Web Annex F. GRADE table and systematic review: should HIV recency testing be used in routine programmatic HIV testing services?
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Should HIV recency testing be used in routine programmatic HIV testing services?

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Abstract

Background

Providing accurate, efficient, and effective HIV testing services (HTS) with linkage to prevention and treatment, including voluntary partner services, is critical for reaching global goals to achieve and maintain low HIV incidence. Programmes are increasingly using HIV recency assays in HTS with the aim of increasing efficiency and effectiveness of services, increasing uptake and adherence to ART, as well as focusing partner services for people with recent HIV infection.

An HIV recency assay is either a serological laboratory-based assay or a rapid test for recent infection (RTRI; also referred to as point-of-care test). It is conducted at a testing site, and it classifies an HIV infection as recent or long-standing. Programmes might use and other relevant clinical information, such as viral load (VL), to determine whether an HIV infection is recent. We conducted a systematic review to evaluate the evidence and determine the impact of adding recency assays into HTS.

Methods

The systematic review was conducted across 5 databases, and experts were contacted to identify additional articles and abstracts through 31 December 2022. Included studies assessed the impact of including recency testing on: the uptake and linkage to ART and appropriate prevention services; the uptake of partner services; the number of people reached through partner services; the number of people with HIV reached through partner services; harms reported following recency testing, and test performance in HTS. For observational studies, risk of bias was assessed using the Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) tool. Certainty of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. Information on user values and preferences, feasibility, harms and resource use were summarized and reported descriptively.

Results

Of the 6,813 citations identified, 11 studies were eligible and included in the review. Evidence from four network contact-tracing studies contributed on clinical effectiveness. There were likely no differences between the proportions of HIV infection identified in the contacts of the index cases in the recency and long-term groups (RR = 1.12), but certainty is very low, and the proportion in the recency group may be three-fifths (0.63) that of the long-term group. There was very low certainty that the number of HIV (yield) of recent infections in the networks in the recency group was 2.66 times that of the networks in the long-term group. This could range from two-thirds (0.65) to ten times that of the long-term group. There was very low certainty that the proportion of recent infection in the contacts of index clients in the recency group was
double that of contacts of the long-term group (RR = 1.89). This could range from two-thirds (0.66) to 5.43 times that of the long-term group.

One study reported on harms including HIV recency testing, positivity yield and intimate partner violence among persons newly diagnosed with HIV. The study found there may be no difference in proportion of intimate partner violence (IPV) after 2–3 follow-up visits between the recent and long-term groups (this could range from 0.78 less than 1.66 more.) Harms, values and preferences were also summarized narratively and one report, published in gray literature, provided information from qualitative research on the values and preference of people providing and receiving assay testing. In these programmes clients sometimes expressed concerns about recency testing, including concern about creating a negative focus in the past by looking back to identify a possible source of HIV infection, which could disrupt the positive messages of HIV counselling. Further there were concerns from both providers and clients that they might be able to identify who had infected them, which could result in feelings of “bitterness”, “stress” and “blame”. There were also concerns about violence towards the person they thought might have infected them, or fear of violence or blame by people whose partners had been told they had recently acquired infections.

No costing or cost–effectiveness studies were identified in the systematic review. The costs of recency tests are high compared with standard HIV tests and have been estimated by one unpublished source to be between US$ 24.50 and US$ 155.60 (2023 US dollars).

Concerns about the feasibility of using recency assays in HTS were identified in the review. These included the complexity of adding additional tests to the diagnostic algorithm and the need for VL testing, where samples have to be transported to laboratories requiring clients to return for a further appointment for their results. Additional staff time and costs were also noted for the administration of the recency assays and VL testing, the provision of information to clients on recency testing, counselling for clients after results, training for testers and quality assurance/quality improvement systems.

The rationale for looking at the performance of recency assays in this PICO was to determine the performance of recency assays used in HTS (point-of-care assays) compared with the performance of assays used in laboratory settings. There were no studies that addressed this. The review did not identify data that corresponded to the PICO question, but it did identify two studies that addressed test performance in laboratory settings.

**Conclusions**

WHO recommends that programmes deliver a strategic mix of HTS, including voluntary partner services and linkage to prevention and treatment services. While WHO recommends use of HIV recency assays within surveillance programmes, no guidance has been issued on use of recency assays in routine service delivery. Despite limited evidence to support utility or effectiveness in increasing efficiency in HTS, HIV recency assays are increasingly being used in routine HIV testing service delivery. This review identified very low certainty evidence that recency testing in programmes led to increased uptake and linkage to ART, uptake of partner services, number of people reached through partner services or number of people with HIV reached through partner services, uncertainties about social harms, concerns about feasibility and no evidence on cost-effectiveness. The use of recency assays in routine HIV testing services is cautioned.

Based on the expert guideline development meeting, including review of the findings of this review, the guideline development group stated that future research on the use of recency assays in routine HTS is not a priority, as there has already been considerable investment and implementation without demonstrable benefit, nor extensive published research.
GRADE table: Contact tracing after index tests recency-positive compared to after index tests positive for long-term infection for HIV Testing Services

This annex summarizes the certainty of evidence according to the GRADE approach. All outcomes in the GRADE table are presented in the order of criticalness determined by the Guideline Development Group. Table 1 illustrates the full rankings of each outcome.

