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A cost-effectiveness analysis of alternative HIV re-testing strategies in sub-Saharan Africa

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Abstract

Background—Guidelines in sub-Saharan Africa on when HIV-seronegative persons should re-test range from never to annually for lower-risk populations and from annually to every 3 months for high risk populations.

Methods—We designed a mathematical model to investigate the most cost-effective frequency with which an HIV-seronegative tester should re-test for HIV. Cost of HIV counseling and testing (HCT), linkage to care, treatment costs, disease progression and mortality, and HIV transmission are modeled for three hypothetical cohorts with annual HIV incidence of 0.8%, 1.3%, and 4.0%, respectively. The model compares costs, quality-adjusted life-years gained, and secondary infections averted from testing intervals ranging from 3 months to 30 years. Input parameters from sub-Saharan Africa were used and explored in sensitivity analyses.

Results—Accounting for secondary infections averted, the most cost-effective testing frequency was every 7.5 years for 0.8% incidence ($701 per quality-adjusted life year (QALY) gained), every 5 years for 1.3% incidence ($681/QALY), and every two years for 4.0% incidence ($635/QALY). Most testing strategies implied a cost per QALY gained at or below the average GDP per

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CONTRIBUTORS

Crump, Ostermann, Reeves and Thielman originated the work. Ostermann, Reeves and Waters developed the analytic framework. Reeves and Waters identified the background information and input parameters for the model. Masnick and Waters streamlined the original analyses and implemented the model in Matlab. Crump, Ostermann and Waters wrote the final article. Bartlett and Thielman contributed to study interpretation, and article editing. All authors contributed to the final version of the article.

capita in sub-Saharan Africa ($2,031/QALY). Optimal testing strategies and their relative cost effectiveness were most sensitive to assumptions about HCT and treatment costs, rates of CD4 decline, and rates of HIV transmission.

Conclusions—Regular re-testing for HIV may be cost-effective for both high- and low-risk populations in sub-Saharan Africa. The most cost-effective testing frequency varies with HIV incidence. Our data demonstrate benefits of tailoring testing intervals to resource constraints and local HIV incidence rates.

Keywords

HIV counseling and testing; re-testing; cost effectiveness; guidelines; Sub-Saharan Africa

BACKGROUND

HIV counseling and testing (HCT) is promoted to increase serostatus awareness and entry into HIV care and treatment programs, particularly in low- and middle-income countries.[1,2] While uncertainty remains about its efficacy in promoting behavior change,[3] the role of HCT in linking HIV-infected persons to care and treatment services is undisputed.[4–7] Moreover, an increased understanding of the relationship between plasma HIV-1 RNA concentration and risk for HIV transmission[8,9] has prompted consideration of antiretroviral therapy (ART) as an HIV prevention strategy[10–12], further increasing the significance of HCT as an entry point into care.

The generalized nature of the HIV epidemic in sub-Saharan Africa has led to the promotion of universal HCT.[13–16] While many campaigns and strategies appropriately emphasize HCT for persons who have never tested,[17–24] the risk for HIV infection for a given individual typically persists beyond the initial HCT encounter,[25] raising the question of when, if at all, seronegative testers should re-test.[26]

For non-pregnant HIV-seronegative testers, recommendations on when to re-test for HIV are varied. Several national guidelines make no mention of the frequency with which a seronegative tester should continue to test;[20,23,24] others specify a single test after 1–3 months in case the initial HIV antibody test was performed prior to development of HIV antibodies; [24,27,28] some promote testing every 3 months or ‘periodically’ for those who engage in high-risk behaviors[19,22] and annual testing for the general population.[22] The World Health Organization (WHO) recently released guidelines on re-testing, advising annual testing for persons living in countries with generalized HIV epidemics who are at high risk for HIV, who do not know the HIV status of their partner, or who have any other ongoing risk behavior.[29] Testing every three months is discouraged in these recommendations, as is re-testing for individuals who do not have new potential exposures to HIV.

