Overview of HIV Testing Practices and Technology

2019 HIV Diagnostics Conference
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Centers for Disease Control and Prevention

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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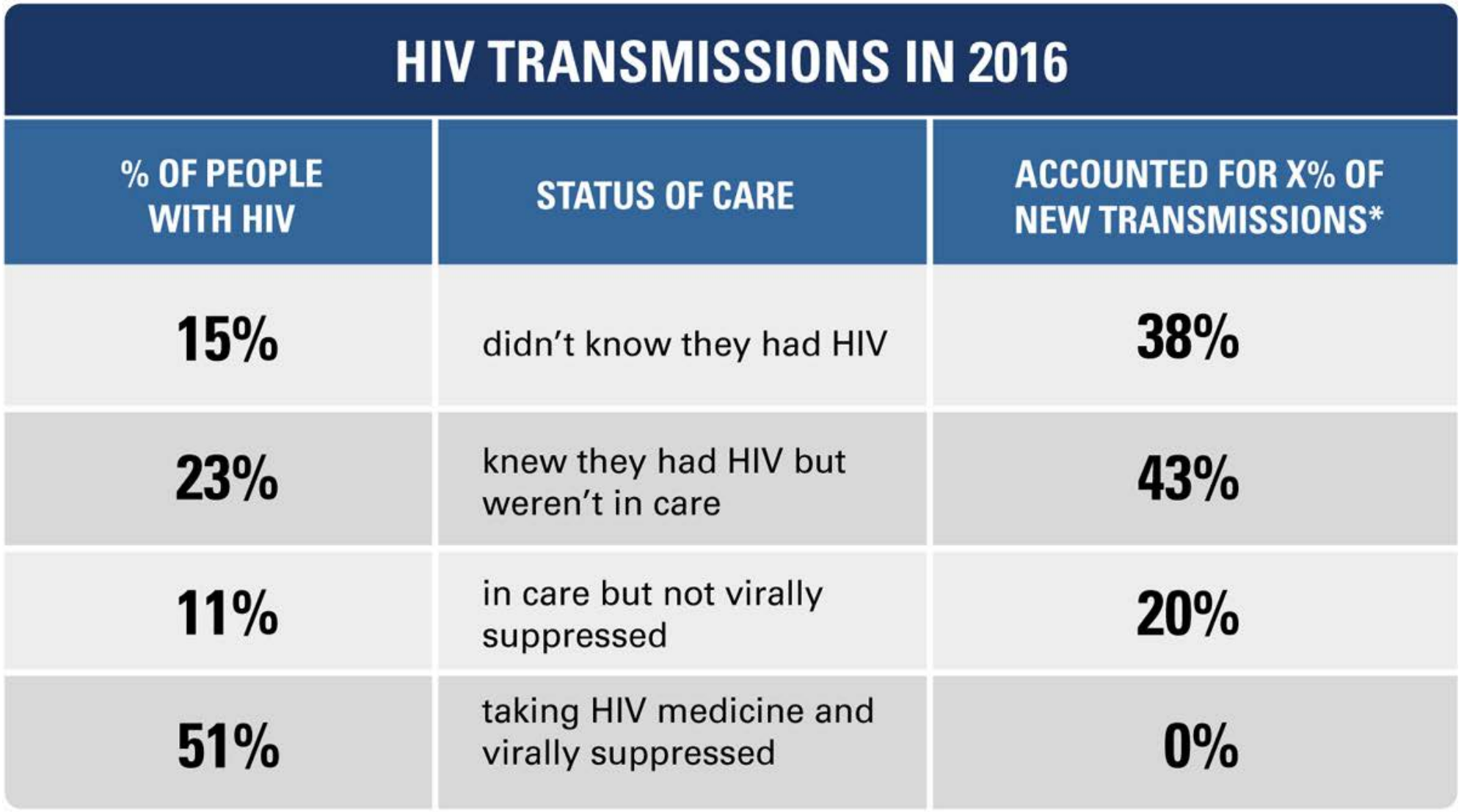


HIV TRANSMISSIONS IN 2016

% OF PEOPLE WITH HIV	STATUS OF CARE	ACCOUNTED FOR X% OF NEW TRANSMISSIONS*
15%	didn't know they had HIV	38%
23%	knew they had HIV but weren't in care	43%
11%	in care but not virally suppressed	20%
51%	taking HIV medicine and virally suppressed	0%

