HEALTH POLICY

Projected Survival Gains from Revising State Laws Requiring Written Opt-in Consent for HIV Testing

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BACKGROUND: Although the Centers for Disease Control and Prevention recommends HIV testing in all settings unless patients refuse (opt-out consent), many state laws require written opt-in consent.

OBJECTIVE: To quantify potential survival gains from passing state laws streamlining HIV testing consent.

DESIGN: We retrieved surveillance data to estimate the current annual HIV diagnosis rate in states with laws requiring written opt-in consent (19.3%). Published data informed the effect of removing that requirement on diagnosis rate (48.5% increase). These parameters then served as input for a model-driven projection of survival based on consent method. Other inputs included undiagnosed HIV prevalence (0.101%); and annual HIV incidence (0.023%).

PATIENTS: Hypothetical cohort of adults (>13 years) living in written opt-in states.

MEASUREMENTS: Life years gained (LYG).

RESULTS: In the base-case, of the 53,036,383 adult persons living in written opt-in states, 0.66% (350,040) will be infected with HIV. Due to earlier diagnosis, revised consent laws yield 1.5 LYG per HIV-infected person, corresponding to 537,399 LYG among this population. Sensitivity analyses demonstrate that diagnosis rate increases of 24.8–72.3% result in 304,765–724,195 LYG. Net survival gains vanish if the proportion of HIV-infected persons refusing all testing in response to revised laws exceeds 18.2%.

CONCLUSIONS: The potential survival gains of increased testing are substantial, suggesting that state laws requiring opt-in HIV testing should be revised.

KEY WORDS: HIV; AIDS; screening; modeling; survival analysis.

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INTRODUCTION

Despite treatment advances,¹ the United States HIV epidemic remains a serious public health dilemma.^{2,3} The Centers for Disease Control and Prevention (CDC) estimates that as of 2006, 1.1 million adults and adolescents were living with HIV, 232,700 (21.0%) of them undiagnosed.⁴ Furthermore, the CDC projects that 56,300 persons became newly infected with HIV during 2006,⁵ many of whom may not seek testing until late-stage infection.⁶

Conventional HIV screening policies have required patients to opt in to testing via stringent written consent procedures exceeding those historically required to screen for other communicable diseases.⁷ Proposals to detect and treat more HIV-infected persons earlier in the course of infection have included streamlining the opt-in consent process by simplifying written consent forms⁸ and accepting verbal consent in lieu of signed forms.^{9,10} In 2006 the CDC recommended an opt-out approach whereby patients in all healthcare settings are tested unless they explicitly decline.¹¹ Observational studies report that each of these streamlined consent strategies yields statistically significant increases in HIV diagnosis rates compared to conventional written opt-in testing.^{8–10,12}

Some states have already changed their HIV testing consent laws in response to the CDC recommendations; however, laws in many states still require conventional opt-in consent.^{13,14} One potential consequence of these written opt-in consent laws is less frequent testing resulting in delays in diagnosis until more advanced immunosuppression. Such delays may be associated with decreased survival for HIV-infected persons due to later initiation of antiretroviral treatment (ART).¹⁵ Our objective was to project the survival gain of revising these state laws, given alternative assumptions regarding the impact of consent laws on rates of HIV diagnosis and linkage to care.

METHODS

Analytic Overview

As of release of the CDC recommendations in September 2006, 21 states required written opt-in consent for HIV testing: AL, AZ, CA, CT, HI, IA, IL, IN, LA, MA, MD, MI, ME, NC, NE, NH, NM, NY, PA, RI, WI.^{13,14} We updated a review of HIV testing state statutes¹⁴ identifying nine states whose laws still required written opt-in consent as of August 2009: AL, HI, MA,

MI, NE, NY, PA, RI, WI.¹³ We then used state testing data from 2006 to estimate current HIV diagnosis rates in these nine states. Numbers of new HIV diagnoses made in each state during 2006 (diagnosis rate numerators) were estimated by accessing state surveillance reports (Table A1, Technical Appendix—available online). Numbers of undiagnosed HIV cases living in each state during 2006 (diagnosis rate denominators) were estimated using CDC reports of the cumulative numbers of persons with diagnosed HIV infection living in each state² and assuming that 21.0%⁴ of HIV cases in each state are undiagnosed. An aggregate diagnosis rate was then calculated for the nine states requiring written opt-in consent (19.3%).

