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Acute HIV Infection and Implications of Fourth-Generation HIV Screening in Emergency Departments

Jason S. Haukoos, MD, MSc*, **Michael S. Lyons, MD, MPH**, **Douglas A. E. White, MD**, **Yu-Hsiang Hsieh, PhD, MSc**, and **Richard E. Rothman, MD, PhD**
Department of Emergency Medicine, Denver Health Medical Center, Denver, CO, the Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, CO, and the Department of Epidemiology, Colorado School of Public Health, Aurora, CO (Haukoos); the Department of Emergency Medicine, University of Cincinnati College of Medicine, Cincinnati, OH (Lyons); the Department of Emergency Medicine, Alameda Health System, Oakland, CA (White); and the Department of Emergency Medicine, Johns Hopkins University, Baltimore, MD (Hsieh, Rothman)

In the United States, more than 1.1 million individuals are infected with HIV, more than 200,000 remain undiagnosed, and approximately 50,000 new infections occur annually.[1] Individuals with undiagnosed HIV infection are responsible for the majority of new infections,[2] and those with acute HIV infection are most likely to transmit the virus because of accompanying high viral loads.[3,4] Identifying HIV infection remains an important public health priority because it affords the opportunity to link patients into specialized care in which treatment may halt disease progression while reducing the likelihood of transmission.[5]

Since 2006, the Centers for Disease Control and Prevention (CDC) has recommended performing non–risk-based (nontargeted) opt-out screening in all health care settings, including emergency departments (EDs), where the undiagnosed HIV prevalence is 0.1% or greater.[6] This ambitious approach was based on the notion that nontargeted opt-out screening would result in larger numbers of individuals tested and identified with HIV infection, and earlier in their course of disease.[7] In 2010, the Office of National AIDS Policy published the National HIV/AIDS Strategy for the United States, in which for the first time the federal government took an aggressive stance in support of broad screening, with the dual goal of reducing the number of individuals with undiagnosed HIV infection to approximately 100,000 (ie, 10% undiagnosed of all individuals with HIV infection) and reducing the number of annual new infections to approximately 37,500 per year (ie, 25% relative reduction in incident cases) by 2015.[8] More recently, in 2013 the US Preventive Services Task Force updated their recommendations in support of routine HIV screening, based principally on evidence that morbidity and transmission may be significantly reduced after diagnosis and initiation of antiretroviral treatment.[9]

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*Corresponding Author. Jason.Haukoos@dhha.org.

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EDs have been a major focus of HIV testing efforts in the United States, prompted by the fact that more than 125 million ED visits occur annually,[10] EDs serve substantial numbers of underserved patients,[11] and they are a common site of missed opportunities for diagnosing HIV infection.[12] Although alignment of federal recommendations provides an important foundation for guiding HIV prevention practices and broad HIV testing initiatives have raised awareness,[13,14] relatively little has been done to ensure translation of such practices into routine emergency medical care.[15,16] It remains unclear which methods of HIV screening are most effective and efficient for use in both academic and community EDs. In fact, the majority of EDs nationally do not routinely screen for HIV infection,[15,16] evidenced by the finding that only approximately 0.3% of all ED visits include HIV testing.[17,18]

