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Introduction: Rapid HIV tests have been widely adopted globally as an important component of HIV prevention and control programs. The INSTI™ HIV-1/HIV-2 antibody test is a second-generation HIV antibody test, available in most countries for use from whole blood, serum, and plasma.

Areas covered: Available data on kit characteristics and current performance data on the INSTI™ HIV-1/HIV-2 antibody test are presented together with six other rapid point-of-care tests (RPOCTs) for HIV antibody. Few published data are available providing direct comparisons of INSTI™ with other RPOCTs for HIV antibody and standard laboratory-based HIV-1/HIV-2 antibody assays. Existing data showed that INSTI™ has comparable performance to other RPOCTs but detected seroconversion later than standard laboratory-based assays.

Expert opinion: The good performance of INSTI HIV-1/HIV-2 antibody test, its ease of use, the rapid availability of results (<5 min), and the lack of specialized equipment required to use the kit make this kit a useful addition to the global market. The unique antigen and flow through technology contained in the kit make it a strong addition to HIV RPOCTs and to rapid/rapid algorithms used in many resource-limited settings.

Keywords: INSTI™ HIV-1/HIV-2 rapid test, rapid HIV testing

1. Introduction

Rapid HIV tests have been widely adopted globally, particularly in resource-limited settings, as an important component of HIV prevention and control programs because they are ideal tools to increase the number of persons who are aware of their HIV status and rapid availability of test results may improve prompt referral to care and treatment services. Demographic and Health Survey data from 13 countries in sub-Saharan Africa before 2006 found that only 2%–27% of population were aware of their HIV status, and uptake of HIV testing ranged from 5 to 25% in men and 4 to 35% in women [1]. Another study in Kenya found that never tested and undiagnosed HIV-infected women had the highest proportion (39%) of missed testing opportunities during an antenatal visit [2]. Although historical estimates of unknown HIV infection in high-resource countries such as the United States have suggested that around 20% are unaware of their HIV status [3], other studies suggested that this may be an overestimate. A study in San Francisco, USA, reported that 10% of HIV-infected persons were not aware of their status while another study in Edmonton, Canada, reported that 5.6% were unaware of their HIV status [4,5]. Those who are unaware of their HIV status play a major role in the transmission of HIV and propagation of the HIV epidemic [6-9].

Current rapid point-of-care tests (RPOCTs) for HIV offer many advantages when compared to standard testing, fulfilling the "ASSURED" criteria (affordable, sensitive, specific, user-friendly, robust and rapid, equipment-free, and deliverable) required for point-of-care testing in developing countries [10]. Rapid HIV tests have been of particular benefit in remote or resource-limited settings that may lack the infrastructure for laboratory-based screening tests, in populations that are
Experts in medicine and diagnostic testing have been influenced by the ability to conduct testing for HIV globally. The INSTI HIV-1/HIV-2 antibody test, a second-generation HIV antibody test, is available for use in most countries for the detection of HIV-1 and HIV-2 from whole blood, serum, and plasma. Available data suggest that INSTI™ has comparable sensitivity and specificity to other select RPOCT HIV antibody tests for the detection of established HIV infection, and limited data suggest that it may be better than other HIV RPOCTs for the detection of early HIV infection. The INSTI HIV-1/HIV-2 antibody test has the fastest time to results when compared to other select RPOCTs for HIV antibody.

This box summarizes key points contained in the article.

2. Description of INSTI HIV-1 and HIV-1/HIV-2 antibody tests

INSTI HIV-1/HIV-2 is made by a Canadian company, bioLytical™ Laboratories, Inc., and was first licensed in Canada for HIV-1 detection in November 2005 and the license was amended to include HIV-2 detection in June 2008. Although the kit contents available in the United States are identical to that used in Canada and elsewhere, it is not yet approved in the USA for HIV-2 detection; the INSTI HIV-1 antibody test is US FDA approved for HIV-1 detection from whole blood, serum, and plasma. The test received CLIA waiver from the US FDA in July 2012. In Canada and elsewhere the INSTI HIV-1/HIV-2 antibody test is available for the detection of HIV-1 and HIV-2 antibodies from whole blood, serum, and plasma.