Mathematical models have been used previously to study the cost-effectiveness of one-time and repeated HIV screening in the United States, Russia and South Africa.[30–35] In simulating repeated screening for HIV, these models take into account long-standing undiagnosed prevalent cases, recent incident cases, and variable uptake of HCT, and have contributed to the formation of new guidelines for HIV screening.[36,37] However, there has been little evaluation of the cost-effectiveness of different frequencies of re-testing for persons who test HIV-seronegative, where re-testing concerns the detection of incident cases. With national testing campaigns gradually raising rates of HIV serostatus awareness,[13,21] cost effectiveness analyses need to be extended to address incidence testing and the costs and benefits of alternative re-testing frequencies.

To evaluate the question of when a seronegative tester should re-test for HIV, we designed a mathematical model that compares the cost-effectiveness of alternative frequencies of HIV re-testing, using input parameters from sub-Saharan Africa when available.

METHODS

Overview

The model follows a cohort of individuals assumed to have tested HIV-seronegative, i.e., HIV prevalence at the start of the model is 0%. The cohort is followed for 45 years. Three different annual incidence rates mimic different HIV-risk environments comparable to those seen in previous studies in sub-Saharan Africa: 0.8% (low), 1.3% (medium), 4.0% (high).[38–42] Twelve HCT strategies compare testing intervals ranging from every 3 months to once after 30 years. No further HIV risk or testing are assumed to occur during the final 15 years of the model. The base-case scenario uses a starting age of 20 years and age-specific mortality data for uninfected persons from South Africa.[43] The primary outcome of interest was the cost per quality-adjusted life year (QALY) gained from each testing strategy when compared with a scenario without HIV testing or treatment. Cost and QALY calculations account for secondary infections averted from effective ART and behavior change (see below). Incremental cost-effectiveness ratios (ICERs) for each strategy were calculated in comparison with the respective next longer re-testing interval, with a single repeat test after 30 years compared with no re-testing. The model is estimated iteratively in 3 month cycles; costs and benefits are discounted at 3 percent per year and expressed in year 2011 United States dollars ($).[44] Table 1 summarizes the base-case assumptions and sensitivity analysis ranges used in the model. Further discussion of the model and input parameters is presented in the Supplementary Appendix. The model was estimated in MATLAB version R2009a (MathWorks Inc, Natick, MA); formulae are available from the authors upon request.

HIV infection and disease progression without treatment

Individuals are infected with HIV per the given incidence rate, but remain undiagnosed until testing. HIV disease progression is modeled by changes in CD4 counts, with associated changes in quality of life values and mortality rates over time. The base case scenario assumes a median time from seroconversion to AIDS of 10.3 years and a 10-year cumulative mortality of 39%.[45–50]

HIV testing, linkage to care, and treatment

Testing frequencies range from re-testing every 3 months to one test after 30 years (Table 1). To avoid biases resulting from different lengths of follow-up after the last test, testing frequencies were chosen such that the last test for all strategies takes place 30 years after the start of the model. To compare the relative cost effectiveness of each strategy, all individuals tested according to the given frequencies (see Supplementary Appendix). HIV tests were assumed to be rapid, point-of-care tests and have 100% sensitivity and specificity. Individuals testing seronegative continue to test at the specified frequency; individuals testing seropositive do not re-test, but are linked to care and then started on 1st-line highly active antiretroviral therapy (HAART) if the CD4 count is 350 cells/mm^3 or less.[51] After initiating HAART, a person may be lost to follow-up (LTFU) at a rate of 10% per year (range: 5–20% yearly in sensitivity analysis).[52] Upon HAART initiation and virologic suppression, a patient's CD4 count gradually increases as a function of the CD4 count at the start of HAART (see Supplemental Appendix).[30,53,54] Failure rates and mortality on 1st- and 2nd-line HAART were assumed to be greatest immediately after initiation of HAART.[55–59] It was assumed to take 6 months for virologic failure to be detected and patients to be switched to 2nd-line HAART. To avoid unrealistic increases in CD4, CD4 counts were

assumed to remain constant during effective 2nd-line therapy in the base-case; the effect was this assumption was explored in sensitivity analysis (see Supplemental Appendix). During non-suppressive therapy, CD4 counts were assumed to drop again. Patients failing 2nd-line therapy are kept on non-suppressive therapy, consistent with guidelines.[51,60,61]

