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ORIGINAL CONTRIBUTIONS

Differences in the Temporal Trends of HIV Seroincidence and Seroprevalence among Sexually Transmitted Disease Clinic Patients, 1989–1998: Application of the Serologic Testing Algorithm for Recent HIV Seroconversion

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The authors compared temporal trends in the prevalence and incidence of human immunodeficiency virus (HIV) infection based upon 34,866 specimens from patients who attended the San Francisco, California, municipal sexually transmitted disease clinic between 1989 and 1998. HIV infection data were collected during annual blinded HIV serologic surveys. Incidence was determined by applying a serologic testing algorithm for recent HIV seroconversion that uses both a sensitive and a less sensitive enzyme immunoassay to stored HIV positive sera. The HIV seroprevalence declined from 15.2% in 1989 to 7.2% in 1998 (odds ratio per year = 0.92, 95% confidence interval (CI): 0.91, 0.94). Among homosexual men, the HIV prevalence declined from 50.9% in 1989 to 19.9% in 1998 (odds ratio per year = 0.86, 95% CI: 0.85, 0.88). The pooled seroincidence was 1.6% and did not change significantly over time (odds ratio per year = 1.0, 95% CI: 0.98, 1.1). The pooled seroincidence among homosexual men was 6.6% per year and remained steady between 1989 and 1998 (odds ratio per year = 0.99, 95% CI: 0.92, 1.1). During a dramatic, 10-year decline in seroprevalence of HIV infection, the incidence of HIV infection remained remarkably stable. *Am J Epidemiol* 2001;153:925–34.

acquired immunodeficiency syndrome; HIV; incidence; prevalence; sexually transmitted diseases

Editor's note: *An invited commentary on this article appears on page 935, and the author's response appears on page 938.*

Sexually transmitted disease (STD) clinics have been identified as important sites for measuring the prevalence of infection with human immunodeficiency virus (HIV) because persons attending STD clinics are at increased risk of HIV infection (1–7). Information on the prevalence of HIV infection within selected populations is necessary to plan for health and social services. However, because prevalence data may not identify those groups in whom new infections are occurring, they are less useful for targeting and evaluating primary prevention efforts.

We applied a newly described HIV testing strategy that can distinguish recent infections from those that are long-standing (8) to archived serum specimens that were collected in annual seroprevalence surveys at a municipal STD clinic between 1989 and 1998. The Serologic Testing Algorithm for Recent HIV Seroconversion (STARHS), also referred to as the sensitive/less sensitive (LS) testing method, relies on a dual test strategy in which HIV antibody-positive specimens are retested by using an LS enzyme-linked immunosorbent assay (EIA). Specimens positive on the sensitive EIA and negative on the less sensitive EIA correspond to seroconversion, on average, within the previous 129 days (95 percent confidence interval (CI): 109, 149 days (8)). Because the prevalence of persons who have recently sero-

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Abbreviations: CI, confidence interval; EIA, enzyme-linked immunosorbent assay; HIV, human immunodeficiency virus; HIV-1, human immunodeficiency virus type 1; IDU, injection drug user; LS, less sensitive; MSM, men who have sex with men; OR, odds ratio; STARHS, Serologic Testing Algorithm for Recent HIV Seroconversion; STD, sexually transmitted disease.

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converted is proportional to incidence, we were able to directly compare the temporal trends in seroprevalence and seroincidence at the San Francisco STD clinic.

MATERIALS AND METHODS

Study population

The San Francisco municipal STD clinic is the only public STD clinic in San Francisco, California. Between 1989 and 1998, an average of 80 patients were evaluated each day, the majority of whom were seen for a new problem. Annual blinded seroprevalence surveys were conducted at the San Francisco STD clinic between 1989 and 1998. Consecutive, unduplicated sera that were obtained for routine serologic syphilis testing from all patients who were seen for a new STD complaint or for a routine STD evaluation were tested for HIV antibody after all personal identifiers had been removed from the specimens (9, 10). The seroprevalence study protocols required sampling of all consecutive sera to continue until at least 200 men who have sex with men (MSM), 500 heterosexual men, and 500 women were tested in each year (9). Thus, the duration and total sample achieved varied each year. The study protocol allowed for patients to be included in the survey only once each calendar year. Patients who were returning for follow-up of a previously diagnosed STD or who were visiting the clinic solely for HIV testing were excluded. Patient risk and demographic data were abstracted from the clinic records and were linked to the HIV test results by using a unique study identification number. Protocols for the blinded seroprevalence surveys have been described in detail elsewhere (4, 9, 10). Information on diagnosis of gonorrhea at the time of HIV testing was available beginning in 1990 and was abstracted from the medical record.

Laboratory methods

Serum specimens were screened for human immunodeficiency virus type 1 (HIV-1) antibodies by using a conventional sensitive EIA (Vironostika HIV-1 Microelisa; Organon Teknika, Durham, North Carolina). Repeatedly reactive specimens were confirmed to be positive by Western blot (Bio-Merieux Vitek, Inc., Rockville, Maryland). After testing, specimens were stored at –20°C.

Positive specimens were removed from storage, thawed, and tested with an LS HIV-1 antibody EIA (3A11-LS). Sample dilution as well as sample and conjugate incubation times were modified from the conventional method (HIV-1 EIA [3A11]; Abbott Laboratories, Abbott Park, Illinois) to render the test LS (8). Specimens with a calculated standard optical density (sample optical density-negative control optical density/positive control optical density) of 1.500 or less were retested in triplicate. Retested specimens that had a mean standard optical density of 0.750 or less were defined as "nonreactive," and those that had a mean standard optical density of more than 0.750 were defined as "reactive" (8).

