World Health Organization

Frequently asked questions – Testing for HIV, including HIV self-testing, in the context of antiretroviral therapy (ART)

The below messages are for testing providers, for programme managers, and for HTS clients.

HIV testing in the context of antiretroviral (ARV) drugs has become increasingly complex.

1. Although not recommended, individuals with a known HIV-positive status on antiretroviral therapy (ART) may seek HIV testing services to "check" their HIV status.

2. Individuals who are HIV-negative and take ARVs (i.e. oral pre-exposure prophylaxis (PrEP)) to prevent HIV acquisition are recommended to test quarterly.

This set of frequently asked questions will focus on the first situation.

There are multiple reasons why individuals who are taking ART will seek re-testing:

- to get a second opinion;
- denial or lack of confidence in and distrust of test results or testing providers;
- desire to "check" or "confirm" one's HIV status because they feel healthy, believe in faith healing, or receive incorrect information that ART can cure HIV;
- interpreting testing provider instructions for viral load/treatment monitoring testing as "to go for diagnostic testing again";
- misconception that an undetectable viral load (i.e. 'being undetectable') is the same as a HIV-negative status
- the need to retest to re-enter care;
- missing documentation and/or errors in records;
- participation in HIV surveys where all consenting individuals are tested irrespective of their HIV status and/or ART exposure; and
- emotional and mental health issues.

WHO (2018)

Some retesting is unavoidable such as need to retest to re-enter care (if moving towns, migration for work), missing records, and when participating in HIV biomarker surveys. Other retesting is motivated by personal reasons such as the misperception that undetectable HIV viral load may mean HIV-negative.

Messages for testing providers

1 Why does WHO recommend that HIV-positive individuals on ART are not offered retesting?

ART, when taken properly, inhibits HIV viral replication and therefore reduces the amount of HIV in the body (viral load) and slows disease progression. As a result, there is a reduction in viral antigens present, which in turn reduces the production of HIV antibodies. Evidence indicates that the earlier the ART is initiated, the more likely the antibody response may be impaired (Merchant M et al. 2014).

Antibodies are the body's immune response to HIV antigens. Serology assays that are used to diagnose HIV infection are based on detection of HIV antigens or antibodies to HIV antigens (rather than to the virus itself).

This means that if your client/patient is taking ART and his/her test result is non-reactive on a serology assay – such as a HIV-1/2 rapid diagnostic test – there is a chance that the test result might not be true. The risk of false negative results is moderate to high. However, the risk of false positive results when on ART is very low.

This does not mean the assays are not performing as expected but means there are less antibodies produced by the individual, which in turns reduces the likelihood of any serology assay being able to detect HIV infection.

The risk of a false negative result becomes high when re-testing individuals who are HIV-positive and are taking ART, as NAT assays are even more affected by the use of ART.

2 But WHO recommends retesting before ART initiation to confirm HIV status – isn't this confusing?

WHO recommends any person newly diagnosed as HIV-positive, be retested before initiation of ART to reduce the risk of misdiagnosis due to random error (WHO, 2015).

Retesting should preferably be conducted at a different testing site, e.g. where ART is initiated. If retesting must take place on the same day and at the same testing site, at least a different operator should conduct the assay, a new specimen should be taken, a different test kit box should be used, and where possible different lots of the test kits should be used.

It is critical that testing providers ask their clients/patients if they are taking ART (as well as PEP or PrEP) before retesting is initiated.

3 Are certain serology assays more affected by ART than others?

Yes, serology assays for detection of antibodies in oral fluid are more affected by ART than whole blood-based serology assays, with reduced sensitivity (Jaspard M et al. 2014).

Furthermore, older generations of serology assays (2nd and 1st generation assays) are more affected than newer generations (3rd and 4th generation assays), with reduced sensitivity (Patel P et al. 2010).

This does not mean the assays that are more affected by ART are not performing as expected. This means that analytical sensitivity (the smallest amount of HIV antibodies that the assay can detect) of such assays is lower than the analytical sensitivity of assays that are less affected by ART.