Costs

With the most significant increase of persons on HAART likely to occur in South Africa, [21] costs for HAART therapy were derived for the drug regimens indicated by the South Africa 2010 guidelines for patients newly starting therapy, tenofovir + emtracitabine/lamivudine + efavirenz/nevirapine, and averaging the costs for the four possible regimens.[62] Costs were similarly modeled for a 2nd-line therapy of zidovudine + lamivudine + ritonavir-boosted lopinavir. HCT cost per tester, laboratory costs and cost of prophylaxis for opportunistic infections per patient-year on HAART, and cost per person for treatment of opportunistic infections were derived from studies in sub-Saharan Africa.[63,64] Costs for health care facilities overhead, salaries of health care workers, costs to the patient for time spent obtaining care are not explicitly included in the model, though significantly higher costs for HAART – where overhead costs can be implicit – were explored in the sensitivity analysis.

Quality of life estimates

The quality of life value for HIV-uninfected persons was assumed to be 1. Quality of life values (see Table 1) for an HIV-infected individual were assumed to be dependent on CD4 counts: CD4 > 350, 200 < CD4 <= 350, CD4 <= 200, with values (in comparison with HIV uninfected persons) of 0.94, 0.82, 0.70, respectively.[65] Table 1 shows the base-case and sensitivity analysis values used.

Secondary transmission of HIV

Differential transmission rates were modeled for the acute, subacute, chronic and AIDS phases. As it was assumed that a test for HIV is 100% sensitive and specific, it was also assumed that any diagnosis of HIV occurs after the acute phase. Combined with the mortality estimates for untreated and undiagnosed HIV disease, the base-case transmission rates, shown in Table 1, result in an undiscounted lifetime average of 0.94 infections per HIV+ person.[8,66] Rates of HIV transmission were assumed to decline by 20% in the base-case scenario (range: 0–50% in sensitivity analysis) if an individual is aware of his/her HIV-infected status, a conservative estimate based on several studies in sub-Saharan Africa and the US.[67–71]

Sensitivity Analysis

Comprehensive sensitivity analyses for each of the three incidence scenarios evaluated the effect of alternative assumptions for the model input parameters. For each variation of a single input parameter, the most cost-effective testing strategy was identified and compared to that of the base-case scenario. The sensitivity of the primary outcome of cost per QALY effect to a 1% change in each input parameter was also evaluated.

RESULTS

Base-case scenario

In low-risk environments, the most cost-effective testing frequency was testing every 7.5 years (Table 2). The total cost per QALY gained from this testing frequency was $998. When cost savings and QALYs gained from preventing secondary HIV infections were taken into account, the overall cost per QALY gained was $701. For testing every 7.5 years,

the total cost per HIV-infected case identified was $2030. Of the total cost, 4.5%, 68.1% and 27.3% were from HCT costs, HAART costs, and laboratory costs, respectively.

In a medium-risk environment, the most cost-effective testing frequency was every 6 years, with a total cost per QALY gained of $977. Factoring in benefits derived from transmission reductions resulted in testing every 5 years being most cost-effective, with a total cost per QALY gained of $681 (Table 2). The cost per HIV-infected case identified for this testing frequency was $2123. Of the intervention cost, 4.0%, 68.5% and 27.4% were from HCT costs, HAART costs, and laboratory costs, respectively.

In a higher-risk environment, testing every 5 years was most cost-effective, with a cost per QALY of $942. Including secondary infections averted into the analysis resulted in testing ever two years being the most cost-effective strategy, with a total cost per QALY gained of $635. For this frequency, cost per HIV-infected case identified was $2325, with 3.2%, 69.2% and 27.6% of the total cost from HCT costs, HAART costs and laboratory costs, respectively. Annual testing and testing every 6 months resulted in ICERs of $833/QALY and $1899/QALY gained, respectively, when compared to the next least effective strategy and when benefits from secondary infections averted are accounted for.

Without testing, counseling, diagnosis, or treatment, the average number of undiscounted secondary infections per HIV-infected individual is 0.94 for the base-case scenarios. Values for reproductive numbers greater than 1.0 were assessed in the sensitivity analysis. Reductions in rates of HIV transmission due to testing, counseling and treatment ranged from 5.4% (testing once after 30 years, 4.0% incidence) to 26.3% (testing every 3 months, 0.8% incidence). The percent reduction in transmission of HIV for each testing scenario is shown in Table 2.

