Technical Guidance on the Use of Recency Assays for HIV Surveillance

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Recency Testing for HIV Surveillance

Advantages / opportunities

- Provide estimate of incidence when correctly used in representative surveys
- Outbreak investigation to understand prevention failure
- Identify sub-populations that have high levels of new infections

Disadvantages / possible pitfalls

- Requires very large sample sizes in surveys; sample size increase as incidence decreases
- Potential biases when interpreting results from HIV testing services or case surveillance
- Complexity of recency testing assay and algorithms
- Risk of collecting recency data if confidentiality or criminalization are an issue
- No individual benefit or clinical utility

Incidence & non-incidence use cases

- Recency assays can be used in population-based surveys to estimate HIV incidence

- Use in routine HIV testing programme data (“non-incidence use”) is more challenging
  - Assay performance – reclassification of recent to long-term
    - Accounting for individuals with undisclosed ART/PrEP use, repeat testers
  - Interpreting data is a challenge for programming purposes
    - Selection bias associated with HIV testing service attendance
    - Geographic clustering is affected by mobility
    - Trends are affected by changes in testing patterns and coverage

Ethical considerations for surveillance use

- Risks if laws that criminalize HIV transmission are in place. Remove any link to personal identifiers. Ensure that recency results will not and can not be used to inform criminal procedures
- Involved groups of people living with HIV in all decisions on how results will be interpreted and messaged. Also include members of key populations if any reference by those groups
- Informed consent is ethically required for any biological testing. Must follow HIV testing guidance (counseling and consent, confidentiality, correct results, connections).
- Substantial refusals will have additional impact on representation and interpretation.

Historical guidance on using recency assays for HIV surveillance

Summary of recency assay use

Full explanation of recency assays based on technology in 2011

2011

2015

Technical update (focus on population-based surveys)

- Use of algorithm including viral load testing
- Laboratory quality assurance
- Cutoff time adjusted from 1 to 2 years
- Sampling requirements for surveys

2018

Technical update (focus on calibrating parameters -- MDRI and FRR)

- Parameters should be locally specific

2022

Updated technical guidance on use of recency for HIV surveillance

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Methods for Guidance Update

Review of evidence

- **Joint call for information from WHO/UNAIDS**
  - Brief survey questionnaire to program managers/technical staff working on surveillance and HIV testing services
  - 48 survey responses from people in 21 countries across 5 WHO regions (AFRO, SEARO, WPRO, PAHO, and EURO) from 28 Oct 2020 to 20 Jan 2021
- **Systematic review of literature**
  - PubMed / Web of Science / grey literature search = 167 final documents
  - Published in JMIR Public Health & Surveillance (Facente et al., 2022 doi: 10.2196/34410)

Stakeholder consultation meeting and written feedback (Aug 24-27, 2021)

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Key messages on use of recency assays for HIV surveillance

1. Recent infection testing algorithms (RITAs) must include additional clinical data to identify false recent results (viral load or ART)
2. Interpret recency results cautiously with consideration of sample
3. When using recency test results as a proxy for incidence, the denominator should be all people at risk of recent infection
4. Adjust the assay parameters (MDRI, FRR) based on the local context
5. Recognize the complexity of undertaking recency testing and consider cost effectiveness of point-of-care testing