To estimate the effect of changes in consent laws on this diagnosis rate, we used data published by the San Francisco Department of Public Health. When written opt-in consent for HIV testing was required, 20.6 positive tests were recorded per 1,000 patient-visits; after removing this requirement by permitting verbal consent, the positive rate rose to 30.6 per 1,000 patient-visits.¹⁰ Assuming that each of these positive HIV tests represents a new HIV diagnosis, these data allowed us to estimate the diagnosis rate increase associated with removing laws requiring written opt-in consent for HIV testing: 48.5% [(30.6–20.6)/20.6]. The 95% confidence interval for the positive HIV test rate after removing the requirement for written opt-in consent was 25.7 to 35.5/1,000 patient-visits. Thus, our sensitivity analyses examined diagnosis rate increases ranging from 24.8% [(25.7–20.6)/20.6] to 72.3% [(35.5–20.6)/20.6].

These diagnosis rate estimates served as inputs for the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) Disease^{1,16,17} and Screening Models.^{18–20} Model outputs projected the effects of revised consent laws on population survival for those states that still require written opt-in consent. Model outcomes of interest included mean survival time per HIV-infected person and proportion of the general population ever infected with HIV. Mean survival times were compared between scenarios of the baseline diagnosis rate (19.3%) vs. higher diagnosis rates reflecting the literature-based estimates of the effects of revised consent laws on testing uptake. These comparisons generated estimated survival gains per HIV-infected person associated with revised laws. Total population survival gains associated with revised consent laws were estimated by multiplying the per capita gains by the model-generated proportion of the population ever infected with HIV and the projected sizes of the populations (≥ 13 years) living in states requiring written opt-in consent, excluding persons already diagnosed with HIV (53,036,383) in 2010.²¹ We further approximated survival gains already achieved by the 12 states which have already removed requirements for written opt-in consent since release of the CDC guidelines in September 2006 (AZ, CA, CT, IA, IL, IN, LA, MD, ME, NC, NH, NM).^{13,14} To this end, we multiplied the same per capita survival gain generated in the base-case analysis by the 2010 population size of these states (77,922,909).²¹

Disease Model Overview

The CEPAC Disease Model is a state-transition simulation of HIV disease, details of which have been previously published.¹ The model simulates HIV-infected persons' lifetimes as series of monthly transitions between 'health states,' representing

chronic (asymptomatic) and acute (symptomatic) infection. The model includes a state representing death, the probability of transition to which reflects both the risk of HIV-related mortality for HIV-infected patients and non-AIDS-related death for all individuals. Each acute and chronic health state is stratified by the patient's HIV disease history, CD4 cell count, and HIV RNA. These health states are designed to predict disease progression, affecting probabilities of transition to other states. HIV RNA level drives the rate of CD4 count decline. CD4 count, in turn, determines the monthly probabilities of transition to an acute state (incidence of opportunistic infection) or the death state (HIV-related mortality). The monthly risk of HIV-related mortality is greater for acute states (opportunistic infection) than for chronic states (wasting).²² The monthly risk of non-AIDS-related death for all individuals is age-specific and sex-specific.²³ The model simulates millions of patients' lifetimes to achieve statistical convergence.

Monthly probabilities of transition between health states are affected by treatment. Opportunistic infection prophylaxis reduces the CD4-dependent risk of acute disease. ART reduces HIV RNA with a concomitant increase in CD4 count, and a resultant decrease in the probabilities of HIV-related death and opportunistic infection. Patients experiencing ART failure (two successive HIV RNA levels indicative of virological rebound) transition to successive lines of treatment (up to 6).¹

Screening Model Overview

Whereas the Disease Model simulates disease progression in HIV-infected persons only, the Screening Model simulates HIV infection and case detection in populations including infected and uninfected individuals.¹⁸ The Screening Model regulates entry into the Disease Model, defining population epidemic characteristics which determine whether and when population members become infected with HIV (undiagnosed prevalence, incidence). In conjunction with the Disease Model, the Screening Model also determines whether and when HIV-infected patients are identified and linked to care, both prerequisites for treatment; HIV diagnosis and linkage to care may occur via either a screening program or presentation with opportunistic infection (diagnostic testing).

