THE COST-EFFECTIVENESS OF SYMPTOM-BASED TESTING AND ROUTINE SCREENING FOR ACUTE HIV INFECTION IN MEN WHO HAVE SEX WITH MEN IN THE UNITED STATES

J.L. JUUSOLA, M.L. BRANDEAU, E.F. LONG, D.K. OWENS, E. BENDAVID

APPENDIX

Overview

We developed a dynamic compartmental model to assess the effectiveness and cost-effectiveness of various strategies of testing for and treating acute HIV infection in men who have sex with men (MSM) in the United States. Figure A1 shows a schematic representation of the model. Table A1 summarizes model notation. The model calculates $X_i(t)$, the number of individuals in each compartment $i = 1, \ldots, 13$ at time t. Individuals transition between compartments and age into or transition out of the system at rates defined by population demographics, disease progression parameters, and screening and treatment interventions. We incorporated epidemiologic, clinical, and economic data in order to estimate HIV prevalence, incidence, quality-adjusted life years (QALYs), and healthcare costs for various testing and treatment strategies. We implemented the model in Microsoft Excel 2007 using a weekly time step and considered a time horizon of 20 years.

Model Compartments

We estimated that there are approximately 6.4 million MSM aged 13-64 in the US [1-6]. We subdivided this population into 13 compartments, based on the following factors:

- HIV infection status (uninfected, infected)
- HIV disease stage if infected (acute infection, asymptomatic HIV: CD4 >350 cells/mm^3, symptomatic HIV: CD4 200-350 cells/mm^3, AIDS: CD4 <200 cells/mm^3)
- Screening status (unidentified, identified)

- Treatment status (receiving antiretroviral therapy (ART), not receiving ART)

Population Dynamics

We assumed that individuals enter the model at age 13 into compartment 1 (uninfected, unidentified) at a rate ρ, calculated based on US population data for males by age group [5, 6]. Individuals exit the population due to death or maturation. Individuals mature out of the population upon turning 65 at rate μ_i. All individuals die from non-AIDS related causes at rate δ_i, and individuals with AIDS (those in compartments 9, 10, and 13) die from AIDS at rate α_i. We allowed μ_i and δ_i to vary by compartment, but assumed that they were the same for all MSM, based on US population data for males [5-7]. In the absence of new interventions, the size of the population of MSM at the end of 20 years matches expected US population growth trends [5].

Interventions

Testing for acute HIV infection can be implemented with either p24 antigen tests or with HIV-1 viral load (VL) testing. Tests for p24 antigen are more specific and less expensive than VL tests, but they are less sensitive [8, 9]. In our analysis, we considered VL testing.

Studies on adding VL testing to routine antibody testing have shown that this additional testing increases the diagnostic yield for HIV infection by 4-10% [10-15]. Most of these screening programs have used pooling schemes, where serum or plasma samples that are negative for HIV antibodies are pooled and then tested using VL testing. Pooling is used to reduce cost and the potential for false positives. The additional cost of pooled VL testing in these programs, as compared to standard antibody screening alone, ranged from $3-17 per processed specimen, in populations with HIV prevalence ranging from 0.6-4.1% [10-12, 15]. Pooled VL testing in populations with higher HIV prevalence, such as the MSM population we modeled, would require more re-testing of positive samples, leading to a higher cost per specimen. Also,

pooling increases the turnaround time for notifying the patient of test results, especially in facilities with low volume of testing. During the acute infection phase, time is of the essence due to high transmission risk. Therefore, although pooling algorithms can be used with VL testing to reduce costs, we assumed in our analysis that all specimens are tested individually. In sensitivity analysis we considered pooled testing for routine VL testing, but not for symptom-based testing.

For symptom-based testing, we assumed that uninfected MSM present with influenza-like symptoms at the baseline rate of influenza in the population and are tested for HIV. This results in extra costs incurred for symptom-based testing strategies.

HIV Transmission

We assumed that HIV transmission occurs via homosexual contact. The total rate of contacts sufficient to transmit infection is the sum of the sufficient contact rates between an uninfected individual in compartment i (i = 1, 2) and an infected individual in compartment j (j = 3, …, 13), which we denote by $\beta_{i,j}(t)$.

We modeled the homosexual contact rate as a binomial process, similar to Long et al. [16, 17]. A "success" is defined as transmission of HIV, and uninfected individuals select $n(1-u_i\kappa)$ risky partners per year (i.e., partnerships involving unprotected sexual contact) with the probability of transmission per partnership being the probability of "success". The rate $\beta_{i,j}(t)$ is affected by condom usage, where the percent of partnerships involving condom usage is u_i, and by condom effectiveness, κ. The annual probability of transmission in a partnership, $\sigma_{i,j}$, assuming no condom usage or ineffective condom usage, depends on the disease stage of the infected individual and whether he is receiving ART. Uninfected individuals choose risky partners from infected compartment j based on the number of risky partnerships individuals in

compartment *j* have (homogeneous mixing). Hence the probability of selecting a risky partner from compartment *j* is:

$$P(select\,j) = \frac{X_j(t)n_j(1-u_j\kappa)}{\sum_k X_k(t)n_k(1-u_k\kappa)}$$

Combining all these factors, $\beta_{i,j}(t)$ can be calculated as follows:

$$\beta_{i,j}(t) = 1 - \left(1 - P(select\,j)\sigma_{i,j}\right)^{n_i(1-u_i\kappa)}$$

Uninfected individuals in compartments $i = 1, 2$ thus acquire HIV infection at time t with probability

$$\sum_{j>2}\beta_{i,j}(t) \quad .$$

We modeled the effects of HIV testing and counseling in reducing risky behavior as reductions in the number of sexual partnerships [16-20].

Disease Progression

After acquiring HIV infection, individuals progress through the disease stages at rate θ_i. These progression rates are inversely proportional to the average length of each stage and are based on previous models of the natural history of HIV infection [16-18]. ART lowers the progression rate θ_{12} and the AIDS death rate α_{13} by increasing the time spent in those states.

System of Equations

We modeled HIV transmission and progression with a system of 13 nonlinear differential equations. The equations describing the change in the number of individuals in each compartment at each time step are listed below. We let X_i denote $X_i(t)$ for ease of notation.

Change in number of unidentified uninfected individuals (compartment 1):

$$\frac{dX_1}{dt} = \rho\sum_i X_i - \left(\sum_{j>2}\beta_{1,j}(t)\right)X_1 - \psi X_1 + \omega_{id}X_2 - \mu_1 X_1 - \delta_1 X_1$$

Change in number of identified uninfected individuals (compartment 2):

$$\frac{dX_2}{dt} = -\left(\sum_{j>2}\beta_{2,j}(t)\right)X_2 + \psi X_1 - \omega_{id}X_2 - \mu_2 X_2 - \delta_2 X_2$$

Change in number of unidentified acutely infected individuals (compartment 3):

$$\frac{dX_3}{dt} = \left(\sum_{j>2}\beta_{1,j}(t)\right)X_1 + \left(\sum_{j>2}\beta_{2,j}(t)\right)X_2 - (\psi + \nu_3)X_3 - \theta_3 X_3 - \mu_3 X_3 - \delta_3 X_3$$