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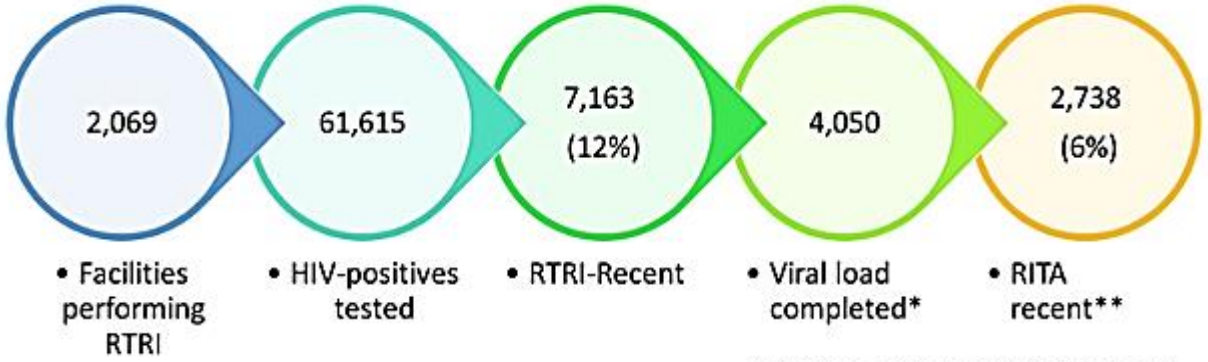
1. Recent infection testing algorithms (RITAs) must include additional clinical data to identify false recent results

Recency assay results from PEPFAR countries



"About 30%-50% of RTRI recent have suppressed VL and are reclassified as long term infections"

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2. Interpret recency results cautiously with consideration of sample

- HIV testing services will include individuals testing for multiple reasons
  - Differences by region/sex/age may be due to selection bias
- Trends are affected by changes in testing patterns and coverage
- Geographic clustering is affected by mobility
- Results from case surveillance should be analysed separately for different populations. Interpretation should be within the context of that population

E.g. Presentation of recency results with potential incorrect interpretation due to selection bias

Population
Gender
Men
Women
Age
15-24
25-34
35-44
45+
Province
A
B
Setting
Antenatal care clinics
Voluntary counselling and testing sites

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3. When using recency test results as a proxy for incidence, denominator should be those at risk

