The cost-effectiveness of symptom-based testing and routine screening for acute HIV infection in men who have sex with men in the USA

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Objective: Acute HIV infection often causes influenza-like illness (ILI) and is associated with high infectivity. We estimated the effectiveness and cost-effectiveness of strategies to identify and treat acute HIV infection in men who have sex with men (MSM) in the USA.

Design: Dynamic model of HIV transmission and progression.

Interventions: We evaluated three testing approaches: viral load testing for individuals with ILI, expanded screening with antibody testing, and expanded screening with antibody and viral load testing. We included treatment with antiretroviral therapy for individuals identified as acutely infected.

Main outcome measures: New HIV infections, discounted quality-adjusted life years (QALYs) and costs, and incremental cost-effectiveness ratios.

Results: At the present rate of HIV-antibody testing, we estimated that 538 000 new infections will occur among MSM over the next 20 years. Expanding antibody screening coverage to 90% of MSM annually reduces new infections by 2.8% and costs US$ 12 582 per QALY gained. Symptom-based viral load testing with ILI is more expensive than expanded antibody screening, but is more effective and costs US$ 22 786 per QALY gained. Combining expanded antibody screening with symptom-based viral load testing prevents twice as many infections compared to expanded antibody screening alone, and costs US$ 29 923 per QALY gained. Adding viral load testing to all annual HIV tests costs more than US$ 100 000 per QALY gained.

Conclusion: Use of HIV viral load testing in MSM with ILI prevents more infections than does expanded annual antibody screening alone and is inexpensive relative to other screening interventions. Clinicians should consider symptom-based viral load testing in MSM, in addition to encouraging annual antibody screening.

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Introduction

In the USA, more than 1.1 million people are living with the human immunodeficiency virus (HIV), and an estimated 56 000 people are infected with HIV annually [1,2]. Men who have sex with men (MSM) account for 53% of new HIV infections in the USA and are an important target group for treatment and prevention programs [1].

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Currently, approximately two-thirds of MSM receive HIV testing at least annually, as recommended by the US Centers for Disease Control and Prevention (CDC) [3–5]. Most screening programs use antibody tests to detect HIV infection. However, current antibody tests fail to detect HIV infection in the first few weeks after infection [6,7]. During the acute infection phase, viral load is very high, and infectivity is much greater than during chronic infection [6,8]. Infection can be detected during this phase with viral load tests. Early identification could reduce disease transmission through interventions to limit risky sexual behavior and early initiation of antiretroviral therapy (ART).

Approximately 70% of people with acute HIV infection develop symptoms of influenza-like illness (ILI), which can sometimes facilitate the early identification of new infections [9–11]. The CDC currently recommends an HIV viral load test in addition to an antibody test for patients with an ILI and recent high-risk behavior [5]. However, decisions about viral load testing are complicated by the lack of sensitivity and specificity of ILI symptoms for acute HIV.

Initiating ART during the acute phase may offer substantial benefits. ART effectively suppresses viral replication during acute infection, suggesting that treatment could be an effective method of reducing transmission [12,13].

Prior studies have assessed the diagnostic yield, costs, and cost-effectiveness of screening for acute infection [7,14–18]. However, no studies included treatment with ART and the associated benefits from reduced transmission. We examined the effectiveness and cost-effectiveness of strategies for expanded testing of MSM, with an emphasis on identifying acutely infected individuals and providing them ART.

Methods

Overview and model structure

We developed a dynamic compartmental model of HIV transmission and progression to compare the effectiveness and cost-effectiveness of alternative testing strategies (additional model details in the Appendix, http://links.lww.com/QAD/A157). We instantiated the model for MSM aged 13–64 years in the USA, consistent with CDC recommendations of routine HIV screening [5]. We implemented the model using weekly time steps and calibrated to estimates of HIV incidence among MSM [1]. We estimated HIV prevalence, incidence, quality-adjusted life years (QALYs), and healthcare costs over a 20-year time horizon. All costs (in 2009 US$) were assessed from a societal perspective, and costs and QALYs were discounted at 3% annually [19]. Table 1 summarizes key model parameters.

The population was segmented by HIV infection status, screening status, HIV disease stage, and treatment status if infected. Initial HIV prevalence in the MSM population was 8.5%, with undetected prevalence of 3.2%, representing an average across the USA [1,2,20,21]. Mortality was decomposed into HIV-related and non-HIV-related death rates.

Testing strategies

We estimated that 67% of MSM were screened annually using antibody tests [3,4]. Pre-test and post-test counseling resulted in a 20% reduction in risky behavior for both infected and uninfected individuals [22–24]. Uninfected tested individuals were eligible for retesting after 1 year. Our antibody screening test had characteristics similar to a rapid-test protocol in which positive results are confirmed by a western blot test, and newly identified individuals received results and counseling at the point of care.

We evaluated testing for acute infection with an individual viral load test following a negative antibody test [7,14]. Costs of testing also included a confirmatory viral load test and western blot at a follow-up visit.

We considered two approaches for acute infection testing: symptom-based viral load testing and adding viral load testing to the annual screening protocol. We also considered expanding screening coverage, alone and in combination with symptom-based testing. We compared alternative strategies to the status quo of 67% of MSM screened annually with antibody tests.

