Q&A February 2024 CQUIN Webinar

"WHO updates-Consolidated Guidelines on HIV Testing Services (HTS), 2023"

1. **Three test algorithm approach:**

Question: Can we have a link to the revised HIV testing guidelines?
Response: hiv-testing-information-note.1.12.2023.pdf (who.int).
2023 update HTS guideline is going to be published end of Q1 or Q2 2024

Question: What are the cost implications of this new strategy on HTS services? For example, for the TB client, a total of 6 test kits needs to be done.
Response: Great question. The cost analysis showed that adding the additional test had no substantial impact on testing costs. You may wonder why that is, but this is because the overall cost of HTS programs is driven by the cost of the first test. Because very few people test positive, very few people need 3 tests and be confirmed positive and therefore as positivity continues to decline overall, very few people will need a positive diagnosis verified before starting life-long treatment. We have looked at the cost of retesting to prevent misdiagnosis and it is not only cost-effective but cost-saving because even if you catch just a few cases, the cost of misdiagnosis and unnecessary initiation of lifelong treatment is very high. Two references here: https://pubmed.ncbi.nlm.nih.gov/28444206/ and https://www.medrxiv.org/content/10.1101/2021.03.31.21254700v1.full

Question: Hi Cheryl, please can you clarify for me why fewer people will need verification testing at ART initiation than those diagnosed using 3 test algorithm "even fewer will need a positive diagnosis verified before starting ART"? My understanding is that WHO recommends that every person diagnosed using 3 tests, will need verification testing (3 tests again) before ART initiation? Thanks
Response: Sorry for any confusion. We recommend every person diagnosed with HIV needs retesting to verify their status. I was only trying to emphasize the point that few people need 3 tests because ***most*** people will be negative. And only those who are diagnosed with HIV, which is declining overall in the testing population, will need retesting to verify diagnosis prior to start treatment.

WHO remains open to receiving new evidence and results from implementation science studies on ways to simplify retesting prior to ART initiation.

Question: Is there guidance for testing blood samples in the blood banks using the 3-test algorithm?
Response: Thank you for this question. WHO recommends use of RDT for routine HIV testing programs. With the 3-test strategy, three essays have to be carefully selected through a verification process and be used in the correct order as the national algorithm. WHO also recommends that the RDT be conducted by appropriately trained providers using the national algorithm. RDTs are simpler to use, getting results within minutes, are also less costly, and much easier to interpret.

For the WHO recommendation regarding blood screening in the context of transfusion can be found through the link below. The objective of screening blood is different of diagnosis so that's why it is not part of the HTS guideline: https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/blood-product-standardization/quality-and-safety/donation-testing#:~:text=Testing%20of%20donated%20blood&text=WHO%20recommends%20that%20all%20blood,B%20and%20C%20and%20syphilis.

Question : Hello everyone, Senegal has been using the three-test algorithm for many years, and it's performed by qualified personnel (biologists) in hospitals and health centers. Is retesting with three tests indicated in this case? ?

Response : Yes, retesting is necessary in this case too, as the causes of erroneous results are not always linked to the test users, but to a problem with a batch of tests, for example. On the other hand, qualified personnel, including biologists, can also make mistakes. In view of the consequences for patients, re-testing for verification is advisable, regardless of the initial tester.

WHO remains open to receiving new information and results for implementation science studies on ways to simplify re-testing before the start of ART. Also, it will be of interest to programs to analyze their data up to the differences between the initial results and the results after retesting.

Question: What is the guidance on retesting before ART initiation? Should every HIV positive case be retested before ART initiation?
Response: The guidance has maintained retesting before ART initiation. It is important to note that retesting prior to ART initiation is related to quality assurance.

As further background, this has been a long-standing recommendation which was emphasized more in programmes when the shift to immediate ART initiation was made and requirements for clinical assessment were removed. Retesting prior to ART initiation has been used in several programmes and when data was analysed overtime there were indications that discrepancies in diagnoses were identified and quality of testing was able to improve over time. L'OMS reste ouverte à receiver les nouvelles informations et résultats pour les études de science de la mise en œuvre sur les manières à simplifier les retests et assurance des qualité avant le début du TAR.

Question: Which of the new recommendations attract strong recommendations in relation to HIV case finding efficiencies and effectiveness
Response: Thanks Vincent, in the wake of new infections as well as case finding gaps, countries need to assess their data to know the gaps and deploy a strategic mix of approaches. for example, screening in at OPD is critical. Additional strategies, including expanding social network testing and self-testing are also important in these new guidelines and highlighted.

