HIV Testing Strategies in PrEP Clients

Eligibility for PrEP initiation or continuation requires confirmation that the person is HIV uninfected, to minimize the risk of HIV drug resistance. The HIV detection period following transmission differs based on the point of care test (see HIV Infection Timeline and Table 1), leaving the possibility that a person may use PrEP with an unknown acute HIV infection. The World Health Organization (WHO) recommends HIV testing strategies to identify HIV infection and therefore, minimize the risk of HIV drug resistance for those using PrEP. GEMS modeling results support WHO recommendations for frequency of HIV testing for PrEP users. Using the WHO recommendations, and this factsheet, policy makers and PrEP project implementers should consider HIV testing strategies specific to their PrEP program; including the use of more sensitive HIV testing methods to identify acute HIV infection.

There are three types of HIV tests used that provide same day results. These tests, along with the GEMS Acute Seroconversion Assessment, available at gems.pitt.edu/toolkit, are recommended for PrEP programs to identify acute or established HIV infection prior to PrEP provision.

Definitions

**Acute Infection:** Occurs immediately after a person contracts HIV; characterized by initial burst of viremia; often includes symptoms such as fever or lymphadenopathy. NAAT and p24 Antigen HIV tests are able to detect acute infection.

**EIA:** Enzyme Immunoassay, also known as the enzyme-linked immunosorbent assay (ELISA), are tests that detect HIV antibodies in your blood.

**Established Infection:** Levels of p24 antigen begin to decline, HIV RNA begins to stabilize at a level that is normally still detectable and HIV antibody levels begin and will continue to rise.

**HIV Antibody:** Antibodies are proteins generated by the immune system as a defense against infections. Antibodies to HIV present distinctive targets for screening tests.

**HIV Diagnostic Testing Window Period:** The time between when a person becomes infected with HIV until the time a test can detect infection.

**HIV Viral Load Testing:** HIV viral load test measures the amount of HIV genetic material (RNA) in the blood.

**HIV Viral p24 Antigen:** A viral protein in blood that antigen assays measure. HIV viral p24 antigen is detectable earlier than HIV antibodies during acute infection.

**Recent Infection:** Typically occurs up to 6 months after infection.

HIV Infection Timeline: For Testing and Diagnosis

11 DAYS
Acute infection phase begins; HIV viral RNA is present in the blood and is the first marker to become detectable by viral load testing. Rapid NAAT test window opens

15 DAYS
Levels of viral p24 Ag start to become detectable

25 DAYS
HIV Ab levels are detectable by 3rd generation rapid tests; peak levels of viral RNA and p24 Ag will also be present

19 DAYS
4th generation rapid test window opens
Table 1: Characteristics of Available Point of Care and Rapid HIV Tests

<table>
<thead>
<tr>
<th>HIV Assay Group</th>
<th>3rd generation point of care rapid diagnostic test (RDT)</th>
<th>4th generation point of care RDT</th>
<th>Rapid NAAT (HIV RNA Viral Load)</th>
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</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>• Detect antibodies only</td>
<td>• Detect both antibodies and the p24 antigen</td>
<td>• Nucleic Acid Amplification Tests (NAAT) measure viral HIV RNA; the first marker to become detectable after a person is infected</td>
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<td></td>
<td>• Currently part of national HIV testing algorithms and WHO recommendations for HIV diagnosis</td>
<td></td>
<td>• Recommended in suspected cases of acute infection</td>
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<tr>
<td><strong>Common Assays</strong></td>
<td>• Determine HIV-1/2</td>
<td>• Alere HIV Combo</td>
<td>• Gene Xpert HIV-1 Viral Load</td>
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<tr>
<td></td>
<td>• STAT-PAK HIV-1/2</td>
<td></td>
<td>• Aptima HIV-1 Quant DX</td>
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<td></td>
<td>• Unigold Recombigen HIV-1/2</td>
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<td></td>
<td>• Oraquick Advance HIV-1/2</td>
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<tr>
<td><strong>Reactive Infection Phase</strong></td>
<td>Established</td>
<td>Acute through established</td>
<td>Acute through established</td>
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<tr>
<td><strong>Test Window Period</strong></td>
<td>26 – 50 days after infection</td>
<td>19 – 31 days after infection</td>
<td>11 days after infection</td>
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<tr>
<td><strong>Allowable specimen types</strong></td>
<td>Fingerstick and venous whole blood, plasma</td>
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<td>Plasma</td>
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<tr>
<td><strong>Time to test completion</strong></td>
<td>20 mins</td>
<td>20 mins</td>
<td>1.5 – 2.5 hrs</td>
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<tr>
<td><strong>Advantages</strong></td>
<td>• Quick and easy to use</td>
<td>• Quick and easy to use</td>
<td>• Able to detect infection the earliest</td>
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<tr>
<td></td>
<td>• Minimal supplies/training required</td>
<td>• Minimal supplies/training required</td>
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<tr>
<td></td>
<td>• No blood processing required</td>
<td>• No blood processing required</td>
<td></td>
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<tr>
<td></td>
<td>• Inexpensive</td>
<td>• Inexpensive compared to Viral Load tests; however, generally more costly than 3rd generation tests</td>
<td></td>
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<tr>
<td><strong>Disadvantages</strong></td>
<td>Least sensitive of all assays; however, some 3rd generation tests are able to detect infection at about four weeks, such as the Determine HIV-1/2.</td>
<td>• Data is still limited on the reliability for detecting infection earlier</td>
<td>• Not a screening/diagnostic assay; an HIV infected person can have an undetectable HIV RNA result</td>
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<td></td>
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<td>• Most expensive to perform/maintain</td>
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<td>• Requires blood processing and skilled technicians</td>
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</table>

*These numbers may vary based on the patient's immune response, the test used and sample type. **Assay specific package inserts must be referenced for specific information about this topic.
HIV Testing Recommendations for PrEP Implementation Programs

Rapid Tests

- HIV point of care or rapid tests are important for immediate HIV diagnosis, are convenient, and easy to use.
- Consider use of a 4th generation test in individuals using PrEP to detect HIV infection as early as possible, if feasible, affordable, and performed according to quality assurance standards.
- Rapid NAAT (viral load) tests are useful for confirming infections detected by rapid tests and helping to identify acute infection.
- False negative test results can occur, especially with oral based tests used for HIV self-testing. Oral fluid-based rapid tests are not recommended for PrEP users.  

Symptomatic PrEP Clients

- If a PrEP user reports recent HIV risk behavior, e.g., unprotected sexual intercourse, needle sharing, and exhibits symptoms reflective of acute infection, conduct HIV testing per the HIV testing algorithm. If the test is negative, consider a confirmatory HIV test to identify an acute infection.
- For confirmation testing, conduct an EIA or supplemental test and an HIV viral load test:
  - A person who has a negative or indeterminate antibody test result, but a detectable viral load, should not use PrEP until additional HIV confirmatory testing is done.
  - If the confirmatory test is not done at the time of the visit, provide condoms and appropriate counseling, and ask the client to return in 30 days for another HIV test.

6. Delaney, et. al. Time Until Emergence of HIV Test Reactivity Following Infection With HIV-1: Implications for Interpreting Test Results and Retesting After Exposure. CID; 2017:64.