We first evaluated expanding annual antibody screening coverage to 90%, without viral load testing, and then we considered symptom-based testing for acute infection with 67 and 90% screening coverage. Approximately 70% of people with acute infection are expected to develop ILI [9–11], and we estimated that 35% of those seek care, based on the percentage of people in the USA who seek healthcare for ILI [10,25]. Our symptom-based strategies assumed that every MSM presenting with febrile ILI received an antibody test followed by a viral load test if the antibody test was negative. We also examined strategies with routine viral load testing for screened individuals whose antibody test was negative, in combination with symptom-based testing.

Antiretroviral therapy

Individuals identified as chronically HIV-infected with a CD4 cell count of 350 cells/μl or lower were offered ART [26]. We assumed a 90% reduction in sexual infectivity due to ART in our base case and varied this in sensitivity analysis [8,22,27]. We incorporated the benefits of ART during chronic infection, including improved quality of life and reduced disease progression and mortality [22,23]. In sensitivity analysis, we examined the effects of individuals initiating ART at a CD4 cell

Table 1. Summary of key model parameters.

Parameter[a]	Value	Range
Demographic parameters		
Total MSM population age 13–64	6 435 210	5.5–7.5 million
HIV prevalence in MSM	8.5%	1–17%
Male mortality rate	0.0043	0.003–0.005
Male maturation rate	0.0106	0.005–0.02
Male entry rate	0.022	0.01–0.04
Disease parameters		
Average disease duration (years)		
Acute HIV	0.25	0.08–0.40
Asymptomatic HIV	7	6–10
Symptomatic HIV	3	1–4
Symptomatic HIV-treated with ART	18	12-30
AIDS	2	1–3
AIDS-treated with ART	5	2–15
Sexual behavior parameters		
Annual transmission probability per MSM partnership ($M_{HIV+} \rightarrow M_{HIV-}$)		
Acute HIV	0.210	0.10–0.40
Asymptomatic HIV	0.039	0.02–0.08
Symptomatic HIV	0.039	0.02–0.08
AIDS	0.160	0.08–0.30
Annual number of male partners	3.0	2.0–5.0
Condom usage with male partners	40%	30–60%
Treatment parameters		
Fraction of acutely infected starting ART after diagnosis	50%	0–100%
Fraction starting ART at CD4 = 350 cells/μl	50%	25–75%
Rate of initiating ART at CD4 < 350 cells/μl	0.05	0–0.10
Reduction in sexual infectivity due to ART	90%	50–99%
Screening parameters		
Fraction of population tested annually	67%	30–90%
Fraction of acutely infected who develop symptoms	70%	40–90%
Fraction of patients with influenza-like symptoms who seek medical attention	35%	10–100%
Identification duration if uninfected (years)	1	0.5–3
Reduction in sexual behavior due to testing and counseling	20%	0–50%
Cost parameters (2009 US$)		
Annual HIV-related healthcare costs		
Acute HIV	30	10–500
Asymptomatic HIV-untreated	4 100	3 000–6 000
Symptomatic HIV-untreated	6 883	5 000–9 000
Symptomatic HIV-treated with ART (excludes ART costs)	6 136	5 000–7 000
AIDS-untreated	21 700	15 000–25 000
AIDS-treated with ART (excludes ART costs)	9 877	6 000–17 000
Annual non-HIV-related healthcare costs	4 028	3 000–6 000
Annual cost of ART	15 475	12 500–19 000
Cost of HIV testing-VL test		
Uninfected	124	51–248
HIV-infected	277	102–344
Cost of HIV testing-antibody test		
Uninfected	13	5–25
HIV-infected	67	50–100
Cost of counselling		
Pre-test counseling	13	0–100
Post-test counseling for HIV-negative persons	7	0–50
Post-test linkage/counseling for HIV-positive persons	14	0–100
Cost of HIV diagnosis	500	125–1 200
Discount rate	3%	0–5%

ART, antiretroviral treatment; MSM, men who have sex with men; VL, viral load.
[a]All rates are annual. See Appendix (http://links.lww.com/QAD/A157) for sources.

count of 500 cells/μl or higher, given recent guidelines recommending earlier ART initiation [28].

We assumed ART reduces infectivity of acutely infected individuals by 90% as well [12,13]. We assumed ART was initiated immediately following diagnosis and continued for 3 months. We estimated that half of those identified as acutely infected would accept ART using data on willingness of chronically infected patients to start ART [22,29]. Thus, in our base case symptom-based strategy, we estimated that 70% of acutely infected individuals develop symptoms, 35% of those seek care and receive viral load testing, and 50% of those identified receive ART, for a total of 12% treated during acute infection.

HIV transmission and progression

We modeled HIV transmission via homosexual contact. The probability of HIV transmission between serodiscordant homosexual partners depended on the number of sexual partners [3,30], average condom use [31], condom effectiveness [32], and the transmission probability per partnership [8,33]. The transmission probability per partnership depended on the HIV disease stage and ART status of the infected individual.

HIV-infected individuals progressed through the four modeled disease stages: acute infection, asymptomatic HIV, symptomatic HIV, and AIDS. Progression rates were based on models of HIV natural history [22,23].

