

Who Are California's Late HIV Testers? An Analysis of State AIDS Surveillance Data, 2000–2006

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ABSTRACT

Objectives. Late HIV testing leads to preventable, severe clinical and public health outcomes. California, lacking a mature HIV surveillance system, has been excluded from documented analyses of late HIV testers in the United States. We identified factors associated with late HIV testing in the California AIDS surveillance data to inform programs of HIV testing and access to treatment.

Methods. We analyzed data from California AIDS cases diagnosed between 2000 and 2006 and reported through November 1, 2007. Late testers were people diagnosed with HIV within 12 months before their AIDS diagnosis. We identified factors significantly associated with late HIV testing using multivariable logistic regression.

Results. Among 28,382 AIDS cases, 61.2% were late HIV testers. Late testing was significantly associated with those ≥ 35 years of age, heterosexual contact or unknown/other reported transmission risk, and being born outside of the U.S. When further classified by country of birth, people born in Mexico were most likely to be HIV late testers who progressed to AIDS.

Conclusions. Our findings support wider implementation of opt-out HIV testing and HIV testing based in emergency departments. Services for HIV testing and treatment should be inclusive of all populations, but especially targeted to populations that may have more limited access.

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Among the more than one million people in the United States estimated to be infected with human immunodeficiency virus (HIV), nearly one-quarter remain undiagnosed.¹ Increasing evidence suggests that earlier antiretroviral therapy (ART) for HIV improves survival compared with deferred therapy.^{2,3} The benefits of HIV diagnosis well before acquired immunodeficiency syndrome (AIDS) diagnosis are clearly documented and include survival benefit for asymptomatic HIV-infected people with early initiation as compared with deferred initiation of ART,² decreased viral transmission due to lower-serum HIV-1 ribonucleic acid levels⁴ as well as risk modification in people who know their HIV serostatus,⁵ and decreased health expenditures.⁶ In Canada, the estimated annual medical cost of a late presenter, after adjusting for patient characteristics, was more than twice that of a non-late presenter, with a difference of more than \$8,000 per person. This discrepancy is mostly due to hospital care costs, which are 15 times higher for those diagnosed late.⁷

Given that the period from primary HIV infection to AIDS is estimated at seven to eight years⁸ and the Centers for Disease Control and Prevention (CDC) guidelines advocate routine HIV testing for all U.S. adults,⁹ late HIV testing (defined as the first diagnosis of HIV within one year of an AIDS diagnosis)¹⁰ should be an unusual clinical outcome. However, national estimates from CDC reported that 45% of people with AIDS at 16 sites in the U.S. were late testers.¹⁰ Among AIDS surveillance cases in San Francisco and South Carolina, 39% and 41%, respectively, were late testers.^{11,12} In the U.S., AIDS diagnoses can be arguably regarded as a measure of diagnostic or treatment failure.

In California, approximately 85% of adult HIV cases are male, 28% are Hispanic, 20% are African American, and 50% are white. Men who have sex with men (MSM) comprise the main risk exposure for men (77%). For women, heterosexual contact is the main risk exposure (52%), followed by injection drug use (23%).¹³ California is home to about 4.4 million Mexican immigrants, about 40% of the total immigrant population in the U.S., and is a key destination for Mexican migrants.^{11,14} Both the U.S. and Mexico have concentrated HIV epidemics, where prevention and testing campaigns prioritize traditionally high-risk groups such as MSM and injection drug users (IDUs).

The role of migration on the vulnerability of immigrants in California, historically considered a low-risk group, is complex and poorly understood but may have a significant impact on the likelihood of becoming infected with HIV while in the U.S.¹⁵ The denominator of Mexican immigrants in California likely varies by structural factors such as agricultural season. The

effect and extent of this varying denominator on HIV/AIDS estimates is not well characterized. In this analysis of California AIDS surveillance data, we identified factors that are significantly associated with late HIV testing in the state.

METHODS

Cases who meet the 1993 CDC AIDS case definition¹⁶ are required by California law to be reported to local health departments, which in turn report them to the state Office of AIDS. We analyzed AIDS cases in adults and adolescents, aged 13 years and older, diagnosed from January 1, 2000, through December 31, 2006, and reported to the California Office of AIDS by November 1, 2007. People whose first diagnosis of HIV was within 12 months of their AIDS diagnosis were defined as late testers. The term “late tester” is used rather than “late presenter” to highlight the differences between the date of testing and the date of presentation for care, which is unavailable. The term “AIDS diagnosis” is used rather than “AIDS onset” because information on the date of onset is unknown. Cases may have had an earlier date of AIDS onset prior to being formally diagnosed with AIDS. The surveillance data used in this analysis do not include information on the dates of presentation for clinical care or AIDS onset.

