Identifying Undiagnosed Human Immunodeficiency Virus

The Yield of Routine, Voluntary Inpatient Testing

Rochelle P. Walensky, MD, MPH; Elena Losina, PhD; Kathleen A. Steger-Craven, RN, MPH; Kenneth A. Freedberg, MD, MSc

Background: Despite current recommendations for human immunodeficiency virus (HIV) counseling and testing among patients admitted to hospitals with at least a 1% prevalence of HIV infection, an estimated 300000 people in the United States remain unaware of their HIV infection.

Methods: We implemented the Think HIV program, which offered voluntary HIV counseling and testing to patients admitted to the medical service of a Boston, Mass, teaching hospital. We compared the results of this effort with testing results from a 15-month historical control period.

Results: Patients admitted during the program period were 3.4 times more likely to undergo testing for HIV than those admitted during the control period (95% confidence interval [CI], 2.8-4.1). The testing program detected approximately 2 new diagnoses of HIV infection per month, compared with 1 per month during the control period. Patients who underwent testing during the program, and who likely would not have done so without this initiative, had an estimated prevalence of HIV infection of 3.8% (95% CI, 1.8%-5.8%).

Conclusions: Testing efforts for HIV targeted to only symptomatic patients are inadequate to identify the one third of HIV-seropositive people in the United States who are unaware of their infection. We have shown that in a single urban hospital, offering voluntary, routine inpatient HIV counseling and testing can be successful as a screening program by identifying a substantial number of patients with undiagnosed HIV. These patients then can be informed, counseled, and linked to care and treatment. Seventy-two hospitals nationwide have demographics similar to those of the study hospital, suggesting that these results are generalizable to many urban hospitals.

Arch Intern Med. 2002;162:887-892

In the past 20 years, acquired immunodeficiency syndrome (AIDS) in the United States has evolved from being virtually unknown to being a leading killer of young adults. Despite its initial onset in specific communities, the epidemic has since crossed all demographic and socioeconomic boundaries, and the number of patients at risk for contracting the human immunodeficiency virus (HIV) has expanded dramatically. Several studies estimate that one third of HIV-infected patients in the United States have not undergone testing. The Centers for Disease Control and Prevention (CDC) report that approximately 300000 people in the United States are infected with HIV and are unaware of their HIV-seropositive status. Among those who undergo testing, most patients begin care late in the course of disease. In Boston, Mass, Samet et al noted that on initial presentation for HIV medical care, 69 (36.5%) of 189 patients had CD4 counts of less than 200 cells/µL. In San Francisco, Calif, 29% of patients had CD4 counts of less than 200 cells/µL at first presentation. A recent study of a national sample of HIV-infected persons receiving medical care in the United States found that 29% of patients already considered themselves sick at the time of HIV diagnosis. Patients continue to present with late disease, despite the 1993 CDC recommendations for routine, voluntary HIV testing in all hospitalized patients in high-prevalence areas. This time lag from infection to initial testing and treatment represents therapeutic opportunity lost and extended risk for HIV transmission to uninfected partners.

We implemented the Think HIV testing program to offer HIV counseling and testing to all patients admitted to the medical service of an inner-city Boston teaching hospital. This approach is in contrast to most inpatient HIV testing programs...
SUBJECTS AND METHODS

We conducted a pilot study from April 1 through December 31, 1999, to offer routine HIV counseling and testing to all patients admitted to the medical service at Boston Medical Center. The population of medical inpatients from which we sampled the patients has a mean age of 52 years and is approximately 39% white, 12% African American, 37% Hispanic, 6% Asian, and 6% other. This pilot project was enhanced by the availability of HIV counseling and testing services through Project TRUST (Teaching, Referral, Understanding, Support, and Testing), a state-funded HIV counseling and testing clinic affiliated with the hospital. On admission, patients were asked by the medical intern, resident, or attending physician if they were interested in speaking with someone about HIV testing. If the patient agreed, a voice-mail message was left for a counselor at Project TRUST. The counselor visited the patient in the hospital, discussed HIV testing, completed standard pretest counseling for confidential testing, and drew the blood for HIV serologic tests. All samples were tested for HIV antibody by means of an enzyme-linked immunoassay (Genetic Systems HIV ELISA; Bio-Rad Laboratories, Redmond, Wash). According to the standard protocol, if the assay results were positive in duplicate, they were confirmed by means of Western blotting (Genetic Systems HIV-1; Bio-Rad Laboratories). All patients were given outpatient appointments to receive their test results 1 week later; if they were still inpatients, then results were given in the hospital when they became available. On return of a positive test result, patients were referred to the HIV Diagnostic Evaluation Unit, an HIV intake unit for linkage to medical care.11