Health outcomes and costs

We calculated discounted costs and QALYs for each strategy. We estimated quality of life for each health state from published literature and adjusted the utilities based on the average age of the modeled population [22,23,34].

Total health-related costs for individuals during the 20-year time frame were calculated from the costs associated with each health state and the costs of HIV testing, counseling, and diagnosis. Baseline medical costs, HIV-related healthcare costs, cost of ART, and costs of counseling were estimated from the published literature [22,35]. Costs of HIV testing protocols were obtained from the Centers for Medicare and Medicaid Services 2009 fee schedules [36]. Discounted lifetime health-related costs and QALYs were also incorporated for the population remaining at the end of the time horizon and for individuals who matured out of the model.

Results

Health outcomes

At current testing and treatment levels, we estimate that 538 371 new HIV infections will occur among MSM in the USA in the next 20 years (Table 2). This incidence can be reduced with the testing and treatment strategies we evaluated. Expanding antibody screening coverage to 90% annually will reduce the number of infections over 20 years by 14 923 (2.8% of the projected total) and yield 183 535 incremental QALYs (Table 2). Symptom-based viral load testing yields greater health benefits. Over 20 years, adding symptom-based testing to current annual screening rates leads to 22 446 fewer new infections and 218 085 more QALYs compared to the status quo. Combining symptom-based viral load testing with expanded antibody screening of MSM averts 30 780 new infections (5.7%) and adds 321 164 QALYs compared to the status quo. Finally, expanded screening with both antibody and viral load tests, in combination with symptom-based viral load testing, provides the most health benefits, with 38 995 (7.2%) infections averted.

Table 2. Benefits and costs of acute HIV testing and treatment strategies over 20 years-base case.

Strategy[a]	New HIV infections[b]	HIV infections prevented[c]	HIV Ab tests administered (millions)	HIV VL tests administered (millions)	Total costs (billion US$)[d]	Total QALYs (millions)[d]	Incremental costs[e] (billion US$)	Incremental QALYs[e]	ICER relative to[f]	
									Status quo (US$)	Next best strategy (US$)
90% annually, Ab + VL + symptom-based	499 376	38 995 (7.2%)	118.28	120.19	1283	176.39	13.65	389 711	35 032	105 398
90% annually, Ab + symptom-based	507 591	30 780 (5.7%)	118.31	38.88	1276	176.32	6.43	321 164	20 013	29 923
67% annually, Ab + VL + symptom-based	510 651	27 720 (5.1%)	95.43	96.85	1280	176.27	10.23	263 663	38 783	Dominated
67% annually, Ab + symptom-based	515 925	22 446 (4.2%)	95.44	38.85	1275	176.22	4.97	218 085	22 786	Dominated
90% annually, Ab	523 448	14 923 (2.8%)	87.68	–	1272	176.19	2.31	183 535	12 582	12 582
Status quo (67% annually, Ab)	538 371		65.46	–	1270	176.00				

[a]Ab, antibody testing; VL, viral load testing.
[b]New HIV infections and HIV infections prevented are undiscounted totals. Discounting infections at 3% annually reduces the number of infections averted for each strategy by approximately 25%.
[c]The values in parentheses are the fraction of total HIV infections prevented.
[d]Costs and quality-adjusted life years (QALYs) are net present values (3% discount rate) over 20 years.
[e]Incremental costs and QALYs are relative to the status quo.
[f]ICER, incremental cost-effectiveness ratio; relative to the status quo or the next-best strategy. Strategies that are dominated yield fewer QALYs at higher cost than the comparator.

Cost-effectiveness

Expanding annual antibody screening coverage to 90% is cost-effective by conventional standards, with an incremental cost-effectiveness ratio (ICER) of US$ 12 582 per QALY gained compared to the status quo (Table 2 and Fig. 1). This expanded screening generates an incremental US$ 2.31 billion in healthcare-related costs compared to the status quo, or US$ 200 000 per infection averted.

Adding symptom-based testing for acute infection to current antibody screening rates is also cost-effective under our base case assumptions, costing US$ 22 786 per QALY gained relative to the status quo (Table 2 and Fig. 1). Combining symptom-based testing with expanded antibody screening provides greater health benefits than does either strategy separately and costs US$ 29 923 per QALY gained compared to expanded antibody screening alone. Symptom-based testing with current or expanded levels of screening is associated with higher healthcare-related costs incremental to the status quo than expanded screening alone, with total costs over 20 years of US$ 4.97 billion at current screening rates and US$ 6.43 billion with expanding screening. These costs include all medical costs (HIV and non-HIV-related) over the lifetime of the cohort; testing costs comprise 76–86% of these totals (Table 3).

In general, we find that symptom-based testing offers substantial gains in health benefits with favorable cost-effectiveness ratios. However, viral load screening of all MSM is substantially more expensive. In particular, annual antibody screening with viral load testing costs US$ 115 325 per QALY gained at current screening rates, or US$ 105 398 per QALY gained with expanded screening coverage (Fig. 1). Routine viral load testing costs more than US$ 10 billion over 20 years incremental to the status quo.

