

SPECIAL ARTICLE

Cost-Effectiveness of Screening for HIV in the Era of Highly Active Antiretroviral Therapy

Gillian D. Sanders, Ph.D., Ahmed M. Bayoumi, M.D., Vandana Sundaram, M.P.H., S. Pinar Bilir, A.B., Christopher P. Neukermans, A.B., Chara E. Rydzak, B.A., Lena R. Douglass, B.S., Laura C. Lazzeroni, Ph.D., Mark Holodniy, M.D., and Douglas K. Owens, M.D.

ABSTRACT

BACKGROUND

The costs, benefits, and cost-effectiveness of screening for human immunodeficiency virus (HIV) in health care settings during the era of highly active antiretroviral therapy (HAART) have not been determined.

METHODS

We developed a Markov model of costs, quality of life, and survival associated with an HIV-screening program as compared with current practice. In both strategies, symptomatic patients were identified through symptom-based case finding. Identified patients started treatment when their CD4 count dropped to 350 cells per cubic millimeter. Disease progression was defined on the basis of CD4 levels and viral load. The likelihood of sexual transmission was based on viral load, knowledge of HIV status, and efficacy of counseling.

RESULTS

Given a 1 percent prevalence of unidentified HIV infection, screening increased life expectancy by 5.48 days, or 4.70 quality-adjusted days, at an estimated cost of \$194 per screened patient, for a cost-effectiveness ratio of \$15,078 per quality-adjusted life-year. Screening cost less than \$50,000 per quality-adjusted life-year if the prevalence of unidentified HIV infection exceeded 0.05 percent. Excluding HIV transmission, the cost-effectiveness of screening was \$41,736 per quality-adjusted life-year. Screening every five years, as compared with a one-time screening program, cost \$57,138 per quality-adjusted life-year, but was more attractive in settings with a high incidence of infection. Our results were sensitive to the efficacy of behavior modification, the benefit of early identification and therapy, and the prevalence and incidence of HIV infection.

CONCLUSIONS

The cost-effectiveness of routine HIV screening in health care settings, even in relatively low-prevalence populations, is similar to that of commonly accepted interventions, and such programs should be expanded.

From Duke Clinical Research Institute, Duke University, Durham, N.C. (G.D.S.); the Center for Primary Care and Outcomes Research, Department of Medicine (G.D.S., V.S., S.P.B., C.P.N., C.E.R., D.K.O.), and the Department of Health Research and Policy (L.C.L., D.K.O.), School of Medicine (M.H.), Stanford University, Stanford, Calif.; the Centre for Research on Inner City Health and Division of General Medicine, St. Michael's Hospital, and the Department of Medicine, University of Toronto — both in Toronto (A.M.B.); and Palo Alto Veterans Affairs Health Care System, Palo Alto, Calif. (V.S., L.R.D., M.H., D.K.O.). Address reprint requests to Dr. Sanders at Duke Clinical Research Institute, P.O. Box 17969, Duke University, Durham, NC 27715, or at gillian.sanders@duke.edu.

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TIMELY IDENTIFICATION OF HUMAN immunodeficiency virus (HIV) infection is critical from both clinical and public health perspectives. A delay in diagnosis until late in the course of HIV infection may be associated with irreversible immunologic damage and related complications. Early identification also provides the opportunity to reduce transmission of HIV through changes in risk behavior.¹⁻³ Treatment with highly active antiretroviral therapy (HAART) most likely reduces infectivity⁴ and may therefore afford an additional public health benefit by further reducing transmission.

Despite these compelling reasons for early identification, the Centers for Disease Control and Prevention (CDC) estimate that up to 20,000 new HIV infections annually can be attributed to people who are unaware of their HIV-positive status. Such people represent up to 280,000 of the approximately 950,000 people infected with HIV in the United States.⁵ CDC data indicate that in 41 percent of HIV-positive patients, the acquired immunodeficiency syndrome (AIDS) develops within a year after they received the diagnosis,⁶ suggesting that opportunities for preventing adverse outcomes were missed.

A fundamental strategy of a new CDC initiative to promote early identification of HIV disease is to make voluntary HIV testing a routine part of medical care.^{7,8} Although we and others previously evaluated the cost-effectiveness of screening,⁹⁻¹² these analyses were performed before HAART became available. Because both the costs and the benefits of screening have changed since these analyses were published, the current cost-effectiveness of screening and the settings in which screening is economically attractive remain uncertain. We sought to evaluate the cost-effectiveness of voluntary HIV screening in health care settings and to assess how incorporating the costs and benefits associated with reductions in HIV transmission would influence the cost-effectiveness of a screening program.

METHODS

We used a decision model to estimate the health benefits and expenditures of performing voluntary HIV screening in health care settings. We adhered to the recommendations of the Panel on Cost-Effectiveness in Health and Medicine for conducting and reporting a reference-case analysis.¹³

DECISION MODEL

We used Decision Maker software (version 2003.11.1, Pratt Medical Group) to develop a Markov model that followed a cohort of patients over their lifetime (details are provided in Figure 1 of the Supplementary Appendix, available with the full text of this article at www.nejm.org). Our model includes voluntary HIV screening of a population, the natural history of HIV and AIDS, the costs and health consequences of transmission of HIV, and the costs and health consequences of HAART for patients so identified. Whenever possible, we based our probability estimates on high-quality published studies^{1-4,7-9,13-165} (Table 1).

PATIENT POPULATION

The target population for our analysis was patients in health care settings whose HIV status was unknown. Reflecting the average age of patients in health care settings, our base-case analysis considered a cohort of 43-year-old men and women.¹⁴ In our base-case analysis we assumed a prevalence of unidentified HIV infection of 1 percent, a value consistent with the CDC recommendation for screening.⁸ The age- and sex-specific incidence of HIV was estimated on the basis of work by Rosenberg (Fig. 3 of the Supplementary Appendix).²¹

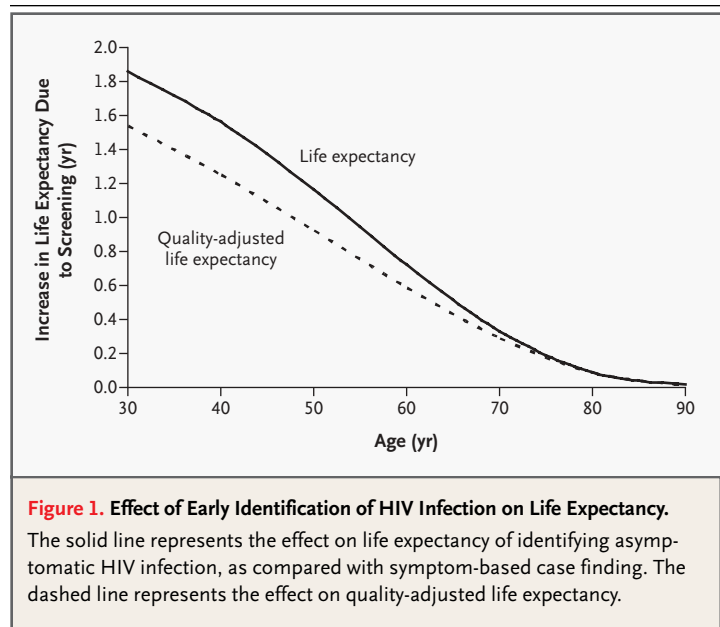


Table 1. Variables and Sources.*

Variable	Base-Case Value	Range	Source
Demographic variables			
Age of patients in screening program (yr)	43	20–80	Kozak et al. ¹⁴
Prevalence of unidentified HIV infection among patients (%)	1.0	0–15	CDC, ⁸ Janssen et al. ¹⁵
Asymptomatic infection (%)	75	50–100	Estimate based on CDC, ⁷ Lemp et al., ¹⁶ Sinclair et al., ¹⁷ Bindman et al., ¹⁸ Bozzette et al., ¹⁹ Zingmond et al. ²⁰
Symptomatic infection (%)	15	0–30	
AIDS (%)	10	0–20	
Annual incidence (%)	0.03	1×–3× baseline	Fig. 3 of Supplementary Appendix; Rosenberg, ²¹ Karon et al. ²²
Proportion of uninfected population who are women (%)	60	50–70	Kozak et al. ¹⁴
HIV-infected population (%)			
Men	75	50–90	HIV/AIDS surveillance report ²³
Men who have sex with men	50	25–75	HIV/AIDS surveillance report ²³
Natural-history variables (cells/mm³)			
CD4 count when infected with HIV	900	750–900	Turner et al. ²⁴
CD4 count at onset of symptoms	350	250–500	Turner et al. ²⁴
Case-finding variables			
CD4 count at which maximal case-finding rate is reached (cells/mm ³)	50	0–350	Assumed
Maximal annual symptom-based case-finding rate (%)	80	50–100	Assumed
HIV testing variables			
Adherence to HIV-screening program (%)	100	50–100	Harris et al., ²⁵ Irwin et al., ²⁶ Kelen et al. ²⁷
Sensitivity of screening test (%)			
First 3 mo after infection	60	11–83	Owens et al., ⁹ Schwartz et al., ²⁸ Mylonakis et al. ²⁹
Established disease	99.5	98.0–99.9	Owens et al., ⁹ Mylonakis et al., ²⁹ CDC ³⁰
Specificity of entire sequence of screening tests (%)	99.9994	99–100	Owens et al., ⁹ Mylonakis et al., ²⁹ MacDonald et al. ³¹
Probability that patient returns to receive HIV test results (%)	80	70–100	Irwin et al., ²⁶ Kelen et al., ³² Kassler et al., ³³ Holman et al., ³⁴ CDC, ^{35,37,38} Erickson et al., ³⁶ Hightow et al., ³⁹ Sullivan et al. ⁴⁰
Months before false positive HIV diagnosis is discovered	2	0–12	Assumed
Frequency of CD4 testing without HAART (mo)	Every 3	Every 3–6	Panel on Clinical Practices ⁴¹
Frequency of HIV testing (mo)	One time	Every 12–108	Assumed
Treatment variables			
CD4 count triggering HAART (cells/mm ³)	350	—	Panel on Clinical Practices, ⁴¹ Yeni et al., ⁴² AVANTI, ⁴³ Erb et al., ⁴⁴ Mocroft et al., ⁴⁵ Rhone et al. ⁴⁶
Viral load triggering HAART (log copies/ml)	4.6	—	
Frequency of CD4 and viral-load testing during HAART treatment (mo)	Every 3	Every 2–6	

Table 1. (Continued.)

