Ability to Identify Acute HIV Infections from Surveillance Data Varies by Diagnostic Testing Algorithm

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Background

An Exciting Time in HIV Prevention

End the HIV Epidemic: The plan will focus efforts on four key strategies (a.k.a., pillars) that together can end the HIV epidemic in the U.S.

Early Diagnosis is Essential to End the HIV Epidemic

- ***Strategy #1: Diagnose*** *all individuals with HIV as early as possible after infection.*
  - Early detection is critical and can lead to quicker results in treatment and prevent transmission to others.
- "As early as possible" – ideally, when first detectable during acute HIV infection

Acute HIV Infection

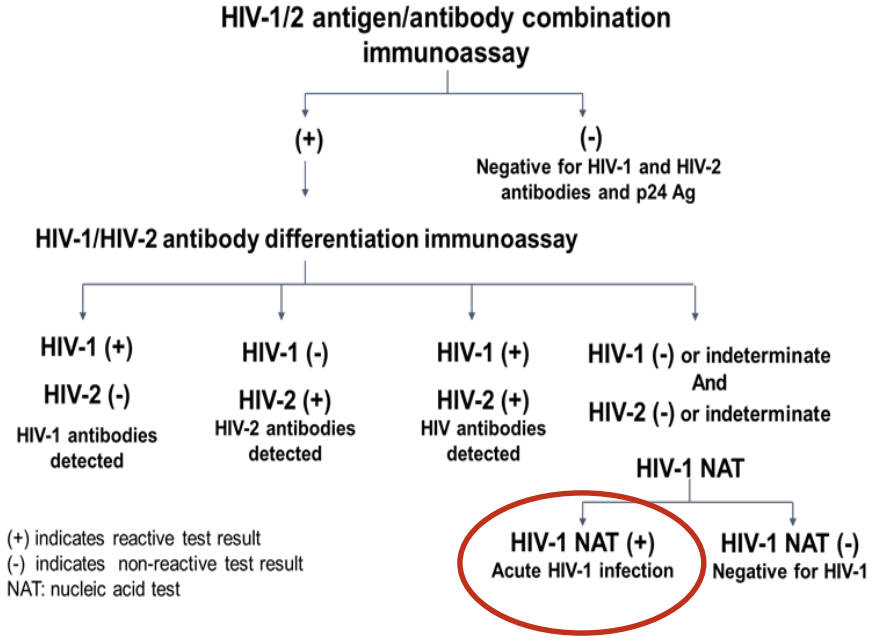
- Acute HIV infection (AHI) is the period from the first appearance of detectable virologic evidence (RNA, DNA, or antigen) from 2-3 weeks after infection until a full antibody response (recognized usually by detection of HIV IgG antibodies) about 6 weeks after infection.
- AHI is associated with viral loads much higher than those in later stages, thus individuals are more likely to be infectious to others during AHI.
- Prompt detection of AHI can optimize early treatment initiation and viral suppression, thereby reducing morbidity and preventing further transmission.

Use of AHI Data for Public Health Action

- Laboratory data indicating AHI are an important resource at both individual and group level for
  - Identifying and intervening in active transmission
  - Prioritizing and focusing efforts where most needed
- Understanding factors related to AHI is useful for
  - Informing on missed opportunities and gaps in prevention;
  - Improving prevention efforts.

Revised Laboratory Testing Algorithm

- In 2014, CDC and APHL recommended a revised laboratory testing algorithm.
  - improved accuracy for diagnosing HIV infection
  - detects and identifies acute HIV infection



www.cdc.gov/hiv/testing/laboratorytests.html

Revised HIV Surveillance Case Definition

- In 2014, CDC also implemented a "stage 0" case definition for HIV surveillance to identify early HIV infection.
- Stage 0 can be identified by a series of discordant test results:
  - include a negative or indeterminate HIV test result ≤180 days before,
  - or ≤60 days after (or on the same date as)
  - the first positive HIV test result.

Revised Surveillance Case Definition for HIV Infection — United States, 2014

www.cdc.gov/mmwr/preview/mmwrhtml/rr6303a1.htm

AHI as a Subcategory of Stage 0

- Stage 0 may be divided into subcategories that are more or less likely to indicate AHI rather than post-acute early HIV infection (PA-EHI).
- A recent study by Selik & Linley* analyzed the combinations of tests used to classify stage 0 and found that a subset of these were associated with high viral load results consistent with AHI.
  - In general, the subcategory that is more likely to indicate AHI may be identified from combinations of HIV test results in which the first positive and the key negative/indeterminate test results are from specimens obtained on the same date or ≤60 days apart from one another.