INSTI has been CE Marked (a valid CE marking affixed to a product indicates that it complies with the relevant European “new Approach” product safety directives) for HIV-1 and HIV-2 detection in Europe since March 2006. This kit is the only licensed assay for HIV RPOCT in Canada with Reveal® G3 Rapid HIV-1 antibody test (MedMira, Inc., Nova Scotia, Canada) licensed for laboratory-based serum and plasma testing only.

Since all countries but the United States have access to the INSTI HIV-1/HIV-2 antibody test and because the majority additional benefits including improved source patient awareness of their HIV sero-status and increased compliance with post-exposure reporting [22-25]. Cost analyses have suggested that RPOCT is cheaper per test result delivered when compared with standard blood testing [26]. However, it has been argued that RPOCT estimates chronically underestimate the additional costs of implementation, staffing, training, and maintenance that are often excluded from estimated costs [27]. RPOCT also creates new challenges with respect to training, maintenance of competence, quality assurance, new kit lot verification, post-marketing surveillance, and maintenance of public health surveillance data [14].
of the available performance data are from this version of the kit, the descriptions that follow have been restricted to this kit.

The INSTI HIV-1/HIV-2 antibody test is a manual, visually read, flow-through immunoassay for the qualitative detection of HIV-1/HIV-2 antibodies in human blood, serum, or plasma (INSTI HIV-1/HIV-2 product monograph). The test contains a synthetic filtration membrane above an absorbent material within a plastic cartridge (the INSTI Membrane Unit). Company sources confirm that the recombinant HIV-1 gp41 and HIV-2 gp36 antigens used in the kit are produced exclusively for bioLytical Laboratories (personal communication, Rick Galli, bioLytical Laboratories, Inc.). In addition, although the flow-through technology used in the kit is not patent protected, the INSTI solutions are proprietary and were developed to work optimally with the HIV antigens (personal communication, Rick Galli, bioLytical Laboratories, Inc.). HIV-1/2 antibodies captured in the test spot react with a proprietary chromatic agent, protein-A-indigo blue, to produce a colored (blue) signal on the membrane. The membrane also contains a procedural control which contains a protein-A treated spot which captures IgG antibodies.

2.1 Kit contents, storage requirements, and procedure for conducting test

There are different package formats of the INSTI HIV-1/HIV-2 assay: single-use one-test kit with support materials including alcohol swab, lancet, and pipette, for RPOCT or package with 24 test units with or without the support materials. The testing components include an INSTI Membrane Unit and three solutions: a sample diluent made of 5 ml Tris-glycerine buffer containing cell lysis reagents (Solution 1), color developer (Solution 2), and clarifying solution (Solution 3) with propriety components. All three vials contain 0.1% sodium azide preservative and INSTI reagents are to be stored at 15–30°C, ambient temperature for most but not all settings.

The test is performed by adding the recommended amount (50 µl) of whole blood, serum, EDTA-plasma, or EDTA whole blood specimen to the vial of sample diluent which lyses the red blood cells. The sample diluent-specimen mixture is then poured into the well of the membrane unit. If present, HIV-1/HIV-2 antibodies (IgG) are captured by the recombinant HIV proteins in the test spot and IgG, normally present in blood, is captured in the control spot. Color developer is then added to the membrane unit. A distinct blue dot should appear in the control spot area and if HIV-1/HIV-2 antibodies are present, a blue color will appear in the test spot area. Clarifying solution is then added to decrease background color and make the control and test spots more distinct.

2.2 Controls

Since IgG antibodies are present in both HIV-negative and -positive human specimens, the internal control spot provides a visual signal that the test was performed correctly and IgG antibodies are present in the sample. If the control spot does not appear then the test is considered invalid.

