been previously described.[17, 18, 38, 42] Mean monthly CD4 cell count decline, determined by HIV RNA level, ranges from 3.0–6.4 cells/μl.[17] Persons initiate ART with a CD4 count <350/μl or if they present with an AIDS-defining opportunistic disease.[20, 21] ART-eligible patients receive a first-line non-nucleoside reverse transcriptase inhibitor-based regimen followed by a second-line regimen using a boosted protease inhibitor. In the absence of clinical trial or large cohort data reporting the efficacy of 2nd-line ART in South Africa, we assumed the same efficacy for 1st and 2nd-line ART (48-week suppression of 75%).[22] CD4 cell counts, among those with successful virologic suppression, increase by 168 cells/μl in the first 48 weeks, followed by an average increase of 3 cells/μl/month until virologic failure.23

We derive the direct medical costs of HIV care (clinic visits, inpatient days, and monitoring tests) using healthcare utilization and unit costs in the CTAC cohort.31, 33 ART costs are from the Clinton Foundation HIV/AIDS Initiative (CHAI) 2009 list of negotiated prices for generic drugs in resource-limited settings (Table 1).[36] The costs of HIV test kits and post-test counseling and referral are applied for patients who receive testing through a routine screening program; these tests costs are not incurred for patients diagnosed with HIV via background testing or development of an opportunistic disease.[32]

RESULTS

Base Case

Clinical and Economic Impact of Screening—In the base case, the discounted quality-adjusted life expectancy of HIV-infected individuals is 180.6 months (15.1 years, undiscounted 285.6 months, or 23.8 years) and the average discounted life expectancy in the overall population is 213.7 months (17.8 years, undiscounted 354.3 months, or 29.5 years) (Table 2). This population life expectancy is consistent with that reported in South Africa.[19] The addition of a single, one-time HIV screen increases quality-adjusted life expectancy to 184.9 months (undiscounted 291.9 months) for HIV-infected individuals and 215.7 months (undiscounted 357.6 months) in the overall population. Screening every five years or annually increases the discounted quality-adjusted life expectancy of HIV-infected persons to 187.6 and 197.2 months (undiscounted 298.3 and 317.2 months). Compared to current practice, all screening strategies increase mean CD4 count at the time of HIV detection.

Expanded screening (one-time, every five years, and annually) increases average per person lifetime costs from $2,330 for current practice to $2,570, $2,740 and $3,330. The fraction of these total per person costs that are directly related to screening range from 0.1% (one-time screen) to 0.3% (screening every five years) to 1.0% (annual screening). The incremental cost-effectiveness of every five year screening weakly dominates one-time screening, with a ratio of $1,570/quality-adjusted life year (QALY), compared to current practice. Compared to screening every five years, annual screening has an incremental cost-effectiveness ratio of $1,720/QALY. Both of these strategies are economically attractive when compared to the WHO's benchmark of South Africa's *per capita* GDP.[15]

Mechanisms of Detection—Under current practice, 25% of infected persons are detected via development of a severe opportunistic disease (Figure 1). Screening once, every five years, or annually decreases the proportion of HIV-infected individuals detected via

severe opportunistic disease to 22%, 20%, or 13%. The percent detected via background or expanded screening increases from 31% with current practice to 66% with annual screening.

Other HIV Prevalence and Incidence Populations—For any given screening strategy, the potential gains in life expectancy are lowest in areas with low baseline HIV prevalence and incidence (Table 2, bottom).[5, 29] Yet even in the Western Cape, the province with the lowest rates of HIV infection, screening annually maintains a favorable cost-effectiveness ratio ($3,090/QALY).

Sensitivity Analyses

ART Initiation Thresholds as a Surrogate for Limited ART Access—For HIV-infected individuals, the discounted quality-adjusted life expectancy benefit associated with annual HIV screening is 16.6 months compared to current practice when there is adequate ART capacity to treat all those with CD4 <350/μl, but decreases to 4.1 months when there is only sufficient ART capacity to treat those with CD4 <50/μl (Figure 2, sum of black, white, and hatched bars). The synergy between effective screening, linkage-to-care and timely ART initiation is illustrated by the greater life expectancies that can be achieved via current screening practices and ART initiation at <200/μl than by annual screening with ART initiation at <50/μl as noted by the dashed, horizontal line in the figure. In a threshold analysis, annual screening compared to screening every five years remains cost-effective ($3,750/QALY) even if expanded screening leads to restricted ART availability for only those with CD4 <100/μl (data not shown).

Limited Test Acceptability and Incomplete Linkage to Care—In a two-way sensitivity analysis, we vary both the test acceptance and linkage-to-care rates from 20% to 100% in 20% increments (25 unique combinations). At the combination with the poorest screening program performance (20% acceptance/20% linkage-to-care), annual HIV screening provides a discounted per person quality-adjusted life expectancy for HIV-infected individuals of 184.7 months (4.1 months more than current practice) and maintains a favorable cost-effectiveness ratio of $2,110/QALY compared to screening every five years (Technical Appendix, Table A2b).