The budgetary consequences of the alternative strategies vary by an order of magnitude. This has important implications because short-term programmatic costs, such as testing costs and costs of ART during acute infection, may have different relevance than long-term costs of providing healthcare to the overall MSM population. In our analysis, the largest cost increment comes with adding viral load testing, since HIV-negative MSM with ILI are also tested due to the nonspecific symptoms (Table 3). Less than 1% of symptom-based viral load tests detect acute HIV infection. Expanded annual antibody screening costs approximately US$ 28 million more per year in testing costs than the status quo, or US$ 560 million over 20 years, whereas symptom-based viral load testing at current screening rates costs US$ 215

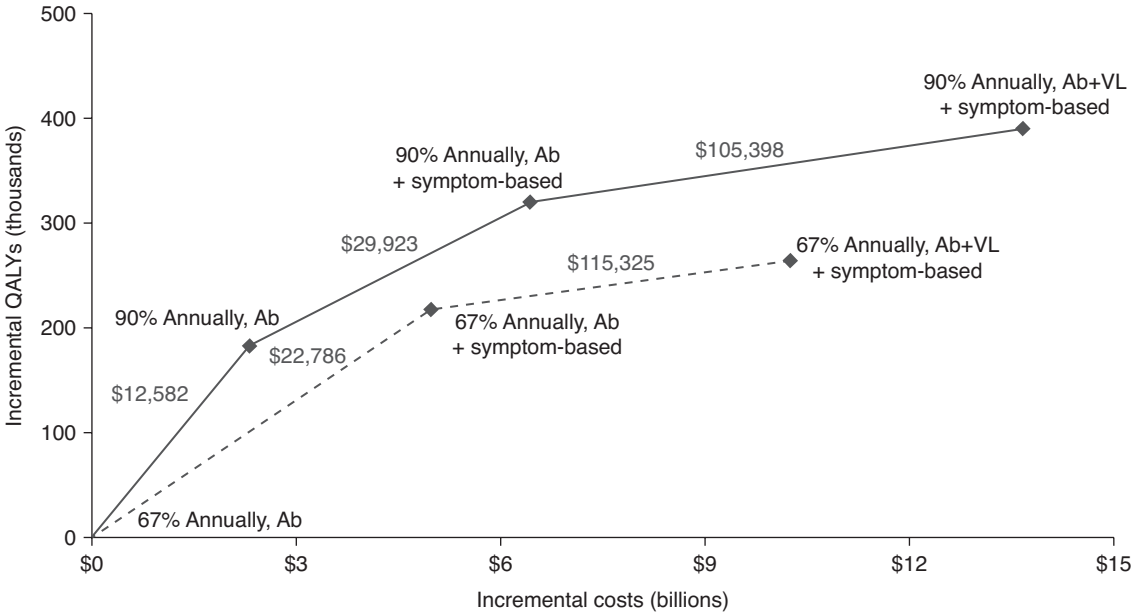

Fig. 1. Cost-effectiveness of testing for and treating acute HIV infection. Incremental costs and quality-adjusted life years (QALYs) are plotted for each strategy of testing for HIV infection, with the origin corresponding to the status quo. Under each strategy, 50% of individuals identified as acutely infected receive antiretroviral therapy (ART) for the duration of their acute infection. The solid lines show the incremental cost-effectiveness ratio (ICER) relative to the next-best alternative. The dashed lines show the ICER relative to the next-best alternative if increasing annual screening coverage is infeasible. Although these strategies are dominated by similar strategies with expanded annual screening coverage, they are relevant if increasing screening coverage is infeasible. Incremental costs and QALYs are calculated over a 20-year time horizon and are discounted to the present at 3% annually. Ab, antibody; VL, viral load; symptom-based = 35% of symptomatic acutely infected MSM receive Ab and VL testing.

Table 3. Costs of acute HIV testing and treatment strategies, incremental to status quo-base case.

Strategy[a]	Incremental non-HIV healthcare costs[b] (million US$)	Incremental HIV healthcare costs[b,c] (million US$)	Incremental ART costs[b] (million US$)	Incremental screening and testing costs[b] (million US$)	Total incremental costs[d] (million US$)
90% annually, Ab + VL + symptom-based	302	214	435	12 304	13 652
90% annually, Ab + symptom-based	272	334	459	4 868	6 428
67% annually, Ab + VL + symptom-based	179	54	238	9 589	10 226
67% annually, Ab + symptom-based	156	89	235	4 294	4 969
90% annually, Ab	200	477	459	560	2 309

[a]Ab, antibody testing; VL, viral load testing.
[b]Costs are net present values (3% discount rate) over 20 years.
[c]HIV healthcare costs do not include costs of ART.
[d]Costs are net present values (3% discount rate) over 20 years and include future lifetime costs (those incurred after individuals age out of the model upon turning 65 until death, and those incurred by the population alive in the model at the end of 20-year time horizon until that population dies out). This column does not equal the sum of the other four columns because of the inclusion of future lifetime costs.

million more per year in testing costs than the status quo, or US$ 4.29 billion over 20 years.