Acute HIV infection, a nonspecific clinical mononucleosis-like syndrome that occurs approximately 1 to 6 weeks after infection, represents a highly infectious phase of disease due to its association with extremely high viral loads.[3] To help identify acute infections, in 2010 the Food and Drug Administration approved the first 4th-generation HIV assay, the Architect HIV Ag/Ab Combo (Abbott Laboratories, Abbott Park, IL); since that time, two other 4th-generation platforms, GS HIV Combo Ag/Ab EIA (Bio-Rad Laboratories, Hercules, CA) and the Alere Determine HIV-1/2 Ag/Ab Combo (Alere Inc, Waltham, MA) have been approved for use in clinical settings. These assays, which detect both HIV-1 and HIV-2 immunoglobulin M and immunoglobulin G antibodies and HIV-1 p24 antigen, offer improved sensitivities (over 3rd generation assays) for identification of acute HIV infection while maintaining high sensitivities for established HIV infection, thereby affording the opportunity to increase the total number of patients identified with HIV infection. The CDC recently endorsed use of 4th generation assays when coupled with a single assay to differentiate between HIV-1 and HIV-2 (eg, Multispot HIV-1/HIV-2 Rapid Test [Bio-Rad Laboratories]), while using nucleic acid testing (NAT) (ie, viral load) for confirmation, when necessary.[19] Notably, for the new testing algorithm, Western blot is no longer recommended for confirmatory HIV testing given its relatively low sensitivity during early stages of HIV infection.

In this volume of *Annals*, Geren et al[20] contribute substantially to our understanding of HIV screening in EDs by reporting programmatic results of nontargeted opt-out screening in a high-volume, urban ED. This study is unique in that it reports, for the first time in an ED setting, the use of fourth-generation HIV testing. During the approximately 30-month study period, 71,556 eligible patients presented to the ED, resulting in 27,952 HIV tests performed and 78 (0.3%) confirmed positive results. Eligibility included patients aged 18 through 64 years, without previous HIV diagnoses, altered mentation, being residents of psychiatric or correctional facilities, or victims of severe trauma. Additionally, patients were not tested for HIV infection if blood was not drawn (32% of those who consented for HIV testing) or, in a very limited number of cases, an order was not entered into their electronic medical record. The results from this implementation study parallel findings from other studies reporting nontargeted opt-out HIV screening in EDs (Table 1),[20–37] including the need to perform a large number of HIV tests to identify a relatively small number of infected individuals (ie, about 350 tests per positive result), a prevalence ranging from 0.2% to 0.6%, and the

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majority of patients not completing testing because they opted out or were ineligible for testing due to the clinical circumstance (eg, severe illness or injury), or because of another practical issue (eg, lack of a blood draw). These limitations raise questions about the overall system-level effectiveness of performing nontargeted HIV screening in an ED, particularly when external resources for integrating this preventive service into practice become increasingly limited.

The most striking finding reported in their article, however, was the number of those identified with acute infections. Of the 78 patients with confirmed positive results, 18 (23%) were identified with acute HIV infection and would not have been identified had an earlier-generation assay been used (ie, testing for antibody only). These patients, most of whom were highly infectious because of extremely elevated viral loads, would have otherwise been told they were uninfected and unknowingly continued to engage in behaviors that contribute to viral transmission. Use of fourth-generation HIV testing thus may significantly mitigate transmission of HIV infection. Furthermore, given the high diagnostic accuracy and comparable costs of fourth-generation testing compared with third-generation testing (ie, approximately $10 per test), we firmly believe that this newer technology should be integrated into ED-based HIV testing programs, if at all possible.

It is difficult, however, to clearly resolve the relatively high proportion of acute HIV infections identified in the Maricopa ED, and it remains uncertain whether these results are generalizable or if they represent a largely untested population or even a microepidemic. Although acute HIV infections represented only 0.06% of all tests performed (ie, approximately 1,667 tests per acute infection identified), the proportion of acute infections among all confirmed diagnoses was remarkably high.[20] Recent programmatic findings from our institutions support the notion that acute infections are identifiable in EDs. However, the proportion of acute infections relative to all confirmed positive results was significantly lower (approximately 10%) than that reported by Geren et al[20] (Table 2). This latter prevalence is similar to what has been reported in other studies, including 5% in an ED in New Orleans.[19,38,39]

Although diagnosing acute HIV infection is important, we should not lose track of how much work remains to solve larger issues related to ED-based HIV screening in general (eg, broader dissemination and implementation and patient selection strategies). Unfortunately, data from across the United States suggest that even when efforts to integrate nontargeted HIV screening are implemented in EDs, only approximately 25% of eligible ED patients actually complete testing (Table 1). Likely contributing to this unsettling statistic is the finding from 2 recent studies that most individuals who opt out do so because they believe they are not at risk for HIV infection.[34,40] In addition, a significant proportion of patients in these studies were still identified relatively late in their disease courses.

