ORIGINAL RESEARCH | Annals of Internal Medicine

The Cost-Effectiveness and Population Outcomes of Expanded HIV Screening and Antiretroviral Treatment in the United States

Elisa F. Long, PhD; Margaret L. Brandeau, PhD; and Douglas K. Owens, MD, MS

Background: Although recent guidelines call for expanded routine screening for HIV, resources for antiretroviral therapy (ART) are limited, and all eligible persons are not currently receiving treatment.

Objective: To evaluate the effects on the U.S. HIV epidemic of expanded ART, HIV screening, or interventions to reduce risk behavior.

Design: Dynamic mathematical model of HIV transmission and disease progression and cost-effectiveness analysis.

Data Sources: Published literature.

Target Population: High-risk (injection drug users and men who have sex with men) and low-risk persons aged 15 to 64 years in the United States.

Time Horizon: Twenty years and lifetime (costs and quality-adjusted life-years [QALYs]).

Perspective: Societal.

Intervention: Expanded HIV screening and counseling, treatment with ART, or both.

Outcome Measures: New HIV infections, discounted costs and QALYs, and incremental cost-effectiveness ratios.

Results of Base-Case Analysis: One-time HIV screening of low-risk persons coupled with annual screening of high-risk persons could prevent 6.7% of a projected 1.23 million new infections and cost $22 382 per QALY gained, assuming a 20% reduction in sexual activity after screening. Expanding ART utilization to 75% of eligible persons prevents 10.3% of infections and costs $20 300 per QALY gained. A combination strategy prevents 17.3% of infections and costs $21 580 per QALY gained.

Results of Sensitivity Analysis: With no reduction in sexual activity, expanded screening prevents 3.7% of infections. Earlier ART initiation when a CD4 count is greater than 0.350×10^9 cells/L prevents 20% to 28% of infections. Additional efforts to halve high-risk behavior could reduce infections by 65%.

Limitation: The model of disease progression and treatment was simplified, and acute HIV screening was excluded.

Conclusion: Expanding HIV screening and treatment simultaneously offers the greatest health benefit and is cost-effective. However, even substantial expansion of HIV screening and treatment programs is not sufficient to markedly reduce the U.S. HIV epidemic without substantial reductions in risk behavior.

Primary Funding Source: National Institute on Drug Abuse, National Institutes of Health, and Department of Veterans Affairs.

Ann Intern Med. 2010;153:778-789. www.annals.org
For author affiliations, see end of text.

Approximately 56 000 persons in the United States acquire HIV annually. This number has not decreased in recent years and highlights the need for expanded HIV screening and treatment (1, 2). Routine HIV screening facilitates early identification of HIV infection, linking infected persons with access to life-saving treatments. If accompanied by an effective counseling program, HIV screening may reduce sexual activity and other risky behavior among participants (3–7). Once identified, persons infected with HIV who are eligible to receive antiretroviral therapy (ART) can benefit from substantially reduced mortality and improved quality of life. Moreover, suppressive ART may reduce overall HIV transmission in the population by reducing a recipient's blood plasma viral load and subsequent infectivity (8–14).

The Centers for Disease Control and Prevention (CDC) estimates that 21% of the approximately 1.1 million persons living with HIV in the United States are unaware of their disease status, implying that expanded screening could directly benefit almost 250 000 persons and their partners (15). In 2006, the CDC published revised guidelines calling for routine HIV screening in all health care settings of patients aged 13 to 64 years, regardless of potential risk behaviors, unless HIV prevalence is less than 0.1% among patients with undiagnosed HIV (3). Many other professional organizations have endorsed this policy (16), and the American College of Physicians recently advised routine screening of patients (17).

Previous studies have demonstrated that HIV screening is cost-effective. Older analyses focused on specific high-risk groups (18, 19) or settings with a relatively high prevalence (20). Because ART therapy is now much more effective than it was early in the epidemic, more recent studies show that HIV screening is cost-effective, even in low-prevalence settings in which HIV prevalence exceeds 0.1% to 0.2% (21–25), in patients older than 55 years (26), and with either conventional

See also:

Print
Editors' Notes 779

Web-Only
Supplement
Conversion of graphics into slides

or rapid testing (24, 27). These studies demonstrate that the cost-effectiveness of screening is critically dependent on the availability of ART. Despite the 2009 U.S. Department of Health and Human Services guidelines recommending ART initiation in patients with CD4 counts from 0.350 to 0.500×10^9 cells/L (28), universal ART utilization has not been fully realized. From 2007 to 2009, the CDC's Expanded Testing Initiative resulted in 10 000 persons with newly diagnosed HIV, linking 75% to care (29). However, among persons with newly diagnosed HIV, 36% develop AIDS within 1 year, and 45% develop AIDS within 3 years (30), suggesting that many persons who are linked to care have advanced HIV disease.

Because neither universal HIV screening nor universal treatment of identified persons has been achieved yet, we evaluated how expanding screening, treatment, or both would affect the HIV epidemic in the United States. Unlike most previous analyses (21, 22, 26, 27), we used a modeling framework that can assess the effect of these programs on the entire U.S. population by tracking HIV transmission among several risk groups and the general population. Our goal was to understand whether the expansion of screening, treatment, or both could substantially diminish the HIV epidemic in the United States and whether allocating resources to screening or treatment was more effective and efficient. We also evaluated the effect of reductions in risk behavior on the epidemic.

Context

The incidence of HIV infections in the United States has remained steady over many years.

Contribution

By using a dynamic model, the investigators found that although expanding HIV testing and treatment simultaneously was more beneficial and cost-effective in reducing new infections than using either method alone, new infections only modestly decreased. However, substantial reduction in risk behavior among patients tested and treated would lead to a marked decrease in the number of new infections.

Caution

The model did not include screening for acute HIV infection.

Implication

To substantially decrease the size of the U.S. HIV epidemic, a multimodal approach of testing, treatment, and behavior change would be needed.

—The Editors

METHODS

Study Design

We extended a dynamic HIV epidemic model that we previously developed to estimate the health benefits and costs of expanded HIV screening and ART in the United States (31). We integrated epidemiologic, clinical, and economic data and calculated population-level outcomes that accrue from varying combinations of the 2 interventions. Our model was calibrated to match empirical estimates of incidence and prevalence (see **Supplement,** available at www.annals.org). We estimated HIV prevalence, incidence, quality-adjusted life-years (QALYs), and health care costs over a 20-year time horizon by using a societal perspective. Our base-case analysis estimates HIV infections averted and incremental cost-effectiveness ratios (ICERs) associated with implementing each program individually or jointly. Because the effects of HIV screening and treatment with ART on risk behavior and disease transmission are uncertain, we varied each intervention's effectiveness. All costs are in 2009 U.S. dollars, and costs and QALYs were discounted at an annual rate of 3% (32). We programmed the model by using Matlab R2010a (MathWorks, Natick, Massachusetts).

HIV Epidemic Model

Our HIV epidemic model captures HIV transmission and progression in the population (**Supplement**). We partitioned the adult population aged 15 to 64 years into compartments on the basis of sex, risk behavior (men who have sex with men [MSM], injection drug users, or low-risk persons), HIV infection status, CD4 cell count if infected, treatment status if infected (receiving or not receiving ART), screening status (identified or unidentified), and male circumcision status.