<table>
<thead>
<tr>
<th>№ of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Contact tracing after index tests recency-positive</th>
<th>After index tests positive for long-term infection</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>3(1,2,4)</td>
<td>observational studies</td>
<td>serious&lt;sup&gt;a&lt;/sup&gt;</td>
<td>serious&lt;sup&gt;b&lt;/sup&gt;</td>
<td>not serious</td>
<td>serious&lt;sup&gt;c&lt;/sup&gt;</td>
<td>none</td>
<td>119/431 (27.6%)</td>
<td>151/1670 (9.0%)</td>
<td>RR 1.12 (0.63 to 2.00)</td>
<td>11 more per 1,000 (from 33 fewer to 90 more)</td>
<td>⬤⬤⬤⬤</td>
<td>very low</td>
</tr>
</tbody>
</table>

Proportion of HIV infection in contacts by network denominator

**HIV recent infection by reported adjusted contact tracing yield ratio (per seed), reported crude odds ratio (per contact) or calculated crude relative risk (per seed)**

| 3(1,2,4)    | observational studies | serious<sup>d</sup> | serious<sup>b</sup> | not serious | serious<sup>e</sup> | none | -/1093 | +/-2175 | rate ratio or odds ratio | 175 more per 1,000 (from 49 fewer to 514 more)<sup>f</sup> | ⬤⬤⬤⬤ | very low | CRITICAL |

Proportion of HIV recency in contacts

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<sup>a</sup>Risk of bias: Down-graded once for serious risk of attrition bias due to missing data (not all contacts identified were located or tested) and lack of adjustment for confounding in Morgan et al. (3) and ICAP and Rwanda Medical Center (2). Morgan et al. (3) matched by baseline age and sex and Nikolopoulos et al. (1) conducted multivariable analyses to control for age, gender, nationality, education, place of residence, unemployment, drug injection and sex work.

<sup>b</sup>Inconsistency: Down-graded once. Statistical heterogeneity was high with I-squared = 76%, which may be explained by subgroup differences such as region and mode of network, but we cannot be certain of the reasons and have marked it down.

<sup>c</sup>Imprecision: The confidence interval is wide, around 1 and the line of appreciable benefit and appreciable harm.

<sup>d</sup>Risk of Bias: Down-graded once for serious risk of attrition bias due to missing data (not all contacts identified were located or tested) and lack of adjustment for confounding in ICAP and Rwanda Medical Center (2) and Williams et al (4). Williams et al. (4) matched by baseline age and sex and Nikolopoulos et al (1) conducted multivariable analyses to control for age, gender, nationality, education, place of residence, unemployment, drug injection and sex work.

<sup>e</sup>This is calculated at a control event rate observed in Nikolopoulos et al (1) of 0.16. CER in Williams et al. (4) was 0.61 and in ICAP and Rwanda Medical Center (2) was 0.005. These are vastly different and may not reflect the actual regional prevalence rates.
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<td>not serious</td>
<td>serious&lt;sup&gt;e&lt;/sup&gt;</td>
<td>none</td>
<td>35/104 (7.3%)</td>
<td>20/2137 (0.9%)</td>
<td>RR 1.76 (0.64 to 4.83)</td>
<td>7 more per 1,000 (from 3 fewer to 36 more)</td>
<td>⬤⬤◯◯◯ very low</td>
<td>CRITICAL</td>
</tr>
</tbody>
</table>

Proportion of IPV after 2–3 follow-up visits

| 1<sup>2</sup> | observational studies | serious<sup>e</sup> | not serious<sup>b</sup> | not serious | serious<sup>e</sup> | none | 22/83 (26.5%) | 198/849 (23.3%) | RR 1.14 (0.78 to 1.66) | 33 more per 1,000 (from 51 fewer to 154 more) | ⬤⬤◯◯ low | CRITICAL |

CI: confidence interval; RR: risk ratio

<sup>a</sup>Risk of Bias: Down-graded once for serious risk of attrition bias due to missing data (not all contacts identified were located or tested) and lack of adjustment for confounding in ICAP and Rwanda Medical Center (2) and Williams et al (4). Williams et al. (4) matched by baseline age and sex and Nikolopoulos et al (1) conducted multivariable analyses to control for age, gender, nationality, education, place of residence, unemployment, drug injection and sex work.

<sup>b</sup>Inconsistency: Down-graded once. Statistical heterogeneity was moderate with I-squared = 64%, which may be explained by subgroup differences such as region and mode of network, but we cannot be certain of the reasons and have marked it down.

<sup>c</sup>Imprecision: The confidence interval is wide, crossed 1 and the line of appreciable benefit and appreciable harm.

<sup>d</sup>Risk of bias: ICAP and Rwanda Medical Center (2) was assessed as a serious risk of bias by the ROBINS-I given that attrition from returning to the clinic for IPV assessment was 23%.

<sup>e</sup>Inconsistency: This cannot be evaluated as it is a single study.
References


