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Missed Opportunities for HIV Prevention: Individuals Who HIV Seroconverted Despite Accessing Healthcare

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Abstract

Individuals with a negative HIV test before a positive one (seroconverters) may represent missed opportunities for prevention. To inform HIV prevention strategies, we aimed to characterize patients who seroconverted despite accessing care. We identified patients at a large, urban healthcare system who seroconverted between 2009 and 2014. Demographics, visits, and HIV-related variables were extracted from the medical records. We performed descriptive statistics, assessed for trends, and tested for associations according to sex. 220 seroconverters were identified: 45% were female, 87% were non-Hispanic Black or Hispanic, and median number of negative tests prior to diagnosis was 2 (IQR 1–3). Overall, 49% reported heterosexual contact as their risk factor and the proportion with heterosexual risk increased over time (24% in 2009 vs. 56% in 2014, $p = 0.03$). Compared to men, women were older at the time of diagnosis (35 vs. 26 years old, $p < 0.01$), had more visits between their latest negative and positive HIV test (4 vs. 2, $p < 0.01$), and were more likely to be diagnosed in the context of screening (64% vs. 56%, $p = 0.05$). We identified a population that became HIV-infected despite multiple healthcare encounters and undergoing HIV testing multiple times. Patients were mostly heterosexual and almost half were female. To avoid missed opportunities for those already accessing care, HIV prevention efforts should include strategies tailored to individuals with less frequently recognized risk profiles.

Keywords

HIV prevention; Seroconverters; Epidemiology; Missed opportunities

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Background

Multiple HIV prevention strategies exist to reduce the risk of HIV transmission: from counseling on safe sex practices, to early initiation of antiretroviral treatment for discordant couples, to, most recently, the introduction of pre-exposure prophylaxis (PrEP) [1, 2]. Many of these strategies, however, remain underutilized [3, 4]. Among the challenges facing large-scale implementation of HIV prevention is identifying individuals at high risk for HIV and engaging them in longitudinal medical care that would provide access to these strategies.

Individuals who test for HIV multiple times and have a positive result after a negative HIV result (“seroconverters”) represent a unique population both because the timeframe of their HIV acquisition is known and because a negative HIV test prior to a positive test may indicate contact with the healthcare system before becoming infected. This critical time between a negative HIV test and first positive test may represent an opportunity for intervention. A better understanding of these seroconverters, including their interactions with the health care system in the time preceding their HIV diagnosis, may provide useful insights for HIV prevention efforts.

The aim of this study was to describe demographic, clinical, and behavioral characteristics of seroconverters to help tailor implementation of HIV prevention strategies.

Methods

Setting

We performed a retrospective study of patients who had at least one negative HIV test followed by a positive test between 2009 and 2014 at the largest provider of healthcare in the Bronx, New York, a region of New York City with an HIV prevalence of 2% [5]. Lab-based HIV testing is available at all clinical sites and point-of-care testing is available at some of the outpatient and Emergency Department (ED) sites of the affiliated healthcare system.

Study Population

We used the Einstein-Rockefeller-CUNY Center for AIDS Research Clinical Database to identify seroconverters. The database contains clinical and demographic information of patients tested for HIV across the affiliated healthcare system since 1997 [6]. HIV-positive patients in the database are demographically representative with respect to age, sex, race/ethnicity, and HIV transmission risk of the overall HIV-positive population in the Bronx, NY that is described by public health surveillance data [7]. We included all patients aged 18 years with at least one negative HIV test followed by a positive test. To ensure the availability of electronic medical records for review, we restricted the study to those whose positive HIV test occurred from 2009 to 2014. A negative HIV test was defined as non-reactive point of care oral swab or lab-based third or fourth generation test. A positive test was defined either as a reactive HIV-1 Western blot performed as confirmation of a third generation test, a reactive differentiation assay for HIV 1 or 2, or detectable HIV viral load performed as confirmation of reactive fourth generation test. All seroconversions were confirmed by manual review of the medical record.