Test-associated Stigma and Diagnosis-associated Stigma—In Figure 3, we enumerate all possible combinations of test-associated and diagnosis-associated stigma that would yield the same clinical outcomes as those obtained under current practice. For example, when test-associated stigma leads to a 0.33 quality of life decrement for one month, the diagnosis-associated stigma decrement could also be as high as 0.34 before losing the clinical benefit of an annual screening program (Arrow). These quality of life decrements are approximately four- to five-fold higher than those used in the base case analysis. One-way sensitivity analysis on the impact of test-associated and diagnosis-associated stigma on quality-adjusted life expectancy are provided in Technical Appendix, Figure A2. When each stigma parameter is varied individually, screening annually remains very cost-effective provided that the test-associated stigma decrement is less than 0.35 in the month of the test ($5,390/QALY) and the monthly diagnosis-associated stigma decrement is less than 0.41, applied for the duration of the lifetime following an HIV diagnosis ($5,360/QALY).

Other Sensitivity Analyses—Results remain robust in sensitivity analyses of other parameters, including increasing test costs (up to ten-fold higher than the base case) and treatment costs (up to two-fold higher than the base case); incorporating additional clinical triggers leading to HIV diagnosis in the absence of screening (including tuberculosis); increasing background testing rates (up to once every five years); changing the mean age at

cohort initiation (23 years to 43 years); increasing ART efficacy; and including a third-line regimen. Please see Technical Appendix for details.

DISCUSSION

Annual routine HIV screening in South Africa increases the per person quality-adjusted life expectancy of an HIV-infected individual by 16.6 months, even when assuming highly constrained rates of acceptance and linkage-to-care. Annual screening is also very cost-effective ($1,720/QALY),[15] a result that remains stable (i.e., below the "very cost-effective" South African GDP threshold of $5,400/QALY) at the lowest reported provincial rates of HIV prevalence/incidence, or when we assume rates as low as 20% for both test acceptance and linkage-to-care and with testing costs greater than ten-fold higher than in the base case.[5, 29] The stability of these cost-effectiveness findings reflects the fact that it is effective antiretroviral therapy, and not screening *per se*, that is the major determinant of both the clinical and economic impact of screening. Thus, the cost-effectiveness ratio of annual HIV screening is only slightly higher than the cost-effectiveness ratio for routine HIV care in South Africa (~$1,200/QALY).[43] While expanded screening at any level would improve upon the current *status quo*, for clinical outcomes, implementation of an intensive annual routine screening program is also very cost-effective, and will provide nearly as good value for money as screening once or every five years.

This analysis underscores the WHO's recommendations that HIV screening should be associated with "assurances of linkage between the site where the test is being conducted and relevant treatment, care and other services,"[44] emphasizing that case detection alone is insufficient to yield improvement in clinical outcomes. We therefore critically examine the impact of a screening program in the setting of both incomplete ART access (Figure 2) and poor rates of linkage to care. We find that annual HIV screening leading to earlier case detection – even in the setting of insufficient resources for guideline-concordant ART – still improves clinical outcomes and is cost-effective as long as ART is initiated at a CD4 count <100/μl or higher. Moreover, because the clinical benefits to those linked to care are so dramatic, linkage rates need only be 20% to continue to demonstrate cost-effectiveness.

The results are also robust to test costs up to ten-fold higher than those used in the base case. Thus, variations in screening programs by site, by testing algorithm, or by operational differences in counseling and referral are unlikely to have an impact on the general results. The stability of the results under these conditions, combined with sensitivity analyses using data from three different South African regions, with varying prevalence/incidence rates, suggests the likely generalizability of our results even outside the South African setting in countries with generalized HIV epidemics.

A persistent challenge to HIV screening is the impact of stigma on health-related quality of life, both as it pertains to the act of obtaining an HIV test and to living with known HIV infection. The very favorable cost-effectiveness findings remain unchanged, even when we assume that the psychosocial impact of testing- and HIV-related stigma on quality of life are four-fold more detrimental than those reported in the literature. Furthermore, South African data collected in the context of increasing ART availability report decreases in stigma over time; <1% of survey respondents in 2005 report fear of non-confidentiality, stigma or job loss as their reason for not being tested.[45]

Despite concerns regarding stigma and the ethics of routine HIV screening, when concerted efforts and resources are dedicated to HIV case identification, the results are clear. Routine HIV screening in one South African urgent care center resulted in a case identification rate of 39 cases per week (newly diagnosed prevalence of 33%).32 Other approaches to routine

screening have also proven feasible in other resource-limited settings, including: large public health campaigns (Botswana);46 testing of male partners in the antenatal period (Uganda);47 home-based testing (Uganda, Zambia);48, 49 and testing in combination with other health care services (Haiti).50