We included HIV transmission through heterosexual and homosexual contact and through needle sharing associated with injection drug use. Heterosexual contact occurs within risk groups (for example, both partners are low risk or both are injection drug users) and across groups (for example, a female injection drug user with a low-risk male partner or a low-risk female with a MSM partner). We assumed proportional mixing, in which persons with many sexual partners are more likely to select a partner who similarly has many partners. The average annual number of sexual partnerships (33–42), average condom use (33, 38–44), and transmission probability per partnership (8, 45–55) for each sexual behavior method was estimated on the basis of published data. The model captures HIV transmission through needle sharing in a similar manner, as a function of the annual number of injections (56–58), average needle-sharing rates (41, 44, 57, 59), and probability of transmission per shared needle (57, 60, 61). The probability of HIV transmission between 2 persons depends on the infected person's sex, disease status, and treatment status and the uninfected person's sex and circumcision status. Finally, the model accounts for changes in risky behavior due to effective HIV screening and counseling (4, 5, 62, 63).

On acquiring HIV, persons progress through a set of health states at a rate inversely proportional to the average

time spent in each health state, based on a Markov model of the natural history of HIV infection (21). The health states are defined approximately according to a person's CD4 T-cell count: asymptomatic HIV (CD4 count $>0.500 \times 10^9$ cells/L), symptomatic HIV (CD4 count from 0.200 to 0.350×10^9 cells/L), and AIDS (CD4 count $<0.200 \times 10^9$ cells/L).

HIV Screening and Treatment

We considered alternative combinations of HIV screening and treatment by varying screening frequency, targeted risk groups, and ART utilization. On the basis of CDC guidelines (3), we considered a strategy offering 1-time screening of low-risk persons, which mostly detects prevalent cases, accompanied by annual screening of high-risk persons, which detects prevalent cases initially and incident cases thereafter. For each strategy, we adjusted the appropriate model measurements to account for changes in sexual behavior and infection transmissibility. We assumed that persons infected with HIV are eligible to initiate ART at a CD4 cell count of 0.350×10^9 cells/L, although we also estimated the effect of initiating ART earlier (28). Persons who receive ART benefit from reduced disease progression and mortality and improved quality of life (21, 64–67). The partners of infected persons may also benefit because ART suppresses a person's viral load, thus reducing the chance of transmitting the virus. We assumed that ART reduces sexual infectivity by 90% (4, 5, 8, 45, 68–71) and infectivity related to injection drug use by 50% (21, 56). We varied these measurements widely in the sensitivity analysis.

Before initiating an ART regimen, persons with HIV must first be identified through an HIV screening program or a symptom-based case finding. We assumed a standard rapid HIV testing protocol of an initial enzyme-linked immunosorbent assay followed by a Western blot test to confirm HIV infection. We included the effects of posttest counseling to accompany screening, and we assumed that only persons with HIV reduce their sexual partnerships by 20% (4, 5, 62, 63) but varied this assumption in the sensitivity analysis.

Target Populations

We assessed relevant demographic data for each risk group, including population sizes, HIV prevalence, entry and maturation rates, and mortality rates (**Table 1**). The model was populated using 2007 data, and we numerically solved the dynamic system to estimate population compartment sizes over a 20-year time horizon. Initial HIV prevalence was 12.6% (MSM), 18.8% (MSM injection drug users), 12.9% (male injection drug users), 17.3% (female injection drug users), 0.10% (low-risk men), and 0.22% (low-risk women). Although HIV prevalence varies across geographic regions, we applied a U.S. average to serve as a basis for estimating the benefits of a national HIV screening and treatment campaign.

We estimated that approximately 50% of infected persons receive ART when they have a CD4 cell count less than 0.350×10^9 cells/L (29, 30), and thereafter, an additional 5% enter treatment regimens annually, resulting in approximately 85% of eligible persons eventually receiving ART. We calculated an overall prevalence of undiagnosed HIV of 0.11% and an annual incidence rate of 0.03% in our target populations.

Economic Model

We calculated net present health benefits (QALYs) and costs for each strategy. The quality of life for each health state was estimated, and the incremental gain in health benefits due to reduced morbidity and mortality was assessed. We measured lifetime health costs on the basis of HIV disease progression and mortality rates and the associated costs of each health state. Finally, we included the per-person cost of HIV screening and counseling and the annual cost of ART. The ICER for each intervention was calculated relative to the next best alternative.

Role of the Funding Source

The National Institute on Drug Abuse, National Institutes of Health, and Department of Veterans Affairs supported this study. The funding sources had no role in the design, conduct, and reporting of the study or in the decision to submit the manuscript for publication.

RESULTS

HIV Infections Prevented

Individual Interventions

Our model projects that approximately 1.23 million new HIV infections will occur over 20 years, with 74% occurring among high-risk persons. Although MSM comprise 4% of adult men, they account for 49% of total new infections, similar to the CDC's estimate of 53% (76).

One-time screening of low-risk persons combined with annual screening of high-risk persons prevents 81 991 infections (6.7% of the projected total), including 23 099 and 58 892 infections among low-risk and high-risk groups, respectively (**Table 2**). For comparison, targeted annual screening of only MSM could avert 58 513 infections, of which 95% are among MSM; however, the feasibility of risk-based screening is questionable (3). Routine screening of all persons every 3 years is less effective, preventing 2.3% of infections, because high-risk persons are screened less frequently. A treatment-focused strategy that instead increases ART utilization (at a CD4 cell count $<0.350 \times 10^9$ cells/L) from 50% to 75% prevents 125 775 infections (10.3% of the total).

Combination Interventions

In general, we found that combination strategies that increase both screening and treatment prevent more HIV infections than the sum prevented from each individual

Table 1. **Summary of Key Model Parameters**

Variable	Value	Range	References
Demographic characteristics			
Total population (aged 15–64 y), *n*			
IDU			
Men	1 000 000	0.5–1.5 million	Calculated (1, 72–75)
Women	450 000	300 00–600 000	Calculated (1, 72–75)
MSM	4 057 194	3–6 million	Calculated (1, 72, 73, 76)
MSM IDU	300 000	200 000–500 000	Calculated (1, 43, 72–77)
General population			
Men	96 022 652	95–100 million	Calculated (1, 72, 73)
Women	101 632 781	100–105 million	Calculated (1, 72, 73)
HIV prevalence, %			
IDU			
Men	12.9	10–20	Calculated (1, 72–75)
Women	17.3	15–30	Calculated (1, 72–75)
MSM	12.6	5–20	Calculated (1, 72, 73, 76)
MSM IDU	18.8	15–30	Calculated (1, 43, 72–76)
General population			
Men	0.10	0.05–0.25	Calculated (1, 72, 73)
Women	0.22	0.10–0.40	Calculated (1, 72, 73)
Annual mortality rate			
Men	0.0041	0.002–0.005	78
Women	0.0024	0.002–0.005	78
IDU (excess)	0.025	0–0.05	57
Annual maturation rate			
Men	0.0111	0.01–0.02	73
Women	0.0122	0.01–0.02	73
Annual entry rate			
Men	0.0227	0.01–0.05	73
Women	0.0213	0.01–0.05	73
Sexual transmission			
Transmission probability per partnership			
Heterosexual (female to male)			
Asymptomatic HIV	0.02	0.01–0.04	8, 45–52
Symptomatic HIV	0.03	0.01–0.04	8, 45–52
AIDS	0.05	0.03–0.06	8, 45–52
Heterosexual (male to female)			
Asymptomatic HIV	0.03	0.02–0.05	8, 45–52
Symptomatic HIV	0.04	0.02–0.05	8, 45–52
AIDS	0.08	0.05–0.10	8, 45–52
Homosexual (male to male)			
Asymptomatic HIV	0.04	0.03–0.06	49, 53–55
Symptomatic HIV	0.05	0.03–0.06	49, 53–55
AIDS	0.10	0.08–0.15	49, 53–55
Annual same-sex partners, *n*			
MSM	3.0	2.0–5.0	37, 40–42
MSM IDU	3.0	2.0–5.0	40–42
Condom use with same-sex partners, %			
MSM	40	30–60	37, 40–43
MSM IDU	40	30–50	41
Annual opposite-sex partners, *n*			
IDU			
Men	3.0	2.0–5.0	39
Women	3.5	2.0–5.0	39
MSM	0.1	0–1.0	37
MSM IDU	0.1	0–1.0	33
General population			
Men	1.1	0.5–2.0	34–38
Women	1.1	0.5–2.0	34–36, 38
Condom use with opposite-sex partners, %			
IDU			
Men	25	15–35	33, 43
Women	25	20–50	39, 44
MSM	30	20–50	41, 43
MSM IDU	30	30–50	33, 41
General population			
Men	20	10–40	38
Women	20	10–40	38