Given the reality of limited existing ED-based prevention resources, alternative screening approaches may be more appropriate, with a focused effort on at-risk subpopulations.[41] As the proportion of undiagnosed HIV infection declines nationally, in accordance with goals of the National HIV/AIDS Strategy, the utility of non–risk-based HIV screening will likely diminish, making more targeted strategies reasonable, practical, and likely cost-effective.[42]

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Though the results are complex and still controversial, recent preliminary work found that risk-based screening using an empirically developed clinical prediction instrument was more strongly associated with identification of newly diagnosed HIV-infected patients than non–risk-based screening.[31] Further focused research is required, however. Of the 18 ED implementation studies published to date, few have directly compared nontargeted screening with alternative screening or testing methods (eg, targeted screening or diagnostic testing), and none have found nontargeted screening to be superior in terms of rates of identification of newly diagnosed HIV infection.[25,32,34] A large multicentered clinical trial is currently under way to help further the understanding of the comparative effectiveness of targeted and nontargeted screening strategies in EDs.[43]

As with the diagnosis of any clinical condition, one must look to actually find it; this holds true for HIV infection and, in particular, acute HIV infection. Fourth-generation HIV testing will improve our ability to identify a small but important group of individuals who are highly infectious and who otherwise do not know about their infections. However, the broader issues of engaging EDs in HIV screening and determining which patients should be tested remain the more fundamental challenge.

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References

1. Centers for Disease Control and Prevention. [Accessed June 23, 2014.] HIV in the United States. 2011. Available at: http://www.cdc.gov/hiv/resources/factsheets/PDF/us.pdf
2. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS. 2006; 20:1447–1450. [PubMed: 16791020]
3. Pilcher CD, Eron JJ Jr, Vemazza PL, et al. Sexual transmission during the incubation period of primary HIV infection. JAMA. 2001; 286:1713–1714. [PubMed: 11594895]
4. 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. [PubMed: 15122514]
5. 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. [PubMed: 21767103]
6. 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. [PubMed: 16988643]
7. Bartlett JG, Branson BM, Fenton K, et al. Opt-out testing for human immunodeficiency virus in the United States: progress and challenges. JAMA. 2008; 300:945–951. [PubMed: 18728268]