Variable	Base-Case Value	Range	Source
Increase in CD4 count at initiation of HAART (cells/mm ³)	110 + $\frac{[535 \times (\text{initial CD4})^{0.98}]}{[(\text{initial CD4})^{0.98} + 260]^{\dagger}}$	—	Cohen Stuart et al., ⁴⁷ Hammer et al., ⁴⁸ Maher et al., ⁴⁹ Drusano and Stein, ⁵⁰ Keita-Perse et al. ⁵¹
Decline in CD4 count with detectable viral load (cells/mm ³)	-79.2 + 33.5 × log viral load	—	Mellors et al., ⁵² Cook et al. ⁵³
Viral load (log copies/ml)‡			
Set point	4.6	3.0–6.0	Bindman et al., ¹⁸ CDC ⁵⁴
During virologic suppression	1.3	1.0–2.7	Raboud et al. ⁵⁵
During virologic rebound	4.1	3.6–4.6	Le Moing et al., ⁵⁶ Deeks et al. ⁵⁷
Incremental rise above set point			
After suppressive therapy failed	0.8	0.0–1.5	CDC, ⁵⁸ de Wolf et al., ⁵⁹ Mellors et al., ⁶⁰ Ioannidis et al., ⁶¹ Keet et al., ⁶² O'Brien et al., ⁶³ Spijkerman et al., ⁶⁴ Henrard et al., ⁶⁵ Sabin et al. ^{66,67}
After suppressive therapy failed and onset of AIDS	1.0	0.0–2.0	
Decrease with nonsuppressive therapy	1.0	0.0–2.0	Lucas et al., ⁶⁸ d'Arminio Monforte et al., ⁶⁹ Bonfanti et al., ⁷⁰ Valdez et al., ⁷¹ Welch et al. ⁷²
Transition rate (events/100 patient-yr)			
From HIV to AIDS	6	2–12	Mellors et al., ⁵² Vlahov et al., ⁷³ Hughes et al. ⁷⁴
From AIDS to death	3	1–10	Vlahov et al. ⁷³
Relative hazard of AIDS			
Per decline in plasma viral load of 1 log copy/ml	0.43	0.28–0.65	O'Brien et al., ^{63,75,83,84} Henrard et al., ⁶⁵ Sabin et al., ⁶⁷ Vlahov et al., ⁷³ Hughes et al., ⁷⁴ Marschner et al., ⁷⁶ Brun-Vezinet et al., ⁷⁷ Coombs et al., ⁷⁸ Galetto-Lacour et al., ⁷⁹ Katzenstein et al., ⁸⁰ Mellors et al., ⁸¹ Montaner et al., ⁸² Pedersen et al., ⁸⁵ Phillips et al., ^{86,87} Welles et al., ⁸⁸ Yerly et al., ⁸⁹ Chêne et al., ⁹⁰ Loveday and Hill ⁹¹
Per increase in CD4 count of 1 log/mm ³	0.0154	0.0002–1.0	
Relative hazard of death from AIDS			
Per decline in plasma viral load of 1 log copy/ml	0.64	0.55–0.75	
Per increase in CD4 count of 1 log/mm ³	0.118	0.064–0.329	
Probability of virologic suppression (%)			Panel on Clinical Practices, ⁴¹ AVANTI, ⁴³ Erb et al., ⁴⁴ Mocroft et al., ⁴⁵ Rhone et al., ⁴⁶ Cohen Stuart et al., ⁴⁷ Hammer et al., ⁴⁸ Maher et al., ⁴⁹ Raboud et al., ⁵⁵ Deeks et al., ⁵⁷ Lucas et al., ⁶⁸ Bonfanti et al., ^{70,112} Valdez et al., ⁷¹ Butcher et al., ⁹² Guardiola et al., ⁹³ Casado et al., ⁹⁴ d'Arminio Monforte et al., ⁹⁵ Kirk et al., ⁹⁶ Roca et al., ^{97,98} van Roon et al., ⁹⁹ Paredes et al., ¹⁰⁰ Kaufmann et al., ¹⁰¹ Hogg et al., ¹⁰² Fätkenheuer et al., ¹⁰³ Montaner et al., ¹⁰⁴ Zolopa et al., ¹⁰⁵ Shulman et al., ¹⁰⁶ Durant et al., ¹⁰⁷ Cohen et al., ¹⁰⁸ Baxter et al., ¹⁰⁹ Carpenter et al., ¹¹⁰ Bernasconi et al., ¹¹¹ Gulick et al., ^{113,114} Ledergerber et al., ¹¹⁵ Moyle et al., ¹¹⁶ Notermans et al., ¹¹⁷ Paris et al., ¹¹⁸ Powderly et al., ¹¹⁹ Salzberger et al., ¹²⁰ Staszewski et al., ¹²¹ Cameron et al., ¹²² Clough et al., ¹²³ De Wit et al., ¹²⁴ Paredes et al., ¹²⁵ Kaufmann et al., ¹²⁶ Bellman, ¹²⁷ Hall et al. ¹²⁸

Table 1. (Continued.)

Variable	Base-Case Value	Range	Source
First regimen	80	30–98	
Second regimen	65	20–80	
Third regimen	30	5–40	
Rates of virologic rebound			
First rebound (% at 2 yr)	15	6–30	AVANTI, ⁴³ Mocroft et al., ⁴⁵ Raboud et al., ^{55,132} d'Arminio Monforte et al., ⁶⁹ Butcher et al., ⁹² Paredes et al., ¹⁰⁰ Montaner et al., ¹⁰⁴ Gulick et al., ^{114,131} Paris et al., ¹¹⁸ Powderly et al., ¹¹⁹ Salzberger et al., ¹²⁰ Pialoux et al., ¹²⁹ Havlir et al., ¹³⁰ Staszewski et al., ¹³³ D'Amato et al., ¹³⁴ Kempf et al., ¹³⁵ Tebas et al. ¹³⁶
Per subsequent regimen (relative hazard)	2.0	1.0–6.0	Kaufmann et al., ¹⁰¹ Salzberger et al., ¹²⁰ Paredes et al., ¹²⁵ Havlir et al. ¹³⁰
Intolerance requiring discontinuation of first regimen (%)	25	5–40	AVANTI, ⁴³ Lucas et al., ⁶⁸ d'Arminio Monforte et al., ^{69,95} Bonfanti et al., ⁷⁰ Butcher et al., ⁹² Guardiola et al., ⁹³ Casado et al., ⁹⁴ Kirk et al., ⁹⁶ Roca et al., ^{97,98} van Roon et al., ⁹⁹ Paredes et al., ¹⁰⁰ Kaufmann et al., ¹⁰¹ Gulick et al., ¹³¹ Staszewski et al., ¹³³ Cameron et al., ¹³⁷ Sullivan et al., ¹³⁸ Safrin and Grunfeld, ¹³⁹ Reijers et al. ¹⁴⁰
Relative risk of discontinuation of second regimen	1.0	1–4	
Relative risk of discontinuation of third regimen	1.4	1–4	
Transmission variables			
Age of patients' sexual partners (yr)	43	20–80	Assumed to be the same as the infected patient
No. of susceptible partners at risk			
Men who have sex with men	2	1–10	Michael et al., ¹⁴¹ Laumann ¹⁴²
Heterosexual men	1	0.5–4.0	Michael et al., ¹⁴¹ Laumann ¹⁴²
Heterosexual women	1	0.5–4.0	Michael et al., ¹⁴¹ Laumann ¹⁴²
Annual probability of infecting a sexual partner (%)			
Men who have sex with men	4	1–5	Samuel et al., ¹⁴³ Keet et al., ¹⁴⁴ Caceres and van Griensven, ¹⁴⁵ Buchbinder et al. ¹⁴⁶
Heterosexual men	3	0.5–5.0	Deschamps et al., ¹⁴⁷ de Vincenzi, ¹⁴⁸ Padian et al., ¹⁴⁹ Operskalski et al., ¹⁵⁰ Musicco et al. ¹⁵¹
Heterosexual women	1	0.5–4.0	Deschamps et al., ¹⁴⁷ de Vincenzi, ¹⁴⁸ Padian et al., ¹⁴⁹ Operskalski et al. ¹⁵⁰
Relative risk of infectivity given change in viral load of 1 log copy/ml	2.45	1–3	Quinn et al. ⁴
Effectiveness of testing and counseling in reducing the number of sexual transmissions (% reduction in infectivity)	20	0–50	NIMH, ¹ Kamb et al., ² DiClemente and Wingood ³

Table 1. (Continued.)

