



2-1-2013

Leveraging a Rapid, Round-the-Clock HIV Testing System to Screen for Acute HIV Infection in a Large Urban Public Medical Center

Katerina A. Christopoulos

Nicola M. Zetola
University of Pennsylvania, nzetola@gmail.com

Jeffrey D. Klausner

Barbara Haller

Brian Louie

See next page for additional authors

Follow this and additional works at: https://repository.upenn.edu/botswana_schol

 Part of the [Immune System Diseases Commons](#)

Recommended Citation

Christopoulos, Katerina A.; Zetola, Nicola M.; Klausner, Jeffrey D.; Haller, Barbara; Louie, Brian; Hare, Bradley; Pandori, Mark; Nassos, Patricia; Roemer, Marguerite; and Pilcher, Christopher D., "Leveraging a Rapid, Round-the-Clock HIV Testing System to Screen for Acute HIV Infection in a Large Urban Public Medical Center" (2013). *Botswana-UPenn Scholarly Publications*. 22.
https://repository.upenn.edu/botswana_schol/22

This paper is posted at ScholarlyCommons. https://repository.upenn.edu/botswana_schol/22
For more information, please contact repository@pobox.upenn.edu.

Leveraging a Rapid, Round-the-Clock HIV Testing System to Screen for Acute HIV Infection in a Large Urban Public Medical Center

Abstract

Methods

The hospital laboratory performed round-the-clock rapid HIV antibody testing on venipuncture specimens from patients undergoing HIV testing in hospital and community clinics, inpatient settings, and the emergency department. For patients with negative results, a public health laboratory conducted pooled HIV RNA testing for acute HIV infection. The laboratories communicated positive results from the hospital campus to a linkage team. Linkage was defined as one outpatient HIV-related visit.

Results

Among 7,927 patients, 8,550 rapid tests resulted in 137 cases of HIV infection (1.7%, 95% CI 1.5%–2.0%), of whom 46 were new HIV diagnoses (0.58%, 95% CI 0.43%–0.77%). Pooled HIV RNA testing of 6,704 specimens (78.4%) resulted in 3 cases of acute HIV infection (0.05%, 95% CI 0.01%–0.14) and increased HIV case detection by 3.5%. Half of new HIV diagnoses and 2/3 of acute infections were detected in the emergency department and urgent care clinic. Rapid test sensitivity was 98.9% (95% CI 93.8%–99.8%); specificity was 99.9% (95% CI 99.7%–99.9%). Over 95% of newly diagnosed and out-of-care HIV-infected patients were linked to care.

Conclusions

Patients undergoing HIV testing in emergency departments and urgent care clinics may benefit from being simultaneously screened for acute HIV infection.

Keywords

HIV serodiagnosis; HIV rapid tests; acute HIV infection; HIV testing in medical settings

Disciplines

Diseases | Immune System Diseases | Medicine and Health Sciences

Author(s)

Katerina A. Christopoulos, Nicola M. Zetola, Jeffrey D. Klausner, Barbara Haller, Brian Louie, Bradley Hare, Mark Pandori, Patricia Nassos, Marguerite Roemer, and Christopher D. Pilcher

Leveraging A Rapid, Round-the-Clock HIV Testing System to Screen for Acute HIV Infection in a Large Urban Public Medical Center

Katerina A. Christopoulos, MD, MPH¹, Nicola M. Zetola, MD, MPH², Jeffrey D. Klausner, MD, MPH³, Barbara Haller, MD, PhD⁴, Brian Louie, BA⁵, C. Bradley Hare, MD¹, Mark Pandori, PhD⁵, Patricia Nassos, PhD⁴, Marguerite Roemer, BA⁴, and Christopher D. Pilcher, MD¹

¹HIV/AIDS Division, San Francisco General Hospital, University of California San Francisco, San Francisco, CA

²Botswana-UPenn Partnership, Division of Infectious Diseases, University of Pennsylvania, Philadelphia, PA

³Infectious Diseases Division, David Geffen School of Medicine, University of California Los Angeles

⁴Department of Laboratory Medicine, San Francisco General Hospital, University of California San Francisco, San Francisco, CA

⁵San Francisco Department of Public Health, San Francisco, CA

Abstract

Objective—To describe the prevalence and location of new and acute HIV diagnoses in a large urban medical center. Secondary objectives were to evaluate rapid HIV test performance, the added yield of acute HIV screening, and linkage to care outcomes.

Design—Cross-sectional study from November 1, 2008, to April 30, 2009.

Correspondence/Reprints: Katerina A. Christopoulos, HIV/AIDS Division, San Francisco General Hospital, 995 Potrero Ave, Bldg 80, Ward 84, Box 0874, San Francisco CA 94114. Tel 415-476-4082 Fax 415-476-6953 christopoulosk@php.ucsf.edu.

Previous Presentation: This work was presented in part at the 2009 National HIV Prevention Conference, Atlanta, GA, and the XVIII International AIDS Conference, July 18–23, 2010, Vienna, Austria.

Conflicts of Interest: Outside of this work, Dr. Christopoulos has received grant funding from Bristol Myers Squibb; Dr. Pilcher has received funding from Gen-Probe and given lectures for Bio-Rad; Dr. Haller has served as a consultant to Ortho Diagnostics and has received research support from Cepheid; Dr. Hare has been a consultant to Bristol Myers Squibb, Abbott, Gilead, Merck, and Tibotec/Janssen, and on the lectures/speakers' bureau of Bristol Myers Squibb, Gilead, Merck, Viiv, and Tibotech/Janssen. All other authors declare no conflicts of interest.

Author Contributions: Dr. Christopoulos had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Zetola, Klausner, Louie, Hare, Pilcher

Acquisition of data: Christopoulos, Haller, Louie, Pandori, Nassos, Roemer, Pilcher

Analysis and interpretation of data: Christopoulos, Zetola, Klausner, Haller, Hare, Nassos, Roemer, Pilcher

Drafting of manuscript: Christopoulos, Pilcher

Critical revision of the manuscript for important intellectual content: Zetola, Klausner, Haller, Louie, Pandori, Hare, Nassos, Roemer

Statistical analysis: Christopoulos, Zetola

Obtaining funding: Zetola, Klausner, Pilcher

Administrative, technical, or material support: Klausner, Haller, Louie, Pandori, Nassos, Roemer

Study supervision: Klausner, Hare, Pilcher

Methods—The hospital laboratory performed round-the-clock rapid HIV antibody testing on venipuncture specimens from patients undergoing HIV testing in hospital and community clinics, inpatient settings, and the emergency department. For patients with negative results, a public health laboratory conducted pooled HIV RNA testing for acute HIV infection. The laboratories communicated positive results from the hospital campus to a linkage team. Linkage was defined as one outpatient HIV-related visit.