*Selik RM, Linley L. Viral Loads Within 6 Weeks After Diagnosis of HIV Infection in Early and Later Stages: Observational Study Using National Surveillance Data. JMIR Public Health Surveill. 2018 Nov 5;4(4):e10770. DOI: 10.2196/10770.

Objective: Detecting AHI in the National HIV Surveillance System

- Using the criteria for AHI established by Selik & Linley, we used laboratory data reported to the National HIV Surveillance System (NHSS) to
  - examine trends in and demographic associations with diagnosis of AHI, and
  - assess differences in detection of AHI by various diagnostic testing algorithms.

Methods

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- We included data from adults and adolescents (aged ≥13 years at diagnosis) with HIV diagnosed during 2012–2017 and reported to NHSS through June 2018.
- To accommodate reporting delay, for assessing the trend in detecting AHI, we examined data from 2012–2016.
- Data from 2015–2017 were used to assess characteristics associated with AHI.

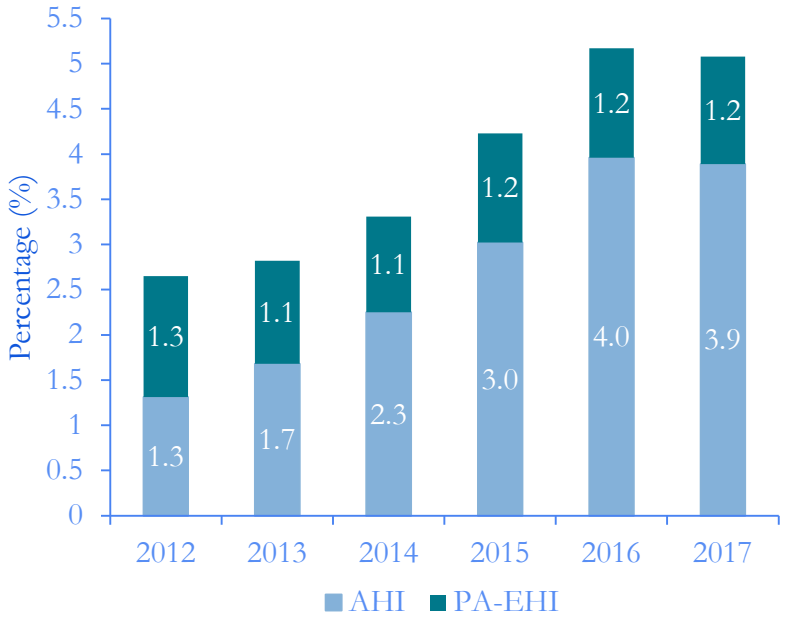
Definitions of Acute HIV Infection (AHI) and Post-Acute Early HIV Infection(PA-EHI)

- **AHI** included the subset of the surveillance stage 0 (early infection) having either:
  - A negative or indeterminate HIV-1 antibody test ≤60 days after the first confirmed positive HIV-1 test, OR
  - A negative/indeterminate antibody test or qualitative HIV-1 nucleic acid test (NAT) ≤180 days before the first positive test, if this first positive test was a NAT or detectable viral load.
- Infections that otherwise met the criteria for stage 0 but not this definition of AHI were classified as **PA-EHI** based on:
  - A negative/indeterminate antibody test or qualitative HIV-1 nucleic acid test (NAT) ≤180 days before the first positive test, if this first positive test was an antibody test.