Variable	Base-Case Value	Range	Source
Cost variables (dollars)			
Negative HIV test	2.50	1–5	Cost of ELISA test at Palo Alto VA
Positive HIV test	64	45–80	Cost of ELISA and Western blot tests at Palo Alto VA
HIV-test counseling	45	25–100	Owens et al. ⁹
Cost of measuring CD4 count per test	92	65–120	Freedberg et al. ¹⁵²
Cost of measuring viral load per test	122	90–200	Freedberg et al. ¹⁵²
Annual cost of HIV infection (CD4, >500 cells per cubic millimeter) with HAART‡	2,978	2,228–3,723	Bozzette et al. ¹⁵³
Annual cost of HIV infection (CD4, 200–500 cells per cubic millimeter) with HAART‡	5,096	3,821–6,369	
Annual cost of HIV infection (CD4, <200 cells per cubic millimeter) with HAART‡	7,596	5,697–9,495	
Annual cost of AIDS with HAART‡	10,998	8,251–13,748	
Cost of three-drug antiretroviral therapy	13,752	8,251–16,307	Panel on Clinical Practices, ⁴¹ Durant et al., ¹⁰⁷ Carpenter et al., ¹¹⁰ Drugs for HIV Infection, ¹⁵⁴ U.S. General Accounting Office ¹⁵⁵
Incremental cost of four-drug antiretroviral therapy	2,477	1,540–12,579	
Annual cost of salvage therapy	16,230	0–28,885	
Cost of HAART side effect per episode	148	98–733	Mole et al., ¹⁵⁶ Keiser et al., ¹⁵⁷ Gable et al. ¹⁵⁸
Quality-of-life variables 			
Current health			Sex- and age-specific quality of life for current health from Fryback et al. ¹⁵⁹
Unknown asymptomatic HIV infection	0.91	0.85–1.00	Honiden et al. ¹⁶⁰
Diagnosed asymptomatic HIV infection			
First year	0.84	0.80–1.00	Honiden et al. ¹⁶⁰
Subsequent years	0.89	0.80–1.00	Honiden et al. ¹⁶⁰
Symptomatic (untreated) HIV infection	0.79	0.45–1.00	Honiden et al., ¹⁶⁰ Tsevat et al., ^{161,162} Revicki et al., ¹⁶³ Tengs and Lin ¹⁶⁴
HIV infection during HAART	0.83	0.45–1.00	Honiden et al., ¹⁶⁰ Tsevat et al., ^{161,162} Revicki et al., ¹⁶³ Tengs and Lin ¹⁶⁴
AIDS	0.73	0.24–0.80	Honiden et al., ¹⁶⁰ Tsevat et al., ^{161,162} Revicki et al., ¹⁶³ Tengs and Lin ¹⁶⁴
Decrease in quality of life due to side effects of HAART (multiplier)	0.53	0.44–0.62	Keiser et al., ¹⁵⁷ Gable et al., ¹⁵⁸ Bayoumi and Redelmeier ¹⁶⁵
Other variables			
Discount rate (annual %)	3	0–5	Weinstein et al. ¹³
Cycle length (mo)	1		Assumed

* All probabilities are annual unless otherwise noted. All costs are in 2004 U.S. dollars. NIMH denotes the National Institute of Mental Health, ELISA enzyme-linked immunosorbent assay, and VA Veterans Affairs.

† We assumed that all patients had an increase in the CD4 count of at least 60 cells per cubic millimeter.

‡ The maximal viral load was 6.0 log copies per milliliter.

§ Treatment costs do not include the cost of HAART.

|| Quality-of-life variables represent a person's preference for a given state of health and are scaled from 0 to 1, with 1 equivalent to perfect health.

HIV DISEASE PROGRESSION

The patients' viral load and CD4 levels together defined their risk of disease progression. We used natural-history data to estimate the rates of disease progression without therapy.^{52,73,74} As the patients' viral load or CD4 count changed, so did their risk of AIDS or death. We estimated the relative hazard of AIDS or death for every change in the viral load of 1 log (on a base 10 scale) copy per milliliter and for every change in the CD4 count of 1 log per cubic millimeter (Table 1 and Fig. 4 of the Supplementary Appendix).

HIV TESTING

Each month, patients could be selected for testing through either an HIV-screening program or symptom-based case finding. We assumed that the frequency with which case finding occurred was constant and high below a CD4 count of 50 cells per cubic millimeter, linearly related to the CD4 count between 50 and 350 cells per cubic millimeter, and not relevant with a CD4 count of more than 350 cells per cubic millimeter, when patients were assumed to be asymptomatic (Fig. 4 of the Supplementary Appendix).

We assumed a standard testing strategy consisting of a serum enzyme-linked immunosorbent assay followed by confirmatory Western blotting (Table 1). The benefits of testing and counseling accrued only if patients received their test results and entered care. Our base-case assumption was that 80 percent of patients who screened positive for HIV would enter care and receive appropriate treatment.

TREATMENT OF HIV INFECTION

In accordance with published treatment guidelines, we assumed that HAART was started when the CD4 count of an identified HIV-infected patient was at or below 350 cells per cubic millimeter.^{41,42} We estimated the viral load for such patients to be 4.6 log copies per milliliter, according to community-based populations of patients who had never received antiretroviral agents.⁴³⁻⁴⁶

After starting a HAART regimen, patients in whom virologic replication was suppressed also had an increase in their CD4 count (Table 1). Each month, patients with virologic suppression (defined as fewer than 500 copies per milliliter) could have treatment-related effects, virologic rebound, or continued virologic suppression (Supplementary Appendix). Patients who had drug-related adverse effects switched to a new antiretroviral regimen.

Patients with incompletely suppressed viral loads owing to the development of resistance were identified when their viral load was determined at three-month intervals. When identified, these patients switched to a new antiretroviral regimen. We assumed that virologic suppression was less likely to be successful with each virologic rebound (Table 1).

If resistance developed to three successive antiretroviral regimens, we assumed that only partial virologic suppression was possible; such patients continued to receive HAART. We assumed that this partial suppression was sustained, reflecting the use of additional nonsuppressive regimens over time. All patients received prophylaxis against opportunistic infections when appropriate.

TRANSMISSION OF HIV

Transmission from an HIV-infected patient to his or her sexual partner depended on the infected patient's sex, type of sexual activity, number of sexual partners, knowledge of HIV status, and viral load (Table 1). On the basis of trials of counseling to prevent transmission of HIV by increasing condom use,¹⁻³ we assumed a 20 percent reduction in transmission for patients with identified HIV infection. We assumed that reductions in viral load further reduced transmission (Table 1).⁴ Our assumptions and methods are in the Supplementary Appendix. In a sensitivity analysis, we included transmission from injection-drug users to their partners.

QUALITY OF LIFE

HIV infection and AIDS can markedly affect the quality of life. Accordingly, we incorporated adjustments for the quality of life in our analysis (Table 1 and Supplementary Appendix).

COSTS

Our analysis included the costs of testing and counseling, follow-up, and treatment for patients identified through screening or case finding (Table 1). We updated all costs to 2004 U.S. dollars (Supplementary Appendix).^{166,167}

Costs for care of HIV-infected patients receiving HAART were separated into drug-related and non-drug-related costs (Table 1). The cost of multidrug HAART was estimated from published wholesale costs of recommended drug regimens. The non-drug-related annual cost of treating patients varied on the basis of the CD4 count and clinical status (Table 1).

Table 2. Lifetime Transmission Rates.*

Strategy	Men Who Have Sex with Men		Heterosexual Men		Heterosexual Women	
	No. of Lifetime Transmissions	Annual Transmission Rate	No. of Lifetime Transmissions	Annual Transmission Rate	No. of Lifetime Transmissions	Annual Transmission Rate
		%		%		%
Natural history	1.16	5.01	0.43	3.74	0.14	1.23
No screening	1.12	2.80	0.42	2.09	0.14	0.69
One-time screening	0.95	2.22	0.35	1.66	0.12	0.55
Recurrent screening	0.93	2.11	0.34	1.58	0.11	0.52

* The annual transmission rate is per partner at risk. These results represent the lifetime and annual transmissions of a patient infected with HIV at the age of 43 years. The base-case transmission rates found in Table 1 are reduced to those shown here through two mechanisms: when an HIV-infected patient is identified and undergoes behavior counseling he or she reduces risky behavior (base-case analysis, 20 percent reduction), and when an identified HIV-infected patient begins HIV-suppressive treatment and lowers his or her viral load, his or her infectivity is also reduced. The natural-history strategy represents a strategy in which HIV-infected patients are never identified and therefore do not receive treatment for their infection. Recurrent screening is every five years.

RESULTS

BENEFIT OF SCREENING DUE TO EARLY IDENTIFICATION OF HIV

We used our model to estimate the increase in the length of life that resulted from the initiation of HAART at a CD4 count of 350 cells per cubic millimeter as compared with the initiation of HAART on the basis of case finding (associated with an average CD4 count of 175 cells per cubic millimeter). In our base-case analysis, early identification and treatment resulted in an increase in life expectancy of the HIV-infected patient of 1.52 years; the benefit decreased for older patients (Fig. 1).

BENEFIT OF SCREENING FROM REDUCED TRANSMISSION OF HIV

Without screening, we estimated that HIV-infected men who have sex with men transmit the virus to 1.12 sexual partners over their lifetime and that heterosexual men and women transmit the virus to 0.42 and 0.14 partner, respectively (Table 2). If a one-time screening program is implemented, the lifetime numbers of transmissions are reduced to 0.95, 0.35, and 0.12 partner among men who have sex with men, heterosexual men, and heterosexual women, respectively. At our base-case incidence, recurrent screening (every five years) had little additional effect on the lifetime numbers of transmissions (Table 2). These lifetime transmissions reflected a 44 percent reduction in the annual transmission rate in the absence of screening, as com-

pared with the natural history of the disease (without any case finding), and a reduction in the annual transmission rate of approximately 21 percent with the use of a screening strategy, as compared with the absence of screening.

ONE-TIME SCREENING

We assessed the cost-effectiveness of screening both with and without considering the benefit to sexual partners. When we considered only the benefit to the identified patient, we found that with an unidentified HIV prevalence of 1 percent, a one-time screening program increased life expectancy by 3.92 days, or 2.92 quality-adjusted days, at a cost of \$333 relative to current practice, for an incremental cost-effectiveness of \$41,736 per quality-adjusted life-year (Table 3). Incorporating costs and benefits to partners, we estimated that one-time screening cost \$194 more than the cost of current practice, while increasing life expectancy by 5.48 days, or 4.70 quality-adjusted days, for an incremental cost-effectiveness of \$15,078 per quality-adjusted life-year (Table 3). As Figure 2A demonstrates, the prevalence of unidentified HIV can be as low as 0.5 percent and still have a cost-effectiveness ratio of less than \$50,000 per quality-adjusted life-year, excluding the benefits to partners. Including the costs and benefits to partners, the prevalence of unidentified HIV can be as low as 0.05 percent before it costs \$50,000 per quality-adjusted life-year gained.