Continued on following page

Table 1—**Continued**

Variable	Value	Range	References
Reduction in heterosexual HIV transmission due to male circumcision, %	50	48–60	79–81
Injection drug use transmission			
Transmission probability per shared injection			
Asymptomatic HIV	0.002	0.001–0.005	57, 60, 61
Symptomatic HIV	0.003	0.001–0.005	57, 60, 61
AIDS	0.003	0.001–0.005	57, 60, 61
Average injections per year, *n*	200	100–500	57, 58
Fraction of injections that are shared, %	20	10–40	41, 44, 57, 59
HIV screening			
Fraction of population tested in past 12 mo, %			
High-risk persons	23	10–30	82
Low-risk persons	10	5–20	82
Annual probability of symptom-based case finding, %			
HIV	10	0–30	21
AIDS	20	10–60	21
Reduction in sexual behavior among persons identified as HIV-positive, %	20	0–50	4, 5, 62, 63
ART			
Fraction starting ART at CD4 cell count of 0.350×10^9 cells/L	50	25–75	Assumed (29, 83)
Annual ART entry rate if CD4 cell count $<0.350 \times 10^9$ cells/L	0.05	0–0.10	Assumed (83)
Reduction in injection infectivity due to ART, %	50	25–75	21, 56
Reduction in sexual infectivity due to ART, %	90	50–99	8–14
Quality-of-life multipliers			
Uninfected	1.0	–	84
Unidentified asymptomatic HIV	0.91	0.85–0.95	64, 65, 67, 85
Identified asymptomatic HIV at 1 y	0.84	0.85–0.95	21, 64, 65, 67, 85
Identified asymptomatic HIV at ≥2 y	0.89	0.85–0.95	21, 64, 65, 67, 85
Unidentified symptomatic HIV	0.79	0.70–0.80	64, 65, 67, 85
Identified symptomatic HIV	0.72	0.70–0.80	64, 65, 67, 85
Symptomatic HIV treated with ART	0.83	0.82–0.87	64, 65, 67, 85
Unidentified AIDS	0.72	0.60–0.75	64, 65, 67, 85
Identified AIDS	0.72	0.60–0.75	64, 65, 67, 85
AIDS treated with ART	0.82	0.82–0.87	64, 65, 67, 85
IDU (multiplier)*	0.90	0.80–1.0	56, 57
Costs (2009 U.S. dollars)			
Annual HIV-related health care costs, $			
Untreated asymptomatic HIV	4125	3000–6000	86, 87
Untreated symptomatic HIV	6925	5000–9000	86, 87
Symptomatic HIV treated with ART	6174	5000–7000	86, 87
Untreated AIDS	21 838	15 000–25 000	86–88
AIDS treated with ART	9938	6000–17 000	21, 87
Annual non–HIV-related health care costs, $	7576	5000–8000	89
Annual cost of ART, $	15 571	12 000–18 000	21, 22, 87, 88
Cost of HIV ELISA antibody test, $	12	10–20	90
Cost of confirmatory Western blot test, $	19	10–50	90
Cost of behavior counseling, $	60	50–100	21, 22, 24
Annual cost of ancillary IDU services, $	2500	1000–4000	57
Annual discount rate, %	3	0–5	32

ART = antiretroviral therapy; ELISA = enzyme-linked immunosorbent assay; IDU = injection drug user; MSM = men who have sex with men.
* Quality of life for all is multiplied by this quantity.

strategy (**Figure 1**). A joint strategy that simultaneously offers 1-time screening to low-risk persons and annual screening to high-risk persons and increases ART utilization to 75% prevents 212 291 infections (17.3% of the total).

We also examined whether a universal annual HIV screening and treatment with ART (with 90% utilization) could theoretically eliminate the HIV epidemic within the next 2 decades. Such a strategy could prevent 24% of new infections but would not prevent more than 40 000 new infections each year. To substantially reduce HIV incidence, expanded screening and treatment programs must be augmented with programs aimed at reducing risky sexual behavior. Incidence of HIV decreases by 65% if (in addition to universal annual HIV screening and 90% ART utilization) high-risk MSM halve their number of sexual partners and injection drug users halve their needle-sharing frequency.

Table 2. **Population Benefits and Costs Over 20 Years of Expanded HIV Screening and Treatment**

Strategy	HIV Infections Over 20 y*	Incremental Costs, $ *(billion)*	Incremental QALYs, *millions*	ICER, $	
				Status Quo	Next Best Alternative
Status quo	1 225 380	–	–	–	–
Expanded screening only					
Screening (low-risk once; high-risk annually)	−81 991 (6.7%)	26.9	1.2	22 382	22 382
Screening (low-risk every 3 y; high-risk annually)	−89 438 (7.3%)	71.7	1.4	51 040	Dominated†
Screening (every 3 y)	−28 132 (2.3%)	60.7	0.5	112 094	Dominated†
Screening (annually)	−94 538 (7.7%)	25.7	1.6	143 930	Dominated†
Expanded ART only					
ART (75% utilization)	−125 775 (10.3%)	63.8	3.1	20 300	20 300
Combination screening and ART					
Screening (low-risk once; high-risk annually) and ART (75% utilization)	−212 291 (17.3%)	92.6	4.5	20 682	21 580
Screening (low-risk every 3 y; high-risk annually) and ART (75% utilization)	−220 027 (18.0%)	138.2	4.7	29 327	192 139
Screening (every 3 y) and ART (75% utilization)	−155 958 (12.7%)	126.5	3.8	33 488	Dominated†
Screening (annually) and ART (75% utilization)	−225 242 (18.4%)	293.1	4.9	59 691	788 706

ART = antiretroviral therapy; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.
* Under the status quo, the total number of projected infections over 20 y is given. For the remaining strategies, a negative number refers to infections prevented compared with the status quo. The values in parentheses are the fraction of total HIV infections prevented. Incremental costs and QALYs are relative to the status quo.
† The strategy is dominated by another strategy and is not an efficient use of resources.

False Diagnoses

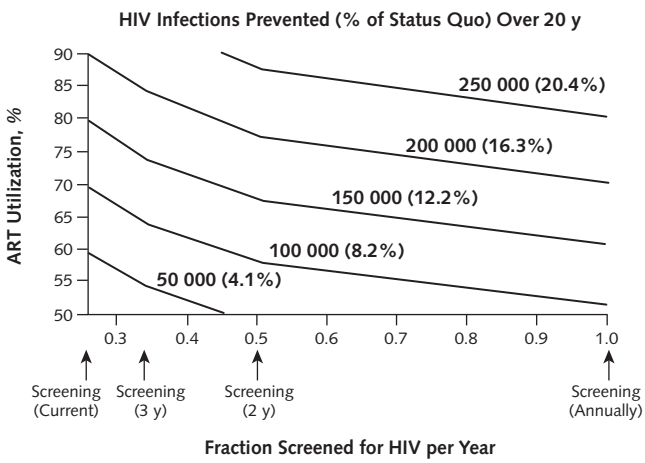
With annual screening of high-risk persons and 1-time screening of low-risk persons, false-positive and false-negative diagnoses will occur. We assumed a testing sequence sensitivity of 0.995 and specificity of 0.999994 (21). In the first year of the intervention, approximately 1162 false-positive and 1034 false-negative results occur, but these decrease to 176 and 189 per year, respectively, over 20 years because low-risk persons are screened only once with this strategy. High-risk persons with a false-negative test result will likely be detected on a future annual screening.