4 Can nucleic acid testing (NAT) assays (like HIV viral load) be used for retesting?

NAT assays are intended to detect HIV itself. HIV is expected to become undetectable when the individual is taking ART properly. Therefore, NAT assays are even more affected by the use of ART and the risk of a false negative result becomes high when re-testing HIV positive individuals taking ART.

This does not mean the NAT assay is not performing as expected, this means that the level of virus is below the limit of detection of the NAT assay.

It is critical to remember that "undetectable" (or target not detected) does not mean HIV-negative although it may mean "untransmittable" (U=U).

NAT assays may be useful to rule in HIV infection but should never be used to rule out HIV infection. Meaning that a detectable NAT test result is indication of being HIV-positive; however, a negative or undetectable NAT test result may not necessarily mean the client is HIV-negative – they could simply be undetectable because they are taking ART.

Messages for programme managers

5

Why does WHO recommend that HIV-positive individuals on ART are not offered retesting?

The risk of false negative test results when a client/patient is taking ART is moderate to high. When ART is consistently and appropriately used, viral reproduction decreases (viral suppression) which leads to lower production of antibodies, which in turn reduces the likelihood of any serology assay being able to detect HIV infection.

However, the risk of false positive results when on ART is very low.

6

What are the implications of testing HIV-positive individuals on ART for HIV surveillance?

For surveillance, either case-based or cross-sectional in design, it is critical to reduce the rate of false non-reactive results that may have been caused by exposure to ART. A recent biomarker surveillance study that included individuals who knew their HIV-positive status and were on ART but did not disclose this to the study investigators contributed to an 11% underestimation of treatment coverage (Kim A et al. 2016).

Furthermore, studies to evaluate HIV incidence assays have observed false recent infection results are common for individuals on ART (Fogel J et al. 2017). Some survey protocols incorporate testing for presence of ART metabolites to determine ART exposure. But mostly, survey protocols incorporate HIV viral load measurement, as a proxy for ART exposure, which is a more accessible and less costly technique than ART metabolite testing.

It is critical that testing providers within surveillance activities ask their clients/patients if they are taking ART (as well as PEP or PrEP) before retesting is initiated.

7

What are the implications of testing donations from HIV-positive individuals on ART in the context of blood and blood product screening?

The risk of onwards transmission of transfusion-transmissible infections is reduced through screening of donations using serological assays, and sometimes using NAT assays. Ensuring high clinical sensitivity for screening is key to assuring the safety of the blood supply. For individuals who know their HIV-positive status and are on ART, there is a possibility that serology assays may be false non-reactive. For NAT screening, it is expected that the test result for individuals who are taking ART will be "undetectable".

Messages for clients

8 Does an "undetectable" HIV viral load result mean I am now HIV-negative?

Regular monitoring of HIV viral load determines when ART is working well. But it is critical to remember that "undetectable" (or "target not detected") does not mean HIV-negative although it may mean "untransmittable" (U=U).

For this reason, NAT assays may be useful to rule in HIV infection but should not be used to rule out HIV infection.

9 What if I am taking treatment and I am retested and my result is negative, what should I do?

In certain circumstances, retesting while taking treatment may be unavoidable, for example, when re-entering care (if moving countries, moving towns, re-commencing treatment).

You should disclose if you are taking treatment to the testing provider immediately, they can use this information to help make a definitive HIV diagnosis.

In some circumstances, additional testing may be required on a case-by-case basis and would need to be conducted at a specialized laboratory.

10 Can I self-test when I am taking treatment?

WHO doesn't recommend that you self-test for HIV when you are taking treatment. This is because treatment changes the way your immune system reacts to HIV and means that certain tests, including rapid tests used for HIV self-tests may be false negative. This is because self-tests for HIV are designed to detect your immune response to HIV. A false negative result means that the test may suggest you do not have HIV while in fact you do have HIV infection.

If you are on treatment and you have self-tested and find the result is negative, seek attention at a HIV testing facility. You should disclose that you are on treatment to the testing provider immediately.

References

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