Sensitivity analysis

We performed sensitivity analysis on all model parameters (ranges in Table 1) and found that the results were stable to nearly all assumptions. Parameters to which results were sensitive are described below (probabilistic sensitivity analysis is presented in the Appendix, http://links.lww.com/QAD/A157). When initial HIV prevalence in the overall MSM population drops below 3% (compared to our base case estimate of 8.5%), symptom-based testing costs more than US$ 50 000 per QALY gained (Fig. 2). If infectivity during acute infection is at least twice as high as in the base case or if MSM have at least 50% more sex partners, symptom-based viral load testing becomes more favorable than expanded antibody screening, with an ICER of US$ 10 000 or less compared to the status quo.

The percentage of symptomatic MSM identified and treated could vary across cities and regions as a result of public health campaigns, and would depend on the proportion visiting a healthcare setting, consenting to or requesting treatment, and lost to follow-up. If none of those identified as acutely infected receive ART, the cost-effectiveness of symptom-based viral load testing decreases to approximately US$ 60 000 per QALY gained. If, on the contrary, every symptomatic infected

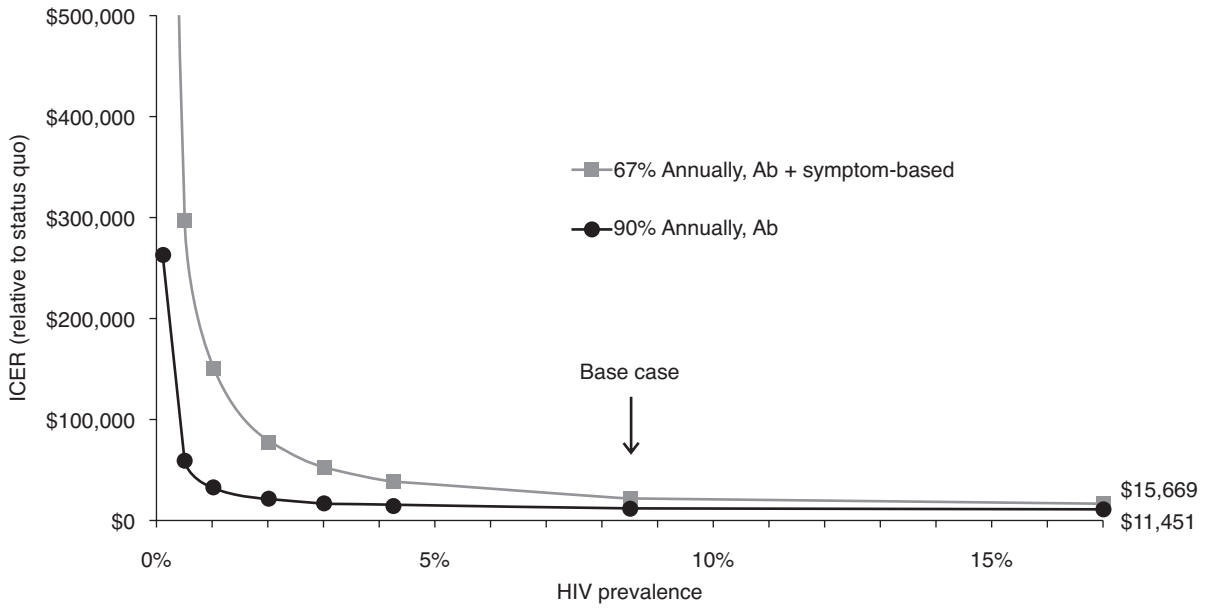

Fig. 2. Incremental cost-effectiveness ratio of testing for and treating acute HIV infection by HIV prevalence. The horizontal axis displays the initial HIV prevalence in the total modeled population, and the vertical axis shows the incremental cost-effectiveness ratio (ICER) relative to the status quo. Under each strategy, 50% of individuals identified as acutely infected receive antiretroviral therapy (ART) for the duration of their acute infection. Incremental costs and quality-adjusted life years (QALYs) used to calculate the ICER are calculated over a 20-year time horizon and are discounted to the present at 3% annually. Ab, antibody; symptom-based = 35% of symptomatic acutely infected MSM receive Ab and viral load testing.

individual could be identified and put on ART, so that 70% of acutely infected individuals receive treatment, symptom-based viral load testing is more effective than with base case assumptions and similarly cost-effective.

We tested the possibility that promoting symptom-based viral load testing would lead to higher rates of uninfected MSM seeking symptom-based testing, as with minor cold symptoms. This would make symptom-based testing less attractive, as the case-finding rate of symptom-based testing would decline. We find that symptom-based testing remains cost-effective at less than US$ 50 000 per QALY gained if up to four times as many uninfected individuals present for viral load testing as in the base case. This could also occur, for example, during a heavy influenza season.

There is not yet conclusive data on long-term effects of early treatment [37], so we assumed in our base case that early treatment has no effect on disease progression or future health outcomes. In sensitivity analysis, we examined the possible contribution of increased long-term adverse events due to early treatment. Our results were insensitive to modest increases in HIV-related mortality as a possible consequence of early ART. We also examined the effects of individuals treated during the acute phase remaining on ART for their entire life, incurring costs of treatment but not receiving any benefit beyond the benefits others obtain when starting ART during chronic infection. This results in more favorable cost-effectiveness for all viral load testing strategies, as the additional infections averted and QALYs gained from guaranteed treatment in later disease stages outweigh the costs of earlier treatment. The results are similar if individuals treated during acute infection remain on ART for 6 months or a year but not indefinitely, as the reduced infectivity from ART produces additional transmission benefits.