Cost-Effectiveness Analysis

In general, strategies that target screening frequency based on risk status or expand ART are cost-effective (**Figure 2** and **Table 2**). One-time screening of low-risk groups and annual screening of high-risk groups add 1.2 million QALYs over 20 years, at a cost of $26.9 billion (discounted) or $22 382 per QALY gained, compared with the status quo. During the first year, this program costs $12.4 billion because of the 1-time screening component. Routine screening every 3 years among all risk groups adds 540 000 QALYs and has an ICER of $112 094 per QALY gained compared with the status quo. This strategy is less effective and more expensive than the former strategy. Annual HIV screening of all adults is less cost-effective at $143 930 per QALY gained.

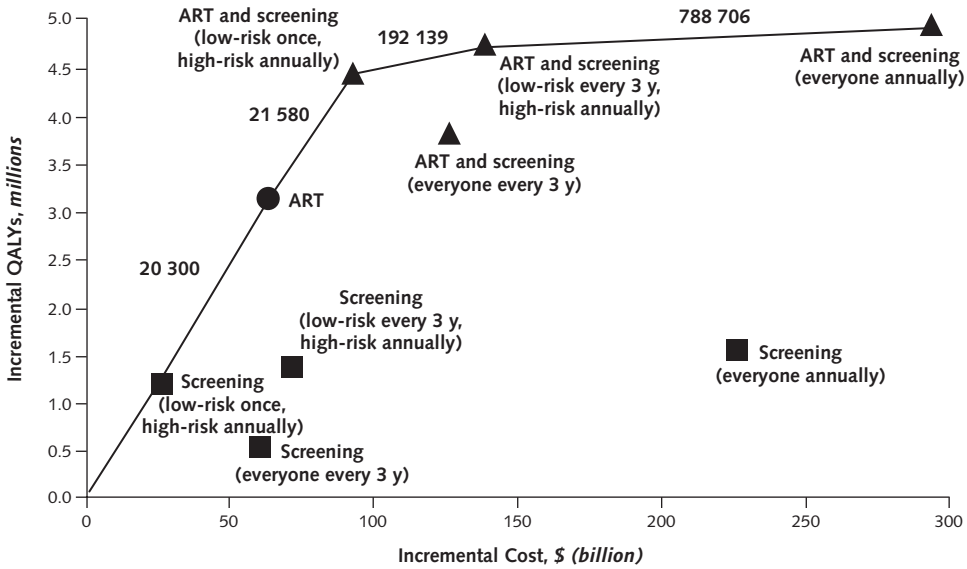
Alternatively, increasing ART utilization to 75% adds 3.1 million QALYs, with an ICER of $20 300 per QALY gained compared with the status quo. A combination program of 1-time low-risk and annual high-risk screening and 75% ART utilization adds 4.5 million QALYs—more than the sum of implementing each program separately—at a cost of $92.6 billion over 20 years ($12.9 billion in the

Figure 1. **Complementary effects of expanded HIV screening and treatment.**



The *x*-axis displays varying levels of HIV screening (current, every 3 y, every 2 y, or annually). The *y*-axis displays ART utilization levels (50%, 60%, 70%, 80%, or 90%). The curves are isocontours showing a given number (and fraction) of HIV infections prevented over 20 y compared with the status quo. The point at the origin corresponds to current screening and treatment levels. HIV screening reduces sexual behavior by 20% among persons identified as HIV-positive, and ART reduces sexual infectivity by 90%. Under the status quo, an estimated 1.23 million HIV infections occur over 20 years. ART = antiretroviral therapy.

Figure 2. **Cost-effectiveness of alternative screening and treatment strategies.**



Incremental costs and QALYs of expanded HIV screening and counseling, expanded access to ART, or a combination of screening and ART. Expanded screening occurs once, annually, or every 3 y. Expanded ART includes treatment utilization of 75%. The cost-effectiveness frontier (*solid line*) includes strategies that may be cost-effective if the incremental cost-effectiveness ratio is less than the accepted threshold. Strategies that are not on the frontier are dominated, meaning that they are not an efficient use of resources. Costs and QALYs are calculated over a 20-y time horizon and are discounted to the present. ART = antiretroviral therapy; QALY = quality-adjusted life-year.

first year) or $21 580 per QALY gained compared with expanded treatment only (**Table 2**).

Sensitivity Analysis

Health outcomes were most sensitive to changes in screening and treatment effectiveness. The effect of viral resistance and other sensitivity analyses are discussed in the **Supplement**.

Screening Effectiveness

Expanded HIV screening can reduce new infections through 2 mechanisms: infected persons are identified at an earlier stage and can initiate treatment sooner, thereby reducing the chance of infecting their partners, and screened persons may reduce their sexual behavior because of counseling. In the base case, we assumed that both mechanisms are in effect, but only persons with HIV reduce their risky behavior after screening and counseling.

Under these assumptions, 1-time low-risk and annual high-risk screening prevents 6.7% of projected HIV infections. With no reduction in sexual partners after screening, nearly 4% of new infections are still prevented because identified persons initiate ART at an earlier stage (**Figure 3**). This strategy remains cost-effective ($31 615 per QALY gained).

Conversely, a counseling program that successfully reduces partnerships by 50% prevents a significant number of new infections (11.7%) with 1-time low-risk and annual high-risk screening and costs $16 321 per QALY gained. Under this assumption, universal screening every year costs approximately $100 000 per QALY gained.

ART Effectiveness

We considered variations in the effectiveness of ART at reducing infectivity through sexual transmission. If ART reduces infectivity by 50% instead of 90%, then expanded ART utilization prevents 59 281 infections over 20 years (vs. 125 775 in the base case) and costs $27 585 per QALY gained. With no reduction in sexual infectivity, expanding ART costs $41 367 per QALY gained because of the enormous increase in health benefits from reduced morbidity and mortality among infected persons. The cost-effectiveness of expanded treatment improves to $16 000 per QALY gained if ART reduces sexual and needle-sharing infectivity completely. Combination screening and treatment cost between $19 000 per QALY and $42 000 per QALY gained if ART is more or less effective, respectively, compared with the next best alternative.

CD4 Cell Count at Initiation of ART

On the basis of recent guidelines recommending earlier treatment of HIV in some patients (28), we considered variations in CD4 cell count at initiation of ART. Because the effect on mortality of ART initiation at a CD4 cell count less than 0.500×10^9 cells/L is uncertain, we did exploratory analysis assuming a 50% survival gain with early initiation of ART (91). If 5% of asymptomatic per-

sons with HIV enter treatment programs each year, more than twice as many (20.6%) HIV infections are prevented (**Table 2**). Under this scenario, 30% of persons with a CD4 cell count greater than 0.350×10^9 cells/L would be receiving ART after 10 years. If 10% of asymptomatic patients begin treatment each year (that is, 50% receive ART after 10 years), 28% of new infections are prevented.