*Values do not equal 100% because of rounding

SOURCE: Vital Signs, 2019 https://www.cdc.gov/vitalsigns/end-hiv/images/vs-infographic-end-hiv1.jpg

Testing Technology

1985
- Viral Lysate IgG HIV-1 EIA

1987
- Western Blot approved as supplemental test

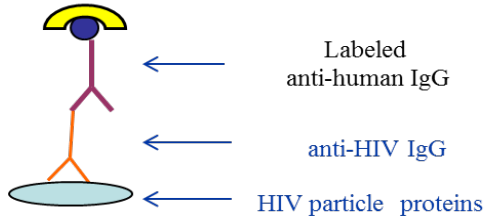
1989
- p24 Antigen EIA
- CDC MMWR 1st HIV diagnostic algorithm

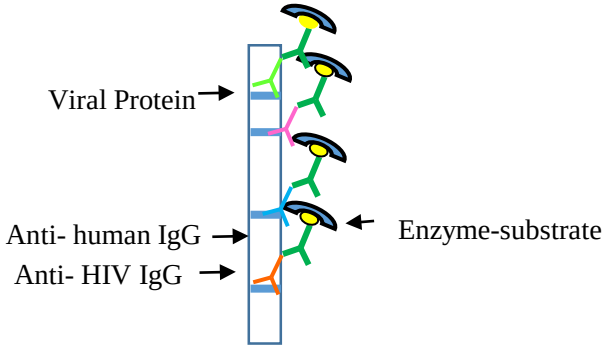
1990
- HIV-2 EIA
- EIA approved for DBS

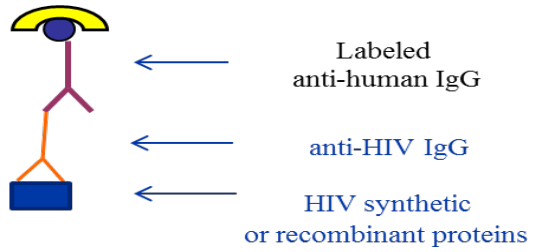
1991
- Recombinant/Peptide HIV-1/HIV-2 EIA

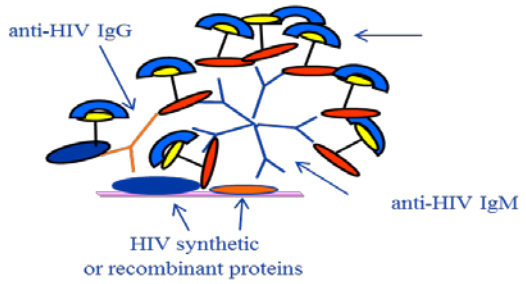
1992
- HIV-1 IFA approved as supplemental test
- HIV-1 Rapid Test (not CLIA waived)
- IgG/IgM HIV-1/HIV-2 EIA

1994
- HIV-1 Oral fluid collection device and oral fluid EIA









1996
- Oral fluid Western blot
- Urine HIV-1 EIA
- HIV-1 Home specimen collection diagnostic system
- Quantitative viral load test

2002
- Rapid IA CLIA waived for whole blood and plasma

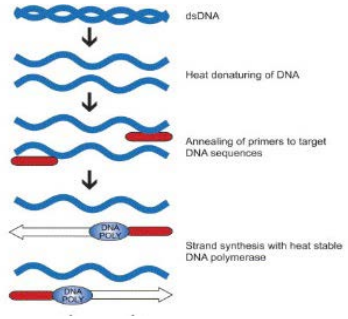
2003
- EIAs Include Group O antigen
- CLIA waived rapid for whole blood

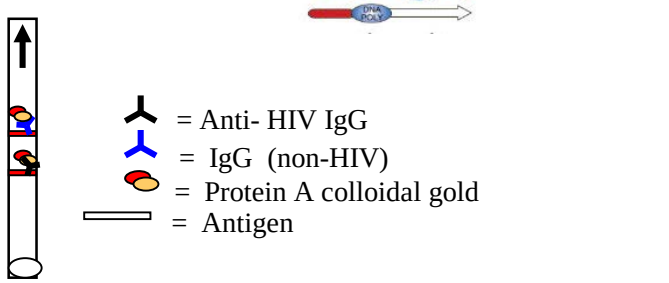
2004
- CLIA waived rapid IA for oral fluid
- Rapid EIA to differentiate between HIV-1 and HIV-2