A panel of quality controls is available from the manufacturer which includes a negative control and two positive controls, one for HIV-1 and a second for HIV-2. Control panels are not run with each sample but rather in accordance with local quality-assurance programs. Invalid results have been observed in

Table 1. Feasibility and acceptability of INSTI™ HIV-1/HIV-2 antibody test.

<table>
<thead>
<tr>
<th>Country</th>
<th>Clinical setting</th>
<th>Feasibility and acceptability</th>
<th>No. of infected cases identified</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Church-based settings</td>
<td>N = 32, 54% were never tested for HIV; 87.5% consented to testing</td>
<td>0</td>
<td>[44]</td>
</tr>
<tr>
<td>Canada</td>
<td>Community outreach – female sex workers</td>
<td>N = 87, 32% were never tested for HIV; 100% consented to testing</td>
<td>0</td>
<td>[42]</td>
</tr>
<tr>
<td>UK</td>
<td>Newly registered patients in primary-care setting</td>
<td>N = 799, 55% were never tested for HIV; 67.4% of males and 80% of females consented to testing</td>
<td>2</td>
<td>[45]</td>
</tr>
<tr>
<td>France</td>
<td>Emergency room</td>
<td>N = 8354, 67.5% consented to testing; 89.2% completed testing</td>
<td>43 with positive screen: 1 false-reactive result, 28 confirmed by WB, 4 known infected cases, 10 confirmatory test results not available</td>
<td>[46]</td>
</tr>
<tr>
<td>Uganda</td>
<td>Clinic in urban market</td>
<td>N = 1104</td>
<td>121 tested positive</td>
<td>[43]</td>
</tr>
<tr>
<td>Canada</td>
<td>Female sex workers</td>
<td>N = 198</td>
<td>40 tested positive, all known infection; 26% declined to receive results at time of testing including 3 with reactive tests</td>
<td>[41]</td>
</tr>
</tbody>
</table>
some patients with low IgG level related to sepsis, immunosuppressed state, or extreme hemodilution; however, in one study, no explanation could be found for two invalid tests [32].

2.3 Quality control (INSTI product monograph)
The manufacturer recommends that controls be run under the following circumstances: for new INSTI operator verification before performing testing on patient specimens, when switching to a new lot number of INSTI test kits, when a new shipment of kits is received, when temperatures in the storage or testing area fall outside the recommended 15 – 30°C (59 – 86°F) and at regular intervals as determined by the user facility.

It is good laboratory practice to include positive and negative test controls at regular intervals as defined by the user depending on the setting and for verification of new kit lot or operator.

2.4 Time to test interpretation (INSTI product monograph)
Total test time varies depending on specimen type as well as pre- and post-analytical processes but the actual performance of the test and results of valid tests are typically available in 1 – 2 min.

2.5 Safety considerations
The membrane unit is designed to filter, absorb, and retain the specimen and all reagents to limit leakage. As with other test kits for HIV, all specimens and controls should be handled as if capable of transmitting infectious diseases and it is recommended that BioSafety Level 2 practices or equivalent precautions be observed [33].

3. Overview of clinical data on INSTI HIV-1/HIV-2 antibody test
There are few published or abstract data directly comparing the INSTI HIV test with other RPOCTs. Available data on the performance characteristics of INSTI HIV-1/HIV-2 antibody test are summarized in Table 2 [32,34-40]. Studies assessing the feasibility and acceptability of the INSTI HIV-1/HIV-2 antibody test in various clinical settings are summarized in Table 1 [41-46].