Discussion

Our analysis provides novel insights into the clinical impact and cost-effectiveness of HIV testing and treatment strategies among MSM in the USA. We show that in this population, in which HIV prevalence often exceeds 10%, expanded annual screening with HIV-antibody tests alone can reduce the number of new infections over the next 20 years by 15 000 and improve quality-adjusted life expectancy. However, we also show that symptom-based viral load testing alone, without expanding antibody testing, can prevent more infections and provide more QALYs than expanded antibody screening, and may be an attractive strategy when expanded annual screening is not feasible. This underscores the importance of curtailing HIV transmission during acute infection, when high infectivity facilitates HIV transmission, and of the use of ART in preventing transmission.

Among the various preventive measures being considered to reduce the HIV epidemic, our analysis illustrates the importance of testing interventions for HIV prevention among MSM. Our demonstration of the efficacy of expanded testing alone provides an important addition to our current understanding of HIV testing.

Although expanding antibody screening to 90% annually represents the best value among our strategies, implementation may be challenging. Current estimated rates of annual testing (67%) are high, and MSM who do not already test annually may be difficult to reach. Alternatively, we show that symptom-based viral load testing, whereas more expensive per QALY gained than expanded antibody testing, is also more effective and is very cost-effective by conventional criteria when compared with the status quo. This suggests a unique opportunity for substantial improvements in health outcomes at an acceptable cost through a strategy that can be implemented by physicians who come in contact with MSM.

A key parameter in our analysis is that only 35% of MSM with symptoms of ILI seek medical attention [25]. A recommendation for MSM to get an HIV viral load test when experiencing influenza-like symptoms may lead some MSM to seek medical attention with mild cold symptoms, and physicians to subsequently recommend HIV viral load testing. We show that even if four times as many uninfected individuals seek HIV testing due to symptoms, symptom-based testing remains cost-effective by conventional criteria.

The budget implications of symptom-based testing and treatment are important. Implementing symptom-based testing would result in an 8% increase in spending on HIV testing and treatment in the MSM population. This is largely due to the high cost of viral load testing, which accounts for 86% of the incremental costs of symptom-based testing. Because of the short duration of acute HIV infection and the nonspecific symptoms, less than 1% of viral load tests detect a case of HIV infection. Increasing the yield of symptom-based viral load testing, for example by encouraging MSM to watch for symptoms after high-risk behaviors, could make the intervention more efficient.

Prior studies assessing the cost-effectiveness of viral load testing for acute infection are limited. Coco [17] assessed the cost-effectiveness of symptom-based testing, and Hutchinson *et al.* [18] evaluated the cost-effectiveness of pooled viral load screening. Coco found symptom-based testing cost approximately US$ 30 000 per QALY gained in a general population with viral symptoms. The analysis did not include the secondary effects of testing on transmission. Hutchinson *et al.* found that pooled viral load testing after a negative antibody test during routine

screening was only likely to cost less than US$ 100 000 per QALY gained in settings with very high HIV incidence, such as a community clinic serving MSM. Our study builds on the findings of each of these studies and illustrates the health benefits that can be achieved in the MSM population with symptom-based viral load testing and use of ART during acute infection.

Our study has several limitations. First, we assumed that treatment with ART during acute infection provides no benefits to the treated individual. Observational studies suggest that ART during acute infection may delay CD4 decline, increase the probability of low plasma viral load after treatment discontinuation, and delay immunological decline [37,38]. Incorporating such benefits would only improve cost-effectiveness estimates and the case for early identification. Second, we assumed that HIV antibody tests are completely insensitive during acute infection. However, the point at which antibodies become detectable varies. A fourth-generation enzyme immunoassay (EIA) that detects infection earlier was approved for use in the USA in June 2010 [6,39]. Standard viral load tests are more sensitive to acute infection, however, and the new fourth-generation EIA does not distinguish between the detection of acute infection or HIV antibodies. Since acutely infected patients must be identified as such in order to receive ART during the acute phase, strategies using fourth-generation EIAs to detect acute infection would require confirmatory testing to identify infections as acute, complicating the testing algorithm and reducing the cost savings from avoiding viral load tests. Thus, viral load tests may be more appropriate for symptom-based testing. Third, we assumed a homogeneous population of MSM, whereas in reality MSM fall along a spectrum of risky behavior. If high-risk MSM are less likely than low-risk men to present to a healthcare setting when they have ILI, the impact of symptom-based viral load testing may be overestimated here; if the converse is true, the impact of symptom-based testing may be underestimated. Fourth, we did not consider the possibility of increased drug resistance, which could be a concern with increased ART use. However, the effects of resistance could be approximated by lower ART efficacy and higher ART cost, to which our results were not sensitive. Fifth, we did not explicitly model non-AIDS-defining events, such as neurocognitive decline, cardiovascular events, renal disease, and cancers, which factor into the life expectancy and quality of life of AIDS patients. However, we account for these in the mortality rates and quality-of-life weights that we use for HIV patients. Lastly, we assumed individual viral load tests. Whereas this is necessary for symptom-based testing and critical for short turnaround times in reporting results and initiating ART, annual viral load screening could make use of pooling schemes to reduce cost. We examine the implications of this in more depth in the Appendix (http://links.lww.com/QAD/A157).