Specimens that were initially positive by the Organon Teknika Vironostika HIV-1 Microelisa were not retested with the standard Abbott [3A11]. Analysis of laboratories performing either test on the Centers for Disease Control Model Performance Evaluation Program HIV-1 antibody panels found comparable sensitivity with their test results (11–13).

Statistical methods

Persons who tested reactive with the sensitive (Vironostika HIV-1) assay and nonreactive with the LS (3A11-LS) assay were classified as having recent HIV infection. The estimated length of the average interval during which persons test reactive on the sensitive assay but nonreactive on the LS assay is 129 days (95 percent CI: 109, 149 days). Persons who tested reactive on both the sensitive assay and the LS assay were considered to have seroconverted sometime beyond the previous 129 days and were classified as having longer-standing infections.

The prevalence of recent HIV infection was estimated as the number of persons with recent infections (Vironostika reactive and 3A11LS nonreactive) divided by the number of uninfected persons (Vironostika nonreactive) plus the number of persons with recent infections (Vironostika reactive and 3A11LS nonreactive). HIV incidence, expressed as percent per year, was estimated by multiplying the prevalence of recent infection by $(365/129) \times 100$. Ninety-five percent confidence intervals for the estimated HIV incidences were constructed by using a Bonferroni procedure described previously (8, appendix 1).

Temporal trends in the demographic characteristics of the clinic population, seroprevalence, and seroincidence were evaluated by using logistic regression models. Changes in the clinic population were assumed to be negligible within any calendar year. To assess the possible influence of temporal changes in the clinic population on the trends in prevalence and incidence, we evaluated trends in prevalence and incidence, controlling for all demographic and risk characteristics in a multivariable logistic regression model for all observations as well as for MSM alone, which is the variable most predictive of HIV infection. In addition, we reestimated the prevalence and incidence trends, directly standardized to the overall distribution of the sex, age, race/ethnicity, and risk group of the clinic population.

RESULTS

Study population

The STD clinic evaluated an average of 11,727 patients each year between 1989 and 1998. The number of patients seen decreased from 13,829 in 1989 to 9,429 in 1998.

Between 1989 and 1998, a total of 34,866 serum samples were collected according to the HIV seroprevalence study protocols (table 1). The demographic characteristics of the sampled population changed modestly during the study period. The distribution of sampled patients by gender was stable until 1998, when the proportion of female patients increased slightly. The proportion of patients under age 25 years declined and that of White patients increased during

TABLE 1. Temporal trends in the characteristics of study patients at the sexually transmitted disease clinic, San Francisco, California, 1989–1998

Characteristic	Total sampled population (1989–1998)		1989		1990		1991		1992		1993	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total no. of clinic patients	117,272		13,829		14,746		14,590		13,606		11,654	
Total no. of specimens	34,866		2,297		3,179		3,569		3,273		3,598	
Gender*												
Male	26,730	76.7	1,788	77.8	2,498	78.6	2,717	76.1	2,496	76.3	2,752	76.5
Female	8,080	23.2	509	22.2	681	21.4	852	23.9	776	23.7	846	23.5
Age (years)†												
≤24	9,689	27.8	749	32.6	983	30.9	1,187	33.3	1,017	31.1	1,035	28.8
25–34	14,972	42.9	953	41.5	1,355	42.6	1,445	40.5	1,396	42.7	1,564	43.5
35–44	7,147	20.5	442	19.2	605	19.0	655	18.4	618	18.9	669	18.6
≥45	2,926	8.4	153	6.7	226	7.1	265	7.4	222	6.8	304	8.5
Race/ethnicity‡												
White	14,449	41.4	916	39.9	1,211	38.1	1,432	40.1	1,321	40.4	1,399	38.9
African American	10,032	28.8	828	36.1	1,178	37.1	1,168	32.7	1,016	31.0	1,110	30.9
Latino	6,760	19.4	371	16.2	564	17.7	675	18.9	683	20.9	720	20.0
Asian/other	3,446	9.9	181	7.9	222	7.0	283	7.9	247	7.6	333	9.4
Risk group												
MSM§	7,437	21.3	440	19.2	626	19.7	695	19.5	650	19.9	700	19.5
MSM and IDU§	737	2.1	114	5.0	90	2.8	80	2.2	50	1.5	46	1.3
IDU	1,402	4.0	153	6.7	152	4.8	171	4.8	137	4.2	109	3.0
Heterosexual/no known risk	25,290	72.5	1,590	69.2	2,311	72.7	2,623	73.5	2,436	74.4	2,743	76.2

Table continues

the study period. The proportion of MSM was stable until 1996, when it increased. Despite these changes, in each time period most of the subjects were male, less than age 35 years, and heterosexual. Whites accounted for 41.4 percent of the subjects during the study period.

