Estimation of HIV Incidence in the United States

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Context Incidence of human immunodeficiency virus (HIV) in the United States has not been directly measured. New assays that differentiate recent vs long-standing HIV infections allow improved estimation of HIV incidence.

Objective To estimate HIV incidence in the United States.

Design, Setting, and Patients Remnant diagnostic serum specimens from patients 13 years or older and newly diagnosed with HIV during 2006 in 22 states were tested with the BED HIV-1 capture enzyme immunoassay to classify infections as recent or long-standing. Information on HIV cases was reported to the Centers for Disease Control and Prevention through June 2007. Incidence of HIV in the 22 states during 2006 was estimated using a statistical approach with adjustment for testing frequency and extrapolated to the United States. Results were corroborated with back-calculation of HIV incidence for 1977-2006 based on HIV diagnoses from 40 states and AIDS incidence from 50 states and the District of Columbia.

Main Outcome Measure Estimated HIV incidence.

Results An estimated 39 400 persons were diagnosed with HIV in 2006 in the 22 states. Of 6864 diagnostic specimens tested using the BED assay, 2133 (31%) were classified as recent infections. Based on extrapolations from these data, the estimated number of new infections for the United States in 2006 was 56 300 (95% confidence interval [CI], 48 200-64 500); the estimated incidence rate was 22.8 per 100 000 population (95% CI, 19.5-26.1). Forty-five percent of infections were among black individuals and 53% among men who have sex with men. The back-calculation (n = 1.230 million HIV/AIDS cases reported by the end of 2006) yielded an estimate of 55 400 (95% CI, 50 000-60 800) new infections per year for 2003-2006 and indicated that HIV incidence increased in the mid-1990s, then slightly declined after 1999 and has been stable thereafter.

Conclusions This study provides the first direct estimates of HIV incidence in the United States using laboratory technologies previously implemented only in clinic-based settings. New HIV infections in the United States remain concentrated among men who have sex with men and among black individuals.

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KNOWLEDGE ABOUT TRENDS AND current patterns of human immunodeficiency virus (HIV) infections is essential for planning and evaluating prevention efforts and for resource allocation. In the past, data on AIDS incidence and, more recently, data on HIV diagnoses and prevalence have been used for planning and targeting HIV prevention programs. Timely information on national HIV incidence among key US populations can provide a more accurate picture of the HIV epidemic and likely lead to improved reach and impact of domestic programs. However, the incidence of HIV infection in the United States has never been directly measured.[1]

In the early 1990s, back-calculation models using AIDS incidence data and the probability distribution of the incubation period from HIV infection to AIDS diagnosis[2-5] provided historical trends of HIV incidence, but these models could not provide timely data on current transmission patterns. In addition, with the change in the AIDS case definition in 1993 and the advent of effective treatments that slow disease progression to AIDS, back-calculation models based exclusively on incident AIDS cases are no longer valid because the incubation period from HIV infection to AIDS diagnosis is difficult to estimate and inconsistently ascertained on a population level. Estimates of the annual number of new in-

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fections in the United States have also been derived from HIV incidence observed in cohort studies.[6] However, this method was based on small, select populations that did not produce population-based estimates and did not provide trends in incidence over time.

The development of laboratory assays that differentiate recent vs long-standing HIV infections now makes it possible to directly measure HIV incidence.[7-9] Building on the existing infrastructure of the Centers for Disease Control and Prevention (CDC) national HIV/AIDS case reporting system, we used the new technology to implement population-based HIV incidence surveillance. As a part of the new system, remnant serum specimens from persons who have a new diagnosis with a confirmed positive HIV antibody test result are tested with a second antibody assay, the BED HIV-1 capture enzyme immunoassay (BED),[8] which distinguishes recent (on average, 156 days after seroconversion on standard diagnostic assays [R.H. Byers, PhD, unpublished data, July 2005]) from long-standing infections. The BED assay uses antibodies to detect all HIV subtypes (ie, HIV-1 subtypes B, E, and D gp41 immunodominant sequences are included on a branched peptide used in the assay). The assay detects levels of anti-HIV IgG relative to total IgG and is based on the observation that the ratio of anti-HIV IgG to total IgG increases with time shortly after HIV infection. If a confirmed HIV-1–positive specimen is reactive on the standard sensitive enzyme immunoassay and has a normalized optical density of less than 0.8 on the BED assay, the source patient is considered recently infected. The combination of diagnostic testing (confirmed HIV antibody–positive) followed by testing for recent infection is known as the serologic testing algorithm for recent HIV seroconversion (STARHS).[9]

Estimation of HIV incidence with extended back-calculation models that incorporate all known infected cases and that attempt to use more information about cases than just their AIDS diagnosis date has been performed in Italy, England, and Australia for about the last 10 years.[10-12] In the United States, national AIDS surveillance data were used historically for back-calculation of HIV incidence[2-5]; information for extended back-calculation was not available. Recent advances in HIV case surveillance in addition to AIDS case surveillance in the United States have made the use of this approach feasible at the national level. The purpose of this analysis was to estimate HIV incidence in the United States in 2006. We estimated incidence based on the STARHS method and corroborated this estimate with an extended back-calculation approach using information on HIV diagnoses and AIDS incidence.