Based on the results of the pilot phase, the Department of Medicine formalized the HIV testing program in January 2000 so that it became departmental procedure for all inpatients to be offered routine, voluntary HIV testing.

RESULTS

Before any specific HIV testing effort was implemented, an average of 9.3 patients per month were referred for HIV counseling and testing on the medical service (Figure 1), with an overall prevalence of HIV seropositivity of 14.3% (95% confidence interval [CI], 8.5%-20.0%) among those referred (Table). The referral rate of all patients admitted to the medical service was 2.0%, derived from a total of 7068 admissions during the control period. Testing was generally performed on patients with 1 or more clear risks for and/or signs of HIV infection.

In the routine testing program, 473 (6.4%) of the 7356 admitted patients underwent counseling and testing for HIV. The testing effort led to an increase of 3.4 times in the likelihood of undergoing testing for admitted patients (95% CI, 2.8-4.1), with a monthly increase in positive test results from 1.3 to 2.3 (Figure 2). The overall prevalence of seropositive test results among those referred decreased to 6.8% (95% CI, 4.5%-9.0%).

We estimated the HIV prevalence among low-risk patients by characterizing the 14.3% HIV-seropositive patients in the control period as high risk by definition. We then varied the assumption that there were also 14.3% high-risk patients during the study period, with the following results of our 5 equations:

(1) No. of Low-Risk Patients Undergoing Testing Each Month = (473 Tests/14 Months) − (140 Tests/15 Months) = 24.5 Tests per Month

(2) Total No. of Low-Risk Patients Undergoing Testing = (24.5 Tests/Month) × 14 Months = 343 Patients Undergoing Testing

(3) No. of Low-Risk HIV-Seropositive Patients Each Month = (32 HIV-Seropositive Patients/14 Months) − (20 HIV-Seropositive Patients/15 Months) = 0.95 Seropositive Patients Each Month

(4) Total No. of Low-Risk HIV-Seropositive Patients = (0.95 HIV-Seropositive Patients/Month) × 14 Months = 13 Low-Risk Patients With HIV

(5) Prevalence of HIV in Low-Risk Population (%) = (13/343) × 100% = 3.8%
patients who were admitted with thrush and a history of multiple sexual partners would be considered at high risk because we assumed they would generally undergo HIV testing, as would patients with a history of injected drug use and pneumonia. These high-risk patients were similar in character, number, and prevalence of HIV infection to patients undergoing testing during the historical control period. We considered low-risk patients to be those who likely would not have undergone testing without a program in place. We calculated the prevalence of HIV among patients in the low-risk category using the following series of equations:

\[
(1) \text{No. of Low-Risk Patients Undergoing Testing Each Month} = \frac{\text{Total Number of Low-Risk Patients Undergoing Testing Each Month}}{14} \\
(2) \text{Total No. of Low-Risk Patients Undergoing Testing} = \text{Total Number of Low-Risk Patients Undergoing Testing Each Month} \times \text{14-Month Program} \\
(3) \text{No. of Low-Risk HIV-Seropositive Patients Each Month} = \frac{\text{Total Number of Low-Risk Patients Undergoing Testing Each Month}}{14} \\
(4) \text{Total No. of Low-Risk HIV-Seropositive Patients} = \frac{\text{Total Number of Low-Risk Patients Undergoing Testing Each Month}}{14} \times \text{14-Month Program} \\
(5) \text{Prevalence of HIV in Low-Risk Population (%) =} \\
\left( \frac{\text{Total No. of Low-Risk HIV-Seropositive Patients \times 100}}{\text{Total Number of Low-Risk Patients Undergoing Testing}} \right) \\
\]