Change in number of identified, untreated acutely infected individuals (compartment 4):

$$\frac{dX_4}{dt} = (\psi + \nu_3)(1 - at_3)X_3 - \theta_4 X_4 \ - \mu_4 X_4 - \delta_4 X_4$$

Change in number of unidentified asymptomatic infected individuals (compartment 5):

$$\frac{dX_5}{dt} = \theta_3 X_3 - (\psi + \nu_5)X_5 - \theta_5 X_5 - \mu_5 X_5 - \delta_5 X_5$$

Change in number of identified asymptomatic infected individuals (compartment 6):

$$\frac{dX_6}{dt} = \theta_4 X_4 + (\psi + \nu_5)X_5 + \theta_{11}X_{11} - \theta_6 X_6 - \mu_6 X_6 - \delta_6 X_6$$

Change in number of unidentified symptomatic infected individuals (compartment 7):

$$\frac{dX_7}{dt} = \theta_5 X_5 - (\psi + \nu_7)X_7 - \theta_7 X_7 - \mu_7 X_7 - \delta_7 X_7$$

Change in number of identified, untreated symptomatic infected individuals (compartment 8):

$$\frac{dX_8}{dt} = \theta_6(1 - \phi_6)X_6 + (\psi + \nu_7)(1 - \phi_7)X_7 - \hat{\phi}_8 X_8 - \theta_8 X_8 - \mu_8 X_8 - \delta_8 X_8$$

Change in number of unidentified individuals with AIDS (compartment 9):

$$\frac{dX_9}{dt} = \theta_7 X_7 - (\psi + \nu_9)X_9 - \alpha_9 X_9 - \mu_9 X_9 - \delta_9 X_9$$

Change in number of identified, untreated individuals with AIDS (compartment 10):

$$\frac{dX_{10}}{dt} = \theta_8 X_8 + (\psi + \nu_9)(1 - \phi_9)X_9 - \hat{\phi}_{10} X_{10} - \alpha_{10} X_{10} - \mu_{10} X_{10} - \delta_{10} X_{10}$$

Change in number of identified, treated acutely infected individuals (compartment 11):

$$\frac{dX_{11}}{dt} = (\psi + \nu_3)at_3 X_3 - \theta_{11} X_{11} - \mu_{11} X_{11} - \delta_{11} X_{11}$$

Change in number of identified, treated symptomatic infected individuals (compartment 12):

$$\frac{dX_{12}}{dt} = \theta_6\phi_6 X_6 + (\psi + \nu_7)\phi_7 X_7 + \hat{\phi}_8 X_8 - \theta_{12} X_{12} - \alpha_{12} X_{12} - \mu_{12} X_{12} - \delta_{12} X_{12}$$

Change in number of identified, treated individuals with AIDS (compartment 13):

$$\frac{dX_{13}}{dt} = (\psi + \nu_9)\phi_9 X_9 + \hat{\phi}_{10} X_{10} + \theta_{12} X_{12} - \alpha_{13} X_{13} - \mu_{13} X_{13} - \delta_{13} X_{13}$$

Health Outcomes and Costs

We computed total costs (in 2009 US dollars) and health benefits over 20 years. When necessary, costs were inflated to 2009 US dollars using the GDP deflator calculated by the Bureau of Economic Analysis [21]. We discounted both costs and QALYs at an annual 3% rate. Because the time step of the model is weekly, we calculated the equivalent weekly discount rate with the following formula:

$$weeklyrate = \left((1 + 0.03)^{1/52}\right) - 1$$

Quality of life was weighted by an average age-specific baseline utility. The average was calculated using time trade-off assessment (TTO) measures for men aged 45-54 and 55-64 from the Beaver Dam Health Outcomes Study [22]. The weighted average utility for the modeled population assumed quality-of-life factor of 1 for ages 13-44.

In our estimates of quality of life for each health state, quality of life decreased with HIV disease progression and was improved by treatment with ART during chronic infection. We also incorporated a decrement in utility for learning of HIV-positive status [23].

The utility for acute infection was calculated based on the utility of influenza- or mononucleosis-like illness and the fraction of those infected who experience symptoms [9, 18, 23-30]. Quality of life during acute infection was not influenced by treatment with ART.

HIV-related healthcare costs during the acute infection phase were calculated based on expected costs for symptomatic patients. We summed the direct medical expenses for an outpatient visit to a physician (including lab fees, consult fees, and prescription medications),

and the cost of over-the-counter medications, and multiplied by the percent of acutely infected individuals who both are symptomatic and choose to visit a physician [9, 24-26, 31-33].

Costs and QALY decrements were incurred for false positives occurring during testing. The sensitivity and specificity of each test was estimated from the literature [8, 18, 26, 34-37], and costs and QALY decrements associated with positive test results were incurred for uninfected people for test specificities less than 1.0. Uninfected individuals who received a false positive test result, whether with an antibody test or a VL test, incurred a QALY decrement of 0.06 times their baseline utility for 14 days [18, 23, 38].

We calculated the number of new HIV infections averted under each strategy over the 20-year time horizon as the difference in the total number of new infections under the strategy and the total number of new infections under the status quo. We reported undiscounted infections, but we also calculated discounted infections, discounted at 3% annually. Discounting infections reduces the number of infections averted for each strategy by approximately 25%.

We calculated the incremental cost-effectiveness ratio (ICER) relative to the status quo and to the next-best strategy for each intervention. To do so, we summed the (discounted) QALYs incurred over the 20-year time horizon for each strategy as well as the status quo. We did the same for all (discounted) costs incurred. The ICER was then calculated as follows:

$$ICER = \frac{Cost_{Strategyi} - Cost_{StatusQuo}}{QALY_{Strategyi} - QALY_{StatusQuo}}$$

$$ICER = \frac{Cost_{Strategyi} - Cost_{NextBest}}{QALY_{Strategyi} - QALY_{NextBest}}$$

Sensitivity Analysis

We performed sensitivity analysis on all model parameters. Results were not significantly affected by most parameters. Table A4 shows results of sensitivity analysis for those parameters that did have an impact on results or that were discussed in the manuscript.

Recent guidelines recommend ART initiation at CD4 cell counts of greater than 350 cells/mm^3 [39]. Accordingly, we examined initiating ART at CD4 cell counts of 500 cells/mm^3 or greater in sensitivity analysis. With earlier ART initiation among the chronically infected in the status quo, assuming a 50% survival gain for those treated earlier, the effectiveness and cost-effectiveness of strategies remained qualitatively similar. Under all assumptions tested, symptom-based VL testing with treatment still cost less than $50,000 per QALY gained.

We analyzed pooled testing for annual VL screening in sensitivity analysis. If the cost per specimen tested is below $40, and if patients can be notified of their results and started on ART within one week, then adding VL testing to the annual screening protocol, in combination with symptom-based testing and expanded annual antibody screening, has a more favorable ICER (less than $30,000 per QALY gained) than symptom-based testing with annual antibody testing alone. At current antibody screening levels, adding VL testing to the annual screening protocol in combination with symptom-based testing has a more favorable ICER than symptom-based testing alone if cost per specimen is below $25. However, if we assume a moderate delay in starting ART during acute infection due to slower turnaround time with pooling (e.g., a delay of over two weeks), results are similar to the base case, with symptom-based testing with annual antibody screening alone being more cost-effective than adding pooled VL testing to the screening protocol.