Table 3. Health and Economic Outcomes.*

Strategy	Cost	Incremental Cost	Life Expectancy	Incremental Life Expectancy	Incremental Cost-Effectiveness	Quality-Adjusted Life Expectancy	Incremental Quality-Adjusted Life Expectancy	Incremental Cost-Effectiveness
	\$	\$	years	days	\$/LY	QALY	QALD	\$/QALY
Index patient only (transmission to partners excluded)								
No screening	51,517		21.063			18.626		
One-time screening	51,850	333	21.073	3.92	31,084	18.634	2.92	41,736
Recurrent screening†	52,086	236	21.076	0.97	88,328	18.636	0.70	123,614
Index patient and sexual partners (transmission to partners included)								
No screening	52,623		21.015			18.576		
One-time screening	52,816	194	21.030	5.48	12,919	18.589	4.70	15,078
Recurrent screening†	53,022	206	21.034	1.52	49,509	18.592	1.31	57,138

* The analysis was based on a 1 percent prevalence of underdiagnosed HIV infection. LY denotes years of life, QALY quality-adjusted years of life, and QALD quality-adjusted days of life.

† Recurrent screening is every five years.

RECURRENT SCREENING

At our base-case annual incidence of 0.03 percent, screening every five years relative to one-time screening cost \$57,138 per quality-adjusted life-year gained, when we included the benefit to partners (Table 3). Because the incidence of HIV infection in health care settings varies, we evaluated the cost-effectiveness of screening when the incidence was increased by a factor of 2 or 3 (Fig. 2B). Recurrent screening became more cost-effective as the incidence increased. For example, if the incidence increased by a factor of 3, screening every five years cost \$29,900 per quality-adjusted life-year gained, as compared with one-time screening.

SENSITIVITY ANALYSES

The reduction in HIV transmission that occurred with screening depended on the effectiveness of counseling, the degree to which HAART reduced infectivity, and the baseline viral levels at the time of transmission. If a 1-log decrease in viral load reduced transmission by a factor of 1.5, screening cost \$24,800 per quality-adjusted life-year, as compared with no screening. If counseling resulted in a reduction in risk behavior of only 10 percent, screening cost \$20,500 per quality-adjusted life-year. If men who have sex with men had only 1 partner at risk and heterosexuals had only 0.5 partner at risk,

screening cost \$25,300 per quality-adjusted life-year, as compared with no screening.

In a sensitivity analysis, we evaluated the cost-effectiveness of screening when a proportion of HIV-positive patients were injection-drug users and accounted for additional transmission that could occur (Supplementary Appendix). In one-way sensitivity analyses, we changed our assumptions about infectivity (from a factor of 2 per 1-log decrease in viral load to no change), the proportion of injection-drug users among HIV-infected patients (from 25 percent to 35 percent), and the effectiveness of counseling in reducing high-risk injections (from 25 percent to 50 percent). The corresponding cost-effectiveness ratios were \$15,900, \$9,700, and \$8,800 per quality-adjusted life-year, respectively.

Given the high specificity of HIV tests, the occurrence of false positive results was very rare. Even at a prevalence of HIV of 0.1 percent, for every 100,000 patients tested, only 0.48 patient would be falsely identified as infected with HIV. In the base-case analysis, we assumed that such persons would be identified as not having HIV within two months after the false positive result. Even if such identification took three years, the cost of screening would be less than \$45,000 per quality-adjusted life-year gained at a prevalence of 0.1 percent.

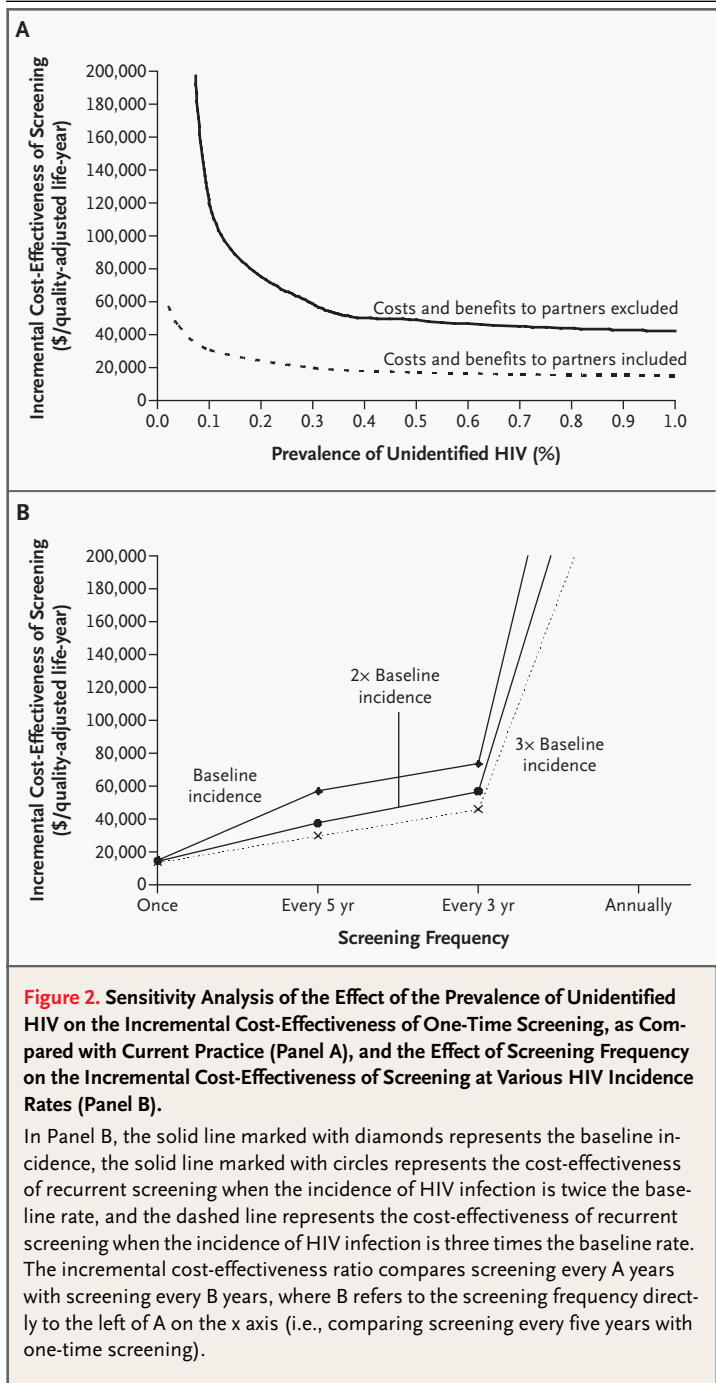
If HAART was started at a lower CD4 count

(e.g., 300 cells per cubic millimeter), screening cost \$14,200 per quality-adjusted life-year.

DISCUSSION

We evaluated the cost-effectiveness of routine screening for HIV infection in the era of HAART. Our analysis indicates that screening for HIV infection is cost-effective relative to other commonly accepted screening programs and medical treatments,¹⁶⁸ even when the prevalence of HIV infection is substantially lower than 1 percent, a prevalence that the CDC has used as general guidance for the initiation of routinely recommended as opposed to targeted screening.⁸ This finding has potential public health implications in that screening for HIV infection is likely to be cost-effective in a much broader range of health care settings than has previously been recognized. Our analysis also highlights the importance of the public health benefit afforded by the identification of HIV infection. The identification of HIV infection can reduce transmission through two mechanisms: reductions in risk behavior and in infectivity from HAART. When we accounted for these important benefits, the cost-effectiveness of screening for HIV became favorable even at infection prevalences of less than 0.1 percent.

The main benefit of screening is that people identified as having HIV can begin lifesaving HAART before severe immunologic destruction has occurred. We assumed that, in patients in whom the infection was diagnosed early, HAART would begin when the CD4 count declined to 350 cells per cubic millimeter, the threshold recommended in current treatment guidelines. However, the best time to begin HAART is controversial.^{44,169-176} The clinical benefit of starting therapy at various CD4 counts has not been evaluated directly in clinical trials. The ongoing Strategies for Management of Antiretroviral Therapy (SMART) study may help determine whether starting treatment when the CD4 count exceeds 350 cells per cubic millimeter and maintaining an undetectable viral load are more clinically beneficial than waiting to start treatment until the CD4 cell count reaches 350 cells per cubic millimeter.¹⁷⁷ Our model-based estimates indicate that identifying patients early and beginning therapy when the CD4 count was 350 cells per cubic millimeter, rather than through case finding and beginning therapy when the CD4 count was, on average, 175 cells per cubic millimeter, resulted in a



survival advantage of about 1.5 years. This substantial survival advantage is the reason that screening reaches conventional levels of cost-effectiveness even when we did not consider the additional benefit from reduced transmission to sexual partners.

When we accounted for changes in risk behavior associated with counseling and the reduction in

transmission related to a decreased viral load during HAART, the rates of HIV transmission with the use of screening dropped by slightly more than 20 percent, as compared with no screening. Both changes in behavior and reduced viral load are important mediators of this benefit: HAART would reduce transmission even if patients who screened positive for HIV did not change their risk behavior (a reduction of 12 percent, as compared with no screening). However, the rate of transmission of HIV depends on many factors, including the number of sexual partners, the type and frequency of sex acts, the length of partnerships, the use or nonuse of condoms, and the viral load of the index patient. These factors will vary among populations that are screened, and there is uncertainty about each of them. Nonetheless, the benefit from reduced transmission remained important in our analyses under a broad range of assumptions.