TABLE 1. Continued

Characteristic	1994		1995		1996		1997		1998	
	No.	%	No.	%	No.	%	No.	%	No.	%
Total no. of clinic patients	10,434		9,795		9,725		9,464		9,429	
Total no. of specimens	3,539		4,046		3,571		3,885		3,909	
Gender*										
Male	2,717	76.8	3,155	78.0	2,748	77.0	2,956	76.1	2,903	74.3
Female	822	23.2	836	20.7	823	23.1	929	23.9	1,006	25.7
Age (years)†										
≤24	1,051	29.7	1,060	26.2	814	22.8	886	22.8	907	23.2
25–34	1,499	42.4	1,758	43.5	1,607	45.0	1,689	43.5	1,706	43.6
35–44	695	19.6	850	21.0	817	23.9	878	22.6	918	23.5
≥45	292	8.3	329	8.1	333	9.3	428	11.0	374	9.6
Race/ethnicity‡										
White	1,316	37.2	1,598	39.5	1,661	46.5	1,781	45.8	1,614	46.4
African American	1,030	29.1	1,123	27.8	812	22.7	870	22.4	897	23.0
Latino	774	21.9	835	20.6	656	18.4	724	18.6	758	19.4
Asian/other	412	11.6	415	10.3	442	12.4	490	12.6	416	10.6
Risk group										
MSM	694	19.6	793	19.6	809	22.7	1,072	27.6	958	24.5
MSM and IDU	65	1.8	81	2.0	64	1.8	95	2.5	52	1.3
IDU	139	3.9	142	3.5	127	3.6	161	4.1	111	2.8
Heterosexual/no known risk	2,641	74.6	3,030	75.0	2,571	72.0	2,557	65.8	2,788	71.3

* Excludes 56 persons for whom gender was not known. Percents based upon total observations.
† Excludes 132 persons for whom age was not known. Percents based upon total observations.
‡ Excludes 179 persons for whom race/ethnicity was not known. Percents based upon total observations.
§ MSM, men who have sex with men; IDU, injection drug users.

TABLE 2. Temporal trends in HIV* seroprevalence at the sexually transmitted disease clinic, San Francisco, California, 1989–1998

Characteristic	Total		1989		1990		1991		1992		1993	
	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+
Total no.	34,866	9.5	2,297	15.2	3,179	13.1	3,569	10.5	3,273	9.4	3,598	9.4
Gender†												
Male	26,730	12.0	1,788	18.9	2,498	15.9	2,717	13.3	2,496	12.0	2,752	11.9
Female	8,080	1.4	509	2.0	681	2.9	852	1.8	776	1.0	846	1.4
Age (years)‡												
≤24	9,689	2.2	749	5.1	983	4.1	1,187	2.2	1,017	2.2	1,035	1.0
25–34	14,972	10.4	953	19.0	1,353	16.0	1,445	13.2	1,396	11.3	1,564	11.2
35–44	7,147	16.6	422	22.6	605	21.2	665	19.1	618	16.7	669	17.0
≥45	2,926	12.0	153	19.0	226	13.7	265	12.5	222	9.9	304	12.8
Race/ethnicity§												
White	14,449	12.6	916	22.8	1,211	18.1	1,432	14.7	1,321	12.3	1,399	14.3
African American	10,032	7.6	828	9.2	1,178	9.4	1,168	6.7	1,016	7.5	1,110	6.0
Latino	6,760	8.1	371	14.0	564	12.1	675	9.9	683	7.8	720	7.9
Asian/other	3,446	4.8	181	5.5	222	7.7	283	6.7	247	5.7	338	3.9
Risk group												
MSM*	7,437	30.4	440	50.9	626	43.0	695	37.7	650	34.8	700	34.3
MSM and IDU*	737	44.9	114	71.1	90	61.1	80	47.5	50	38.0	46	47.8
IDU	1,402	6.5	153	11.1	152	7.2	171	7.0	137	5.8	109	7.3
Heterosexual/no known risk	25,290	2.5	1,590	1.6	2,311	3.5	2,623	2.4	2,436	2.2	2,743	2.5
Diagnosis of gonorrhea												
No	29,717	7.7	N/A¶		2,882	12.2	3,086	8.6	2,953	8.5	3,466	8.9
Yes	2,852	23.7			297	21.6	483	23.2	320	17.2	132	23.5

Table continues

HIV seroprevalence

The pooled prevalence of all HIV infections was 9.5 percent. HIV prevalence was higher among men (12.0 percent), persons aged 35–44 years (16.6 percent), Whites (12.6 percent), MSM who were also injection drug users (IDU) (44.9 percent), MSM who did not inject drugs (30.4 percent), and patients with incident gonorrhea (23.7 percent) (table 2). The seroprevalence was highest in 1989 (15.2 percent) and declined significantly to 7.2 percent in 1998 (odds ratio (OR) per year = 0.92, 95 percent CI: 0.91, 0.94) (table 2, figure 1). The seroprevalence declined significantly among all demographic and risk groups evaluated except African Americans and heterosexual non-IDUs. MSM, including MSM who injected drugs, exhibited a greater than 50 percent decline in seroprevalence. The prevalence of HIV among persons with gonorrhea increased significantly between 1990 and 1998 (OR per year = 1.1, 95 percent CI: 1.0, 1.1). In the multiple logistic regression models, the decline in prevalence for the clinic total remained after we controlled for all demographic and risk variables (OR per year = 0.89, 95 percent CI: 0.87, 0.90). Similarly, among MSM only, the decline in prevalence remained after adjustment for other demographic variables in the multiple logistic regression model (OR per year = 0.85, 95 percent CI: 0.84, 0.87). Similarly, direct standardization to the overall clinic demographic and risk group distribution did not alter our estimates of the trends in seroprevalence (data not shown).

HIV seroincidence

Of the 3,314 HIV-positive specimens tested as part of the seroprevalence survey, 3,225 (97 percent) were tested by using STARHS. There were 89 HIV-positive specimens that were unable to be retested using STARHS because of insufficient sera quantity or incomplete identification of the specimen.