Our analysis did not consider some factors specific to the strategies themselves that could be key to their implementation. The clinical and ethical ramifications of discontinuing treatment after the acute infection phase is over should be examined in more detail. Additionally, symptom-based testing may depend on patient and physician education, as a large proportion of MSM do not disclose same-sex activities to their primary care provider [40]. Convincing MSM to seek HIV testing upon onset of viral symptoms, and to comply with an ART regimen, may require evidence of individual health benefits, as transmission benefits alone may not be viewed as an impetus for treatment.

Our study indicates that augmenting annual HIV-antibody testing of MSM with viral load testing in patients with influenza-like symptoms could prevent more than 30 000 new HIV infections over 20 years, while costing less than many interventions accepted as cost-effective. Targeted viral load testing of symptomatic MSM provides approximately 80% of the benefit of universal viral load testing at less than half the cost. Identifying persons with acute HIV can prevent future new infections through behavior modification as well as early initiation of ART, and testing only symptomatic patients considerably narrows the pool of eligible MSM to test, although this strategy will invariably miss detecting persons with acute HIV who are asymptomatic. These findings can assist clinicians and MSM in making decisions about the value of testing and can inform policymakers' decisions about how to allocate limited HIV screening resources.

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Conflicts of interest

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References

1. Centers for Disease Control and Prevention (CDC). *Estimates of new HIV infections in the United States*. 2008; http://www.cdc.gov/hiv/topics/surveillance/resources/factsheets/incidence.htm. [Accessed 30 September 2009]
2. Centers for Disease Control and Prevention (CDC). *HIV prevalence estimates: United States, 2006; 2008*. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5739a2.htm. [Accessed 30 September 2009]
3. Centers for Disease Control and Prevention (CDC). *HIV/AIDS Surveillance Special Report, Number 5: HIV Testing Survey, 2002; 2006*. http://www.cdc.gov/hiv/topics/surveillance/resources/ reports/2004spec_no5/default.htm. [Accessed 27 January 2010]
4. Centers for Disease Control and Prevention (CDC). **Human immunodeficiency virus (HIV) risk, prevention, and testing behaviors: United States, National HIV Behavioral Surveillance System: Men who have sex with men, November 2003–April 2005**. *MMWR Morbid Mortal Wkly Rep* 2006; **55**:1–16.
5. Centers for Disease Control and Prevention (CDC). **Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings.** *MMWR Recomm Rep* 2006; **55**:1–17 [quiz CE11–CE14].
6. Pilcher CD, Christopoulos KA, Golden M. **Public health rationale for rapid nucleic acid or p24 antigen tests for HIV.** *J Infect Dis* 2010; **201 (Suppl 1)**:S7–S15.
7. Patel P, Klausner JD, Bacon OM, Liska S, Taylor M, Gonzalez A, *et al*. **Detection of acute HIV infections in high-risk patients in California.** *J Acquir Immune Defic Syndr* 2006; **42**:75–79.
8. McCormick AW, Walensky RP, Lipsitch M, Losina E, Hsu H, Weinstein MC, *et al*. **The effect of antiretroviral therapy on secondary transmission of HIV among men who have sex with men.** *Clin Infect Dis* 2007; **44**:1115–1122.
9. Vergis EN, Mellors JW. **Natural history of HIV-1 infection.** *Infect Dis Clin North Am* 2000; **14**:809–825; v-vi.
10. Schacker T, Collier AC, Hughes J, Shea T, Corey L. **Clinical and epidemiologic features of primary HIV infection.** *Ann Intern Med* 1996; **125**:257–264.
11. Daar ES, Little S, Pitt J, Santangelo J, Ho P, Harawa N, *et al*. **Diagnosis of primary HIV-1 infection. Los Angeles County Primary HIV Infection Recruitment Network.** *Ann Intern Med* 2001; **134**:25–29.
12. Pantazis N, Touloumi G, Vanhems P, Gill J, Bucher HC, Porter K. **The effect of antiretroviral treatment of different durations in primary HIV infection.** *AIDS* 2008; **22**:2441–2450.
13. Hoen B, Dumon B, Harzic M, Venet A, Dubeaux B, Lascoux C, *et al*. **Highly active antiretroviral treatment initiated early in the course of symptomatic primary HIV-1 infection: results of the ANRS 053 trial.** *J Infect Dis* 1999; **180**:1342–1346.
14. Pilcher CD, Fiscus SA, Nguyen TQ, Foust E, Wolf L, Williams D, *et al*. **Detection of acute infections during HIV testing in North Carolina.** *N Engl J Med* 2005; **352**:1873–1883.
15. Priddy FH, Pilcher CD, Moore RH, Tambe P, Park MN, Fiscus SA, *et al*. **Detection of acute HIV infections in an urban HIV counseling and testing population in the United States.** *J Acquir Immune Defic Syndr* 2007; **44**:196–202.
