Acute Infections, Cost and Time to Reporting of HIV Test Results in U.S. State Public Health Laboratories

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Introduction

- In 2014, the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) recommended an HIV diagnostic testing algorithm: 4th-generation immunoassay (IA) that detects HIV-1 antigen and HIV antibody followed, when repeatedly reactive, by an HIV-1/HIV-2 differentiation antibody IA. When that test is negative or indeterminate, an HIV-1 nucleic acid test (NAT) is conducted (Figure 1). Positive NAT results indicate acute infection.
- The algorithm detects HIV-1 infection earlier, reduces indeterminate results, and identifies HIV-2 infections.
- Evaluating the algorithm in state public health laboratories (PHLs) is critical to ensuring its future success.
- There are few data on the cost of the recommended algorithm in U.S. state PHLs.

Objectives

- In three U.S. PHLs, we characterized the yield of acute infections, time to reporting of acute and antibody-positive HIV-1 infections, and cost per positive specimen.

Methods

- Routine HIV testing data were collected from 7/1/2012- 6/30/2013 for Massachusetts (MA) and Maryland (MD) PHLs, and from 11/27/2012- 6/30/2013 for Michigan (MI) PHL.
- MA and MI used the recommended algorithm with NAT conducted by a public health referral laboratory.
- MD PHL used a modified algorithm; 4th-generation IA repeatedly reactive specimens were followed by Western Blot (WB). Those with negative or indeterminate WB results were tested with an HIV-1/HIV-2 differentiation IA and a HIV-1 NAT, and if positive by NAT, confirmed by a different HIV-1 NAT. Specimens with positive HIV-1 WB results at increased risk for HIV-2 were tested with an HIV-1/HIV-2 differentiation IA. HIV-2 positive specimens on an HIV-1/HIV-2 differentiation IA were tested with HIV-2 WB and a differential HIV-1/HIV-2 proviral DNA polymerase chain reaction (PCR).
- For each PHL, we determined the total number of non-reactive and repeatedly reactive specimens on the fourth-generation IA.
- Among repeatedly reactive specimens, we classified testing outcomes as confirmed HIV-1 antibody positive, acute infection, IA false positive (i.e. WB or HIV-1/HIV-2 differentiation IA negative or indeterminate and NAT not reactive), and HIV-2 positive.

Figure 1: HIV diagnostic testing algorithm recommended by Centers for Disease Control and Prevention and the Association of Public Health Laboratories

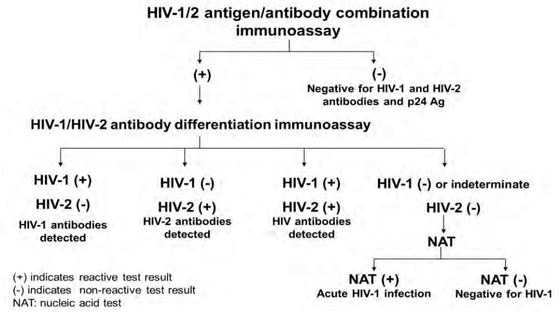

Table 1: Results of HIV testing in three U.S. State Public Health Laboratories.

	Massachusetts State Public Health Laboratory, Boston MA	Michigan State Public Health Laboratory, Lansing MI	Maryland State Public Health Laboratory, Baltimore MD
4th-generation immunoassay	Bio-Rad GS HIV Antigen/Antibody Combo	Bio-Rad GS HIV Antigen/Antibody Combo	Abbott Architect HIV Antigen/Antibody Combo
Prospective time period	7/1/2012- 6/30/2013	11/27/12- 6/30/2013	7/1/2012- 6/30/2013
4th-generation immunoassay test results			
Total	7914	6069	36266
Non-reactive	7652 (96.69%)	5898 (97.18%)	35232 (97.15%)
Repeatedly reactive	262	171	1034
Results of supplemental testing in specimens with repeatedly reactive results			
Confirmed HIV-1 antibody positive (a)	246 (3.11%)	163 (2.68%)	983 (2.71%)
Acute infection (b)	8 (0.10%)	1 (0.02%)	19 (0.05%)
IA false positive (c)	7 (0.09%)	5 (0.08%)	29 (0.08%)
HIV-2 positive (d)	1 (0.01%)	0 (0.00%)	1 (0.003%)
Other	0 (0.00%)	2 (0.03%)(e)	2 (0.005%)(f)

(a) HIV-1 positive by Western blot (WB) or HIV-1/HIV-2 antibody test
(b) Immunoassay (IA) repeatedly reactive, WB or HIV-1/HIV-2 differentiation IA negative or indeterminate, reactive nucleic acid test (NAT)
(c) IA repeatedly reactive, WB or HIV-1/HIV-2 differentiation IA negative or indeterminate, NAT not reactive
(d) Positive for HIV-2 by HIV-1/HIV-2 differentiation IA or HIV-2 WB or differential HIV-1/HIV-2 proviral DNA conventional polymerase chain reaction
(e) IA repeatedly reactive, HIV-1/HIV-2 differentiation IA undifferentiated, WB positive, NAT not reactive (n=1); IA repeatedly reactive, HIV-1/HIV-2 differentiation IA undifferentiated, NAT not reactive (n=1)
(f) IA repeatedly reactive, WB indeterminate, HIV-1/HIV-2 differentiation IA positive, NAT not reactive (n=1); IA repeatedly reactive, WB indeterminate, HIV-1/HIV-2 differentiation IA negative, NAT not reactive (n=1)

Methods (cont.)