There are several limitations to this analysis. First, we have not included any transmission benefits associated with HIV screening. A recent meta-analysis found that HIV VCT clients in resource limited settings were 70% less likely to engage in unprotected sex compared to those without access to VCT.[51] Results of this analysis would be even more favorable if additional benefits in risk reduction and transmission were achieved among both HIV-infected and uninfected individuals. Second, cost-effectiveness analysis is an inappropriate tool with which to evaluate the ethical considerations associated with resource allocation policies for HIV prevention and treatment.[52] In a resource-limited setting, affordability is as important as cost-effectiveness. While budget impact is beyond the scope of the present paper, it merits more attention than it has received to date in the HIV-related literature.[53] Although many univariate and multi-way assessments were conducted, a more complete sensitivity analysis might examine the question of cost-effectiveness over a range of willingness-to-pay thresholds and examine the simultaneous interaction of all input parameters. Recognizing the difficulties of conducting this type of analysis alongside first-order, Monte Carlo microsimulation, we have adhered to the guidance of both the US Panel on Cost-effectiveness in Health and Medicine and the ISPOR Task Force on Good Modeling Practice with regard to the appropriate use of deterministic methods in sensitivity analysis.[14, 54, 55]

While we use lifetime projections to forecast the optimal HIV screening policy recommendations today, secular changes in South Africa will require a reevaluation of these results over a five- to ten-year time horizon. Finally, routine screening will require additional health care infrastructure. This analysis, by convention, excluded fixed costs associated with scaling up a routine screening program, but sensitivity analyses examined a possible surrogate for their inclusion -- a two-fold increase in total HIV care costs -- and still found annual testing to be very cost-effective.[14]

As researchers worldwide begin to address the potential of “HIV treatment as prevention” strategies, an initial critical question is whether frequent HIV screening is clinically beneficial and economically viable.[56, 57] Annual screening in South Africa is likely not immediately achievable; it will require dedicated political will and financial investment. Although cost-effectiveness is just one of many criteria for policy decision-making, when used to understand the impact and value of routine HIV screening in South Africa, the conclusions are clear. Case identification is required to access life-saving antiretroviral therapy; HIV screening in South Africa would provide more clinical benefit than virtually any other screening program for any disease that has been reported.[58] The unchecked HIV epidemic in South Africa warrants a major and comprehensive response. That response should include frequent routine, voluntary HIV screening, ensuring that those identified as HIV-infected receive the highly effective antiretroviral therapy that is currently the standard of HIV care in South Africa.

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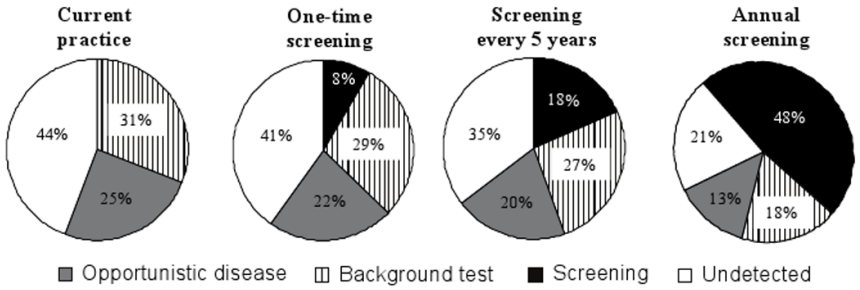


FIGURE 1.
Mechanisms of HIV detection in South Africa.