METHODS

Additional details of the study methods are provided in the eMethods (available at http://www.jama.com). In brief, since 1982, all 50 US states and the District of Columbia have reported AIDS cases to the CDC using a standardized case report form. In 1994, the CDC implemented data management for national reporting of HIV integrated with AIDS case reporting, at which time 25 states with confidential, name-based HIV reporting started submitting case reports to the CDC. Over time, additional states implemented name-based HIV reporting and started reporting these cases to the CDC. In 2004, the CDC funded selected areas to implement HIV incidence surveillance.[13]

All data were collected as part of routine HIV/AIDS surveillance as mandated by state or local laws or regulations. In reviews according to the CDC's Guidelines for Defining Public Health Research and Public Health Non-Research[14] and based on Title 45 Part 46 of the Code of Federal Regulations,[15] the CDC determined in 2005 and again in 2007 that HIV incidence surveillance is not a research activity and therefore does not require review by an institutional review board. Demographic information, including race/ethnicity, is collected from medical records as part of routine HIV and AIDS surveillance. Because the rates of HIV/AIDS vary widely by race/ethnicity[16] and this information is used to prioritize populations for HIV prevention and care efforts and resource allocation, we included analyses by race/ethnicity. The data analyses for this article were generated using SAS version 9.1.3 (SAS Institute Inc, Cary, North Carolina)[17] and APL*PLUS III (Manugistics Inc, Rockville, Maryland).[18]

Stratified Extrapolation Approach

Analyses were based on all individuals 13 years or older with HIV (HIV diagnosed with or without concurrent AIDS diagnosis) diagnosed in 2006 in 22 states (Alabama, Arizona, Colorado, Connecticut, Florida, Georgia, Illinois, Indiana, Louisiana, Michigan, Mississippi, Missouri, New Jersey, New York, North Carolina, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Virginia, and Washington) that had confidential, name-based HIV case reporting and HIV incidence surveillance implemented in 2006. Information on HIV cases was reported to the CDC through June 2007. The incidence surveillance areas represent approximately 73% of all AIDS cases diagnosed in 2006 in the United States.

Information was obtained on age, sex, race/ethnicity (white, black, Hispanic, Asian/Pacific Islander, American Indian/Alaska Native), transmission category (men who have sex with men [MSM], injection drug use [IDU], MSM and IDU [MSM/IDU], heterosexual contact, other), HIV testing history, STARHS result, and antiretroviral treatment. Infections in persons diagnosed with AIDS concurrently or within 6 months after HIV diagnosis were classified as long-standing infections.

We estimated population-based HIV incidence using a statistical approach analogous to that used to estimate a population total from a sample survey.[19] In a sample survey, the weight for a sampled person is the inverse of the sampling probability, and the population total (ie, the number of persons in the sampling frame [which includes un-

tested HIV-positive individuals]) is the sum of the estimated weights. All infections in a year were estimated using the probability of testing within 1 year of infection (described by the term p_1 in the eMethods at http://www.jama.com for the stratified extrapolation approach). Each individual identified as recently infected is assigned a weight that is then used to estimate the total incidence, including the "hidden" group of untested HIV-positive individuals. All persons infected in 2006 (including those not diagnosed) represented the sampling frame, and those identified as recently infected represented the sample selected from the sampling frame. Each sampled case was weighted according to the inverse of the estimated probability that a case of similar demographic and risk characteristics was in the sample. The estimated weight depends on the estimated probability that an infected person was tested within 1 year after infection, the probability that a person diagnosed with HIV had a BED test result, and the probability that the BED result for a person tested within 1 year after infection was "recent." The probability of being tested within 1 year after infection was estimated separately for those whose first HIV test result was positive (first-time testers) and those who had a previous negative result (repeat testers). For persons previously tested, this probability was estimated assuming that the infection date was uniformly distributed from the date of the last HIV-negative result to the date of the first HIV-positive result. For persons with no previous test, this probability was estimated from a competing-events model, the events being an HIV test or an AIDS diagnosis, assuming that HIV testing hazard (likelihood of having an HIV test) was a constant after infection until AIDS diagnosis.

Because HIV testing history and BED results were not available for most cases diagnosed in 2006 (TABLE 1), a 20-fold multiple imputation procedure[20] was used (12 067 individuals [36%] had information on testing history and 6864 [30%] with HIV [no AIDS diagnosis within 6 months] had a BED test). First we imputed BED values (recent or long-term infection) for HIV cases without AIDS (no AIDS diagnosis within 6 months after HIV diagnosis) and missing BED test results; then we imputed previous testing status (previously tested or not tested) for cases with missing information on this variable. The time from the last HIV-negative test result to the first HIV-positive result was

Table 1. Estimated Incidence of Human Immunodeficiency Virus Infection, 50 US States and the District of Columbia