Data Collection and Measures

The variables of interest for this study included those known or suspected to be associated with HIV risk or health-seeking behaviors [8–11] and were accessible either from the database or through systematic manual review of the medical record. The following variables were extracted from the database: sex at birth; age at time of first positive HIV test; race/ethnicity (Non-Hispanic black, Hispanic, non-Hispanic white, other/unknown); dates and results of all HIV tests during the study period; HIV transmission risk factor (men who have sex with men [MSM], injection drug use, heterosexual contact, other/unknown); and first CD4 count after diagnosis. Systematic manual review of medical records was performed to collect gender identity (male, female, transgender); indication for performing the first positive HIV test (diagnostic if provider noted signs or symptoms suggestive of HIV, screening if no HIV-related signs or symptoms documented); history of sexually transmitted infection (STI) at any point prior to seroconversion (documentation or laboratory evidence of chlamydia, gonorrhea, or syphilis); history of hepatitis B (HBV) exposure (documentation or laboratory evidence of acute or chronic HBV, or clearance of acute HBV); history of hepatitis C (HCV) exposure (documentation or laboratory evidence of acute or chronic HCV, or clearance of acute HCV); history of substance use prior to seroconversion (documentation or laboratory evidence of cocaine, heroin, amphetamines, or other illicit drug use); mental health diagnosis at time of seroconversion (documented diagnosis and pharmacologic or behavioral treatment); number of visits to the healthcare system between the last negative and first positive HIV test (including ED visits, outpatient visits, and inpatient admissions); use of pre-exposure prophylaxis prior to seroconversion; acute HIV infection at time of diagnosis (detectable HIV RNA concomitant with a negative HIV antibody test or provider documentation of acute infection); and presence of an opportunistic infection at time of HIV diagnosis.

Statistical Analyses

We performed primarily descriptive statistics. Because of known differences in health-seeking and HIV testing behaviors according to sex [8, 12, 13], we assessed bivariate associations between our variables of interest and sex with Chi square or Wilcoxon tests, as appropriate. Temporal trends in HIV risk factors were assessed using the Chi square test for trend. Analyses were performed with SAS 9.3. This study was approved by the Institutional Review Board of Albert Einstein College of Medicine. As a retrospective study only using data acquired during the course of clinical care, the IRB provided a waiver of informed consent.

Results

Demographic Characteristics of Study Sample

Over the course of the study period, a total of 278,047 unique individuals were tested for HIV across the affiliated healthcare system. The annual number of tests increased from 42,098 in 2009 to 71,284 in 2014. Among tested individuals, we identified 220 seroconverters (Table 1). Overall, more than 85% of seroconverters were non-Hispanic Black or Hispanic, and almost half were women. The most common risk factor for HIV

acquisition was heterosexual contact. The proportion of individuals reporting heterosexual contact as their risk factor increased from 24% in 2009 to 56% in 2014, $p = 0.03$) (Fig. 1).

Frequency of HIV Testing and Healthcare Encounters

Overall, patients had a median of 2 (interquartile range [IQR] 1–3) negative HIV tests before a positive test, and the median interval between negative tests was 1 year (IQR 0.6–1.6). The median interval between the last negative test and the positive test was 2.1 years (IQR 1–3.8) and 22% of patients had a negative test within 1 year of seroconversion. Patients had a median of 3 (IQR 1–5) health-care encounters between their last negative test and the positive test.

Indicators of HIV Risk

Almost 40% of our patients had at least one STI prior to seroconversion and 19% had a history of substance use. Prior exposure to HBV and HCV was present in 5% of patients for each virus. 11% of individuals had a diagnosis of a mental health disorder at the time of HIV diagnosis.

Indication for HIV Testing and Clinical Characteristics at Time of Diagnosis

For the majority of patients (60%), HIV was diagnosed in the context of routine screening. Only 26 (12%) of individuals were diagnosed in the setting of a diagnostic workup, including 9 (4%) patients diagnosed in the setting of acute HIV infection and 3 (1%) in the setting of an opportunistic infection. Of note, while PrEP was approved for HIV prevention approximately mid-way through the study period, it had not been prescribed to any of the seroconverters. The median CD4 count at the time of diagnosis was 507 cells/ μ l (IQR 349–724). Over two-thirds of patients were linked to HIV care within 30 days after the diagnosis.

Comparison of Characteristics by Sex

Women were older than men at the time of diagnosis (35 vs. 26 years old, $p < 0.01$) and had a greater number of visits between their last negative and positive HIV test (4 vs. 2, $p < 0.01$). Compared to men, women were more likely to be diagnosed with HIV in the context of screening (64% vs. 56%, $p = 0.05$) and had higher CD4 counts at diagnosis (588 vs. 474 cells/ μ l, $p = 0.02$).