Results—Among 7,927 patients, 8,550 rapid tests resulted in 137 cases of HIV infection (1.7%, 95% CI 1.5%–2.0%), of whom 46 were new HIV diagnoses (0.58%, 95% CI 0.43%–0.77%). Pooled HIV RNA testing of 6,704 specimens (78.4%) resulted in 3 cases of acute HIV infection (0.05%, 95% CI 0.01%–0.14) and increased HIV case detection by 3.5%. Half of new HIV diagnoses and 2/3 of acute infections were detected in the emergency department and urgent care clinic. Rapid test sensitivity was 98.9% (95% CI 93.8%–99.8%); specificity was 99.9% (95% CI 99.7%–99.9%). Over 95% of newly diagnosed and out-of-care HIV-infected patients were linked to care.

Conclusions—Patients undergoing HIV testing in emergency departments and urgent care clinics may benefit from being simultaneously screened for acute HIV infection.

Keywords

HIV serodiagnosis; HIV rapid tests; acute HIV infection; HIV testing in medical settings

INTRODUCTION

In 2006, the Centers for Disease Control and Prevention (CDC) recommended routine screening for HIV infection in patients aged 13–64 years in all health care settings where the prevalence of HIV infection is above 0.1%.¹ HIV-infected persons who do not know their status often present to medical settings and fail to be diagnosed, leading to late detection, higher morbidity, and prolonged transmission risk.^{2–4} Hospitals and their satellite clinics, therefore, are ideal settings to scale up HIV testing, especially since access to on-site HIV specialists has been shown to improve linkage to care for newly diagnosed and out of care HIV-infected patients.⁵

Historically, a significant barrier to expanding HIV testing in the medical center setting has been the use of testing technologies with long turnaround time, e.g., enzyme immunoassay (EIA) testing. EIA testing, conducted in “batches” several times a week, is not well-suited to settings with rapid patient turnover, as it may delay appropriate clinical management and has been associated with high failure-to-notify rates.^{6,7}

Rapid HIV testing has the potential to increase testing in medical settings.⁸ Indeed, rapid HIV testing has been implemented successfully in medical settings such as labor and delivery, the emergency department, and the inpatient wards.^{9–13} To date, however, the use of rapid HIV testing in medical settings has been limited to specific hospital departments. In addition, these initiatives have generally relied on point-of-care technology requiring ancillary staff, curtailing the ability to provide round-the-clock testing for large numbers of patients. As yet, a system for the effective application of rapid HIV testing across all care settings of a hospital and its satellite clinics has not been demonstrated.

An additional point regarding the adoption of rapid HIV testing is that the optimal testing technology for identifying HIV infection in medical settings has not been determined, especially since acute HIV infection may be relatively common in certain clinical venues, such as the urgent care clinic.^{14,15} Persons with acute HIV infection are highly infectious and may unknowingly transmit HIV infection if they remain unaware of their status.^{16–18}

Fourth-generation immunoassays that can detect both HIV antibody and p24 antigen are a potentially appealing option. In addition, these assays can be run on automated platforms (as opposed to manual third-generation EIAs).¹⁹ However, little data exist on the prevalence of acute HIV infection across all inpatient and outpatient medical settings to justify a universal shift to this more sensitive testing format.

We therefore sought to investigate the potential contribution of acute HIV infection to hospital-wide HIV diagnosis. We drew upon a unique testing system developed at San Francisco General Hospital to execute this project. Key features of this testing system were laboratory-based, round-the-clock, rapid HIV testing on venipuncture specimens from all medical center care settings closely integrated with the services of an HIV clinic-based linkage to care team. Building on this system, we developed and implemented a program to screen rapid-test negative specimens for HIV RNA and link acutely HIV infected individuals to care. Thus, the primary objective of this study was to describe the prevalence all HIV cases, new HIV diagnoses, and acute HIV infections across medical center sites. Secondary objectives were to: 1) determine the increase in HIV case detection conferred by screening for acute HIV infection; 2) calculate rapid test performance characteristics against a “gold standard” of pooled HIV RNA screening, and; 3) ascertain disclosure and linkage to care outcomes.

METHODS

Study Design

We conducted a six-month cross-sectional study of medical center rapid HIV testing with an algorithm that included pooled HIV RNA testing for acute HIV infection. The implementation of pooled HIV RNA testing and all evaluation procedures were approved by the University of California San Francisco Committee on Human Research.

Population, Sites, and Consent Procedures

The study included all patients undergoing HIV antibody testing via the San Francisco General Hospital (SFGH) Clinical Laboratory between November 1, 2008 and April 30, 2009, a period during which there were department-specific initiatives to increase HIV testing in the emergency department and the adult urgent care clinic. SFGH is a 300-bed acute care public hospital and a major provider for the estimated 150,000 people in San Francisco who have public insurance or are uninsured. HIV testing sites included medical/surgical specialty clinics located on the hospital campus, 18 community health centers, the emergency department, and all inpatient wards. In accordance with California state law, clinicians obtained verbal consent prior to rapid HIV testing, which was offered in an opt-in fashion. Several sites using the hospital laboratory for HIV testing were excluded from the pooled HIV RNA protocol because of: 1) preference for individually managing patients at risk for acute HIV infection (occupational health, labor and delivery, the nursery); 2) a high number of individuals with known HIV infection (an on-site HIV primary care clinic, an off-site HIV skilled nursing facility), or; 3) special administrative requirements (the outpatient jail, research studies).

Rapid Antibody Testing Protocol

The hospital Clinical Laboratory used the Uni-Gold Recombigen HIV Test (Trinity Biotech, Bray, Ireland) to conduct rapid HIV antibody testing on serum or plasma specimens during every shift, seven days a week. A negative rapid antibody test was reported as rapid HIV antibody “negative,” and, if an additional BD Vacutainer (Franklin Lakes, NJ) plasma preparation tube (PPT) was also collected according to protocol, it was sent to the San Francisco Department of Public Health (SFDPH) Laboratory on the next business day to be

placed in the queue for twice-weekly pooled HIV RNA testing (Figure 1). Rapid test results were available in the electronic medical record (EMR) within two hours after specimen receipt. A positive rapid HIV antibody result was reported as “preliminary positive.” Rapid test “preliminary positive” specimens underwent EIA testing with a third-generation test (Genetic Systems HIV-1/HIV-2 Plus O EIA, Bio-Rad, Redmond, WA) Mondays, Wednesdays, and Fridays, and were confirmed with immunofluorescence (IFA) testing (Fluorognost HIV-1 IFA, Sanochemia Pharmazeutika, Vienna, Austria). If the EIA and IFA were both negative, then a final HIV antibody test was reported as “negative.” If the EIA and IFA were both positive, then a final HIV antibody test was reported as “positive.” If the EIA was positive and the IFA was negative or indeterminate, the rapid test specimen was sent to the SFDPH Laboratory for Western blot testing; in addition, if a PPT specimen was available, it was sent to the SFDPH Laboratory for individual HIV RNA testing.