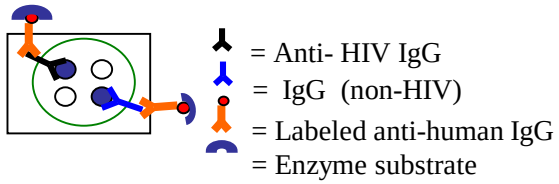
2006
- Random access microparticle HIV1/2/0 chemilumenesence test
- HIV-1 nucleic acid test approved for diagnostic applications
- Revised recommendations for HIV testing in clinical settings

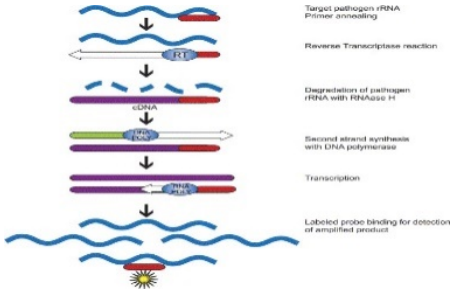
2008
- CLIA waiver requirements revised

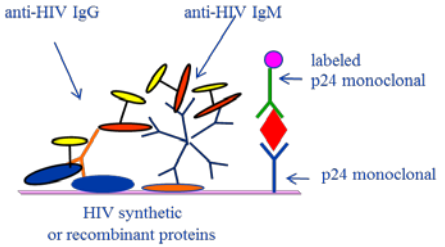
2010
- HIV1/2 antigen/antibody combo test approved











2012

- CLIA waived rapid IA that gives almost immediate results
- Over the counter rapid IA for use with oral fluid

2013

- Rapid antigen/antibody IA

2014

- CLIA waived rapid antigen/antibody IA
- Dual Path supplemental assay to distinguish HIV-1 from HIV-2
- Updated guidelines for laboratory testing for HIV
- Pre-exposure prophylaxis (PrEP) guidelines issued

2015

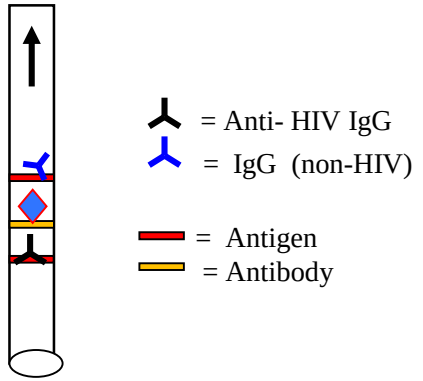
- Multiplex flow immunoassay for detection and differentiation of HIV p24 antigen and antibodies to HIV-1 (group M and group O) and/or HIV-2

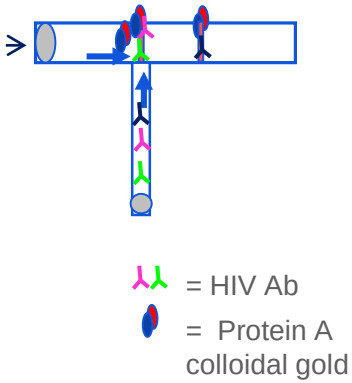
2017

- Minor modification to guidelines for laboratory testing for HIV to include rapid Ag/Ab assay with plasma

2018

- PrEP guidelines updated
- FDA advisory committee meeting on HIV test down-classification





CDC Preferred Nomenclature for Initial Tests

Test Category	Analyte targets	Previous Designation
Ag/Ab combo laboratory-based	HIV-1 p24 Ag, IgM/IgG Ab to HIV-1/HIV-2	4th generation
Ag/Ab combo rapid test (POC)	HIV-1 p24 Ag, IgM/IgG Ab to HIV-1/HIV-2	4th generation
IgM/IgG-sensitive laboratory-based	IgM/IgG Ab to HIV-1/HIV-2	3rd generation
IgM/IgG-sensitive rapid test (POC)	IgM/IgG Ab to HIV-1/HIV-2	3rd generation
IgG-sensitive tests (lab-based or POC)	IgG Ab to HIV-1 or HIV-1/HIV-2	1st/2nd generation

