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HIV Seroprevalence Surveys in Sexually Transmitted Disease Clinics

IDA M. ONORATO, MD
EUGENE MC CRAY, MD
MARGUERITE PAPPAIOANOU, DVM, PhD
ROBERT JOHNSON, MD
SEVGI ARAL, PhD
ANN M. HARDY, DrPH
TIMOTHY J. DONDERO, Jr., MD, MPH

The authors are with the Centers for Disease Control, Public Health Service. Dr. Onorato, Dr. McCray, Dr. Pappaioanou, and Dr. Dondero are with the Division of HIV/AIDS, Center for Infectious Diseases. Dr. Johnson and Dr. Aral are with the Division of STD/HIV Prevention, Center for Prevention Services. Dr. Hardy is with the National Center for Health Statistics.

Tearsheet requests to CDC, Technical Information Activity, Mail Stop G29, Atlanta, GA 30333.

Synopsis

The Centers for Disease Control, in cooperation with State and local health departments, is conducting human immunodeficiency virus, type 1 (HIV), seroprevalence surveys, using standard protocols, in sexually transmitted disease (STD) clinics in selected metropolitan areas throughout the United States. The surveys are blinded (serologic test results not identified with a person) as well as nonblinded (clients voluntarily agreeing to participate).

STD clinics are important sentinel sites for the surveillance of HIV infection because they serve persons who are at increased risk as a result of certain behaviors, such as unprotected sex, homosexual exposure, or intravenous drug use. HIV seroprevalence rates will be obtained in the sentinel clinics each year so that trends in infection can be assessed over an extended period of time. Behaviors that place clients at risk for infection, or protect against infection, are being evaluated in voluntary, nonblinded surveys to define groups for appropriate interventions and to detect changes in response to education and prevention programs.

Although inferences drawn from the surveys are limited by the scope of the clinics and clients surveyed, HIV trends in STD clinic client populations should provide a sensitive monitor of the course of the acquired immunodeficiency syndrome (AIDS) epidemic among persons engaging in high-risk sexual behaviors.

HUMAN immunodeficiency virus, type 1 (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS), is transmitted by sexual contact between homosexual and bisexual men as well as through heterosexual activity by bisexual or heterosexual men and women. The present extent of HIV transmission among sexually active persons, and changes now taking place in that transmission, are unknown.

Sexually transmitted disease (STD) clinics are important sentinel sites for surveillance of HIV infection because they serve persons who practice behaviors known to be associated with transmission of HIV. AIDS cases have been reported principally among homosexual and bisexual men and among intravenous drug users and their heterosexual partners. In addition to those in risk behavior groups, heterosexually active men and women who seek diagnosis and treatment of STD are likely to have engaged, knowingly or unknowingly, in risk behaviors that increased their exposure to HIV as well. Such behaviors include having multiple sex partners, having sex with persons not well known to them, not using condoms, and engaging in sex practices that increase exposure to blood and rectal mucosa.

Recent studies suggest that STDs characterized by genital ulceration (syphilis, chancroid, and genital herpes) or genital warts may facilitate HIV transmission (*1–3*). While the prevalence of STD has declined among homosexual men in some areas (*4*), recent outbreaks of syphilis and chancroid associated with drug use and heterosexual prostitution among minority group clients of STD clinics pose the possibility of increased HIV transmission among heterosexuals (*5, 6*).

In 1987, the Centers for Disease Control (CDC) conducted a systematic search for published and unpublished information on the seroprevalence of HIV in the United States (*7*). Twenty-three surveys of STD clinics conducted during the period 1985–87 were reviewed. STD clinic HIV prevalence rates were 0.5 to 15.2 percent (median, 3.5 percent). Homosexual and bisexual men had the highest seroprevalence (median, 32.2 percent). Heterosexuals who used drugs intravenously had a median rate of 3.5 percent (range, 0 to 45.2 percent), compared with generally lower rates (median, 1.1 percent; range, 0 to 3 percent) in those not acknowledging drug use or homosexual activity.

Seroprevalence rates in the 23 surveys were difficult to compare because of differences in methodology. Most of the survey subjects were STD clinic clients who volunteered for HIV testing, or clients recruited because they were thought to be at risk of HIV infection. Surveys of self-selected persons will give biased estimates of seroprevalence (*8*). Information on risk behaviors, a factor particularly relevant to STD clients, was not routinely collected in all surveys or was collected using different techniques, such as interview assessments, self-administered questionnaires, and reinterviews of HIV-positive clients.