Pooled HIV RNA Testing Protocol

Given the use of pooled HIV RNA testing in public health practice,^{20–24} the institutional review board and hospital administration did not require separate consent or additional orders for pooled HIV RNA testing. Clinical staff were educated via administrative meetings on the need to draw additional specimen for pooled HIV RNA testing but were not systematically encouraged to target patients with symptoms consistent with acute HIV infection. Sites received monthly reports detailing the proportion of specimens screened for acute HIV infection.

The SFPDH Laboratory assembled aliquots from rapid antibody negative patients into pooled samples at a 10:1 ratio. Pooled HIV RNA testing was performed twice a week using a qualitative HIV RNA assay (APTIMA HIV-1 RNA; Gen-Probe Inc, San Diego CA) with a lower limit of detection of 30 copies/ml, theoretically permitting detection of individual specimens with 300 copies/ml in a master pool with a 1:10 dilution. Positive pools were deconstructed and each individual specimen underwent qualitative HIV RNA testing. Individual HIV RNA-positive specimens were then quantified (Abbott RealTime HIV-1 Assay, Abbott Laboratories, Des Plaines, IL) before being reported as “HIV-1 RNA Detected” in the SFGH electronic medical record (EMR). EIA-positive/IFA-negative or indeterminate specimens also underwent qualitative HIV RNA testing with subsequent quantification if positive. Negative pools were reported in the EMR as “HIV-1 RNA Not Detected” within 2–6 days, while HIV RNA-positive results were available within 4–8 days of rapid antibody testing.

Procedures for Disclosure and Linkage to Care

The hospital Clinical Laboratory paged all “preliminary positive” HIV rapid test results to a linkage to care team based in an on-site HIV primary care clinic in real-time during business hours (8am–5pm) and on the next business day for results reported on evenings and weekends. Patients on the hospital campus were eligible for linkage to care team services (Figure 2). For both admitted and non-admitted patients, the linkage to care team, which consisted of a nurse, nurse practitioner, and social work associate, worked with the ordering clinician to ensure disclosure. Ordering clinicians were encouraged to disclose with linkage team support, but linkage team members also disclosed results directly, especially if the ordering clinician was not available. For patients still on-site, the linkage team met with the patient to provide counseling and an appointment for confirmatory results. For outpatients with “preliminary positive” results reported on nights or weekends, the linkage to care team contacted ordering clinicians and patients within one business day to ensure disclosure and a follow-up appointment. With regard to pooled HIV RNA results, the SFDPH Laboratory notified the ordering clinician, the linkage to care team, and the SFDPH HIV notification and partner services unit when specimens were confirmed RNA-positive.²⁵ For patients with

prior HIV diagnoses, the linkage to care team ascertained care status through review of EMR appointment data and direct patient query.

Data Collection and Analyses

We obtained test data and demographics on all individuals undergoing HIV testing from the EMR and laboratory databases. For individuals with confirmed HIV infection, we assessed prior testing history, HIV care status, and linkage to care, defined as attendance at one outpatient HIV-related visit at any time, using the EMR, linkage to care team logs, and laboratory/public health databases. As outlined above, patients with EIA/IFA positive results were considered to have confirmed HIV infection. Acute HIV infection was defined as being: 1) EIA-negative/HIV RNA-positive; 2) EIA-positive/IFA-negative/HIV RNA-positive, or; 3) EIA-positive/IFA-indeterminate/HIV RNA-positive. We report data on the total number of tests processed by the hospital laboratory as well as the number of tests from sites eligible for pooled HIV RNA testing, along with test outcomes and the proportion of HIV diagnoses considered to be new (previously unknown). The increase in HIV case detection attributable to pooled HIV RNA testing was calculated using only those samples with adequate specimen available for further testing. Rates of disclosure and linkage to care were calculated considering HIV-infected inpatients and outpatients who were tested on the hospital campus and thus eligible for linkage team services. Descriptive statistics were calculated using Stata SE/10 (College Station, TX). Test performance characteristics were calculated using an open-source software program (Open-Epi, version 2.3.1; Emory Rollins School of Public Health, Atlanta, GA).

Role of Funding Sources

Funding and materials for the implementation of pooled HIV RNA testing were provided by the California HIV Research Program and Gen-Probe, Inc. Neither of these entities played a role in the design, conduct, or reporting of this study.

RESULTS

Prevalence of HIV Infection Among Hospital System Testers

Between November 1, 2008, and April 30, 2009, there were 9,938 specimens rapid tested for HIV antibody by the hospital Clinical Laboratory (Table 1), of which 8,550 specimens were from patients seen at sites participating in pooled HIV RNA testing (5,809 specimens from the hospital campus and 2,741 specimens from 18 off-site community clinics). These 8,550 specimens were drawn from 7,927 unique patients. Approximately 76,811 unique patients were seen at testing sites during the study period, thus about 10% of patients were tested for HIV. Patients had a median age of 40 years (interquartile range 28, 52), were evenly divided between men and women, and were 61.8% racial/ethnic minority (Table 2). As detailed in Table 1, there were 137 cases of HIV infection (prevalence 1.7%, 95% CI: 1.5%-2.0%) from sites participating in pooled HIV RNA testing (134 confirmed HIV infections, 2 acute infections with inconclusive antibody results, and 1 antibody-negative acute infection). Of these 137 cases, there were 46 (33.6%) new diagnoses of HIV infection for a prevalence of newly diagnosed HIV infection = 0.58%, 95% CI: 0.43%-0.77% and a prevalence of acute HIV infection = 0.05%, 95% CI: 0.01%-0.14% (as calculated by dividing the acute cases by the number of unique individuals undergoing pooling). The median CD4 cell count for newly diagnosed patients was 331 cells/ μ L (interquartile range 260, 517). Half of the cases of new HIV infection were from the ED or adult urgent care clinic. Indeed, the three cases of acute HIV infection were from the emergency department, the adult urgent care clinic, and a “drop-in” visit at a community health center. All were Latino men who identified their HIV risk factor as having sex with men. When considering just the yield of new and acute cases

from the ED and adult urgent care clinic, estimates doubled to 1.2%, 95% CI: 0.8%-1.9% and 0.1%, 95% CI: 0.01%, 0.4%, respectively.