Results: Improved Detection of AHI in NHSS, 2012-2017

(Summary of Data Presented at CROI 2019; Linley et al., Poster #0847)

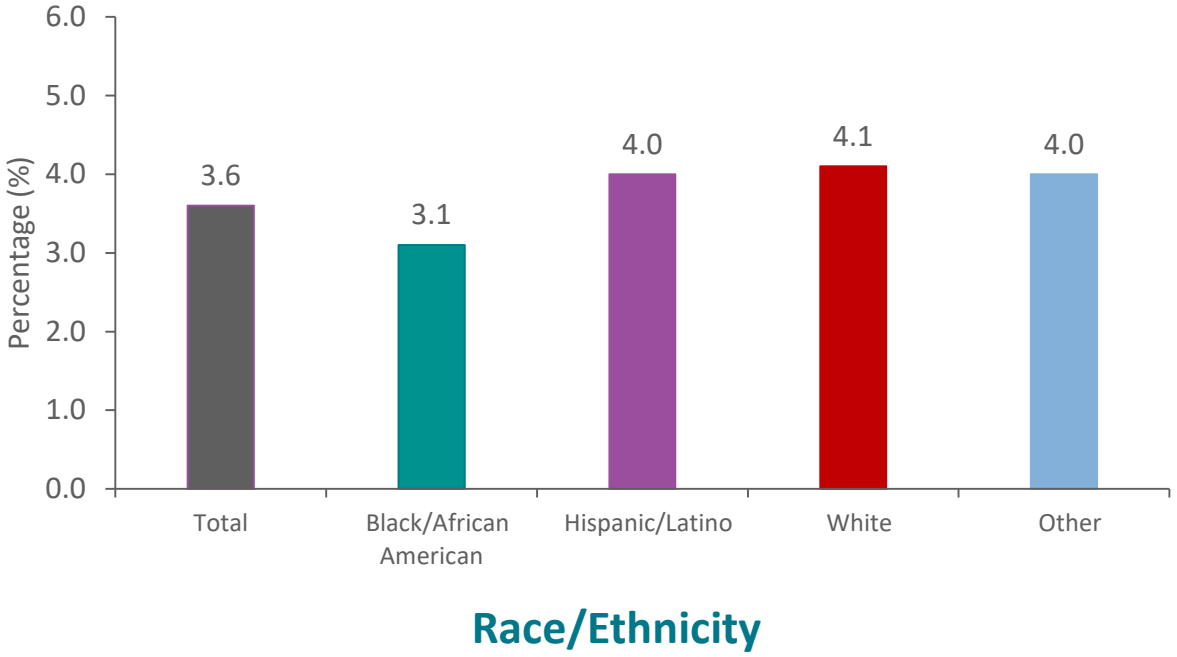
Percentage of Persons Aged ≥13 Years with Diagnosed HIV Classified as Stage 0 Subcategories of Acute or Post-Acute Early HIV Infection at Diagnosis, by Year of Diagnosis, National HIV Surveillance System, 2012–2017



- From 2012 to 2016, while the annual numbers of HIV diagnoses remained stable, the percentage of those that were classified as acute at diagnosis increased from 1.3% (535 of 40,939) to 4.0% (1,563/39,459).
- The percentage of HIV diagnoses classified as post-acute early HIV remained stable from 2012–2016.

Note: Data for the year 2017 are considered preliminary because they are based on only a 6-month reporting delay. Data for the year 2017 should not be used when assessing trends.

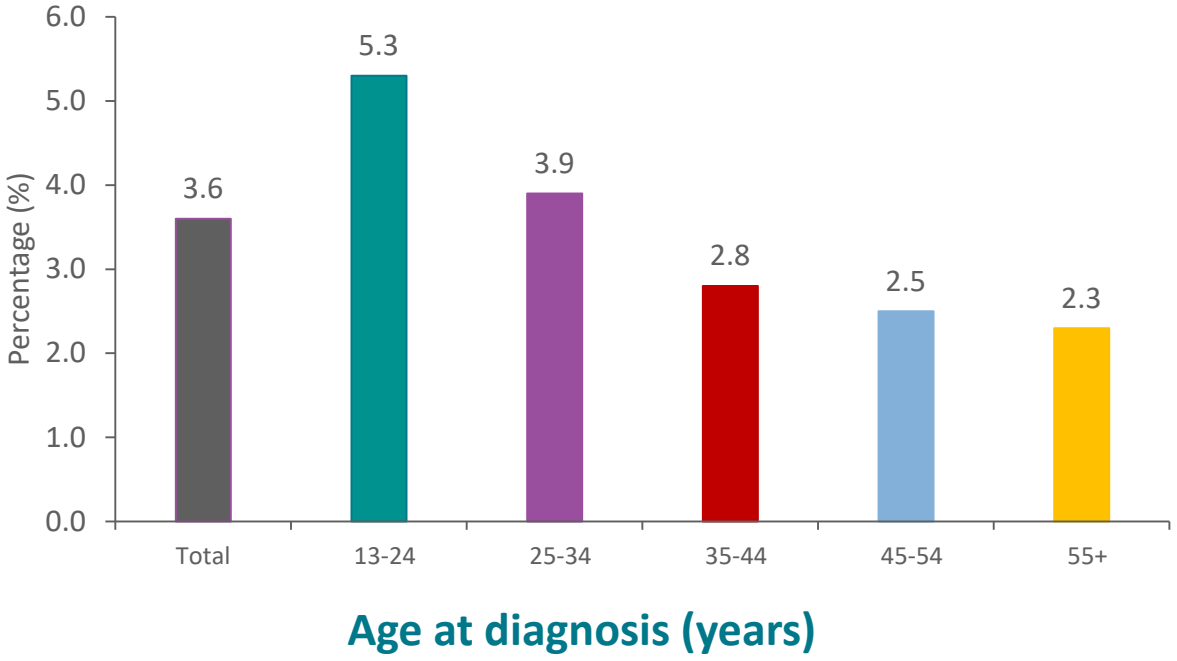
Percentage of Acute HIV Infections Among Persons Aged ≥13 Years with Diagnosed HIV, by Race/Ethnicity, National HIV Surveillance System, 2015–2017