Probabilistic Sensitivity Analysis

We conducted probabilistic sensitivity analysis using a Monte Carlo simulation with 10,000 runs. We chose and fitted distributions to each parameter, generally using beta distributions for parameters that ranged from 0 to 1 (e.g., probabilities, utilities) and gamma distributions for nonnegative, uncapped parameters (e.g., costs). Table A5 shows the distribution type and the fitted parameters for each value. The distributions in Table A5 were parameterized using the means and ranges from Tables 1 and A3. We ran "goal seek" in Excel to fit the relevant type of distribution to the inputs we obtained from the literature (e.g., base case value being mean or mode, and range being 95% confidence interval). We then calculated the relevant parameters for the fitted distribution (e.g., alpha and beta for beta distributions). These parameterized distributions were then used in the Monte Carlo simulation. In each simulation run, we sampled from the distribution for each listed input and calculated model results with the resulting set of inputs. All parameters in Table A5 were included in the sensitivity analysis.

After running 10,000 simulations and collecting the outputs of total discounted costs and QALYs for each strategy, we calculated the net benefit for each strategy in each simulation. Net benefit is calculated as $\lambda \times \text{QALYs} - \text{Cost}$, where λ is the willingness to pay for a QALY gained.

Results of the probabilistic sensitivity analysis supported base case results, as seen from the cost-effectiveness acceptability curves and frontier in Figures A2 and A3. Figure A3 shows that increasing annual antibody screening to 90% coverage without testing for acute infection is the optimal decision if willingness to pay for a QALY gained is less than approximately $20,000 per QALY gained. If willingness to pay is within the range of $20,000 – $80,000 per QALY gained, it is optimal to add symptom-based testing and treatment for acute HIV infection. Adding VL testing to the screening protocol is only optimal if willingness to pay for a QALY gained is closer to $100,000.

Table A1: Model Parameters and Notation

Parameter	Description
Demographic Parameters	
$X_i(t)$	Number of people in compartment *i* at time *t*
ρ	Entry rate of individuals into the model at age 13
μ_i	Maturation rate out of compartment *i*
δ_i	Non-AIDS death rate for compartment *i*
r	Annual discount rate
HIV Progression Parameters	
θ_i	HIV disease progression rate for compartment *i*
α_i	AIDS death rate for compartment *i*
Sexual Behavior Parameters	
n_i	Annual number of male partners of individuals in compartment *i*
u_i	Condom usage with male partners by individuals in compartment *i*
$\sigma_{i,j}$	Annual probability of HIV transmission per unprotected sexual partnership between uninfected (compartment *i*) and infected (compartment *j*) individuals
Transmission Variables	
$\beta_{i,j}(t)$	Sufficient contact rate at time *t* between uninfected (compartment *i*) and infected (compartment *j*) individuals
Treatment Parameters	
at_i	Fraction of acutely infected individuals (in compartment $i = 3$) starting ART after diagnosis
ϕ_i	Fraction of individuals in compartment *i* starting ART at CD4=350 cells/mm^3
$\hat{\phi}_i$	Rate of individuals in compartment *i* starting ART at CD4<350 cells/mm^3
ε_{hs}	ART efficacy in reducing sexual infectivity in infected individuals
Screening Parameters	
ψ	Probability of screening
ν_i	Probability of symptomatic testing or case-detection for individuals in compartment *i*
$\frac{1}{\omega_{id}}$	Average duration of identification status for uninfected individuals
p_{id}	Reduction in sexual behavior due to screening and counseling

Table A2: Summary of Key Model Parameters with Sources

Parameter*	Value	Range	Source
Demographic Parameters			
Total MSM population age 13-64	6,435,210	5.5-7.5 million	Calculated [1-6]
HIV prevalence in MSM	8.5%	1-17%	Calculated [1-6]
Male mortality rate	0.0043	0.003-0.005	Calculated [7]
Male maturation rate	0.0106	0.005-0.02	Calculated [5, 6]
Male entry rate	0.022	0.01-0.04	Calculated [5, 6]
Disease Parameters			
Average disease duration (years)			
Acute HIV	0.25	0.08-0.40	[9, 40-43]
Asymptomatic HIV	7	6-10	[16, 17, 44, 45]
Symptomatic HIV	3	1-4	[16, 17, 44, 45]
Symptomatic HIV – Treated with ART	18	12-30	[16, 17, 46, 47]
AIDS	2	1-3	[16, 17, 44, 45]
AIDS – Treated with ART	5	2-15	[16, 17, 46, 47]
Sexual Behavior Parameters			
Annual transmission probability per MSM partnership ($M_{HIV+} \rightarrow M_{HIV-}$)			
Acute HIV	0.210	0.10-0.40	[48-50]
Asymptomatic HIV	0.039	0.02-0.08	[16, 48-50]
Symptomatic HIV	0.039	0.02-0.08	[16, 48-50]
AIDS	0.160	0.08-0.30	[16, 48-50]
Annual number of male partners	3.0	2.0-5.0	[16, 51-53]
Condom usage with male partners	40%	30-60%	[16, 54-57]
Treatment Parameters			
Fraction of acutely infected starting ART after diagnosis	50%	0-100%	Assumed
Fraction starting ART at CD4=350 cells/mm^3	50%	25-75%	Estimated [16-18, 58]
Rate of initiating ART at CD4<350 cells/mm^3	0.05	0-0.10	Estimated [16-18]
Reduction in sexual infectivity due to ART	90%	50-99%	[16-18, 49, 59-66]
Screening Parameters			
Fraction of population tested annually	67%	30-90%	[51, 67, 68]
Fraction of acutely infected who develop symptoms	70%	40-90%	[9, 24-26, 34]
Fraction of patients with influenza-like symptoms who seek medical attention	35%	10-100%	Estimated [24, 32, 33] (Range assumed)
Identification duration if uninfected (years)	1	0.5-3	Assumed

Parameter*	Value	Range	Source
Reduction in sexual behavior due to testing and counseling	20%	0-50%	[16, 18-20]
Cost Parameters (2009 US $)			
Annual HIV-related healthcare costs			
Acute HIV	30	10-500	Calculated [9, 24-26, 31-33]
Asymptomatic HIV – Untreated	4,100	3,000-6,000	[16, 69, 70]
Symptomatic HIV – Untreated	6,883	5,000-9,000	[16, 69, 70]
Symptomatic HIV – Treated with ART (excludes ART costs)	6,136	5,000-7,000	[16, 69, 70]
AIDS – Untreated	21,700	15,000-25,000	[16, 69-72]
AIDS – Treated with ART (excludes ART costs)	9,877	6,000-17,000	[16, 18, 70]
Annual non-HIV-related healthcare costs	4,028	3,000-6,000	[73]
Annual cost of ART	15,475	12,500-19,000	[16, 18, 70, 72]
Cost of HIV testing – VL test			
Uninfected	124	51-248	[74]
HIV-Infected	277	102-344	[74]
Cost of HIV testing – antibody test			
Uninfected	13	5-25	[74]
HIV-Infected	67	50-100	[74]
Cost of counseling			
Pre-test counseling	13	0-100	[75, 76]
Post-test counseling for HIV-negative persons	7	0-50	[75, 76]
Post-test linkage/counseling for HIV-positive persons	14	0-100	[75, 76]
Cost of HIV diagnosis	500	125-1,200	[74]
Discount Rate	3%	0-5%	[77]