Input Data (Table 1)

In addition to baseline diagnosis rates, other Screening Model inputs included 0.101% undiagnosed HIV prevalence in written opt-in states, as determined using the estimates of numbers of unidentified HIV-infected persons derived from CDC data.^{2,4} We assumed 0.023% annual incidence based on CDC calculations.⁵ Published data provided estimates of HIV test sensitivity (99.6%) and specificity (97.5%) and the linkage-to-care probability for newly-diagnosed HIV-infected persons (75.0%).¹⁸

The monthly probabilities of transition between health states in the Disease Model reflect data from cohort studies and randomized clinical trials. Data describing the natural history of untreated HIV (CD4 count decline, incidence of opportunistic infection, and HIV-related mortality) and distributions of CD4 counts and HIV RNA in the HIV-infected population are derived from the Multicenter AIDS Cohort

Table 1. Model Parameter Inputs

Parameter	Base-case	Range	Sources
Epidemic characteristics*			
Undx'd prevalence (written opt-in states)	0.101%	0.096–0.106%	2,44
Annual HIV incidence (all states)	0.023%	0.020–0.026%	5
HIV testing			
Written opt-in baseline diagnosis rate	19.3%	9.6–38.5%	Table A1
Diagnosis rate increase	48.5%	24.8–72.3%	10
Linkage-to-care rate	75.0%	50–100%	18
HIV test characteristics			
Sensitivity	99.6%†	95–100%	18
Specificity	97.5%‡	95–100%	18
Baseline HIV-infected population			
Mean CD4 cells/mm ³ (SD)			22,24
Acute HIV infection	534 (164)	400–600	
Chronic HIV infection, asymptomatic	280 (100)	200–400	
Chronic HIV infection, symptomatic	100 (50)	0–200	
Baseline HIV RNA (% of cohort)			22
≤ 500 copies/ml	8%	0–100%	
501–3,000 copies/ml	16%	0–100%	
3,001–10,000 copies/ml	25%	0–100%	
10,001–30,000 copies/ml	25%	0–100%	
>30,000	26%	0–100%	
Antiretroviral treatment efficacy			
Probability of viral suppression at 48 wks (mean rise in CD4 cells/mm ³ at 48 wks)			
1st line (EFV + TDF + FTC)	80.8% (190)	64.5–100%	27,33
2nd line (ATV/r + TDF + FTC)	70.0% (110)	55.0–91.6%	29,30
3rd line (LPV/r + TDF + FTC + AZT)	58.0% (121)	46.0–76.6%	29,30
4th line (RAL + OBR)	64.5%§ (102)§	48.4–80.6%	31
5th line (ENF + OBR)	40.0%§ (121)	30.0–50.0%	32
6th line (OBR)	15.0%§ (45)	11.3–18.8%	32

Abbreviations: ATV/r—atazanavir sulfate with ritonavir; AZT—zidovudine; EFV—efavirenz; FTC—emtricitabine; LPV/r—lopinavir with ritonavir; OBR—optimized background regimen as chosen with the aid of genotypic and phenotypic HIV resistance testing; RAL—raltegravir; SD—standard deviation; ENF—enfuvirtide; TDF—tenofovir disoproxil fumarate

* Estimates derived from national data sources; prevalence values were validated using the opt-in state prevalence estimates calculated in Table 2

† Value is for patient post-seroconversion; pre-seroconversion sensitivity parameter set to 2.5%¹⁸

‡ Pre- and post-seroconversion specificities assumed to be equivalent¹⁸

§ Data are for probability of viral suppression at 24 weeks

Study²² and the literature.²⁴ Patient care is assumed to conform to national guidelines: quarterly CD4 and HIV RNA measurements²⁵ to dictate initiation, termination, or switching of opportunistic infection prophylaxis²⁶ and ART regimens.²⁵ The effects of these treatments on patients' monthly transition probabilities reflect data on the efficacy (Table 1) of ART^{27–33} and OI prophylaxes.^{34–40}

Additional Sensitivity Analyses

First, to evaluate concerns that a switch to opt-out testing might discourage people from accessing healthcare, we examined the survival effects of scenarios in which the diagnosis rate among HIV-infected persons in written opt-in states decreased by 25%, 50%, 75%, and 100% in response to a transition to verbal consent. Second, we varied the baseline diagnosis rate estimate for written opt-in states from half (9.6%) to double (38.5%) the 19.3% base-case value. Third, we considered scenarios of high and low combined undiagnosed prevalence and incidence with input ranges based on the confidence intervals of CDC estimates of national prevalence ($\pm 4.5\%$ of baseline undiagnosed prevalence)⁴ and incidence ($\pm 14.5\%$ of baseline incidence).⁵ Additional sensitivity analyses examined the impact of varying other major Disease and Screening Model parameter inputs from 50–200% of base-case

values, including ART efficacy, opportunistic infection incidence rates, and cohort viral load distribution.