The information collected on AIDS cases includes demographic and risk characteristics, country of birth, opportunistic illnesses (OIs) at the time of AIDS diagnosis, and the dates and results of the first and subsequent periodic CD4 T lymphocyte cell and viral-load tests. Additionally, the surveillance data include the date of the patient’s first positive HIV test obtained either from a laboratory report or by physician documentation of HIV infection listed in the medical record. In 2001, the information collected on patients reported with AIDS was expanded to include the date of patient’s self-report of first positive HIV test, and this analysis includes this date for the variable “age at HIV diagnosis.”

The categorization of race/ethnicity is generally based on the self-reported information from medical records. We use the term “Latino” interchangeably with the census term “Hispanic.” We classified the region of birth as one of the following: the U.S. (includes U.S.-dependent areas), Mexico, and foreign-born (other than Mexico). The foreign-born race/ethnicity categories include Mexico-born (all races/ethnicities), Latino foreign-born (not born in Mexico), and other foreign-born. Due to small numbers, Asian race/ethnicity cases could not be analyzed separately.

The HIV exposure risk categories were (1) MSM,

including men who have sex with both men and women; (2) IDUs; (3) MSM who are IDUs; and (4) heterosexuals or people with other risk factors or no risk factor identified. For the time period used in this analysis, the AIDS surveillance data in California could not separate out heterosexual transmission from other risk factors. This has since changed, and current surveillance data are able to differentiate between these categories.

We assessed differences in the distribution of demographic and clinical characteristics using Pearson's Chi-square test for categorical variables. Independent predictors of late testing that were significant at $p < 0.1$ were entered into the model. We assessed factors significantly associated with late testing by using multivariable logistic regression. We conducted the likelihood ratio test and the Hosmer and Lemeshow Chi-square goodness-of-fit test to assess model fit. We determined the prevalence of OIs for late and non-late testers.

RESULTS

A total of 28,382 cases of AIDS were diagnosed in California from 2000 to 2006 and reported to the California Office of AIDS by November 1, 2007. Among these AIDS cases, 17,364 (61.2%) were late testers, and this proportion was stable during the seven years of the data (Table 1). In univariate analysis, late testing occurred more frequently among people aged 35 years and older at HIV diagnosis ($p < 0.001$), people whose risk for HIV infection was heterosexual contact or without a reported risk ($p < 0.001$), people born outside of the U.S. ($p < 0.001$), and people whose AIDS diagnosis included an OI ($p < 0.001$). In multivariable analysis, while controlling for gender in the model, factors that were significantly associated with an increased likelihood of late testing were age 35 years and older at the time of HIV diagnosis (odds ratio [OR] = 2.4, 95% confidence interval [CI] 2.3, 2.6, as compared with the 25–34-year age group) and heterosexual or unknown HIV risk factor (OR=2.4, 95% CI 2.2, 2.6, as compared with MSM).

Additionally, as compared with white U.S.-born cases, Mexico-born cases (OR=3.4, 95% CI 3.1, 3.7), foreign birth among Latinos (category excludes Mexico) (OR=2.1, 95% CI 1.9, 2.4), and cases having an OI at the time of AIDS diagnosis (OR=1.7, 95% CI 1.6, 1.7) were also significantly associated (Table 1). Furthermore, foreign-born Latinos (those born in Mexico and elsewhere) were more likely to be HIV late testers as compared with U.S.-born Latinos in the univariate and multivariable analyses. Separate univariate analyses on race/ethnicity and country of birth were significant

and showed an increased risk of late testing (data not shown). Limiting Mexico-born cases to Latinos removed 18 cases and did not change the OR or its 95% CI, and combining all foreign-born Latinos (cases that identified as Latino or born in Mexico) was still significant for late testing (OR=3.0, 95% CI 2.8, 3.2). Due to issues with the small number of Asian cases in the dataset and the potentially identifying information, we were unable to analyze that specific group. The likelihood ratio test was significant ($p < 0.05$) and the Hosmer and Lemeshow Chi-square goodness-of-fit test was not significant ($p > 0.05$). Both tests indicated the model was well-fitting.