The percentage of AHI detected at diagnosis was lowest among blacks/African Americans.

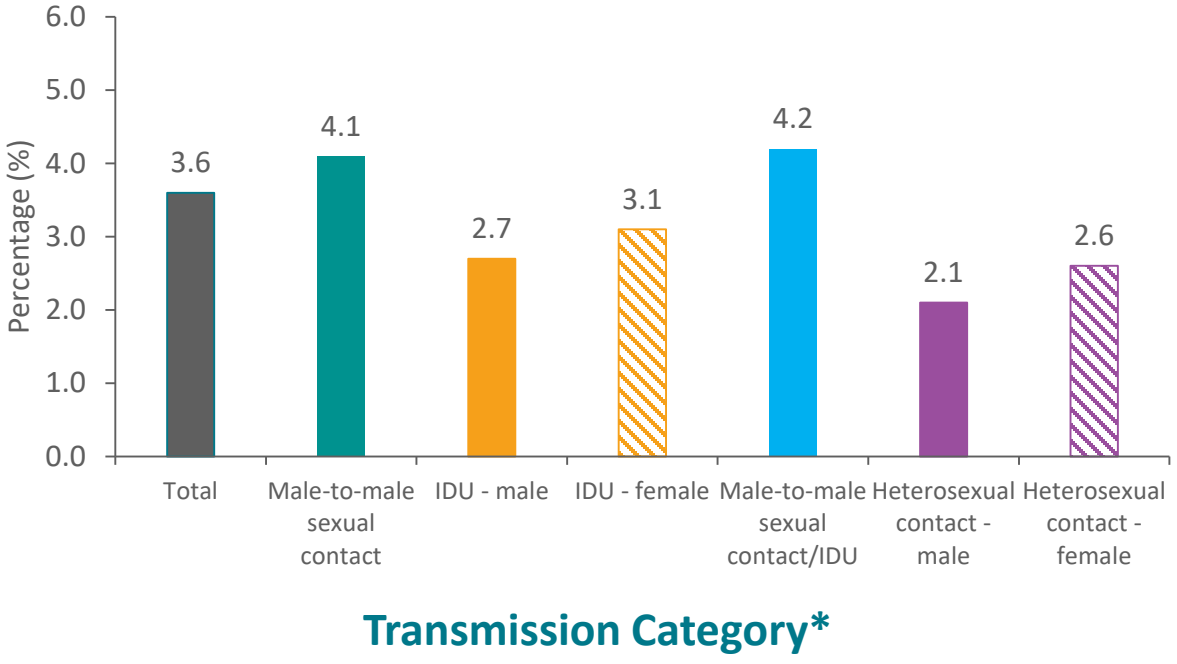
Of the 117,465 cases diagnosed during 2015–2017, 4,251 (3.6%) were AHI. AHI was associated with all demographic characteristics examined.

