Identification of Acute HIV Infection Using Fourth-Generation Testing in an Opt-Out Emergency Department Screening Program

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Study objective: Acute HIV infection is a clinical diagnosis aided by technology. Detecting the highly infectious acute stage of HIV infection is critical to reducing transmission and improving long-term outcomes. The Maricopa Integrated Health System implemented nontargeted, opt-out HIV screening with a fourth-generation antigen/antibody combination HIV assay test in our adult emergency department (ED) at Maricopa Medical Center to assess the prevalence of both acute and chronic unrecognized HIV.

Methods: Eligible patients aged 18 to 64 years were tested for HIV if they did not opt out and had blood drawn as part of their ED care. Patients were not eligible if they had a known HIV or AIDS diagnosis, exhibited altered mental status, were a current resident of a long-term psychiatric or correctional facility, or prompted a trauma activation. Reactive test results were delivered by a physician with the assistance of a linkage-to-care specialist. Specimens with a reactive fourth-generation assay result underwent confirmatory testing.

Results: From July 11, 2011, through January 5, 2014, 27,952 HIV screenings were performed for 22,468 patients tested for HIV; 78 (0.28%) had new HIV diagnoses. Of those, 18 (23% of all new diagnoses) were acute HIV infections, and 22 patients (28%) had a CD4 count of less than 200 cells/mL, or an opportunistic infection.

Conclusion: HIV testing with a fourth-generation antigen/antibody laboratory test producing rapid results is feasible in an ED. Unexpectedly, nearly one fourth of patients with undiagnosed HIV had acute infections, which would have been more difficult to detect with previous testing technology. [Ann Emerg Med. 2014;64:537-546.]

Please see page 538 for the Editor's Capsule Summary of this article.

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SEE EDITORIAL, P. 547.

INTRODUCTION

Background

Acute HIV infection clinical syndrome is notoriously difficult to diagnose because of vague symptoms and imperfect testing technology. Until 2009, only third-generation antibody HIV assays were available for use in the United States.[1] Although effective at detecting chronic HIV infections, third-generation assay tests do not detect the p24 HIV antigen. This methodology could not diagnose HIV infection before antibody production, leaving HIV ribonucleic acid (RNA) detection the only other method of diagnosis. Detecting HIV RNA is an expensive, tedious process, especially in screening programs, because it combines numerous samples that are tested together; a positive result in the pool then requires identification of the particular sample that contains HIV RNA.[2] The advent of a fourth-generation antigen/antibody HIV test allows detection of both the p24 HIV antigen and HIV antibodies. Although this technique detects an HIV core protein rather than the RNA, it does provide earlier and easier detection of HIV.[3] Thus, previously invisible acute HIV infections are now evident. Mathematical models and studies screening for HIV RNA suggest that acute HIV infections generally compose between 5% and 20% of all new HIV diagnoses.[3]

Importance

Individuals infected with acute HIV are responsible for 7% to 50% of transmissions and subsequent infections[4-7] because of the combination of increased infectivity of the virus, high plasma viral loads, and the actions of those with acute HIV because they are generally unaware of their HIV status.[1,3] Early identification of HIV improves outcomes for individual patients and enhances prevention efforts. The International Antiviral Society–USA Panel 2012 revised recommendations now support early treatment of HIV with antiretroviral therapy to reduce long-term morbidity and mortality.[8] By controlling viral loads and

Editor's Capsule Summary

What is already known on this topic

HIV screening is recommended for emergency department (ED) patients, but commonly used antibody tests will not identify acute HIV infection.

What question this study addressed

Nontargeted HIV screening was performed on ED patients in a Phoenix, AZ, public hospital, using a newer testing algorithm that incorporates p24 antigen to identify acute infection.

What this study adds to our knowledge

Among 22,468 patients tested, 78 (0.28%) had newly identified HIV infection, and 23% of these were acute infections that would have gone undetected by standard screening.

How this is relevant to clinical practice

Newer HIV testing algorithms could identify a greater number of acute HIV infections, but cost and time constraints remain barriers to HIV screening in the ED.

addressing risky behaviors of patients with HIV, treatment of HIV also prevents transmission.[9]

Goals of This Investigation

Our goal was to assess the prevalence of both acute and chronic unrecognized HIV infections through TESTAZ (Test, Educate, Support, Treat Arizona), a nontargeted, opt-out HIV testing program using a fourth-generation antigen/antibody HIV test in a metropolitan emergency department (ED) with a medically underserved population. A brief preliminary synopsis of the first 20 months of laboratory testing was published.[10] This article expands on the screening program, testing process, and outcome data.

MATERIALS AND METHODS

Study Design and Setting

In this observational program evaluation, we performed nontargeted, opt-out HIV testing according to the Maricopa Integrated Health System protocol for TESTAZ. Implementation occurred in the adult ED of a single, urban, Level I trauma center with a census of 45,000 patients per year. An academic hospital with an emergency medicine residency program located in Maricopa County, AZ, this ED mainly serves minority, underinsured, and uninsured patients. TESTAZ was developed by the Grants Department at Maricopa Integrated Health System. During a 6-month period, 22 departments met to construct the mechanics of the program. TESTAZ was approved by the Maricopa Integrated Health System Institutional Review Board. ED staff training occurred through modules available on the Maricopa Integrated Health System intranet, and physicians received preparation through a lecture.

