POLICY BRIEF

WHO ENCOURAGES COUNTRIES TO ADAPT HIV TESTING STRATEGIES IN RESPONSE TO CHANGING EPIDEMIC

NOVEMBER 2019

World Health Organization

HIV testing services (HTS) and anti-retroviral therapy (ART) have been scaled up substantially. It is estimated that, globally, nearly 80% of people with HIV now know their status. With the offer of immediate ART initiation and improved treatment options, access to and uptake of treatment have increased, too. Now, most people with HIV who know their status are obtaining treatment and care.

As HTS and ART scale-up close testing and treatment gaps, fewer people with HIV need HIV testing, diagnosis and linkage to treatment and care. Consequently, national HTS positivity – the proportion of HIV-positive results among those undergoing HTS – have also declined. Such trends are most apparent in high HIV burden settings such as eastern and southern Africa (Fig. 1).

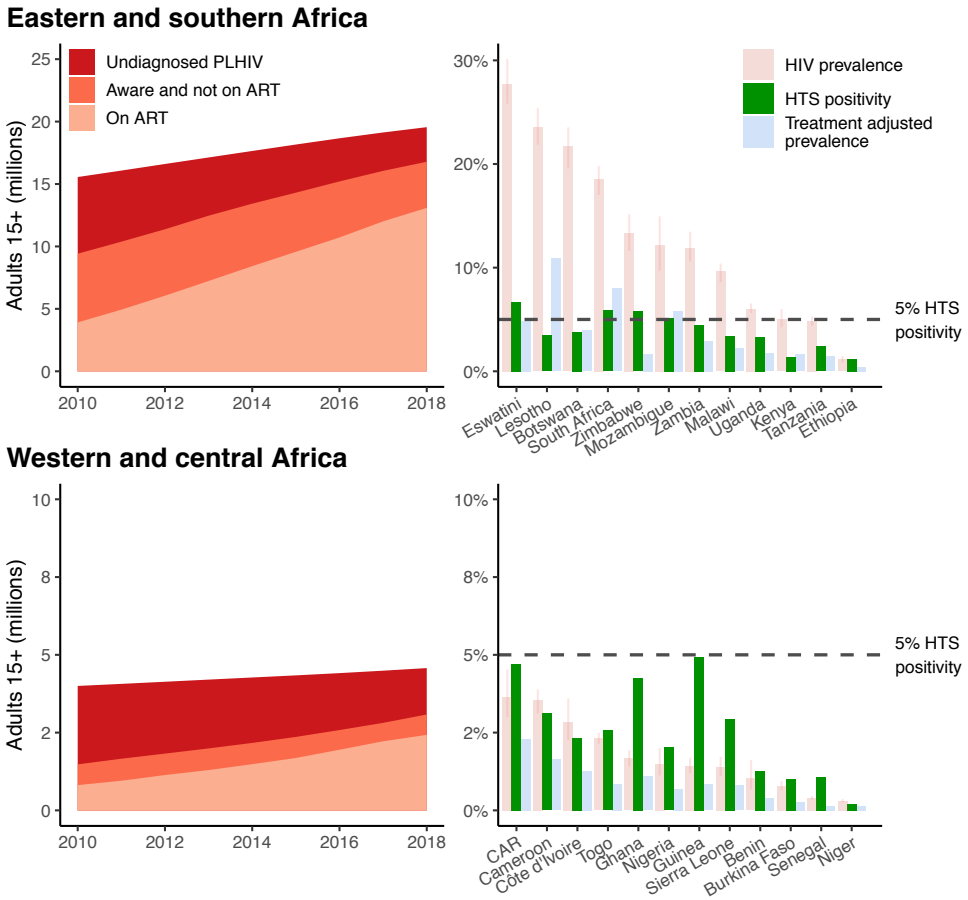
In response to these changes in the global HIV epidemic, WHO is encouraging countries to use three consecutive reactive tests for an HIV-positive diagnosis as their treatment-adjusted prevalence and national HTS positivity fall below 5%.

WHO is encouraging countries currently using two consecutive reactive tests for an HIV-positive diagnosis to move toward using three consecutive reactive tests for an HIV-positive diagnosis as their treatment-adjusted HIV prevalence and national HTS positivity fall below 5%.

Rationale for guidance

Providing correct HIV diagnoses, as quickly as possible, is critical to all HIV testing services and national programmes. To achieve accurate results, WHO recommends that countries use an HIV testing strategy/algorithm whereby a combination of rapid diagnostic tests (RDTs) and/or enzyme immunoassays (EIAs), used together, achieves at least a 99% positive predictive value (that is, less than one false positive per 100 people diagnosed with HIV).

