Diagnostic accuracy of 8 HIV RDTs and 2 simple confirmatory assays on specimens from 5 sub-Saharan African countries

Cara S. Kosack[a], Anne-Laure Page[b], Greet Beelaert[c], Tumwesigye Benson[d], Aboubacar Savane[e], Anne Ng'ang'a[f], Bita Andre[g], Jean-Paul B. N. Zahinda[h], Leslie Shanks[a], Katrien Fransen[c]

[a]Médecins sans Frontières, Amsterdam, Netherlands, [b]Epicentre, Paris, France, [c]Institute of Tropical Medicine, Antwerp, Belgium, [d]Ministry of Health Uganda, Kampala Uganda, [e]Laboratoire National de Reference, Conakry, Guinea, [f]National AIDS and Sexually Transmitted Infections Control Programme, Nairobi, Kenya, [g]Regional Delegation of Public Health for the Littoral Region, Cameroon, [h]Programme National de Lutte contre le Sida et les IST (PNLS), Democratic Republic of Congo

Background

- In resource-constrained settings, HIV testing is based on rapid diagnostic tests (RDT) combined in an algorithm.
- Despite good performance of RDTs in recent WHO evaluations, an unacceptably high frequency of false reactive test and algorithm results have been reported in some MSF missions and by other actors.
- No systematic heat-to-head evaluation of RDT accuracy with specimens from diverse settings has been carried out recently
- We conducted a standardized multi-centric study in six HIV testing and counselling (HTC) programmes in sub-Saharan Africa
- Here, we describe the diagnostic accuracy of 8 HIV diagnostic RDTs and 2 simple confirmatory assays

Methods

- **Design**: laboratory-based diagnostic evaluation study
- **Population**: all clients >5 years of age attending one of the study HTC clinics for HIV testing and providing informed consent
- **Sample size:** At least 220 HIV-positive and 220 HIV-negative (according to on-site algorithm) per site. The sample was consecutive in sites with HIV positivity > 40%, and stratified in sites with HIV positivity <40%. In addition, all clients with indeterminate results were included.
- **Recruitment**: After informed consent, venous blood was collected and EDTA plasma was prepared and sent to the reference laboratory.
- **Reference algorithm**: ELISA (Vironostika HIV Uni Form II Ag/Ab, bioMérieux), followed by INNO-LIA HIV I/II (Innogenetics NV, Belgium) Score for confirmation of positive results were performed at the AIDS reference laboratory at Institute of Tropical Medicine, Belgium.
- **Rapid tests**: the following rapid tests were performed at the reference laboratory according to manufacturer's recommendation
  - Determine HIV-1/2, Alere, USA
  - Uni-Gold HIV, Trinity Biotech, Ireland
  - Genie Fast HIV 1/2, BioRad Laboratories, USA
  - Vikia HIV 1/2, bioMérieux, France
  - HIV 1/2 Stat-Pak, Chembio, USA
  - INSTI HIV-1/HIV-2 antibody tests, bioLytical, Canada
  - SD Bioline HIV 1/2 3.0, Standard Diagnostics Inc, Korea
  - First Response HIV 1-2.O, PMC, India
- **Simple confirmatory assays**:
  - ImmunoComb II HIV 1&2 CombFirm, Orgenics, Alere, Israel
  - Geenius HIV 1/2 confirmatory assay, BioRad, USA

Results

- Samples from 2785 clients from six study sites in Africa were included in the study. The main results are presented in the Table below.
- Weak bands were reported only with the SD Bioline and First Response tests and represented up to 50% for HIV-2 lines for these tests.
- Specificity of the HIV-2 line was 89.8% for SD Bioline and 96.1% for First Response. Sensitivity could not be established due to the low number of HIV-2 infection (n=1).
- A multivariate analysis showed several factors associated with a risk of false positive results, including male gender (Genie Fast, Vikia and INSTI), being referred for testing (Determine), and inclusion site (INSTI, SD Bioline, First Response).

Table 1. Summary of main results of the performance of HIV rapid diagnostic tests and simple confirmatory assays

	Sensitivity	Specificity					
	Total	Total	Guinea Conakry	Uganda Kitgum	Uganda Arua	Kenya Homa Bay	Cameroon Douala	DRC Baraka
	(N=1474)	(N=1307)	(N=222)	(N=214)	(N=212)	(N=224)	(N=214)	(N=221)
Rapid diagnostic tests								
Determine HIV 1/2	100.0	93.3	99.0	93.1	94.4	94.4	92.4	91.9
Uni-Gold HIV	99.5	97.8	99.2	98.2	96.9	99.0	97.8	96.5
Genie Fast HIV 1/2	100.0	94.1	97.5	93.5	88.0	96.5	95.2	95.7
Vikia HIV 1/2	99.6	97.2	99.0	96.8	96.3	96.9	97.5	96.8
Stat-Pack HIV 1/2	99.5	99.7	100.0	100.0	99.9	98.6	99.6	99.9
INSTI HIV-1/HIV-2	100.0	90.6	98.0	96.3	90.4	96.8	84.9	80.4
SD Bioline HIV 1/2	100.0	97.6	99.7	98.6	95.6	96.8	98.7	96.6
First Response HIV 1/2.0	98.8	90.4	98.0	90.4	77.0	85.3	99.8	93.2
Confirmatory assays								
ImmunoComb	100.0	98.8	99.7	98.3	97.7	100.0	99.1	98.5
ImmunoComb OCA*	100.0	99.5	99.7	98.3	99.3	100.0	100.0	99.9
Geenius	99.7	98.4	98.4	98.3	97.0	100.0	98.9	98.4

** Different interpretation from manufacturer's recommendations, where all results with 1-2 positive spots are considered indeterminate*

Discussion

- Sensitivity of the tests was in line with WHO evaluation, but specificity was generally lower.
- Specificity varied highly by test and by origin of specimens. The differences per site could be partly explained by differences in population (such as the proportion of males, or mode of entry), but site-specific geographical differences remained for INSTI, SD Bioline and First Response.
- Weak bands could not explain the low specificity since they were rarely reported.
- Although confirmatory assays are presumed to have higher specificity than RDT, the simple confirmatory assays evaluated here also had imperfect and varying specificity and cannot provide a universal solution to the problem of false positive results.
- Finally, these results highlight the need for local assessment of HIV RDTs and testing algorithms