Selection of Participants

The Figure illustrates the participant selection process, as well as the workflow used to obtain and act on an HIV test result. Eligible patients were aged 18 to 64 years and did not meet any exclusion criteria: a previously known HIV or AIDS diagnosis, altered mental status, a current resident of a long-term psychiatric or correctional facility, or a trauma activation. Patients younger than 18 years were not tested because of disclosure and consent-to-treatment issues in minors and because these patients are cared for in the pediatric ED (a physically and administratively separate department). Critically ill patients were included if there was time for the patient to opt out and he or she did not meet any exclusion criteria.

During the ED triage process, the triage nurse asked and documented in the electronic medical record whether the patient

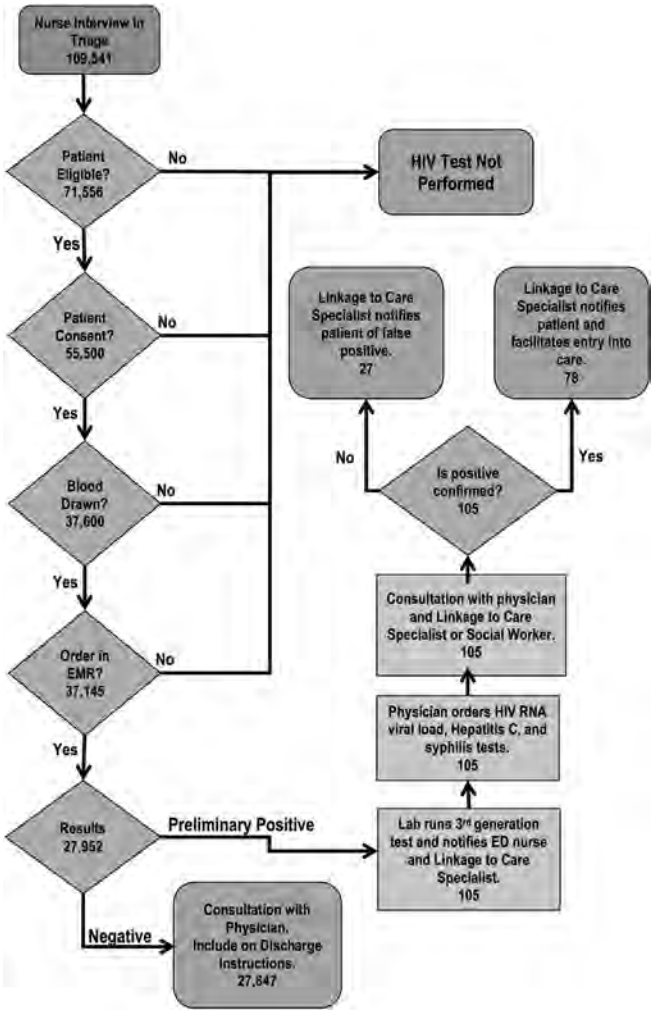

Figure. Selection of participations and workflow to obtain and act on an HIV test result (encounter level). *EMR*, Electronic medical record.

had previously been tested for HIV, the result of the previous test, if any, and whether the most recent test was conducted in the past 12 months. The triage nurse obtained explicit verbal consent, using this script: "In accordance with CDC [Centers for Disease Control and Prevention] recommendations, all routine blood work includes an HIV test. This will be completed at no additional cost to you. Here is our HIV informed consent information brochure."

To improve workflow, HIV tests were performed only on patients who had venipuncture as part of their ED care. The Architect HIV Ag/Ab Combo Test, a fourth-generation antigen/antibody rapid assay from Abbott Laboratories (Abbott Park, IL), was performed with whole blood by the hospital laboratory. Within 1 hour, negative test results were entered in the electronic medical record and the patient was notified. For workflow purposes, a patient's ED discharge was not delayed by a pending Architect HIV Ag/Ab Combo Test result. Delayed notification occurred in the event of a reactive fourth-generation HIV test in a patient who had already been discharged from the ED. As soon as the reactive test result was obtained, the patient was called back to the ED for counseling and confirmatory testing.

As outlined in the Figure, within an hour a reactive Architect HIV Ag/Ab Combo Test, considered a preliminary positive test result, prompted a telephone call from the laboratory to the ED nurse caring for the patient and the linkage-to-care specialist. In turn, the nurse notified the emergency physician. The linkage-to-care specialist, available at all times, immediately went to the ED and was with the emergency physician for patient result notification. Later, the ED social workers received training on HIV and how to deliver the news of a preliminary reactive HIV test. Since month 21, the ED social worker, rather than the linkage-to-care specialist, has assisted the emergency physician with preliminary positive result notifications. After the physician explained the reactive test result, the linkage-to-care specialist or social worker spent approximately 30 minutes with the patient explaining the testing methodology, implications, and next steps for a preliminary positive test result. Patients were informed of the need for confirmatory testing before a final diagnosis of HIV infection could be made. The physician returned later to answer any further questions from the patient.