The validity of this technique relies on the consistency of medical admissions over time, a relatively stable monthly rate of testing, and equal rates of testing refusal regardless of HIV status. When we examined the number of admissions during the control and program periods, we found that they were similar. Data collected monthly from the testing site suggest that monthly testing rates were also relatively consistent. Because these calculations are also based on an assumption of a background of HIV prevalence among high-risk patients, we varied this prevalence in 5% increments ± 50% to estimate HIV prevalence among low-risk patients within reasonable rates of error in our assumption.

To examine the generalizability of our findings to other US hospitals, we used the American Hospital Association 1995 Annual Survey database. We determined the percentage of patients discharged at Boston Medical Center with Medicaid insurance and cross-referenced this feature with other demographic characteristics of the hospital. We searched for the number of hospitals that resembled Boston Medical Center in the following ways: (1) at least 40% of patients discharged insured by Medicaid; (2) more than 200 licensed beds; and (3) more than 1 million people in the metropolitan area where the hospital is located. We were then able to determine the number of similar facilities nationally that might achieve comparable results should HIV counseling and testing programs be implemented there.

Therefore, among patients who would not have undergone testing without a testing program in place in this hospital, we found an estimated prevalence of undiagnosed HIV infection of 3.8% (95% CI, 1.8%-5.8%). A sensitivity analysis examining the durability of this conclusion is shown in Figure 3. If the prevalence in high-risk patients is substantially higher than the estimated 14.3% (eg, 20%), then the prevalence in low-risk patients would be 1.9%. On the other hand, if the prevalence in high-risk patients is only 8.5%, then the prevalence in low-risk patients would be 6.0%. Regardless of whether the baseline assumption is high or low, within a plausible range of error, the prevalence of HIV infection among patients who would not otherwise have undergone testing lies between 1% and 6%.

Using the American Hospital Association database, we examined how many hospitals in the United States are demographically similar to the study institution. The search of the database retrieved 72 hospitals nationwide with similar characteristics to Boston Medical Center and for which we believe these results are likely generalizable. Assuming the prevalence of HIV is similar among inpatients in these hospitals and that HIV-infected patients present as inpatients at the same frequency, we can
Human immunodeficiency virus is now a highly treatable disease. However, one third of HIV-infected Americans have not undergone testing, and many of them are aware of their high-risk behavior. We sought to pilot a program that follows the 1993 CDC recommendations for routine, voluntary inpatient HIV testing in a high-prevalence institution. Our results demonstrate a sharp increase in the number of HIV tests performed by the medical service and a decrease in HIV prevalence among those tested. This decrease in prevalence compared with the historical control period was expected, because as testing increases, more tests will likely be performed in individuals with a lower pretest probability of having HIV infection. However, the absolute yield of testing nearly doubled, from 1.3 to 2.3 new cases of HIV diagnosed per month (Figure 2). This finding suggests that lowering the threshold for testing will identify a substantially increased number of undiagnosed cases of HIV.

One of the most striking results of this analysis is our estimation of an HIV prevalence of 3.8% among patients who would not have undergone testing if this policy not been implemented. This finding suggests that at this institution, with approximately 500 medical admissions per month, voluntary testing of all inpatients might detect 19 patients with previously undiagnosed HIV per month, compared with the 1.3 patients per month identified by results of targeted testing. Although not all facilities nationwide should adopt this screening policy, it is potentially a powerful intervention for the 72 urban institutions that are demographically similar to Boston Medical Center.