The available evidence strongly indicates that current approaches to testing are inadequate. As noted, AIDS developed in 41 percent of the patients reported in CDC surveillance data within a year after they learned of their HIV-positive status.⁶ In an ongoing cohort study of veterans, 20 percent of patients had an AIDS-defining illness at presentation for HIV care and 41 percent had a CD4 count of 200 cells per cubic millimeter or less (Justice AC: personal communication). Another study of veterans found that of almost 14,000 patients identified as at risk, only about one third to one half had documentation of HIV testing.¹⁷⁸ Together these studies indicate that many patients at risk are not tested at all and that of those who are identified, many have advanced disease.

Given the inadequacies of current testing, we believe the case for systematic voluntary HIV screening in health care settings is now compelling. When implementing screening, providers must decide whether to recommend routine screening for all patients or targeted screening based on risk-behavior

assessment. The CDC recommends providers consider the type of setting, prevalence of HIV, and behavioral and clinical HIV risk of individual patients when they are deciding between targeted and routinely recommended screening.⁸ The guideline suggests that a prevalence of 1 percent can be used as a general threshold for recommending routine (as compared with targeted) screening, but it also notes that routine screening may be recommended at lower prevalences depending on available resources and circumstances. Our findings suggest that routine screening would be cost-effective if the prevalence of undiagnosed HIV infection were as low as 0.05 percent. Although the prevalence of undiagnosed HIV infection is largely unknown, it is likely to reach 0.05 percent in many settings, including urgent care clinics, emergency departments, and some primary care clinics. For example, in a blinded serologic survey, we found that the prevalence of undiagnosed HIV infection ranged from 0.13 percent to 2.9 percent in unselected outpatients at six Department of Veterans Affairs health care systems.¹⁷⁹ Outpatient populations are rarely offered routine HIV screening. Because the prevalence of HIV infection in these populations is low, the HIV tests that are used should have very high specificity, ensuring low rates of false positive results.

Our analysis indicated that screening would be more effective than current practice and that the cost-effectiveness of screening is well within the range of that of other commonly accepted health care interventions. In addition, we demonstrated that screening is likely to be cost-effective at a substantially lower prevalence than previously recognized. This finding suggests that in many health care settings, HIV screening will provide important health benefits for a reasonable investment in health care resources.

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REFERENCES

1. The NIMH Multisite HIV Prevention Trial: reducing HIV sexual risk behavior. *Science* 1998;280:1889-94.
2. Kamb ML, Fishbein M, Douglas JM Jr, et al. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. *JAMA* 1998;280:1161-7.
3. DiClemente RJ, Wingood GM. A randomized controlled trial of an HIV sexual risk-reduction intervention for young African-American women. *JAMA* 1995;274:1271-6.
4. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000;342:921-9.
5. Advancing HIV prevention: new strategies for a changing epidemic, 2004. (Accessed January 18, 2005, at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5215a1.htm>.)
6. Neal JJ, Fleming PL. Frequency and predictors of late HIV diagnosis in the United States, 1994 through 1999. In: Proceedings of the 9th Conference on Retroviruses and Opportunistic Infections, Seattle, February 24-28, 2002. abstract.
7. Advancing HIV prevention: new strategies for a changing epidemic — United States, 2003. *MMWR Morb Mortal Wkly Rep* 2003;52:329-32.
8. Revised guidelines for HIV counseling,

- testing, and referral. *MMWR Recomm Rep* 2001;50(RR-19):1-57.
9. Owens DK, Nease RF Jr, Harris RA. Cost-effectiveness of HIV screening in acute care settings. *Arch Intern Med* 1996;156:394-404.
 10. Phillips KA, Feryak S. The cost-effectiveness of expanded HIV counselling and testing in primary care settings: a first look. *AIDS* 2000;14:2159-69.
 11. McCarthy BD, Wong JB, Munoz A, Sonnenberg FA. Who should be screened for HIV infection? A cost-effectiveness analysis. *Arch Intern Med* 1993;153:1107-16.
 12. Lurie P, Avins AL, Phillips KA, Kahn JG, Lowe RA, Ciccarone D. The cost-effectiveness of voluntary counseling and testing of hospital inpatients for HIV infection. *JAMA* 1994;272:1832-8. [Erratum, *JAMA* 1995;273:1000.]
 13. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-Effectiveness in Health and Medicine. *JAMA* 1996;276:1253-8.
 14. Kozak LJ, Owings MF, Hall MJ. National Hospital Discharge Survey: 2001 annual summary with detailed diagnosis and procedure data. *Vital and health statistics. Series 13. No. 156.* Hyattsville, Md.: National Center for Health Statistics, 2004:1-198.
 15. Janssen RS, St Louis ME, Satten GA, et al. HIV infection among patients in U.S. acute care hospitals: strategies for the counseling and testing of hospital patients. *N Engl J Med* 1992;327:445-52.
 16. Lemp GF, Hirozawa AM, Givertz D, et al. Seroprevalence of HIV and risk behaviors among young homosexual and bisexual men: the San Francisco/Berkeley Young Men's Survey. *JAMA* 1994;272:449-54.
 17. Sinclair M, Bor R, Evans A, Glass D, Levitt D, Johnson MA. The sociodemographic profile, risk categories and prevalence of HIV infection among people attending a London same-day testing clinic, 2000-2001. *Int J STD AIDS* 2004;15:33-7.
 18. Bindman AB, Osmond D, Hecht FM, et al. Multistate evaluation of anonymous HIV testing and access to medical care. *JAMA* 1998;280:1416-20.
 19. Bozzette SA, Berry SH, Duan N, et al. The care of HIV-infected adults in the United States. *N Engl J Med* 1998;339:1897-904.
 20. Zingmond DS, Wenger NS, Crystal S, et al. Circumstances at HIV diagnosis and progression of disease in older HIV-infected Americans. *Am J Public Health* 2001;91:1117-20.
 21. Rosenberg PS. Scope of the AIDS epidemic in the United States. *Science* 1995;270:1372-5.
 22. Karon JM, Fleming PL, Steketee RW, De Cock KM. HIV in the United States at the turn of the century: an epidemic in transition. *Am J Public Health* 2001;91:1060-8.
 23. Centers for Disease Control and Prevention. HIV/AIDS surveillance report 2002. Vol. 14. (Accessed January 18, 2005, at <http://www.cdc.gov/hiv/stats/hasr1402/2002SurveillanceReport.pdf>.)
 24. Turner BJ, Hecht FM, Ismail RB. CD4+ T-lymphocyte measures in the treatment of individuals infected with human immunodeficiency virus type 1: a review for clinical practitioners. *Arch Intern Med* 1994;154:1561-73.
 25. Harris RL, Boisauvin EV, Salyer PD, Semands DE. Evaluation of a hospital admission HIV antibody voluntary screening program. *Infect Control Hosp Epidemiol* 1990;11:628-34.
 26. Irwin K, Olivo N, Schable CA, Weber JT, Janssen R, Ernst J. Performance characteristics of a rapid HIV antibody assay in a hospital with a high prevalence of HIV infection. *Ann Intern Med* 1996;125:471-5.
 27. Kelen GD, Shaham JB, Quinn TC. Emergency department-based HIV screening and counseling: experience with rapid and standard serologic testing. *Ann Emerg Med* 1999;33:147-55.
 28. Schwartz JS, Kinoshian BP, Pierskalla WP, Lee HL. Strategies for screening blood for human immunodeficiency virus antibody: use of a decision support system. *JAMA* 1990;264:1704-10.
 29. Mylonakis E, Paliou M, Lally M, Flanagan TP, Rich JD. Laboratory testing for infection with the human immunodeficiency virus: established and novel approaches. *Am J Med* 2000;109:568-76.
 30. Update: serologic testing for antibody to human immunodeficiency virus. *MMWR Morb Mortal Wkly Rep* 1988;36:833-40, 845.
 31. MacDonald KL, Jackson JB, Bowman RJ, et al. Performance characteristics of serologic tests for human immunodeficiency virus type 1 (HIV-1) antibody among Minnesota blood donors: public health and clinical implications. *Ann Intern Med* 1989;110:617-21.
 32. Kelen GD, Hexter DA, Hansen KN, et al. Feasibility of an emergency department-based, risk-targeted voluntary HIV screening program. *Ann Emerg Med* 1996;27:687-92.
 33. Kassler WJ, Dillon BA, Haley C, Jones WK, Goldman A. On-site, rapid HIV testing with same-day results and counseling. *AIDS* 1997;11:1045-51.
 34. Holman S, Sorin MD, Crossette J, LaChance-McCullough ML. A state program for postpartum HIV counseling and testing. *Public Health Rep* 1994;109:521-9.
 35. HIV counseling and testing in publicly funded sites: annual report 1997 and 1998. Atlanta: Centers for Disease Control and Prevention, 2001.
 36. Erickson B, Wasserheit J, Rompalo AM, Brathwaite W, Glasser D, Hook E III. Routine voluntary HIV screening in STD clinic clients: characterization of infected clients. *Sex Transm Dis* 1990;17:194-9.
 37. Voluntary HIV testing as part of routine medical care — Massachusetts, 2002. *MMWR Morb Mortal Wkly Rep* 2004;53:523-6.
 38. Routinely recommended HIV testing at an urban urgent-care clinic — Atlanta, Georgia, 2000. *MMWR Morb Mortal Wkly Rep* 2001;50:538-41.
 39. Hightow LB, Miller WC, Leone PA, Wohl D, Smurzynski M, Kaplan AH. Failure to return for HIV posttest counseling in an STD clinic population. *AIDS Educ Prev* 2003;15:282-90.
 40. Sullivan PS, Lansky A, Drake A. Failure to return for HIV test results among persons at high risk for HIV infection: results from a multistate interview project. *J Acquir Immune Defic Syndr* 2004;35:511-8.
 41. Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Bethesda, Md.: Department of Health and Human Services, March 23, 2004. (Accessed January 18, 2005, at http://aidsinfo.nih.gov/guidelines/adult/AA_102904.pdf.)
 42. Yeni PG, Hammer SM, Hirsch MS, et al. Treatment for adult HIV infection: 2004 recommendations of the International AIDS Society-USA Panel. *JAMA* 2004;292:251-65.
 43. The AVANTI Steering Committee. Analysis of HIV-1 clinical trials: statistical magic? *Lancet* 1999;353:2061-4.
 44. Erb P, Battegay M, Zimmerli W, Rickenbach M, Egger M. Effect of antiretroviral therapy on viral load, CD4 cell count, and progression to acquired immunodeficiency syndrome in a community human immunodeficiency virus-infected cohort: Swiss HIV Cohort Study. *Arch Intern Med* 2000;160:1134-40.
 45. Mocroft A, Gill MJ, Davidson W, Phillips AN. Predictors of a viral response and subsequent virological treatment failure in patients with HIV starting a protease inhibitor. *AIDS* 1998;12:2161-7.
 46. Rhone SA, Hogg RS, Yip B, et al. The antiviral effect of zidovudine and zalcitabine in combination amongst HIV-infected adults: results from a community-based study. *AIDS* 1998;12:619-24.
 47. Cohen Stuart JW, Schuurman R, Burger DM, et al. Randomized trial comparing zalcitabine soft gelatin capsules versus zidovudine as part of triple therapy (CHEESE study). *AIDS* 1999;13:F53-F58.
 48. Hammer SM, Squires KE, Hughes MD, et al. A controlled trial of two nucleoside analogues plus zidovudine in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. *N Engl J Med* 1997;337:725-33.
 49. Maher K, Klimas N, Fletcher MA, et al. Disease progression, adherence, and response to protease inhibitor therapy for HIV infection in an urban Veterans Affairs medical center. *J Acquir Immune Defic Syndr* 1999;22:358-63.
 50. Drusano GL, Stein DS. Mathematical modeling of the interrelationship of CD4