The incidence of HIV was 1.6 percent per year for the period 1989–1998. Incidence was highest among men (1.9 percent per year), persons aged 35–44 years (2.0 percent per year), Whites (2.5 percent per year), MSM (6.6 percent per year), and MSM IDU (8.2 percent per year) (table 3).

For the period 1989–1998, the incidence of HIV infection fluctuated (range, 0.76–2.3 percent per year) but did not demonstrate a temporal trend (OR per year = 1.0, 95 percent CI: 0.98, 1.1) (figure 1, table 3). The incidence declined among persons aged less than 25 years, from 2.0 percent per year in 1989 to 0.32 percent per year in 1998 (OR = 0.88, 95 percent CI: 0.77, 1.0). African Americans also experienced a significant decline in incidence, from 1.5 percent per year in 1989 to 0.68 percent per year in 1998 (OR = 0.84 per year, 95 percent CI: 0.72, 0.97). The incidence increased among persons aged 35–44 years, from zero in 1989 to 4.5 percent per year in 1998 (OR per year = 1.2, 95 percent CI: 1.1, 1.3). The incidence among all other demographic and risk groups was relatively stable between 1989 and 1998. In the multiple logistic regression model of recent HIV infection, a significant temporal trend in incidence was not observed after controlling for all demographic and risk

TABLE 2. Continued

Characteristic	1994		1995		1996		1997		1998		OR*	95% CI*
	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+	No. tested	% HIV+		
Total no.	3,539	8.0	4,046	9.1	3,571	8.1	3,885	8.0	3,909	7.2	0.92	0.91, 0.94
Gender†												
Male	2,717	10.1	3,155	11.0	2,748	10.2	2,956	10.1	2,903	9.4	0.93	0.91, 0.94
Female	822	0.9	836	1.6	823	1.1	929	1.1	1,006	0.7	0.89	0.83, 0.95
Age (years)‡												
≤24	1,051	1.7	1,060	2.3	814	1.4	886	1.1	907	1.0	0.84	0.80, 0.89
25–34	1,499	8.3	1,758	9.3	1,607	7.3	1,689	6.6	1,706	6.6	0.87	0.86, 0.89
35–44	695	14.8	850	15.5	817	15.4	878	15.8	918	13.0	0.94	0.92, 0.96
≥45	292	12.3	329	12.2	333	9.9	428	11.5	374	10.7	0.96	0.92, 0.96
Race/ethnicity§												
White	1,316	11.2	1,598	12.3	1,661	9.9	1,781	9.7	1,814	7.9	0.89	0.88, 0.92
African American	1,030	7.5	1,123	7.0	812	6.8	870	7.8	897	8.0	0.98	0.96, 1.01
Latino	774	5.7	835	6.0	656	6.1	724	6.4	758	6.7	0.91	0.89, 0.94
Asian/other	412	3.4	415	3.9	442	6.6	490	4.1	416	3.4	0.94	0.89, 0.96
Risk group												
MSM*	694	29.1	793	28.0	809	25.0	1,072	20.6	958	19.9	0.86	0.85, 0.88
MSM and IDU*	65	49.2	81	28.4	64	26.6	95	31.6	52	26.9	0.82	0.78, 0.86
IDU	139	5.8	142	4.2	127	3.2	161	6.8	111	5.4	0.92	0.86, 0.99
Heterosexual/no known risk	2,641	1.5	3,030	3.9	2,571	2.5	2,557	1.8	2,788	2.5	1.0	0.97, 1.0
Diagnosis of gonorrhea												
No	3,241	6.7	3,666	7.6	3,302	6.5	3,557	6.0	3,564	5.3	0.91	0.90, 0.93
Yes	298	21.5	380	23.7	269	26.8	328	29.3	345	26.4	1.1	1.0, 1.1

* HIV, human immunodeficiency virus; OR, odds ratio; CI, confidence interval; MSM, men who have sex with men; IDU, injection drug users.
† Excludes 56 persons for whom gender was not known. Percents based upon total observations.
‡ Excludes 132 persons for whom age was not known. Percents based upon total observations.
§ Excludes 179 persons for whom race/ethnicity was not known. Percents based upon total observations.
¶ Information on diagnosis of gonorrhea was not collected in 1989.

variables (OR per year = 0.99, 95 percent CI: 0.94, 1.0). Similarly, among MSM only, a significant trend in incidence was not observed after adjustment for other demographic variables in the multiple logistic regression model (OR per year = 0.99, 95 percent CI: 0.94, 1.1). In addition, direct standardization to the overall clinic demographic and risk group distribution did not alter our estimates of the trends in seroincidence (data not shown).

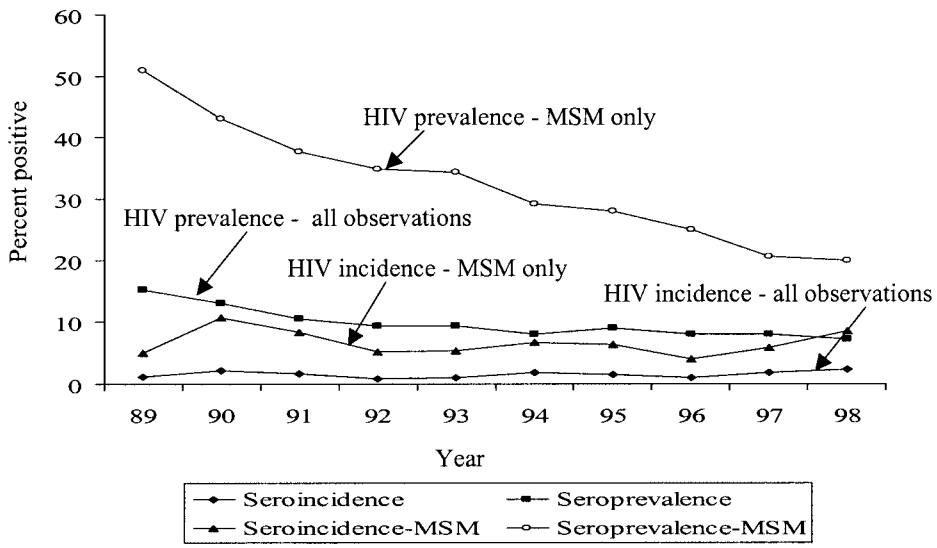

FIGURE 1. Trends in HIV seroincidence and seroprevalence, San Francisco, California, 1989–1998.