Discussion

We identified a cohort of seroconverters who were diagnosed with HIV between 2009 and 2014 despite accessing medical care. Most individuals had multiple healthcare encounters before their positive test and underwent HIV testing multiple times. Half of the patients reported heterosexual contact as their risk factor, and almost half were women. These findings have important implications for HIV prevention efforts.

While the high prevalence of STIs, exposure to hepatitis viruses, and mental health diagnoses suggests that our population was at high risk for HIV infection, the number and frequency of healthcare encounters suggest that they were able to access care. The median time between negative HIV tests was 1 year, which is consistent with current guidelines for

adults at high risk [14]. Although the frequency of testing may be partially attributable to contemporaneous public health efforts to increase routine HIV screening, including a 2010 mandate from New York State to routinely offer HIV testing in clinical settings, prior studies have shown that implementation of these efforts are suboptimal [15–18]. Therefore, these efforts are unlikely to be the sole explanation for this finding and it is likely that the frequency of testing may also indicate an awareness of HIV risk on the part of the patients and/or the providers. Our finding of frequent testing is also consistent with both national and local data showing that between 21 and 56% of high risk individuals are tested for HIV within a year prior to diagnosis [12, 19, 20], and with data reporting that more than 90% of heterosexuals at high risk encountered a medical setting offering HIV testing in the year prior to diagnosis [12]. Access to care and awareness of HIV risk by patients and/or providers is also suggested by the high proportions of patients who were diagnosed in the context of a screening test, had a CD4 count > 500 cells/ μ l at time of diagnosis, and were linked to care within 30 days. As a comparison, the median CD4 count at HIV diagnosis in New York City is 378 cells/ μ l [21].

Understanding the local epidemiology of HIV is crucial for the effective planning and implementation of prevention strategies. While national statistics continue to indicate that the population at the highest risk of contracting HIV is MSM, particularly black and Hispanic MSM [22], almost half of seroconverters in our sample were heterosexual women. This finding differs from the most recent data on HIV epidemic in New York City where women represent only 20% of new diagnoses. Similar to what is seen in the wider New York City area, however, the women we identified were predominantly black or Hispanic and older than their male counterparts [5]. One factor contributing to our finding of a high proportion of women newly infected with HIV may be related to differences in sex-specific health-seeking behaviors. By definition, our cohort required patients to have at least two HIV tests (one negative and one positive) within a single healthcare system. Studies have shown that women access care more frequently than men [13] and better access to care is predictive of HIV testing [12]. Therefore, our cohort represents a selection of patients who are both at risk for HIV infection and access healthcare longitudinally.

In addition to identifying a higher proportion of women among the seroconverters than expected, we also observed an increase in the proportion of seroconverters with heterosexual risk over time. Considering that 27% of the women in our study had an unknown HIV risk factor, because it has been shown that unrecognized or undisclosed risk behaviors in women usually represents heterosexual exposure [23, 24], it is likely that our reported proportion of seroconverters with heterosexual risk actually represents and underestimation. This increasing representation of heterosexual risk over time among the seroconverters may be related to the secular changes in HIV testing patterns during the course of the study period emphasizing routine, rather than targeted, HIV screening. This is supported by recent literature suggesting an increase in frequency of HIV testing among individuals with heterosexual risk factors, especially women [8]. Our findings of a high proportion of women and increasing proportion of individuals whose HIV risk is heterosexual sex among the seroconverters suggests that while ongoing outreach efforts are critical to engage populations at highest risk for HIV who are not accessing care, our healthcare systems must also be cognizant of at-risk populations that are actively accessing care despite not fitting the

traditional risk profile, and should tailor prevention strategies and accordingly. Provider education and implementation of routine screening strategies might help avoid missed opportunities.

Our study has some limitations. First, the database only includes individuals whose HIV tests were performed within the affiliated healthcare system, a population that may not be representative of those who test repeatedly across different health systems before seroconversion. However, we believe this limitation is attenuated because several major urban centers in the U.S. with high HIV prevalence and similar demographic profiles to the Bronx (e.g., Baltimore, Philadelphia, Washington, DC) [25] have a similar landscape of medical care characterized by multiple large healthcare systems in close proximity which frequently provide overlapping care to the local population. Second, our inferences may be influenced by the retrospective study design. On one hand, it is possible that not all of our variables of interest were systematically documented in the course of clinical care. On the other hand, use of real-life clinical data is frequently the first step in recognizing local epidemiologic trends, which can later be borne-out with more rigorously structured study designs. Finally, although most patients had multiple visits and HIV tests within the healthcare system prior to seroconversion, because location of HIV testing (ED, outpatient clinic, inpatient setting) is not systematically included in our database it is difficult to discern whether these tests were sent as part of engagement in consistent, longitudinal care rather than in the context of episodic acute care, or how much routine HIV screening for perinatal care accounts for some of the differences observed between men and women. Nonetheless, the number of HIV tests and healthcare encounters we observed suggest that the patients did have some level of longitudinal access to the healthcare system.