Epidemic Elimination

We assessed whether the HIV epidemic could theoretically be eliminated under the following optimistic assumptions: annual screening of all risk groups, 50% reduction in sexual partners among persons who know they have HIV, 100% ART utilization at CD4 cell count less than 0.350×10^9 cells/L, and rapid scale-up of ART for CD4 cell count greater than 0.350×10^9 cells/L (60% after 1 year, 80% after 2 years, and 95% after 4 years). This prevents 69% of new infections, but 18 000 infections still occur each year, with more than 60% among injection drug users, largely because ART reduces needle-sharing infectivity only by 50%. If both sexual and needle-sharing infectivity are reduced by 90%, then 9000 infections occur each year. Even with these unrealistic assumptions, it is not possible to eliminate the HIV epidemic in the United States without additional concomitant preventive measures and behavior modification.

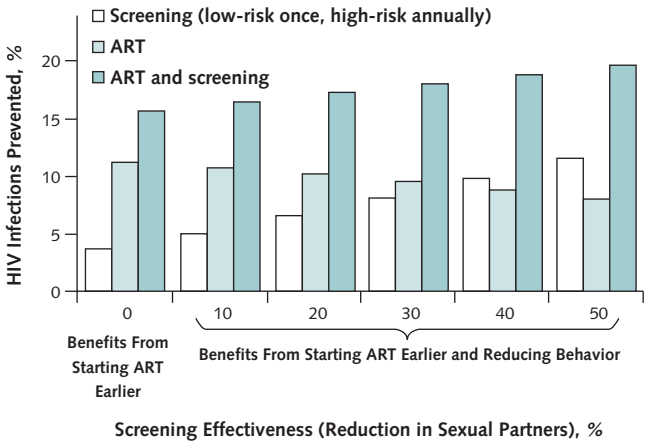
Initial HIV Prevalence

In general, as HIV prevalence increases, expanded screening becomes more cost-effective and vice versa. With 50% lower HIV prevalence levels, expanded screening (1-time screening for low-risk persons and annual screening for high-risk persons) costs $31 789 per QALY gained (vs. $22 382 in the base case) but is dominated by expanded ART, which costs $19 829 per QALY gained. Conversely, if HIV prevalence is doubled, both strategies cost less than $22 000 per QALY gained. Screening for HIV is more sensitive to variations in prevalence because of the higher cost of detecting an infected person in a low-prevalence U.S. setting.

DISCUSSION

We aimed to assess the population-wide effects of expanded HIV treatment and screening on the HIV epidemic in the United States. Although previous studies have addressed the effectiveness and cost-effectiveness of either expanded HIV screening (21, 22, 24, 26) or treatment (92–94), they were not designed to fully evaluate how such programs would influence HIV transmission in the overall population or the course of the epidemic. To our knowledge, our study is the first to evaluate the population-wide effects (new HIV infections and other health outcomes) and the cost-effectiveness of alternative combinations of HIV screening and treatment in the United States.

Figure 3. **Fraction of HIV infections prevented with varying HIV screening effectiveness.**



Each bar corresponds to the fraction of HIV infections prevented over 20 y, with varying degrees of screening effectiveness by reducing sexual partners among persons identified as HIV-positive (base case, 20%). The benefits from starting ART earlier are due to infected persons who are identified through a screening program and can initiate treatment, thereby reducing their infectivity. The benefits from reduced behavior result from reduced sexual partnerships among persons identified as HIV-positive (and hence reduced HIV transmission) after screening and counseling. Expanded screening occurs once for low-risk persons and annually for high-risk persons. Expanded ART includes treatment utilization of 75%. Under the status quo, an estimated 1.23 million HIV infections occur over 20 y. ART = antiretroviral therapy.

Our study has several key findings. First, we found that expanding HIV screening and treatment could prevent 200 000 to 300 000 infections over 20 years or approximately 17% to 24% of new infections, adding up to 6.8 million QALYs to the population. To prevent 24% of new infections, routine HIV screening would need to occur annually, with antiretroviral treatment available for essentially all symptomatic patients. Our analysis assumes that persons identified as HIV-infected reduce risk behaviors by 20%; even with modest reductions in risk behavior, expansion of screening and treatment would provide enormous health benefits. If persons with HIV reduce risk behavior further, as some studies suggest (7), the health benefit could be substantially higher than we have estimated. Annual HIV screening and counseling leading to 50% behavior reduction in infected persons, along with 90% ART initiation in symptomatic patients, reduces new infections to fewer than 35 000 per year. Even under such optimistic assumptions, the U.S. HIV epidemic is unlikely to be completely eliminated without additional preventive measures.

Second, our analysis highlights the importance of emphasizing risk behavior reduction as HIV screening and treatment becomes increasingly available. For example, in addition to expanded screening and treatment, a 50% reduction in sexual risk behaviors among MSM and needle sharing among injection drug users could prevent 65% of new infections, reducing HIV incidence to approximately

20 000 cases per year. This suggests that programs to reduce risk behavior among high-risk persons will probably be a key component of a successful prevention program. If, however, uninfected persons increase risk behavior after screening, some of the benefits would be attenuated.

Our third finding is that the net benefit of implementing both interventions is greater than the sum from implementing each program individually. A substantial increase in HIV screening or treatment could prevent 95 000 or 198 000 new infections, respectively, whereas a combination program could avert 300 000 infections (an increase of 7000 infections prevented or 2%). Programs to expand screening and treatment will be most effective if they are implemented together, because each program complements the other. Essential to achieving these levels of infections averted is patient receipt of test results after diagnosis, as well as linkage to care, which has been shown to improve with nurse-initiated counseling (95) and health worker follow-up interviews with patients with new diagnoses (96).

The effectiveness of screening and counseling in reducing sexual activity will probably vary among health care settings because of the differences in risk behavior and the length, content, and intensity of counseling services. Even with no reduction in risk behavior, 1-time screening of low-risk groups and annual screening of high-risk groups could prevent nearly 4% of new infections by identifying infected persons and linking them to treatment programs. Augmenting this strategy with expanded ART prevents 16% of new infections. This suggests that preventing future infections through increased ART becomes increasingly important as the effectiveness of screening and counseling diminishes. In settings in which counseling is unavailable or ineffectual, increased utilization of ART can help ensure that expanded screening will lead to reductions in HIV transmission.

Finally, we find that expanded utilization of ART (to 75% or 90% initiating ART at a CD4 cell count less than 0.350×10^9 cells/L) is very cost-effective, as is 1-time screening of low-risk groups and annual screening of high-risk groups. Combination strategies prevent more HIV infections and increase QALYs more than either individual strategy. As noted, our analysis specifically accounts for the effect of combination screening and treatment on population-wide HIV transmission, which is a strength of our modeling framework. As routine HIV screening for adults increases across health care settings due to recently revised CDC guidelines (3), it is important to ensure that ART utilization increases at a concomitant rate. Further expanding HIV screening and counseling services, without expanding the proportion of infected persons receiving ART, does not realize the potential benefits of implementing these 2 complementary interventions.

Compared with other disease screening programs in the United States, 1-time HIV screening of low-risk persons and annual screening of high-risk persons is economically attractive, with a cost-effectiveness ratio less than $23 000 per QALY gained. This compares favorably with other accepted interventions, including screening for type 2 diabetes (97) and breast cancer mammography (98).