Percentage of Acute HIV Infections Among Persons Aged ≥13 Years with Diagnosed HIV, by Age at Diagnosis, National HIV Surveillance System, 2015–2017



The percentage of AHI detected at diagnosis was highest among those aged 13–24 years.

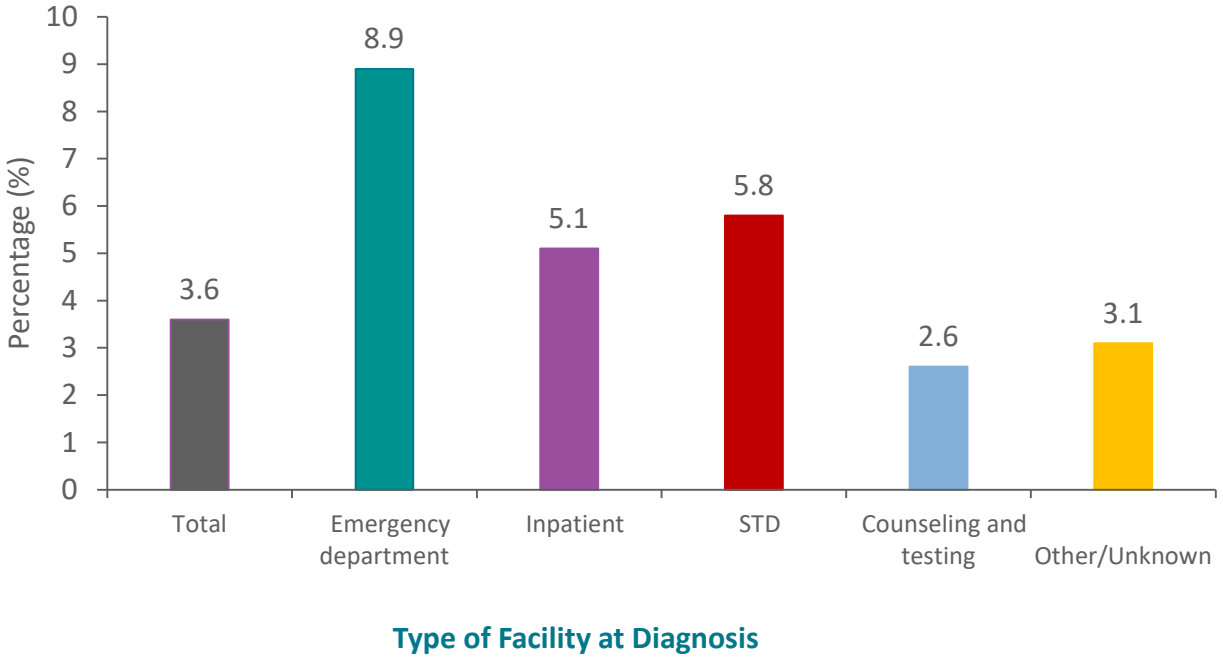
Percentage of Acute HIV Infections Among Persons Aged ≥13 Years with Diagnosed HIV, by Transmission Category, National HIV Surveillance System, 2015–2017



The percentage of AHI detected at diagnosis was highest among those who had HIV infection attributable to both male-to-male sexual contact and injection drug use or male-to-male sexual contact alone.

* Data have been statistically adjusted to account for missing transmission category. “Heterosexual contact” is heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

Percentage of Acute HIV Infections Among Persons Aged ≥13 Years with Diagnosed HIV, by Type of Facility at Diagnosis, National HIV Surveillance System, 2015–2017



The percentage of persons whose HIV infection was acute at diagnosis was higher when diagnoses were made in emergency departments, STD clinics, or inpatient settings.