TABLE 3. Temporal trends in HIV* seroincidence at the sexually transmitted disease clinic, San Francisco, California, 1989–1998†

Characteristic	Total		1989		1990		1991		1992		1993	
	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)
Total no.	174/31,726	1.6	8/1,957	1.2	21/2,784	2.1	19/3,212	1.7	8/2,974	0.76	12/3,271	1.0
Gender‡												
Male	161/23,697	1.9	6/1,456	1.2	19/2,121	2.5	18/2,374	2.2	6/2,205	1.0	11/2,436	1.3
Female	12/7,981	0.43	2/501	1.1	2/663	0.85	1/838	0.34	0/788	0	1/835	0.34
Age (years)§												
≤24	31/9,512	0.92	5/716	2.0	4/947	1.2	6/1,167	1.5	3/998	0.85	1/1,026	0.28
25–34	86/13,507	1.8	3/775	1.1	13/1,151	3.2	8/1,262	1.8	5/1,243	1.1	6/1,396	1.2
35–44	43/6,001	2.0	0/342	0	4/481	2.4	4/534	2.1	0/515	0	1/556	0.51
≥45	13/2,586	1.4	0/124	0	0/195	0	1/233	1.2	0/200	0	4/268	4.2
Race/ethnicity¶												
White	113/12,737	2.5	3/710	1.2	10/1,002	2.8	10/1,232	2.3	6/1,164	1.5	9/1,208	2.1
African American	29/9,302	0.88	4/756	1.5	8/1,075	2.1	6/1,096	1.6	0/940	0	2/1,045	0.54
Latino	24/6,239	1.1	1/320	0.88	2/498	1.1	2/610	0.93	2/632	0.90	1/664	0.43
Asian/other	7/3,287	0.60	0/171	0	1/208	1.4	1/265	0.07	0/233	0	0/325	0
Risk group												
MSM*	124/5,302	6.6	4/220	5.1	14/371	10.7	13/446	8.3	8/432	5.2	9/469	5.4
MSM and IDU*	12/418	8.2	2/35	16.2	1/36	7.9	0/42	0	0/31	0	0/24	0
IDU	77/1,318	7.5	1/137	2.1	1/142	2.0	2/161	3.5	0/129	0	0/101	0
Heterosexual/no known risk	31/24,668	0.36	1/1,565	0.18	5/2,235	0.63	4/2,563	0.44	0/2,382	0	3/2,677	0.32
Diagnosis of gonorrhea												
No	119/27,545	1.2	NA#		13/2,543	**	13/2,835	**	5/2,706	**	10/3,168	**
Yes	4/72,224	6.0	NA		8/241	**	6/337	**	3/268	**	2/103	**

Table continues

TABLE 3. Continued

Characteristic	1994		1995		1996		1997		1998		OR*	95% CI*
	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)	No. HIV+/ no. tested	Rate (%/year)		
Total no.	21/3,278	1.8	19/3,697	1.5	12/3,295	1.0	24/3,600	1.9	30/3,658	2.3	1.0	0.98, 1.1
Gender‡												
Male	19/2,461	2.2	15/2,824	1.5	12/2,481	1.4	23/2,680	2.4	30/2,659	3.2	1.1	1.0, 1.1
Female	2/817	0.69	3/826	1.0	0/814	0	1/920	0.31	0/999	0	0.85	0.69, 1.1
Age (years)§												
≤24	4/1,037	1.1	2/1,038	0.55	1/804	0.35	4/880	1.3	1/899	0.32	0.88	0.77, 1.0
25–34	11/1,385	2.3	9/1,603	1.6	6/1,495	1.1	12/1,590	2.1	13/1,607	2.3	1.0	0.93, 1.1
35–44	5/597	2.4	5/723	2.0	5/695	2.0	6/745	2.3	13/812	4.5	1.2	1.1, 1.3
≥45	1/257	1.1	2/291	2.0	0/300	0	2/381	1.5	3/337	2.5	1.1	0.90, 1.4
Race/ethnicity¶												
White	15/1,184	3.6	13/1,414	2.6	5/1,502	0.94	20/1,628	3.5	22/1,693	3.7	1.1	1.0, 1.1
African American	2/955	0.59	2/1,046	0.54	3/760	1.2	0/802	0	2/827	0.68	0.84	0.72, 0.97
Latino	4/734	1.5	2/770	0.74	2/618	0.92	3/681	1.3	5/712	2.0	1.1	0.92, 1.3
Asian/other	0/398	0	1/400	0.71	2/415	1.4	1/471	0.60	1/403	0.70	1.1	0.80, 1.4
Risk group												
MSM	12/504	6.7	13/586	6.3	9/616	4.1	18/864	5.9	24/791	8.6	0.99	0.92, 1.1
MSM and IDU	2/35	16.2	0/58	0	1/48	5.9	5/70	20.2	1/39	7.3	1.1	0.88, 1.3
IDU	2/133	3.7	0/136	0	0/123	0	0/150	0	1/106	2.7	0.89	0.68, 1.2
Heterosexual/no known risk	5/2,606	0.54	6/2,919	0.58	2/2,508	0.23	1/2,511	0.11	4/2,722	0.42	0.98	0.87, 1.1
Diagnosis of gonorrhea												
No	20/3,043	**	15/3,403	**	9/3,095	**	19/3,363	**	15/3,389	**		
Yes	1/235	**	4/294	**	3/200	**	5/237	**	15/269	**		

