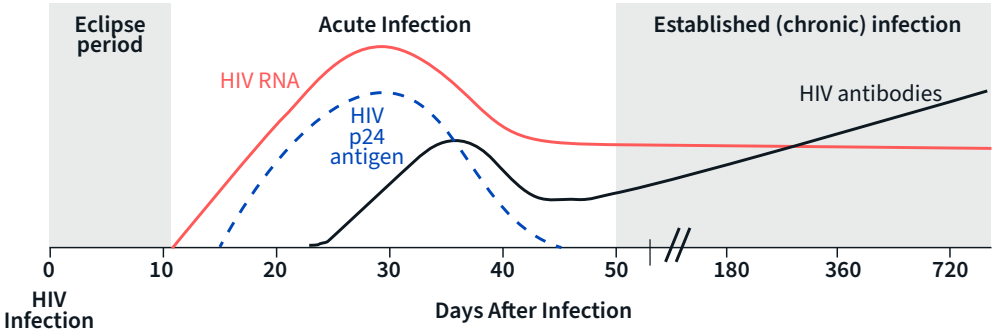
Human Immunodeficiency Virus (HIV) Screening and Diagnosis

In 2021, approximately 30,000 new HIV diagnoses were made in the United States.[1] Timely diagnosis of infection and linkage to care of all persons with HIV is crucial for achieving optimal clinical outcomes and preventing HIV transmission. The HIV diagnostic algorithm illustrated below[2] relies on the detection of laboratory markers that appear with kinetics.

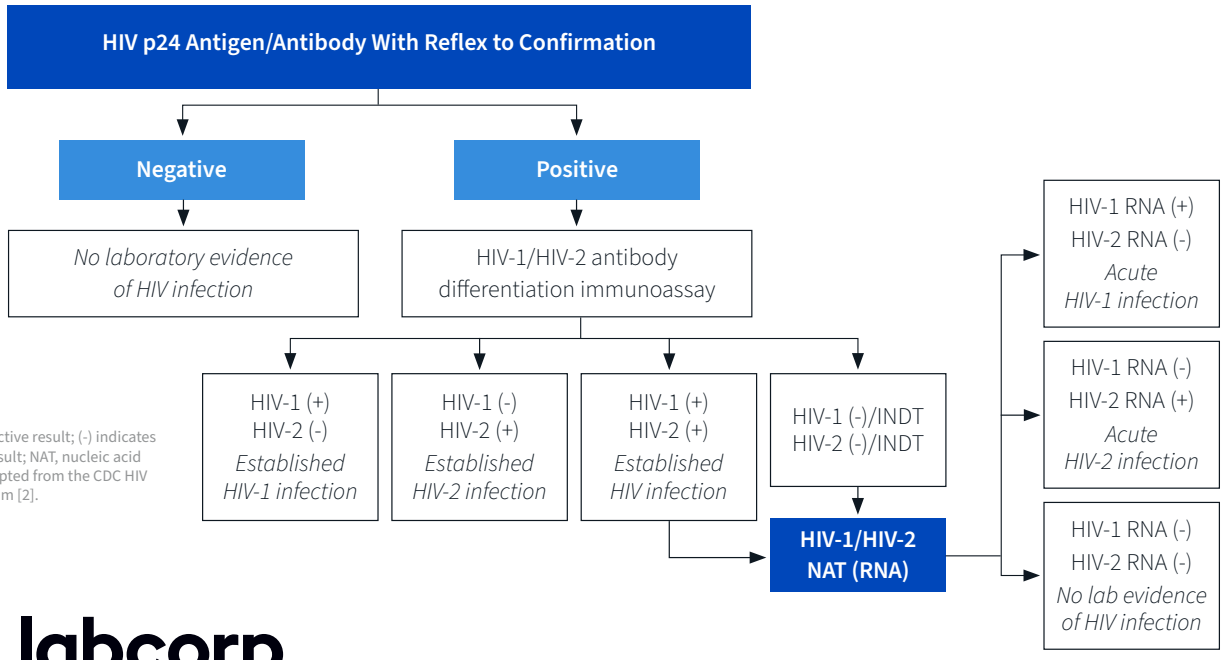
Temporal Appearance of Laboratory Markers of HIV Infection