Time to Test Reactivity

Clinical Infectious Diseases

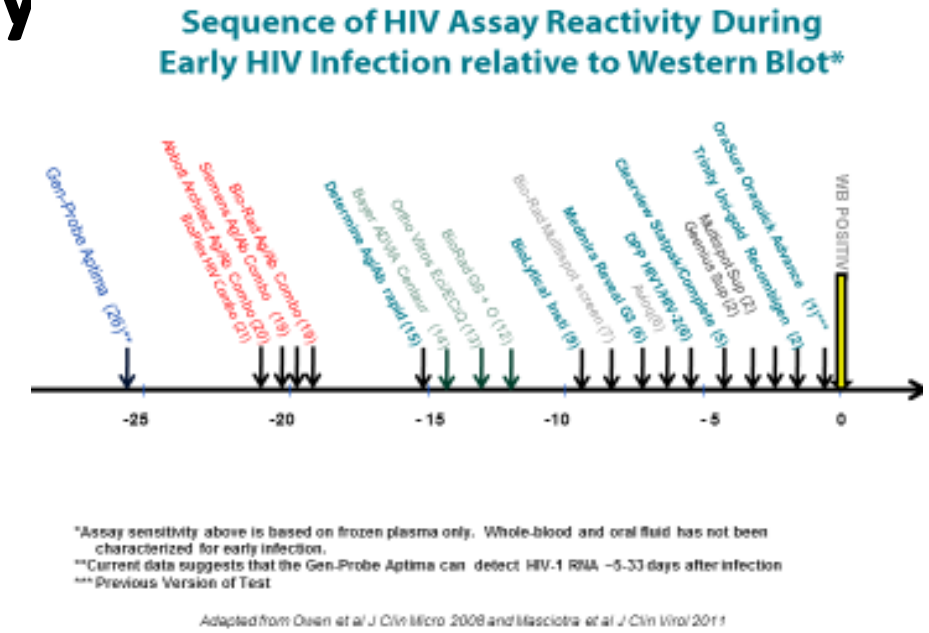
MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Time Until Emergence of HIV Test Reactivity Following Infection With HIV-1: Implications for Interpreting Test Results and Retesting After Exposure

Kevin P. Delaney,[1] Debra L. Hanson,[1] Silvina Masciotra,[1] Steven F. Ethridge,[1] Laura Wesolowski,[1] and Sherry Michele Owen[2]

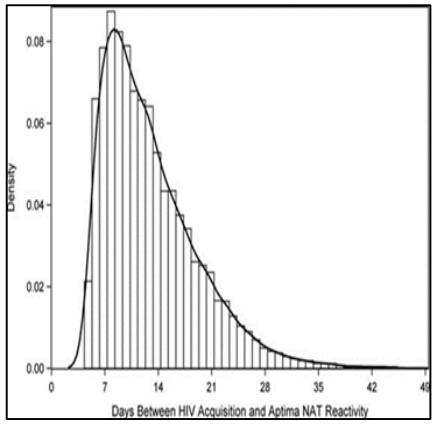
[1]Division of HIV/AIDS Prevention, and [2]Office of the Director, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