RESULTS

Survival Gains Associated with Consent Law

In the base-case scenario, a 48.5% diagnosis rate increase in written opt-in states from 19.3% to 28.7% results in improved patient outcomes (Table 2). Mean CD4 count at detection increases from 315 cells/mm³ to 357 cells/mm³ after consent law revision. These improved clinical outcomes correspond to a survival gain of 0.1 months (0.01 years) per member of the general population and 18.4 months (1.5 years) per HIV-infected person. The model-projected proportion of individuals who will become infected prior to death is 0.66% in written opt-in states. Based on US Census Bureau state population size estimates and CDC data on the numbers of persons already diagnosed with HIV, the estimated sizes of the population residing in these states during 2010 is 53,036,383.²¹ Thus, the base-case total survival gain associated with passage of revised HIV consent laws is (53,036,383 * 0.66% * 1.5 years) 537,399 life years gained (LYG). The projected survival gains achieved by the 12 states which have already removed the requirement for written opt-in consent since release of the

Table 2. Model Projected Clinical Outcomes for the Population Residing in Written Opt-in States Following Passage of Revised Consent Laws

Outcomes	Scenario	
	Baseline*	Revised Consent Laws
General population		
Mean survival time (mo.)	515.8	515.9
Survival gain (mo.)	–	0.1
HIV-infected persons		
CD4 count at diagnosis (cells/mm ³)	315	357
OIs (/1,000)	1,302	1,254
Mean survival time (mo.)	357	376
Survival gain (mo.)†	–	18.4

OI: opportunistic infection

* Column represents current HIV testing practice

† Reported values are differentials compared to current HIV testing practice (no diagnosis rate increase)

CDC HIV testing recommendations is (77,922,909 * 0.66% * 1.5 years) 789,565 LYG.

These total survival gains due to new consent laws are affected by the diagnosis rate increase associated with those laws. A diagnosis rate increase of 24.8% results in a survival gain of 304,765 LYG for states currently requiring written opt-in consent and 447,772 LYG already achieved by previously written opt-in consent states. A diagnosis rate increase of 72.3% corresponds to a survival gain of 724,195 LYG for states currently requiring written opt-in consent and approximately 1,064,012 LYG already achieved by previously written opt-in consent states.

Potential Impact of Healthcare Avoidance

Regarding scenarios in which HIV-infected persons living in written opt-in states avoid HIV testing in response to laws relaxing consent requirements, 18.2% of HIV-infected persons must cease all testing to offset survival gains (solid arrow, Fig. 1). Alternatively, 37.3% of the HIV-infected population must receive testing half as often as they do with written opt-in consent to negate survival gains (hollow arrow, Fig. 1).

Variations in Baseline Diagnosis Rate

The estimated baseline diagnosis rate in written opt-in states also affects survival gain projections (Fig. 2a). Survival gains are stable when the current diagnosis rate is reduced by half from 19.3% to 9.6% (triangles, Fig. 2a): a 48.5% diagnosis rate increase with the low baseline diagnosis rate results in a total survival gain of 491,503 LYG (solid arrow, Fig. 2a). However, a 48.5% diagnosis rate increase when the current diagnosis rate is doubled from 19.3% to 38.5% results in a total survival gain of 377,568 LYG (hollow arrow, Fig. 2a).

Variations in Baseline HIV Incidence/Prevalence

Projected survival gains also rely upon the undiagnosed HIV prevalence and incidence of the population living in written

opt-in states (Fig. 2b). In a scenario of high undiagnosed prevalence (0.106%) and incidence (0.026%), a 48.5% diagnosis rate increase yields 612,213 LYG (solid arrow, Fig. 2b). In a scenario of low undiagnosed prevalence (0.096%) and incidence (0.020%), the same diagnosis rate increase yields 454,187 LYG (hollow arrow, Fig. 2b).