	Stratified Extrapolation Approach				
	22 States, No. (%)[a]				
Characteristic	BED Tested[b]	2006 Diagnoses[c]	2006 Incidence	50 States + DC, 2006 Incidence, No. (%) [95% CI][d]	Extended Back-Calculation Approach, 50 States + DC, Incidence per Year, 2003-2006, No. (%) [95% CI][d]
Total	6864	39 400	40 800	56 300 [48 200-64 500]	55 400 [50 000-60 800]
Sex					
Male	4892 (71)	28 900 (73)	29 300 (72)	41 400 (73) [35 100-47 700]	42 000 (76) [37 400-46 600]
Female	1972 (29)	10 600 (27)	11 500 (28)	15 000 (27) [12 600-17 300]	13 400 (24) [11 000-15 800]
Race/ethnicity[e]					
White	1707 (25)	11 400 (29)	13 100 (33)	19 600 (35) [16 400-22 800]	17 700 (32) [14 700-20 700]
Black	3825 (56)	20 000 (51)	19 600 (49)	24 900 (45) [21 100-28 700]	27 800 (50) [24 200-31 400]
Hispanic	1190 (17)	7000 (18)	6800 (17)	9700 (17) [7900-11 600]	8600 (16) [6200-11 000]
Asian/Pacific Islander	78 (1)	440 (1)	590 (1)	1200 (2) [490-1900]	1000 (2) [200-1800]
American Indian/ Alaska Native	21 (<1)	130 (<1)	180 (<1)	290 (1) [60-500]	300 (<1) [50-700]
Age, y					
13-29	2790 (41)	13 100 (33)	14 100 (35)	19 200 (34) [16 300-22 200]	21 200 (38) [17 000-25 400]
30-39	1892 (28)	12 100 (31)	12 500 (31)	17 400 (31) [14 600-20 200]	16 800 (30) [13 600-20 000]
40-49	1539 (22)	9800 (25)	9900 (24)	13 900 (25) [11 700-16 100]	12 300 (22) [9100-15 500]
50-99	643 (9)	4400 (11)	4300 (11)	5800 (10) [4600-7100]	5100 (9) [2900-7300]
Transmission category					
MSM	3582 (52)	18 400 (48)	20 100 (51)	28 700 (53) [24 300-33 100]	31 200 (56) [25 400-37 000]
IDU	749 (11)	5600 (15)	4900 (12)	6600 (12) [5300-7900]	5900 (11) [3500-8300]
MSM/IDU	182 (3)	1200 (3)	1400 (3)	2100 (4) [1500-2700]	1600 (3) [400-2800]
Heterosexual	2328 (34)	13 100 (34)	13 100 (33)	16 800 (31) [14 200-19 400]	16 400 (30) [12 600-20 200]

Abbreviations: BED, BED human immunodeficiency virus 1 capture enzyme immunoassay; CI, confidence interval; IDU, injection drug use; MSM, men who have sex with men.
[a] Alabama, Arizona, Colorado, Connecticut, Florida, Georgia, Illinois, Indiana, Louisiana, Michigan, Mississippi, Missouri, New Jersey, New York, North Carolina, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Virginia, Washington.
[b] Numbers do not count individuals diagnosed with AIDS at or within 6 mo after human immunodeficiency virus diagnosis; these were risk redistributed but not adjusted for reporting delay.
[c] Numbers for 2006 diagnoses were adjusted for reporting delay and risk redistribution.
[d] Confidence intervals reflect random variability affecting model uncertainty but may not reflect model-assumption uncertainty; thus, they should be interpreted with caution.
[e] Race/ethnicity and transmission category subgroup numbers may not sum to the overall total because cases with unknown race/ethnicity or unknown transmission categories are excluded. However, percentages are adjusted for the exclusion and sum to 100%.

also generated for cases with missing information on previous test date but assigned to the previously tested group through imputation. See the eMethods at http://www.jama.com for more details.

Case counts were adjusted for reporting delays.[21] Cases reported without risk factor information were redistributed among transmission categories based on the classification of transmission category (by sex, race/ethnicity, and region) of cases diagnosed 3 to 10 years earlier and initially reported without risk factor information but later reclassified based on information obtained through follow-up investigations.[22] Incidence data from the 22 states were extrapolated to all 50 states and the District of Columbia. We assumed that the ratio of HIV incidence to AIDS incidence in the 22 states was equal to the ratio in the other areas when cases were stratified by sex, race/ethnicity, age, and transmission category.

Point estimates are the mean values of the estimates from the 20 multiple imputation data sets. Confidence interval (CI) estimates were obtained by normal approximation with standard errors of estimates derived using the delta method and include the variability among the 20 data sets.[20,23] We conducted sensitivity analyses to determine whether data on individuals who sought testing because of a specific exposure event would bias incidence estimates. During 2006, information was collected on reasons for testing newly diagnosed persons in the areas participating in incidence surveillance (reasons included potential exposure to HIV in the past 6 months, getting tested on a regular basis [eg, once a year or every 6 months], checking to confirm HIV-negative status, or testing required [eg, insurance, military, or court order]).

Crude incidence rates per 100 000 population were calculated by sex, race/ethnicity, and age (population denominators were not available by transmission category). Population denominators for rates were based on official postcensus estimates for 2006 from the US Census Bureau[24] and on bridged-race estimates for 2006 obtained from the CDC's National Center for Health Statistics.[25]

Extended Back-Calculation Approach

We used an extended back-calculation model based on the earliest time that individuals were known to be infected with HIV[11] and a dichotomous measure of disease severity at diagnosis: whether the individuals received an AIDS diagnosis in the same year they were first diagnosed as HIV-positive. We estimated the national HIV incidence per year for 1977-2006 using information from the national HIV/AIDS Reporting System on individuals 13 years or older diagnosed with HIV prior to the end of 2006 and reported to the CDC by the end of June 2007. AIDS cases were reported by all states and the District of Columbia for the entire reporting period. Forty states provided both HIV and AIDS diagnoses, while 10 states (California, Delaware, Hawaii, Illinois, Maryland, Massachusetts, Montana, Oregon, Rhode Island, Vermont) and the District of Columbia provided only AIDS diagnoses. We included year of HIV diagnosis, year of AIDS diagnosis, state of residence at diagnosis, sex, race/ethnicity, transmission category, and age at first diagnosis.