4. Alternative technologies and comparison with INSTI HIV-1/HIV-2 antibody test
Seven RPOCTs for the detection of HIV antibody are currently approved for use by the US FDA: OraQuick ADVANCE® Rapid HIV-1/2 antibody test (OraSure Technologies), Reveal® G3 Rapid HIV-1 antibody test (MedMira), Uni-Gold™ Recombigen® HIV (Trinity BioTech), Multispot HIV-1/ HIV-2 Rapid Test (Bio-Rad Laboratories), Clearview® COMPLETE HIV-1/2 and Clearview® HIV-1/2 STAT-PAK® (Chembio Diagnostics), and the INSTITM HIV-1 antibody test.

Table 3 summarizes features of the six US FDA-approved kits and the INSTI HIV-1/HIV-2 antibody test. All of these tests use either immunochromatography (lateral flow) or immunoconcentration (flow-through) techniques and contain antigens that correspond to envelope regions of HIV-1 (gp41, gp120, or both). Two of the tests (INSTI HIV-1/HIV-2 antibody test and the Bio-Rad Multispot HIV-1/HIV-2 test) also contain HIV type 2 (HIV-2) envelope (gp36) antigens.

A recent study evaluated six tests (not including INSTI HIV-1/HIV-2 antibody test) and showed reported high sensitivity (95.38 – 99.44%) and high specificity (99.35 – 99.98%) when compared to a Bio-Rad Enzyme Immunoassay (EIA)/WB algorithm [47]. Of note, confidence intervals overlapped among different tests and for different specimen types. The sensitivity of some rapid tests was slightly lower in specimens obtained from participants receiving antiretroviral therapy but the differences did not reach statistical significance. This study also compared the sensitivity of the rapid tests for detecting acute seroconversion to an IgM-sensitive EIA. The EIA detected two WB-positive specimens that had negative results on all rapid tests. In this study the decreased sensitivity of rapid tests in detecting seroconversion relative to the IgM-sensitive EIA was not statistically significant despite the high prevalence and high incidence of HIV infections in the population studied. This is in contrast to other studies using HIV RNA to detect HIV seroconversion [48,49]. Persons with a recent potential exposure who may be seroconverting to HIV should be counseled and retested or tested with a nucleic acid amplification test [7].

There are no published data directly comparing INSTI with other rapid HIV tests and third- and fourth-generation HIV EIAs. A study done at the Laboratory Branch, Division of HIV AIDS Prevention, Centers for Disease Control and Prevention using plasma samples from HIV seroconvertors showed that INSTI had higher sensitivity compared to the six rapid tests in Delaney’s study in terms of earlier detection of HIV antibodies before positive WB for these individuals (Personal communication, Dr. Michele Owen, Centers for Disease Control, Atlanta, USA). In the same evaluation, INSTI detected seroconversion later than third- and fourth-generation laboratory assays.

In addition to the seven US FDA-approved rapid tests, there are many more rapid HIV tests on the global market that have not received FDA approval (PATH) [50]. Performance of these assays in the developing world has been well characterized in a variety of settings [51-54]. A recent meta-analysis of RPOCT HIV kits also found that oral HIV tests had lower sensitivity and lower positive predictive value (PPV) than blood-based specimens in low-prevalence populations than RPOCT that uses blood samples [55].

5. Conclusion

The use of RPOCT for HIV has changed HIV testing practices worldwide and has vastly enhanced access to HIV testing
globally. In the maternal setting, particularly labor and delivery, RPOCT allows directed antiretroviral therapy to be given to reduce mother-to-child transmission of HIV. In recipients of blood and body fluid exposures, the availability of a rapid test result in the source patient limits use of unnecessary HIV post-exposure prophylaxis (PEP) and reduces anxiety in the recipient. Finally, RPOCT for HIV has allowed populations to be reached that could not previously be reached in traditional health-care settings.

Despite these many advantages, RPOCT for HIV has resulted in new challenges to health systems. For example, false-positive results with the RPOCT may result in unnecessary confirmatory tests so ideally; an equally rapid confirmatory test represents a currently unmet need in this setting unless a dual RPOCT algorithm becomes universally accepted practice. Interestingly in the study by Tyndall et al., some patients undergoing RPOCT declined to receive the test results at the time of the test, including some who tested positive, suggesting that HIV RPOCT may not be the solution for HIV screening in all patients [41].