Detection of AHI by Type of Diagnostic Testing Algorithm

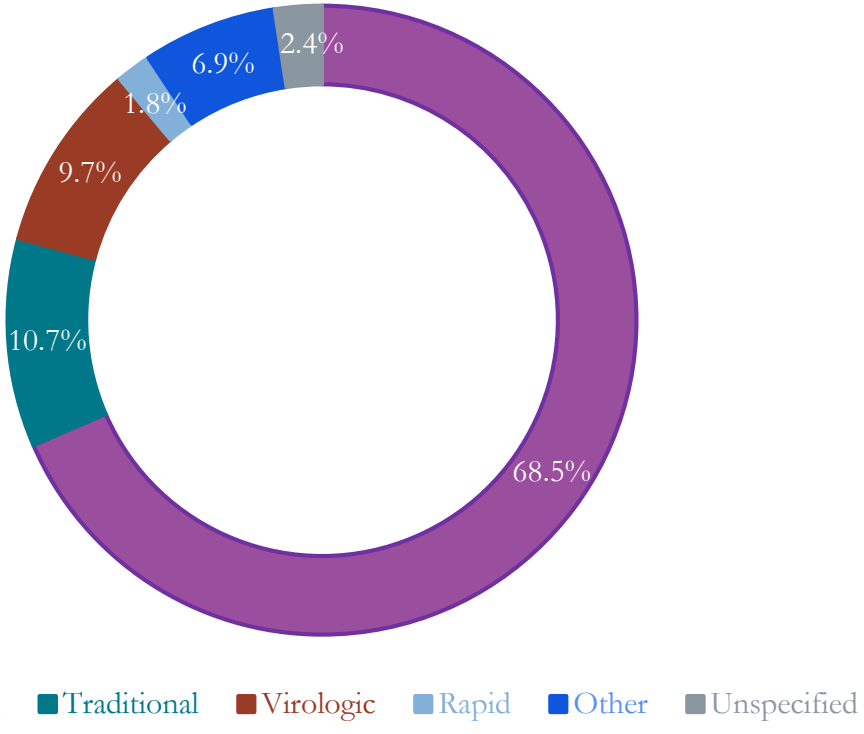
Testing Algorithm Classification[2]

- Based on sequence of HIV tests used at diagnosis that were reported to NHSS:
  - **Recommended:** initial HIV antigen/antibody immunoassay followed by a HIV-1/2 type-differentiating antibody test;
  - **Traditional:** initial HIV antibody immunoassay followed by a Western blot or immunofluorescence antibody test;
  - **Virologic:** first positive test was a quantitative or qualitative NAT, HIV-1 culture, or antigen-only test;
  - **Rapid:** two CLIA-waived rapid tests on same date;
  - **Other:** another combination of tests;
  - **Unspecified:** HIV diagnosis documented by a physician, before any laboratory tests were documented.

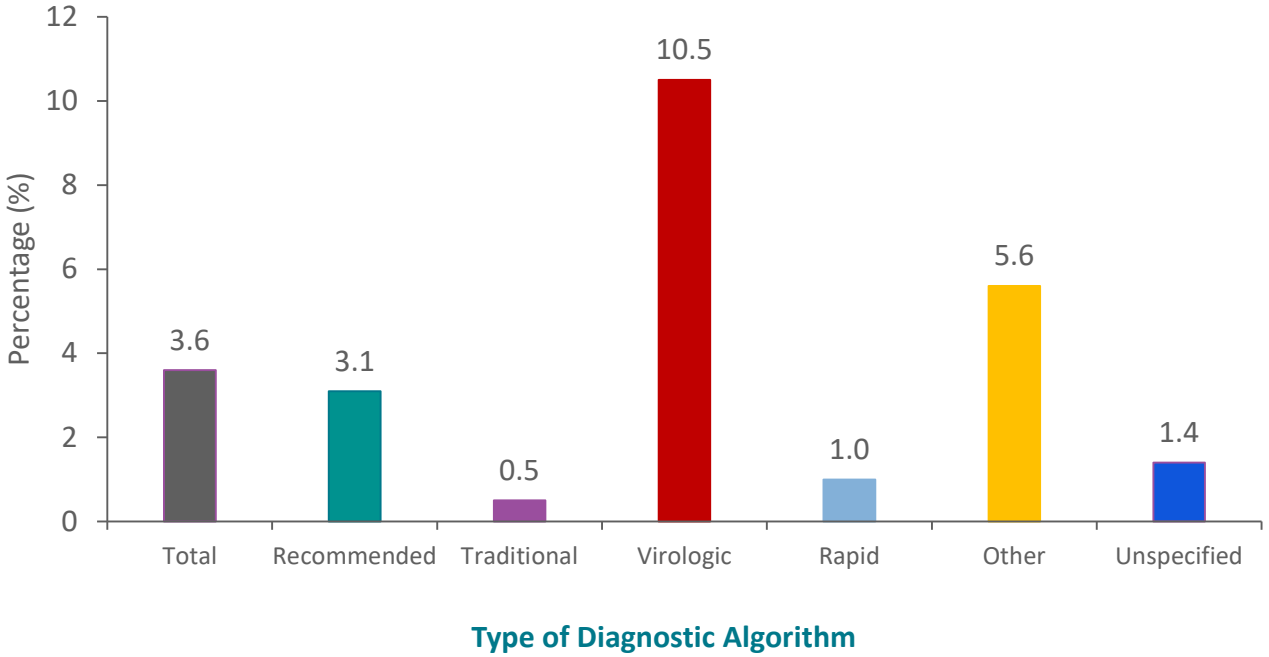
[2] Peruski AH, Dong X, Selik RM. Trends in testing algorithms used to diagnose HIV infection, 2011-2015, United States and 6 dependent areas. J Clin Virol. 2018 Jun;103:19-24. [Link] DOI:10.1016/j.jcv.2018.03.008. Epub 2018 Mar 27.