- lymphocyte count and viral load changes induced by the protease inhibitor indinavir. *Antimicrob Agents Chemother* 1998;42:358-61.
51. Keita-Perse O, Roger PM, Pradier C, Pugliese P, Cottalorda J, Dellamonica P. Do viral load and CD8 cell count at initiation of tritherapy influence the increase of CD4 T-cell count? *AIDS* 1998;12:F175-F179.
52. Mellors JW, Munoz A, Giorgi JV, et al. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. *Ann Intern Med* 1997;126:946-54.
53. Cook J, Dasbach E, Coplan P, et al. Modeling the long-term outcomes and costs of HIV antiretroviral therapy using HIV RNA levels: application to a clinical trial. *AIDS Res Hum Retroviruses* 1999;15:499-508.
54. Diagnosis and reporting of HIV and AIDS in states with integrated HIV and AIDS surveillance — United States, January 1994–June 1997. *MMWR Morb Mortal Wkly Rep* 1998;47:309-14.
55. Raboud JM, Montaner JS, Conway B, et al. Suppression of plasma viral load below 20 copies/ml is required to achieve a long-term response to therapy. *AIDS* 1998;12:1619-24.
56. Le Moing V, Chene G, Carrieri MP, et al. Predictors of virological rebound in HIV-1-infected patients initiating a protease inhibitor-containing regimen. *AIDS* 2002;16:21-9.
57. Deeks SG, Hecht FM, Swanson M, et al. HIV RNA and CD4 cell count response to protease inhibitor therapy in an urban AIDS clinic: response to both initial and salvage therapy. *AIDS* 1999;13:F35-F43.
58. Report of the NIH Panel to Define Principles of Therapy of HIV Infection. *MMWR Recomm Rep* 1998;47(RR-5):1-41.
59. de Wolf F, Spijkerman I, Schellekens PT, et al. AIDS prognosis based on HIV-1 RNA, CD4+ T-cell count and function: markers with reciprocal predictive value over time after seroconversion. *AIDS* 1997;11:1799-806.
60. Mellors JW, Kingsley LA, Rinaldo CR Jr, et al. Quantitation of HIV-1 RNA in plasma predicts outcome after seroconversion. *Ann Intern Med* 1995;122:573-9.
61. Ioannidis JP, Cappelleri JC, Lau J, Sacks HS, Skolnik PR. Predictive value of viral load measurements in asymptomatic untreated HIV-1 infection: a mathematical model. *AIDS* 1996;10:255-62.
62. Keet IP, Janssen M, Veugelers PJ, et al. Longitudinal analysis of CD4 T cell counts, T cell reactivity, and human immunodeficiency virus type 1 RNA levels in persons remaining AIDS-free despite CD4 cell counts <200 for >5 years. *J Infect Dis* 1997;176:665-71.
63. O'Brien TR, Rosenberg PS, Yellin F, Goedert JJ. Longitudinal HIV-1 RNA levels in a cohort of homosexual men. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;18:155-61.
64. Spijkerman IJ, Prins M, Goudsmit J, et al. Early and late HIV-1 RNA level and its association with other markers and disease progression in long-term AIDS-free homosexual men. *AIDS* 1997;11:1383-8.
65. Henrard DR, Phillips JF, Muenz LR, et al. Natural history of HIV-1 cell-free viremia. *JAMA* 1995;274:554-8.
66. Sabin CA, Devereux H, Phillips AN, et al. Course of viral load throughout HIV-1 infection. *J Acquir Immune Defic Syndr* 2000;23:172-7.
67. Sabin CA, Devereux H, Phillips AN, Janossy G, Loveday C, Lee CA. Immune markers and viral load after HIV-1 seroconversion as predictors of disease progression in a cohort of haemophilic men. *AIDS* 1998;12:1347-52.
68. Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: risk factors for virologic failure and adverse drug reactions. *Ann Intern Med* 1999;131:81-7.
69. d'Arminio Monforte A, Lepri AC, Rezza G, et al. Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naive patients. *AIDS* 2000;14:499-507.
70. Bonfanti P, Valsecchi L, Parazzini F, et al. Incidence of adverse reactions in HIV patients treated with protease inhibitors: a cohort study. *J Acquir Immune Defic Syndr* 2000;23:236-45.
71. Valdez H, Lederman MM, Woolley I, et al. Human immunodeficiency virus 1 protease inhibitors in clinical practice: predictors of virological outcome. *Arch Intern Med* 1999;159:1771-6.
72. Welch K, Morse A, Clark R, Ogbuokiri T. Factors associated with incomplete virological response to highly active antiretroviral therapy. *Clin Infect Dis* 2000;30:407-8.
73. Vlahov D, Graham N, Hoover D, et al. Prognostic indicators for AIDS and infectious disease death in HIV-infected injection drug users: plasma viral load and CD4+ cell count. *JAMA* 1998;279:35-40.
74. Hughes MD, Johnson VA, Hirsch MS, et al. Monitoring plasma HIV-1 RNA levels in addition to CD4+ lymphocyte count improves assessment of antiretroviral therapeutic response. *Ann Intern Med* 1997;126:929-38.
75. O'Brien WA, Hartigan PM, Daar ES, Simberkoff MS, Hamilton JD. Changes in plasma HIV RNA levels and CD4+ lymphocyte counts predict both response to antiretroviral therapy and therapeutic failure. *Ann Intern Med* 1997;126:939-45.
76. Marschner IC, Collier AC, Coombs RW, et al. Use of changes in plasma levels of human immunodeficiency virus type 1 RNA to assess the clinical benefit of antiretroviral therapy. *J Infect Dis* 1998;177:40-7.
77. Brun-Vezinet F, Boucher C, Loveday C, et al. HIV-1 viral load, phenotype, and resistance in a subset of drug-naive participants from the Delta trial. *Lancet* 1997;350:983-90.
78. Coombs RW, Welles SL, Hooper C, et al. Association of plasma human immunodeficiency virus type 1 RNA level with risk of clinical progression in patients with advanced infection. *J Infect Dis* 1996;174:704-12.
79. Galetto-Lacour A, Yerly S, Perneger TV, Baumberger C, Hirschel B, Perrin L. Prognostic value of viremia in patients with longstanding human immunodeficiency virus infection. *J Infect Dis* 1996;173:1388-93.
80. Katzenstein DA, Hammer SM, Hughes MD, et al. The relation of virologic and immunologic markers to clinical outcomes after nucleoside therapy in HIV-infected adults with 200 to 500 CD4 cells per cubic millimeter. *N Engl J Med* 1996;335:1091-8. [Erratum, *N Engl J Med* 1997;337:1097.]
81. Mellors JW, Rinaldo CR Jr, Gupta P, White RM, Todd JA, Kingsley LA. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma. *Science* 1996;272:1167-70. [Erratum, *Science* 1997;275:14.]
82. Montaner JS, DeMasi R, Hill AM. The effects of lamivudine treatment on HIV-1 disease progression are highly correlated with plasma HIV-1 RNA and CD4 cell count. *AIDS* 1998;12:F23-F28.
83. O'Brien TR, Blattner WA, Waters D, et al. Serum HIV-1 RNA levels and time to development of AIDS in the Multicenter Hemophilia Cohort Study. *JAMA* 1996;276:105-10.
84. O'Brien WA, Hartigan PM, Martin D, et al. Changes in plasma HIV-1 RNA and CD4+ lymphocyte counts and the risk of progression to AIDS. *N Engl J Med* 1996;334:426-31.
85. Pedersen C, Katzenstein T, Nielsen C, Lundgren JD, Gerstoft J. Prognostic value of serum HIV-RNA levels at virologic steady state after seroconversion: relation to CD4 cell count and clinical course of primary infection. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;16:93-9.
86. Phillips AN, Eron JJ, Bartlett JA, et al. HIV-1 RNA levels and the development of clinical disease. *AIDS* 1996;10:859-65.
87. Phillips AN, Eron J, Bartlett J, et al. Correspondence between the effect of zidovudine plus lamivudine on plasma HIV level/CD4 lymphocyte count and the incidence of clinical disease in infected individuals. *AIDS* 1997;11:169-75.
88. Welles SL, Jackson JB, Yen-Lieberman B, et al. Prognostic value of plasma human immunodeficiency virus type 1 (HIV-1) RNA levels in patients with advanced HIV-1 disease and with little or no prior zidovudine therapy. *J Infect Dis* 1996;174:696-703.
89. Yerly S, Perneger TV, Hirschel B, et al. A critical assessment of the prognostic value of HIV-1 RNA levels and CD4+ cell counts in HIV-infected patients: the Swiss HIV Cohort Study. *Arch Intern Med* 1998;158:247-52.
90. Chêne G, Binquet C, Moreau JF, et al. Changes in CD4+ cell count and the risk of opportunistic infection or death after highly active antiretroviral treatment. *AIDS* 1998;12:2313-20.