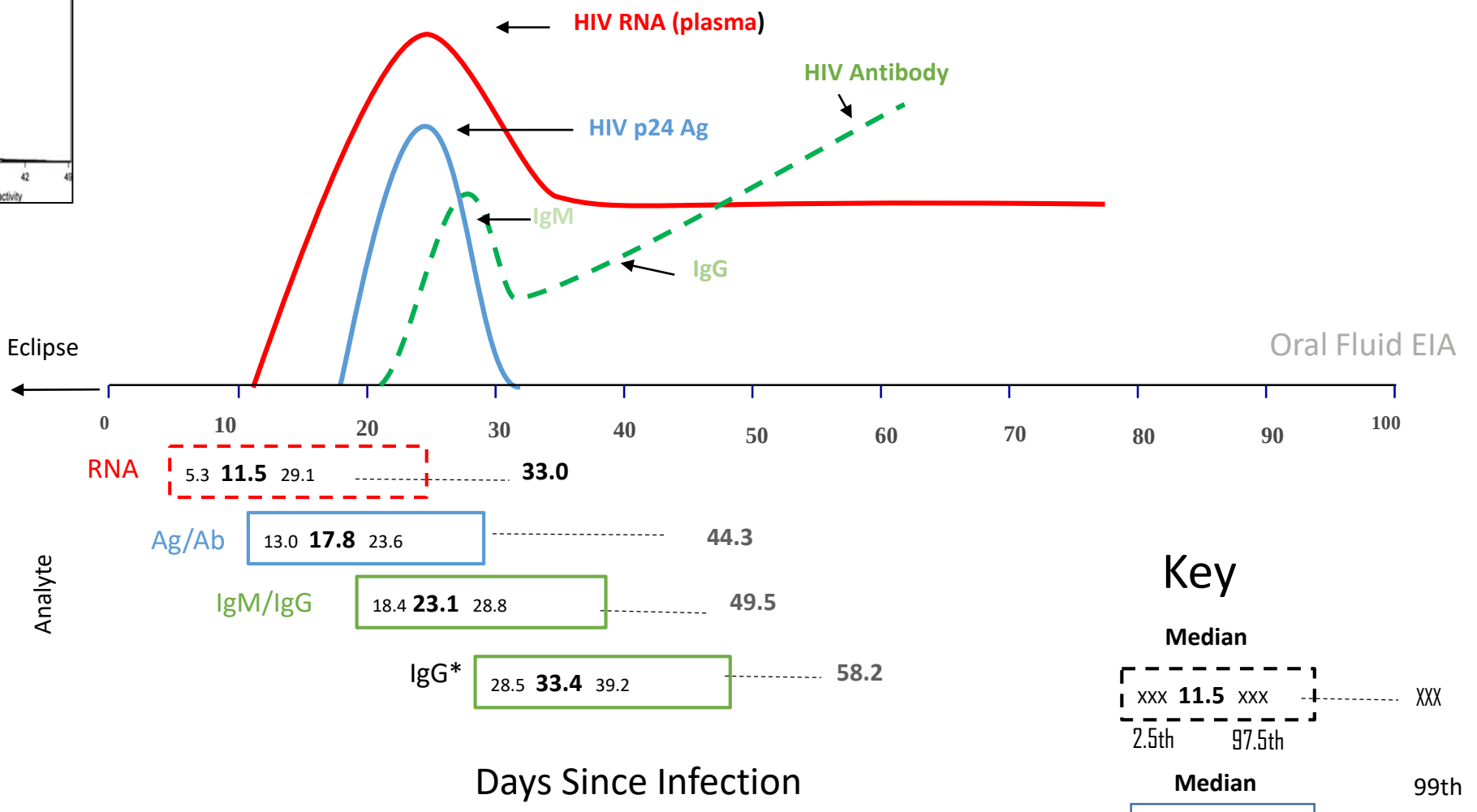


*Assay sensitivity above is based on frozen plasma only. Whole-blood and oral fluid has not been characterized for early infection.
**Current data suggests that the Gen-Probe Aptima can detect HIV-1 RNA ~5-33 days after infection
*** Previous Version of Test

Adapted from Owen et al J Clin Micro 2008 and Masciotra et al J Clin Virol 2011

- Seroconversion panel data used to compare tests in context of time since RNA reactivity
  - Inter-test reactivity interval (ITRI)
- Eclipse period simulated from published data and combined with ITRI data
- Why?
  - Valuable to testing providers for interpreting negative HIV test results
  - Counseling individuals on when to retest after an exposure





Delaney et al CID, 2016

Luo et al J Clin Virol, 2013

Resources

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

SEARCH

CDC A-Z INDEX

HIV/AIDS

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HIV/AIDS > HIV Testing

Laboratory Tests

This section focuses on FDA-approved diagnostic HIV tests for use in moderate and high complexity laboratories.

Laboratory Testing Guidance

- New Item January 2018 2018 Quick Reference Guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens
- Updated January 2019 APHL Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm
- Full Version of the Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations
- Technical Update on HIV-1/2 Differentiation Assays, August 2016
- Technical Update: Use of the Determine HIV 1/2 Ag/Ab Combo Test with Serum or Plasma in the Laboratory Algorithm for HIV Diagnosis