We believe that our data are extremely relevant to ongoing HIV prevention efforts. Our findings suggest that in addition to outreach efforts among high-risk populations not in care, health systems should also avoid missed opportunities for HIV prevention by tailoring strategies to those at risk who might not be recognized as such and are actively engaged in care. For these patients, indicators of HIV risk such as STIs, substance use, mental health disorders, exposure to HBV or HCV, or even a concern for HIV-risk as suggested by repeatedly negative HIV testing, should prompt providers to consider appropriate HIV prevention counseling, including PrEP.

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Fig. 1. Changes in HIV risk factors among seroconverters over time. *MSM* men who have sex with men, *IDU* injection drug use

Table 1

Demographic and clinical characteristics of seroconverters, 2009–2014

	Total N = 220	Female N = 100	Male^a N = 120	p value^b
Age	30 (23–42)	35 (28–46)	26 (21–36)	< 0.01
Race/ethnicity				
Black, non-hispanic	104 (47)	51 (51)	53 (44)	0.72
Hispanic	88 (40)	37 (37)	51 (43)	
White, non-hispanic	10 (5)	5 (5)	5 (4)	
Other	18 (8)	7 (7)	11 (9)	
Risk factor				
Heterosexual	97 (44)	71 (71)	26 (22)	< 0.01
MSM	70 (32)	-	70 (58)	
IDU	6 (3)	2 (2)	4 (3)	
Other/unknown	47 (21)	27 (27)	20 (17)	
Negative tests prior to diagnosis	2 (1–3)	1 (1–3)	2 (1–)	0.36
Number of visits between last negative and positive test	3 (1–5)	4 (1–)	2 (0–4)	< 0.01
Years between negative tests	1.0 (0.6–1.7)	1.0 (0.6–1.4)	1.1 (0.7–1.8)	0.28
Years between last negative and positive test	2.2 (1.0–3.8)	2.2 (1.1–3.9)	2.2 (1.0–3.7)	0.69
STIs prior to HIV seroconversion				
Yes	86 (39)	37 (37)	49 (41)	0.34
No	118 (54)	58 (58)	60 (50)	
Missing	16 (7)	5 (5)	11 (9)	
Hepatitis B virus exposure				
Yes	12 (5)	2 (2)	10 (8)	0.11
No	196 (89)	93 (93)	103 (86)	
Missing	12 (5)	5 (5)	7 (6)	
Hepatitis C virus exposure				
Yes	12 (5)	8 (8)	4 (3)	0.19
No	196 (89)	85 (85)	111 (93)	
Missing	12 (5)	7 (7)	5 (4)	
Substance use prior to seroconversion				
Yes	41 (19)	18 (18)	23 (19)	0.31
No	142 (65)	61 (61)	81 (68)	
Missing	37 (17)	21 (21)	16 (13)	
Mental health diagnosis at time of seroconversion				
Yes	25 (11)	12 (12)	13 (11)	0.75
No	174 (79)	77 (77)	97 (81)	
Missing	21 (10)	11 (11)	10 (8)	
Test indication at seroconversion				
Screening	131 (60)	64 (64)	67 (56)	0.05
Diagnostic	26 (12)	6 (6)	20 (17)	

	Total N = 220	Female N = 100	Male^a N = 120	p value^b
Missing	63 (29)	30 (30)	33 (28)	
CD4 count at HIV diagnosis (cells/μl)	507 (349–724)	588 (364–799)	474(343–683)	0.02
Linkage to care within 30 days of HIV diagnosis				
Yes	149 (68)	72 (72)	77 (64)	0.46
No	30 (14)	12 (12)	18 (15)	
Missing	41 (19)	16 (16)	25 (21)	

Numbers represent frequencies (%) or median (IQR) as appropriate

MSM men who have sex with men, *IDU* intravenous drug users, *RF* risk factors, *STI* sexually transmitted infection

^a 4 transgender patients with male sex at birth identified as female

^b Associations were assessed using Chi squared or Wilcoxon tests as appropriate