Adjustments were made to the surveillance data to obtain the estimated number of HIV diagnoses by year and disease severity (ie, whether an individual had AIDS). Adjustments were made for reporting delay, underreporting of cases, detection and elimination of duplicate reports, and misclassification of the first diagnosis date; these adjustments were based on information from prior studies.[21,26]

Original back-calculation models used the date of AIDS diagnosis to estimate HIV incidence. These models estimated the distribution of the time of infection of the observed AIDS cases using assumptions about the distribution of the incubation period for an AIDS diagnosis following HIV infection and the possible shape of the HIV incidence curve. The assumptions about the incubation period also indicated the proportions of infected individuals by year of infection who would be expected to be AIDS-free at the date specified for the analysis. The 2 sets of estimates were then combined to provide estimates of HIV incidence by year.

By contrast, in our extended back-calculation model the disease history information of interest was the calendar year in which the individual was first diagnosed with HIV, along with an indicator of whether the individual was also diagnosed with AIDS during the same calendar year.

The relevant incubation period in our extended back-calculation model was the time from infection to first HIV diagnosis. The distribution of this period depends both on the rate of progression to AIDS diagnosis and on the rate of diagnosis by HIV testing prior to AIDS among undiagnosed infected individuals. That is, to remain undiagnosed from infection to some later period, an infected individual must avoid diagnosis by either of those reasons in each intervening period. Since treatments only occur after initial HIV diagnosis, they do not affect the type of incubation period used in the extended model.

The extended model estimates the year of infection conditional on both the calendar year first diagnosed and the stage of disease at diagnosis; ie, for diagnoses from any particular year, patients with an AIDS diagnosis at or soon after the initial HIV diagnosis will have a different distribution for the estimated year infected compared with those without an AIDS diagnosis at or near the initial diagnosis. Individuals with a simultaneous AIDS diagnosis will have an earlier estimated average year of infection compared with those without a simultaneous AIDS diagnosis.

The estimation of the year of infection involves 3 sets of parameters: (1) AIDS hazards (the AIDS hazard in a designated year is the probability that an individual is diagnosed with AIDS in that year, given that he or she was AIDS-free at the beginning of the year) by time since infection in untreated infected individuals; (2) HIV testing rate by year in infected individuals prior to AIDS di-

agnosis; and (3) number of HIV infections by year.

The AIDS diagnosis hazards were based on the published literature and assumed to have been correctly specified in our model. The 2 sets of parameters for HIV testing hazards and the number of HIV infections were estimated by the model subject to assumptions about the relationship of the parameters within each set, which are necessary to ensure the stability of the model. Within each set we grouped together calendar years to form periods in which the parameters within a set were assumed to be constant. For example, for HIV incidence, the 30 years covered by the analysis (1977-2006) was reduced to a smaller number of intervals, eg, the model was forced to estimate that the same number of infections occurred in the years 2000, 2001, and 2002. It is important to note that the HIV testing parameters estimated herein do not represent the rate of HIV testing in the general population. Rather, they reflect the rate of removal by HIV testing from the pool of undiagnosed infected individuals who are not close to an AIDS diagnosis. In the simple version of the model, for which these rates depend only on calendar time but not time since infection, the estimated HIV testing rate for a single calendar year would be calculated as a proportion, with the numerator equal to the number of new HIV diagnoses without an AIDS diagnosis in that year divided by a denominator equal to the estimated number of undiagnosed cases carried over from the previous calendar year, plus new infections occurring in the current calendar year minus the number of new diagnoses that are simultaneous HIV/AIDS cases in the current year.

While fitting models, estimates and goodness-of-fit statistics were examined to determine whether any adjustments needed to be made to the specified periods (eg, whether periods needed to be broken into shorter periods). The defining of periods required a compromise between avoiding too many periods (and thereby unstable models due to more estimated parameters) and the need for smaller periods (especially for the early years of the epidemic) to capture the variation likely to be present in the data. The number and lengths of the intervals used to estimate HIV incidence were chosen based both on prior information about the likely shape of the incidence curve at different stages of the epidemic (eg, steep increases in incidence in the early 1980s, relatively stable incidence from the mid 1990s to the present) and experience gained by evaluating a variety of models with varying numbers of intervals and interval lengths. We used an approach based on approximating the shape of the incidence curve with a step function that uses a moderate number of intervals having varying lengths.

The results presented herein, ie, 2-year intervals in the early part of the epidemic vs 3-year or 4-year intervals in the latter part of the epidemic, reflect that estimated incidence changed more rapidly in the early part of the epidemic. When estimating total US incidence, the number of intervals could have been reduced; ie, the estimates in some contiguous intervals were essentially equal. However, we wished to directly illustrate these small differences rather than only stating that the estimates were similar. Additionally, at other levels, eg, analysis by risk group, race, or sex, the estimated incidences were not so similar as to justify combining the intervals. The HIV testing rates were restricted to be dependent on calendar time, not on time since infection.[27] However, this assumption does not preclude the possibility that within any year there may be groups of infected individuals with different rates of HIV testing (eg, variation by time since infection). Rather, the assumption merely requires that the average probability of diagnosis via HIV testing is the same across years that were grouped together.