* All rates are annual. ART = antiretroviral treatment, MSM = men who have sex with men, VL = viral load

Table A3: Summary of Additional Model Inputs

Parameter*	Value	Range	Source
Disease Parameters			
Quality-of-life factors			
Uninfected	1.00	---	[16, 17, 22]
Acute HIV – Unidentified	0.92	0.73-0.97	Calculated [9, 24-30]
Acute HIV – Identified	0.86	0.68-0.91	Calculated [9, 18, 23-30]
Acute HIV – Treated with ART	0.86	0.68-0.94	Calculated [9, 18, 23-30]
Asymptomatic HIV – Unidentified	0.91	0.85-0.95	[17, 18, 23]
Asymptomatic HIV – Identified (Year 1)	0.84	0.84-0.95	[17, 18]
Asymptomatic HIV – Identified (Years 2+)	0.89	0.85-0.95	[17, 18]
Symptomatic HIV – Unidentified	0.79	0.70-0.80	[17, 18, 78, 79]
Symptomatic HIV – Identified	0.72	0.70-0.80	[17, 23]
Symptomatic HIV – Treated with ART	0.83	0.82-0.87	[16-18, 78]
AIDS – Unidentified	0.72	0.60-0.75	[16-18]
AIDS – Identified	0.72	0.60-0.75	[16, 17, 78, 79]
AIDS – Treated with ART	0.82	0.82-0.87	[16, 17, 78]
Age-specific multiplier	0.96	0.887-1	[22, 80, 81]
Sexual Behavior Parameters			
Condom effectiveness	90%	85-95%	[64]
Screening Parameters			
Weekly probability of influenza-like symptoms in general population	1.7%	0.5-3.1%	[31, 33, 82]
Annual probability of symptom-based case finding			
Symptomatic HIV	10%	0-30%	[16, 18]
AIDS	20%	10-60%	[16, 18]
Sensitivity of VL test, pre-seroconversion	100%	98-100%	[8, 26, 34]
Specificity of VL test, pre-seroconversion	98%	95-99.9%	[8, 26, 34]
Sensitivity of antibody test, post-seroconversion	99.5%	98.0-99.9%	[18, 35-37]
Specificity of antibody test, post-seroconversion	99.9994%	99-100%	[18, 35-37]
Quality decrement for false-positive result (multiplier to above quality-of-life factors)	0.12	0-0.48	Calculated [18, 23, 38]

* ART = antiretroviral treatment, VL = viral load

Table A4: Results of Key Sensitivity Analyses

Strategy*	HIV Infections Prevented¶†	Incremental Costs¥‡ (billions)	Incremental QALYs¥‡	ICER relative to§	
				Status Quo	Next Best
Base-Case Scenario					
90% Annually, Ab+VL + Symptom-based	38,995 (7.2%)	$13.65	389,711	$35,032	$105,398
90% Annually, Ab + Symptom-based	30,780 (5.7%)	$6.43	321,164	$20,013	$29,923
67% Annually, Ab+VL + Symptom-based	27,720 (5.1%)	$10.23	263,663	$38,783	Dominated
67% Annually, Ab + Symptom-based	22,446 (4.2%)	$4.97	218,085	$22,786	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582
Initial HIV Prevalence 3%					
90% Annually, Ab+VL + Symptom-based	16,045 (7.7%)	$13.62	156,445	$87,030	$268,039
90% Annually, Ab + Symptom-based	12,483 (6.0%)	$5.74	127,054	$45,157	$77,620
67% Annually, Ab+VL + Symptom-based	11,766 (5.6%)	$10.46	109,269	$95,725	Dominated
67% Annually, Ab + Symptom-based	9,481 (4.5%)	$4.80	89,808	$53,442	Dominated
90% Annually, Ab	5,695 (2.7%)	$1.24	69,059	$17,896	$17,896
Infectivity During Acute 2x Higher					
90% Annually, Ab+VL + Symptom-based	70,717 (11.4%)	$12.01	651,245	$18,448	$44,782

90% Annually, Ab + Symptom-based	52,789 (8.5%)	$5.39	503,313	$10,708	$12,270
67% Annually, Ab+VL + Symptom-based	53,932 (8.7%)	$8.86	479,163	$18,493	Dominated
67% Annually, Ab + Symptom-based	42,838 (6.9%)	$3.95	385,867	$10,233	$10,233
90% Annually, Ab	18,614 (3.0%)	$2.33	216,725	$10,739	Dominated
5 Annual Sexual Partners					
90% Annually, Ab+VL + Symptom-based	192,093 (12.9%)	$8.33	1,608,567	$5,178	$15,836
90% Annually, Ab + Symptom-based	149,274 (10.0%)	$3.03	1,274,189	$2,381	$2,995
67% Annually, Ab+VL + Symptom-based	142,109 (9.5%)	$6.19	1,169,223	$5,297	Dominated
67% Annually, Ab + Symptom-based	114,360 (7.7%)	$2.06	948,818	$2,171	$2,171
90% Annually, Ab	66,326 (4.5%)	$1.97	618,992	$3,190	Dominated
0% of MSM Identified as Acutely Infected Receive ART					
90% Annually, Ab+VL + Symptom-based	26,318 (4.9%)	$14.11	284,780	$49,550	$243,982
90% Annually, Ab + Symptom-based	22,709 (4.2%)	$6.72	254,491	$26,408	$62,170
67% Annually, Ab+VL + Symptom-based	16,776 (3.1%)	$10.61	172,990	$61,340	Dominated
67% Annually, Ab + Symptom-based	14,167 (2.6%)	$5.26	149,550	$35,178	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582

25% of MSM Identified as Acutely Infected Receive ART					
90% Annually, Ab+VL + Symptom-based	32,727 (6.1%)	$13.88	337,805	$41,086	$146,840
90% Annually, Ab + Symptom-based	26,773 (5.0%)	$6.57	288,050	$22,820	$40,797
67% Annually, Ab+VL + Symptom-based	22,300 (4.1%)	$10.42	218,734	$47,623	Dominated
67% Annually, Ab + Symptom-based	18,336 (3.4%)	$5.11	184,048	$27,787	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582
75% of MSM Identified as Acutely Infected Receive ART					
90% Annually, Ab+VL + Symptom-based	45,125 (8.4%)	$13.43	440,533	$30,486	$82,432
90% Annually, Ab + Symptom-based	34,731 (6.5%)	$6.28	353,841	$17,759	$23,337
67% Annually, Ab+VL + Symptom-based	33,040 (6.1%)	$10.04	307,797	$32,611	Dominated
67% Annually, Ab + Symptom-based	26,499 (4.9%)	$4.83	251,669	$19,177	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582
100% of Symptomatic Acutely Infected MSM Identified and Receive ART					
90% Annually, Ab+VL + Symptom-based	62,415 (11.6%)	$20.09	590,562	$34,022	$142,447
90% Annually, Ab	57,141	$13.83	546,584	$25,298	$31,726