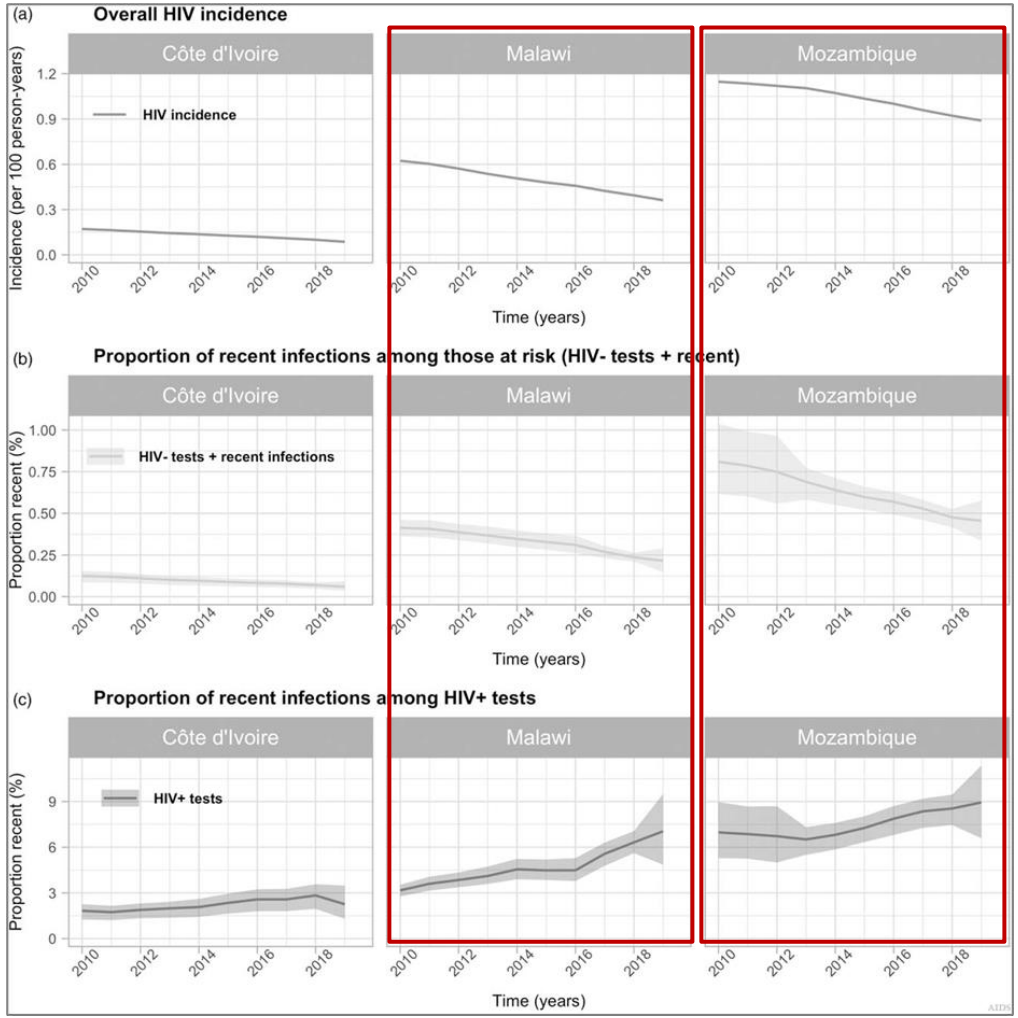
Godin et al. AIDS, 2021

Inferring population HIV incidence trends from surveillance data of recent HIV infection among HIV testing clients

True incidence

Recent infections
/
HIV negative + recent

Recent infections
/
HIV positive



4. Adjust the assay parameters (MDRI, FRR) based on the local context

- Published MDRI often does not reflect the “effective MDRI” accounting for individuals with undisclosed ART/PrEP use, repeat testers
- Parameters can change based on HIV sub-type and other local characteristics
- FRR can change based on treatment coverage, testing rates (or time from infection to diagnosis)
- 2022 Technical guidance will be complemented by web tools:
  - Assist in the calculation of locally adjusted MDRI and FRR parameters
  - Calculate incidence from recency data

5. Recognize the complexity of recency testing, consider cost effectiveness of point of care testing

Potential issues when implementing a RITA in the field, with suggested actions, MESH, 2021	
Issues	**Considerations and potential actions**
Availability of assays	Quantities may be limited, unavailable for shipment into country. Programs should project needs/discuss w manufacturer well in advance
Specimen / assay transport	Assays, specimens, control panels need cold chain If using DBS, ensure proper specimen drying/packaging/transport
Training and performance	All testers need to be trained in advance. Training/assay panels available from CDC and should be sought
External quality assurance	All labs and testing sites need to participate in external QA program to ensure confidence in testing procedures and assays.
Reporting results	Users should be clear on which assay was used and the cut-offs applied

Clinical Utility

Scoping Literature review & Programmatic Survey

Current WHO guidance on recency:

- **WHO does not recommend the use of recency testing for the clinical management of individuals or their partners, as there is currently insufficient evidence of their clinical utility**
- **Results should not be returned to individuals**
- **No WHO pre-qualified recency products or any in the pipeline**
- **Not to be used in national diagnostic algorithms**

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Scoping literature review (26 studies)

Assay performance

- Addition of clinical indicators leads to significant reclassification from recent to non-recent infections
  - Adding clinical information (e.g., viral load) improves accuracy but adds logistical complexity & cost
  - Order of operations often unclear for multi-step RITA
- Little data (one study) on performance of rapid assays in clinical settings, despite widespread programmatic use

Operational considerations

- Limited feasibility and implementation challenges
  - Long turn-around times
  - Lost to follow-up
  - Difficulties operationalizing RITA
  - Supply procurement
- Field-based readings
  - Differing levels of agreement between lab and field-based settings
  - Quality issues reported

Clinical utility

- No consensus on perceptions of utility among providers and patients: some found it acceptable, others had concerns about costs, time, effort and harm
- Little data on adverse events and social harms, insufficient ethical and human rights considerations identified
- No studies provide evidence that recency testing increases linkage to prevention, care or treatment initiation

Programmatic survey (17 countries - 15 PEPFAR funded)