Our study has several limitations. First, we assumed proportional mixing among sexual partners and needle-sharing contacts, which simplifies the complex network structure of partnership formation and dissolution. Second, although we stratified the population according to sex and risk behavior, we did not include variations by race or ethnicity. To fully account for such granularity, we would need to accurately estimate sexual and needle-sharing behavior within and between races, which would be difficult to do. Moreover, significant disparities in treatment rates, background mortality, and comorbid conditions exist, and our model cannot account for these additional factors. A third limitation of our study is the omission of acute HIV screening, which would require a different model structure and specific assumptions about the benefits and costs associated with identification and treatment of acute HIV infection. The degree to which acute infection contributes to transmission is uncertain, and estimates vary (47, 99–103). Fourth, we used a simplified HIV treatment model that does not include the intricacies of individual HIV disease management; drug toxicities; CD4 cell count monitoring; or the presence of comorbid conditions, such as coronary heart disease, diabetes, and various types of cancer. Our results, however, are broadly consistent with those from more complicated models of HIV disease progression (21–24, 92, 104). Finally, we did not explicitly model development of resistance to ART, although we believe our assumptions about the benefits of ART are conservative given the introduction of new classes of ART, such as integrase inhibitors and entry inhibitors, and we evaluated scenarios that included resistance in sensitivity analyses.

Expanded HIV screening and counseling in the United States can prevent a substantial number of new HIV infections, adding millions of QALYs to the population. Programs that simultaneously expand ART utilization can prevent more HIV infections than expanding either intervention alone. Our analysis indicates that over the next 2 decades, HIV incidence in the United States could be reduced by 24% with a comprehensive expansion of screening and treatment. If these programs are accompanied by additional interventions that halve risky sexual and needle-sharing behavior, the epidemic could be reduced by 65%, suggesting the need for a comprehensive portfolio of HIV prevention, screening, and treatment.

From the Yale School of Management, New Haven, Connecticut; Stanford University, Stanford, California; and Veterans Affairs Palo Alto Health Care System, Palo Alto, California.

Grant Support: By the National Institute on Drug Abuse, National Institutes of Health (R-01-DA-15612), and Department of Veterans Affairs.

Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M10-0968.

Reproducible Research Statement: *Study protocol and data set*: Not available. *Statistical code*: Additional details may be available by contacting Dr. Long (e-mail, elisa.long@yale.edu), although the exact code is not available in the public domain.

Requests for Single Reprints: Elisa F. Long, PhD, Yale School of Management, 135 Prospect Street, New Haven, CT 06520; e-mail, elisa.long@yale.edu.

Current author addresses and author contributions are available at www.annals.org.

References

1. **Centers for Disease Control and Prevention (CDC).** Estimates of New HIV Infections in the United States; 2008. Accessed at www.cdc.gov/hiv/topics/surveillance/resources/factsheets/incidence.htm on 1 August 2010.
2. **Hall HI, Song R, Rhodes P, Prejean J, An Q, Lee LM, et al; HIV Incidence Surveillance Group.** Estimation of HIV incidence in the United States. JAMA. 2008;300:520-9. [PMID: 18677024]
3. **Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al; 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. [PMID: 16988643]
4. **The NIMH Multisite HIV Prevention Trial: reducing HIV sexual risk behavior.** The National Institute of Mental Health (NIMH) Multisite HIV Prevention Trial Group. Science. 1998;280:1889-94. [PMID: 9632382]
5. **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;280:1161-7. [PMID: 9777816]
6. **Koblin B, Chesney M, Coates T; EXPLORE Study Team.** Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomized controlled study. Lancet. 2004;364:41-50. [PMID: 15234855]
7. **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;39:446-53. [PMID: 16010168]
8. **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;342:921-9. [PMID: 10738050]
9. **Vernazza P, Hirschel B, Bernasconi E, Flepp M.** Les personnes seropositives ne souff rant d'aucune autre MST et suivant un traitment antiretroviral effi cie ne transmettent pas le VIH par voie sexuelle. Bull Med Suisses. 2008;89:165-69.
10. **Castilla J, Del Romero J, Hernando V, Marincovich B, García S, Rodríguez C.** Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. J Acquir Immune Defic Syndr. 2005;40:96-101. [PMID: 16123689]
11. **Porco TC, Martin JN, Page-Shafer KA, Cheng A, Charlebois E, Grant RM, et al.** Decline in HIV infectivity following the introduction of highly active antiretroviral therapy. AIDS. 2004;18:81-8. [PMID: 15090833]
12. **Vernazza PL, Troiani L, Flepp MJ, Cone RW, Schock J, Roth F, et al.** Potent antiretroviral treatment of HIV-infection results in suppression of the seminal shedding of HIV. The Swiss HIV Cohort Study. AIDS. 2000;14:117-21. [PMID: 10708281]
13. **Zhang H, Dornadula G, Beumont M, Livornese L Jr, Van Uitert B, Henning K, et al.** Human immunodeficiency virus type 1 in the semen of men receiving highly active antiretroviral therapy. N Engl J Med. 1998;339:1803-9. [PMID: 9854115]
14. **Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Suleiman JM, Miller MD, et al; 903 Study Group.** Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naive patients: a 3-year randomized trial. JAMA. 2004;292:191-201. [PMID: 15249568]
15. **Centers for Disease Control and Prevention (CDC).** HIV and AIDS in the United States; 2010. Accessed at www.cdc.gov/hiv/resources/factsheets/us.htm on 1 August 2010.
16. **Bartlett JG, Branson BM, Fenton K, Hauschild BC, Miller V, Mayer KH.** Opt-out testing for human immunodeficiency virus in the United States: progress and challenges. JAMA. 2008;300:945-51. [PMID: 18728268]
17. **Qaseem A, Snow V, Shekelle P, Hopkins R Jr, Owens DK; Clinical Efficacy Assessment Subcommittee, American College of Physicians.** Screening for HIV in health care settings: a guidance statement from the American College of Physicians and HIV Medicine Association. Ann Intern Med. 2009;150:125-31. [PMID: 19047022]
18. **Brandeau ML, Owens DK, Sox CH, Wachter RM.** Screening women of childbearing age for human immunodeficiency virus. A cost-benefit analysis. Arch Intern Med. 1992;152:2229-37. [PMID: 1444682]
19. **Brandeau ML, Owens DK, Sox CH, Wachter RM.** Screening women of childbearing age for human immunodeficiency virus. A model-based policy analysis. Manage Sci. 1993;39:72-92.
20. **Owens DK, Nease RF Jr, Harris RA.** Cost-effectiveness of HIV screening in acute care settings. Arch Intern Med. 1996;156:394-404. [PMID: 8607724]
21. **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;352:570-85. [PMID: 15703422]
22. **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;352:586-95. [PMID: 15703423]
23. **Walensky RP, Freedberg KA, Weinstein MC, Paltiel AD.** Cost-effectiveness of HIV testing and treatment in the United States. Clin Infect Dis. 2007;45 Suppl 4:S248-54. [PMID: 18190295]
24. **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. [PMID: 17146064]
25. **Owens DK, Sundaram V, Lazzeroni LC, Douglass LR, Sanders GD, Taylor K, et al.** Prevalence of HIV infection among inpatients and outpatients in Department of Veterans Affairs health care systems: implications for screening programs for HIV. Am J Public Health. 2007;97:2173-8. [PMID: 17971545]
26. **Sanders GD, Bayoumi AM, Holodniy M, Owens DK.** Cost-effectiveness of HIV screening in patients older than 55 years of age. Ann Intern Med. 2008;148:889-903. [PMID: 18559840]
27. **Sanders GD, Anaya HD, Asch S, Hoang T, Golden JF, Bayoumi AM, et al.** Cost-effectiveness of strategies to improve HIV testing and receipt of results: economic analysis of a randomized controlled trial. J Gen Intern Med. 2010;25:556-63. [PMID: 20204538]
28. **U.S. Department of Health and Human Services Panel on Clinical Practices for Treatment of HIV Infection.** Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents; 2009. Accessed at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf on 1 August 2010.
29. **Centers for Disease Control and Prevention (CDC).** CDC's HIV Prevention Progress in the United States; 2010. Accessed at www.cdc.gov/hiv/resources/factsheets/PDF/cdcprev.pdf on 1 August 2010.
30. **Centers for Disease Control and Prevention (CDC).** Late HIV testing - 34 states, 1996-2005. MMWR Morb Mortal Wkly Rep. 2009;58:661-5. [PMID: 19553901]
31. **Long EF, Brandeau ML, Owens DK.** Potential population health outcomes and expenditures of HIV vaccination strategies in the United States. Vaccine. 2009;27:5402-10. [PMID: 19591796]
32. **Gold MR, Siegel JE, Russell LB, Weinstein MC, eds.** Cost-Effectiveness in Health and Medicine. New York: Oxford Univ Pr; 1996.
33. **Bacon O, Lum P, Hahn J, Evans J, Davidson P, Moss A, et al.** Commercial sex work and risk of HIV infection among young drug-injecting men who have sex with men in San Francisco. Sex Transm Dis. 2006;33:228-34. [PMID: 16565643]
34. **Brisson M, Boily MC, Mâsse BR, Adrien A, Léaune V.** Highlights of the sexual activity of the heterosexual population in the province of Quebec. Sex Transm Infect. 1999;75:296-9. [PMID: 10616351]
35. **Fryar CD, Hirsch R, Porter KS, Kottiri B, Brody DJ, Louis T.** Drug use and sexual behaviors reported by adults: United States, 1999-2002. Adv Data. 2007:1-14. [PMID: 17668724]
36. **Johnson AM, Mercer CH, Erens B, Copas AJ, McManus S, Wellings K, et al.** Sexual behaviour in Britain: partnerships, practices, and HIV risk behav-