+ Symptom-based	(10.6%)				
67% Annually, Ab+VL + Symptom-based	56,197 (10.4%)	$17.13	522,863	$32,769	Dominated
67% Annually, Ab + Symptom-based	53,200 (9.9%)	$12.89	497,563	$25,916	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582
HIV-uninfected MSM Present with Febrile ILI 4x More Often					
90% Annually, Ab+VL + Symptom-based	43,547 (8.1%)	$25.30	436,294	$57,995	$112,852
90% Annually, Ab + Symptom-based	37,392 (6.9%)	$19.55	385,354	$50,744	$85,448
67% Annually, Ab+VL + Symptom-based	37,429 (7.0%)	$22.48	373,031	$60,253	Dominated
67% Annually, Ab + Symptom-based	33,805 (6.3%)	$18.69	342,648	$54,543	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582
50% Increased HIV-related Mortality Due to Early ART					
90% Annually, Ab+VL + Symptom-based	39,106 (7.3%)	$13.56	388,724	$34,891	$105,508
90% Annually, Ab + Symptom-based	30,852 (5.7%)	$6.37	320,557	$19,874	$29,641
67% Annually, Ab+VL + Symptom-based	27,815 (5.2%)	$10.15	262,820	$38,617	Dominated
67% Annually, Ab + Symptom-based	22,519 (4.2%)	$4.91	217,460	$22,587	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582

MSM Treated During Acute Remain on Lifelong ART					
90% Annually, Ab+VL + Symptom-based	97,021 (18.0%)	$25.61	1,058,455	$24,192	$37,854
90% Annually, Ab + Symptom-based	69,022 (12.8%)	$14.31	759,911	$18,825	$20,812
67% Annually, Ab+VL + Symptom-based	78,499 (14.6%)	$20.64	846,958	$24,367	Dominated
67% Annually, Ab + Symptom-based	61,615 (11.4%)	$13.00	666,857	$19,495	Dominated
90% Annually, Ab	14,923 (2.8%)	$2.31	183,535	$12,582	$12,582

* Ab = antibody testing, VL = viral load testing. In the base-case scenario, initial HIV prevalence is 8.5%, annual transmission probability per partnership during acute infection is 21%, MSM have 3 partners annually on average, 50% of acutely infected individuals who are identified receive ART, 0.6% of HIV-uninfected MSM present for VL testing with ILI symptoms per week, and individuals receiving ART during acute infection remain on ART for 3 months and experience no future harms or benefits.
¶ HIV infections prevented are undiscounted totals.
† The values in parentheses are the fraction of total HIV infections prevented.
¥ Costs and quality-adjusted life years (QALYs) are net present values (3% discount rate) over 20 years.
‡ Incremental costs and QALYs are relative to the status quo.
§ 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.

Table A5: Distributions for Probabilistic Sensitivity Analysis

Parameter*	Distribution Type†	Parameter 1	Parameter 2
Demographic Parameters			
Total MSM population age 13-64	Normal	6,435,210	628,221
HIV prevalence in MSM	Beta	4.59	49.41
Male mortality rate	Beta	29.20	6,777.90
Male maturation rate	Beta	6.18	574.63
Male entry rate	Beta	7.57	33.59
Disease Parameters			
Average disease duration (weeks)			
Acute HIV	Gamma	11.07	1.08
Asymptomatic HIV	Gamma	23.62	15.41
Symptomatic HIV	Gamma	36.65	4.26
Symptomatic HIV – Treated with ART	Gamma	10.96	85.40
AIDS	Gamma	17.71	5.87
AIDS – Treated with ART	Gamma	2.66	97.59
Quality-of-life factors (weekly)			
Acute HIV – Unidentified	Beta	681.08	37,982.92
Acute HIV – Identified	Beta	640.22	38,023.78
Acute HIV – Treated with ART	Beta	177.84	10,562.16
Asymptomatic HIV – Unidentified	Beta	725.55	40,734.45
Asymptomatic HIV – Identified	Beta	705.17	40,754.83
Symptomatic HIV – Unidentified	Beta	984.46	63,815.54
Symptomatic HIV – Identified	Beta	138.86	9,890.03
Symptomatic HIV – Treated with ART	Beta	329.14	20,291.66
AIDS – Unidentified & Identified	Beta	452.69	32,241.49
AIDS – Treated with ART	Beta	303.93	18,969.41
Age-specific multiplier	Beta	43.86	1.83
Sexual Behavior Parameters			
Annual transmission probability per MSM partnership ($M_{HIV+} \rightarrow M_{HIV-}$)			
Acute HIV	Beta	4.44	16.69
Asymptomatic HIV	Beta	4.56	112.31
Symptomatic HIV	Beta	4.56	112.31
AIDS	Beta	5.30	27.81
Annual number of male partners	Gamma	10.99	0.27
Condom usage with male partners	Beta	8.80	13.21

Parameter*	Distribution Type†	Parameter 1	Parameter 2
Condom effectiveness	Beta	13.47	1.50
Treatment Parameters			
Fraction starting ART at CD4=350 cells/mm^3	Beta	6.38	6.38
ART entry rate if CD4<350 cells/mm^3	Beta	5.00	95.00
Reduction in sexual infectivity due to ART	Beta	3.43	0.38
Screening Parameters			
Fraction of acutely infected who develop symptoms	Beta	9.60	4.11
Identification duration if uninfected (weeks)	Gamma	1.65	31.60
Reduction in sexual behavior due to testing and counseling	Beta	1.69	6.77
Weekly probability of influenza-like symptoms in general population	Beta	6.83	398.17
Weekly probability of symptom-based case finding			
Symptomatic HIV	Beta	1.13	558.87
AIDS	Beta	0.88	205.41
Sensitivity of VL test, pre-seroconversion	Beta	499.95	0.05
Specificity of VL test, pre-seroconversion	Beta	366.00	10.00
Sensitivity of antibody test, post-seroconversion	Beta	164.61	0.83
Specificity of antibody test, post-seroconversion	Beta	4,999.97	0.03
Quality decrement for false-positive result (subtracted from above quality-of-life factors)	Gamma	0.82	2.45
Cost Parameters ($)			
Annual HIV-related healthcare costs			
Acute HIV	Gamma	6.00	5.00
Asymptomatic HIV – Untreated	Gamma	21.42	191.45
Symptomatic HIV – Untreated	Gamma	43.07	159.81
Symptomatic HIV – Treated with ART	Gamma	196.20	31.27
AIDS – Untreated	Gamma	177.38	122.33
AIDS – Treated with ART	Gamma	9.29	1,036.08
Annual non-HIV-related healthcare costs	Gamma	19.37	207.91
Annual cost of ART	Gamma	80.73	191.70
Cost of HIV testing – VL test			
Uninfected	Gamma	5.30	23.39
HIV-Infected	Gamma	69.75	3.97
Cost of HIV testing – antibody test			

Parameter*	Distribution Type†	Parameter 1	Parameter 2
Uninfected	Gamma	6.14	2.12
HIV-Infected	Gamma	24.94	2.69
Cost of counseling			
Pre-test counseling	Gamma	1.06	12.31
Post-test counseling for HIV-negative persons	Gamma	1.23	5.71
Post-test linkage/counseling for HIV-positive persons	Gamma	1.09	12.86
Cost of HIV diagnosis	Gamma	3.01	166.00
Discount Rate	Beta	10.52	340.17

* All rates are annual. ART = antiretroviral treatment, MSM = men who have sex with men, VL = viral load

† Parameters 1 and 2 for each type of distribution are as follows: normal: mean, standard deviation; beta: alpha, beta; gamma: alpha, beta

FIGURES

Figure A1: Model Schematic

This figure presents a schematic of the dynamic compartmental model. Each square represents a compartment of the MSM population, identified by HIV infection status, HIV disease stage if infected, screening status, and treatment status. The number within each square denotes the index number of that compartment (i = 1, …, 13). The arrows depict population movement from one compartment to another and into and out of the population, with the associated parameters representing the rates of change. Descriptions of the parameters can be found in Table A1.