Performance of Rapid HIV Testing vs. Rapid Testing Plus HIV RNA Testing

Pooled HIV RNA testing was performed on 6,704 (78.4%) specimens from HIV rapid test negative patients. Compliance with specimen submission, defined as submission of both a rapid test specimen and the plasma preparation tube necessary for pooled RNA testing, increased from 54.4% in the first month of the observation period to 87.0% in the last month. The number of monthly rapid HIV tests from the hospital campus rose from 632 during the first month of the study to 1,101 during the last month of the study. Although the rapid test plus HIV RNA testing algorithm identified three cases that met our study definition of acute HIV infection, only one of these was rapid test negative/HIV-RNA positive (one was rapid test positive/EIA positive/IFA negative/HIV RNA-positive and one was rapid test positive/EIA positive/IFA indeterminate/HIV RNA-positive). All had quantitative viral loads >500,000 copies/ml and subsequent complete seroconversion (Figure 1). The single rapid-test negative/HIV-RNA positive specimen was also negative on a third-generation EIA test. Using the number of confirmed cases sent with a PPT tube (and hence eligible for pooled HIV RNA screening had these specimens been rapid test negative) as the denominator, these three cases represented 3.5% of all HIV cases and 10.3% of new HIV cases. However, because two of the three acute HIV cases would have been detected (though not confirmed) by the rapid test alone, the addition of pooled HIV RNA screening identified only one case that would have been completely missed, representing 1.2% of all cases and 3.5% of new cases.

The performance of the Uni-Gold rapid HIV test was assessed using EIA/IFA/HIV RNA testing as the gold standard. The sensitivity of the rapid test was 98.9% (95% CI 93.8%-99.8%) and the specificity was 99.9% (95% CI 99.7%-99.9%). The positive predictive value was 90.5% (95% CI 82.0%-94.9%) and the negative predictive value was 100% (95% CI 99.9%-100%).

Disclosure and Linkage to Care Outcomes

There were 98 patients with a “preliminary positive” rapid HIV test result diagnosed on the hospital campus and thus eligible for linkage to care team services (Table 1). Of these patients, 12 had a false-positive rapid HIV test result and 1 was an infant with maternal antibodies and a negative quantitative HIV viral load, while 54 rapid test results were in patients who proved to have confirmed, previously diagnosed HIV infection (Figure 3). Of the 31 patients who were rapid test positive and subsequently confirmed as new HIV diagnoses, 9 admitted patients and 18 of 22 outpatients received their test results during the same clinical encounter. Of the remaining four outpatients, three patients were disclosed to 5–9 days later and one learned his diagnosis after representing to the ED for care. The one patient with rapid test negative/HIV RNA positive acute HIV infection received his final test results one week after testing negative on the rapid test. This patient was already in care with a community physician with HIV expertise. All newly diagnosed patients who lived in the county and did not have insurance incompatible with the SFGH clinic system were confirmed as linked to care. Time to linkage was calculated as time from diagnosis to first outpatient HIV visit except for those patients admitted after diagnosis, in which case time to linkage was time from hospital discharge to first outpatient HIV visit. The median time to linkage to care was 3.5 days (interquartile range 2–8.5, range 0 to 70). Of those with prior HIV diagnoses, the majority (74%) were in care. Of the 12 patients who were not in care, 11 were re-linked to care. Thus, the overall proportion of patients linked to care was 97.5% (95% CI: 86.8%–99.9%).

DISCUSSION

We leveraged the novel features of a hospital laboratory-based rapid testing system to add pooled HIV RNA testing for a period of six months. We found that screening for acute HIV infection in rapid test negative patients from an urban medical center contributed only minimally (1.2%) to the total number of HIV cases identified. Perhaps more importantly, we found that by using round-the-clock rapid testing, the hospital laboratory was able to provide preliminary results that had both high positive and negative predictive value within two hours of specimen receipt. Use of an HIV clinic-based linkage to care team resulted in very high rates of linkage to care. These results support round-the-clock, laboratory-based, rapid testing as a successful approach to medical center HIV testing. In addition, this testing system has the potential to sustain efforts to expand HIV testing, as it provides these round-the-clock and rapid results without requiring dedicated staff to conduct point-of-care testing.

This study demonstrated that there are several clinical locations, particularly those that provide “drop-in” care, that diagnose a large number and proportion of new HIV infections. Half of the new HIV infections in this study were identified in the emergency department and adult urgent care clinic, including two of the three acute infections. In these important sites of health care for vulnerable urban populations,² scaling up testing to identify new and acute cases remains a challenge, as busy providers in these settings face numerous barriers to performing HIV testing.²⁶ Screening for acute HIV infection by pooled HIV RNA testing requires too lengthy a turnaround time to guide clinical management in real time. However, the recent FDA approval of two fourth-generation immunoassays offers the potential for both acute HIV screening and relatively fast (perhaps same day) test turnaround.²⁷ Indeed, a preliminary recommendation for new laboratory HIV testing guidelines advocates for screening with the most sensitive immunoassay available, i.e. a fourth-generation test, followed by an antibody test that can distinguish between HIV-1 and HIV-2.^{28,29}

However, several points bear mentioning. First, even same-day results may not be fast enough for locations such as the emergency department and urgent care clinic, where a cornerstone of HIV testing has been the availability of truly rapid results. Second, the fourth-generation tests currently available in the U.S. do not distinguish between acute and established HIV infection, making it necessary to investigate the discordance between a reactive fourth-generation test and a negative confirmatory test (such as a Western blot) with HIV RNA testing. In our study, two of three acute infections were rapid test positive, negative or indeterminate by confirmatory IFA testing, and RNA positive. These two cases highlight the importance of resolving discordant test results.

While screening for acute HIV infection may be important in the emergency department and urgent care clinic, its impact in other medical settings will likely be less pronounced. In the inpatient setting – and even in many outpatient clinics – HIV testing is frequently used to confirm a patient’s HIV status, as prior test results may not be readily available and clinical management decisions need to be made. In our study, two-thirds of patients testing HIV positive were found to have previously tested HIV positive. Reasons for this finding bear further investigation but may include the need to document HIV status, lack of immediate disclosure of HIV status, and denial of HIV status. Moreover, some previously diagnosed HIV-infected individuals had lapsed in care, and reporting positive rapid test results to the linkage team facilitated effective re-engagement for these patients.