Nationwide, approximately 11,000 federally funded anonymous and confidential HIV testing and counseling sites provide about 2.5 million HIV tests annually. Rates of positive test results in these sites in 1997 ranged from 3.5% in prisons to 2.1% in community health centers to 1.5% in clinics for sexually transmitted diseases, all of which are lower than the overall 6.8% prevalence found by the medical service in our study. Since 1993, the CDC has recommended screening and testing for active HIV risk factors in all patients with potential infection, not just outpatients who seek testing on their own. These recommendations include counseling and testing for inpatients at acute care hospitals where HIV seroprevalence exceeds 1%, or where the AIDS discharge diagnosis rate is greater than 1/1000. These recommendations are fueled by data from emergency departments with a high prevalence of HIV, where half of infected patients are unaware of their seropositive status. Other studies among pregnant women have documented that HIV testing by risk factor assessment identifies 41% to 57% of HIV-seropositive patients, whereas routine voluntary testing has detected up to twice as many (87%). The CDC has directly advocated that “voluntary [HIV] testing will need to be increased in settings where persons at risk of HIV infection seek care for non–HIV-related reasons,” but little evidence exists of this happening on a systematic basis.

In July 2001, the CDC circulated a draft updating the 1993 recommendations on HIV counseling, testing, and referral. Highlights of the revision emphasize the importance of making these services more accessible to patients and decreasing the numbers of HIV-infected individuals who are unaware of their HIV status. The draft continues to advocate routine voluntary testing of all individuals in high-prevalence areas, defined as those with an HIV seropositive rate of at least 1%. Even in low-prevalence areas, the CDC recommends that HIV counseling and testing be based on assessment of risk, which is often neglected in the provision of routine medical care.

Why is HIV testing important? The diagnosis of AIDS is preceded by a median 11 years when patients harbor relatively quiescent HIV disease. Many investigators have reported that health care workers generally do not recognize patients early in the course of this long, clinically subtle period. Patients are most often identified as HIV infected when they present with clinical symptoms or an opportunistic infection. However, these years represent therapeutic opportunities lost. Starting antiretroviral therapy before the onset of opportunistic

**Figure 2.** Mean monthly number of positive results of human immunodeficiency virus (HIV) testing.

**Figure 3.** Estimated prevalence of human immunodeficiency virus (HIV) among low-risk patients, based on prevalence among the high-risk group. Dotted lines represent 95% upper and lower confidence intervals. High- and low-risk factors are described in the “Subjects and Methods” section.
infections diminishes the incidence of these infections and allows patients to sustain their immunologically potent native CD4 lymphocyte levels.\textsuperscript{20} Identifying patients before the onset of an opportunistic infection also spares them the attributable morbidity and mortality associated with such a history.\textsuperscript{21,22} Antiretroviral therapy diminishes transmission through altered risk behavior and through decreased plasma and semen HIV RNA levels.\textsuperscript{23-26} Data by Weinhardt et al\textsuperscript{23} show that after HIV counseling and testing, HIV-seropositive participants and HIV-discordant couples decreased their frequency of unprotected intercourse and increased their condom use relative to participants not undergoing testing. Testing for HIV infection, therefore, is also an effective means of secondary prevention for those patients.

Our data from a single urban site indicate that more vigorous inpatient testing strategies than those currently in place are needed. The explanation for the failure to implement large-scale inpatient HIV testing programs likely centers on resource constraints. Even in this study, when avid attempts were made for global screening and an HIV counselor was readily available, we were able to offer testing to only 6.4\% of admitted patients. Expanding testing to a higher percentage of patients would likely decrease the overall prevalence of positive test results, but would further increase the total number of HIV-seropositive patients identified. In addition, cost-effectiveness analyses of patients with HIV have repeatedly shown that antiretroviral therapy and prophylaxis for opportunistic infections are extremely cost-effective compared with other uses of health care resources.\textsuperscript{27,28} Two independent analyses showed that with an HIV prevalence of 1\%, routine counseling and testing were highly cost-effective, although these analyses were performed before the era of combination antiretroviral therapy.\textsuperscript{29,30} Our study showed that, even when accounting for possible errors in assumptions, prevalence of HIV infection among inpatients at Boston Medical Center meets or exceeds this threshold. Moreover, we found that results of inpatient HIV testing could yield higher prevalence rates than results of testing targeted to clinics for treatment of sexually transmitted disease, prisons, and drug treatment centers.\textsuperscript{15} Although all institutions clearly do not have the counseling and testing services available as we did from Project TRUST, our results suggest that investing in personnel devoted to HIV counseling and testing may be an effective use of HIV-related resources.