Accurate classification of surveyed clients according to risk behaviors is necessary because many factors may affect seroprevalence estimates, such as changes in behaviors over a period of time, the proportion of the population practicing various behaviors, and the potentially changing HIV risk associated with those behaviors. But more important, knowledge of the characteristics of clients who engage in certain risk behaviors may be used in developing effective, culturally appropriate prevention programs and in directing them to the appropriate audience.

Objectives

Seroprevalence surveys in STD clinics are one component of the CDC family of surveys program (*9*). The STD clinic surveys have five objectives, which are to

- Develop standard procedures for conducting seroprevalence surveys in participating STD clinics,
- Evaluate the prevalence of HIV infection in STD clinic clients,
- Assess risk behaviors associated with seropositivity,
- Monitor trends in infection and risk behaviors over a period of time, and
- Direct HIV prevention programs to appropriate groups and evaluate the effectiveness of the programs.

Survey Methods

Selection of metropolitan areas and clinics. Thirty-nine metropolitan areas are participating in the family of surveys program. Metropolitan areas were selected, beginning in October 1987, on the basis of AIDS and STD case rates, willingness to participate, and geographic diversity. From one to eight STD clinics in each metropolitan area are participating in the survey. Clinics were selected for participation after a review by the local health department of clinics in that area that primarily provide STD services.

The criteria for selection of clinics included a large number of clients served per week, the variety of demographic subgroups served, the clinics' locations in different parts of the city, and the willingness of clinic staff members to participate in the annual surveys. All STD clinics that were supported by State or local health departments were enrolled. Privately funded STD clinics, usually gay- or feminist-sponsored, were included in some cities.

Eligibility criteria for participants. The following criteria apply in order for STD clinic clients to be included in nonblinded surveys (in which clients voluntarily agree to participate), or for serums to be included in blinded surveys (in which serologic test results are not identified with a person). The clinic visit must be the first for a new STD problem, and the client may not have visited the clinic within the previous 90 days, or since the beginning of the survey, whichever is more

recent. Clients attending for followup visits are excluded. Clients who come to the STD clinic specifically to obtain an HIV test are excluded. They are considered to be a biased group, either more likely to be seropositive than persons primarily seeking treatment for STD, because they may be aware of their risk behaviors, or less likely to be seropositive, because they may be the so-called worried well.

Blinded surveys. Blinded surveys are used to estimate HIV seroprevalence among clients of participating STD clinics. Clinic staff members routinely record demographic information for each client on the clinic record. At many STD clinics, staff members routinely assess possible risk behaviors, such as drug use and promiscuity, during the medical interview as part of the clinical evaluation. Information obtained in the clinic visits is abstracted on standardized data collection forms that are coded only by a unique survey number not related to patient numbers or names. Information associated with the specimen, such as the date of the visit, the client's age group, and residence, is aggregated so that individual clients cannot be identified. The information collected is shown in the accompanying box.

STD clinics routinely obtain venous blood for testing for syphilis and other sexually transmitted diseases. Most clinics follow a standard procedure in which new clients and those who have not been tested for syphilis within the past 3 months receive a blood test for syphilis as part of their clinic visit regardless of the reason for the visit. Clinics in areas of high syphilis incidence may test clients at each visit. After the serum is tested as requested by the clinician, client-identifying information is removed and the remaining serum is sent to a separate laboratory for testing for antibodies to HIV. The serum is accompanied only by the CDC survey number. HIV test results and the CDC data collection forms are sent separately to the survey coordinator and merged through the CDC HIV family of surveys software system. Summary seroprevalence rates are returned to the clinic by the survey coordinator in tabular form, without survey numbers or listings of individual data.

Nonblinded surveys. HIV education and counseling and testing services are offered in all publicly funded STD clinics (*10*). Clients receiving HIV testing and who are eligible for the nonblinded survey are interviewed using a risk assessment questionnaire, after obtaining their consent. When the client returns for test results and posttest counseling, risk behaviors are again assessed, using the posttest, nonblinded survey questionnaire, to validate previously reported risks.

