

Diagnostic accuracy of simulated HIV testing algorithms following the latest WHO recommendations

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Background

- In resource-constrained settings, HIV testing is based on rapid diagnostic tests (RDT) combined in an algorithm.
- According to the latest WHO guidelines (2012 and 2015), the algorithm is composed of 3 RDTs used sequentially according to the HIV prevalence in the tested population (Figure 1).
- These algorithms have not yet been widely adopted and there is limited data on their accuracy in different settings.
- We have used the results of a multi-centric study of the accuracy of HIV testing in 6 sites in 5 sub-Saharan African countries to simulate the WHO-recommended algorithms and present accuracy data of selected algorithms globally and on specimens from DRC, where individual RDTs showed the lowest specificity.

Methods

- Design:** laboratory diagnostic evaluation study
- Samples:** At least 220 HIV-positive and 220 HIV-negative (according to on-site algorithm) specimens were obtained from each of six African sites in five countries (Guinea, Uganda, Kenya, Cameroon, Democratic Republic of Congo) and sent to the AIDS reference laboratory at Institute of Tropical Medicine, Belgium.
- Rapid tests :** Eight rapid tests were performed according to manufacturer's recommendations at the reference laboratory.

Results

- 2785 specimens were included in the study (438-500 per site)
- Table 1 shows the adjusted performance of selected algorithms on all specimens, and Table 2 illustrates the results on specimens from DRC

Table 2. Performance of selected simulated algorithms using Determine as first test on specimens from Baraka, DRC (N=497)

2nd test	3rd test	Sensitivity %	Specificity %	PPV %	NPV %	Inconclusive n (adjusted %)
3-test algorithms for high HIV settings						
Uni-Gold HIV	Stat-Pak	100.0	99.0	89.2	100.0	3 (0.1)
Genie Fast HIV 1/2	Stat-Pak	100.0	98.7	86.8	100.0	1 (0.0)
Vikia HIV 1/2	Stat-Pak	100.0	97.3	75.8	100.0	1 (0.0)
SD Bioline HIV1.2 3.0	Stat-Pak	100.0	99.5	94.3	100.0	3 (0.1)
HIV 1/2 Stat-Pak	Uni-Gold	100.0	99.9	98.7	100.0	6 (1.0)
HIV 1/2 Stat-Pak	SD Bioline	100.0	99.9	98.7	100.0	3 (0.5)
3-test algorithms for low HIV settings						
Uni-Gold HIV	Stat-Pak	99.6	99.9	99.6	99.9	5 (0.9)
Genie Fast HIV 1/2	Stat-Pak	99.6	99.9	98.7	99.9	10 (1.1)
Vikia HIV 1/2	Stat-Pak	99.6	99.9	98.7	99.9	16 (2.4)
SD Bioline HIV1.2 3.0	Stat-Pak	100.0	100.0	100.0	100.0	3 (0.5)
HIV 1/2 Stat-Pak	Uni-Gold	100.0	99.9	99.6	100.0	3 (0.1)
HIV 1/2 Stat-Pak	SD Bioline	100.0	100.0	100.0	100.0	3 (0.1)

Discussion

- The algorithms selected here all contained Determine as first test, since this is currently the first test used in most settings, and HIV 1/2 Stat-Pak as second or third test since this test showed better specificity than all other tests in the evaluation of individual RDTs.
- The performance of the algorithms for high HIV settings varies greatly with the choice of the second test, with the algorithms using HIV 1/2 Stat-Pak as second test showing significantly better specificity and PPV than most other algorithms.
- All the algorithms for low HIV settings presented here (and all including HIV 1/2 Stat-Pak) showed good performance, with slightly different proportions of inconclusive results.
- The variety of results on specimens from DRC, which showed the highest proportion of false-reactive results in the RDT evaluation, illustrates the need for a proper local evaluation of different tests and algorithms for selection of an appropriate algorithm.
- Further modelling of the predictive values with varying prevalence should be performed for a more generalizable assessment of the performance in high- and low-prevalence settings.