Sensitivity Analysis

Tables 3–5 display the effects of varying the input parameters, one at a time, on the most cost-effective testing frequency, taking into account benefits from secondary infections averted. For the low, medium and high HIV-risk scenarios, the sensitivity analysis produced ranges of every 3 to 30 years, every 2 to 15 years, and every 6 months to 7.5 years, respectively, as the most cost-effective testing frequencies. For no scenario evaluated in the sensitivity analysis was testing every 3 months the most cost-effective frequency. The greatest variation in the optimal testing strategy were produced by varying assumptions about HCT cost, annual declines in CD4 counts for untreated HIV, and rates of HIV transmission: decreasing HCT costs, faster CD4 count decline, and greater reductions in HIV transmissions from diagnosis and treatment favored more frequent testing. Varying the time to detection of virologic failure did not change the relative cost-effectiveness of the strategies. Importantly, while some variations of parameters did not change which frequency was most cost-effective, all variations affected the cost per QALY gained from each testing strategy.

DISCUSSION

Using a mathematical model, we compared alternative testing strategies for HIV with best estimates for input parameters from sub-Saharan Africa. Expectedly, the most cost-effective testing frequency depended on the risk-environment, with higher risk indicating more frequent testing. Most strategies implied a cost per QALY below the average per capita gross domestic product in sub-Saharan African countries of $ 2,031 in 2007.[72]

Our sensitivity analysis shows that the most cost-effective strategy can vary with changes in the input parameters. HCT cost, assumptions about the effect of a seropositive diagnosis on

HIV transmission, and the cost of 1st-line HAART had the greatest effects across risk settings; rates of linkage to care, rates of CD4 count decline for untreated HIV, assumptions about quality of life values, rates of HIV transmission for untreated HIV, and cost of 2nd-line HAART altered the optimal testing strategy for some risk scenarios.

The effect of the cost of HAART on Tables 3–5 merits further attention. While HAART and laboratory costs are the primary drivers of overall cost in most scenarios considered, the percentage of total cost from HCT greatly influences the relative cost-effectiveness of the testing strategies. Lower treatment costs result in HCT costs comprising a greater percentage of the total intervention cost, approaching 67% for some testing strategies (data not shown), which creates a bias against frequent testing despite overall lower cost per QALY gained. For example, testing once after 30 years is the most cost-effective strategy for low-risk settings when 1st-line HAART is set at $50 per patient-year (Table 3). Yet for this variation, even annual testing costs less per QALY gained that the most cost-effective strategy in the base-case.

The results for the high-risk scenario approximate the recommendation for annual testing for high-risk individuals recently released from the WHO,[29] particularly if the cost of HCT per tester can be minimized. The WHO guidelines also discourage re-testing for individuals who have no new exposure after a seronegative HIV test. While our results do not disagree with this recommendation, certainty of no new exposure may be difficult in the setting of a generalized epidemic.[13–16] In such cases, our results suggest that encouraging populations of much lower risk, if certainty of no exposure cannot be guaranteed, to re-test approximately every 5–7 years may be the most efficient use of resources, though the sensitivity analysis did produce a wide variation.

Aside from uncertainties introduced by the input parameters, our model has several structural limitations and could be extended in several ways. Behavior change associated with HCT, for which there is mixed evidence,[3,73] would alter our cost-effectiveness estimates. Including a background of ongoing symptom-based case-identification or exposure-related self-initiated testing at interim time points would affect the cost-effectiveness of the strategies, as would allowing a mechanism for those who are lost to follow-up to later return to care. Treatment side-effects and development of resistant strains that affect available HAART options are not currently modeled. False positive and false negative test results are not taken into account, which would gain importance at more frequent testing intervals. While studies have shown that CD4 counts at seroconversion vary with age, sex and exposure group,[45,46] and that rates of CD4 decline vary significantly with HIV-1 subtype,[46] these factors were not included in the model, and would be pertinent for certain subpopulations of testers. Though costs for health care personnel and overhead were not built into the model, these costs can be absorbed into the treatment costs, which are studied in the sensitivity analysis. An extension of the model to incorporate these factors as well as modeling of disease progression and cost at the individual rather than cohort level is required for a comprehensive cost effectiveness analysis of re-testing strategies.