OIs reported at AIDS diagnosis differed for Mexico-born and U.S.-born people (Table 2). Mexico-born AIDS cases (all races/ethnicities) were more likely to present with tuberculosis, both pulmonary and extra-pulmonary, than U.S.-born cases (14% vs. 3%, respectively, $p < 0.001$). Mexico-born AIDS cases were also more likely to present with reactivated disease from the environmental pathogens of cryptococcus, toxoplasmosis, or histoplasmosis than U.S.-born AIDS cases. When comparing late testers with non-late testers, late testers were more likely to present with tuberculosis, both pulmonary and extra-pulmonary (7% vs. 4%), cryptococcus (7% vs. 3%), toxoplasmosis (4% vs. 2%), and *Pneumocystis jirovecii* pneumonia (37% vs. 21%) than non-late testers (all $p < 0.001$) (data not shown).

DISCUSSION

Our analysis found that almost two-thirds (61%) of reported AIDS cases in California were late testers. A literature review from industrialized countries reported prevalence of late testers, defined as CD4/microliter < 200 , among people diagnosed with HIV infection ranging from 24% to 43%, with the U.S. having the highest prevalence.⁷ In San Francisco, among 2,139 AIDS cases reported between 2001 and 2005, 39% were late testers using a definition of late tester similar to the one used in this analysis.¹¹ It is important to note the denominator used when comparing late diagnosis incidence. A proportion of HIV cases may never develop AIDS. As a result, using HIV cases as a denominator will result in a smaller percentage and be more reflective of a population prevalence, as compared with the prevalence of late testers in the population of AIDS cases.

Consistent with most prior studies, we found late testing was more common among groups not traditionally considered, and/or who may not consider themselves, to be at high risk of infection and who may not actively be offered or seek HIV testing. Studies^{11,17–19}

have reported that late HIV testing was less common among MSM and IDUs compared with heterosexuals and those reporting an unknown mode of transmission. Also consistent with most,^{17,20} but not all,¹¹ prior studies, we found older age was associated with late diagnosis. Older age was found to be the strongest risk factor for

disease progression from HIV to AIDS or death within one and three years in a population-based analysis in the U.S.²¹ U.S.-born Latinos in our study were found to be at increased risk for late testing when compared with U.S. white people. This was also reported in a study in 16 U.S. sites between 2000 and 2003.¹⁰

Table 1. Late HIV testing among people with AIDS in California, 2000–2006: prevalence, characteristics, and independent predictors^a

Characteristic	Total N	Late tester N (percent)	P-value ^b	AOR (95% CI)
Total	28,382	17,364 (61.2)		
Year of AIDS diagnosis				
2000	4,490	2,854 (63.6)		
2001	4,363	2,845 (65.2)		
2002	4,610	2,821 (61.2)		
2003	4,264	2,519 (59.1)		
2004	3,769	2,260 (60.0)		
2005	3,546	2,074 (58.5)		
2006	3,340	1,991 (59.6)		
Gender			0.305	
Male	24,643	15,105 (61.3)		1.8 (1.7, 2.0)
Female	3,739	2,259 (60.4)		Referent
Age group (in years) at HIV diagnosis			<0.001	
13–24	2,633	940 (35.7)		0.5 (0.5, 0.6)
25–34	9,081	4,511 (49.7)		Referent
35–44	10,227	6,926 (67.7)		2.4 (2.3, 2.6)
≥45	6,441	4,987 (77.4)		4.0 (3.7, 4.3)
Risk factor			<0.001	
MSM	16,219	9,540 (58.8)		Referent
IDU	3,324	1,916 (57.6)		1.0 (0.9, 1.1)
MSM and IDU	2,281	971 (42.6)		0.6 (0.5, 0.7)
Heterosexual/other ^c	6,558	4,937 (75.3)		2.4 (2.2, 2.6)
Race/ethnicity and country of birth			<0.001	
U.S.-born white	10,933	5,783 (52.9)		Referent
U.S.-born Latino	3,711	2,416 (65.1)		2.0 (1.8, 2.1)
U.S.-born black	5,562	3,201 (57.6)		1.2 (1.1, 1.3)
U.S.-born other	605	364 (60.2)		1.6 (1.3, 1.9)
Foreign-born/other	1,559	1,109 (71.1)		2.1 (1.8, 2.3)
Mexico-born	4,468	3,422 (76.6)		3.4 (3.1, 3.7)
Foreign-born/other Latino	1,544	1,069 (69.2)		2.1 (1.9, 2.4)
Initial AIDS diagnosis			<0.001	
CD4 count <200 (14%)	18,749	10,653 (56.8)		Referent
Opportunistic illness	9,621	6,705 (69.7)		1.7 (1.6, 1.7)

^aPredictors with $p < 0.1$ were entered into the model. Model was controlled for gender. Good model fit was assessed according to the likelihood ratio test and the Hosmer and Lemeshow test.