Sensitivity analyses were conducted for the effect of the specified AIDS hazards. We assessed the sensitivity of the model results to the particular values we used by refitting the back-calculation model using alternative values for the AIDS hazards that were proportionally larger or smaller than the original values (up to 20% larger or smaller).

RESULTS

Stratified Extrapolation Approach

A total of 33 802 persons 13 years or older were diagnosed with HIV in 2006 in the 22 incidence surveillance states and reported to the CDC through June 2007 (39 400 adjusted for reporting delays). A total of 6864 persons with HIV who were not diagnosed with AIDS within 6 months after HIV diagnosis had BED results (2133 [31%] were classified as having recent infections and 4731 as having long-term infections). Of 12 067 cases with information on having had a previous test, 7604 (63%) had a previous negative test result. Among the individuals who had their specimens BED tested, a slightly higher proportion were black and in younger age groups compared with all cases diagnosed in the 22 states in 2006 (Table 1).

An estimated 56 300 adolescents and adults were newly infected with HIV in 2006 in the United States (95% confidence interval [CI], 48 200-64 500) (Table 1), with a rate of 22.8 per 100 000 population (95% CI, 19.5-26.1) (**TABLE 2**). Seventy-three percent of the infections occurred among males, 45% among blacks, 35% among whites, and 17% among Hispanics (Table 1). More than half (53%) of the infections were attributed to MSM. The HIV incidence rate was 7 times as high among blacks (83.7; 95% CI, 70.9-96.5) as among whites (11.5; 95% CI, 9.6-13.4) (Table 2). The rate among Hispanics (29.3; 95% CI, 23.8-35.0) was almost 3 times as high as that among whites.

Sensitivity analyses based on data from individuals who sought testing because of a specific perceived exposure event showed that the incidence estimate would be less than 7% lower than our current estimate, which is within the 95% CI of our estimate.

Back-Calculation Approach

Through June 2007, 1.230 million individuals (aged ≥13 years at diag-

nosis) had been reported to the CDC as having been diagnosed with HIV infection (with or without AIDS diagnosis) by the end of 2006. Accounting for reporting delays, state systems providing only AIDS cases, and underreporting of HIV cases, an estimated 247 000 additional individuals were diagnosed with HIV by the end of 2006 but not yet reported to the CDC.

The model estimates indicated that HIV incidence increased sharply after 1977, with a peak in 1984-1985 of approximately 130 000 infections per year (FIGURE 1). Incidence decreased after 1985 and reached a low point in the early 1990s, with approximately 49 000 infections per year. Incidence again peaked in the late 1990s at approximately 58 000 incident infections and decreased to 55 000 per year in the most recent intervals (ie, 2000-2002 and 2003-2006). Incidence among males mirrored the overall trend, but among females, incidence increased more slowly until the late 1980s, decreased toward the early 1990s, and then remained relatively stable.

Throughout most of the epidemic, except in the late 1980s and early 1990s, MSM (not including MSM/IDU) had the largest estimated incidence (FIGURE 2). The trend in HIV incidence for MSM has been steadily increasing since the early 1990s. For 2003-2006, MSM continued to account for more than half of the estimated incidence (Table 1). Blacks, whites, and Hispanics, respectively, accounted for about one-half, one-third, and one-sixth of current incidence. HIV incidence increased sharply after 1977 among whites, with a peak in 1984-1985 of more than 72 000 infections per year (FIGURE 3). Incidence increased more gradually after 1977 among blacks and Hispanics, with peak incidence during the late 1980s of approximately 46 000 infections per year among blacks and approximately 16 000 infections per year among Hispanics.

Sensitivity analyses based on reanalyzing the data using different values for the AIDS hazards (±20%) while retaining the same set of periods for the testing hazards and the numbers of infections did not change results substantially (data not shown).

COMMENT

The national HIV incidence estimates for the United States for 2006 from both methods used are within the range of estimates from back-calculation models in the early to mid 1990s but higher than the CDC estimate from 2001.[6] A back-calculation that accounted for the age-dependent AIDS incubation distributions estimated 55 000 new infections (95% CI, 49 500-60 700) for the United States each year during 1987-1991.[3] Using an alternative back-calculation method, Rosenberg[4] later reported an average of 40 000 to 80 000 new infections each year from 1987 to 1992. The prior back-calculation estimates were based on national AIDS surveillance data provided by the CDC. Another method extrapolating from incidence estimates from studies among convenience samples of MSM to the general US population estimated HIV incidence at approximately 40 000 infections per year.[6]