- In each PHL, we determined the time from specimen receipt to laboratory reporting of HIV test results.
- The cost per positive in each of the PHLs was calculated by summing laboratory testing and labor costs and dividing by the number of HIV-1and 2 positive specimens.
- The cost per test was obtained by multiplying the cost per test adjusted for the use of controls by the number of specimens tested with that test. This was summed for all tests in the algorithm.
- Labor costs per test were calculated from the product of the labor hours per specimen, the total number of specimens tested, and the labor cost per hour. This was summed for all tests in the algorithm.

Table 2: Unadjusted and adjusted test costs, labor costs, and cost per positive in three U.S. State Public Health Laboratories.

Type of Test	Test costs		Reference laboratory fee	Total specimens	Total tests cost	Total labor cost†††	Total cost††††	Total cost per positive †††††
	Cost per test	Adjusted cost per test						
	Massachusetts State Public Health Laboratory, Boston MA							336.41
GS HIV Combo	2.78	3.44		8438	29025.80 ††	28376.63	57402.44	
Multispot	26.78	80.34		262	21049.08	6403.07	27452.15	
APTIMA HIV-1 RNA NAT	40.00	54.55		15	818.18	112.78	930.96	
	Michigan State Public Health Laboratory, Lansing MI							281.19
GS HIV Combo	3.50	4.46		6411	28609.09 ††	7388.11	35997.20	
Multispot	25.70	35.98		170	6116.60	3563.37	9679.97	
APTIMA HIV-1 RNA NAT			90†	8	720.00	0	720.00	
	Maryland State Public Health Laboratory, Baltimore MD							221.25
Architect HIV Combo	3.00	3.09		38334	118287.7 7††	21223.98	139511.7 5	
HIV-1 Western Blot	30.33	37.91		1034	39195.06	6931.42	46126.48	
Multispot	23.52	33.60		574	19286.40	14621.67	33908.07	
HIV-2 Western Blot	0	0		0	0	0	0	
HIV-1/HIV-2 proviral DNA PCR		22.00		1	22.00	74.48	96.48	
LTR real time PCR		20.00		51	1020.00	811.19	1831.19	
bDNA		6.00		19	114.00	21.33	135.33	
Real time PCR gag pol		6.00		19	114.00	189.62	303.62	

†In MI PHL, the estimated cost reimbursed to Florida PHL as part of a CDC/Association of Public Health Laboratories (APHL) NAT demonstration project was $90.
††Total tests costs of 4th-generation IAs was estimated using the following formula: (adjusted cost per test × positive screening IAs × 3) + (adjusted cost per test × negative screening IAs)
†††Labor cost per hour was determined by Bureau of Labor Statistics' estimate for the 2013 mean salary (including benefits). Labor hours per test were calculated either by being directly observed at the laboratory or from the estimates from literature.
††††Includes tests and labor cost. ††††† Includes HIV-1 and HIV-2.
-All costs are reported in 2013 US dollars

Results

- Among 7,914 specimens from MA PHL, 6,069 from MI PHL and 36,266 from MD PHL, 8, 1 and 19 acute infections were identified, respectively (Table 1).
- The median time from specimen receipt to laboratory reporting of test results for acute infections was 8, 11 and 7 days and for HIV-1 antibody-confirmed infections was 3, 2 and 3 days for MA, MI, and MD PHLs respectively.
- Overall, the cost per HIV positive specimen was $336 in MA PHL, $281 in MI PHL and $221 in MD PHL (Table 2).

Limitations

- MD PHL used a modified HIV testing algorithm as compared to MA and MI PHLs, which used the recommended algorithm. Therefore, comparison across sites regarding the cost and time to reporting of test results may not be possible.
- The analysis is based on specimens and not individuals; there may be instances where more than one specimen belongs to the same individual.

Conclusions

- 4th-generation IA, coupled with antibody tests and NAT, detected acute infections in PHLs that may have been missed if an antibody-only test such as the Western Blot had been used as a confirmatory test.
- Few HIV-1 nucleic acid tests were needed due to 4th-generation IA false positive results.
- Major cost of the algorithm was driven by the screening 4th-generation IA in the PHLs; reduction in their cost may help reduce the overall laboratory cost of diagnosing HIV infections.
- Continued efforts are needed to reduce the time to receipt of results for acute infections to interrupt potential transmissions.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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