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8. The White House Office of National AIDS Policy. [Accessed June 23, 2014.] National HIV/AIDS Strategy for the United States. 2010. Available at: http://www.whitehouse.gov/sites/default/files/uploads/NHAS.pdf
9. Moyer VA. Screening for HIV: US Preventive Services Task Force recommendation statement. Ann Intern Med. 2013; 159:51–60. [PubMed: 23698354]
10. [Accessed June 23, 2014.] National Hospital Ambulatory Medical Care Survey: emergency department summary tables. 2010. Available at: http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2010_ed_web_tables.pdf
11. Pitts SR, Carrier ER, Rich EC, et al. Where Americans get acute care: increasingly, it's not at their doctor's office. Health Aff (Millwood). 2010; 29:1620–1629. [PubMed: 20820017]
12. Jenkins TC, Gardner EM, Thrun MW, et al. Risk-based human immunodeficiency virus (HIV) testing fails to detect the majority of HIV-infected persons in medical care Settings. Sex Transm Dis. 2006; 33:329–333. [PubMed: 16547450]
13. Centers for Disease Control and Prevention. Results of the Expanded HIV Testing Initiative–25 Jurisdictions, United States, 2007–2010. MMWR Morb Mortal Wkly Rep. 2011; 60:805–810. [PubMed: 21697804]
14. Centers for Disease Control and Prevention. [Accessed June 23, 2014.] High-impact HIV prevention: CDC's approach to reducing HIV infection in the United States. 2011. Available at: http://www.cdc.gov/hiv/nhas/dhap/pdf/nhas_booklet.pdf
15. Rothman RE, Hsieh YH, Harvey L, et al. 2009 US emergency department HIV testing practices. Ann Emerg Med. 2011; 58(suppl 1):S3–S9. e4. [PubMed: 21684405]
16. Haukoos JS, Hopkins E, Hull A, et al. HIV testing in emergency departments in the United States: a national survey. Ann Emerg Med. 2011; 58(suppl 1):S10–S16. e8. [PubMed: 21684387]
17. Hsieh YH, Rothman RE, Newman-Toker DE, et al. National estimation of rates of HIV serology testing in US emergency departments 1993–2005: baseline prior to the 2006 Centers for Disease Control and Prevention recommendations. AIDS. 2008; 22:2127–2134. [PubMed: 18832876]
18. Merchant RC, Catanzaro BM. HIV testing in US EDs, 1993–2004. Am J Emerg Med. 2009; 27:868–874. [PubMed: 19683120]
19. Centers for Disease Control and Prevention. Routine HIV screening in two health-care settings–New York City and New Orleans–2011–2013. MMWR Morb Mortal Wkly Rep. 2014; 63:537–541.
20. Geren, KI.; Lovecchio, F.; Knight, J., et al. Identification of acute HIV infection using fourth generation testing in an opt-out emergency department screening program. Ann Emerg Med. 2014. http://dx.doi.org/10.1016/j.annemergmed.2014.05.021
21. Silva A, Glick NR, Lyss SB, et al. Implementing an HIV and sexually transmitted disease screening program in an emergency department. Ann Emerg Med. 2007; 49:564–572. [PubMed: 17113684]
22. Mehta SD, Hall J, Lyss SB, et al. Adult and pediatric emergency department sexually transmitted disease and HIV screening: programmatic overview and outcomes. Acad Emerg Med. 2007; 14:250–258. [PubMed: 17331918]
23. Walensky RP, Arbelaez C, Reichmann WM, et al. Revising expectations from rapid HIV tests in the emergency department. Ann Intern Med. 2008; 149:153–160. [PubMed: 18678842]
24. 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. [PubMed: 18990468]
25. 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(suppl 1):S89–S95. [PubMed: 21684416]
26. d'Almeida KW, Kierzek G, de Truchis P, et al. Modest public health impact of nontargeted human immunodeficiency virus screening in 29 emergency departments. Arch Intern Med. 2011; 172:12–20. [PubMed: 22025095]
27. Wilbur L, Huffman G, Lofton S, et al. The use of a computer reminder system in an emergency department universal HIV screening program. Ann Emerg Med. 2011; 58(suppl 1):S71–S73. e1. [PubMed: 21684412]