Clients who are found to be seropositive may recall or acknowledge behaviors not reported in the pretest interview. Confidentiality, counseling, and posttest services, such as partner notification and tuberculosis testing, are provided in accord with CDC recommendations and local policies. The protocol for nonblinded surveys has been reviewed and approved by the CDC Institutional Review Board. Approval by an appropriately constituted local board is required as well.

Pretest and posttest risk assessment questionnaires are administered by a trained interviewer. The question-

Client Information Collected in STD Clinic Blinded Surveys

Date of this visit: month and year

Date of last visit: month and year

Residence: State, county, and zip code

Sex: male, female

Age group: younger than 15 years, 5-year age groups, older than 45 years

Race: white, black, Hispanic (Mexican, Puerto Rican, Cuban, other), Asian or Pacific Islander, American Indian or Native Alaskan, other

Risk exposures since 1978: man who had sex with a man, man who had sex with men and women, intravenous drug use, person with hemophilia, female sex partner of bisexual man, sex partner of intravenous drug user, sex partner of person with HIV or AIDS, sex partner of person with hemophilia, born in pattern-II country,[1] sex partner of person born in pattern-II country, received blood or blood products in the period 1978–85, heterosexual, person who gave or received drugs or money for sex, smoked crack cocaine since 1978, or no information available

Reason for clinic visit: requesting HIV test, followup STD visit, STD examination or treatment, premarital screening, symptomatic for HIV or AIDS, asymptomatic or worried about HIV, other, or no information available

Referral source: HIV-positive sex partner, sex partner with STD, health department for HIV test, health department for STD examination, private doctor or blood bank or hospital referral for HIV test, private doctor or blood bank or hospital referral for STD examination

STD diagnosis: gonorrhea, nongonococcal urethritis, penile-vaginal discharge, syphilis, genital ulcers, warts, other

Syphilis test result: nonreactive, reactive, not available

[1] A pattern-II country, by World Health Organization definition, is one in which HIV is transmitted primarily through heterosexual activity.

'The purpose of the nonblinded survey is to assess the risk behaviors that are associated with HIV infection, rather than to estimate seroprevalence.'

naires are used to assess behaviors that increase exposure to HIV and behaviors that may protect against infection. The pretest questionnaire consists of 58 questions for men and 43 questions for women. Detailed questions on sexual and drug-using behaviors are skipped if the client answers *no* to general screening questions. The types of information obtained in the pretest questionnaire are demographic data, medical history, history of drug use, sexual history, experience with prostitution, changes in sexual and drug-using behavior, STD diagnosis, and syphilis and hepatitis B test results. The clinical diagnosis and laboratory results are recorded from the STD clinic record. The posttest questionnaire consists of 13 questions for women and 16 questions for men. (A copy of the STD risk assessment questionnaire may be obtained from CDC, Mail Stop G29, HIV Seroepidemiology Branch, Atlanta, GA 30333.)

Questionnaire data are entered and merged with the results of enzyme immunoassay and Western blot tests, using a unique survey number, through the CDC HIV family of surveys software system. Client names are not entered into the data set.

Nonblinded surveys are conducted concurrently with blinded surveys in STD clinics participating in the CDC family of surveys. Thus, clients in the nonblinded surveys are a self-selected sample of the client population tested in the blinded survey. Demographic information is collected for clients eligible for nonblinded surveys who refuse to participate so that comparisons with patients surveyed can be made; the participation rate for eligible clients is calculated.

Sample size, blinded surveys. The duration of the blinded survey in a given STD clinic depends on the time required to collect the target number of samples. The recommended sample size is based upon the number of observations required for estimating seroprevalence within certain bounds (95 percent confidence interval) in different groups of clients. These sample size estimates require an assumption of the expected seroprevalence in the various groups. If seroprevalence in homosexual men is 10 to 50 percent, testing at least 200 serums from this group per clinic per survey period would produce reasonably precise estimates at a level of significance of 0.05 (table 1). Sample sizes for heterosexual men and women, groups generally expected to have low prevalence of HIV infection, are at least 500 serums for each group per clinic for each survey period. Larger sample sizes will allow more precise estimates of seroprevalence.

A limitation on sample size is the number of clients in the various subgroups visiting the clinic during the survey period. STD clinics usually serve more men than women. For simplicity, STD clinics estimate the period of time needed to obtain serums from at least 500 women and survey the entire eligible clinic population for that period. The total clinic sample size then ranges from 1,500 to 2,500 serums, depending on the proportion of male and female clients. Clinics with small client populations may test for an entire year to obtain the desired sample size.