The available data suggest that INSTI has comparable performance to other US FDA-approved RPOCT assays. However, despite the potential public health benefits of RPOCT for HIV, this form of testing also has limitations compared to standard laboratory-based testing with lower sensitivity, failing to identify cases of early HIV seroconversion [56]. Laboratory-based study suggested that rapid fourth-generation HIV Ag/Ab testing assays might address this concern [49]. However, further studies are required as initial field studies using an RPOCT combo assay: Determine® HIV-1/2 Ag/Ab Combo rapid test did not confirm this advantage [57,58]. Some preliminary data suggest that the INSTI™ HIV-1/HIV-2 antibody test. Depending on sample type: sensitivity: 99.2 – 99.6%; specificity: 99.4 – 99.9%

Table 2. Summary of published data on the performance of the INSTI™ HIV-1/HIV-2 antibody test.

<table>
<thead>
<tr>
<th>Population (country)</th>
<th>Specimen type</th>
<th>N (positive)</th>
<th>Performance characteristic % (95% CI)</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Finger stick blood</td>
<td>200 (196*)</td>
<td>Sensitivity: 99 (96.3 – 99.7)</td>
<td>[37]</td>
</tr>
<tr>
<td>Adults with documented HIV-1 or HIV-2 infection (France)</td>
<td>Serum (stored)</td>
<td>49 (34)</td>
<td>Sensitivity: 69.4 (54.6 – 81.8)</td>
<td>[38]</td>
</tr>
<tr>
<td>Individuals with early seroconversion HIV infection (Canada)</td>
<td>Serum</td>
<td>1708 (25)</td>
<td>Sensitivity: 100 (no CI available)</td>
<td>[32]</td>
</tr>
<tr>
<td>Pregnant women, source individuals in blood and body fluid exposures, acutely ill adults (Canada)</td>
<td>Finger prick specimens</td>
<td>123 (2)</td>
<td>Sensitivity: 100 (no CI available)</td>
<td>[39]</td>
</tr>
<tr>
<td>High-risk adults in outreach settings (Canada)</td>
<td>Finger prick specimens</td>
<td>4180 (71.6% male)</td>
<td>Sensitivity: 99.7% (99.5 – 99.9%); positive predictive value 82.4%</td>
<td>[35]</td>
</tr>
<tr>
<td>Anonymous HIV testing clinic (Canada)</td>
<td>Serum and whole blood</td>
<td>3467 RPOCTs; 3462 whole blood EDTA samples; 3462 plasma samples; 1384 serum samples</td>
<td>Sensitivity: &lt; 18 months: 97.6)</td>
<td>[37]</td>
</tr>
<tr>
<td>Archival and prospective samples in community and hospital-based clinics (Canada)</td>
<td>Finger prick specimens</td>
<td>123 (2)</td>
<td>Sensitivity: 99.9% (99.5 – 99.9%); positive predictive value: 82.4%</td>
<td>[35]</td>
</tr>
<tr>
<td>Anonymous HIV testing clinic (Canada)</td>
<td>Finger prick specimens</td>
<td>4180 (71.6% male)</td>
<td>Sensitivity: 99.7% (99.5 – 99.9%); positive predictive value: 82.4%</td>
<td>[35]</td>
</tr>
<tr>
<td>Infants born to HIV positive mothers</td>
<td>Serum (stored)</td>
<td>273 (192)</td>
<td>Sensitivity: 70.3 (65.3 – 75.40)</td>
<td>[36]</td>
</tr>
<tr>
<td>HIV-exposed infants of known HIV status (South Africa)</td>
<td>Whole blood</td>
<td>872 &lt; 18 months: 254 &lt; 3 months: 227</td>
<td>Sensitivity: &lt; 18 months: 95.7 (92.4 – 97.6) &lt; 3 months: 98.7 (96.2 – 99.6)</td>
<td>[40]</td>
</tr>
<tr>
<td>HIV-exposed infants (South Africa)</td>
<td>Finger prick specimens</td>
<td>4180 (71.6% male)</td>
<td>Sensitivity: &lt; 18 months: 95.7 (92.4 – 97.6)</td>
<td>[40]</td>
</tr>
</tbody>
</table>