16. Stekler J, Swenson PD, Wood RW, Handsfield HH, Golden MR. **Targeted screening for primary HIV infection through pooled HIV-RNA testing in men who have sex with men.** *AIDS* 2005; **19**:1323–1325.
17. Coco A. **The cost-effectiveness of expanded testing for primary HIV infection.** *Ann Fam Med* 2005; **3**:391–399.
18. Hutchinson AB, Patel P, Sansom SL, Farnham PG, Sullivan TJ, Bennett B, *et al*. **Cost-effectiveness of pooled nucleic acid amplification testing for acute HIV infection after third-generation HIV antibody screening and rapid testing in the United States: a comparison of three public health settings.** *PLoS Med* 2010; **7**:e1000342.
19. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in health and medicine*. New York: Oxford University Press; 1996.
20. Centers for Disease Control and Prevention (CDC). *HIV/AIDS Surveillance Report*. Vol. 18; 2006; http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2006report/default.htm. [Accessed 30 September 2009]
21. U.S. Census Bureau PD. *U.S. Interim Projections by Age, Sex, Race, and Hispanic Origin: 2000–2050; 2001*. http://www.census.gov/population/www/projections/usinterimproj/. [Accessed 25 March 2010]
22. Long EF, Brandeau ML, Owens DK. **Health outcomes and costs of expanded HIV screening and antiretroviral treatment in the United States**. *Ann Intern Med* 2010; **153**.
23. Sanders GD, Bayoumi AM, Sundaram V, Bilir SP, Neukermans CP, Rydzak CE, *et al*. **Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy.** *N Engl J Med* 2005; **352**:570–585.
24. Marks G, Crepaz N, Senterfitt JW, Janssen RS. **Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs.** *J Acquir Immune Defic Syndr* 2005; **39**:446–453.
25. Molinari NA, Ortega-Sanchez IR, Messonnier ML, Thompson WW, Wortley PM, Weintraub E, *et al*. **The annual impact of seasonal influenza in the US: measuring disease burden and costs.** *Vaccine* 2007; **25**:5086–5096.
26. Hammer SM, Eron JJ Jr, Reiss P, Schooley RT, Thompson MA, Walmsley S, *et al*. **Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel.** *JAMA* 2008; **300**:555–570.
27. Wilson DP, Law MG, Grulich AE, Cooper DA, Kaldor JM. **Relation between HIV viral load and infectiousness: a model-based analysis.** *Lancet* 2008; **372**:314–320.
28. U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*; 2011. http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. [Accessed 11 May 2011]
29. Teshale EH, Kamimoto L, Harris N, Li J, Wang H, McKenna MT. **Estimated number of HIV-infected persons eligible for and receiving HIV antiretroviral therapy, 2003: United States** (abstract #167). In: *Proceedings of the 12th Conference on Retroviruses and Opportunistic Infections*; 2005.
30. Koblin BA, Chesney MA, Husnik MJ, Bozeman S, Celum CL, Buchbinder S, *et al*. **High-risk behaviors among men who have sex with men in 6 US cities: baseline data from the EXPLORE Study.** *Am J Public Health* 2003; **93**:926–932.
31. Pathela P, Hajat A, Schillinger J, Blank S, Sell R, Mostashari F. **Discordance between sexual behavior and self-reported sexual identity: a population-based survey of New York City men.** *Ann Intern Med* 2006; **145**:416–425.
32. Long EF, Brandeau ML, Galvin CM, Vinichenko T, Tole SP, Schwartz A, *et al*. **Effectiveness and cost-effectiveness of strategies to expand antiretroviral therapy in St. Petersburg, Russia.** *AIDS* 2006; **20**:2207–2215.
33. Xiridou M, Geskus R, De Wit J, Coutinho R, Kretzschmar M. **The contribution of steady and casual partnerships to the incidence of HIV infection among homosexual men in Amsterdam.** *AIDS* 2003; **17**:1029–1038.
34. Honiden S, Sundaram V, Nease RF, Holodniy M, Lazzeroni LC, Zolopa A, *et al*. **The effect of diagnosis with HIV infection on health-related quality of life.** *Qual Life Res* 2006; **15**:69–82.
35. Schackman BR, Gebo KA, Walensky RP, Losina E, Muccio T, Sax PE, *et al*. **The lifetime cost of current human immunodeficiency virus care in the United States.** *Med Care* 2006; **44**:990–997.
36. Centers for Medicare & Medicaid Services; 2009; http://www.cms.hhs.gov/home/medicare.asp. [Accessed 9 April 2010]
37. Cohen MS, Shaw GM, McMichael AJ, Haynes BF. **Acute HIV-1 infection.** *N Engl J Med* 2011; **364**:1943–1954.
38. Fidler S, Fox J, Porter K, Weber J. **Primary HIV infection: to treat or not to treat?** *Curr Opin Infect Dis* 2008; **21**:4–10.
39. FDA approves first-of-its-kind HIV test which can detect HIV days earlier than current U.S. tests. In Abbott Press Release; 2010.
40. Daskalakis D, Silvera R, Bernstein K, Stein D, Hagerty R, Hutt R, *et al*. **Implementation of HIV testing at 2 New York City bathhouses: from pilot to clinical service.** *Clin Infect Dis* 2009; **48**:1609–1616.