Larger sample sizes are needed to detect a change in estimates of seroprevalence from one survey period to the next (table 2). For example, if serums from 500 heterosexual men show a prevalence of 1 percent in the first survey period, testing 500 serums from this group in the second survey period will likely find a change to be statistically significant only if seroprevalence increases to at least 4.1 percent. Smaller increases between any 2 years may not be detected with statistical validity. Sample sizes for subsequent survey periods should be based on the seroprevalence observed in earlier surveys and the detected increase or decrease in rates that is desired. Subsequent surveys should be conducted at the same time each year to minimize the impact of seasonal variation of STD on the comparability of annual survey data.

Sample size, nonblinded surveys. The purpose of the nonblinded survey is to assess the risk behaviors that are associated with HIV infection, rather than to estimate seroprevalence. Sufficient numbers of clients should be enrolled to obtain risk assessment questionnaires both from seropositive and seronegative patients. Sample sizes similar to those recommended for blinded surveys will yield information from infected and uninfected clients, assuming that both groups consent equally to participate in the nonblinded survey. The number of clients recruited for the nonblinded survey depends on the expected participation rate and the availability of resources, including trained interviewers and counselors and space for confidential interviews in the clinic. Clinics at which resources are limited may sample every 10th client, for example, until the desired sample size is reached.

Laboratory methods. Serums are tested according to manufacturers' recommendations by an enzyme immu-

Table 1. Confidence intervals (95 percent) for estimates of seroprevalence rates (percent positive) by observed seroprevalence and sample size of survey

Observed rate (percent)	Sample size						
	100	200	300	500	1,000	2,000	4,000
0	0 – 3	0 – 1.5	0 – 1	0 – 0.6	0 – 0.4	0 – 0.2	0 – 0.1
1	0.02– 5.5	0.1– 3.6	0.2– 2.9	0.3– 2.3	0.5– 1.8	0.6– 1.5	0.7– 1.4
2	0.2 – 7	0.6– 5	0.7– 4.3	1 – 3.6	1.2– 3.1	1.4– 2.7	1.6– 2.5
5	2 –11	2 – 9	3 – 8	3 – 7	3.7– 6.5	4 – 6	4.3– 5.7
10	5 –18	6 – 15	7 – 14	8 – 13	8.2– 12	8.7– 11.4	9.1– 11
20	13 –29	15 – 26	16 – 25	17 – 24	17.6– 22.6	18.3– 21.8	18.8– 21.3
50	40 –60	43 – 57	44 – 56	46 – 54	46.9– 53.2	47.8– 52.2	48.4– 51.6

EXAMPLE: If a sample of 300 serums is tested and none found positive, one can be 95 percent confident that the true seroprevalence is 0 to 1 percent. If 3 of the 300 (1 percent) specimens are positive, then one can be 95 percent confident that the true seroprevalence is 0.2 to 2.9 percent. The size of the interval can be narrowed by increasing sample size. For example, if 600 specimens are collected and none are positive, one can be 95 percent confident that the true seroprevalence is 0 to 0.5 percent; if 6 are positive (1 percent), the true seroprevalence falls within 0.4 to 2.2 percent.

noassay for HIV antibody that is licensed by the Food and Drug Administration (FDA). Repeatedly reactive serums are tested by an FDA-licensed Western blot assay. The presence or absence of each virus-specific band is reported to CDC. Laboratories testing serums from clinic surveys are required to participate in a quality assurance program provided by CDC (*11*).

Applications of Data

Data from STD clinic surveys will be used in providing baseline estimates of infection and monitoring trends over a period of time. STD clinic surveys are the principal sources of information about populations at greatest risk of infection, including homosexual men and intravenous drug users who are not in drug treatment programs. Infection rates in minority groups and among adolescents are of great importance for future prevention efforts and their assessment will be particularly emphasized in the surveys. The surveys of STD clinics each year will be useful indicators of the direction of the AIDS epidemic. The surveys also may be used to infer the rate of new infections occurring in clinic clients.

Blinded surveys will provide the best estimates of the prevalence of HIV infection that are or will be available because they are standardized and are not biased by self-selection. Nonblinded surveys, by assessing the presence or absence of different risk behaviors among HIV-positive persons, are the best way to establish the presence of infection in persons exposed through heterosexual contact. The surveys will provide the earliest warning of the sexual spread of HIV infection in those heterosexually active populations in which there is a significant reservoir of persons with HIV infection related to intravenous drug use.