Percentage of Persons Diagnosed with HIV, by Type of Diagnostic Testing Algorithm Used at Diagnosis, National HIV Surveillance System, 2015–2017

- Of the 117,465 persons diagnosed with HIV during 2015–2017, the majority (80,518, 68.5%) were diagnosed using the recommended algorithm.
  - The percentage of cases diagnosed using the recommended algorithm increased by 8.9% from 2015 (59%) to 2016 (69%).



Percentage of Acute HIV Infections Among Persons Aged ≥13 Years with Diagnosed HIV, by Type of Diagnostic Algorithm, National HIV Surveillance System, 2015–2017



Compared with the traditional algorithm, which yielded only 65 (0.5%) AHI, detection of AHI was significantly higher among cases diagnosed using any other algorithm: recommended (3.1%), virologic (10.5%), rapid (1.0%), or other (5.6%).

Number and Percentage of Acute HIV Infections Among Persons Aged ≥13 Years with Diagnosed HIV, National HIV Surveillance System, 2015-2017

Type of diagnostic algorithm	2015		2016		2017 (preliminary data)		Total 2015-2017	
	No. AHI/HIV Diagnoses	% AHI	No. AHI/HIV Diagnoses	% AHI	No. AHI/HIV Diagnoses	% AHI	No. AHI/HIV Diagnoses	% AHI
Recommended	585/25,305	**2.3**	954/27,229	**3.5**	933/27,984	3.3	2,472/80,518	3.1
Traditional	25/6,208	0.4	29/3,959	0.7	11/2,367	0.5	65/12,534	0.5
Virologic	405/3,816	10.6	392/3,740	10.5	400/3,826	10.5	1,197/11,382	10.5
Rapid	7/776	0.9	11/688	1.6	3/592	0.5	21/2,056	1.0
Other	164/2,679	6.1	166/2,863	5.8	126/2,558	4.9	456/8,100	5.6
Unspecified	18/1,040	1.7	11/980	1.1	11/855	1.3	40/2,875	1.4
Total	1,204/39,824	3.0	1,563/39,459	4.0	1,484/38,182	3.9	4,251/117,465	3.6

- Detection of AHI using the recommended algorithm **increased by 52.2%,** from 2.3% in 2015 to 3.5% in 2016; preliminary data from 2017 support these findings.

Summary

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- An increasing proportion of all cases have been diagnosed with the recommended laboratory HIV testing algorithm, improving the ability to identify AHI in surveillance data.
- The recommended algorithm detected at least 6 times the percentage of AHI compared with the traditional algorithm.
- The percentage of AHI detected by other algorithms, particularly the virologic algorithm, may indicate testing performed specifically when there is a high suspicion of AHI.

Considerations

- Demographic distribution of AHI suggest groups of persons who may benefit from more focused outreach efforts to discern reasons for these differences and address these disparities.
- Data on AHI are a key indicator in the initiative to end the HIV epidemic:
  - identifying and promptly treating those with HIV as early as possible,
  - for understanding where transmission is actively occurring and for focusing efforts in response to new clusters of active transmission.
- Health departments should ensure complete and accurate collection of laboratory data and prompt recognition of AHI to prioritize follow-up and optimize opportunities for treatment and prevention.
- Future changes to the HIV laboratory testing algorithm should consider the ability to identify AHI both clinically and in surveillance data.

Disclaimer

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

Questions?