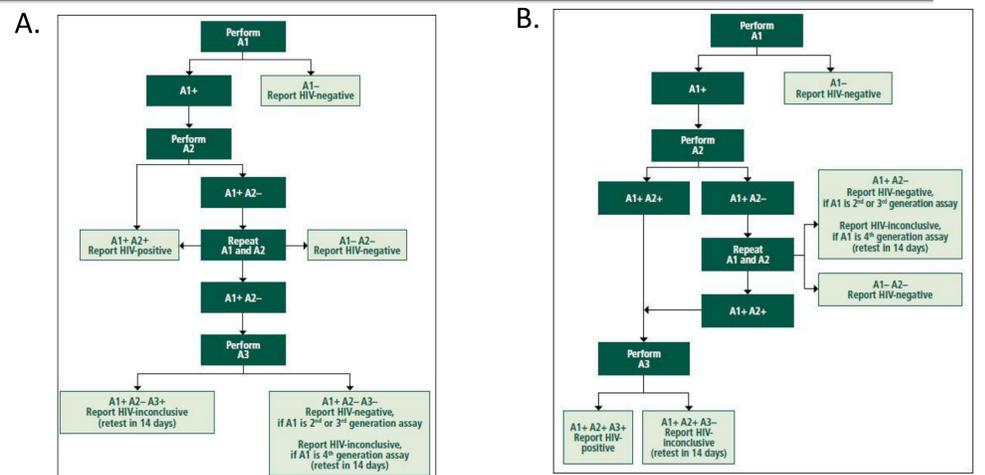


Figure 1. WHO-recommended algorithms for high (A) and low (B) prevalence settings

- Reference algorithm:** ELISA (Vironostika HIV Uni Form II Ag/Ab, bioMérieux, France), followed by INNO-LIA HIV I/II (Innogenetics, Belgium) Score for confirmation of positive results were performed at the reference laboratory.
- Analysis:** Different HIV testing algorithms were simulated using the RDT results obtained at the reference laboratory. A weighted analysis was used to estimate the performance of these simulated algorithms compared to the reference algorithm, while accounting for the sampling strategy that under-represented negative specimens by the on-site algorithm.

Table 1. Global performance of selected simulated HIV testing algorithms according to WHO recommendations for high and low HIV settings using Determine as first test (N=2785)

2nd test (A2)	3rd test (A3)	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)	Inconclusive n (adjusted %)
Algorithm for high HIV prevalence settings						
Uni-Gold HIV	Stat-Pak	99.6 (98.0-99.9)	99.6 (99.0-99.8)	98.4 (96.6-99.2)	99.9 (99.5-100)	6 (0.1)
Genie Fast HIV 1/2	Stat-Pak	100 (99.7-100)	99.0 (98.3-99.4)	96.5 (94.3-97.9)	100 (99.7-100)	1 (0)
Vikia HIV 1/2	Stat-Pak	99.6 (98.1-99.9)	98.2 (97.4-98.7)	93.8 (91.3-95.6)	99.6 (99.5-100)	1 (0)
INSTI HIV-1/HIV-2	Stat-Pak	100 (99.7-100)	99.0 (98.4-99.4)	96.5 (94.5-97.9)	100 (99.7-100)	2 (0.1)
SD Bioline HIV1/2 3.0	Stat-Pak	100 (99.7-100)	99.6 (99.0-99.8)	98.4 (96.5-99.3)	100 (99.7-100)	7 (0.1)
First Response HIV 1-2.0	Stat-Pak	99.7 (97.8-100)	98.7 (97.9-99.2)	95.3 (92.7-97.0)	99.9 (99.4-100)	19 (0.3)
HIV 1/2 Stat-Pak	Uni-Gold	99.6 (98.0-99.9)	99.9 (99.8-100)	99.7 (99.1-99.9)	99.9 (99.5-100)	13 (0.4)
HIV 1/2 Stat-Pak	SD Bioline	100 (99.7-100)	99.9 (99.7-100)	99.7 (99.1-99.9)	100 (99.7-100)	12 (0.5)
Algorithms for low HIV prevalence settings						
Uni-Gold HIV	Stat-Pak	99.5 (98.1-99.9)	99.9 (99.9-100)	99.9 (99.8-100)	99.9 (99.5-100)	11 (0.4)
Genie Fast HIV 1/2	Stat-Pak	99.9 (99.8-100)	99.9 (99.8-100)	99.7 (99.1-99.9)	99.9 (99.9-100)	23 (0.8)
Vikia HIV 1/2	Stat-Pak	99.6 (98.1-99.9)	99.9 (99.8-100)	99.7 (99.1-99.9)	99.9 (99.5-100)	41 (1.4)
INSTI HIV-1/HIV-2	Stat-Pak	100 (99.7-100)	99.9 (99.8-100)	99.8 (99.3-99.9)	100 (99.7-100)	28 (0.9)
SD Bioline HIV1/2 3.0	Stat-Pak	99.9 (99.7-100)	100 (99.7-100)	100 (99.7-100)	99.9 (99.9-100)	12 (0.5)
First Response HIV 1-2.0	Stat-Pak	98.8 (97.7-99.4)	99.9 (99.9-100)	99.9 (99.7-100)	99.7 (99.4-99.8)	24 (1.1)
HIV 1/2 Stat-Pak	Uni-Gold	99.5 (98.1-99.8)	99.9 (99.9-100)	99.9 (99.8-100)	99.9 (99.5-100)	6 (0.1)
HIV 1/2 Stat-Pak	SD Bioline	99.5 (98.1-99.8)	100 (99.7-100)	100 (99.7-100)	99.9 (99.5-100)	7 (0.1)

Adjusted analysis correcting for the verification bias due to the sampling strategy