For our findings to provide guidance, policy makers need to understand variations in local HIV incidence rates and resource availability in order to select optimal testing strategies. This includes differential rates of HIV infection in population subgroups, and an understanding of the cost and uptake of alternative HCT options, such as provider-initiated testing, mobile HCT, fixed-venue HCT, and home-based testing. Selection biases associated with seeking HIV testing and variation in the cost per test have the potential to greatly influence the relative cost-effectiveness of each strategy in different venues. With limited resources there is also a need to balance re-testing against the more pressing need to detect as yet undiagnosed prevalent cases. While guidelines on re-testing can assist clients already

presenting for HIV testing, significant obstacles still remain in decreasing stigma and promoting uptake of HIV testing by those who have yet to ever test.[13] Care also needs to be taken to ensure that no individual wishing to test at 'greater-than-optimal' frequencies is denied or feels discouraged to do so.

While our model is theoretical, it has direct implications for HIV testing and treatment policy and practice. The results suggest substantial benefits from periodic re-testing for HIV for groups other than high-risk populations. These findings also show (Table 2) substantial savings in cost and QALYs from reduced HIV transmission due to periodic re-testing and linkage to care, consistent with the paradigm of treatment as prevention.[10–12] Recognizing the need for most sexually active adults to re-test for HIV at regular intervals may help to decrease stigma, as testing might no longer be seen as acknowledgement of "bad behavior," a reason that keeps some individuals from ever testing.[74,75] Further work in this area and the convergence of several models on similar outcomes as presented here would provide more robust evidence in support of the adoption of guidelines for HIV re-testing for lower-risk populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Input parameters

Variable	Base-case assumption	Sensitivity analysis range	References
	Population and testing		
Annual incidence rates (%)	0.8, 1.3, 4.0	--	38–42
Age of starting cohort	20 years old	20–30 years	Assumed
Years with constant incidence rate	30 years	5–10 years	Assumed
Mortality rates of HIV-uninfected persons (% per year)	Age 20–24: 0.35 Age 25–34: 1.26 Age 35–44: 1.67 Age 45–54: 1.75 Age 55–65: 2.32	For studies on length of follow-up: Ages 65–74: 4.21 Ages 75+: 13.14	43
Testing frequencies studied (yrs)	3 mo, 6 mo, 1, 2, 3, 4†, 5, 6, 7.5, 10, 15, 30	--	Given
Cycle length	3-months	--	Given
Discount rate	3% per year	--	44
	HIV disease progression		
Average CD4 count at seroconversion (cells/mm^3); standard deviation	600; SD 240	(see ave CD4 decline)	45–49
Average CD4 decline per year, untreated	39 cells/year	22–75 cells/year	45–49
Mortality rates (%), untreated HIV per CD4 count; per year	>500: as HIV-uninfected 350–499: 4.60% 200–349: 7.98% 50–199: 25.54% <50: 48.54%	0.75–1.5 × base (see Supp. Material).	47,48,50,76
	HIV care and treatment		
Rate of linkage from diagnosis to care	70% in 1st year post-test 10% thereafter	30–100%	77
Criteria for starting HAART	CD4 <= 350 cells/mm^3	--	51
Loss to follow-up from HIV care	10.33% yearly	0%–20% yearly	52
Maximum possible rise in CD4 due to HAART, by baseline CD4 count (cells/microL)*	300–350: 300 250–300: 295 200–250: 285 150–200: 270 100–150: 247 50–100: 218 0–50: 154	150–450 for all strata	53,54,78,79
Failure rates on 1st-line HAART	27% 1st year 7.8% thereafter	1%–40% 1st year 1%–15% thereafter	55–57
Failure rates on 2nd-line HAART	27% 1st year 7.8% thereafter	1%–40% 1st year 1%–15% thereafter	55–57,59
Mortality rates while on HAART, by CD4 count	see Supp.Appendix	0.5–2 × base	80
Time to detect virologic failure	6 months	0–18 months	Assumed
	Transmission of HIV		