Other Sensitivity Analyses

Plausible variation in other major Disease and Screening Model input parameters generally did not result in material or informative changes in outcomes. Study results remained largely unchanged although to the extent that simulated care was less effective (e.g., poor ART efficacy or availability), survival gains decreased.

DISCUSSION

This analysis projects a survival gain exceeding half a million LYG associated with a 48.5% increase in HIV diagnosis rate which may be achieved by revising consent laws in nine states requiring written opt-in consent. Based on this same diagnosis rate increase, we further estimate a survival gain of 789,565 LYG achieved by the 12 states which have already removed the requirement for written opt-in consent since release of the CDC recommendations for opt-out HIV testing. These survival gains are sensitive to the diagnosis rate increase associated with revised laws. Varying this parameter according to the confidence interval reported by Zetola et al. (24.8-72.3%)¹⁰ results in survival gains ranging from 304,765 to 724,195 LYG

Figure 1. Impact of nonparticipation on survival gains. Nonparticipation is quantified by the percent decrease in diagnosis rates compared to current (written opt-in) testing practice (horizontal axis) and the proportion of the HIV-infected population exhibiting that decrease (vertical axis). The solid line represents the frontier along which expanded screening yields exactly zero survival gains. The space above and to the right of the frontier represents scenarios in which nonparticipation offsets and reverses the base-case scenario survival gains attributable to revised consent laws, leading to a net survival loss. In contrast, the space below and to the left of the frontier represents scenarios in which nonparticipation is insufficient to offset all survival gains due to expanded screening. To offset survival gains, 18.2% would need to cease all testing (solid arrow) or 37.3% of the HIV-infected population would need to decrease their testing rates half (hollow arrow) in response to revised consent laws.

Figure 2. a. Impact of baseline diagnosis rate on survival gains. Base-case survival gains are similar in scenarios of base-case (diamonds) and half of base-case (triangles) baseline diagnosis rates. Assuming a 48.5% diagnosis rate increase given the low baseline diagnosis rate resulted in a total survival gain of 491,503 LYG (solid arrow); the slightly lower value when compared to the base-case is likely attributable to the smaller magnitude of diagnosis rate increase. Scenarios with the baseline diagnosis rate set to double the base-case value (squares) resulted in survival gains significantly lower than those for base-case scenarios, reflecting a leveling off of survival gains as diagnosis rates rise. Assuming a 48.5% diagnosis rate increase given the high baseline diagnosis rate resulted in a total survival gain of 377,568 LYG (hollow arrow). b. Impact of undiagnosed prevalence and incidence on survival gains. Base-case survival gains assume 0.101% undiagnosed prevalence and 0.023% incidence (diamonds). In scenarios of high undiagnosed prevalence (0.106%) and incidence (0.026%) survival gains are higher (squares), reaching 612,213 LYG assuming a 48.5% diagnosis rate increase (solid arrow). Conversely, in scenarios of low undiagnosed prevalence (0.096%) and incidence (0.020%) survival gains are lower (triangles), reaching 454,187 LYG assuming a 48.5% diagnosis rate increase (hollow arrow).

in states still requiring written opt-in consent and from 447,772 to 1,064,012 LYG in states which have already removed this requirement.

These survival gains compare favorably with those of other accepted health policy initiatives. The survival gain of 0.12 months per member of the general population exceeds that for vaccinating infants against measles, mumps, rubella, or pertussis; vaccinating adults against hepatitis B; or biennial mammography for women >50 years of age.⁴¹ Furthermore, there is an extensive literature suggesting that expansion of HIV testing as simulated by this study would be cost-effective.^{18–20}

Our finding that new consent laws might yield substantial survival gains is robust to broad sensitivity analyses. Notably, nearly one-fifth of HIV-infected persons would need to suspend all contact with the healthcare system in response to new laws to yield a net survival loss. This result speaks to concerns voiced since the early days of the HIV epidemic regarding measures to streamline the testing consent process. Specifically, some have noted that if streamlined consent laws were misinterpreted as an endorsement of involuntary testing, it is possible that diagnosis rates would decrease as infected persons refuse to present to healthcare facilities.⁴² To our

knowledge, there are no data to suggest that any such avoidance would result from streamlining the consent process.