All patients with a reactive Architect HIV Ag/Ab Combo Test result received additional testing. A preliminary positive result triggered an automatic third-generation test by Multispot HIV-1/HIV-2 Rapid Test from Bio-Rad Laboratories (Hercules, CA). Initially, confirmatory testing was completed by HIV-1 Western blot (qualitative antibody test) from Cambridge Biotech Corporation (Rockville, MD) and RealTime HIV-1 Assay (quantitative polymerase chain reaction) from Abbott Laboratories. In anticipation of changing recommendations from the CDC, the confirmation strategy for a reactive fourth-generation antigen/antibody test changed in month 9. The Western blot was no longer used, leaving the RealTime HIV-1 Assay as the confirmatory study. Confirmatory testing was usually completed in 1 to 3 days.

Within 1 to 3 days of the reactive fourth-generation HIV test result, the linkage-to-care specialist contacted the patient to provide support and answer remaining questions. The specialist was responsible for following up on confirmatory testing and subsequent result notification. In the event of a false-positive result, the specialist explained the result implications and referred the patient to primary care. In the event of a confirmed positive HIV infection, the specialist assisted with active linkage to follow-up HIV medical care and support services. In addition to helping with entry to care (including health insurance enrollment, social support, and a health literacy assessment), the specialist had the option of attending the first physician visit and continued to follow up for a year with patients receiving a new diagnosis. Patients with a new HIV diagnosis were linked to medical care at the Maricopa Integrated Health System HIV clinic. This process improved when the clinic moved to a larger location and hired an additional provider. The clinic is physically colocated with an organization that provides numerous community resources, easing a patient's transition to HIV treatment. Communicable disease reporting required by state and federal regulations was completed by Maricopa Integrated Health System.

Outcome Measures

Our goal was to assess the prevalence of both acute and chronic unrecognized HIV infections through TESTAZ, a nontargeted, opt-out HIV testing program using a fourth-generation antigen/antibody. The primary outcome measure of this observational program evaluation was to describe the number and percentage of patients with HIV infections detected by the fourth-generation antigen/antibody test in the ED. Although acute HIV infection is a clinical diagnosis, for the purpose of this program evaluation, we defined acute HIV infection consistent with the CDC's proposed algorithm for a "stage 0" diagnosis.[11,12] This definition was consistent with Fiebig Classification stages II, III, and IV (p24 antigen positive, enzyme-linked immunosorbent assay positive and Western blot positive or negative, respectively).[13] A preliminary positive test result was a reactive fourth-generation Architect HIV Ag/Ab Combo Test result without further confirmatory testing. AIDS was defined as an initial CD4 count of less than 200/μL or the presence of an opportunistic infection at diagnosis. Secondary outcome measures included linkage-to-care timing after the diagnosis of HIV and the initial viral load and CD4 count of patients receiving a diagnosis of HIV through TESTAZ.

Primary Data Analysis

The data from patients were self-reported. A report from the adult ED was reviewed by the HIV program manager each day. The demographics of eligible, tested, and excluded patients were obtained from the electronic medical record. The data were extracted from the electronic medical record into Microsoft Excel 2010. Review of patient identifiable information was authorized by the institutional review board and Maricopa Integrated Health System Compliance Department. About 10% of the data collected was reviewed during the first part of TESTAZ to ensure validity. Descriptive statistics were calculated and regularly evaluated by the Office of HIV Prevention of the Arizona Department of Health Services. Each patient visit was considered

a separate encounter. Ninety-five percent confidence intervals (CIs) were calculated for test outcomes.

RESULTS

Main Results

Results were obtained from July 11, 2011, through January 5, 2014. Table 1 shows the main results. A total of 27,952 HIV screening tests were conducted for 22,468 patients. This accounts for 25.5% of total ED encounters, 53.6% of patients who did not decline testing, and 90.3% of patients who did not decline and had blood drawn. The reactive tests are categorized as false-positive results, acute HIV infections, and chronic HIV infections in Table 2. The total number of preliminary positive HIV test results by fourth-generation antigen/antibody testing was 105 (0.38%; 95% CI 0.30% to 0.45%). Of these 105 preliminary positive results, 27 (25.7%; 95% CI 17.9% to 35.3%; 0.097% of all tests) were false positives. The total number of confirmed HIV infections was 78, for an overall prevalence of 0.28% (95% CI 0.22% to 0.35%). Of the confirmed diagnoses, 18 (23.1%; 95% CI 14.5% to 34.2%) were acute HIV infections. At the confirmed diagnosis, 22 patients (28.2%; 95% CI 18.8% to 39.7%) presented with AIDS. Chronic infections included 2 patients who may have previously received a diagnosis of HIV but did not inform the triage nurse and were not excluded from testing. Details of confirmed HIV-positive patients, such as demographics, risk profiles, linkage-to-care time frame, and mean and median initial viral load and CD4 count, are described in Table 3. Eighty-two percent of patients with confirmed HIV did not have health insurance, and 72% were linked into HIV care within 90 days.