Indeed, the ability of the testing system to facilitate linkage team follow up of positive HIV test results in real time and across a range of hospital settings is a unique feature that merits attention. As hospitals and acute care settings look for sustainable and cost-effective ways to

scale up HIV testing, we believe elements of this testing system hold great promise, with or without screening for acute HIV infection.

There were several limitations to our analysis. This was a lab-based study designed to screen for acute HIV infection, rather than an effort to actively promote hospital-wide HIV case finding. Because not all medical center patients were tested for HIV, the true prevalence of acute and non-acute HIV infection is not known. Furthermore, because this was an observational study, we cannot evaluate the separate effects of rapid testing, pooled RNA screening, and the linkage to care team on patient outcomes. Finally, we do not formally assess labor requirements and cost, though we are able to document that this rapid testing system allowed the hospital campus to nearly double the monthly number of tests without need for additional laboratory staff while maintaining excellent diagnostic test performance.

CONCLUSIONS

Clinical laboratory-based rapid HIV testing with integrated linkage to care works well for many medical settings and has the potential to sustain HIV testing efforts. However, patients in certain clinical venues, such as the emergency department and the urgent care clinic, may benefit from being screened for acute HIV infection. While pooled RNA testing can aid in the detection of acute HIV infection, its long turnaround time may limit its application in these settings. Fourth-generation immunoassays performed in a rapid fashion may be one option for these locations.

Acknowledgments

Source of Funding: Funding and materials for the implementation of pooled HIV RNA testing were provided by California HIV Research Program (CHRP) grants RN07-SF-722 and CH05-SMCHC-612, and Gen-Probe, Inc. Neither entity played a role in the design or conduct of the study, collection, management, analysis, and interpretation of the data, or the preparation, review and approval of the manuscript. This publication was made possible by grant number UL1 RR024131 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and the NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR. Information on NCRR is available at <http://www.ncrr.nih.gov/>. Information on Re-engineering the Clinical Research Enterprise can be obtained from <http://nihroadmap.nih.gov/clinicalresearch/overview-translational.asp>. This work was also supported by NIH grants T32 AI60530 and K23 MH 09220 (K.A.C.) and R34 MH 096606 (C.D.P).

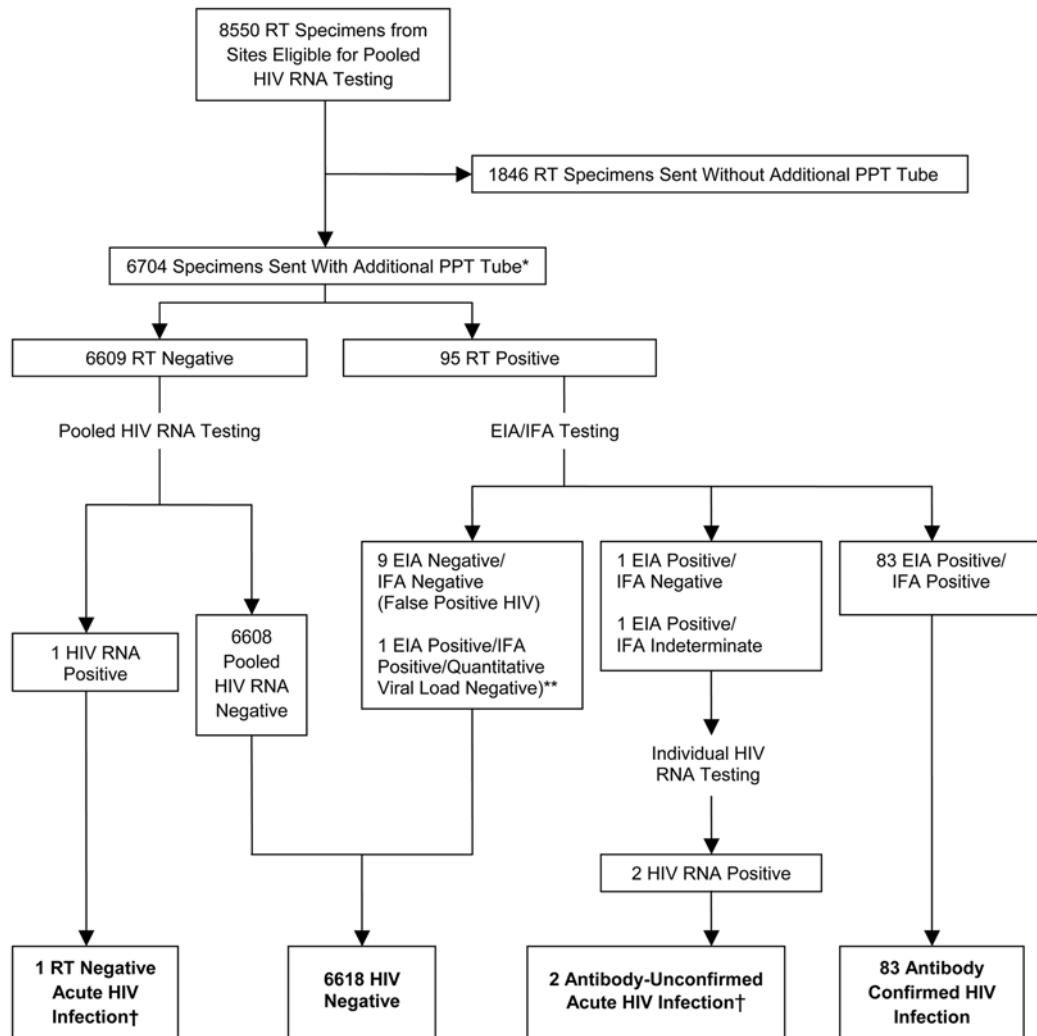
The authors wish to thank the following individuals, without whom this project and its evaluation would not have been possible: Diane Jones, RN, Clarissa Ospina-Norvell, NP, and Alida Marrero-Calderon of the San Francisco General Hospital Positive Health Program for their dedication in linking HIV-infected patients to care, Sally Liska, PhD, of the San Francisco Department of Public Health Laboratory for technical guidance, and Fred Strauss, MD, of the San Francisco General Hospital for medical informatics support. For the data used in this study, we thank Margaret Wong of the San Francisco General Hospital Clinical Laboratory, Paul Norris, AB, and Ketty Mobed, PhD, of the UCSF THREDS program, and Kyle Bernstein, PhD, and Robert Kohn, MPH, of the San Francisco Department of Public Health STD Prevention and Control Services. We thank Wendy Hartogensis, PhD, of the San Francisco General Hospital HIV/AIDS Division for assembling the final datasets, and Jane Drake, MPH, of the UCSF Global Health Sciences for administrative support.

