Journal of Clinical Virology 103 (2018) 19–24

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Trends in testing algorithms used to diagnose HIV infection, 2011–2015, United States and 6 dependent areas

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ARTICLE INFO

Keywords:
HIV
Testing algorithms
Linkage to care

ABSTRACT

Background: In 2014 the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) issued updated laboratory testing recommendations for the diagnosis of HIV infection.
Objectives: To examine trends in the use of HIV diagnostic testing algorithms, and determine whether the use of different algorithms is associated with selected patient characteristics and linkage to HIV medical care.
Study design: Analysis of HIV infection diagnoses during 2011–2015 reported to the National HIV Surveillance System through December 2016. Algorithm classification: traditional = initial HIV antibody immunoassay followed by a Western blot or immunofluorescence antibody test; recommended = initial HIV antibody IA followed by HIV-1/2 type-differentiating antibody test; rapid = two CLIA-waived rapid tests on same date.
Results: During 2011–2015, the percentage of HIV diagnoses made using the traditional algorithm decreased from 84% to 16%, the percentage using the recommended algorithm increased from 0.1% to 64%, and the percentage using the rapid testing algorithm increased from 0.1% to 2%. The percentage of persons linked to care within 30 days after HIV diagnosis in 2015 was higher for diagnoses using the recommended algorithm (59%) than for diagnoses using the traditional algorithm (55%) ($p < 0.05$).
Conclusions: During 2011–2015, the percentage of HIV diagnoses reported using the recommended and rapid testing algorithms increased while the use of the traditional algorithm decreased. In 2015, persons with HIV diagnosed using the recommended algorithm were more promptly linked to care than those with diagnosis using the traditional algorithm.

1. Background

The Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention Strategic Plan 2017–2020 has four main goals for prevention of human immunodeficiency virus (HIV) infection: 1) prevent new HIV infections, 2) improve health outcomes for persons living with HIV, 3) reduce HIV-related disparities and health inequities, and 4) continually improve effectiveness and efficiency of operations [1].

Testing and diagnosis is the first step in the HIV "continuum of care" [2], and people who are aware that they are infected and have had counseling services, are more likely to behave in a way that lowers their risk of transmitting HIV to others, compared to those who are unaware [3]. Linkage to HIV medical care generally occurs after confirmation of the diagnosis by a supplemental antibody test, but there are many variations on the laboratory criteria that satisfy the HIV case definition used by the National HIV Surveillance System (NHSS) [4]. Little is known about whether the types of tests or testing algorithms used to diagnose HIV infection may be associated with linkage to care. Several studies found that reluctance to schedule healthcare appointments for additional testing to confirm the diagnosis was associated with a longer time for persons with HIV infection to receive care [5–8].

In 1985, the US Food and Drug Administration approved the first HIV diagnostic test that detected IgG antibodies. The IgG test was sensitive but had a long window period and a high false-positive rate especially in low-risk populations [9,10]. As a result, a second level of testing was added to improve specificity, and by 1989 the most commonly used HIV diagnostic testing algorithm consisted of an HIV antibody immunoassay (IA) as the initial test, followed by a Western blot (WB) or immunofluorescence assay (IFA) as the supplemental antibody test to confirm reactive results from the initial test [11]. In 2014 the

Abbreviations: APHL, The Association of Public Health Laboratories; CDC, Centers for Disease Control and Prevention; CLIA, Clinical Laboratory Improvement Amendments; EAPC, estimated annual percent change; HIV, human immunodeficiency virus; NHSS, National HIV Surveillance System; IA, immunoassay; IFA, immunofluorescence assay; NAT, nucleic acid test; WB, Western blot

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https://doi.org/10.1016/j.jcv.2018.03.008
Received 19 January 2018; Received in revised form 9 March 2018; Accepted 19 March 2018

Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) issued updated laboratory testing recommendations for the diagnosis of HIV infection to improve the recognition of acute HIV-1 infections and to reduce the time to make a definitive determination of a patient's HIV status [12–16]. The 2014 algorithm consists of an HIV-1 IA that can detect both HIV antigen and antibody, followed by a supplemental IA that can detect HIV antibodies and differentiates between HIV-1 and HIV-2 antibodies. If the supplemental IA is negative or indeterminate, a qualitative RNA test is done to confirm the diagnosis of HIV. There are various algorithms that may meet the surveillance case definition for HIV infection, including a sequence of two different point-of-care rapid tests [4].

Little is known about the extent to which laboratories have adopted the recommended diagnostic testing algorithm or alternative testing algorithms to diagnose HIV infection. The APHL surveyed US public health laboratories in early 2015 regarding their adoption of the recommended algorithm. They found that 55% of the responding laboratories had adopted the recommended algorithm [17].

2. Objectives

We examined the trends in testing algorithms used for diagnoses of HIV infection reported to CDC's NHSS, and determined whether the algorithms used varied with selected patient characteristics and whether the percentage of persons with diagnosed HIV infection who were linked to care within 30 or 90 days after diagnosis varied with the type of algorithm.