LIMITATIONS

Acute HIV infection is the body's reaction to the HIV virus and therefore a clinical entity. As a result, laboratory testing fails to capture all clinical acute HIV infections. Although fourth-generation testing is a technological improvement, acute HIV infections, specifically Fiebig stage I infections (viral RNA positive only), may have been missed. How many infections were missed is unknown because nonreactive samples do not undergo criterion standard pooled viral load testing. The various definitions for acute HIV infection influenced the results. Although the parameters we chose included a reactive fourth-generation test result with a negative third-generation and negative or indeterminate Western blot antibody test result coupled with a measurable HIV viral load, other definitions include clinical symptoms, a documented negative test result within the previous 6 months, and a viral load threshold.[1,3,12,14] The definition also does not account for clinically acute infections when both antigen and antibodies were present. Last, had Western blot testing not been discontinued in month 9 of TESTAZ, we believe that the number of acute infections would have been higher because a negative or indeterminate Western blot result together with a reactive or nonreactive third-generation test result and a measurable viral load would have been considered an acute infection rather than an established infection.

At the beginning of the program, a number of barriers in the HIV testing workflow were identified. A major deficiency was the exclusion of patients because an HIV test order was not placed in the electronic medical record by the treating physician despite eligibility, consent, and blood being drawn. This was remedied when the triage nurse, instead of the physician, started placing orders for the HIV test in the electronic medical record. Additionally, patients who did not have blood drawn may have believed they tested negative for HIV. An alteration to the discharge paperwork now prompts the discharge nurses to remind patients who did not have blood drawn as part of their ED stay that an HIV test was not performed.

The patients included in this program had different risk profiles from those who were excluded or declined. For example, patients in the custody of corrections facilities, who are known to have a higher rate of HIV,[15] were excluded because many received an HIV test as part of their jail care. Patients from psychiatric institutions, who are also known to have higher rates of HIV compared with the overall US population,[16] were excluded because of questions about their ability to consent to testing. The reasons patients declined an HIV test were not studied; however, anecdotally, patients often stated they did not believe they were at risk or did not want to know their HIV status. These statements are consistent with previous studies evaluating why patients decline HIV testing.[17,18]

It is possible that HIV infections identified through TESTAZ were already diagnosed. Although patients were asked in triage about previous HIV testing and the results of those tests, 2 patients did not disclose that they may have previously received a diagnosis of HIV. After further interviews with these patients, a review of the electronic medical record, and feedback from the county health department, it was determined that one of these patients did not disclose a preliminary positive test result without confirmatory testing; the other patient did not provide sufficient information to confirm a previous diagnosis. Because medical records from other facilities were not obtained and the public health department could not definitely confirm that each patient had received a new diagnosis, it is possible the number of new HIV diagnoses is slightly overestimated.

Most important, this program was conducted at a single institution with a large number of ethnic minority, underinsured, and uninsured patients. Thus, generalizability of these findings to other clinical settings and different populations may be limited.

DISCUSSION

The CDC 2006 revised recommendations for HIV testing of adults, adolescents, and pregnant women in health care settings suggests universal screening for HIV in populations with a prevalence of undiagnosed infections greater than 0.1%,[19] defined as 1 or more new HIV infections per 1,000 tests. With an overall positivity rate of 0.28%, this program well surpasses

Table 1. TESTAZ population characteristics (July 11, 2011, to January 5, 2014).

	Unduplicated Patients, n=63,077		Did Not Decline, n=41,033		Declined, n=22,044		Excluded, n=38,195		Tested, n=27,952	
Demographic Category	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**
Testing status										
Screened for HIV	22,468	35.6	21,981	53.6	487	2.2	0	0	27,952	100.0
Not screened for HIV	40,609	64.4	19,052	46.4	21,557	97.8	38,195	100.0	0	0
Sex										
Female	30,763	48.8	21,445	52.3	9,318	42.3	16,912	44.3	15,708	56.2
Male	32,314	51.2	19,588	47.7	12,726	57.7	21,283	55.7	12,244	43.8
Age range, y										
18–24	9,690	15.4	6,670	16.3	3,020	13.7	6,153	16.1	3,889	13.9
25–44	28,401	45.0	19,300	47.0	9,101	41.3	17,182	45.0	12,509	44.8
45–64	20,978	33.3	14,030	34.2	6,948	31.5	11,562	30.3	10,741	38.4
≥65	4,008	6.4	1,033	2.5	2,975	13.5	3,298	8.6	813	2.9
Race/ethnicity										
American Indian or Alaska Native	1,706	2.7	888	2.2	818	3.7	1,179	3.1	595	2.1
Asian or Pacific Islander	716	1.1	393	1.0	323	1.5	462	1.2	252	0.9
Black	9,017	14.3	5,965	14.5	3,052	13.8	5,587	14.6	4,095	14.7
Hispanic or Latino	30,554	48.4	21,794	53.1	8,760	39.7	17,034	44.6	14,932	53.4
White	18,481	29.3	10,708	26.1	7,773	35.3	11,943	31.3	7,478	26.8
Other or unknown	2,603	4.1	1,285	3.1	1,318	6.0	1,990	5.2	600	2.1
Payer category										
Private insurance	2,993	4.7	1,829	4.5	1,164	5.3	1,899	5.0	1,109	4.0
Medicaid	14,352	22.8	10,064	24.5	4,288	19.5	7,938	20.8	7,842	28.1
Medicare	4,302	6.8	1,883	4.6	2,419	11.0	2,911	7.6	1,784	6.4
No insurance	37,878	60.1	26,424	64.4	11,454	52.0	22,384	58.6	16,672	59.6
Corrections	2,479	3.9	200	0.5	2,279	10.3	2,331	6.1	164	0.6
Other insurance	1,073	1.7	633	1.5	440	2.0	732	1.9	381	1.4