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28. Casalino E, Bernot B, Bouchaud O, et al. Twelve months of routine HIV screening in 6 emergency departments in the Paris area: results from the ANRS URDEP study. PLoS One. 2012; 7:e46437. [PubMed: 23056308]
29. Haukoos JS, Hopkins E, Bender B, et al. Use of kiosks and patient understanding of opt-out and opt-in consent for routine rapid human immunodeficiency virus screening in the emergency department. Acad Emerg Med. 2012; 19:287–293. [PubMed: 22435861]
30. Hack CM, Scarfi CA, Sivitz AB, et al. Implementing routine HIV screening in an urban pediatric emergency department. Pediatr Emerg Care. 2013; 29:319–323. [PubMed: 23426243]
31. Haukoos JS, Hopkins E, Bender B, et al. Comparison of enhanced targeted rapid HIV screening using the Denver HIV risk score to nontargeted rapid HIV screening in the emergency department. Ann Emerg Med. 2013; 61:353–361. [PubMed: 23290527]
32. Lyons MS, Lindsell CJ, Ruffner AH, et al. Randomized comparison of universal and targeted HIV screening in the emergency department. J Acquir Immune Defic Syndr. 2013; 64:315–323. [PubMed: 23846569]
33. Brown J, Shesser R, Simon G, et al. Routine HIV screening in the emergency department using the new US Centers for Disease Control and Prevention guidelines: results from a high-prevalence area. J Acquir Immune Defic Syndr. 2007; 46:395–401. [PubMed: 18077831]
34. Haukoos JS, Hopkins E, Conroy AA, et al. Routine opt-out rapid HIV screening and detection of HIV infection in emergency department patients. JAMA. 2010; 304:284–292. [PubMed: 20639562]
35. Sattin RW, Wilde JA, Freeman AE, et al. Rapid HIV testing in a southeastern emergency department serving a semiurban-semirural adolescent and adult population. Ann Emerg Med. 2011; 58(suppl 1):S60–S64. [PubMed: 21684410]
36. 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. [PubMed: 21630105]
37. Hoxhaj S, Davila JA, Modi P, et al. Using nonrapid HIV technology for routine, opt-out HIV screening in a high-volume urban emergency department. Ann Emerg Med. 2011; 58:S79–S84. [PubMed: 21684414]
38. Dubravac T, Gahan TF, Pentella MA. Use of the Abbott Architect HIV antigen/antibody assay in a low incidence population. J Clin Virol. 2013; 58(suppl 1):e76–e78. [PubMed: 24342481]
39. Manlutac AL, Giesick JS, McVay PA. Identification of early HIV infections using the fourth generation Abbott ARCHITECT HIV Ag/Ab Combo chemiluminescent microparticle immunoassay (CIA) in San Diego County. J Clin Virol. 2013; 58(suppl 1):e44–e47. [PubMed: 24342477]
40. 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. [PubMed: 19172703]
41. Haukoos JS. The impact of nontargeted HIV screening in emergency departments and the ongoing need for targeted strategies. Arch Intern Med. 2012; 172:20–22. [PubMed: 22025100]
42. Holtgrave DR. Costs and consequences of the US Centers for Disease Control and Prevention's recommendations for opt-out HIV testing. PLoS Med. 2007; 4:e194. [PubMed: 17564488]
43. Haukoos, JS.; Hopkins, E.; Bucossi, MM., et al. [Accessed June 23, 2014.] The HIV Testing Using Enhanced Screening Techniques in Emergency Departments (TESTED) Trial. Available at: http://www.DenverEDHIV.org. (ClinicalTrials.gov Identifier: NCT01781949.)
44. Freeman AE, Sattin RW, Miller KM, et al. Acceptance of rapid HIV screening in a southeastern emergency department. Acad Emerg Med. 2009; 16:1156–1164. [PubMed: 20053236]

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Table 1

Peer-reviewed studies to date (N=18) reporting effectiveness of nontargeted HIV screening in EDs since 2006, stratified by consent method.