2. HIV Self Testing Recommendations:

Question: With PEP, I think acute infection needs to be considered and addressed in counseling, so self-testing might not be a good strategy. Thoughts?
Response: Good question, we have looked at this in our guidance and there is really no substantial difference in the ability of standard testing and self-testing to detect acute infection. Acute infection is rare and declining as well. We have looked at the impact and the benefits of using HIVST outweigh risks. There is a new paper on this in Lancet HIV showing the potential public health impact of using HIVST to promote uptake of PrEP and is applicable to PEP. https://www.medrxiv.org/content/10.1101/2021.03.31.21254700v1.full. HIVST was actually used as early as 2010 in Kenya to promote uptake of PEP among health workers and can be a way to help people start PEP as early as possible which is important to its effectiveness.

Question: Under what circumstances would HIVST replace use of validated HIV Testing eligibility screening tools at OPD?
Response: If, and when resources allow!! This is why epidemic contexts are important, and also use of data for programs. Self-tests can be a good option in some facilities where high coverage remains important. WHO's review on screening tools and the risks of missing cases is here: https://pubmed.ncbi.nlm.nih.gov/35147855/. Programmes using screening tools may find implementation varies across sites, could lead to missing too many individuals with HIV and that cost savings are not substantial and that self-tests may be a better value. See recent paper from Uganda that may be of interest: https://www.mdpi.com/2414-6366/9/2/37

3. Caregiver Testing:

Question: Kindly explain more the recommendation on not using caregiver testing
Response: We have not recommended for or against caregiver assisted testing. We have reported that based on the review of evidence there was insufficient information and in the absence of information we point countries to prioritize evidence-based strategies for case-finding that may need to be scaled-up further, funded and prioritized for attention. The pre-print is available here: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4706355

Question: Why is WHO recommending guidance with insufficient evidence?
Response: WHO is not recommending caregiver testing. The slide was summarizing that we made no recommendation and that countries should continue to prioritize evidence-based approaches for children and adolescents. The pre-print is available here: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4706355

Question: Have the Western blots been completely discontinued as part of HIV diagnostics?
Response: WHO encourages countries to move away from Western Blot (WB) and line Immuno Assay (IA) because it has poorer sensitivity for early HIV infection compared to RDT/IA. They have higher rates of HIV inconclusive/indeterminate status and longer test procedure than RDTs/IAs. They have more complex interpretation and use more staff. The cost per test is also higher than RDTs/IAs. WHO has also issued a negative listing on the EDL for WB and IA.

4. Retesting as an entry point for Re-engagement

Question: If someone is re-engaging in care after an interruption in treatment, and self-reports HIV diagnosis but prior documentation of HIV infection is not available, is WHO recommending 6 tests before re-initiating ART?
Response: Retesting as an entry point for re-engagement in treatment and care (NOT for everyone). For Example:

- Those who re-engage through HIV testing services on their own should be welcomed back
- Those who say they are HIV positive without any evidence should be re-tested using the full algorithm as long as they are not taking ART
- Those who say they were on ART in the past and want to be given medication without any documentation can be tested using full algorithm for re-engagement

WHO does NOT recommend re-testing individuals on ART – the risk of false negative. However, if they have a concern about their test results this should be discussed with appropriate follow-up actions.

Question: If someone is re-engaging in care after an interruption in treatment, and self-reports HIV diagnosis but prior documentation of HIV infection is not available, is WHO recommending 6 tests before re-initiating ART?
Response: Céline answered this live [detailed above], but I would just add that in the absence of documentation and information retesting maybe wise here. We have reviewed and reported previously in a systematic review that cases of misdiagnosis have been picked up in these situations. In the context of lifelong treatment, it is important to do whatever we can to avoid misdiagnosis and unnecessary initiation of lifelong treatment.

WHO remains open to receiving new evidence and results from implementation science studies on ways to simplify retesting prior to ART initiation. Further, it may be beneficial for programmes doing retesting to review and analyse their data to see if and where there are discrepancies.

5. Recency Surveillance Testing:

Question: Kindly clarify more on Recency Surveillance Testing. What does it mean to say that it should not be part of routine HIV testing services?
Response: WHO guidance on the use of recency assays in surveillance recommends the use of recency in relation to incidence measurement and in representative population samples. Routine HTS sites as a whole do not provide a representative sample. There remains no patient benefit to recency, and it can detract from the HTS program and poorly affect client services. We are saying in the guidelines that recency should not be used in your standard routinely offered HIV testing services program and should not be used to return results.