STD clinic data are sufficiently focused by type of risk and by demographic and geographic subgroup to be useful in directing appropriate prevention activities to specific clinics and groups of clients. One method for effectively allocating limited resources for treatment of persons infected with HIV is to provide services first to clinics and communities where the estimated risk of HIV infection is highest. The services may include voluntary counseling and testing; partner notification; street outreach and community-based services; and followup services for infected persons, such as medical assessment, contraception, and antiviral and prophylactic therapy for opportunistic infections.

Data from STD clinic surveys can be used to evaluate prevention programs. Comparing seroprevalence rates in blinded surveys with voluntary HIV testing in STD patients in the same clinic will measure the proportion of infected clinic clients who were reached by counseling and testing programs.

Table 2. Testing for changes[1] in seroprevalence rates between two survey periods, showing the minimum rates which are detectable for second period by rates for first period, by various sample sizes[2]

Sample size	First period seroprevalence rate (percent)						
	0.01	1	2	5	10	20	50
50	18.6	20.8	22.9	28.3	36.1	49.3	79.4
100	9.9	12.1	14.2	19.4	26.9	39.7	70.1
200	5.1	7.3	9.2	14.0	21.0	33.4	64.9
300	3.4	5.6	7.4	12.0	18.7	30.7	62.2
400	2.6	4.7	6.4	10.8	17.3	29.1	60.5
500	2.1	4.1	5.8	10.1	16.5	28.1	59.4
600	1.8	3.7	5.3	9.5	15.8	27.3	58.6
1,000	1.1	2.9	4.4	8.4	14.4	25.6	56.6
2,000	0.5	2.2	3.6	7.3	13.0	23.9	54.7
5,000	0.2	1.7	2.9	6.4	11.8	22.4	52.9

[1]One-tailed test on proportions, a = 0.05, power 1-B = 0.90.
[2]Reference 12.

'Blinded surveys will provide the best estimates of the prevalence of HIV infection that are or will be available because they are standardized and are not biased by self-selection.'

Interpretation of Data

STD clinics serve as sentinel sites for HIV surveillance, permitting trends to be monitored. STD clinics are not representative of all clinics; neither are clinic patients representative of all persons with STD, or of all persons sharing the behaviors that facilitate their transmission. Despite careful adherence to protocols, specific situations and procedures in STD clinics may bias the estimates of HIV infection that are obtained.

For example, persons who primarily want HIV counseling and testing, but do not want to say so, may come to the clinic ostensibly for evaluation of a STD and be inadvertently included in the survey. In some clinics, clients who ask solely for HIV testing are offered a STD examination; if they accept, they may be included inappropriately in the survey as STD patients.

In the blinded surveys, HIV testing is performed on serums remaining after the routine serologic test for syphilis. Policies for routine syphilis testing may vary between clinics in the same metropolitan area and even between physicians in the same clinic. These variations, if they result in systematic inclusion or exclusion of some types of clients, may affect observed seroprevalence rates. In some clinics, a syphilis test is more likely to be ordered for clients perceived to be at increased risk for syphilis, such as homosexual men and prostitutes, whereas some types of patients at lower risk for HIV infection may not receive the test, such as women with yeast infection or chlamydia.

Patients with syphilis may be more likely to be infected with HIV. Certain risk behaviors may increase exposure to both infections. Moreover, syphilis and other genital ulcer diseases may facilitate transmission of HIV. Several serums from an HIV-infected client, drawn to monitor the treatment of syphilis, if included in the survey, may falsely elevate seroprevalence rates.

Strict adherence to the survey protocol is necessary to minimize sampling problems.

Conclusion

Surveys of clients attending STD clinics are an important surveillance system for monitoring HIV infection in persons with increased risk of infection. Methods for blinded and nonblinded surveys have been standardized to permit comparability of data from the various STD clinics participating in the CDC family of surveys program. STD clinic surveys will continue to monitor trends in infection for several years. Information from the nonblinded surveys is expected to evaluate the association between HIV infection and changes in such risky practices as unprotected sex and drug use as education programs are implemented. Use of this method will assist in evaluating the success of prevention efforts.

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