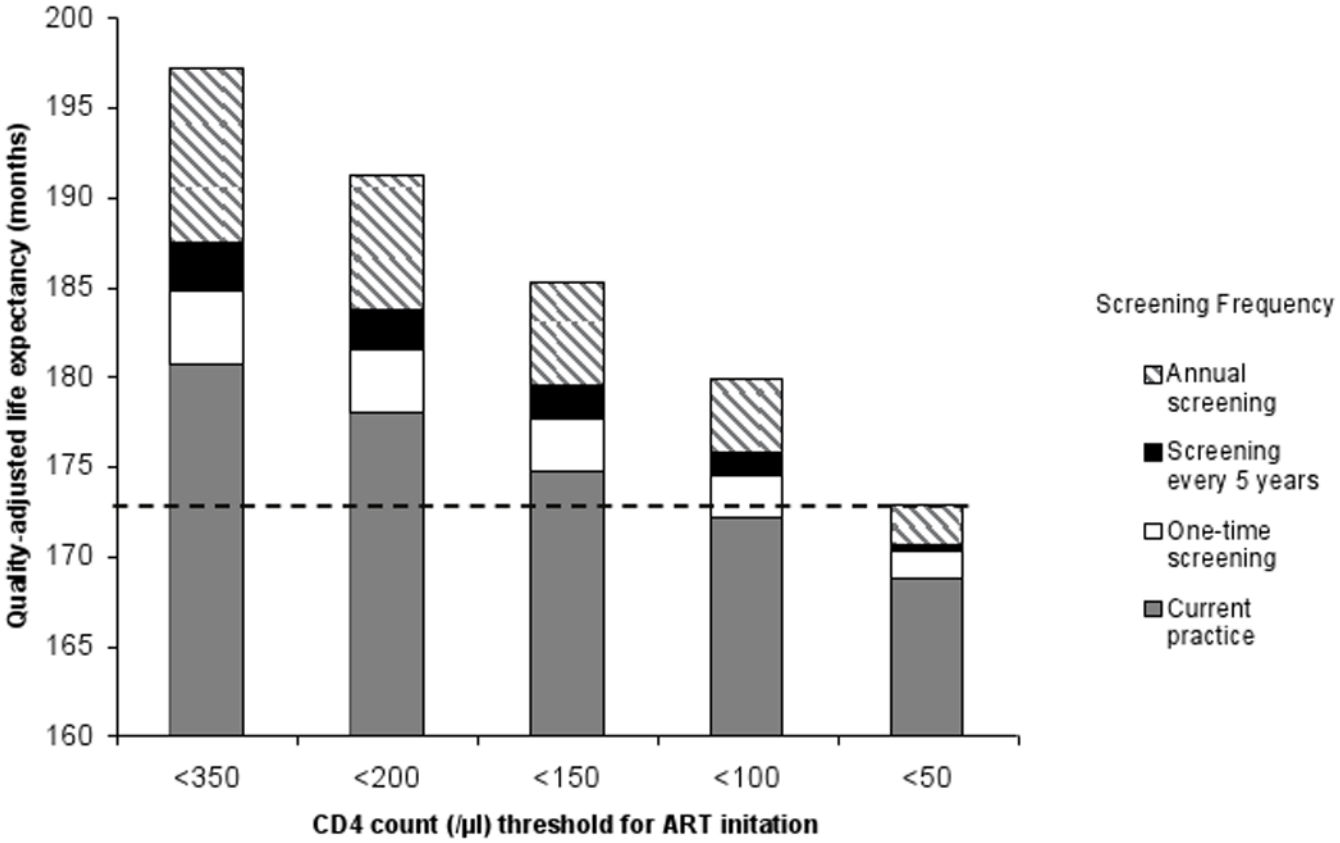


FIGURE 2.
Quality-adjusted life expectancy for HIV-infected individuals under varying thresholds for ART initiation and HIV screening frequencies.

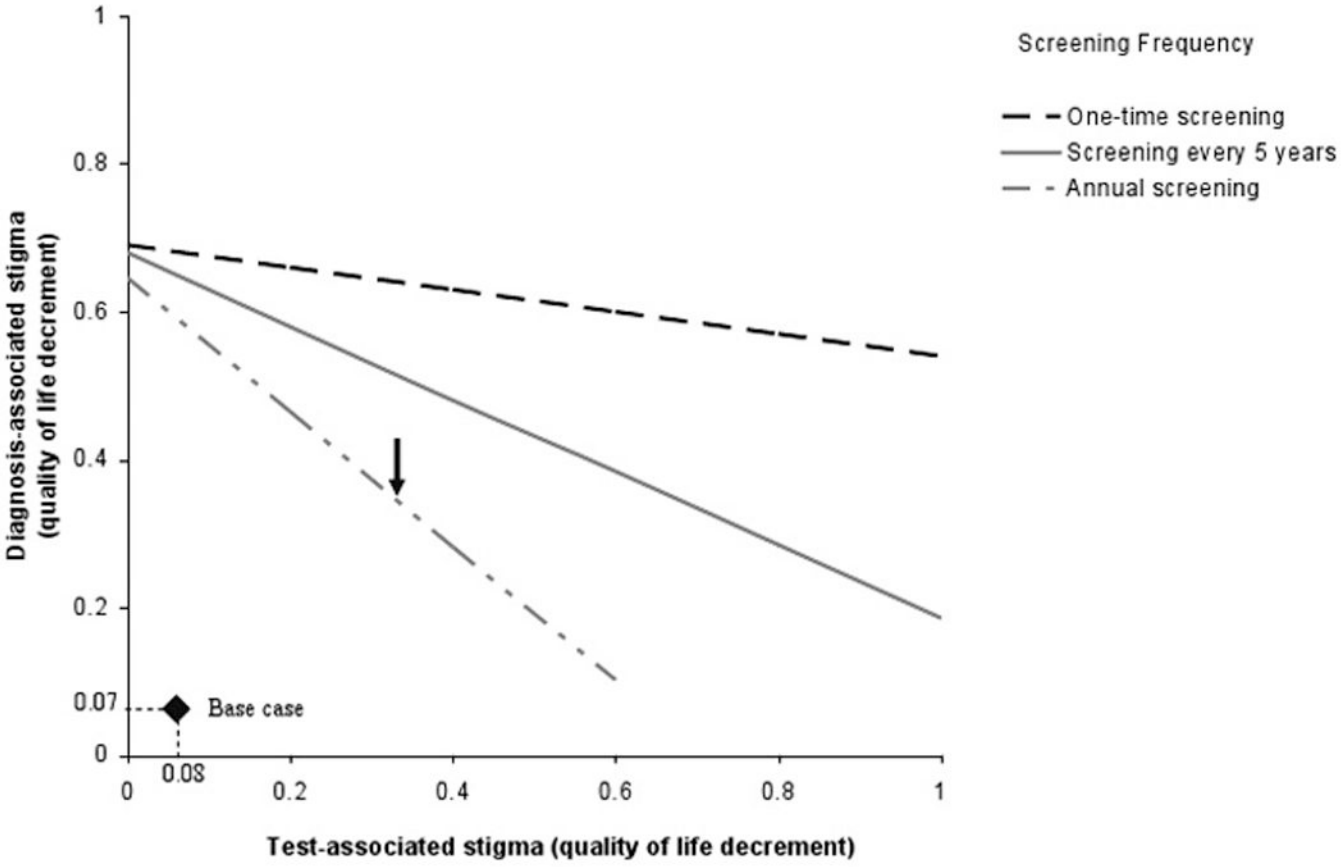


FIGURE 3.
Two-way sensitivity analysis on test-associated and diagnosis-associated stigma.