Table 2. Preliminary positive classifications (July 11, 2011, to January 5, 2014).

	Preliminary Positive Results, n=105, Prevalence 0.38% (95% CI 0.30%–0.45%)						Confirmed Positive Results, n=78, Prevalence 0.28% (95% CI 0.22%–0.35%)					
Testing Description	**Number**	**Percent**	**95% CI**	**Total Number**	**Total Percent**	**95% CI**	**Number**	**Percent**	**95% CI**	**Total Number**	**Total Percent**	**95% CI**
False positive												
Reactive fourth generation Nonreactive third generation Negative or indeterminate Western blot* Viral load not detected	3	2.9	0.74–8.7	27	25.7	17.9–35.3						
Reactive fourth generation Nonreactive third generation Viral load not detected	24	22.9	15.4–32.2									
Acute infection												
Reactive fourth generation Nonreactive third generation Negative or indeterminate Western blot* Measurable viral load	3	2.9	0.74–8.7	18	17.1	10.7–26.0	3	3.8	0.99–11.5	18	23.1	14.5–34.2
Reactive fourth generation Reactive third generation Negative or indeterminate Western blot* Measurable viral load	2	1.9	0.33–7.3				2	2.6	0.44–9.8			
Reactive fourth generation Nonreactive third generation Measurable viral load	13	12.4	7.01–20.5				13	16.7	9.5–27.1			
Chronic infection (including possibly previously diagnosed)												
Reactive fourth generation Reactive third generation Positive Western blot result* Measurable viral load	7	6.7	2.9–13.7	59	56.2	46.1–65.7	7	9.0	3.9–18.1	59	75.6	64.3–84.3
Reactive fourth generation Reactive third generation Measurable viral load	52	49.5	39.6–59.3				52	66.7	54.9–76.6			
Unknown												
Reactive fourth generation Nonreactive third generation Viral load unknown: patient left ED against medical advice	1	1.0	0.04–5.9	1	1.0	0.04–5.9	1	1.3	0.06–7.9	1	1.3	0.06–7.9

*Western blot tests were discontinued in March 2012.

Table 3. Confirmed HIV diagnoses population characteristics (July 11, 2011, to January 5, 2014).