The survival gains projected by our analysis are based on a diagnosis rate increase estimate extrapolated from a San Francisco-based study examining changes in rates of positive HIV test results associated with the transition from written to verbal opt-in HIV testing.¹⁰ While positive test rates are not necessarily equivalent to diagnosis rates, they are likely to be a much closer approximation than are the testing rates otherwise reported in the literature.^{8,12} Nevertheless, there is a paucity of literature informing the effect of consent law on diagnosis rates and the generalizability of the San Francisco results is uncertain. Moreover, a recent study found that New York state increased HIV testing rates by 31.4% by merely simplifying its consent form.⁸ This finding suggests the diagnosis rate change following removal of written opt-in consent will be unique in each state, depending on the extent to which each jurisdiction's consent form poses a testing barrier, yet our study assumes a uniform effect in all states.

While further research might consider the heterogeneity in written opt-in states' consent forms, the absence of such site-specific data now makes it difficult to interpret the implications of the uniform effect assumption for our results. Regardless, our study likely understates the possible survival benefits of consent law revision as the 48.5% base-case diagnosis rate increase value used is that reported for the transition from written opt-in to verbal opt-in consent rather than the more ambitious transition recommended by the CDC¹¹ to opt-out consent. Indeed, data from England indicate that the transition from written opt-in to opt-out consent as recommended by the CDC could yield a testing rate increase of 85.7%.¹² Furthermore, the base-case applies a 48.5% diagnosis rate increase only to states requiring written opt-in consent, ignoring potential survival gains that may be attributed to transitioning to opt-out consent in verbal opt-in states.

This study has several additional limitations. First, the model is not dynamic; consequently, the simulations assumed a constant incidence rate, likely a reasonable assumption over at least the next ten years. Second, the model does not simulate survival gains from preventing secondary transmission due to HIV-infected persons' earlier knowledge of their serostatus, an omission likely to underestimate the survival benefits of revised consent laws. Third, the model does not simulate members of future generations whom may become infected with HIV and so would eventually benefit from law changes facilitating more frequent testing now, another limitation likely to bias our results against revised laws. Finally, the assumption that all monitoring and treatment of HIV-infected persons conforms to national guidelines portrays screening favorably. Our sensitivity analyses confirm that the survival gains of expanded screening depend upon treatment access and efficacy. Expanded screening becomes less attractive to the extent that certain populations receive substandard care.⁴³

Opt-in state HIV testing consent laws exemplify "HIV exceptionalism," a legacy of the early HIV epidemic during which the disease was poorly understood, untreatable, and primarily confined to well-defined risk groups already stigmatized by society.⁴² In that context opt-in testing protected HIV-infected persons from a diagnosis associated with discrimination and little medical benefit. Patient protection and consent remain important today, but now must be balanced against

the dramatic health benefits made possible by ART.¹ The CDC's recommendations offer a pragmatic approach to achieving this balance, aligning the HIV testing process with that used when screening for other treatable communicable diseases. While many states have adjusted their laws accordingly, numerous states still require opt-in consent.¹⁴ For those states whose laws continue to require written opt-in testing, this study highlights the potential value of urgent legislation to remove any requirement for written opt-in consent. Failure to revise these obsolete laws is to risk an opportunity cost which in aggregate may exceed half a million years of human life.