References

1. 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*. Sep 22; 2006 55(RR-14):1–17. quiz CE11–14. [PubMed: 16988643]
2. Klein D, Hurley LB, Merrill D, Quesenberry CP Jr. Review of medical encounters in the 5 years before a diagnosis of HIV-1 infection: implications for early detection. *J Acquir Immune Defic Syndr*. Feb 1; 2003 32(2):143–152. [PubMed: 12571523]
3. Liddicoat RV, Horton NJ, Urban R, Maier E, Christiansen D, Samet JH. Assessing missed opportunities for HIV testing in medical settings. *J Gen Intern Med*. Apr; 2004 19(4):349–356. [PubMed: 15061744]

4. Jenkins TC, Gardner EM, Thrun MW, Cohn DL, Burman WJ. Risk-based human immunodeficiency virus (HIV) testing fails to detect the majority of HIV-infected persons in medical care Settings. *Sex Transm Dis.* May; 2006 33(5):329–333. [PubMed: 16547450]
5. Marks G, Gardner LI, Craw J, Crepaz N. Entry and retention in medical care among HIV-diagnosed persons: a meta-analysis. *AIDS.* Nov 13; 2010 24(17):2665–2678. [PubMed: 20841990]
6. Wolf LE, Donoghoe A, Lane T. Implementing routine HIV testing: the role of state law. *PLoS One.* 2007; 2(10):e1005. [PubMed: 17925853]
7. Kendrick SR, Kroc KA, Withum D, Rydman RJ, Branson BM, Weinstein RA. Outcomes of offering rapid point-of-care HIV testing in a sexually transmitted disease clinic. *J Acquir Immune Defic Syndr.* Feb 1; 2005 38(2):142–146. [PubMed: 15671798]
8. Lubelchek R, Kroc K, Hota B, et al. The role of rapid vs conventional human immunodeficiency virus testing for inpatients: effects on quality of care. *Arch Intern Med.* Sep 26; 2005 165(17):1956–1960. [PubMed: 16186464]
9. Bulterys M, Jamieson DJ, O’Sullivan MJ, et al. Rapid HIV-1 testing during labor: a multicenter study. *JAMA.* Jul 14; 2004 292(2):219–223. [PubMed: 15249571]
10. Christopoulos KA, Schackman BR, Lee G, Green RA, Morrison EA. Results from a New York City emergency department rapid HIV testing program. *J Acquir Immune Defic Syndr.* Mar 1; 2010 53(3):420–422. [PubMed: 20190591]
11. White DA, Scribner AN, Schulden JD, Branson BM, Heffelfinger JD. Results of a rapid HIV screening and diagnostic testing program in an urban emergency department. *Ann Emerg Med.* Jul; 2009 54(1):56–64. [PubMed: 18990468]
12. Jain CL, Jue JS, MacKay R, Wallach F, Factor SH, Wyatt CM. Acceptance of rapid HIV testing among medical inpatients in New York City. *AIDS Patient Care STDS.* Aug; 2008 22(8):657–662. [PubMed: 18721054]
13. Siegel M, Kennedy L, Rexroth K, et al. Better but not ideal acceptance of routine inpatient HIV point-of-care testing among veterans in a high prevalence area. *J Acquir Immune Defic Syndr.* Oct 1; 2010 55(2):205–210. [PubMed: 20502345]
14. Rosenberg ES, Caliendo AM, Walker BD. Acute HIV infection among patients tested for mononucleosis. *N Engl J Med.* Mar 25.1999 340(12):969. [PubMed: 10094651]
15. Pincus JM, Crosby SS, Losina E, King ER, LaBelle C, Freedberg KA. Acute human immunodeficiency virus infection in patients presenting to an urban urgent care center. *Clin Infect Dis.* Dec 15; 2003 37(12):1699–1704. [PubMed: 14689354]
16. Yerly S, Vora S, Rizzardi P, et al. Acute HIV infection: impact on the spread of HIV and transmission of drug resistance. *AIDS.* Nov 23; 2001 15(17):2287–2292. [PubMed: 11698702]
17. Brenner BG, Roger M, Routy JP, et al. High rates of forward transmission events after acute/early HIV-1 infection. *J Infect Dis.* Apr 1; 2007 195(7):951–959. [PubMed: 17330784]
18. Pilcher CD, Tien HC, Eron JJ Jr, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis.* May 15; 2004 189(10):1785–1792. [PubMed: 15122514]
19. Ly TD, Laperche S, Brennan C, et al. Evaluation of the sensitivity and specificity of six HIV combined p24 antigen and antibody assays. *J Virol Methods.* Dec 15; 2004 122(2):185–194. [PubMed: 15542143]
20. Pilcher CD, McPherson JT, Leone PA, et al. Real-time, universal screening for acute HIV infection in a routine HIV counseling and testing population. *JAMA.* Jul 10; 2002 288(2):216–221. [PubMed: 12095386]
21. Pilcher CD, Fiscus SA, Nguyen TQ, et al. Detection of acute infections during HIV testing in North Carolina. *N Engl J Med.* May 5; 2005 352(18):1873–1883. [PubMed: 15872202]
22. Stekler J, Swenson PD, Wood RW, Handsfield HH, Golden MR. Targeted screening for primary HIV infection through pooled HIV-RNA testing in men who have sex with men. *AIDS.* Aug 12; 2005 19(12):1323–1325. [PubMed: 16052089]
23. Patel P, Klausner JD, Bacon OM, et al. Detection of acute HIV infections in high-risk patients in California. *J Acquir Immune Defic Syndr.* May; 2006 42(1):75–79. [PubMed: 16763493]
24. Priddy FH, Pilcher CD, Moore RH, et al. Detection of acute HIV infections in an urban HIV counseling and testing population in the United States. *J Acquir Immune Defic Syndr.* Feb 1; 2007 44(2):196–202. [PubMed: 17312561]