FDA Approved HIV Tests

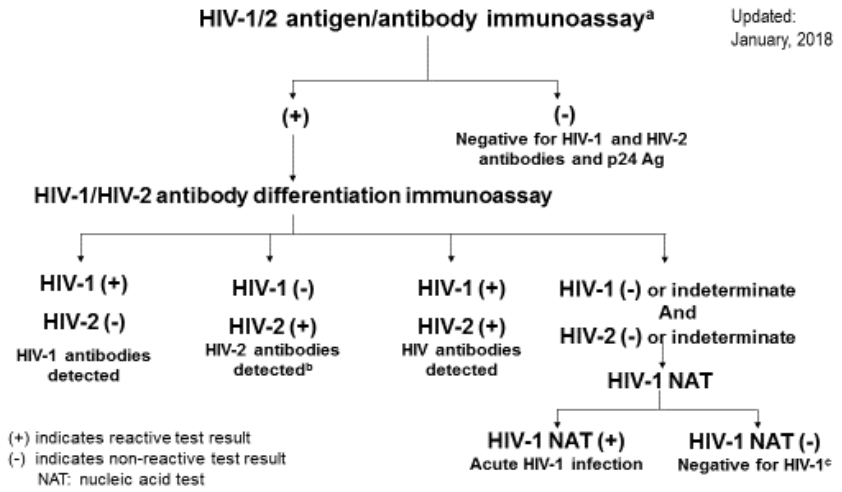
- Updated June 2018 Advantages and Disadvantages of Different Types of HIV tests
- Updated March 2018 Laboratory Screening Tests
- Laboratory Screening Tests
- Updated Feburary 2019 Supplemental Tests for Laboratory Settings
- Moderate Complexity Rapid HIV Tests for Clinical Settings
- Updated June 2018 CLIA-waived rapid HIV tests

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

Laboratory Algorithm

Objectives of 2014 Laboratory Algorithm

- Improve diagnosis of acute HIV infection
- Accurate diagnosis of HIV-2
- Decrease turn-around time for results
- No substantial change in cost for testing