Question: When WHO says that recency testing is not recommended, does it mean that we are no longer required to offer this test to all newly diagnosed HIV positive clients?
Response: WHO has guidance on the use of recency testing for surveillance. However, WHO does NOT recommend recency testing in routine HIV testing programs, for the following reasons:

- No clinical benefit because all positives are offered immediate ART, regardless of when HIV was acquired.
- Recency assays do not identify acute HIV infection, so there is no clinical benefit. Currently, rapid recency tests cannot detect AHI.
- No evidence that it can identify case clusters, or hotspots – is not supported by evidence.
- Currently - there are no WHO Prequalified recency tests

Question: Recency testing is being implemented in dozens of countries as program-based surveillance that is cost effective and provides critical information about ongoing transmission. It is not part of the HTS services but extends program-based surveillance. Data from many countries and several publications support the use of recent infection surveillance. This recommendation that recent infection surveillance is counter-productive and confusing to many countries.
Response: We recommend the use of recency assay in surveillance activities within surveillance specific protocol but not in routine testing service. We will disseminate further this information throughout 2024 to avoid confusion in countries. The WHO guidance here is still relevant: https://www.unaids.org/en/resources/documents/2023/using-recency-assays-HIV-surveillance

Question: Countries like Uganda are scaling up HIV Recency testing. Yet current recommendation from WHO is contrary. What is the way forward now?
Response: I think it might be good to check in with both surveillance and HTS program colleagues to align your strategy. We would be more than happy to follow-up to have a call with countries needing support to unpack the next steps specific to their situation. Please email Cheryl Johnson at *johnsonc@who.int*.

Also review to WHO guidance here: https://www.unaids.org/en/resources/documents/2023/using-recency-assays-HIV-surveillance

Question: *From the WHO Information Note:* It will be helpful to understand how VL testing, performed as part of the Recent Infection Testing Algorithm (RITA), delays return of HIV diagnostic results?
Response: This point is addressed in relation to responding to questions on the clinical utility and potential feasibility to use recency assays within routine HTS which is not recommended. When reviewing evidence on the challenges of using recency in routine HTS programmes, it has been reported by studies that implementing RITA, which requires VL at minimum to rule out false recent results, is challenging. This is particularly the case if a programme is using a rapid test for recent infection (RTRI) in a testing site where they need to send out samples for VL testing. Studies have reported this leads to increased logistical needs, high costs and delays turnaround time in results.

Question: Are there countries that have been using recency testing as part of the routine HTS? And if so, why?

Response: The uses of recency has varied in some countries over time. Some countries have used recency testing in routine HTS sites, sometimes in effort to contribute to surveillance efforts and sometimes as part of studies to identify if there may be some clinical benefit. In some situation the uses of recency tests at clinical and surveillance level in a country have overlapped. For example, in a WHO/UNAIDS 2022 report it was identified that at least 10 countries were returning recency tests results directly to patients and some of the practices documented included efforts to use recency tests to prioritize partner services, initiate rapid ART and provide revised counselling messages sometimes prior to VL confirmation and use of RITA.

Within surveillance efforts, adding in recency testing in routine HTS has limited value. WHO guidance has previously underscored that interpreting recency indicators from routine HTS is challenging and is not advised because selection bias associated with HIV testing attendance, thus it is important to consider recency surveillance in populations with consistent and high HIV status ascertainment (i.e. ANC) as opposed to implementation in routine HTS sites. Further, the proportion testing recent does not - on its own - indicate incidence, or relatively high levels of transmission between groups, and may vary considerably based on the underlying HIV testing and care cascade and trends may still be wrong if FRR and MDRI are not adjusted for local context, and the denominator of all people at risk of recent infection is not used.

6. Quality of HIV Testing Services:

Question : Please, why are you now advising the use of the laboratory quality management system and/or screening?
Response : The quality management system has been recommended for a long time, and the WHO simply wants to reinforce the importance of this system to guarantee the quality of screening. It's not new, but we want to see what the level of implementation of these activities is in countries, and what we could do to extend its implementation

7. Post-market surveillance

Question: Thank you for the excellent presentations. Is there a generic tool or protocol for post-market surveillance (active/ passive) of IVDs, similar to the WHO verification protocol for rapid HIV testing?

Response: This is the current guidance on post-market surveillance: https://www.who.int/publications/i/item/9789240015319. Contact Anita Sands *sandsa@who.int* for the tools.