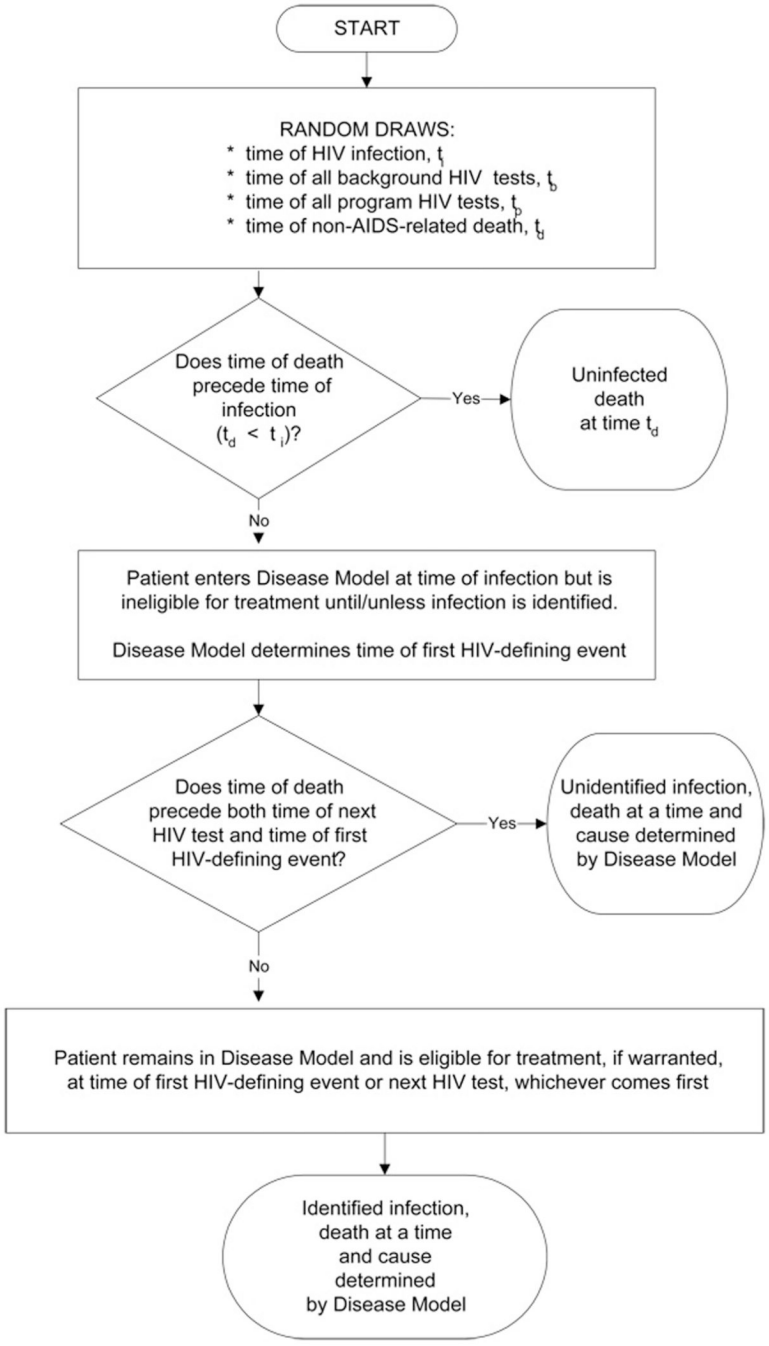
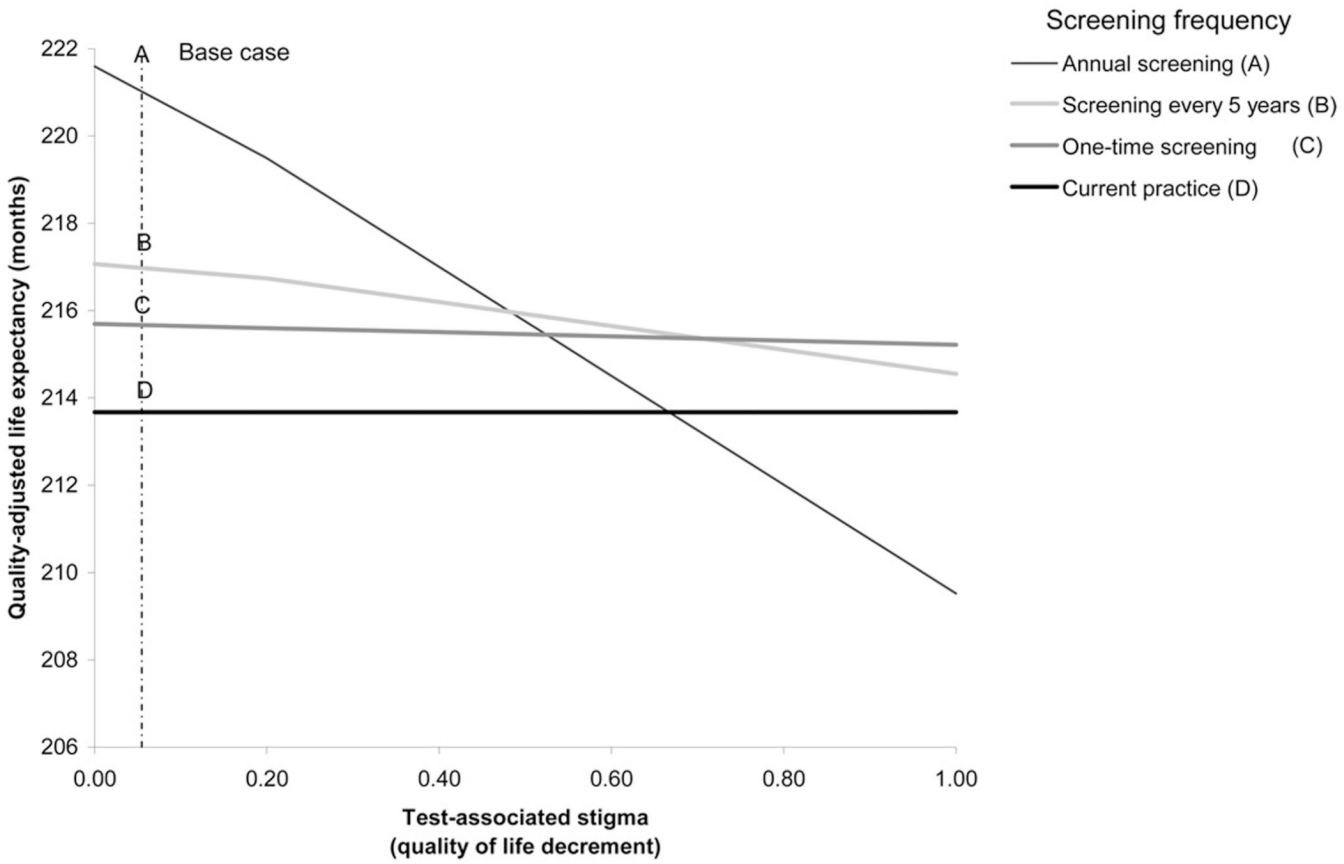