	Total, n=78			Acute Infections, n=18			Chronic and Unknown Infections, n=60		
Demographic Category	**Number**	**Percent**	**95% CI**	**Number**	**Percent**	**95% CI**	**Number**	**Percent**	**95% CI**
Sex									
Female	12	15.4	8.5–25.7	4	22.2	7.3–48.0	8	13.3	6.3–25.1
Male	66	84.6	74.2–91.4	14	77.8	51.9–92.6	52	86.7	74.8–93.6
Age range, y									
18–24	14	17.9	10.5–28.6	4	22.2	7.3–48.0	10	16.7	8.7–28.9
25–44	38	48.7	37.3–60.2	11	61.1	36.1–81.7	27	45.0	32.3–58.3
45–64	26	33.3	23.3–45.0	3	16.7	4.4–42.2	23	38.3	26.3–51.8
≥65	0	0	0–5.8	0	0	0–21.8	0	0	0–7.4
Race/ethnicity									
American Indian or Alaska Native	0	0	0–5.8	0	0	0–21.8	0	0	0–7.4
Asian/Pacific Islander	0	0	0–5.8	0	0	0–21.8	0	0	0–7.4
Black	22	28.2	18.8–39.7	6	33.3	14.3–58.8	16	26.7	16.4–39.8
Hispanic or Latino	37	47.4	36.1–58.9	7	38.9	18.2–63.8	30	50.0	37.7–62.2
White	19	24.4	15.6–35.6	5	27.8	10.7–53.5	14	23.3	13.7–36.3
Other or unknown	0	0	0–5.8	0	0	0.0–21.8	0	0	0–7.4
Payer category									
Private	1	1.3	0.06–7.9	1	5.6	0.29–29.3	0	0	0–7.4
Medicaid	10	12.8	6.6–22.7	1	5.6	0.29–29.3	9	15.0	7.5–27.0
Medicare	0	0	0–5.8	0	0	0–21.8	0	0	0–7.4
None	64	82.1	71.3–89.4	16	88.9	63.9–98.0	48	80.0	67.2–88.8
Corrections	2	2.6	0.44–9.8	0	0	0–21.8	2	3.3	0.57–12.5
Other	1	1.3	0.06–7.9	0	0	0–21.8	1	1.7	0.08–10.1
Risk factor									
Heterosexual	22	28.2	18.8–39.7	6	33.3	14.3–58.8	16	26.7	16.4–39.8
IDU	5	6.4	2.3–14.9	0	0	0–21.8	5	8.3	3.1–19.1
MSM	35	44.9	33.7–56.5	7	38.9	18.2–63.8	28	46.7	33.8–59.9
MSM/IDU	6	7.7	3.1–16.5	1	5.6	0.29–29.3	5	8.3	3.1–19.1
Other or unknown	10	12.8	6.6–22.7	4	22.2	7.3–48.0	6	10.0	4.1–21.1
Linkage to medical care									
0 to 30 days	20	25.6	16.7–36.9	8	44.4	22.4–68.6	12	20.0	11.1–32.7
31 to 60 days	22	28.2	18.8–39.7	2	11.1	1.9–36.0	20	33.3	22.0–46.7
61 to 90 days	14	17.9	10.5–28.6	5	27.8	10.7–53.5	9	15.0	7.5–27.0
91 days or longer	8	10.3	4.8–19.7	0	0	0–21.8	8	13.3	6.3–25.1
Lost to follow-up	8	10.3	4.8–19.7	1	5.6	0.29–29.3	7	11.7	5.2–23.1
Other	6	7.7	3.1–16.5	2	11.1	1.9–36.0	4	6.7	2.1–17.0
Medical indicators									
Mean initial viral load	1,512,000 cpy/mL (SD=3,054,703)		834,094–2,189,906	4,630,000 cpy/mL (SD=4,238,333)		2,672,026–6,587,974	527,000 cpy/mL (SD=1,663,088)		106,188–947,812
Median initial viral load	105,400 cpy/mL (IQR=990,140)		64,163–324,546	3,636,000 cpy/mL (IQR=9,196,000)		691,343–10,000,001	59,310 cpy/mL (IQR=215,280)		29,476–109,222
Mean initial CD4	344/mL (SD=251)		288–400	537/mL (SD=237)		428–646	296/mL (SD=233)		237–355
Median initial CD4	318/mL (IQR=295)		239–427	469/mL (IQR=209)		327–848	239/mL (IQR=297)		213–403

the CDC's suggested threshold for universal screening. The total number of new HIV diagnoses was unexpected. Maricopa County, which encompasses greater Phoenix, is not considered an epicenter for HIV, with an incidence of 12.8 new HIV infections per 100,000 population,[20] lower than the national incidence rate of 15.9 per 100,000 population.[21] As a result, we anticipated a lower number of infections than we encountered. This speaks to the importance of HIV detection in varying locations and populations. Because of the fourth-generation test, a quarter of the new HIV infections detected in this study were acute. If the more common third-generation test had been used, the result would have been a false negative, and 16 of our patients would have been told they were HIV negative when they were in fact experiencing acute HIV infection, at which time medical interventions are most beneficial on morbidity and mortality. Alternatively, 1 of 4 new HIV infections likely would have been missed with third-generation antibody-only technology. Given the time course of transmission, some patients were able to identify a particular instance of possible disease acquisition.

TESTAZ was conducted in the only public, safety-net hospital in Arizona. As a result, the characteristics of our patient population suggest they may be at greater risk of both acute and chronic HIV infections. Although the United States Census Bureau Small Area Health Insurance Estimates for 2011 calculated that 19.6% of Arizonans did not have health insurance,[22] 60.1% of unduplicated ED patients during the review period presented with no health insurance at their most recent encounter. Uninsured patients are known to be at high risk for HIV.[23] This study supports this finding as uninsured patients account for 82.1% of newly diagnosed HIV infections and 88.9% of acute infections.

Nearly half of the patients treated in this ED are Hispanic/Latino. Although they represented only 16% of the US population in 2009, this community accounted for 20% of the new HIV infections.[24] Underreported risk factors (because of fear of deportation from illegal intravenous drug use or relations with commercial sex workers), stigma and discrimination against homosexuality, language and education barriers, and lack of access to health care are thought to explain low HIV testing rates among the Hispanic/Latino community.[25,26] Indeed, Table 3 shows that 47% of the HIV diagnoses made through TESTAZ are for Hispanic/Latino patients. Because they are members of a community with a higher HIV prevalence than the national rate and are notoriously undertested,[24] the ED may be a rare opportunity for them to be tested for and potentially receive a diagnosis of HIV.