The historical control design of the study produces some limitations. We have explored the possibility of changes in discharge diagnoses in the hospital population over time and believe that this is a relatively short period for any large variations to occur. We have confirmed that no change in the Boston Medical Center proportion of discharge diagnoses for substance abuse has occurred (Jeffrey Samet, MD, MA, MPH, Medical Director of the Boston Public Health Commission and Substance Abuse Treatment Services, written communication, August 2001). We are also unaware of any secular trends nationally or locally that might account for changes in HIV testing rates during the 15 months before our study, during which the historical controls were drawn.

Although these results may incorporate some biases of testing, we believe that these biases are likely to be evenly distributed. Some house staff or attending physicians particularly interested in HIV may offer more tests than those without such a focus. However, patients admitted to the general medical service were assigned from the emergency department to medical personnel in a fashion that should not lead to a significant bias in either direction. We believe that another possible bias is the refusal rate for HIV testing (3.1 tests refused per month during the program period). For this analysis, we assumed that patients were equally likely to refuse a test, regardless of HIV status. However, in a small clinical sample, it appeared that those who refused testing had a relatively high rate of signs and symptoms suggestive of HIV, eg, unexplained adenopathy or thrush. This type of bias would lead our findings to underestimate the true prevalence of HIV infection. Other assumptions, such as the stability of medical admissions and tests offered per month, were reasonable given our data and did not affect the overall results.

The stigma associated with HIV infection continues to plague aggressive testing endeavors. We advocate, as does the American Medical Association, confidential HIV testing strategies that guarantee patient autonomy.\textsuperscript{31} This strategy does not conflict with, and is compatible with, efforts to identify and refer for treatment all HIV-infected patients.\textsuperscript{8} In fact, it is our hope that with widespread screening for HIV and treatment of infected persons, the stigma associated with testing will decrease. Studies have shown that acceptance rates for HIV screening among pregnant women are higher when it is routinely offered (\textless=96\%) than when it is offered by risk factor assessment.\textsuperscript{10,17}

**CONCLUSIONS**

This study explores the impact of implementing the recommended CDC policy of routine inpatient HIV testing. Although the resources to expand this effort nationally would be extensive, analyses exploring the outcomes, cost-effectiveness, and viability of this type of study support such a goal. We have shown that in a single urban hospital like many others around the country, routine voluntary inpatient HIV testing can be successful as a screening program and can identify a substantial number of patients with undiagnosed HIV. These patients then can be informed, counseled, and linked to care and treatment.\textsuperscript{11} Physicians must make the commitment to enroll patients in such a testing program if it is to have an impact. This study can serve as an example for other facilities to establish similar screening efforts so that most of the estimated 300000 people with undiagnosed HIV infection in the United States can be identified and provided with appropriate care.

Accepted for publication September 26, 2001.

This study was supported by the AIDS Bureau, Massachusetts Department of Public Health, Boston; cooperative agreement U64/CCU119325 from the Centers for Disease Control and Prevention, Atlanta, Ga; grant R01AH2006 from the National Institute of Allergy and Infectious Disease.
cases, Bethesda, Md; and grant 5T32HS00020-15 from the Agency for Healthcare Research and Quality, Rockville, Md.

We thank Jeffrey Samet, MD, MA, MPH, and A. David Paltiel, PhD, for their reviews of the manuscript; Jackie Gutierrez for providing counseling and testing; and Jon Hall for assistance with data collection.

Corresponding author and reprints: Rochelle P. Walensky, MD, MPH, Massachusetts General Hospital, Division of General Internal Medicine, 50 Staniford St, Ninth Floor, Boston, MA 02114 (e-mail: rwalensky@partners.org).

REFERENCES