FIGURE A1.
Conceptual framework for the Screening Model



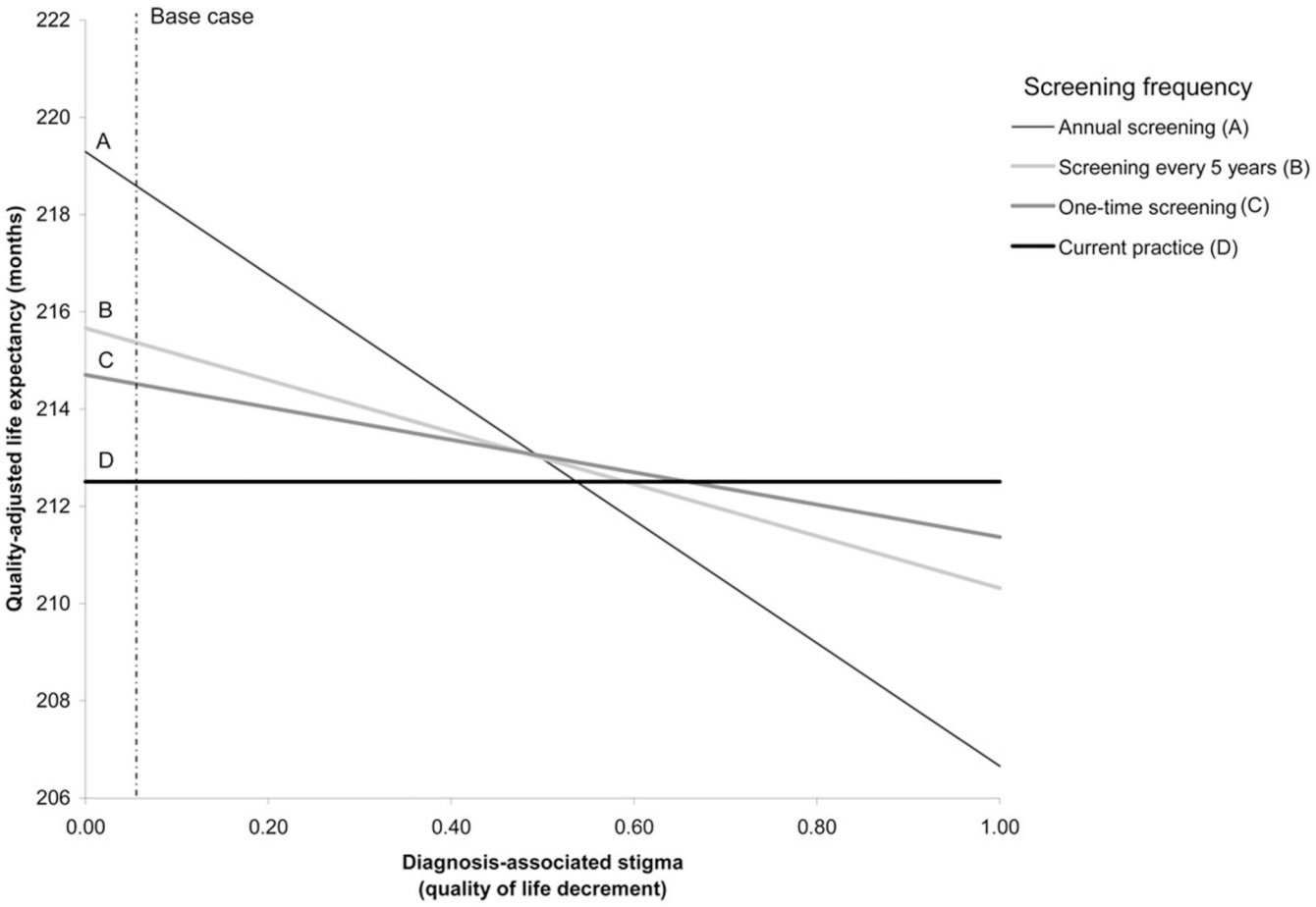


FIGURE A2.

a: One-way sensitivity analysis on the impact of test-associated stigma on quality-adjusted life expectancy.

b: One-way sensitivity analysis on the impact of diagnosis-related stigma on quality-adjusted life expectancy.

Table 1

Model input parameters.

Variable	Base Case Value (SD)	Range Examined	Reference
Baseline cohort characteristics			
HIV prevalence (%)			
Asymptomatic, chronic HIV+	11.4	2.6–17.6%	39
Symptomatic, chronic HIV+	5.2	1.2–8.0%	39
Acute, primary HIV infection	0.3	0.05–0.4%	Assumption
Total	16.9	3.9–26.0%	5, 29
Annual HIV incidence (%)	1.3	0.4–1.6%	5, 29
Age, mean years ± SD	32.8 ± 9.2		18
Male subjects (%)	54.6		18
HIV testing protocols			
Average background HIV test frequency	Every 10 years	0–10 years, detection by OD	39
Sensitivity* (%)	99.6		37
Specificity* (%)	98.0		37
Test acceptance rate (%)	48.6	20–100	32
Rate of HIV-infected return for test results and linkage to care (%)	46.8	20–100	39
Distribution of initial CD4, mean cells/μl (SD)			
Acute, primary HIV infection†	534 (164)		10
Chronic HIV infection‡	288 (331)	288–320	39
HIV RNA distribution (%)			35
>100,000 copies/ml	42.5	0–100	
30,001 – 100,000 copies/ml	28.3	0–100	
10,001 – 30,000 copies/ml	17.9	0–100	
3,001 – 10,000 copies/ml	7.8	0–100	
501 – 3,000 copies/ml	2.3	0–100	
<500 copies/ml	1.2	0–100	
Natural history of disease			
Mean monthly CD4 cell decline by HIV RNA level (cells/μl)			17
>30,001 – 100,000 copies/ml	6.4		
10,001 – 30,000 copies/ml	5.4		
3,001 – 10,000 copies/ml	4.6		
501 – 3,000 copies/ml	3.7		
<500 copies/ml	3.0		