* HIV, human immunodeficiency virus; MSM, men who have sex with men; IDU, injection drug users; OR, odds ratio; CI, confidence interval.
† The HIV incidence was calculated as number of recent infections/number of recent infections + number HIV-negative) and annualized by multiplying this number by (129/365).
‡ Excludes 56 persons for whom gender was not known. Percents based upon total observation.
§ Excludes 132 persons for whom age was not known. Percents based upon total observations.
¶ Excludes 179 persons for whom race/ethnicity was not known. Percents based upon total observations.
# Information on diagnosis of gonorrhea was not collected in 1989.
** Incidence of HIV could not be calculated for persons with incident gonorrhea.

Gonorrhea among persons with recent HIV infection

Forty-seven (28 percent) of the 166 persons with recent HIV infection between 1990 and 1998 had gonorrhea at the time of HIV testing. Although the proportion of persons with recent HIV infection who were diagnosed with gonorrhea fluctuated between 1990 and 1998, a significant trend was not observed. However, 50 percent of the persons with recent HIV infection in 1998 were diagnosed with gonorrhea at the time of their HIV test.

DISCUSSION

To our knowledge, this is the first published application of the STARHS testing strategy to assess HIV incidence in a STD clinic. Although studies have attempted to estimate trends in HIV incidence among STD clients through serial cross-sectional seroprevalence surveys (9, 10) and record-based incidence studies (6), our data indicate that temporal trends in the prevalence of HIV infections do not reflect trends in seroincidence. During a 10-year period of steady and dramatic declines in the prevalence of HIV infections, the rate of new HIV infections among San Francisco STD clients remained relatively stable. Our results support other findings that persons attending STD clinics are at high risk of HIV infection (1–7) and that declines in prevalence are not necessarily accompanied by declines in incidence in this population (14–17). In the case of our STD clinic, the decline in seroprevalence, seen in virtually all demographic and risk groups evaluated, is probably due to persons with long-standing infection, who by virtue of receiving HIV-related care elsewhere stopped attending the STD clinic in later years.

STARHS testing in sentinel sites such as STD clinics may prove superior to other methods of estimating HIV incidence. The STARHS testing strategy is inexpensive ($30 per specimen), needs to be performed only on those specimens that are HIV antibody positive by conventional testing, and can be performed on fresh or archived specimens (8). The STARHS testing method is not only markedly less expensive than traditional cohort studies but also avoids some of the biases of cohorts. In particular, with closed cohorts, the number of susceptible persons declines over time, the personal characteristics of persons who enroll and remain in cohort studies usually differ from the population of interest, and the behavioral interventions provided in cohort studies may affect the behavior of the participants (18–20). Although the high prevalence of HIV infection among MSM in San Francisco may have reduced the size of the susceptible population, this is likely to have been offset by the ongoing influx of at-risk persons moving to San Francisco and through the aging of uninfected children and teens.

Our large sample sizes of over 30,000 specimens allowed assessment of temporal trends for HIV incidence within demographic and risk subgroups. The decline in incidence among African Americans and persons under age 25 years may have been due to the small numbers of seroconversions, including 2 years during which there were no new infections among African Americans. To overcome this limitation, we reanalyzed the seroincidence trends among African Americans and persons under age 25 years in linear, 2-year blocks. The decline in seroincidence remained significant for African Americans (OR per year = 0.69, 95 percent CI: 0.52, 0.92) and for persons under age 25 years (OR = 0.78, 95 percent CI: 0.60, 1.0). Whether these trends are the result of decreases in higher-risk persons attending the clinic in later years or reflect true declines in HIV incidence is unknown.

The prevalence of both recent and long-standing HIV infection among persons who were coinfected with gonorrhea was very high. Our findings support other studies that have documented the association of HIV infection with gonorrhea (21–23). The occurrence of gonorrhea among persons with long-standing HIV infection highlights the need to target prevention efforts to HIV-infected persons to prevent secondary HIV transmission (24).

Within this study population, the high prevalence of recent and long-standing HIV infection among persons with gonorrhea appears to be predominately among MSM. The prevalence of all HIV infections among MSM with gonorrhea was 45.7 percent, much higher than the prevalence of all HIV infection among non-MSM with gonorrhea (6.7 percent). Of the 47 persons with both gonorrhea and recent HIV infection, 43 (91 percent) were MSM (data not shown). These differences demonstrate that MSM are most likely to acquire HIV sexually and that non-MSM, even those attending the STD clinic, acquire HIV infection through other types of exposures. The high rates of HIV infection among MSM with gonorrhea is particularly worrisome because of the recent increase in rectal gonorrhea and high-risk sexual behavior among MSM in San Francisco (25–27) and increases in other bacterial STD among MSM elsewhere (28). Our findings clearly support recommendations for HIV prevention through the early detection and treatment of STD and through HIV testing and counseling among STD clinic patients (29, 30).