- **All LMIC site/country respondents (15) were funded by PEPFAR and used Asante.**
  - **Most (but not all) used VL to confirm recency, but RITA not always used increasing risk of misclassification of recent infection**. Respondents from Ethiopia, Zimbabwe, Tanzania and Thailand documented that RITA not used.
- **Identified reports that countries are returning results to individuals, against WHO guidance to:**
  - Clients, Providers and Communities
  - Countries with respondents reporting that results were returned directly to clients at some point in programme included: Central America, Rwanda, Burundi, Ukraine, South Africa, Thailand, Cambodia, Namibia, Kenya and Viet Nam
- **Identified confusion with implementation,** including use of recency results for clinical management
  - Rapid recency test embedded within national diagnostic algorithm diagrams and being done in parallel with 2nd test in national algorithm prior to HIV positive diagnosis with 3rd test, including in very low prevalence settings
  - Different counselling messages for people with rapid recent results, including those delivered prior to further confirmation of recent infection
  - Policies, documents and reports of practices prioritizing index testing and ART for those with recent infection
- **Few details on monitoring of adverse events,** although some programmes reported having a system in place
- **No information on how recency results were used to improve/change programmes** and/or increase linkage to ART or prioritizing prevention
- **Costs – recency RDT ≈$4.50-8.50 + VL≈ $20 + training, QA, logistics**
  - Lowest price not widely available because it requires large volume procurement per country (i.e. +1 million kits)

Summary of findings on use of recency for clinical use

Accuracy

30-50% reclassification rate;
Validity results varied widely (lab vs field);
Limited information in clinical setting;
Clinical information & VL improves accuracy;
Some countries reported returning results to clients without VL confirmation

Feasibility & Complexity

Additional time & effort w/ limited staff
Supply procurement & Service challenges;
VL ↑ accuracy, but ↓feasibility;
Return of recency results delayed:
Long turn-around times & lost to follow-up;
Confusion with order of operations and steps (i.e., counselling message and patient pathway)

Costs

cost to procure and run tests and return results; current costs of POCT $4.50-8.50 per kit; VL costs for confirmation additional

Acceptability?

Some acceptability to patients and providers; but not everyone agreed helpful, worried about harm, and did not like the additional time and costs

Impact?

No consensus on perceptions of utility; similar percentage of partner notification comparing recent to non-recent infections;
No studies provide evidence that recency testing increases linkage to care or treatment initiation.

Social harm & Adverse events?

Little data on adverse events and social harms.
Some monitoring systems noted, but few details.
Critical need to protect human rights noted.

Research gaps is main finding of this review & programme survey

Next steps?

- Document COP22 reports and scale-up plans
- WHO updating systematic review and critical to have access to published and unpublished data to support this
- Community consultations

Theoretical benefits?

Evidence on potential use case in clinical individual use <u>not</u> identified at this time

Conclusions - 1

- Evidence on recency assays for incidence use cases in representative surveys is robust and extensively validated
- Interpreting recency indicators from case surveillance or HIV testing programmes is challenging:
  - Selection bias associated with HIV testing attendance
    - Consider recency surveillance in populations with consistent & high HIV status ascertainment e.g. ANC
  - 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
  - Trends may still be wrong if FRR and MDRI are not adjusted for local context
  - When using recency test results as a proxy for incidence, the denominator should be all people at risk of recent infection
- Use a **RITA**, not just a single assay
  - Viral load, tests for ARVs can reduce false recency
- Recognize the complexity of undertaking recency testing and consider cost-effectiveness of point-of-care testing
  - Other programme data like new HIV diagnoses may be sufficient for programme aims

Conclusions - 2

- There is general lack of evidence regarding clinical utility of recency testing within HIV testing services for programme or individual benefit
  - Not enough evidence to make WHO recommendation at this time
  - No WHO PQ product available or in the pipeline
  - Ethical issues are critical to consider

- All new HIV diagnoses are important for programme planning
  - Phylogenetic data from HPTN071 indicates ~76% of new infections were from those who were themselves infected >1 year ago
  - Clients with recent and long-term infections should be offered the same opportunities for treatment, partner services etc.

- WHO, UNAIDS will continue to review data as it becomes available

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Thank you

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