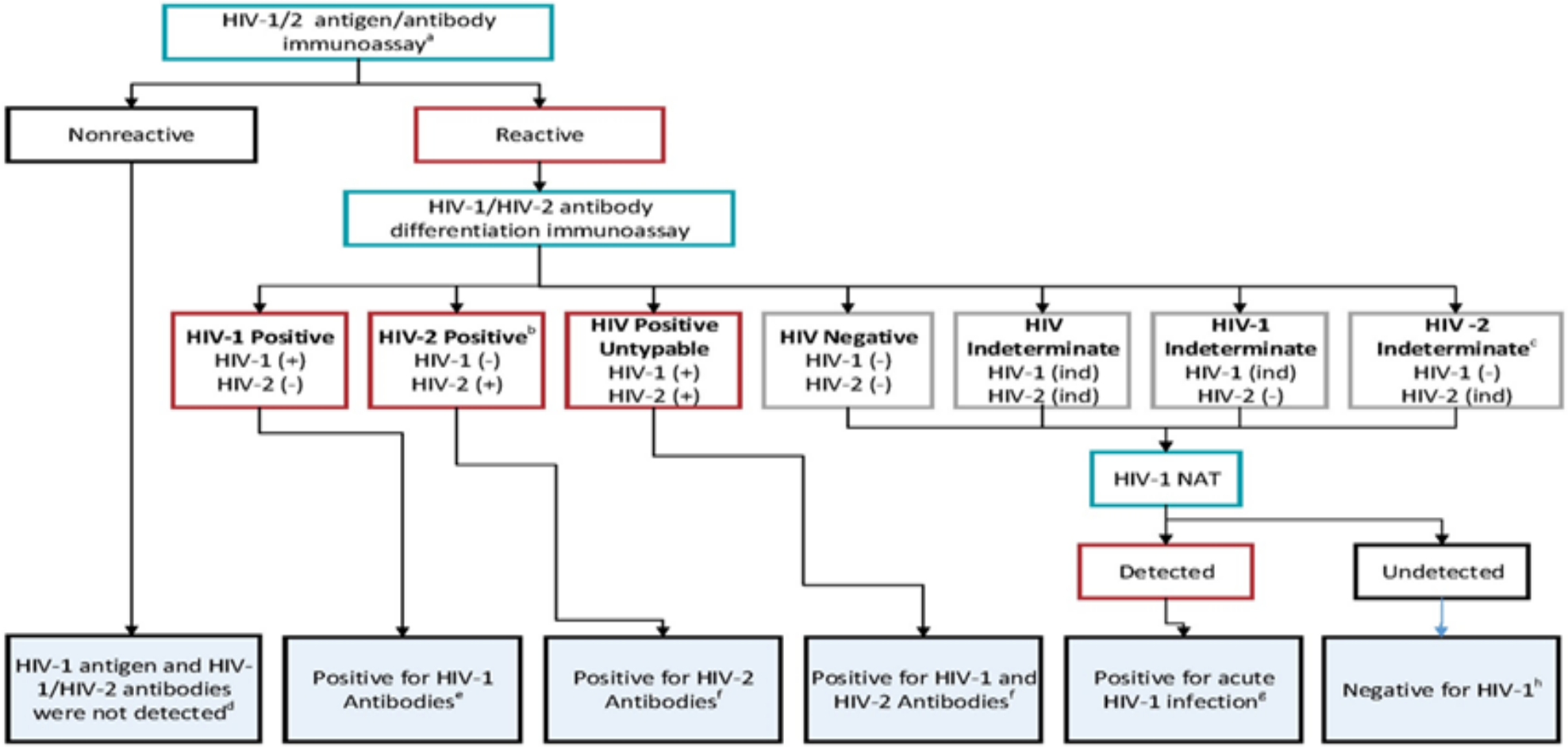
https://stacks.cdc.gov/view/cdc/23447

Determine HIV 1/2 Ag/Ab Combo Test in the Laboratory Algorithm for HIV Diagnosis

- CDC and APHL continue to recommend an instrumented, laboratory based antigen/antibody (Ag/Ab) HIV immunoassay as the first step in the laboratory algorithm.
- Determine can detect infection earlier than IgM/IgG sensitive (antibody-only) immunoassays when used with plasma[1,2]
- Laboratories in which instrumented Ag/Ab testing is not feasible, Determine can be used with **serum/plasma** as the first step in the laboratory algorithm
- Laboratories using Determine are advised to acknowledge the limitations of the testing procedure when reporting results
- Ag only reactivity can be followed with parallel testing of Ab (differentiation assay) and NAT
  - Data needed for a definitive recommendation and potential algorithm updates
- **https://stacks.cdc.gov/view/cdc/48472**

[1]Delaney et al, *Clinical Infectious Diseases*, 2016, [2] Masciotra et al. *Journal Clinical Virology*, 2013 and 2017

Figure 2: HIV Laboratory Testing Algorithm in Serum/Plasma (modified from 2014 algorithm figure and CDC Quick Reference Guide)



a. The FDA-approved single-use rapid HIV-1/HIV-2 antigen/antibody immunoassay can be used as the initial assay in the laboratory HIV testing algorithm for serum or plasma. If any instrumented antigen/antibody test is available, it is preferred due to its superior sensitivity for detecting HIV during acute infection. **b.** This includes specimens reported as HIV-2 positive with HIV-1 cross reactivity. **c.** Per the Geenius Package Insert, specimens with this final assay interpretation should be retested with a new cartridge. If the final assay interpretation is again HIV-2 indeterminate, it should be reported as such and followed with an HIV-1 NAT. **d.** If recent HIV exposure is suspected or reported, conduct HIV-1 NAT or request a new specimen and repeat the algorithm according to CDC Guidance. **e.** Link patient to HIV medical care and provide appropriate prevention counseling. **f.** Link patient to HIV medical care and provide appropriate prevention counseling. Provider may consider additional testing. **g.** Link patient to HIV medical care and provide appropriate prevention counseling immediately to expedite prevention practices. **h.** A negative HIV-1 NAT result and repeatedly HIV-2 indeterminate or HIV indeterminate antibody differentiation immunoassay result should be referred for testing with a different validated supplemental HIV-2 test (antibody test or NAT) if available. Alternatively, redraw and repeat algorithm in 2-4 weeks to assess HIV-2 infection.