There are several limitations to consider when interpreting the results of this study. Four percent of the persons at the end stage of the acquired immunodeficiency syndrome may have low levels of HIV antibody and be falsely classified by STARHS as having early HIV infection (8). However, persons with end-stage acquired immunodeficiency syndrome are less likely to be sexually active and more likely to receive their medical care, including testing for STD, from their regular medical providers. In addition, this population represents only a very small proportion of persons seeking services at the San Francisco STD clinic and would be unlikely to substantially affect our results.

A more significant limitation is that misclassification may also occur because some persons who receive antiretroviral treatment that includes a protease inhibitor early in the course of their infection may have a decline in antibody and revert to a negative test with the less sensitive assay (31). Protease inhibitors were introduced in 1996 but were initially recommended only for persons with severe immunodeficiency (32). Treatment with protease inhibitors for HIV-infected persons with relatively intact immune systems was first recommended after those years (33).

Thus, it is possible that our calculations of the seroincidence in 1997 and 1998 were overestimates of the actual

incidence in those years. Unfortunately, we did not have data on the use of protease inhibitors in our study population. For 1997 and 1998, we did have information on persons who reported a prior positive HIV test. This allowed us to conduct a supplementary analysis in which we reclassified recently infected persons who reported a prior positive HIV test as having long-standing infections. This would have the effect of excluding persons who may have been receiving protease therapy and who may have been misclassified as having recently seroconverted. Exclusion of these persons did not substantially alter our results. Incidence changed from 1.9 to 1.7 percent per year in 1997 and from 2.3 to 1.4 percent per year in 1998. The change was somewhat greater for MSM in whom the prevalence of recent infection decreased from 5.9 to 4.9 percent per year in 1997 and from 8.6 to 4.7 percent per year in 1998. Among MSM, these changes resulted in a marginally significant linear trend ($p = 0.04$), although the incidence in 1989 (5.1 percent per year) was similar to that in 1998 (4.7 percent per year). Unfortunately, excluding persons who have a history of positive test results probably also excludes those who have seroconverted within the 4-month window period of the LS assay. Thus, the incidence probably lies somewhere between the two estimates. Future studies that use STARHS methodology should include information on known HIV infection and the use of antiretroviral therapies.

Misclassification due to the optical density cutoff levels of LS assay, although estimated to be small (0.4 percent), may have biased our overall estimate of incidence (8). However, because this is a nondifferential misclassification, it would not bias our temporal findings or correlates of increased incidence.

The application of the STARHS testing strategy to estimate incidence in the STD clinic patients may be problematic, since the base population is not known and its size and composition may have varied during the study period both in absolute numbers and relative to the larger San Francisco population. For example, if the decline in the number of patients seen at the STD clinic during the period reflects a true decline in sexual risk behaviors in the population, then the stable HIV incidence we observed would reflect a decline in incidence in the base population.

Although the reduction in HIV incidence that occurred in the early 1980s has been credited, at least in part, to prevention programs in San Francisco, it appears that these efforts have, at best, been effective only to the point of holding incidence levels stable in this decade. Preventive vaccines, reduction in viral load through optimal antiretroviral therapies in HIV-infected persons, as well as new prevention tools may be necessary for further reductions in the rate of new HIV infections. If, in fact, persons with early HIV infection are more infectious than persons in later stages of disease (34), then the ability to identify these persons may provide the opportunity to interrupt transmission through more focused behavioral efforts, treatment, and partner notification (35). The STARHS testing strategy may be one of the new tools that will help drive the incidence of HIV infection down.

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REFERENCES

1. Quinn TC, Glasser D, Cannon RO, et al. Human immunodeficiency virus infection among patients attending clinics for sexually transmitted diseases. N Engl J Med 1988;318:197–203.
2. Cannon RO, Schmid GP, Moore PS, et al. Human immunodeficiency virus (HIV) seroprevalence in persons attending STD clinics in the United States, 1985–1987. Sex Transm Dis 1989; 16:184–9.
3. Chiasson MA, Stoneburner RL, Lifson AR, et al. Risk factors for human immunodeficiency virus type 1 (HIV-1) infection in patients at a sexually transmitted disease clinic in New York City. Am J Epidemiol 1990;131:208–20.
4. Schwarcz SK, Bolan GA, Kellogg TA, et al. Comparison of voluntary and blinded human immunodeficiency virus type 1 (HIV-1) seroprevalence surveys in a high prevalence sexually transmitted disease clinic population. Am J Epidemiol 1993; 137:600–8.
5. Lehner T, Chiasson MA. Seroprevalence of human immunodeficiency virus type 1 and sexual behaviors in bisexual African-American and Hispanic men visiting a sexually transmitted disease clinic in New York City. Am J Epidemiol 1998; 147:269–72.
6. Weinstock H, Sweeney S, Satten GA, et al. HIV seroincidence and risk factors among patients repeatedly tested for HIV attending sexually transmitted disease clinics in the United States, 1991–1996. J Acquir Immune Defic Syndr Hum Retrovirol 1998;19:506–12.
7. Kassler W, Zenilman JM, Erickson B, et al. Seroconversion in patients attending sexually transmitted disease clinics. AIDS 1994;8:351–5.
8. Janssen RS, Satten GA, Stramer SL, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. JAMA 1998;280: 42–8.
9. Dondero TJ, Pappaioanou M, Curran JW. Monitoring the levels and trends of HIV infection: the Public Health Satlervice's HIV Surveillance Program. Public Health Rep 1990;103:213–20.
10. Pappainoanou M, Dondero TJ Jr, Peterson LR, et al. The family of HIV seroprevalence surveys: objectives, methods, and uses of sentinel surveillance for HIV in the United States. Public Health Rep 1990;105:113–19.
11. Centers for Disease Control and Prevention. Analysis of the January 26, 1998 performance evaluation HIV-1 antibody testing results. Model Performance Evaluation Program (MPEP): testing for HIV-1 antibody. Atlanta, GA: Centers for Disease Control and Prevention, 1998.
12. Centers for Disease Control and Prevention. Analysis of the August 17, 1998 performance evaluation HIV-1 antibody testing results. Model Performance Evaluation Program (MPEP): testing for HIV-1 antibody. Atlanta, GA: Centers for Disease Control and Prevention, 1999.
13. Centers for Disease Control and Prevention. Analysis of the January 25, 1999 performance evaluation HIV-1 antibody testing results. Model Performance Evaluation Program (MPEP): testing for HIV-1 antibody. Atlanta, GA: Centers for Disease Control and Prevention, 1999.
14. Peterman TA, Zaidi AA, Wroten J. Decreasing prevalence hides a high HIV incidence: Miami. AIDS 1995;9:965–70.