25. Ahrens K, Kent CK, Kohn RP, et al. HIV partner notification outcomes for HIV-infected patients by duration of infection, San Francisco, 2004 to 2006. *J Acquir Immune Defic Syndr*. Dec 1; 2007 46(4):479–484. [PubMed: 18077837]
26. Arbelaez C, Wright EA, Losina E, et al. Emergency Provider Attitudes and Barriers to Universal HIV Testing in the Emergency Department. *J Emerg Med*. E pub 2009/10/16.
27. Bischof JJ, Kuruc JD, Embry JA, et al. Prospective study of the ARCHITECTHIV Ag/Ab Combo fourth generation assay to detect HIV infection in sexually transmitted infection clinics. *AIDS*. Sep 24; 2011 25(15):1927–1929. [PubMed: 21811138]
28. Pandori MW, Branson BM. 2010 HIV Diagnostics Conference. *Expert Rev Anti Infect Ther*. Jun; 2010 8(6):631–633. [PubMed: 20521890]
29. CLSI. CLSI document M53-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2011. *Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection Approved Guidelines*.
30. Rosenberg NE, Kamanga G, Phiri S, et al. Detection of acute HIV infection: a field evaluation of the determine(R) HIV-1/2 Ag/Ab combo test. *J Infect Dis*. Feb; 2012 205(4):528–534. [PubMed: 22207651]



RT=Rapid Test, PPT=Plasma Preparation Tube, EIA =Enzyme Immunoassay, IFA=Immunofluorescence
 * Specimens represent 6,284 unique individuals
 **Represents an infant of an HIV-infected mother who was tested with quantitative viral load testing
 †Quantitative viral load >500,000 copies/mL and full seroconversion confirmed on repeat testing

Figure 1.
Disposition of Specimens Undergoing Rapid HIV Testing and Pooled HIV RNA Testing

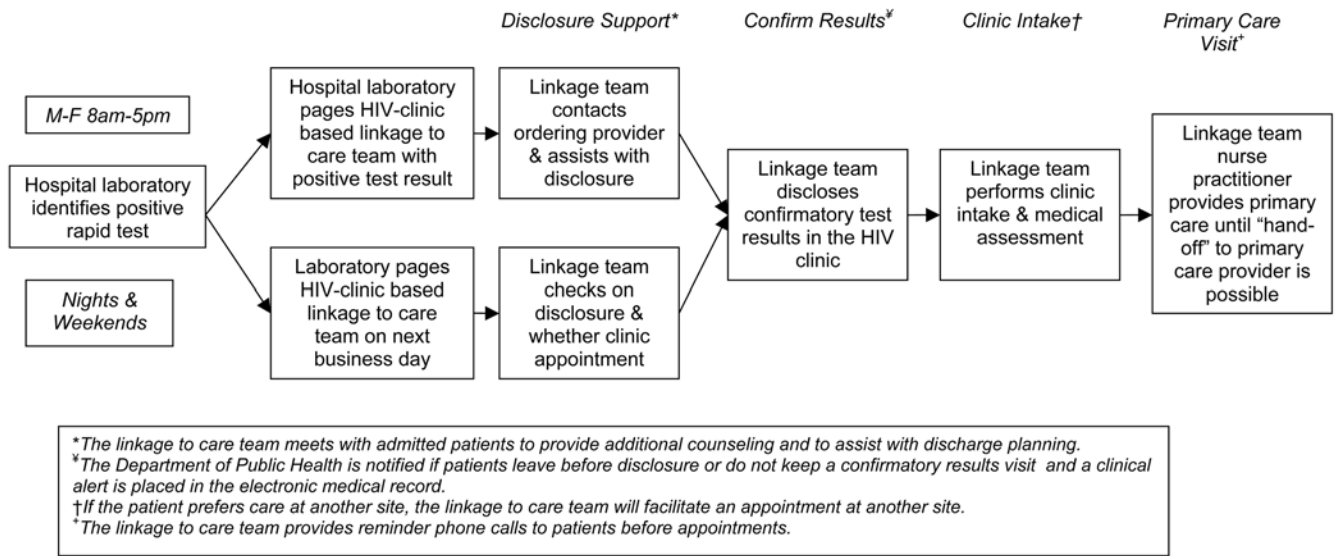


Figure 2.
 Coordination Between the Hospital Laboratory and an HIV Clinic-Based Linkage to Care Team