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REFERENCES

1. Walensky RP, Paltiel AD, Losina E, et al. The survival benefits of AIDS treatment in the United States. *J Infect Dis*. 2006;194(1):11–19.
2. CDC. *HIV/AIDS surveillance report, 2006*. Vol 18. Atlanta: Centers for Disease Control and Prevention; 2008. Accessed 5 Jan 2011. Available from <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2006report/pdf/2006SurveillanceReport.pdf>.
3. District of Columbia DOH. *District of Columbia HIV/AIDS epidemiology update, 2008*. Washington, DC: District of Columbia Department of Health; 2009. Accessed 5 Jan 2011. Available from http://doh.dc.gov/doh/lib/doh/pdf/dc_hiv-aids_2008_updatereport.pdf.
4. Campsmith ML, Rhodes PH, Hall HI, Green TA. Undiagnosed HIV prevalence among adults and adolescents in the United States at the end of 2006. *J Acquir Immune Defic Syndr*. 2010;53(5):619–624.
5. Hall HI, Song R, Rhodes P, et al. Estimation of HIV incidence in the United States. *JAMA*. 2008;300(5):520–529.
6. CDC. Persons tested for HIV–United States, 2006. *MMWR Morb Mortal Wkly Rep*. 2008;57(31):845–849.
7. Bayer R, Fairchild AL. Changing the paradigm for HIV testing—the end of exceptionalism. *N Engl J Med*. 2006;355(7):647–649.
8. Wing C. Effects of written informed consent requirements on HIV testing rates: Evidence from a natural experiment. *Am J Public Health*. 2009;99(6):1087–1092.
9. Zetola NM, Grijalva CG, Gertler S, et al. Simplifying consent for HIV testing is associated with an increase in HIV testing and case detection in