Variable	Base-case assumption	Sensitivity analysis range	References
HIV transmission per person-year, untreated HIV by CD4 count	Acute** 0.58 Subacute: 0.10 >350: 0.05 200–349: 0.072 <200: 0.18	Acute** 0.23–0.64 Subacute: 0.04–0.12 >350: 0.02–0.06 200–349: 0.03–0.09 <200: 0.09–0.21	8,66
Decline in HIV transmission rate from testing and counseling	20%	0–50%	67–71
HIV transmission, on suppressive HAART, per person-year	0.0037	0.001–0.02	8
Reduction in transmission due to non-suppressive HAART	20%	0–70%	81 –83
	Costs (2011 USD)		
VCT cost	$8.17 per person per test	$2–50	63
1st-line therapy (see text)	$560 per person per year	$50–1000	62
2nd-line therapy: AZT+3TC+LPV/r	$752 per person per year	$200–2000	62
Laboratory costs	$254 per person per year	$50–600	64
Cost for treatment of opportunistic infections	$519 per person	$100–1500	64
	Quality of life values		
Quality of life value, HIV-uninfected persons	1	--	Assumed
Quality of life value, HIV-infected persons, by CD4 count	>350: 0.94 200–349: 0.82 <200: 0.70	>350: 0.70–0.98 200–349: 0.50–0.90 <200: 0.30–0.80	65

† The testing frequency of every 4 years is actually every 4.29 years (derived from 7 equal intervals over 30 years).

* Rise in CD4 occurs gradually over a period of two years, and treatment failure or death can prevent maximum rise from being reached.

** See supplemental appendix for further explanation on the role of acute HIV transmission in the model

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Table 2

Base-case results for selected HIV re-testing frequencies

	Selected HIV re-testing frequencies							
	3 mo	**1 yr**	**2 yrs**	**3 yrs**	**5 yrs**	**7.5 yrs**	**10 yrs**	**30 yrs**
0.8% incidence								
HCT cost per case identified ($)	2792	696	347	231	139	95	73	36
Total cost ($) per person	898	507	435	405	366	322	279	59
Percent cost from HCT (%)	56.8	24.7	14.1	9.9	6.3	4.5	3.7	3.1
QALYs gained per person	0.41	0.41	0.40	0.39	0.36	0.32	0.28	0.05
CE ratio ($/QALY)	2196	1251	1096	1045	1008	998	999	1198
Reduction in transmission of HIV (%)	29.8	26.8	24.8	23.5	21.5	18.9	16.4	4.9
CE ratio ($/QALY), accounting for infections averted	1565	866	760	726	704	701	704	716
ICER (d$/dQALY), accounting for infections averted	51604	4324	1938	1166	779	701	#	#
1.3% incidence								
HCT cost per case identified ($)	1734	433	217	145	87	60	46	22
Total cost ($) per person	1079	707	635	601	551	488	423	85
Percent cost from HCT (%)	44.6	16.7	9.2	6.3	4.0	2.9	2.3	2.0
QALYs gained per person	0.63	0.63	0.61	0.60	0.56	0.50	0.43	0.07
CE ratio ($/QALY)	1703	1127	1033	1002	981	978	982	1181
Reduction in transmission of HIV (%)	29.6	26.7	24.7	23.4	21.4	18.7	16.2	4.6
CE ratio ($/QALY), accounting for infections averted	1180	765	707	690	681	684	689	703
ICER (d$/dQALY), accounting for infections averted	30942	2650	1312	886	681	#	#	#
4.0% incidence								
HCT cost per case identified ($)	589	149	75	51	31	22	17	8
Total cost ($) per person	1787	1497	1425	1376	1281	1138	981	144
Percent cost from HCT (%)	20.3	6.0	3.2	2.2	1.4	1.0	0.8	0.7
QALYs gained per person	1.54	1.52	1.49	1.45	1.36	1.20	1.03	0.12
CE ratio ($/QALY)	1163	984	956	947	942	947	955	1157
Reduction in transmission of HIV (%)	29.1	26.1	24.1	22.8	20.8	18.0	15.4	3.3

	Selected HIV re-testing frequencies							
	3 mo	**1 yr**	**2 yrs**	**3 yrs**	**5 yrs**	**7.5 yrs**	**10 yrs**	**30 yrs**
CE ratio ($/QALY), accounting for infections averted	749	641	635	636	640	651	660	671
ICER (d$/dQALY), accounting for infections averted	8781	833	635	#	#	#	#	#

QALY = quality-adjusted life-year

= dominated testing strategy

All cost and benefits have been discounted at a rate of 3% per year. ICER are compared with the next most frequent testing interval, some of which are not shown in the table. (Testing every 6 months, 4 years, 6 years, and 15 years are not shown).