HIV Testing Algorithm

The HIV testing algorithm recommended by the U.S. Centers for Disease Control and Prevention (CDC) is a multistep process that identifies both chronic and acute (pre-seroconversion) HIV infection. The first step of the algorithm is the HIV p24 antigen/antibody screen, which can detect the HIV-1 p24 antigen, and both IgG and IgM HIV-1 and HIV-2 antibodies. Repeated reactivity on the HIV antigen/antibody screen triggers a reflex to a secondary immunoassay that detects and differentiates between HIV-1 and HIV-2 antibodies. A positive secondary antibody assay is consistent with established HIV infection. If the secondary antibody assay is negative or indeterminate, a nucleic acid test (NAT) is performed for HIV-1 and HIV-2 RNA. A positive nucleic acid test, combined with a reactive screen and negative/indeterminate secondary antibody test, indicates acute infection. The complete algorithm and interpretations are illustrated below.[2] This testing cascade is available from Labcorp as part of the HIV p24 Antigen/Antibody with Reflex to Confirmation [083935] test.

HIV Testing Algorithm



+) indicates reactive result; (-) indicates non-reactive result; NAT, nucleic acid test. Figure adapted from the CDC HIV Testing Algorithm [2].

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HIV Testing Recommendations

General Population
Per CDC recommendations, everyone ages 13-64 years old should get tested for HIV at least once using HIV p24 Antigen/Antibody With Reflex to Confirmation [083935].[3]

High-Risk Populations
People at high risk for HIV infection include men who have sex with men, people who inject drugs and their sex partners, people who exchange sex for money or drugs, sex partners of people with HIV, and those who have had or whose partners have had multiple sex partners since their most recent HIV test. All persons initiating treatment for tuberculosis or a sexually transmitted infection (STI) should also be screened for HIV. Per CDC guidelines, annual HIV screening is recommended for these high-risk populations using HIV p24 Antigen/Antibody With Reflex to Confirmation [083935].[4]

People Taking HIV Pre-Exposure Prophylaxis (PrEP)
Prior to initiating PrEP, patients should be screened for HIV infection using the HIV p24 Antigen/Antibody With Reflex to Confirmation [083935]. Because PrEP can alter the timing of laboratory markers of HIV infection,[5] the CDC recommends the addition of an HIV RNA test to baseline testing for all patients who have taken PrEP/PEP (post-exposure prophylaxis) within three months or received a PrEP injection within 12 months. Addition of an HIV RNA test is also recommended for patients who have not taken PrEP but have reported possible exposure in the four weeks prior to their initial PrEP visit and have experienced signs/symptoms of acute HIV during that time.[5]

HIV p24 Antigen/Antibody With Reflex to Confirmation [083935] and an HIV RNA test are both recommended every three months for patients taking oral PrEP; for those on injectable PrEP, the tests should be performed at the one-month follow-up, and every two months subsequently. Both assays should also be performed at discontinuation of oral or injectable PrEP. The HIV RNA test can be either qualitative [139825] or quantitative [550430].[5]

While Labcorp's PrEP panels are aligned with the CDC recommendations, it is important to note that the adoption of HIV RNA testing varies among clinicians.

Recent Exposure
HIV RNA is the earliest detectable laboratory marker of HIV infection. When acute retroviral syndrome is suspected, the Human Immunodeficiency Virus 1 & 2 (HIV-1/HIV-2), Qualitative, RNA [139825] test may identify HIV infection earlier than the HIV p24 Antigen/Antibody Screen With Reflex to Confirmation test; therefore, the tests should be used in conjunction in situations where recent HIV exposure may have occurred.[4]

Pregnant Women
Per guidelines from the U.S. Department of Health and Human Services (DHHS), pregnant women should be tested for HIV infection using HIV p24 Antigen/Antibody With Reflex to Confirmation [083935] as early as possible in pregnancy to minimize the risk of vertical HIV transmission. For women at increased risk of HIV acquisition, repeat testing is recommended during the third trimester. Repeat testing is also recommended for patients with an STI or signs/symptoms of acute HIV infection.[6]

Neonates
Because of transplacental transfer of antibodies from mothers with HIV to infants, serologic testing, including antigen/antibody testing, should not be used in infants less than 18 months old. Instead, assays that detect HIV nucleic acid should be used. HIV DNA and HIV RNA polymerase chain reaction (PCR) assays are recommended as preferred virologic assays by the DHHS guidelines; however, the guidelines also caution that maternal antiretroviral therapy or infant HIV prophylaxis may affect HIV-1 RNA and DNA test results.[7]

Please consult the CDC and DHHS guidelines for complete HIV testing recommendations.