This requirement was the basis of previous WHO recommendations that, to maintain at least a 99% positive predictive value, settings with a national HIV prevalence of 5% or more should use two consecutive reactive tests to make an HIV-positive diagnosis. However, for settings with a



Between 2010 and 2018…

…in eastern and southern Africa

- The number of adult PLHIV unaware of their HIV status decreased from 6.1 million to 2.8 million.
- Adult HIV prevalence decreased from 7.1% to 7.0%.
- The proportion of adults with undiagnosed HIV decreased from 2.8% to 1.0%.
- In countries with 20% HIV prevalence and above, in 2018, national HTS positivity was close to or below 5%.
- National HTS positivity was much closer to the treatment-adjusted prevalence (which excludes adults with HIV on ART) than national HIV prevalence.
- Countries where national HTS positivity is lower than the treatment-adjusted prevalence there may be a need to further optimize HTS.

…in western and central Africa

- The number of adult PLHIV unaware of their HIV status decreased from 2.5 million to 1.5 million.
- The prevalence of HIV among adults decreased from 1.6% to 1.5%.
- The proportion of adults with undiagnosed HIV infection decreased from 1.0% to 0.5%.
- National HTS positivity was below 5% in all countries.
- Countries where national HTS positivity exceeded overall HIV prevalence likely reflects highly focused HTS in key populations, priority locations and patients with HIV-related symptoms.

PLHIV: People living with HIV; ART: antiretroviral therapy; HTS: HIV testing services; CAR: Central African Republic.
HTS positivity presented in this figure is based on national programme data reported to 2018 UNAIDS Global AIDS Monitoring. National HTS positivity refers to the number of tests conducted where an HIV-positive result was returned to a person in the calendar year.
Treatment-adjusted prevalence refers to the estimated national HIV prevalence, adjusted to exclude people with HIV who are on ART from the numerator and the denominator. Treatment-adjusted prevalence includes: people with HIV who are undiagnosed, people with HIV who know their status but have not initiated treatment, and people with HIV who previously initiated treatment but have disengaged from care.
Source: Estimates shared in personal communication from K Giugere, M Maheu-Giroux, JW Eaton, October 2019; UNAIDS/WHO, 2019; Marsh K, Eaton JW, Mahy M, Sabin K, Autenrieth C, Wanyeki I, Daher J, Ghys PD. Global, regional and country-level 90-90-90 estimates for 2018: assessing progress towards the 2020 target. AIDS. 2019. doi: 10.1097/QAD.0000000000002355.

Fig. 1. Closing the gap in the number of undiagnosed people living with HIV (2010–2018)

national HIV prevalence below 5%, to maintain at least a 99% positive predictive value, WHO recommended the use of three consecutive reactive tests to make an HIV-positive diagnosis.[1]

The positive predictive value is the probability that an HIV-positive diagnosis is correct. At a population level, the percentage of people testing for HIV who receive an HIV-positive diagnosis affects the ability to provide the correct diagnosis. As HTS and ART coverage increase, and fewer people undergoing HIV testing services are HIV-positive, the chances that a reactive test result is false increase (see Box 1 as an example).

Because national HTS positivity has and will continue to decline, WHO is encouraging high HIV burden countries, and reminding low HIV burden countries, to use three consecutive reactive tests to make an HIV-positive diagnosis. By making this shift, countries will be able to ensure accurate HIV diagnoses even as national HTS positivity continues to decline.

Programmes with low national HTS positivity and low treatment-adjusted HIV prevalence should prioritize this shift to prevent misdiagnoses and unnecessary initiation of lifelong treatment. Some countries will continue to have national HTS positivity above 5% (see Fig. 1). These countries may continue to use two consecutive reactive tests to provide an HIV-positive diagnosis. It will be important for these countries to monitor national HTS positivity and to start transitioning to using three consecutive reactive tests to provide an HIV-positive diagnosis when national HTS positivity starts to fall below 5%.

Simultaneously using two consecutive reactive tests for some settings or for certain populations or clients, and three consecutive reactive tests for others is not advised.

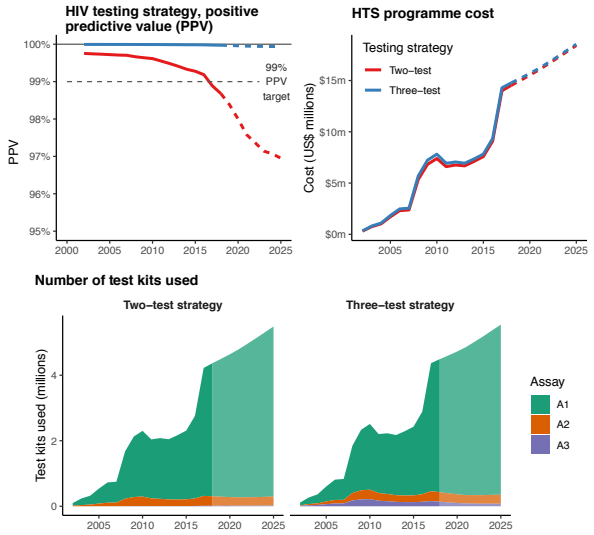
[1] This is based on the assumption that each test (assay) used in the strategy and algorithm has at least 98% specificity.