As expected, some of the reactive fourth-generation HIV test results were false positives. The false-positive rate with this fourth-generation HIV test was 0.097% of all tests, comparable to the 0.227% false-positive rate stated in the test's package insert.[27] Although uncomfortable for patients and an additional complication for TESTAZ, as a public health measure, false-positive results are preferable to false-negative ones. Also, the CD4 counts and viral loads of patients receiving a diagnosis of HIV through this program evaluation show a significant yet expected difference, depending on the classification of the infection. These numbers cannot be compared with those of other ED HIV testing programs because only antibody testing was available.[28] Given that only chronic HIV infections could be diagnosed during previous studies, both CD4 counts and viral load levels would be lower in those studies. Although lower viral load levels in chronic infections may seem counterintuitive, the acute phase of HIV infection is characterized by extremely high viral loads that decrease and stabilize over time.[3] Table 3 shows that initial viral load levels in the acute infections identified through TESTAZ are much higher than in the chronic infections.

Patients receiving a diagnosis through TESTAZ had an active referral to our HIV clinic, the largest provider of HIV medical care in the state of Arizona. Seventy-two percent of TESTAZ patients entered into care within 90 days of diagnosis, which is similar to the 76% found in a meta-analysis of other ED studies and better than the 67% found in a meta-analysis of community venues.[29] The US National HIV/AIDS Strategy released in July 2010 calls for 85% of patients to be linked into care within 90 days of a new HIV diagnosis by 2015.[30] Although a lofty goal, this program shows that it is achievable.

ED HIV programs differ in many respects: who is tested (nontargeted versus targeted), when testing is done (continuously versus certain days and times), how consent is obtained (opt out versus opt in), who obtains consent for the HIV test (triage nurse versus registration versus specialized HIV staff versus physician), who obtains the test (nurse versus specialized HIV staff), type of test performed (antigen/antibody versus antibody alone; phlebotomy versus finger stick versus oral swab), and exclusion criteria.[31,32] As a result, comparisons between programs based on process characteristics are difficult. Of the total individual patients treated in triage, 35.6% received testing, which is a higher percentage than that of most nontargeted or universal screening programs.[33] Eighty-five percent of TESTAZ patients did not decline an HIV test when offered one by a triage nurse, which is on par with a program that used trained HIV staff to discuss consent.[34] Allowing patients to opt out of testing, rather than opt in, likely increased acceptance.[35] Although some question whether ED HIV testing can be routinely conducted without dedicated staff,[32,36] the construction of this program focused on sustainability by adapting existing ED workflow and staff rather than creating a parallel workflow. The only additional program staffing required for TESTAZ has been the linkage-to-care specialist. Although the specialist continues to be integral to confirmatory testing follow-up and linkage to care, ED social workers have assumed primary responsibility for ED result notification; thus, no additional staff is required in the ED.

One of the greatest concerns about this program was asking an already overburdened, underresourced ED and its staff to perform a public health function. By making nontargeted, opt-out HIV screening an organizational priority, the ED has become a long-term investment in the health of the community rather than simply a location for acute care.

Our program shows that fourth-generation antigen/antibody HIV testing with rapid results is feasible in a metropolitan ED. The

total number of new HIV infections was unexpected. Even more surprising, one fourth of patients with undiagnosed HIV had acute infections. This program may serve as a model for the success of nontargeted, opt-out public health measures in an acute care setting. To this end, Maricopa Integrated Health System hosted a symposium to offer information and help to other organizations considering an HIV screening program. Although many were interested and enthusiastic, the lack of organizational support and up-front costs were cited as major barriers to implementation. In addition to continuous improvement of TESTAZ, Maricopa Integrated Health System recently implemented a similar model in our health system's urgent care clinic, using point-of-care technology, and will expand nontargeted HIV screening to our outpatient clinics and psychiatric care.