https://stacks.cdc.gov/view/cdc/76017

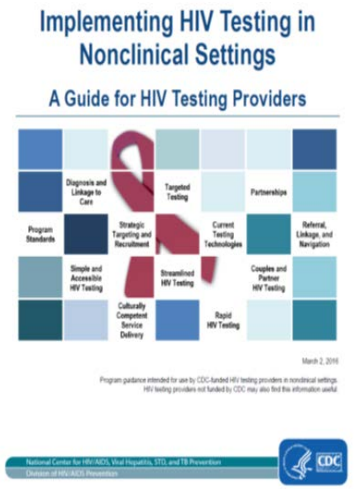
Point of Care and Self Testing


Eddie's
BE SURE

Considerations for POC Testing

- Viable option for locations/populations where lab testing is not feasible
- Successfully used to improve linkage
- Assay characteristics
  - High sensitivity and specificity in established infections and no ART
  - Whole blood assays detect infections later than laboratory assays
  - Oral fluid assays will likely miss acute infections and some early infections
- Guidance available

https://www.cdc.gov/hiv/testing/nonclinical/index.html



Self-testing

- Recent systematic review by Stevens et al[1] indicates the following:
  - Generally high sensitivity and specificity of assays but with wide ranges in some studies
  - Acceptability generally high
  - Most individuals were capable of performing self-testing
    - Education level and language were linked to lower performance
  - To date little evidence of harm related to self-testing
- WHO recommended self-testing in 2016[2]
- One FDA approved assay in the U.S. [3]
  - FDA analysis predicted public health benefit
- RCT in U.S. indicate feasibility and potential for public health benefit [4]
- Barriers in U.S. [1,4]
  - Cost
  - Assay choice

[1]*Stevens et al AIDS Behav 2018* [2]*https://www.who.int/hiv/pub/vct/hiv-self-testing-guidelines/en/*
[3]http://www.fda.gov/BiologicsBloodVaccines/Blood BloodProducts/ApprovedProducts/PremarketApprovalsPMAs/ucm091994.htm
[4] *MacGowan et al. AIDS and Behav 2018*

Testing in the Context of PrEP

- Evidence that testing in the context of PrEP can result in ambiguous results
  - False negative – altered window periods for test reactivity
  - False positive- technical issues, repeated testing ???
- Resistance can develop if PrEP is initiated or continued in infected individuals
- Resolution of ambiguous results important to prevent harm
  - Proper Counseling
  - Additional testing
- PrEPline 855-448-7737 (11 am-6pm EST)
  - Report ambiguous results
  - Advice on patient management related to ambiguous results

Open Forum Infectious Diseases

MAJOR ARTICLE

A Strategy for PrEP Clinicians to Manage Ambiguous HIV Test Results During Follow-up Visits

Dawn K. Smith, William M. Switzer, Philip Peters, Kevin P. Delaney, Timothy C. Granade, Silvina Masciotra, Luke Shouse, and John T. Brooks

Division of HIV/AIDS Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

Prompt determination of HIV infection status is critical during follow-up visits for patients taking pre-exposure prophylaxis (PrEP) medication. Those who are uninfected can then continue safely taking PrEP, and those few who have acquired HIV infection can initiate an effective treatment regimen. However, a few recent cases have been reported of ambiguous HIV test results using common testing algorithms in PrEP patients. We review published reports of such cases and testing options that can be used to clarify true HIV status in these situations. In addition, we review the benefits and risks of 3 antiretroviral management options in these patients: (1) continue PrEP while conducting additional HIV tests, (2) initiate antiretroviral therapy for presumptive HIV infection while conducting confirmatory tests, or (3) discontinue PrEP to reassess HIV status after a brief antiretroviral-free interval. A clinical consultation resource is also provided.

Keywords. PrEP; pre-exposure prophylaxis; HIV testing; seroconversion.

Rapid/POC/TNT/Dual Claim NATs

- Available outside the U.S., but none are FDA approved
  - AlereQ HIV-1/2 Detect
  - Xpert HIV-1 Qual
  - SAMBA II Qual
  - COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Qualitative Test v2.0 (CE)
  - Aptima HIV-1 Quant Dx Assay (CE-IVD)

- Potential for earlier diagnosis and to conduct NAT in more locations
- Potential to impact current laboratory testing algorithm
- Potential to impact care
- Status for the U.S.?

Summary

- Diagnostic assays continue to evolve
- Current HIV Laboratory Testing Algorithm recommended June 2014 with minor updates in 2018
- New data on Inter-test reactivity interval (ITRI) should improve interpretation of negative test results and counseling for retesting
- Rapid and HST will likely play an important role in “Ending the HIV Epidemic”
- Testing in the context of PrEP introduces the potential for new opportunities and challenges
- NAT technology available outside the U.S. would likely improve HIV testing in the U.S.

Thanks!
Questions?
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