Table 3

Selected sensitivity analysis outcomes for incidence of 0.008

Variable	Variable low-end	Base-case 7.5 yrs					Variable high-end	Elasticity†
Years with HIV incidence	7.5 yrs	--	--	--			n/a	--
Ave. CD4 decline/yr, untreated	22 cells/μL/yr	--	--	--	6 yrs	5 yrs	75 cells/μL/yr	0.459
Time to detect virologic failure	3 mo.	--	--	--	--	--	24 mo.	0.028
Reduction in transmission due to diagnosis	0%	15 yrs	10 yrs	--	6 yrs	5 yrs	50%	0.686
VCT cost, per tester	$2	3 yrs	5 yrs	--	10 yrs	15 yrs	$50	0.052
1st-line HAART cost, per patient-year	$50	30 yrs	10 yrs	--	6 yrs	6 yrs	$1000	0.384
2nd-line HAART cost, per patient-year	$200	--	--	--	6 yrs	6 yrs	$2000	0.322
Linkage from diagnosis to care*	30% +	30 yrs	--	--	6 yrs	6 yrs	100%	0.046
Mortality rate, on effective ART	½ base	6 yrs	--	--	--	--	2 × base	−0.045
Failure rates on 1st-line HAART*	1% +	--	--	--	--	--	40% +	0.191
Failure rates on 2nd-line HAART*	1% +	6 yrs	--	--	--	--	40% +	0.052
HIV transmission rates, no treatment (reproductive number)	R0 = 0.5	--	--	--	--	6 yrs	R0 = 1.2	−0.353
HIV transmissions, on ART (per person-year)	0.001	--	--	--	--	6 yrs	0.045	0.019
Quality of life values**	Small differential	--	--	--	6 yrs	6 yrs	Large differential	−0.471
Maximal rise in CD4 count due to suppressive HAART	½ base	6 yrs	--	--	--	--	1.5 × base	--
Length of follow-up after year 30 (base = 15 years)	n/a			--	--	6 yrs	40 yrs	--

The center column represents the base-case, represented with a dash. Outer columns represent the variable low and high values, while the columns between the base-case and outer extremes represent an intermediate value. Dashes indicate that the most cost-effective frequency is the same as for the base-case; otherwise, the frequency is indicated. Secondary infections averted were accounted for in the comparison of testing frequencies.

* Linkage to care starts at 30% linked to care in the first year after diagnosis and 3% each year thereafter. The failure rates from HAART range from 1% failure each year, to 40% failure during the first year with 15% failing each year thereafter.

** Quality of life differentials refers to the magnitude of the difference between the values for the highest CD4 strata (>350) and lowest (<200).

† The elasticity refers to the ratio of a percent change in the CE ratio (with secondary infections accounted for) to a corresponding percent change in the parameter.

Table 4

Selected sensitivity analysis outcomes for incidence of 0.013.

Variable	Variable low-end	Base-case 5 yrs					Variable high-end	Elasticity†
Years with HIV incidence	5 years	--	--	--			n/a	--
Ave. CD4 decline/yr, untreated	22 cells/μL/yr	7.5 yrs	6 yrs	--	--	4 yrs	75 cells/μL/yr	0.459
Time to detect virologic failure	3 mo.	--	--	--	--	--	24 mo.	0.025
Reduction in transmission due to diagnosis	0%	7.5 yrs	6 yrs	--	--	4 yrs	50%	0.734
VCT cost, per tester	$2	2 yrs	4 yrs	--	7.5 yrs	15 yrs	$50	0.047
1st-line HAART cost, per patient-year	$50	7.5 yrs	7.5 yrs	--	--	--	$1000	0.383
2nd-line HAART cost, per patient-year	$200	6 yrs	6 yrs	--	--	--	$2000	0.326
Linkage from diagnosis to care*	30% +	7.5 yrs	6 yrs	--	--	--	100%	0.048
Mortality rate, on effective ART	½ base	--	--	--	--	6 yrs	2 × base	−0.047
Failure rates on 1st-line HAART*	1% +	6 yrs	6 yrs	--	--	--	40% +	0.191
Failure rates on 2nd-line HAART*	1% +	--	--	--	--	6 yrs	40% +	0.052
HIV transmission rates, no treatment (reproductive number)	R0 = 0.5	6 yrs	6 yrs	--	--	--	R0 = 1.2	−0.369
HIV transmissions, on ART (per person-year)	0.001	--	--	--	--	--	0.045	0.019
Quality of life values**	Small differential	6 yrs	--	--	--	4 yrs	Large differential	−0.458
Maximal rise in CD4 count due to suppressive HAART	½ base	--	--	--	6 yrs	6 yrs	1.5 × base	--
Length of follow-up after year 30 (base = 15 years)	n/a			--	--	--	40 yrs	--