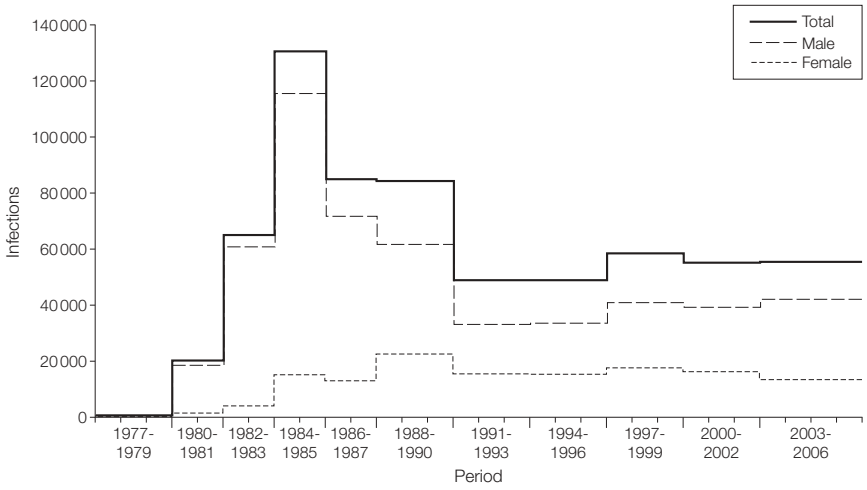
The independence of the methods we used and time frames studied suggest that the similar results for 2006 have validity. The discrepancy between our estimate for 2006 based on the stratified extrapolation method and the CDC's earlier estimate of 40 000 new infections per year[6] could be due to bias in the current estimate, limitations of the methods used for our previous estimate (eg, incidence may not have been

Table 2. Estimated Rates of New Human Immunodeficiency Virus Infections, 50 US States and the District of Columbia, 2006[a]

Characteristic	Rate (95% CI)[b]
Total	22.8 (19.5-26.1)
Sex	
Male	34.3 (29.1-39.5)
Female	11.9 (10.0-13.7)
Race/ethnicity	
White	11.5 (9.6-13.4)
Black	83.7 (70.9-96.5)
Hispanic	29.3 (23.8-35.0)
Asian/Pacific Islander	10.3 (4.2-16.3)
American Indian/ Alaska Native	14.6 (3.0-25.2)
Age, y	
13-29	26.8 (22.8-31.0)
30-39	42.6 (35.7-49.4)
40-49	30.7 (25.8-35.6)
50-99	6.5 (5.1-7.9)

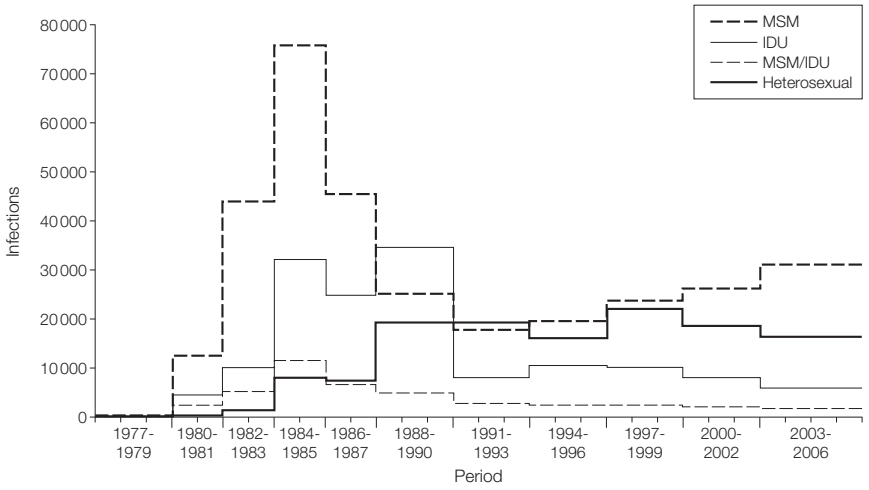
Abbreviation: CI, confidence interval.
[a] Stratified extrapolation approach. See Table 1 for numerator information.
[b] Per 100 000 population; postcensus estimates from the US Bureau of the Census.

Figure 1. Estimated New Human Immunodeficiency Virus (HIV) Infections, Extended Back-Calculation Model, 50 US States and the District of Columbia, 1977-2006



Tick marks denote beginning and ending of a year. The model specified periods within which the number of HIV infections was assumed to be approximately constant.

Figure 2. Estimated New Human Immunodeficiency Virus (HIV) Infections by Transmission Category, Extended Back-Calculation Model, 50 US States and the District of Columbia, 1977-2006



Tick marks denote beginning and ending of a year. The model specified periods within which the number of HIV infections was assumed to be approximately constant. MSM indicates men who have sex with men; IDU, injection drug use.

as low as 40 000), or an increase in HIV incidence.

Our incidence estimate based on the STARHS method could be an overestimate if the proportion of cases classified as recently infected in our sample was higher than that which would have been observed in the general population of individuals diagnosed with HIV or if we underestimated the probability of testing within 1 year after infection. Individuals who get tested more frequently are more likely to get tested within 1 year after infection and to be identified as having been recently infected. National surveys show differences in testing frequency; for example, a higher proportion of MSM report having had a test within the preceding 12 months,[28] compared with individuals in the general population.[29,30] However, we attempted to control for a possible bias in our sample by multiple imputation and stratified analyses.

The minor differences between our estimates within some of the subpopulations are likely due to differences between the methods and also because the stratified extrapolation approach provides estimates for 2006, while the extended back-calculation model provides estimates averaged over 4 years (ie, the CIs reflect model uncertainty but cannot be used to compare the models). The extended back-calculation approach is less suited to identify very recent changes in trends. However, the extended back-calculation model also can provide prevalence estimates that, in context with reported HIV diagnoses and deaths, further corroborate the plausibility of our estimates.