CDC-aligned HIV PrEP Laboratory Panels

	Sex Assigned at Birth	PrEP Type	Test No.	Test Name	HIV Ag/Ab + HIV RNA	HIV Ag/Ab with Reflex*
Initiate PrEP (Baseline)	Male	Oral	**254842**	PrEP, Male, Oral Baseline + HIV RNA	●	
		Injectable	**254972**	PrEP, Male, Injectable Baseline + HIV RNA	●	
	Female	Oral	**254855**	PrEP, Female, Oral Baseline + HIV RNA	●	
		Injectable	**254988**	PrEP, Female, Injectable Baseline + HIV RNA	●	
Manage PrEP (Monitor)	Male	Oral	**254868**	PrEP, Male, Oral Monitor + HIV RNA	●	
		Injectable	**254736**	PrEP, Male, Injectable Monitor + HIV RNA	●	
	Female	Oral	**254880**	PrEP, Female, Oral Monitor + HIV RNA	●	
		Injectable	**254801**	PrEP, Female, Injectable + HIV RNA	●	
Manage PrEP (Monitor without HIV RNA)	Male	Oral	**254892**	PrEP, Male, Oral Monitor (No HIV RNA)		●
		Injectable	**254937**	PrEP, Male, Injectable Monitor (No HIV RNA)		●
	Female	Oral	**254905**	PrEP, Female, Oral Monitor (No HIV RNA)		●
		Injectable	**254951**	PrEP, Female, Injectable Monitor (no HIV RNA)		●

*Samples positive on the HIV Ag/Ab assay reflex to HIV antibody differentiation and HIV RNA as appropriate.
CDC-aligned HIV PrEP lpanels include additional testing for STIs, renal function, lipids and pregnancy as recommended.

Frequently Asked Questions

Q: What is the rate of false-positives on the HIV p24 Antigen/Antibody Screen?
A: The false-positive rate of the HIV p24 Antigen/Antibody screen, which is the first step of the HIV p24 Antigen/Antibody With Reflex to Confirmation [083935] test, has been investigated in several studies and ranged from 0.035% to 0.223%.[8-13]

Q: What are possible reasons for false-positive HIV serology?
A: Possible triggers of false-positive HIV results include infections such as viral hepatitis,[14] Epstein-Barr virus (EBV),[15] cytomegalovirus (CMV),[16] babesiosis[17] and schistosomiasis[18]; malaria[19]; SARS-CoV-2[20-23]; autoimmune diseases including lupus,[24] rheumatoid arthritis[24] and autoimmune hepatitis[25-26]; malignancy, including lymphoma[27-28] and metastatic cancer[15]; heterophilic antibody interference[29]; recent immunization[30]; and investigational products administered in an HIV vaccine trial.[31]

Q: A patient previously diagnosed with HIV is on antiretroviral therapy (ART), but an attempt to confirm the diagnosis using serologic assays produced a negative result. What are the possible reasons for these findings? What tests are available for further evaluation of the patient's HIV status?
A: These findings may reflect a well-documented decline in HIV-1 antibodies (seroreversion) associated with early initiation of ART and prolonged viral suppression.[32-41] Erroneous initial HIV diagnosis is also possible. Qualitative and quantitative HIV-1 RNA tests may produce negative/undetectable results for patients on ART and therefore may not be suitable for confirming HIV diagnosis in such cases. Assays that detect HIV-1 DNA, which is less affected by ART,[42] may provide confirmation of infection. However, inability to produce a result on a DNA-based assay does not exclude HIV infection. The final clinical assessment should be based on all available data including the patient's immune status, risk factors and history.

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