*Four were weakly positive.
Table 3. Overview of select RPOCT for HIV antibody.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Multispot HIV-1/HIV-2 rapid test</th>
<th>OraQuick ADVANCE® rapid HIV-1/2 antibody test</th>
<th>Reveal® G3 rapid HIV-1 antibody test</th>
<th>Uni-Gold™ STAT_PAK® HIV</th>
<th>Clearview® COMPLETE HIV 1/2</th>
<th>INSTI™ HIV-1/HIV-2 antibody test*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1/HIV-2 differentiation</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>HIV antigen and antigen peptides</td>
<td>gp41, gp36</td>
<td>gp41, gp36</td>
<td>gp41, gp120</td>
<td>gp41, gp120</td>
<td>gp41, gp120</td>
<td>gp41, gp36</td>
</tr>
<tr>
<td>Test type</td>
<td>Flow through</td>
<td>Lateral flow</td>
<td>Flow through</td>
<td>Lateral flow</td>
<td>Lateral flow</td>
<td>Flow through</td>
</tr>
<tr>
<td>Test temperature range (°C)</td>
<td>20 – 30</td>
<td>15 – 37</td>
<td>15 – 27</td>
<td>15 – 27</td>
<td>18 – 30</td>
<td>15 – 30</td>
</tr>
<tr>
<td>Sample types</td>
<td>Serum, plasma</td>
<td>Whole blood, plasma</td>
<td>Serum, plasma</td>
<td>Whole blood, serum, plasma</td>
<td>Whole blood, serum, plasma</td>
<td>Whole blood, serum, plasma</td>
</tr>
<tr>
<td>Specimen volume required (µL)</td>
<td>30</td>
<td>5</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Time to result (min)</td>
<td>Serum and plasma: 20 – 40</td>
<td>5</td>
<td>Serum: 99.8</td>
<td>10</td>
<td>15 – 20</td>
<td>1</td>
</tr>
<tr>
<td>Sensitivity (95% CI) [47]</td>
<td>(98.4 - 99.7)</td>
<td>(99.2 - 100)</td>
<td>(99.7)</td>
<td>(99.5 - 100)</td>
<td>(99.7)</td>
<td>(99.9 - 100)</td>
</tr>
<tr>
<td></td>
<td>Whole blood: 99.6 (98.5 – 99.9)</td>
<td>Plasm: 99.8</td>
<td>Whole blood: 99.7 (98.9 – 100)</td>
<td>Whole blood: 99.9 (99.6 – 100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plasma: 99.6 (98.9 – 99.8)</td>
<td></td>
<td>Plasma: 99.9 (98.9 – 99.8)</td>
<td>Whole blood: 99.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity (95% CI) [47]</td>
<td>Serum: 99.9</td>
<td>Serum: 99.8</td>
<td>Serum: 99.9</td>
<td>Whole blood: 99.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(99.8 - 100)</td>
<td>(99.4 - 99.9)</td>
<td>(99.0 - 100)</td>
<td>(99.6 – 100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plasma: 99.9</td>
<td>Plasma: 98.6</td>
<td>Plasma: 98.6</td>
<td>Ser/Pl: 99.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(99.8 - 100)</td>
<td></td>
<td>(98.4 – 98.8)</td>
<td>(99.3 – 100)</td>
<td></td>
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</tbody>
</table>

Adapted from Campbell, 2009 [11], Cook, 2010 [38], Delaney, 2011 [47] and O’Connell, 2007 [61].