Box 1. Estimates and projections for HIV rapid test kit usage (2000-2025), Malawi, and implications for HIV testing outcomes

In Malawi the total number of adults with HIV has been increasing and is projected to continue to increase through 2025 as people with HIV live longer on ART. At the same time, due to scale-up of HTS and ART, the proportion of people with HIV who are **undiagnosed** has declined rapidly, from an estimated 78% in 2005 to 14% in 2017 and is projected to continue declining to around 6% in 2025.

This shift in the HIV epidemic is contributing to rapid declines in the proportion of HIV-positive test results (HTS positivity) and in the percentage of **new** HIV-positive diagnoses among individuals who undergo HIV testing. Although the annual number of people tested doubled between 2015 and 2017, positivity decreased by 50% and the number of people with HIV newly diagnosed has continued to decline since 2016. By 2025 national HTS positivity is expected to reach 1.5%, while overall adult HIV prevalence is projected to be 8.4%.

A model-based triangulation of epidemiological estimates and HTS programme data suggests that almost half of the new HIV-positive tests recorded in programme data are people with HIV who know their status but are retesting. Discounting these retesters, who already know their positive status, further reduces the proportion of new HIV-positive diagnoses to 1.7% in 2017, and a projected 0.5% in 2025



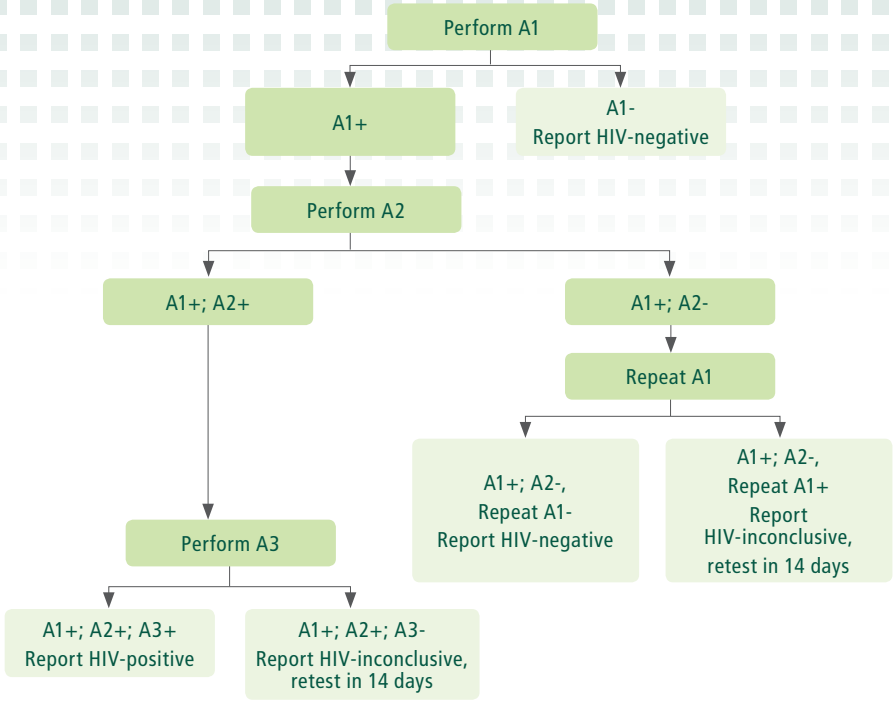
The two-test strategy in this diagram refers to using two consecutive reactive tests to provide an HIV positive diagnosis. The three-test strategy in this diagram refers to using three consecutive reactive tests to provide an HIV-positive diagnosis. The WHO testing strategy is depicted in Fig.2. for reference. Estimates of PPV assume 98% specificity for each independent assay (test) in the algorithm, and does not include retesting to verify HIV-positive status. Projections for PPV, costs, and assay usage assume that rates of HIV testing by sex, age, and HIV status remain at 2018 levels through 2025.

This sharp decline in national HTS positivity, in the population being tested in Malawi, will reduce the positive predictive value of the current testing strategy. Thus, by 2025, if the testing strategy in Malawi used two consecutive reactive tests each with 98% specificity to provide an HIV-positive diagnosis, the testing algorithm's positive predictive value would be below 97% (even if tests used performed in the field according to minimum WHO prequalification requirements). In contrast, if three consecutive reactive tests are used to provide an HIV-positive diagnosis, the positive predictive value will be above 99.9%.