Percent monthly risk of severe opportunistic diseases§ (%)			18
Bacterial	0.08–0.71		
Fungal	0.02–2.22		

Variable	Base Case Value (SD)	Range Examined	Reference
Tuberculosis	0.21–1.96		
Toxoplasmosis	0.00–0.06		
Non-tuberculous mycobacteriosis	0.00–0.30		
Pneumocystis jiroveci pneumonia	0.00–0.12		
Other WHO stage 4-defining diseases	0.25–2.57		
Percent monthly risk of mild opportunistic diseases (%)			18
Fungal	0.59–3.51		
Other	2.51–3.10		
Efficacy of co-trimoxazole (% reduction in probability of infection)			
Severe bacterial	49.8		30, 38
Mild fungal infections[//]	−46.4		30, 38
Toxoplasmosis	83.3		30, 38
Pneumocystis jiroveci pneumonia	97.3		42
Other WHO stage 4-defining diseases	17.9		30
Efficacy of ART (% patients with HIV RNA suppression, CD4 increase at 48 weeks)			
First line (NNRTI + 2 NRTIs)	75%, 168 cells/μl	42%–84%	22, 23
Second line (PI + 2 recycled NRTIs)	75%, 168 cells/μl	35%–71%	22, 23
Stigma (quality of life decrement)[¶]			
Test-associated stigma	0.08	0.00–1.00	27
Diagnosis-associated stigma	0.07	0.00–1.00	28
Discount Rate	3%	0%–3%	14
Costs (2006 US$)			
HIV testing			
Rapid HIV test	1.20	1–10 times base case	32
Confirmatory rapid test	1.78	1–10 times base case	32
Pre-test counseling	3.51	1–10 times base case	32
HIV care			
Co-trimoxazole prophylaxis (monthly)	1.02		34
First-line ART (monthly)	18		36
Second-line ART (monthly)	49		36
Minor drug toxicity	11		18, 33, 34
Major drug toxicity	1,548		18, 33, 34
Routine care (range by CD4, monthly)	9.85–129.41	1–10 times base case	18, 31, 33
Inpatient hospital care, per day	221.14	1–10 times base case	33
Outpatient hospital care, per visit	11	1–10 times base case	33
CD4 count test	9	1–10 times base case	34