Figure A1: Model Schematic

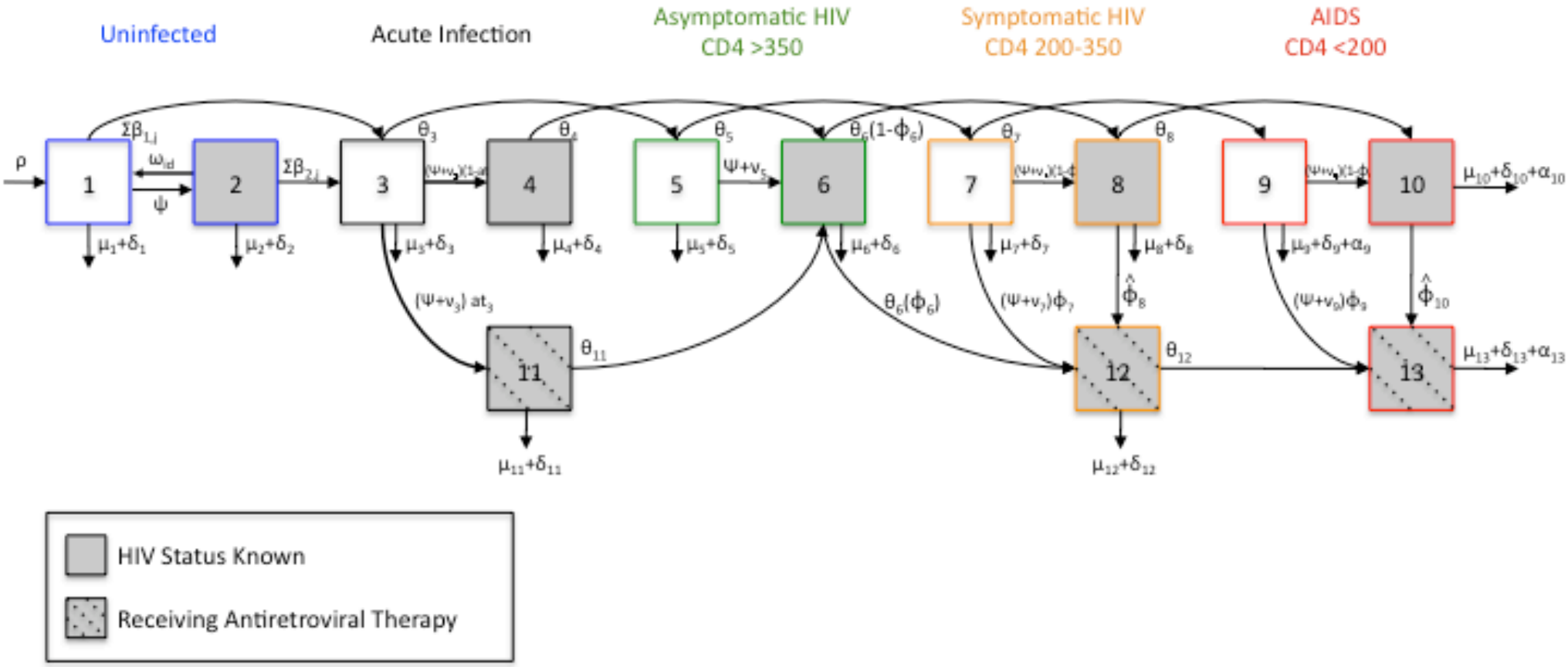
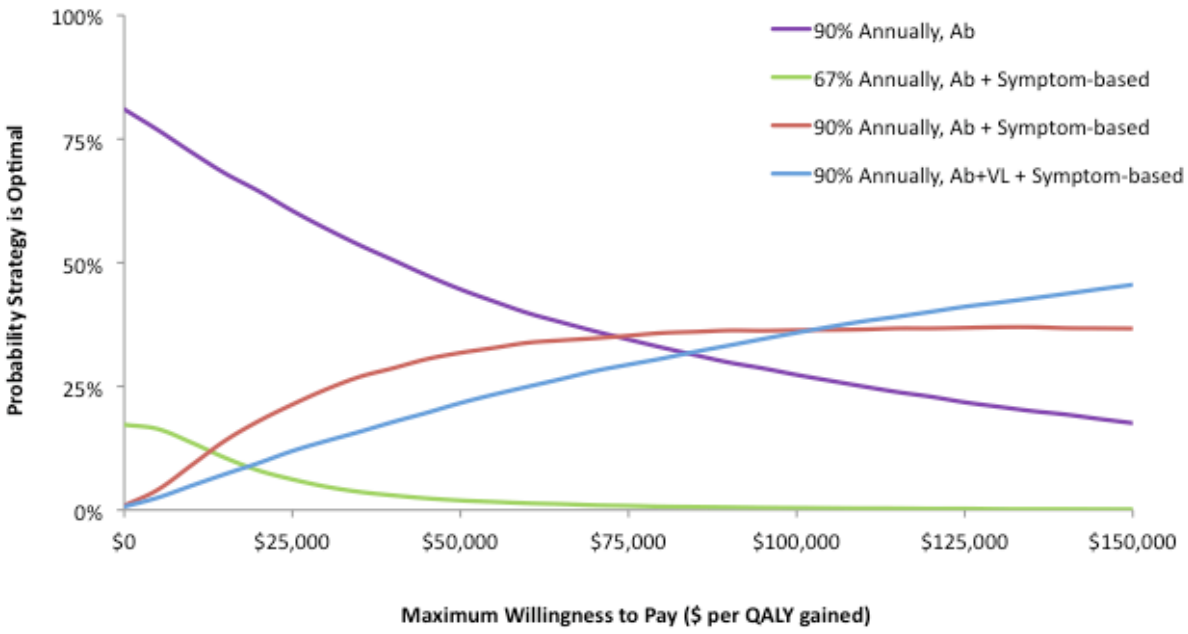