*INSTI data from product monograph.
NA: Not available.
post-marketing surveillance, and maintenance of public health surveillance data.

6. Expert opinion

The available data on the INSTI HIV-1/HIV-2 antibody test demonstrate comparable performance to other FDA-approved rapid HIV tests with slightly earlier detection of infection than other RPOCT assays ([47], personal communication, Dr. Michele Owen). The studies have demonstrated excellent performance when the test is conducted in near-site laboratory settings as well as in the field. The kit meets the WHO’s “ASSURED” criteria (affordable, sensitive, specific, user-friendly, robust and rapid, equipment-free, and deliverable) with results available in most instances within 5 min, the fastest time to results compared to many other tests on the global market. The plastic container which contains the test well ensures that potentially infectious samples are enclosed thereby reducing biological hazards, which makes it logistically easier and safer to use in some field settings compared to some other RPOCT formats.

The INSTI HIV-1/HIV-2 antibody test contains a unique antigen and a novel flow-through technology, which makes it an important addition to the field of HIV RPOCT for screening as well as incorporation into a rapid/rapid testing algorithm.

Three unmet areas have been identified for rapid HIV diagnostics: i) the determination of acute HIV infection; ii) early infant diagnosis; and iii) vaccine-induced seroreactivity, whereby individuals who have received HIV vaccines may screen positive on rapid tests making distinguishing vaccination and disease impossible [14]. Better combination antigen/antibody rapid assays or rapid tests based on nucleic acid detection need to be developed to improve the diagnosis of acute HIV seroconversion. Rapid tests based on antigen detection with high sensitivity and specificity or rapid assays based on nucleic acid are also needed for early infant diagnosis. At the present time, RPOCTs for HIV nucleic acid detection are not commercially available but are in development [60]. Vaccine-induced seroreactivity is a difficult area that requires diagnostic assays that can distinguish between antigens unique to the vaccine versus natural viral antigens.

It is likely that HIV RPOCTs will have maximum impact in areas that central laboratory testing cannot efficiently service [27]. To optimize the use of RPOCT HIV, an assessment of the use of any given kit in a particular setting before implementation will be important to determine if the inclusion of this type of testing has a positive effect on the epidemiology (e.g., incidence) or patient outcomes [14]. Introduction of the kit must be individualized to each setting particularly where other tests and testing algorithms are already in place. Local epidemiologic data should be used to determine the sites that will be involved so that public health impact is maximized. Even though the majority of HIV RPOCTs are easy to perform and appropriate for nonlaboratory settings, it is critical that the accuracy and reliability of testing are ensured by developing quality-assurance programs around the tests themselves as well as ensuring that all testers are adequately trained [14]. Field trials of these assays are necessary to validate assay performance demonstrated in laboratory settings.

In developed countries where access to fourth-generation laboratory-based HIV screening is readily available, caution should be used when RPOCT is deployed in high-risk settings. Parallel standard laboratory testing or follow-up testing should be considered to ensure detection of highly infectious patients with early acute HIV infection. However, in resource-limited settings, even when a rapid point-of-care technology is less sensitive or specific than the reference standard, its implementation may still yield very important public health benefits when standard laboratory testing is not accessible [27].

Future devices should combine rapid testing for multiple infections (e.g., HIV, HBV, HCV, syphilis) and should further explore newer rapid test technologies (e.g., fourth-generation HIV antibody/antigen tests, and nucleic acid detection assays). Finally, additional studies will be required to ensure that test results are translated into the relevant services, e.g., linking of HIV-infected infants to immediate care for initiation of treatment as per WHO recommendations and newly diagnosed HIV-positive persons to counseling and care services [14,59].

Declaration of interest

The authors state no conflict of interest and have received no payment in preparation of this manuscript.
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