Variable	Base Case Value (SD)	Range Examined	Reference
HIV RNA test	47	1–10 times base case	34

SD: Standard deviation; OD: Opportunistic disease; WHO: World Health Organization;

ART: Antiretroviral therapy; NNRTI: non-nucleoside reverse transcriptase inhibitor;

NRTI: nucleoside reverse transcriptase inhibitor; PI: protease inhibitor

*Sensitivity and specificity refer to the characteristics of a single rapid test, not the confirmatory process; test specificity is assumed to be zero during the acute infection window period (approximately 2 months)

†Starting CD4 cell count for incident cases

‡Starting CD4 cell count, on average, for prevalent cases

§Range indicated by CD4 count; details on risk by CD4 stratum are provided in the technical appendix.

//The percent monthly risk of mild fungal infections is increased by 46.4% in the presence of co-trimoxazole.[30]

¶Quality of life decrement reduces quality of life on a 0.00–1.00 scale where 1.00 represents perfect health and 0.00 represents death. By intentionally limiting quality of life decrements to these two forms of stigma (and assuming all other health states are “perfect” = 1.00), we bias results against HIV screening.

Table 2

Base case results and selected sensitivity analyses of an HIV screening analysis in South Africa.

	HIV Screening Frequency			
	Current Practice*	**One-time**	**Every 5 years**	**Annually**
Base Case, South Africa				
Prevalence 16.9%, Annual Incidence 1.3%				
HIV+ Population				
Undiscounted per person quality-adjusted life expectancy (months)	285.6	291.9	298.3	317.2
Discounted per person quality-adjust life expectancy (months)	180.6	184.9	187.6	197.2
Mean CD4 at detection (/μl)				
Prevalent cases	195	233	235	259
Incident cases	337	337	357	410
General Population				
Undiscounted per person quality-adjusted life expectancy (months)	354.3	357.6	361.0	371.2
Discounted per person quality-adjusted life expectancy (months)	213.7	215.7	216.8	221.0
Per person costs ($)	2,330	2,570	2,740	3,330
*Cost-effectiveness ratio ($/**QALY**)*[§,//]	-----	dominated[†]	1,570	1,720
Sensitivity Analysis, Western Cape				
Prevalence 5.3%, Annual Incidence 0.4%				
HIV+ Population				
Undiscounted per person quality-adjusted life expectancy (months)	314.9	320.2	326.3	344.6
Discounted per person life expectancy (months)	194.7	198.0	199.7	209.6
General Population				
Undiscounted per person life expectancy (months)	420.3	421.2	422.2	424.7
Discounted per person life expectancy (months)	243.4	243.9	244.1	245.1
Per person costs ($)	830	910	980	1,220
*Cost-effectiveness ratio ($/**QALY**)*[§,//]	-----	1,650	dominated[†]	3,090
Sensitivity Analysis, KwaZulu Natal				
Prevalence 25.8%, Annual Incidence 2.0%				
HIV+ Population				
Undiscounted per person life expectancy (months)	264.6	271.9	277.9	297.2
Discounted per person life expectancy (months)	170.1	175.0	176.6	187.9
General Population				
Undiscounted per person life expectancy (months)	313.5	318.1	321.7	334.2
Discounted per person life expectancy (months)	194.4	197.5	198.3	204.8
Per person costs ($)	3,240	3,610	3,830	4,630
*Cost-effectiveness ratio ($/**QALY**)*[§,//]	-----	dominated[†]	dominated[†]	1,590

QALY: Quality-adjusted life-year

* In the absence of routine screening, HIV infection is detected via background screening (on average, every ten years) or with the development of one of the following severe opportunistic infections: Isosporiasis, *Mycobacterium avium* complex, Toxoplasmosis, *Pneumocystis jirovecii* pneumonia (PCP), and other WHO stage 4-defining non-bacterial diseases.

[†] "dominated" strategies are eliminated because they cost more and deliver fewer years of life saved than the comparative combination of strategies.[14]

[§] In order to accentuate the effects of HIV-related stigma, it is assumed that all health states prior to HIV testing have quality of life equivalent to perfect health. Quality of life decrements are then applied only to states involving either an HIV test or time spent living with an HIV diagnosis.

[//] Cost-effectiveness ratios were calculated prior to rounding quality-adjusted life expectancy and costs.