				Eligible Patients,	Offered Testing		Patients Tested		Confirmed Positive	
Authors	**Year Published**	**Setting***	**External Staff**	**N†**	**N_1**	**%**	**N_2**	**%**	**N_3**	**%**
Opt-in consent										
Silva et al[21]	2007	U, I	Y	3,030	NR	–	1,428	47	8	0.56
Mehta et al[22]	2007	U, A, I	Y	NR	2,924	–	1,428	–	8	0.56
Walensky et al[23]	2008	U, A	Y	2,356	1,397	59	854	36	5	0.59
White et al[24]	2009	U, A, I	N	118,324	45,159	38	7,923	7	55	0.69
White et al[25‡]	2011	U, A, I	N	23,236	6,479	28	4,053	17	8	0.20§
d'Almeida et al[26]	2011	MI	N	78,411	20,962	27	12,754	16	18	0.14§
Wilbur et al[27]	2011	U, A, I	Y	5,794	1,484	26	1,121	19	5	0.45
Casalino et al[28]	2012	MI	N	183,957	11,401	6	7,215	4	40	0.55§
Haukoos et al[29‡]	2012	U, A, I	N	5,985	5,781	97	389	6	0	0
Hack et al[30]	2013	U, A, P	Y	2,645	300	11	224	8	0	0
Haukoos et al[31]	2013	U, A, I	N	29,510	19,634	67	3,591	12	7	0.20§
Lyons et al[32]	2013	U, A, I	Y	5,501	4,692	85	1,911	35	6	0.31§
Median						33		16		0.20§
Range						6–97		4–47		0.14–0.55§
Opt-out consent										
Brown et al[33]	2007	U, A, I	Y	13,240	4,187	32	2,486	19	9	0.36
Haukoos et al[34]	2010	U, A, I	N	28,043	NR	–	6,933	25	15	0.22§
Sattin et al[35‖]	2011	U, A, I	Y	13,035	9,343	72	8,504	65	35	0.41
Wheatley et al[36]	2011	U, A	Y	NR	8,922	–	7,616	–	129	1.7
White et al[25‡]	2011	U, A, I	N	26,757	20,280	76	4,679	18	21	0.45§
Hoxhaj et al[37]	2011	U, A, I	N	24,686	NR	–	14,093	57	80	0.57§
Haukoos et al[29‡]	2012	U, A, I	N	6,842	6,602	97	886	13	2	0.23§
Geren et al[20]	2014	U, A, I	N	71,556	55,500	78	27,952	39	78	0.28

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				Eligible Patients,	Offered Testing		Patients Tested		Confirmed Positive	
Authors	**Year Published**	**Setting***	**External Staff**	**N†**	**N_1**	**%**	**N_2**	**%**	**N_3**	**%**
Median						76		25		0.34§
Range						32–97		13–65		0.22–0.57§

–, Undefined; *U*, urban; *I*, Level I trauma center; *NR*, not reported; *A*, academic; *MI*, multiple institutions; *P*, pediatric only.

*Setting.

†Eligibility varied by study.

‡Reported in the same study.

§Specifically indicates new HIV diagnoses.

||Reports more complete results that overlap with those of a previous publication.[44]

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Table 2

Fourth-generation HIV testing, confirmed HIV prevalence, and acute HIV infection prevalence among 4 urban EDs.

			Total Tests Performed,	Confirmed HIV Positive		Acute HIV Infections	
Site	**Date Range**	**Fourth-Generation Assay Type***	**N**	**N_1**	**%**	**N_2**	**%**
Alameda Health System, Highland Hospital, Oakland, CA	January 2014–April 2014	Architect HIV Ag/Ab Combo	1,930	23	1.2	2	0.09†
Denver Health Medical Center, Denver, CO	April 2014–June 2014	Determine HIV-1/2 Ag/Ab Combo	1,985	11	0.6	0	0†
Johns Hopkins Hospital, Baltimore, MD	July 2013–May 2014	Architect HIV Ag/Ab Combo	6,991	25	0.4	2	0.03‡
Maricopa Integrated Health System, Maricopa Medical Center, Phoenix, AZ[20]	July 2011–January 2014	Architect HIV Ag/Ab Combo	27,952	78	0.3	18	0.06‡
Total			38,858	137	0.4	22	0.06

Ag, Antigen; *Ab*, antibody.

*Testing algorithms: Highland Hospital: Architect HIV Ag/Ab Combo, followed by Western blot and viral load. Denver Health Medical Center: Determine HIV-1/2 Ag/Ab Combo, followed by viral load. Johns Hopkins Hospital: Architect HIV Ag/Ab Combo, followed by Bio-Rad Multispot HIV-1/HIV-2 Rapid Test and viral load.

†Acute HIV infection defined serologically as antigen positive, antibody negative, and detectable HIV nucleic acid.

‡Acute HIV infection defined serologically as antigen positive or immunoglobulin M antibody positive, immunoglobulin G antibody negative, and detectable HIV nucleic acid.