Our incidence estimates continue to demonstrate the disproportionate distribution of HIV infection among blacks (incidence rate, 83.7/100 000) and Hispanics (29.3/100 000) compared with whites (11.5/100 000).[16] The CDC is working with public health partners and community leaders to address disparities in HIV disease through the Heightened National Response to the HIV/AIDS Crisis Among African Americans.[16] Not only will novel, sustained efforts be needed to reduce incidence among African Americans and Hispanics, but increasing the availability of programs will be critical as well.

Overall trends in HIV incidence can mask trends in subpopulations. Based on the back-calculation results, for example, incidence increased nationally in the late 1990s; however, among those exposed through IDU, incidence remained relatively stable throughout the mid and late 1990s and then decreased. Overall, HIV incidence among individuals exposed through IDU has decreased approximately 80% in the United States. Over that time, those exposed through IDU have reduced needle sharing by using sterile syringes available through needle exchange programs or pharmacies and have reduced the number of individuals with whom they share needles.[31,32] However, the relative contribution of each of these interventions has been difficult to determine.

Currently, we do not have STARHS-based trend data to determine whether the changes in HIV diagnoses in recent years are due to changes in HIV transmission or testing for HIV.[33,34] The results from the extended back-calculation model suggest that HIV incidence among MSM was lowest in the early 1990s and increased thereafter. During this time, annual HIV diagnoses decreased until 1999 and then increased in the 25 states with low-to-moderate prevalence that had HIV reporting.[35] Increases in HIV diagnoses have also been observed in other Western countries.[36] This suggests that without incidence data, delays may occur in recognizing a resurgence of HIV infections among certain populations, which in turn may delay implementation of needed prevention efforts.

Based on the back-calculation results, incidence trends are also different for the various racial/ethnic groups. The annual HIV incidence among blacks surpassed the incidence among whites in the late 1980s, when incidence among whites decreased. Incidence among blacks did not decrease substantially until the early 1990s. Incidence among Hispanics, while lower, mirrors the trends among blacks rather than among whites. Incidence is low among Asians/Pacific Islanders and American Indians/Alaska Natives; therefore, trends are more difficult to interpret.

Our estimates depend on a number of assumptions that may affect the accuracy of the results. In the stratified extrapolation approach, we assumed that information on previous tests and BED results were missing at random after accounting for all variables known to be associated with missing values in the multiple imputation models. For example, HIV incidence surveillance was implemented in some areas by first enrolling public laboratories to submit specimens for BED testing and then adding additional laboratories; therefore, we controlled for facility type in the imputation models. However, the possibility exists that unobserved variables were associated with missing previous test or BED results and that associations cannot be explained by the observed variables.

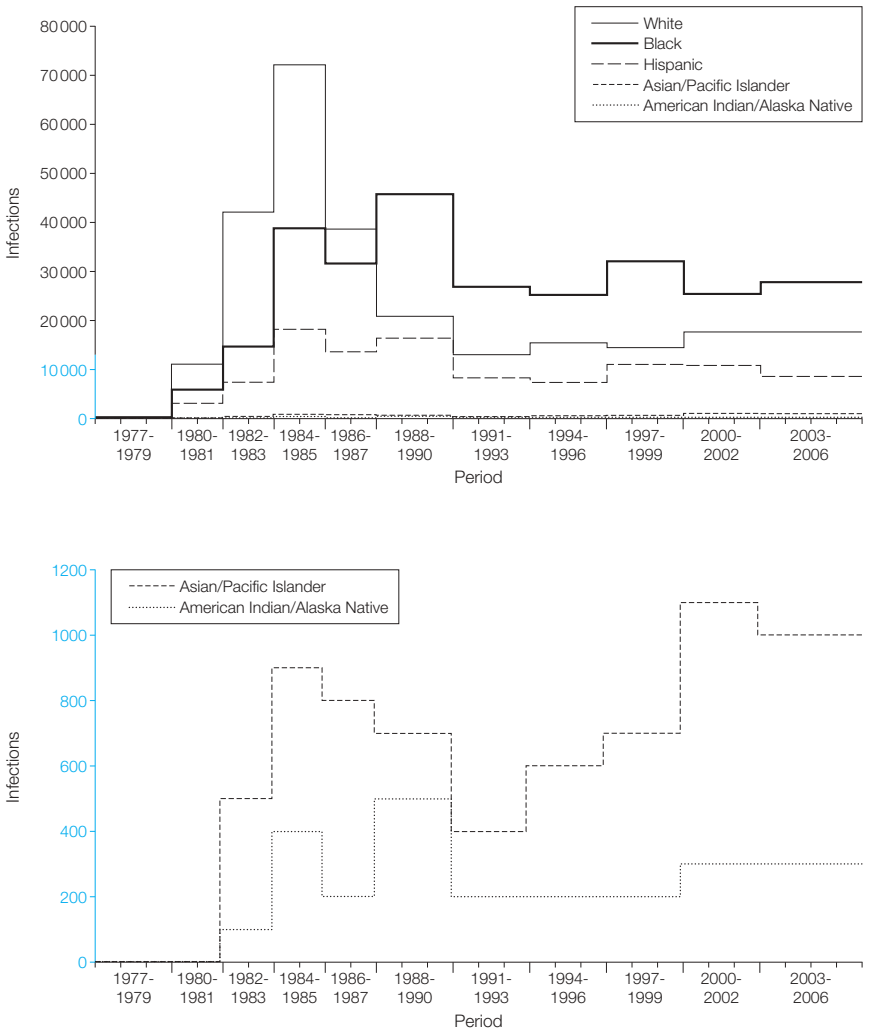
We further assumed that testing behavior has not changed substantially over several years, which would affect the probability of testing within 1 year after infection. Evidence exists that testing rates have changed little,[37] and such changes would have a small effect on our results because a large proportion of persons diagnosed with HIV have been previously tested.