- highest risk groups, San Francisco January 2003-June 2007. *PLoS ONE*. 2008;3(7):e2591.
10. **Zetola NM, Klausner JD, Haller B, Nassos P, Katz MH.** Association between rates of HIV testing and elimination of written consents in San Francisco. *JAMA*. 2007;297(10):1061-1062.
11. **Branson BM, Handsfield HH, Lampe MA, et al.** Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep*. 2006;55(RR-14):1-17; quiz CE1-4.
12. **Stanley B, Fraser J, Cox NH.** Uptake of HIV screening in genitourinary medicine after change to "opt-out" consent. *BMJ*. 2003;326(7400):1174.
13. **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(8):945-951.
14. **Mahajan AP, Stemple L, Shapiro MF, King JB, Cunningham WE.** Consistency of state statutes with the centers for disease control and prevention HIV testing recommendations for health care settings. *Ann Intern Med*. 2009;150(4):263-269.
15. When To Start Consortium, Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: A collaborative analysis of 18 HIV cohort studies. *Lancet*. 2009;373(9672):1352-1363
16. **Freedberg KA, Losina E, Weinstein MC, et al.** The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med*. 2001;344(11):824-831.
17. **Freedberg KA, Scharfstein JA, Seage GR 3rd, et al.** The cost-effectiveness of preventing AIDS-related opportunistic infections. *JAMA*. 1998;279(2):130-136.
18. **Paltiel AD, Weinstein MC, Kimmel AD, et al.** Expanded screening for HIV in the United States—an analysis of cost-effectiveness. *N Engl J Med*. 2005;352(6):586-595.
19. **Paltiel AD, Walensky RP, Schackman BR, et al.** Expanded HIV screening in the United States: Effect on clinical outcomes, HIV transmission, and costs. *Ann Intern Med*. 2006;145(11):797-806.
20. **Walensky RP, Weinstein MC, Kimmel AD, et al.** Routine human immunodeficiency virus testing: An economic evaluation of current guidelines. *Am J Med*. 2005;118(3):292-300.
21. CDC WONDER On-line Database. *Population projections, United States, 2004-2030, by state, age and sex*. Atlanta: Centers for Disease Control and Prevention; 2005. Accessed 5 Jan 2011. Available from <http://wonder.cdc.gov/population-projections.html>.
22. **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(12):946-954.
23. **Arias E.** United States life tables, 2003. *Natl Vital Stat Rep*. 2006;54(14):1-40.
24. **Walensky RP, Goldie SJ, Sax PE, et al.** Treatment for primary HIV infection: Projecting outcomes of immediate, interrupted, or delayed therapy. *J Acquir Immune Defic Syndr*. 2002;31(1):27-37.
25. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*. Rockville: Department of Health and Human Services; 2009. Accessed 5 Jan 2011. Available from <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.
26. **Kaplan JE, Benson C, Holmes KH, et al.** Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Recommendations from CDC, the National Institutes of Health, and the HIV medicine association of the Infectious Diseases Society of America. *MMWR Recomm Rep*. 2009;58(RR-4):1-207. quiz CE1-4.
27. **Gallant JE, DeJesus E, Arribas JR, et al.** Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. *N Engl J Med*. 2006;354(3):251-260.
28. **Cole SR, Hernan MA, Robins JM, et al.** Effect of highly active antiretroviral therapy on time to acquired immunodeficiency syndrome or death using marginal structural models. *Am J Epidemiol*. 2003;158(7):687-694.
29. **Johnson M, Grinsztejn B, Rodriguez C, et al.** Atazanavir plus ritonavir or saquinavir, and lopinavir/ritonavir in patients experiencing multiple virological failures. *AIDS*. 2005;19(7):685-694.
30. **Johnson M, Grinsztejn B, Rodriguez C, et al.** 96-week comparison of once-daily Atazanavir/ritonavir and twice-daily Lopinavir/ritonavir in patients with multiple virologic failures. *AIDS*. 2006;20(5):711-718.
31. **Grinsztejn B, Nguyen BY, Katlama C, et al.** Safety and efficacy of the HIV-1 integrase inhibitor raltegravir (MK-0518) in treatment-experienced patients with multidrug-resistant virus: A phase II randomised controlled trial. *Lancet*. 2007;369(9569):1261-1269.
32. **Nelson M, Arasteh K, Clotet B, et al.** Durable efficacy of enfuvirtide over 48 weeks in heavily treatment-experienced HIV-1-infected patients in the T-20 versus optimized background regimen only 1 and 2 clinical trials. *J Acquir Immune Defic Syndr*. 2005;40(4):404-412.
33. **Pozniak AL, Gallant JE, DeJesus E, et al.** Tenofovir disoproxil fumarate, emtricitabine, and efavirenz versus fixed-dose zidovudine/lamivudine and efavirenz in antiretroviral-naïve patients: Virologic, immunologic, and morphologic changes—a 96-week analysis. *J Acquir Immune Defic Syndr*. 2006;43(5):535-540.
34. **Girard PM, Landman R, Gaudebout C, et al.** Dapsone-pyrimethamine compared with aerosolized pentamidine as primary prophylaxis against pneumocystis carinii pneumonia and toxoplasmosis in HIV infection. the PRIO study group. *N Engl J Med*. 1993;328(21):1514-1520.
35. **Havlic DV, Dube MP, Sattler FR, et al.** Prophylaxis against disseminated mycobacterium avium complex with weekly azithromycin, daily rifabutin, or both. California collaborative treatment group. *N Engl J Med*. 1996;335(6):392-398.
36. **El-Sadr WM, Murphy RL, Yurik TM, et al.** Atovaquone compared with dapsone for the prevention of pneumocystis carinii pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. Community program for clinical research on AIDS and the AIDS clinical trials group. *N Engl J Med*. 1998;339(26):1889-1895.
37. **Benson CA, Williams PL, Cohn DL, et al.** Clarithromycin or rifabutin alone or in combination for primary prophylaxis of mycobacterium avium complex disease in patients with AIDS: A randomized, double-blind, placebo-controlled trial. The AIDS clinical trials group 196/Terry Bein community programs for clinical research on AIDS 009 protocol team. *J Infect Dis*. 2000;181(4):1289-1297.
38. **Ioannidis JP, Cappelleri JC, Skolnik PR, Lau J, Sacks HS.** A meta-analysis of the relative efficacy and toxicity of pneumocystis carinii prophylactic regimens. *Arch Intern Med*. 1996;156(2):177-188.
39. **Nightingale SD, Cameron DW, Gordin FM, et al.** Two controlled trials of rifabutin prophylaxis against mycobacterium avium complex infection in AIDS. *N Engl J Med*. 1993;329(12):828-833.
40. **Carr A, Tindall B, Brew BJ, et al.** Low-dose trimethoprim-sulfamethoxazole prophylaxis for toxoplasmic encephalitis in patients with AIDS. *Ann Intern Med*. 1992;117(2):106-111.
41. **Wright JC, Weinstein MC.** Gains in life expectancy from medical interventions—standardizing data on outcomes. *N Engl J Med*. 1998;339(6):380-386.
42. **Bayer R.** Public health policy and the AIDS epidemic. An end to HIV exceptionalism? *N Engl J Med*. 1991;324(21):1500-1504.
43. **Giordano TP, Gifford AL, White AC Jr, et al.** Retention in care: A challenge to survival with HIV infection. *Clin Infect Dis*. 2007;44(11):1493-1499.
44. CDC. HIV prevalence estimates—United States, 2006. *MMWR Morb Mortal Wkly Rep*. 2008;57(39):1073-1076.