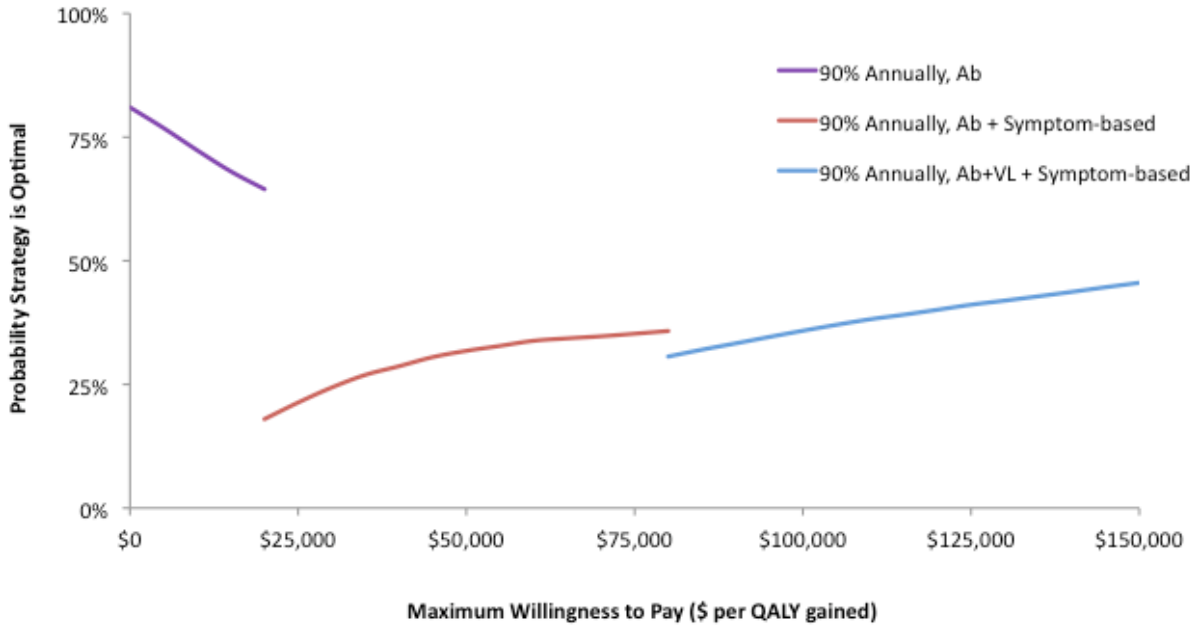
Figure A2: Cost-Effectiveness Acceptability Curves



The cost-effectiveness acceptability curves show the proportion of the 10,000 simulations where each strategy is optimal, for each value of λ, the willingness to pay per QALY gained, shown on the x-axis. A strategy is optimal in a given simulation when it is associated with the highest net benefit, where net benefit = λ×QALYs − Cost.

Note: Ab = antibody, VL = viral load, Symptom-based = 35% of symptomatic acutely infected MSM receive Ab & VL testing.

Figure A3: Cost-Effectiveness Acceptability Frontier



The cost-effectiveness acceptability frontier represents both uncertainty and the identification of the optimal strategy. It shows the cost-effectiveness acceptability curve for the intervention with the highest expected net benefit for each value of λ, the willingness to pay per QALY gained, shown on the x-axis. At each value of λ, the frontier identifies which strategy should be chosen (based on expected net benefit calculated from the 10,000 simulations), and the probability that the strategy will be optimal.

Note: Ab = antibody, VL = viral load, Symptom-based = 35% of symptomatic acutely infected MSM receive Ab & VL testing.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). *2008 Report on the Global AIDS Epidemic*. Geneva, Switzerland: United Nations; 2008.
2. 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 September 30, 2009.
3. Centers for Disease Control and Prevention (CDC). HIV/AIDS Surveillance Report, Volume 18. 2006; http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2006report/default.htm. Accessed September 30, 2009.
4. Centers for Disease Control and Prevention (CDC). HIV Prevalence Estimates -- United States, 2006. 2008; http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5739a2.htm. Accessed September 30, 2009.
5. 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 March 25, 2010.
6. CensusScope. United States Age Distribution. 2000; http://www.censusscope.org/us/chart_age.html. Accessed September 30, 2009.
7. Arias E. United States life tables, 2004. *Natl Vital Stat Rep* 2007,**56**:1-39.
8. Coco A. The cost-effectiveness of expanded testing for primary HIV infection. *Ann Fam Med* 2005,**3**:391-399.
9. Vergis EN, Mellors JW. Natural history of HIV-1 infection. *Infect Dis Clin North Am* 2000,**14**:809-825, v-vi.
10. 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.
11. 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.
12. 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.
13. Truong HM, Grant RM, McFarland W, Kellogg T, Kent C, Louie B*, et al.* Routine surveillance for the detection of acute and recent HIV infections and transmission of antiretroviral resistance. *AIDS* 2006,**20**:2193-2197.
14. 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.
15. Morris SR, Little SJ, Cunningham T, Garfein RS, Richman DD, Smith DM. Evaluation of an HIV nucleic acid testing program with automated Internet and voicemail systems to deliver results. *Ann Intern Med* 2010,**152**:778-785.

16. Long EF, Brandeau ML, Owens DK. Potential population health outcomes and expenditures of HIV vaccination strategies in the United States. *Vaccine* 2009,**27**:5402-5410.
17. 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**.
18. 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.
19. Steward WT, Remien RH, Higgins JA, Dubrow R, Pinkerton SD, Sikkema KJ*, et al.* Behavior change following diagnosis with acute/early HIV infection-a move to serosorting with other HIV-infected individuals. The NIMH Multisite Acute HIV Infection Study: III. *AIDS Behav* 2009,**13**:1054-1060.
20. 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.
21. Bureau of Economic Analysis (BEA). Table 1.1.9. Implicit Price Deflators for Gross Domestic Product. 2010; http://www.bea.gov/national/nipaweb/TableView.asp?SelectedTable=13&ViewSeries=NO&Java=no&Request3Place=N&3Place=N&FromView=YES&Freq=Year&FirstYear=1929&LastYear=2008&3Place=N&AllYearsChk=YES&Update=Update&JavaBox=no#. Accessed
22. Fryback DG, Dasbach EJ, Klein R, Klein BE, Dorn N, Peterson K*, et al.* The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. *Med Decis Making* 1993,**13**:89-102.
23. 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.
24. 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.
25. Bollinger RC, Brookmeyer RS, Mehendale SM, Paranjape RS, Shepherd ME, Gadkari DA*, et al.* Risk factors and clinical presentation of acute primary HIV infection in India. *JAMA* 1997,**278**:2085-2089.
26. 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.
27. Khazeni N, Hutton DW, Garber AM, Hupert N, Owens DK. Effectiveness and cost-effectiveness of vaccination against pandemic influenza (H1N1) 2009. *Ann Intern Med* 2009,**151**:829-839.
28. Turner DA, Wailoo AJ, Cooper NJ, Sutton AJ, Abrams KR, Nicholson KG. The cost-effectiveness of influenza vaccination of healthy adults 50-64 years of age. *Vaccine* 2006,**24**:1035-1043.
29. O'Brien BJ, Goeree R, Blackhouse G, Smieja M, Loeb M. Oseltamivir for treatment of influenza in healthy adults: pooled trial evidence and cost-effectiveness model for Canada. *Value Health* 2003,**6**:116-125.