A further assumption is that testing and infection are independent; however, persons recently infected may have a tendency to be tested in the period immediately following HIV infection. Sensitivity analyses performed on data from those who sought testing because of a possible exposure event showed that the incidence estimate would be less than 7% lower than our estimate, which is within the 95% CI of our estimate. Bias due to heterogeneity of testing frequency and other possible reasons for early testing, such as having a concomitant sexually transmitted disease, is also minimized by stratifying the population as in our model. Bias due to testing because of a sexually transmitted disease is controlled for using the surrogate variable facility of diagnosis as a stratification variable in the imputation model.

The accuracy of the information on whether cases had a previous negative test result is unknown; future studies are needed to validate this information. We extrapolated estimates of HIV incidence from the 22 incidence surveillance states to 50 states and Washington DC, assuming that the ratio of HIV incidence to AIDS incidence in the 22 states is similar to the ratio in the other areas after adjusting for sex, race/ethnicity, age, and transmission categories. As a proxy, we compared the ratio of HIV diagnoses to AIDS diagnoses in the 22 states included in our analyses to that ratio in other areas with HIV reporting that were not part of our analyses and found similar results. The CIs presented reflect random variability and may not reflect model-assumption uncertainty; therefore, they should be interpreted with caution. Finally, population denominator data are needed to calculate rates for at-risk populations in the future.

Concerns have been raised about the accuracy of the BED test, because incidence appeared to be overestimated when using BED results in Africa and Thailand.[38,39] The primary concern is

Figure 3. Estimated New Human Immunodeficiency Virus (HIV) Infections, by Race/Ethnicity, Extended Back-Calculation Model, 50 US States and the District of Columbia, 1977-2006



Tick marks denote beginning and ending of a year. The model specified periods within which the number of HIV infections was assumed to be approximately constant. Y-axis in blue indicates values in the range of 0-1200.

the misclassification of specimens as recent among persons with long-term HIV infection or AIDS, which overestimates the proportion of specimens classified as recent. To reduce this concern in the United States, the BED test is not used for persons with AIDS. Instead, incidence surveillance systems collect information on disease severity (whether an individual had AIDS) and we classified infections among individuals diagnosed with AIDS within 6 months after HIV diagnosis as long-term. However, we cannot rule out potential misclassification among those who have been infected for several years but not diagnosed with AIDS. Other factors also differ between the United States and some other countries; for example, in the United States there are low levels of chronic coinfection (that is, few individuals have hypergammaglobulinemia that may yield false recent BED results), and additional information is collected (eg, last negative test result).[40]

Several factors may affect the accuracy of incidence estimates from the extended back-calculation approach, resulting in underestimates or overestimates of incidence. First, accurate adjustments for reporting delay, underreporting of cases, detection and elimination of duplicate reports, and misclassification of the first diagnosis date need to be made to the surveillance data. Errors in assumptions about contributions from reporting delays and duplicate reports will have much larger effects on estimates of diagnoses in recent years (eg, 2005, 2006) compared with earlier years. Such errors then would also have a similar pattern of effects on estimates of HIV incidence. The method further depends on accurate specification of the AIDS incubation distribution. Variation in the AIDS diagnosis hazard appeared to have little effect on results. While fitting models, periods are combined (ie, with similar incidence), and an estimate for a particular year may change considerably depending on the period in which that year is placed. Finally, for the version of the model presented herein it was assumed that the HIV testing hazard is mostly dependent on calendar time and not on time since infection. However, this simplification generally does not distort the HIV incidence estimates as long as the model contains a sufficiently large number of periods for the HIV testing hazards.

Since 2002, the CDC has launched new prevention initiatives that included expanding HIV prevention to individuals living with HIV, increasing HIV testing,[41] and expanding the use of proven behavioral interventions in prevention programs for high-risk populations.[42] Condoms are highly effective in preventing the sexual transmission of HIV infection[43] but frequently are not used.[44] HIV counseling and testing has been found to reduce high-risk behavior by approximately 68% among individuals who find they are infected with HIV.[45] Most behavioral interventions reduce risk behavior by 20% to more than 40%.[46] Many of these interventions have been implemented in prevention programs across the country, but their reach must be considerably expanded to accelerate progress. An estimated one quarter of individuals living with HIV do not know it, and over a recent 1-year period only approximately 15% of MSM participated in individual-level and 8% in group-level interventions, among the most effective behavioral interventions available.[44] A substantial reduction in HIV incidence will require wider implementation of the effective interventions currently available and the development of additional interventions, such as antiretroviral chemoprophylaxis or a vaccine. These new HIV incidence data can help ensure that HIV prevention resources are allocated to the populations with greatest need and in the future might be used to monitor the success of these prevention efforts.

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Acquisition of data: Hall, Prejean, Lee, McKenna.
Analysis and interpretation of data: Hall, Song, Rhodes, Prejean, An, Karon, Brookmeyer, Kaplan, McKenna, Janssen.
Drafting of the manuscript: Hall, Song, Rhodes, Janssen.
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Additional Information: eMethods are available at http://www.jama.com.

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