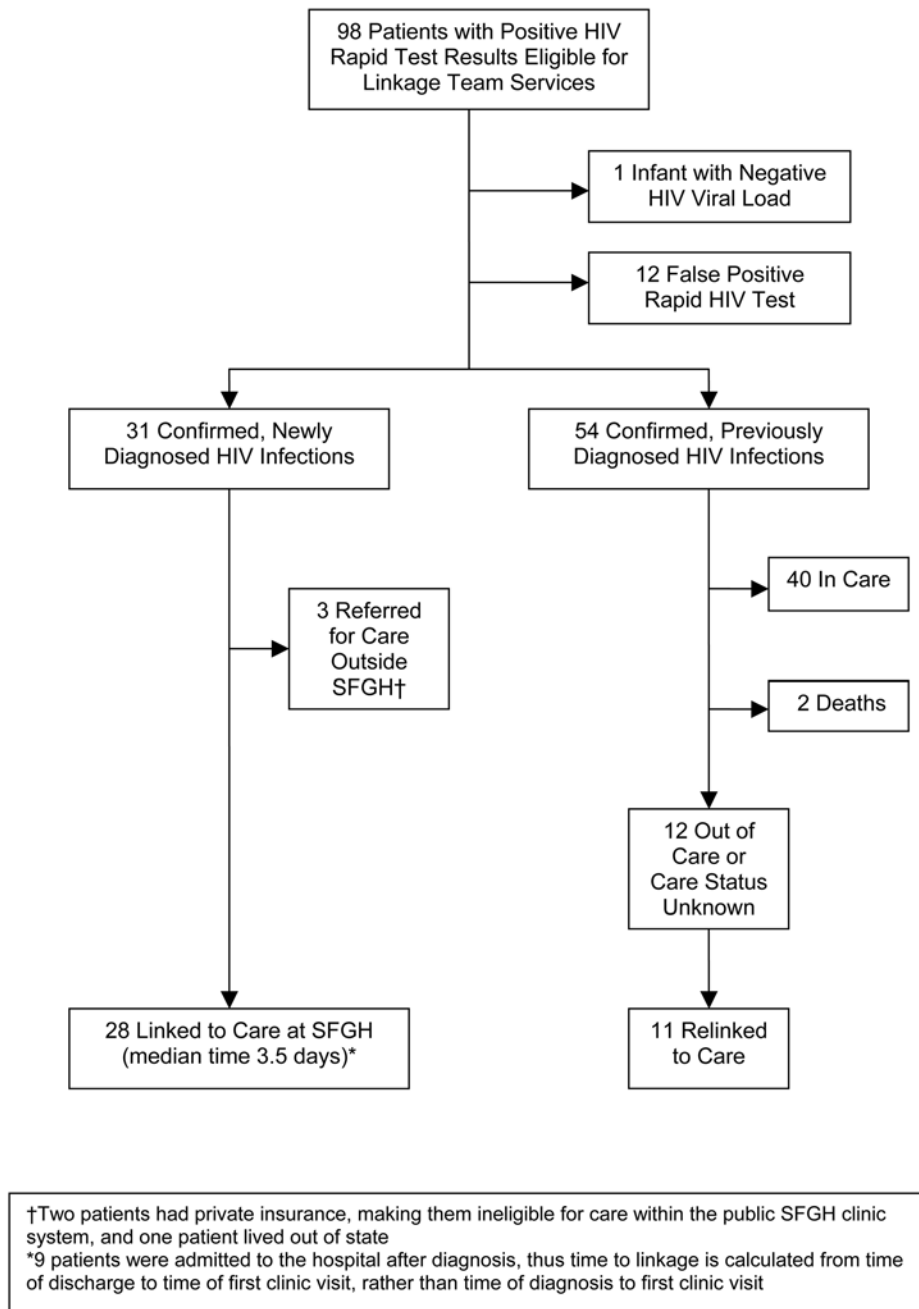


Figure 3. Linkage to Care Outcomes for Patients Newly Diagnosed on the Hospital Campus

Table 1

Rapid Test Results, Pooled HIV RNA Results, and Newly Diagnosed HIV Infections by Medical Center Testing Site

Testing Site	Rapid Tests (RT)	Adequate Specimen for Pooled RNA n (%)	RT+ n (%)	RT+/EIA+/IFA+ (Confirmed +)	RT+/EIA-/IFA-(False Positive)	RT+/EIA+/IFA- or Indeterminate/Pooled RNA +	RT-/Pooled RNA+	New HIV Diagnoses n (%)
Hospital Campus Testing Sites Included in Pooled HIV RNA Testing								
Emergency Department	1,921	1,456 (75.8%)	47 (2.5%)	43	3	1	0	15 (0.8%)
Urgent Care Clinics	604	521 (86.3%)	10 (1.7%)	8	1	1	0	8 (1.3%)
Family Health	774	681 (88.0%)	7 (0.9%)	6	1	0	0	2 (0.26%)
Internal Medicine	342	293 (85.7%)	0 (0.0%)	0	0	0	0	0
Medicine/Surgical Specialty	84	75 (89.3%)	3 (3.6%)	3	0	0	0	2 (2.4%)
Methadone	393	373 (94.9%)	3 (0.8%)	1	2	0	0	0
TB	80	61 (76.3%)	2 (2.5%)	2	0	0	0	2 (2.5%)
Women's Clinic	280	261 (93.2%)	2 (0.7%)	1	1	0	0	1 (0.36%)
Prenatal Clinic	450	412 (91.6%)	6 (1.3%)	3	3	0	0	1 (0.22%)
Abortion	191	73 (38.2%)	1 (0.5%)	1	0	0	0	0
Pediatric Clinic	118	72 (61.0%)	2 (1.7%)	1*	1	0	0	0
Inpatient Wards								
Medical/Surgical	339	218 (64.3%)	12 (3.5%)	12	0	0	0	0
Psychiatry	233	184 (79.0%)	3 (1.3%)	3	0	0	0	0
Hospital Campus Total	5,809	4,681 (80.6%)	98 (1.7%)	83	12	2	0	31(0.53%)
Off-site Community Health Centers Included in Pooled HIV RNA Testing (n=18)								
Off-Site Clinic Total	2,741	2,024 (73.8%)	53 (1.9%)	51	2	0	1	15 (0.55%)
Eligible Site Sub-Total	8,550	6,704 (78.4%)	151 (1.8%)	134	14	2	1	46 (0.54%)
Medical Center Sites Excluded from Pooled HIV RNA Testing								
Nursery	578	N/A	0	0	0	0	0	0
Outpatient Jail	272	N/A	6	6	0	0	0	1
Labor and Delivery	170	N/A	0	0	0	0	0	0
Occupational Health	102	N/A	0	0	0	0	0	0

Testing Site	Rapid Tests (RT)	Adequate Specimen for Pooled RNA n (%)	RT+ n (%)	RT+/EIA+/IFA+ (Confirmed +)	RT+/EIA-/IFA-(False Positive)	RT+/EIA+/IFA- or Indeterminate/Pooled RNA +	RT-/Pooled RNA+	New HIV Diagnoses n (%)
HIV Clinic/HIV Nursing Facility	109	N/A	76	75	0	1**	0	0
Research Studies	116	N/A	3	3	0	0	0	N/A
Lab QC/Unknown Location	41	N/A	6	6	0	0	0	N/A
Excluded Site Sub-Total	1,388		91	90	0	1	0	1
TOTAL	9,938	N/A	242	223	15	3	1	47

* Represents an infant with maternal antibodies but negative quantitative HIV viral load, hence considered HIV-uninfected

** Patient was rapid-test positive at another facility prior to coming to the HIV clinic

Table 2

Demographics of Persons Tested for HIV and New HIV Diagnoses from Medical Center Sites Eligible for Pooled HIV RNA Testing

	All Patients	New HIV Diagnoses
Total *	7,927	46
Age, median (IQR)	40 (28,52)	38.5 (30, 46)
Sex		
Male	4,026 (50.8%)	35 (76.1%)
Female	3,901 (49.2%)	11 (23.9%)
Race/Ethnicity		
White	1,581 (19.9%)	14 (30.4%)
Black	1,894 (23.9%)	12 (26.1%)
Hispanic	2,081 (26.3%)	13 (28.3%)
Asian/Pacific Islander	919 (11.6%)	2 (4.3%)
Other/Unknown	1,452 (18.3%)	5 (10.9%)
Primary Language		
English	5,117 (64.5%)	34 (73.9%)
Spanish	1,469 (18.5%)	7 (15.2%)
Other/Unknown	1,341 (17.0%)	5 (10.9%)
CD4 cell count median, (IQR) †	N/A	331 (260, 517)
CD4 cell count		
<200 cells/ μ L	N/A	9 (20.9%)
\geq 200 cells/ μ L	N/A	34 (79.1%)

* Though the total number of eligible HIV tests during the study period was 8550, there were 7927 unique patients.

† CD4 cell counts available for 43/46 newly diagnosed patients.