3. Study design

We analyzed test results for HIV infections diagnosed during 2011–2015 and reported to the NHSS through December 2016. Data were available from 50 US states, Washington DC, and six dependent areas. We interpreted various combinations of test results as representing diagnostic testing algorithms or diagnosis types and classified them into the following 6 categories:

- Traditional algorithm: the first positive test was any HIV-1 (or combination HIV-1/2) antibody IA that was not a point-of-care rapid test, followed within 30 days by a positive WB or IFA. A prior positive result from the initial IA was presumed if the first reported result was from a WB or IFA.
- Recommended algorithm: the first positive test was an HIV-1 IA that could detect both HIV antigen and antibody and was not a point-of-care rapid test, followed within 30 days by a supplemental IA that could detect HIV antibodies and differentiated between HIV-1 and HIV-2 antibodies. This classification did not depend on whether the result of the supplemental test was positive or negative or followed by a NAT. A positive result from an initial IA was presumed if the first reported result was from a supplemental IA that could detect HIV antibodies and differentiated between HIV-1 and HIV-2 antibodies.
- Rapid testing algorithm: the first positive test was a point-of-care rapid IA, followed by another positive point-of-care rapid IA, on the same day. These were assumed not to be duplicate reports of a single test only if they were both reported on the same document.
- Virologic test: the first positive test result was a quantitative HIV-1 NAT, a qualitative HIV-1 NAT, HIV-1 culture, or a stand-alone HIV-1 antigen test.
- Other algorithms: a sequence of tests that does not fit into the other defined categories of algorithms.
- Unspecified diagnostic methods: HIV diagnosis was documented by a physician, before any laboratory tests were documented.

To determine whether there was a significant trend in the annual number of diagnoses made using each category of testing algorithm, the estimated annual percent change (EAPC) in diagnoses and its 95% confidence interval (CI) were calculated by fitting a logistic regression model using calendar year as the regressor [18]. A trend was considered statistically significant at $p < 0.05$. We classified race/ethnicity as "Hispanic/Latino" if the ethnicity was Hispanic or Latino. Hispanic/Latino persons could be of any race. Persons in other categories of race/ethnicity were not known to be of Hispanic/Latino ethnicity.

The analysis of linkage to HIV care was based on data for persons whose infections were diagnosed in 2015 and who resided in one of the 38 jurisdictions with complete reporting of HIV-related laboratory test results at the time of diagnosis. Jurisdictions were classified as having complete reporting if they had laws or regulations in place before 2015 that required laboratories to report to the health department all levels of CD4 T-lymphocyte test results and all viral load results, laboratories reporting HIV-related testing had reported a minimum of 95% of the HIV-related test results to the jurisdiction and these health departments had reported to NHSS ≥95% of the test results they received by December 2016. Linkage to care was recognized if at least one reported CD4 test or viral load measurement was done within the specified time period (i.e., within 30 days or 90 days after diagnosis, but not on the same date as diagnosis). The date of HIV diagnosis was defined as the date of specimen collection for the first positive HIV test. Only data with complete specimen collection dates or dates of diagnosis were used in this analysis. Univariate logistic regression analysis, using linkage to care as a binary outcome and algorithm category as the only independent variable, was used to evaluate statistical differences in linkage to care among the different algorithm categories. All analyses were performed using SAS v9.4 (Cary, NC).

4. Results

The percentage of diagnoses of HIV infection that used the traditional algorithm decreased from 84% in 2011–16% in 2015, while the percentage that used the recommended algorithm increased from 0.1% to 64%, the percentage that used the rapid testing algorithm increased from 0.1% to 2%, the percentage that used a virologic test as the first test to diagnose HIV increased from 8% to 10%, the percentage that used the other algorithms increased from 5% to 7% and the percentage that used unspecified diagnostic methods decreased from just over 2% to just under 2% (Table 1, Fig. 1).

During 2011–2015, there were 202,725 reported diagnoses of HIV infection; the annual number of diagnoses decreased 1% during this period. The annual number of diagnoses of HIV infection using the traditional algorithm and unspecified diagnostic methods decreased by 30% and 6.5% per year respectively, while the annual number using the recommended algorithm, rapid testing algorithm, virologic tests and other algorithms increased by 150%, 71%, 5% and 8% per year respectively. These trends were significant ($p < 0.01$) (Table 1).

The distribution of the 40,084 reported diagnoses of HIV infection in 2015 by the category of testing algorithm used was as follows: traditional algorithm: 6198 (16%), recommended algorithm: 25,585 (64%), rapid testing algorithm: 758 (2%), virologic test: 4132 (10%), other algorithms: 2710 (7%), unspecified diagnostic methods: 701 (2%). Stratifying by patient characteristics showed that the recommended algorithm was the most commonly used algorithm, accounting for > 60% of diagnoses among most age groups, racial/ethnic groups, regions, and facility types (Table 2).

During 2015 there were 27,973 reported diagnoses of HIV infection among persons who resided in any of the 38 jurisdictions with complete laboratory reporting in that year. Of these persons, 15,654 (56%) were linked to care within 30 days after diagnosis, 21,277 (76%) were linked to care within 90 days after diagnosis (Table 3), and 25,009 (89%) were ever linked to care (including linkages more than 90 days after diagnosis reported through December 2016, data not shown).

Persons whose disease was diagnosed using the recommended algorithm were more likely to be linked to care within 30 days after