15. Otten MW, Zaidi AA, Peterman TA, et al. High rate of HIV seroconversion among patients attending urban sexually transmitted disease clinics. AIDS 1994;8:549–53.
16. Batter V, Matela B, Nsuami M, et al. High HIV-1 incidence in young women masked by stable overall seroprevelance among childbearing women in Kinshasa, Zaire: estimating incidence from serial seroprevalence data. AIDS 1994;8:811–17.
17. Wawer MJ, Serwadder D, Gray RH, et al. Trends in HIV-1 prevalence may not reflect trends in incidence in mature epidemics: data from the Rakai population-based cohort, Uganda. AIDS 1997;11:1023–30.
18. Brookmeyer R, Quinn T, Sheperd M, et al. The AIDS epidemic in India: a new method for estimating current human immunodeficiency virus (HIV) incidence rates. Am J Epidemiol 1995;142:709–13.
19. Heyward W, Osmanov S, Saba J, et al. Preparation for phase III HIV vaccine efficacy trials: methods for determination of HIV incidence. AIDS 1994;8:1285–92.
20. Laga M, Alary M, Nzila N, et al. Condom promotion, sexually transmitted disease treatment, and declining incidence of HIV-1 infection in female Zairian sex workers. Lancet 1994;344: 246–8.
21. Cohen MS, Hoffman IF, Royce RA, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for HIV prevention of sexual transmission of HIV-1. Lancet 1997;349:1868–73.
22. Laga M, Alary M, Nzila N, et al. Condom promotion, sexually transmitted disease treatment, and declining incidence of HIV-1 infection in female Zairian sex workers. Lancet 1994; 344:246–8.
23. Laga M, Monaka A, Kivuvu M, et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS 1993;7:95–102.
24. Marks G, Burris S, Peterman TA. Reducing sexual transmission of HIV from those who know they are infected: the need for personal and collective responsibility. AIDS 1999;13;297–306.
25. Centers for Disease Control and Prevention. Increases in unsafe sex and rectal gonorrhea among men who have sex with men—San Francisco, California, 1994–1997. MMWR Morbid Mortal Wkly Rep 1999;48:45–8.
26. Ekstrand M, Paul J, Stall R, et al. Increasing rates of unprotected anal intercourse among San Francisco gay men include high UAI rates with a partner of unknown or different serostatus. Presented at the X11 World AIDS Conference, Geneva, Switzerland, June 28 to July 3, 1998 (Abstract 23118).
27. Osmond D, Charlebois E, Page-Shafer K, et al. Increasing risk behavior has not led to higher HIV incidence rates in the San Francisco Young Men's Health Study: 1993–1998. Presented at the XII World AIDS Conference, Geneva, Switzerland, June 28 to July 3, 1998 (Abstract 23115).
28. Williams LA, Klausner JD, Whittington WLH, et al. Elimination and reintroduction of primary and secondary syphilis. Am J Public Health 1999;89:1093–7.
29. Centers for Disease Control and Prevention. HIV prevention through early detection and treatment of other sexually transmitted diseases—United States: Recommendations of the Advisory Committee for HIV and STD Prevention. MMWR Morbid Mortal Wkly Rep 1998;47:14, 17.
30. Centers for Disease Control and Prevention. Public Health Service guidelines for counseling and antibody testing to prevent HIV infection and AIDS. MMWR Morbid Mortal Wkly Rep 1987;36:509–15.
31. Rowal, BD, Hecht FM, Kahn J, et al. Application of a novel "detune" HIV EIA to qualify and monitor anti-retroviral therapy trials in patients with early infection. Presented at the XII World AIDS Conference, Geneva, Switzerland, June 26 to July 3 1998 (Abstract 42118).
32. Carpenter CC, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1996: recommendations of an international panel. JAMA 1996;276:146–54.
33. Carpenter CC, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1997: Updated recommendations of the International AIDS Society—USA panel. JAMA 1997; 27:1962–9.
34. Jacquez JA, Koopman JS, Simon CP, et al. Role of the primary infection in epidemics of HIV infection in gay cohorts. J Acquir Immune Defic Syndr Hum Retrovir 1994;7:1169–84.
35. Cates W Jr, Chesney MA, Cohen MS. Primary HIV infection—a public health opportunity. Am J Public Health 1997; 87:191–3.