91. Loveday C, Hill A. Prediction of progression to AIDS with serum HIV-1 RNA and CD4 count. *Lancet* 1995;345:790-1.
92. Butcher D, Greene J, Duong P, Markson L. Virologic response associated with a change in protease inhibitor therapy. *Arch Intern Med* 2000;160:394-5.
93. Guardiola JM, Domingo P, Vazquez G. Switching HIV-1 protease inhibitor therapy: which? When? And why? *Arch Intern Med* 1999;159:194-5.
94. Casado JL, Perez-Elias MJ, Antela A, et al. Predictors of long-term response to protease inhibitor therapy in a cohort of HIV-infected patients. *AIDS* 1998;12:F131-F135.
95. d'Arminio Monforte A, Testa L, Adorni F, et al. Clinical outcome and predictive factors of failure of highly active antiretroviral therapy in antiretroviral-experienced patients in advanced stages of HIV-1 infection. *AIDS* 1998;12:1631-7.
96. Kirk O, Katzenstein TL, Gerstoft J, et al. Combination therapy containing ritonavir plus saquinavir has superior short-term antiretroviral efficacy: a randomized trial. *AIDS* 1999;13:F9-F16.
97. Roca B, Gomez CJ, Arnedo A. A randomized, comparative study of lamivudine plus stavudine, with indinavir or nelfinavir, in treatment-experienced HIV-infected patients. *AIDS* 2000;14:157-61.
98. Roca B, Gomez CJ, Arnedo A. Stavudine, lamivudine and indinavir in drug abusing and non-drug abusing HIV-infected patients: adherence, side effects and efficacy. *J Infect* 1999;39:141-5.
99. van Roon EN, Verzijl JM, Juttman JR, Lenderink AW, Blans MJ, Egberts AC. Incidence of discontinuation of highly active antiretroviral combination therapy (HAART) and its determinants. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999;20:290-4.
100. Paredes R, Puig T, Arno A, et al. High-dose saquinavir plus ritonavir: long-term efficacy in HIV-positive protease inhibitor-experienced patients and predictors of virologic response. *J Acquir Immune Defic Syndr* 1999;22:132-8.
101. Kaufmann GR, Duncombe C, Cunningham P, et al. Treatment response and durability of a double protease inhibitor therapy with saquinavir and ritonavir in an observational cohort of HIV-1-infected individuals. *AIDS* 1998;12:1625-30.
102. Hogg RS, Rhone SA, Yip B, et al. Antiviral effect of double and triple drug combinations amongst HIV-infected adults: lessons from the implementation of viral load-driven antiretroviral therapy. *AIDS* 1998;12:279-84.
103. Fätkenheuer G, Theisen A, Rockstroh J, et al. Virological treatment failure of protease inhibitor therapy in an unselected cohort of HIV-infected patients. *AIDS* 1997;11:F113-F116.
104. Montaner JS, Reiss P, Cooper D, et al. A randomized, double-blind trial comparing combinations of nevirapine, didanosine, and zidovudine for HIV-infected patients: the INCAS Trial: Italy, the Netherlands, Canada and Australia Study. *JAMA* 1998;279:930-7.
105. Zolopa AR, Shafer RW, Warford A, et al. HIV-1 genotypic resistance patterns predict response to saquinavir-ritonavir therapy in patients in whom previous protease inhibitor therapy had failed. *Ann Intern Med* 1999;131:813-21.
106. Shulman NS, Zolopa AR, Passaro DJ, et al. Efavirenz- and adefovir dipivoxil-based salvage therapy in highly treatment-experienced patients: clinical and genotypic predictors of virologic response. *J Acquir Immune Defic Syndr* 2000;23:221-6.
107. Durant J, Clevenbergh P, Halfon P, et al. Drug-resistance genotyping in HIV-1 therapy: the VIRADAPT randomised controlled trial. *Lancet* 1999;353:2195-9. [Erratum, *Lancet* 1999;354:1128.]
108. Cohen C, Hunt S, Sension M, et al. Phenotypic resistance testing significantly improves response to therapy (Tx): a randomized trial (VIRA 3001). In: Proceedings of the 7th Conference on Retroviruses and Opportunistic Infections, San Francisco, January 30–February 2, 2000. abstract.
109. Baxter JD, Mayers DL, Wentworth DN, et al. A randomized study of antiretroviral management based on plasma genotypic antiretroviral resistance testing in patients failing therapy. *AIDS* 2000;14:F83-F93.
110. Carpenter CC, Cooper DA, Fischl MA, et al. Antiretroviral therapy in adults: updated recommendations of the International AIDS Society-USA Panel. *JAMA* 2000;283:381-90.
111. Bernasconi E, Magenta L, Piffaretti JC, Carota A, Moccetti T. Are nelfinavir-containing regimens effective as second-line triple therapy? *AIDS* 2000;14:95-6.
112. Bonfanti P, Capetti A, Di Mattei P, Niero F, Rizzardini G. Virological treatment failure of highly active antiretroviral therapy in an unselected cohort of HIV-infected patients. *AIDS* 1998;12:1111.
113. Gulick RM, Mellors JW, Havlir D, et al. Treatment with indinavir, zidovudine, and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral therapy. *N Engl J Med* 1997;337:734-9.
114. Gulick RM, Mellors JW, Havlir D, et al. Simultaneous vs sequential initiation of therapy with indinavir, zidovudine, and lamivudine for HIV-1 infection: 100-week follow-up. *JAMA* 1998;280:35-41.
115. Ledergerber B, Egger M, Opravil M, et al. Clinical progression and virological failure on highly active antiretroviral therapy in HIV-1 patients: a prospective cohort study: Swiss HIV Cohort Study. *Lancet* 1999;353:863-8.
116. Moyle G, Pozniak A, Opravil M, et al. The SPICE study: 48-week activity of combinations of saquinavir soft gelatin and nelfinavir with and without nucleoside analogues: Study of Protease Inhibitor Combinations in Europe. *J Acquir Immune Defic Syndr* 2000;23:128-37.
117. Notermans DW, Jurriaans S, de Wolf F, et al. Decrease of HIV-1 RNA levels in lymphoid tissue and peripheral blood during treatment with ritonavir, lamivudine and zidovudine. *AIDS* 1998;12:167-73.
118. Paris D, Ledergerber B, Weber R, et al. Incidence and predictors of virologic failure of antiretroviral triple-drug therapy in a community-based cohort. *AIDS Res Hum Retroviruses* 1999;15:1631-8.
119. Powderly WG, Saag MS, Chapman S, Yu G, Quart B, Clendeninn NJ. Predictors of optimal virological response to potent antiretroviral therapy. *AIDS* 1999;13:1873-80.
120. Salzberger B, Rockstroh J, Wieland U, et al. Clinical efficacy of protease inhibitor based antiretroviral combination therapy—a prospective cohort study. *Eur J Med Res* 1999;4:449-55.
121. Staszewski S, Morales-Ramirez J, Tashima KT, et al. Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults. *N Engl J Med* 1999;341:1865-73.
122. Cameron DW, Japour AJ, Xu Y, et al. Ritonavir and saquinavir combination therapy for the treatment of HIV infection. *AIDS* 1999;13:213-24.
123. Clough LA, D'Agata E, Raffanti S, Haas DW. Factors that predict incomplete virological response to protease inhibitor-based antiretroviral therapy. *Clin Infect Dis* 1999;29:75-81.
124. De Wit S, Cassano P, Hermans P, et al. Salvage therapy with ritonavir-saquinavir plus two nucleoside reverse transcriptase inhibitors in patients failing with amprenavir-zidovudine-lamivudine. *AIDS* 1999;13:864-5.
125. Paredes R, Mocroft A, Kirk O, et al. Predictors of virological success and ensuing failure in HIV-positive patients starting highly active antiretroviral therapy in Europe: results from the EuroSIDA study. *Arch Intern Med* 2000;160:1123-32.
126. Kaufmann D, Pantaleo G, Sudre P, Telet A. CD4-cell count in HIV-1-infected individuals remaining viraemic with highly active antiretroviral therapy (HAART): Swiss HIV Cohort Study. *Lancet* 1998;351:723-4.
127. Bellman PC. Clinical experience with adding delavirdine to combination therapy in patients in whom multiple antiretroviral treatment including protease inhibitors has failed. *AIDS* 1998;12:1333-40.
128. Hall CS, Raines CP, Barnett SH, Moore RD, Gallant JE. Efficacy of salvage therapy containing ritonavir and saquinavir after failure of single protease inhibitor-containing regimens. *AIDS* 1999;13:1207-12.
129. Pialoux G, Raffi F, Brun-Vezinet F, et al. A randomized trial of three maintenance regimens given after three months of induction therapy with zidovudine, lamivudine,