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REFERENCES

1. Bodach S, Braunstein S, Bernard MA, et al. Integrating acute HIV infection within routine public health surveillance practices in New York City. *Public Health Rep*. 2012;127:451-459.
2. Karris MY, Anderson CM, Morris SR, et al. Cost savings associated with testing of antibodies, antigens, and nucleic acids for diagnosis of acute HIV infection. *J Clin Microbiol*. 2012;50:1874-1878.
3. Branson BM, Stekler JD. Detection of acute HIV infection: we can't close the window. *J Infect Dis*. 2012;205:521-524.
4. Brenner BG, Roger M, Routy JP, et al. High rates of forward transmission events after acute/early HIV-1 infection. *J Infect Dis*. 2007;195:951-959.
5. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. *J Infect Dis*. 2008;198:687-693.
6. Pilcher CD, Tien HC, Eron JJ Jr, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis*. 2004;189:1785-1792.
7. Gray RH, Wawer MJ. Probability of heterosexual HIV-1 transmission per coital act in sub-Saharan Africa. *J Infect Dis*. 2012;205:351-352.
8. Thompson MA, Aberg JA, Hoy JF, et al. Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International Antiviral Society–USA panel. *JAMA*. 2012;308:387-402.
9. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365:493-505.
10. Centers for Disease Control and Prevention (CDC). Detection of acute HIV infection in two evaluations of a new HIV diagnostic testing algorithm—United States, 2011-2013. *MMWR Morb Mortal Wkly Rep*. 2013;62:489-494.
11. Schneider E, Whitmore S, Glynn KM, et al. Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged <18 months and for HIV infection and AIDS among children aged 18 months to <13 years—United States, 2008. *MMWR Recomm Rep*. 2008;57:1-12.
12. Selik RM, Mokotoff ED, Branson B, et al. Revised surveillance case definition for HIV infection—United States, 2014. *MMWR Recomm Rep*. 2014;63:1-10.
13. Fiebig EW, Wright DJ, Rawal BD, et al. Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. *AIDS*. 2003;17:1871-1879.
14. Cohen MS, Gay CL, Busch MP, et al. The detection of acute HIV infection. *J Infect Dis*. 2010;202(suppl 2):S270-S277.
15. Wakeman SE, Rich JD. HIV treatment in US prisons. *HIV Ther*. 2010;4:505-510.
16. Rosenberg SD, Goodman LA, Osher FC, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *Am J Public Health*. 2001;91:31-37.
17. Christopoulos KA, Weiser SD, Koester KA, et al. Understanding patient acceptance and refusal of HIV testing in the emergency department. *BMC Public Health*. 2012;12:3.
18. Brown J, Kuo I, Bellows J, et al. Patient perceptions and acceptance of routine emergency department HIV testing. *Public Health Rep*. 2008;123(suppl 3):21-26.
19. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep*. 2006;55:1-17; quiz CE1-4.
20. Arizona Department of Health Services. HIV epidemiology program, 2012 annual report. July 2012. Available at: http://www.azdhs.gov/phs/edc/odis/documents/hiv-epidemiology/2012/2012-state-of-arizona.pdf. Accessed September 26, 2013.
21. Centers for Disease Control and Prevention. HIV surveillance report, 2011. 2011;23. Available at: http://www.cdc.gov/hiv/pdf/statistics_2011_HIV_Surveillance_Report_vol_23.pdf#Page=84. Accessed September 26, 2013.
22. United States Census Bureau. Small area health insurance estimates interactive data tool. Available at: http://www.census.gov/did/www/sahie/data/interactive/#view=data&utilBtn=&yLB=0&stLB=0&aLB=0&sLB=0&iLB=0&rLB=0&countyCBSelected=false&insuredRBG=pu_&multiYearSelected=false&multiYearAlertFlag=false. Accessed September 26, 2013.
23. Kates J, Levi J. Insurance coverage and access to HIV testing and treatment: considerations for individuals at risk for infection and for those with undiagnosed infection. *Clin Infect Dis*. 2007;45(suppl 4):S255-S260.
24. Arya M, Amspoker AB, Lalani N, et al. HIV testing beliefs in a predominantly Hispanic community health center during the routine

HIV testing era: does English language ability matter? *AIDS Patient Care STDS*. 2013;27:38-44.
25. del Rio C. Latinos and HIV care in the southeastern United States: new challenges complicating longstanding problems. *Clin Infect Dis*. 2011;53:488-489.
26. Gindi RM, Erbelding EJ, Page KR. Sexually transmitted infection prevalence and behavioral risk factors among Latino and non-Latino patients attending the Baltimore City STD clinics. *Sex Transm Dis*. 2010;37:191-196.
27. Architect i1000[M] [package insert]. Abbott Park, IL: Abbott Laboratories; 2010.
28. Brown J, White DA, Magnus M, et al. CD4 counts in patients diagnosed with HIV through routine HIV screening in two urban emergency departments. *J Acquir Immune Defic Syndr*. 2010;54:e15-e16.
29. Marks G, Gardner LI, Craw J, et al. Entry and retention in medical care among HIV-diagnosed persons: a meta-analysis. *AIDS*. 2010;24:2665-2678.
30. White House. National HIV/AIDS strategy for the United States. Available at: http://www.whitehouse.gov/sites/default/files/uploads/NHAS.pdf. Accessed April 10, 2014.
31. Merchant RC, Seage GR, Mayer KH, et al. Emergency department patient acceptance of opt-in, universal, rapid HIV screening. *Public Health Rep*. 2008;123(suppl 3):27-40.
32. White DA, Scribner AN, Schulden JD, et al. Results of a rapid HIV screening and diagnostic testing program in an urban emergency department. *Ann Emerg Med*. 2009;54:56-64.
33. Torres GW, Heffelfinger JD, Pollack HA, et al. HIV screening programs in US emergency departments: a cross-comparison of structure, process, and outcomes. *Ann Emerg Med*. 2011;58:S104-S113.
34. Wheatley MA, Copeland B, Shah B, et al. Efficacy of an emergency department–based HIV screening program in the deep South. *J Urban Health*. 2011;88:1015-1019.
35. White DA, Scribner AN, Vahidnia F, et al. HIV screening in an urban emergency department: comparison of screening using an opt-in versus an opt-out approach. *Ann Emerg Med*. 2011;58:S89-S95.
36. Walensky RP, Reichmann WM, Arbelaez C, et al. Counselor- versus provider-based HIV screening in the emergency department: results from the Universal Screening for HIV Infection in the Emergency Room (USHER) randomized controlled trial. *Ann Emerg Med*. 2011;58(1 suppl 1):S126-S132.e1-4.

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