^bTesting for differences between proportions

^cIncludes heterosexual, other risk factors, no reported risk, and unknown risk

HIV = human immunodeficiency virus

AIDS = acquired immunodeficiency syndrome

AOR = adjusted odds ratio

CI = confidence interval

MSM = men who have sex with men

IDU = injection drug user

Table 2. Top-10 common opportunistic illnesses present at AIDS diagnosis among Mexico-born cases compared with U.S.-born cases, California, 2000–2006

<i>Opportunistic illness</i>	<i>Total N</i>	<i>Mexico-born N (percent)</i>	<i>U.S.-born N (percent)</i>	<i>P-value^a</i>
Total	8,511	1,624 (100.0)	6,887 (100.0)	
Pneumocystis jirovecii pneumonia	2,792	446 (27.5)	2,346 (34.1)	<0.001
Wasting syndrome	1,596	302 (18.6)	1,294 (18.8)	0.858
Candidiasis esophageal	1,212	219 (13.5)	993 (14.4)	0.333
Chronic mucocutaneous herpes	694	107 (6.6)	587 (8.5)	<0.05
Kaposi's sarcoma	651	85 (5.2)	566 (8.2)	<0.001
Cryptococcosis	509	184 (11.3)	325 (4.7)	<0.001
Mycobacterial tuberculosis	442	228 (14.0)	214 (3.1)	<0.001
Cytomegalovirus disease	252	47 (2.9)	205 (3.0)	0.860
Toxoplasmosis of brain	232	107 (6.6)	125 (1.8)	<0.001
Candidiasis lungs	176	42 (2.6)	134 (2.0)	0.103

^aTesting for differences between proportions

AIDS = acquired immunodeficiency syndrome

Immigrants in our California study, especially those born in Mexico, were more likely to be late HIV testers compared with white people born in the U.S. Migrants in other countries have been found to be at increased risk of HIV late presentation compared with people born in the country of study.^{17,18,22–24} Analysis from an unlinked HIV serosurvey of 61,120 specimens from sexually transmitted disease (STD) clinic attendees in Los Angeles County found that HIV-infected Mexican and Central American immigrants had an average age at immigration of 20.7 years and had been in the U.S. an average of 10 years.²⁵ This finding suggests that most of the Mexican and Central American HIV-infected immigrants in this Los Angeles County STD clinic survey were infected after immigrating to the U.S.

Length of time living in the U.S. seems to affect HIV risk among Latino immigrants in California. In one Northern California study, Latino immigrant men who had been in the U.S. fewer than five years compared with immigrants who had been in the U.S. more than five years were less likely to have a main sex partner, less likely to report ever being HIV tested, and more likely to report commercial sex worker use.²⁶ There are various possible reasons as to why California immigrants are more likely to be late testers. Latino immigrants may be less likely to access and use prevention and care services because of their language, culture, and work or community environments.^{27,28} Latino immigrant MSM are less likely to identify as gay compared with U.S.-born MSM²⁹ and, as a result, may not be reached by social marketing campaigns aimed at gay-identified MSM. Linguistically and culturally appropriate HIV materials and information may not always permeate Latino community sites for work and leisure. Immigrants may also feel stigmatized, not fully understand

health-care services available in California, and prefer not accessing health-care services in the U.S.

Limitations

Our study had several limitations. We used AIDS surveillance data, which exclude HIV-infected people who may never progress to AIDS. In most states, AIDS cases are more likely to be reported with a low CD4 count rather than an AIDS indicator disease/OI. This would make our reported OIs representative of OIs at AIDS diagnosis rather than the prevalence of OIs. We were unable to control for important socioeconomic variables, such as education level or insurance status. We were also unable to control for area of residence as urban, suburban, or rural. Emigration, specifically as immigrants leave the U.S. after an HIV or AIDS diagnosis, could not be controlled nor assessed in this analysis. The limited published information on Mexican migrants and immigrants made it difficult to assess the true impact of late testing considering the unstable denominator. Despite these limitations, the prevalence and associations of late testing in our study are generally consistent with research in other settings. The profile of late HIV testers may be of particular relevance in California at this moment given the severe 2009–2010 state budget reductions to the Office of AIDS.³⁰

CONCLUSIONS

Prevention and testing campaigns for California populations need to reach those who are likely to be late HIV testers: people aged 35 years and older, heterosexuals, Latinos, and immigrants. Among all groups, but perhaps especially among Latinos, prevention campaigns

need to have a range of cultural contexts and sexual identities. This outreach would be supported through wide implementation of CDC-recommended routine adult HIV testing in all health-care settings⁹ as well as emergency department-based testing.^{31,32}

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This study was entirely the work of the authors and in no way reflects the opinion or analysis process of the CDPH Office of AIDS.

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