30. Neuner JM, Hamel MB, Phillips RS, Bona K, Aronson MD. Diagnosis and management of adults with pharyngitis. A cost-effectiveness analysis. *Ann Intern Med* 2003,**139**:113-122.
31. Lachance JA, Bendavid E, Cotter LE, Enanoria W, Misegades LK, Reingold A*, et al.* Cost-Effectiveness of a Hand and Respiratory Hygiene Intervention in Reducing Influenza-like Illness among University Students. *In submission.* 2009.
32. 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.
33. Rothberg MB, Rose DN. Vaccination versus treatment of influenza in working adults: a cost-effectiveness analysis. *Am J Med* 2005,**118**:68-77.
34. Hecht FM, Busch MP, Rawal B, Webb M, Rosenberg E, Swanson M*, et al.* Use of laboratory tests and clinical symptoms for identification of primary HIV infection. *AIDS* 2002,**16**:1119-1129.
35. Owens DK, Nease RF, Jr., Harris RA. Cost-effectiveness of HIV screening in acute care settings. *Arch Intern Med* 1996,**156**:394-404.
36. Mylonakis E, Paliou M, Lally M, Flanigan TP, Rich JD. Laboratory testing for infection with the human immunodeficiency virus: established and novel approaches. *Am J Med* 2000,**109**:568-576.
37. Greenwald JL, Burstein GR, Pincus J, Branson B. A rapid review of rapid HIV antibody tests. *Curr Infect Dis Rep* 2006,**8**:125-131.
38. Paltiel AD, Weinstein MC, Kimmel AD, Seage GR, 3rd, Losina E, Zhang H*, et al.* Expanded screening for HIV in the United States--an analysis of cost-effectiveness. *N Engl J Med* 2005,**352**:586-595.
39. 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 May 11, 2011.
40. Pilcher CD, Tien HC, Eron JJ, Jr., Vernazza PL, Leu SY, Stewart PW*, et al.* Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis* 2004,**189**:1785-1792.
41. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. *J Infect Dis* 2008,**198**:687-693.
42. Pinkerton SD. How many sexually-acquired HIV infections in the USA are due to acute-phase HIV transmission? *AIDS* 2007,**21**:1625-1629.
43. Xiridou M, Geskus R, de Wit J, Coutinho R, Kretzschmar M. Primary HIV infection as source of HIV transmission within steady and casual partnerships among homosexual men. *AIDS* 2004,**18**:1311-1320.
44. Mellors JW, Munoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P*, et al.* Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. *Ann Intern Med* 1997,**126**:946-954.
45. Dunn D, Woodburn P, Duong T, Peto J, Phillips A, Gibb D*, et al.* Current CD4 cell count and the short-term risk of AIDS and death before the availability of effective antiretroviral therapy in HIV-infected children and adults. *J Infect Dis* 2008,**197**:398-404.

46. May M, Sterne JA, Sabin C, Costagliola D, Justice AC, Thiebaut R*, et al.* Prognosis of HIV-1-infected patients up to 5 years after initiation of HAART: collaborative analysis of prospective studies. *AIDS* 2007,**21**:1185-1197.
47. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *Lancet* 2008,**372**:293-299.
48. 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.
49. 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.
50. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O*, et al.* Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005,**191**:1403-1409.
51. 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 January 27, 2010.
52. 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.
53. Colfax GN, Buchbinder SP, Cornelisse PG, Vittinghoff E, Mayer K, Celum C. Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion. *AIDS* 2002,**16**:1529-1535.
54. 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.
55. Harawa NT, Greenland S, Bingham TA, Johnson DF, Cochran SD, Cunningham WE*, et al.* Associations of race/ethnicity with HIV prevalence and HIV-related behaviors among young men who have sex with men in 7 urban centers in the United States. *J Acquir Immune Defic Syndr* 2004,**35**:526-536.
56. MacKellar DA, Valleroy LA, Behel S, Secura GM, Bingham T, Celentano DD*, et al.* Unintentional HIV exposures from young men who have sex with men who disclose being HIV-negative. *AIDS* 2006,**20**:1637-1644.
57. Rietmeijer CA, Wolitski RJ, Fishbein M, Corby NH, Cohn DL. Sex hustling, injection drug use, and non-gay identification by men who have sex with men. Associations with high-risk sexual behaviors and condom use. *Sex Transm Dis* 1998,**25**:353-360.
58. 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). *12th Conference on Retroviruses and Opportunistic Infections* 2005.
59. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F*, et al.* Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med* 2000,**342**:921-929.
60. Vernazza P, Hirschel B, Bernasconi E, Flepp M. HIV transmission under highly active antiretroviral therapy. *Lancet* 2008,**372**:1806-1807; author reply 1807.

61. 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.
62. The National Institute of Mental Health (NIMH) Multisite HIV Prevention Trial Group. The NIMH Multisite HIV Prevention Trial: reducing HIV sexual risk behavior. *Science* 1998,**280**:1889-1894.
63. Kamb ML, Fishbein M, Douglas JM, Jr., Rhodes F, Rogers J, Bolan G*, et al.* Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. Project RESPECT Study Group. *JAMA* 1998,**280**:1161-1167.
64. 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.
65. Abbas UL, Anderson RM, Mellors JW. Potential impact of antiretroviral therapy on HIV-1 transmission and AIDS mortality in resource-limited settings. *J Acquir Immune Defic Syndr* 2006,**41**:632-641.
66. Cohen MS, Gay C, Kashuba AD, Blower S, Paxton L. Narrative review: antiretroviral therapy to prevent the sexual transmission of HIV-1. *Ann Intern Med* 2007,**146**:591-601.
67. 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.
68. Manning SE, Thorpe LE, Ramaswamy C, Hajat A, Marx MA, Karpati AM*, et al.* Estimation of HIV prevalence, risk factors, and testing frequency among sexually active men who have sex with men, aged 18-64 years--New York City, 2002. *J Urban Health* 2007,**84**:212-225.
69. Bozzette SA, Joyce G, McCaffrey DF, Leibowitz AA, Morton SC, Berry SH*, et al.* Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. *N Engl J Med* 2001,**344**:817-823.
70. 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.
71. Gebo KA, Chaisson RE, Folkemer JG, Bartlett JG, Moore RD. Costs of HIV medical care in the era of highly active antiretroviral therapy. *AIDS* 1999,**13**:963-969.
72. Hutchinson AB, Farnham PG, Dean HD, Ekwueme DU, del Rio C, Kamimoto L*, et al.* The economic burden of HIV in the United States in the era of highly active antiretroviral therapy: evidence of continuing racial and ethnic differences. *J Acquir Immune Defic Syndr* 2006,**43**:451-457.
73. Meara E, White C, Cutler DM. Trends in medical spending by age, 1963-2000. *Health Aff (Millwood)* 2004,**23**:176-183.
74. Centers for Medicare & Medicaid Services. 2009; http://www.cms.hhs.gov/home/medicare.asp. Accessed April 9, 2010.
75. Farnham PG, Hutchinson AB, Sansom SL, Branson BM. Comparing the costs of HIV screening strategies and technologies in health-care settings. *Public Health Rep* 2008,**123 Suppl 3**:51-62.

76. Paltiel AD, Walensky RP, Schackman BR, Seage GR, 3rd, Mercincavage LM, Weinstein MC*, et al.* Expanded HIV screening in the United States: effect on clinical outcomes, HIV transmission, and costs. *Ann Intern Med* 2006,**145**:797-806.
77. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press; 1996.
78. Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997,**16**:54-62.
79. Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. *Med Decis Making* 2002,**22**:475-481.
80. Nyman JA, Barleen NA, Dowd BE, Russell DW, Coons SJ, Sullivan PW. Quality-of-life weights for the US population: self-reported health status and priority health conditions, by demographic characteristics. *Med Care* 2007,**45**:618-628.
81. Sullivan PW, Ghushchyan V. Preference-Based EQ-5D index scores for chronic conditions in the United States. *Med Decis Making* 2006,**26**:410-420.
82. Bridges CB, Thompson WW, Meltzer MI, Reeve GR, Talamonti WJ, Cox NJ*, et al.* Effectiveness and cost-benefit of influenza vaccination of healthy working adults: A randomized controlled trial. *JAMA* 2000,**284**:1655-1663.