If rates of HIV testing stay at current levels, an estimated 120 000 A3 tests would be required to implement the new strategy in 2019, declining to 79 000 in 2025. These quantities are substantially lower when compared with the need for more than 4 million A1 tests and 270 000 A2 tests each year. The projected incremental cost of using three consecutive reactive tests to provide an HIV-positive diagnosis (three-test strategy), versus using two consecutive reactive tests to provide an HIV-positive diagnosis (two-test strategy), is less than 2% greater in 2019 and declines to around 0.6% greater in 2025.

The cost difference is small because the primary driver of total HIV testing programme costs is the volume of clients who receive the first test, A1. In contrast, the cost of HIV misdiagnoses is high, as it includes unnecessary treatment costs as well as individual and social costs.

Source: WHO/UNAIDS/Malawi Department of HIV/AIDS, 2019 derived from Maheu-Giroux M, Marsh K, Doyle C, Godin A, Lanièce Delaunay C, Johnson L, et al. National HIV testing and diagnosis coverage in sub-Saharan Africa: a new modeling tool for estimating the "first 90" from program and survey data. AIDS 2019. DOI: 10.1097/QAD.0000000000002386.



- All individuals are tested on Assay 1 (A1). Anyone with a non-reactive test result (A1–) is reported HIV-negative.
- Individuals who are reactive on Assay 1 (A1+) should then be tested on a separate and distinct Assay 2 (A2).
- Individuals who are reactive on both Assay 1 and Assay 2 (A1+; A2+) should then be tested on a separate and distinct Assay 3 (A3).
  - Report HIV-positive if Assay 3 is reactive (A1+; A2+; A3+)
  - Report HIV-inconclusive if Assay 3 is non-reactive (A1+; A2+; A3–). The individual should be asked to return in 14 days for additional testing.
- Individuals who are reactive on Assay 1 but non-reactive on Assay 2 (A1+; A2–) should be repeated on Assay 1
  - If repeat Assay 1 is non-reactive (A1+; A2–; repeat A1–), the status should be reported as **HIV-negative**;
  - If repeat Assay 1 is reactive (A1+; A2–; repeat A1+), the status should be reported as **HIV-inconclusive**, and the individual asked to return in 14 days for additional testing.

A1: Assay 1 (first test); A2: Assay 2 (second test); A3: Assay 3 (third test).

Fig. 2. WHO HIV testing strategy using three consecutive reactive tests as basis for HIV-positive diagnosis

Countries should consider using both national HTS positivity and treatment-adjusted HIV prevalence to help determine when to begin changing their testing strategy and algorithm.

Treatment-adjusted HIV prevalence provides an indication of the proportion of people with HIV in the testing population, by excluding those on ART. Treatment-adjusted HIV prevalence can be calculated by subtracting the number of people (age 15+) with HIV on ART from the numerator (total population with HIV, age 15+) and denominator (total population, age 15+) of national HIV prevalence estimates. Treatment-adjusted HIV prevalence includes: people with HIV who are undiagnosed, people with HIV who know their status but have not initiated treatment, and people with HIV who previously initiated treatment but have disengaged from care.

Fig. 2 shows the WHO recommended testing strategy using three reactive results to make a diagnosis of HIV-positive.

WHO continues to recommend that programmes retest people diagnosed with HIV prior to ART initiation. This retesting to verify an HIV-positive diagnosis is intended to catch human errors such as mislabeling of test results.

Implementation considerations

- Many different HIV RDTs or EIAs can be used in a national testing algorithm. When modifying a national algorithm by introducing a new test, it is critical to verify that the newly selected test works well in combination with the other two tests. Most important is to maximize the specificity of the products chosen as the new third test in a strategy/algorithm. Countries should review and consider products that are WHO prequalified; see https://www.who.int/diagnostics_laboratory/evaluations/PQ_list/en/.

- Efforts to reduce costs and optimize delivery of HTS using the WHO HIV testing strategy are needed and should focus on efficient delivery of the first test in the strategy, since it accounts for by far the largest total cost among the three tests. Scaling up task sharing and utilizing approaches such as HIV self-testing and test for triage may make shifting to the WHO HIV testing strategy more feasible in some settings. In these approaches people first test often at home or in the community, and all those with reactive results are referred to a facility for further testing using the full national testing algorithm.

- Countries changing their national HIV testing strategy and algorithm will need to develop a plan and identify the optimal time for the transition. To assure that all the necessary resources are in place, it will be important to align and coordinate changes in tendering, selection and procurement of new tests (including an A3 test), verification of the testing algorithm, logbook and register updates, training and supportive supervision, and national and site-level policy and guidance.

For more information, contact:

World Health Organization
Department of HIV/AIDS
20, Avenue Appia
1211 Geneva 27
Switzerland

E-mail: hiv-aids@who.int
www.who.int/hiv

WHO/CDS/HIV/19.34