The center column represents the base-case, represented with a dash. Outer columns represent the variable low and high values, while the columns between the base-case and outer extremes represent an intermediate value. Dashes indicate that the most cost-effective frequency is the same as for the base-case; otherwise, the frequency is indicated. Secondary infections averted were accounted for in the comparison of testing frequencies.

* Linkage to care starts at 30% linked to care in the first year after diagnosis and 3% each year thereafter. The failure rates from HAART range from 1% failure each year, to 40% failure during the first year with 15% failing each year thereafter.

** Quality of life differentials refers to the magnitude of the difference between the values for the highest CD4 strata (>350) and lowest (<200).

† The elasticity refers to the ratio of a percent change in the CE ratio (with secondary infections accounted for) to a corresponding percent change in the parameter.

Table 5

Selected sensitivity analysis outcomes for incidence of 0.040

Variable	Variable low-end	Base-case 2 yrs					Variable high-end	Elasticity†
Years with HIV incidence	2 years	--	--	--			n/a	--
Ave. CD4 decline/yr, untreated	22 cells/μL/yr	3 yrs	3 yrs	--	--	--	75 cells/μL/yr	0.447
Time to detect virologic failure	3 mo.	--	--	--	--	--	24 mo.	0.022
Reduction in transmission due to diagnosis	0%	4 yrs	3 yrs	--	--	--	50%	0.863
VCT cost, per tester	$2	6 mo	1 yr	--	4 yrs	7.5 yrs	$50	0.038
1st-line HAART cost, per patient-year	$50	4 yrs	3 yrs	--	--	--	$1000	0.383
2nd-line HAART cost, per patient-year	$200	3 yrs	3 yrs	--	--	1 yr	$2000	0.334
Linkage from diagnosis to care*	30% +	3 yrs	--	--	--	--	100%	0.058
Mortality rate, on effective ART	½ base	--	--	--	--	3 yrs	2 × base	−0.059
Failure rates on 1st-line HAART*	1% +	3 yrs	--	--	--	--	40% +	0.190
Failure rates on 2nd-line HAART*	1% +	--	--	--	--	--	40% +	0.055
HIV transmission rates, no treatment (reproductive number)	R0 = 0.5	4 yrs	3 yrs	--	--	--	R0 = 1.2	−0.416
HIV transmissions, on ART (per person-year)	0.001	--	--	--	--	--	0.045	0.022
Quality of life values**	Small differential	3 yrs	--	--	--	--	Large differential	−0.418
Maximal rise in CD4 count due to suppressive HAART	½ base	--	--	--	--	3 yrs	1.5 × base	--
Length of follow-up after year 30 (base = 15 years)	n/a			--	--	--	40 yrs	--

The center column represents the base-case, represented with a dash. Outer columns represent the variable low and high values, while the columns between the base-case and outer extremes represent an intermediate value. Dashes indicate that the most cost-effective frequency is the same as for the base-case; otherwise, the frequency is indicated. Secondary infections averted were accounted for in the comparison of testing frequencies.

* Linkage to care starts at 30% linked to care in the first year after diagnosis and 3% each year thereafter. The failure rates from HAART range from 1% failure each year, to 40% failure during the first year with 15% failing each year thereafter.

** Quality of life differentials refers to the magnitude of the difference between the values for the highest CD4 strata (>350) and lowest (<200).

† The elasticity refers to the ratio of a percent change in the CE ratio (with secondary infections accounted for) to a corresponding percent change in the parameter.