- and indinavir in previously untreated HIV-1-infected patients. *N Engl J Med* 1998;339:1269-76.
130. Havlir DV, Marschner IC, Hirsch MS, et al. Maintenance antiretroviral therapies in HIV-infected subjects with undetectable plasma HIV RNA after triple-drug therapy. *N Engl J Med* 1998;339:1261-8.
131. Gulick RM, Mellors JW, Havlir D, et al. 3-Year suppression of HIV viremia with indinavir, zidovudine, and lamivudine. *Ann Intern Med* 2000;133:35-9.
132. Raboud JM, Rae S, Vella S, et al. Meta-analysis of two randomized controlled trials comparing combined zidovudine and didanosine therapy with combined zidovudine, didanosine, and nevirapine therapy in patients with HIV. *J Acquir Immune Defic Syndr* 1999;22:260-6.
133. Staszewski S, Miller V, Sabin C, Berger A, Hill AM, Phillips AN. Rebound of HIV-1 viral load after suppression to very low levels. *AIDS* 1998;12:2360.
134. D'Amato RM, D'Aquila RT, Wein LM. Management of antiretroviral therapy for HIV infection: modelling when to change therapy. *Antivir Ther* 1998;3:147-58.
135. Kempf DJ, Rode RA, Xu Y, et al. The duration of viral suppression during protease inhibitor therapy for HIV-1 infection is predicted by plasma HIV-1 RNA at the nadir. *AIDS* 1998;12:F9-F14.
136. Tebas P, Patick AK, Kane EM, et al. Virologic responses to a ritonavir-saquinavir-containing regimen in patients who had previously failed nelfinavir. *AIDS* 1999;13:F23-F28.
137. Cameron DW, Heath-Chiozzi M, Daner S, et al. Randomised placebo-controlled trial of ritonavir in advanced HIV-1 disease. *Lancet* 1998;351:543-9.
138. Sullivan AK, Nelson MR, Moyle GJ, Newell AM, Feher MD, Gazzard BG. Coronary artery disease occurring with protease inhibitor therapy. *Int J STD AIDS* 1998;9:711-2.
139. Saffin S, Grunfeld C. Fat distribution and metabolic changes in patients with HIV infection. *AIDS* 1999;13:2493-505.
140. Reijers MHE, Weigel HM, Hart AAM, et al. Toxicity and drug exposure in a quadruple drug regimen in HIV-1 infected patients participating in the ADAM study. *AIDS* 2000;14:59-67.
141. Michael RT, Wadsworth J, Feinleib J, Johnson AM, Laumann EO, Wellings K. Private sexual behavior, public opinion, and public health policy related to sexually transmitted diseases: a US-British comparison. *Am J Public Health* 1998;88:749-54.
142. Laumann EO. The social organization of sexuality: sexual practices in the United States. Chicago: University of Chicago Press, 1994.
143. Samuel MC, Hessol N, Shiboski S, Engel RR, Speed TP, Winkelstein W Jr. Factors associated with human immunodeficiency virus seroconversion in homosexual men in three San Francisco cohort studies, 1984-1989. *J Acquir Immune Defic Syndr* 1993;6:303-12.
144. Keet IP, Albrecht van Lent N, Sandfort TG, Coutinho RA, van Griensven GJ. Oro-genital sex and the transmission of HIV among homosexual men. *AIDS* 1992;6:223-6.
145. Caceres CF, van Griensven GJ. Male homosexual transmission of HIV-1. *AIDS* 1994;8:1051-61.
146. Buchbinder SP, Douglas JM Jr, McKirnan DJ, Judson FN, Katz MH, MacQueen KM. Feasibility of human immunodeficiency virus vaccine trials in homosexual men in the United States: risk behavior, seroincidence, and willingness to participate. *J Infect Dis* 1996;174:954-61.
147. Deschamps MM, Pape JW, Hafner A, Johnson WD Jr. Heterosexual transmission of HIV in Haiti. *Ann Intern Med* 1996;125:324-30.
148. de Vincenzi I. A longitudinal study of human immunodeficiency virus transmission by heterosexual partners. *N Engl J Med* 1994;331:341-6.
149. 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.
150. Operskalski EA, Stram DO, Busch MP, et al. Role of viral load in heterosexual transmission of human immunodeficiency virus type 1 by blood transfusion recipients. *Am J Epidemiol* 1997;146:655-61.
151. Musico M, Lazzarin A, Nicolosi A, et al. Antiretroviral treatment of men infected with human immunodeficiency virus type 1 reduces the incidence of heterosexual transmission. *Arch Intern Med* 1994;154:1971-6.
152. Freedberg KA, Losina E, Weinstein MC, et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med* 2001;344:824-31.
153. Bozzette SA, Joyce G, McCaffrey DF, et al. Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. *N Engl J Med* 2001;344:817-23.
154. Drugs for HIV infection. *Med Lett Drugs Ther* 2000;42:1-6.
155. HIV/AIDS drugs: funding implications of new combination therapies for federal and state programs. Washington, D.C.: General Accounting Office, October 1998. (GAO/HEHS-99-2.)
156. Mole L, Ockrim K, Holodniy M. Decreased medical expenditures for care of HIV-seropositive patients: the impact of highly active antiretroviral therapy at a US Veterans Affairs Medical Center. *Pharmacoeconomics* 1999;16:307-15.
157. Keiser P, Kvanli MB, Turner D, et al. Protease inhibitor-based therapy is associated with decreased HIV-related health care costs in men treated at a Veterans Administration hospital. *J Acquir Immune Defic Syndr Hum Retrovirology* 1999;20:28-33.
158. Gable CB, Tierce JC, Simison D, Ward D, Motte K. Costs of HIV+/AIDS at CD4+ counts disease stages based on treatment protocols. *J Acquir Immune Defic Syndr Hum Retrovirology* 1996;12:413-20.
159. Fryback DG, Dasbach EJ, Klein R, et al. The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. *Med Decis Making* 1993;13:89-102.
160. Honiden S, Nease RF, Sundaram V, Holodniy M, Owens DK. The effect of diagnosis with HIV infection on quality of life. *Med Decis Making* 2002;22:560. abstract.
161. Tsevat J, Solzan JG, Kuntz KM, et al. Health values of patients infected with human immunodeficiency virus: relationship to mental health and physical functioning. *Med Care* 1996;34:44-57.
162. Tsevat J, Sherman SN, McElwee JA, et al. The will to live among HIV-infected patients. *Ann Intern Med* 1999;131:194-8.
163. Revicki DA, Wu AW, Murray MI. Change in clinical status, health status, and health utility outcomes in HIV-infected patients. *Med Care* 1995;33:Suppl 4:AS173-AS182.
164. Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. *Med Decis Making* 2002;22:475-81.
165. Bayoumi AM, Redelmeier DA. Preventing *Mycobacterium avium* complex in patients who are using protease inhibitors: a cost-effectiveness analysis. *AIDS* 1998;12:1503-12.
166. Budget of the United States government, section 10 — gross domestic product and implicit outlay deflators. 2004. (Accessed January 18, 2005, at <http://www.gpoaccess.gov/usbudget/fy05/hist.html>.)
167. Mankiw NG. Principles of economics. 2nd ed. Fort Worth, Tex.: Harcourt College, 2001.
168. Stone PW, Teutsch S, Chapman RH, Bell C, Goldie SJ, Neumann PJ. Cost-utility analyses of clinical preventive services: published ratios, 1976-1997. *Am J Prev Med* 2000;19:15-23.
169. Opravil M, Ledergerber B, Furrer H, et al. Clinical efficacy of early initiation of HAART in patients with asymptomatic HIV infection and CD4 cell count > 350 × 10⁶/l. *AIDS* 2002;16:1371-81.
170. Cozzi Lepri A, Phillips AN, d'Arminio Monforte A, et al. When to start highly active antiretroviral therapy in chronically HIV-infected patients: evidence from the ICONA study. *AIDS* 2001;15:983-90.
171. Ahdieh-Grant L, Yamashita TE, Phair JP, et al. When to initiate highly active antiretroviral therapy: a cohort approach. *Am J Epidemiol* 2003;157:738-46.
172. Hogg RS, Yip B, Chan KJ, et al. Rates of disease progression by baseline CD4 cell count and viral load after initiating triple-drug therapy. *JAMA* 2001;286:2568-77.
173. Anastos K, Barron Y, Miotti P, et al. Risk of progression to AIDS and death in women infected with HIV-1 initiating highly active antiretroviral treatment at different stages of disease. *Arch Intern Med* 2002;162:1973-80.

174. Phillips AN, Lepri AC, Lampe F, Johnson M, Sabin CA. When should antiretroviral therapy be started for HIV infection? Interpreting the evidence from observational studies. *AIDS* 2003;17:1863-9.
175. Palella FJ Jr, Deloria-Knoll M, Chmiel JS, et al. Survival benefit of initiating antiretroviral therapy in HIV-infected persons in different CD4+ cell strata. *Ann Intern Med* 2003;138:620-6.
176. Ferrer E, Santamarina E, Santin M, et al. Progression to AIDS/death is higher in patients initiating antiretroviral therapy with CD4 counts below 350 cells/ μ L. In: *Proceedings of the 10th Conference on Retroviruses and Opportunistic Infections*, Boston, February 10-14, 2003:910. abstract.
177. A comparison of two ways to manage anti-HIV treatment (the SMART Study). 2004. (Accessed January 18, 2005, at <http://www.clinicaltrials.gov/ct/show/nct00027352>.)
178. Owens DK, Sundaram V, Lazzeroni LC, et al. HIV testing appropriateness and predictors of HIV infection in Department of Veterans Affairs health care systems. *Med Decis Making* 2002;22:534. abstract.
179. Owens DK, Sundaram V, Douglass L, et al. Seroprevalence of HIV infection at VA health care systems. *Med Decis Making* 2003;23:569. abstract.

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