iours. Lancet. 2001;358:1835-42. [PMID: 11741621]
37. **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;145:416-25. [PMID: 16983129]
38. **Davis JO, Smith TW; National Opinion Research Center.** General Social Surveys (GSS), 1972-2008.
39. **Tyndall MW, Patrick D, Spittal P, Li K, O'Shaughnessy MV, Schechter MT.** Risky sexual behaviours among injection drugs users with high HIV prevalence: implications for STD control. Sex Transm Infect. 2002;78 Suppl 1:i170-5. [PMID: 12083439]
40. **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;35:526-36. [PMID: 15021318]
41. **Kral AH, Lorvick J, Ciccarone D, Wenger L, Gee L, Martinez A, et al.** HIV prevalence and risk behaviors among men who have sex with men and inject drugs in San Francisco. J Urban Health. 2005;82:i43-50. [PMID: 15738321]
42. **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;20:1637-44. [PMID: 16868445]
43. **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;25:353-60. [PMID: 9713915]
44. **Spittal PM, Craib KJ, Wood E, Laliberté N, Li K, Tyndall MW, et al.** Risk factors for elevated HIV incidence rates among female injection drug users in Vancouver. CMAJ. 2002;166:894-9. [PMID: 11949985]
45. **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;41:632-41. [PMID: 16652038]
46. **Downs AM, De Vincenzi I.** Probability of heterosexual transmission of HIV: relationship to the number of unprotected sexual contacts. European Study Group in Heterosexual Transmission of HIV. J Acquir Immune Defic Syndr Hum Retrovirol. 1996;11:388-95. [PMID: 8601226]
47. **Hollingsworth TD, Anderson RM, Fraser C.** HIV-1 transmission, by stage of infection. J Infect Dis. 2008;198:687-93. [PMID: 18662132]
48. **Kaplan EH.** Modeling HIV infectivity: must sex acts be counted? J Acquir Immune Defic Syndr. 1990;3:55-61. [PMID: 2293643]
49. **Mastro TD, de Vincenzi I.** Probabilities of sexual HIV-1 transmission. AIDS. 1996;10 Suppl A:75-82.
50. **Nicolosi A, Corrêa Leite ML, Musicco M, Arici C, Gavazzeni G, Lazzarin A.** The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: a study of 730 stable couples. Italian Study Group on HIV Heterosexual Transmission. Epidemiology. 1994;5:570-5. [PMID: 7841237]
51. **Padian NS, Shiboski SC, Glass SO, Vittinghoff E.** Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: results from a ten-year study. Am J Epidemiol. 1997;146:350-7. [PMID: 9270414]
52. **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;191:1403-9. [PMID: 15809897]
53. **Caceres CF, van Griensven GJ.** Male homosexual transmission of HIV-1. AIDS. 1994;8:1051-61. [PMID: 7986400]
54. **Jacquez JA, Koopman JS, Simon CP, Longini IM Jr.** Role of the primary infection in epidemics of HIV infection in gay cohorts. J Acquir Immune Defic Syndr. 1994;7:1169-84. [PMID: 7932084]
55. **Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP.** Per-contact risk of human immunodeficiency virus transmission between male sexual partners. Am J Epidemiol. 1999;150:306-11. [PMID: 10430236]
56. **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;20:2207-15. [PMID: 17086061]
57. **Zaric GS, Barnett PG, Brandeau ML.** HIV transmission and the cost-effectiveness of methadone maintenance. Am J Public Health. 2000;90:1100-11. [PMID: 10897189]
58. **Taylor A, Hutchinson S, Lingappa J, Wadd S, Ahmed S, Gruer L, et al.** Severe illness and death among injecting drug users in Scotland: a case-control study. Epidemiol Infect. 2005;133:193-204. [PMID: 15816144]
59. **Harris ZK.** Efficient allocation of resources to prevent HIV infection among injection drug users: the Prevention Point Philadelphia (PPP) needle exchange program. Health Econ. 2006;15:147-58. [PMID: 16145716]
60. **Wall SD, Olcott EW, Gerberding JL.** AIDS risk and risk reduction in the radiology department. AJR Am J Roentgenol. 1991;157:911-7. [PMID: 1927808]
61. **Kaplan EH, Heimer R.** A model-based estimate of HIV infectivity via needle sharing. J Acquir Immune Defic Syndr. 1992;5:1116-8. [PMID: 1403641]
62. **Cleary PD, Van Devanter N, Rogers TF, Singer E, Shipton-Levy R, Steilen M, et al.** Behavior changes after notification of HIV infection. Am J Public Health. 1991;81:1586-90. [PMID: 1746654]
63. **Higgins DL, Galavotti C, O'Reilly KR, Schnell DJ, Moore M, Rugg DL, et al.** Evidence for the effects of HIV antibody counseling and testing on risk behaviors. JAMA. 1991;266:2419-29. [PMID: 1920748]
64. **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. [PMID: 16411032]
65. **Tengs TO, Lin TH.** A meta-analysis of utility estimates for HIV/AIDS. Med Decis Making. 2002;22:475-81. [PMID: 12458977]
66. **Joyce VR, Barnett PG, Bayoumi AM, Griffin SC, Kyriakides TC, Yu W, et al.** Health-related quality of life in a randomized trial of antiretroviral therapy for advanced HIV disease. J Acquir Immune Defic Syndr. 2009;50:27-36. [PMID: 19295332]
67. **Schackman BR, Goldie SJ, Freedberg KA, Losina E, Brazier J, Weinstein MC.** Comparison of health state utilities using community and patient preference weights derived from a survey of patients with HIV/AIDS. Med Decis Making. 2002;22:27-38. [PMID: 11833663]
68. **Vernazza P, Hirschel B, Bernasconi E, Flepp M.** HIV transmission under highly active antiretroviral therapy [Letter]. Lancet. 2008;372:1806-7. [PMID: 19027479]
69. **Wilson DP, Law MG, Grulich AE, Cooper DA, Kaldor JM.** Relation between HIV viral load and infectiousness: a model-based analysis. Lancet. 2008; 372:314-20. [PMID: 18657710]
70. **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;44:1115-22. [PMID: 17366461]
71. **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. [PMID: 17438318]
72. **Joint United Nations Programme on HIV/AIDS (UNAIDS).** 2008 Report on the Global AIDS Epidemic. Accessed at www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp on 1 August 2010.
73. **CensusScope.** United States Age Distribution. 2000. Accessed at www.censusscope.org/us/chart_age.html on 1 August 2010.
74. **Evans JL, Hahn JA, Page-Shafer K, Lum PJ, Stein ES, Davidson PJ, et al.** Gender differences in sexual and injection risk behavior among active young injection drug users in San Francisco (the UFO Study). J Urban Health. 2003; 80:137-46. [PMID: 12612103]
75. **Friedman SR, Tempalski B, Cooper H, Perlis T, Keem M, Friedman R, et al.** Estimating numbers of injecting drug users in metropolitan areas for structural analyses of community vulnerability and for assessing relative degrees of service provision for injecting drug users. J Urban Health. 2004;81:377-400. [PMID: 15273263]
76. **Centers for Disease Control and Prevention (CDC).** HIV and AIDS among Gay and Bisexual Men. Accessed at www.cdc.gov/nchhstp/newsroom/docs/FastFacts-MSM-FINAL508COMP.pdf on 1 August 2010.
77. **Centers for Disease Control and Prevention (CDC).** Cases of HIV Infection and AIDS in the United States and Dependent Areas, 2006. HIV/AIDS Surveillance Report, Volume 18. Accessed at www.cdc.gov/hiv/topics/surveillance/resources/reports/2006report/default.htm on 1 August 2010.
78. **Arias E, Rostron BL, Tejada-Vera B.** United States life tables, 2005. Natl Vital Stat Rep. 2010;58:1-132. [PMID: 20578408]
79. **Siegfried N, Muller M, Deeks JJ, Volmink J.** Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2009:CD003362. [PMID: 19370585]
80. **Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A.**

Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Med. 2005;2:e298. [PMID: 16231970]

81. **Desai K, Boily MC, Garnett GP, Mâsse BR, Moses S, Bailey RC.** The role of sexually transmitted infections in male circumcision effectiveness against HIV—insights from clinical trial simulation. Emerg Themes Epidemiol. 2006;3:19. [PMID: 17187662]

82. **Centers for Disease Control and Prevention (CDC).** Persons tested for HIV—United States, 2006. MMWR Morb Mortal Wkly Rep. 2008;57:845-9. [PMID: 18685551]

83. **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]. Proceedings of the 12th Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts, 22–25 February 2005.

84. **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. [PMID: 8483408]

85. **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. [PMID: 9377126]

86. **Bozzette SA, Joyce G, McCaffrey DF, Leibowitz AA, Morton SC, Berry SH, et al; HIV Cost and Services Utilization Study Consortium.** Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. N Engl J Med. 2001;344:817-23. [PMID: 11248159]

87. **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;44:990-7. [PMID: 17063130]

88. **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;43:451-7. [PMID: 16980906]

89. **World Health Organization (WHO).** Global Health Observatory. Accessed at www.who.int/gho/en/ on 1 August 2010.

90. **Centers for Medicaid and Medicare Services.** Medicaid Fee Schedule. Accessed at www.med-quest.us/PDFs/Provider%20Memos/Medicaid%20Fee%20Schedule.pdf on 1 August 2010.

91. **Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, Justice AC, et al; NA-ACCORD Investigators.** Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med. 2009;360:1815-26. [PMID: 19339714]

92. **Freedberg KA, Losina E, Weinstein MC, Paltiel AD, Cohen CJ, Seage GR, et al.** The cost effectiveness of combination antiretroviral therapy for HIV disease. N Engl J Med. 2001;344:824-31. [PMID: 11248160]

93. **Bendavid E, Wood R, Katzenstein DA, Bayoumi AM, Owens DK.** Expanding antiretroviral options in resource-limited settings—a cost-effectiveness analysis. J Acquir Immune Defic Syndr. 2009;52:106-13. [PMID: 19448557]

94. **Goldie SJ, Yazdanpanah Y, Losina E, Weinstein MC, Anglaret X, Walensky RP, et al.** Cost-effectiveness of HIV treatment in resource-poor settings—the case of Côte d'Ivoire. N Engl J Med. 2006;355:1141-53. [PMID: 16971720]

95. **Anaya HD, Hoang T, Golden JF, Goetz MB, Gifford A, Bowman C, et al.** Improving HIV screening and receipt of results by nurse-initiated streamlined counseling and rapid testing. J Gen Intern Med. 2008;23:800-7. [PMID: 18421508]

96. **Zetola NM, Bernstein K, Ahrens K, Marcus JL, Philip S, Nieri G, et al.** Using surveillance data to monitor entry into care of newly diagnosed HIV-infected persons: San Francisco, 2006-2007. BMC Public Health. 2009;9:17. [PMID: 19144168]

97. **Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M.** Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. Ann Intern Med. 2004;140:689-99. [PMID: 15126252]

98. **Plevritis SK, Kurian AW, Sigal BM, Daniel BL, Ikeda DM, Stockdale FE, et al.** Cost-effectiveness of screening BRCA1/2 mutation carriers with breast magnetic resonance imaging. JAMA. 2006;295:2374-84. [PMID: 16720823]

99. **Hollingsworth TD, Anderson RM, Fraser C.** Has the role of primary HIV been overstated? [Abstract]. Proceedings from the 13th Conference on Retroviruses and Opportunistic Infections, Denver, Colorado, 5–8 February 2006.

100. **Kelly JA, Morin SF, Remien RH, Steward WT, Higgins JA, Seal DW, et al.** Lessons learned about behavioral science and acute/early HIV infection. The NIMH Multisite Acute HIV Infection Study: V. AIDS Behav. 2009;13:1068-74. [PMID: 19504179]

101. **Kerndt PR, Dubrow R, Aynalem G, Mayer KH, Beckwith C, Remien RH, et al.** Strategies used in the detection of acute/early HIV infections. The NIMH Multisite Acute HIV Infection Study: I. AIDS Behav. 2009;13:1037-45. [PMID: 19495954]

102. **Pinkerton SD.** How many sexually-acquired HIV infections in the USA are due to acute-phase HIV transmission? AIDS. 2007;21:1625-9. [PMID: 17630558]

103. **Prabhu VS, Hutchinson AB, Farnham PG, Sansom SL.** Sexually acquired HIV infections in the United States due to acute-phase HIV transmission: an update [Letter]. AIDS. 2009;23:1792-4. [PMID: 19684485]

104. **Walensky RP, Weinstein MC, Kimmel AD, Seage GR 3rd, Losina E, Sax PE, et al.** Routine human immunodeficiency virus testing: an economic evaluation of current guidelines. Am J Med. 2005;118:292-300. [PMID: 15745728]

Current Author Addresses: Dr. Long: Yale School of Management, 135 Prospect Street, New Haven, CT 06520.
Dr. Brandeau: Department of Management Science and Engineering, Stanford University, 262 Huang Engineering Center, Stanford, CA 94305.
Dr. Owens: Center for Primary Care and Outcomes Research, Stanford University, 117 Encina Commons, Stanford, CA 94305.

Author Contributions: Conception and design: E.F. Long, M.L. Brandeau, D.K. Owens.
Analysis and interpretation of the data: E.F. Long, M.L. Brandeau.
Drafting of the article: E.F. Long.
Critical revision of the article for important intellectual content: E.F. Long, M.L. Brandeau, D.K. Owens.
Final approval of the article: E.F. Long, M.L. Brandeau, D.K. Owens.
Obtaining of funding: M.L. Brandeau, D.K. Owens.
Collection and assembly of data: E.F. Long.