Evaluation and Implementation of Rapid HIV Tests: The Experience in Eleven African Countries

729

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Abstract

Background: Access to HIV testing is a critical component of HIV prevention and care services. Because of their ease of use, rapid HIV tests are being widely used to provide HIV testing services in resource-poor countries, and country-based evaluations and quality assurance of point-of-service testing are important steps in establishing high-quality testing. To date there is limited information concerning the outcomes of these evaluations and of the performance of rapid tests in clinical settings.

Methods: A questionnaire regarding evaluation and implementation of rapid HIV tests was administered to personnel in ministries of health and reference laboratories in 11 African countries where the Centers for Disease Control and Prevention has assisted in improving laboratory capacity. Existing HIV testing algorithms in each country served as the gold standard for measuring rapid test performance.

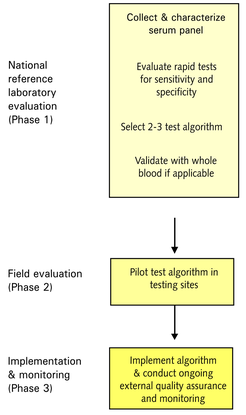
Results: Results are available from rapid HIV test evaluations conducted between 2001 and 2003 in reference laboratories in 10 of the 11 countries. In all, 15 different rapid tests were evaluated. Median sensitivity for each test ranged from 92.5% to 100% and exceeded 99% for 10 tests. Median specificity ranged from 97.4% to 100% and exceeded 99% for 13 tests. Subsequent evaluations at point-of-service sites in 5 countries yielded results comparable with those of reference laboratory evaluations. To date, a standard rapid testing algorithm has been implemented in 10 countries in over 600 sites including voluntary counseling and testing centers, antenatal clinics, blood donation centers, hospitals, and clinics. A median of 96,000 (range: 15,000 to 315,000) people were tested in each country in 2003. Six countries used a serial (consecutive) testing algorithm and 4 countries used a parallel algorithm. Quality assurance in 4 countries involved retesting a sample of positive and negative specimens. Median concordance between on-site rapid testing and reference laboratory retesting was 98.7% (range: 95.7% to 99.5%).

Conclusions: In-country evaluations of rapid HIV tests throughout sub-Saharan Africa yield results comparable to those obtained in more controlled evaluations. Furthermore, quality assurance data show the accuracy of point-of-service testing conducted by persons with varying levels of technical skill. As rapid testing is widely implemented in many countries, ongoing quality assurance is essential for maintaining high-quality HIV testing services.

Introduction

- HIV/AIDS has become the leading cause of death among young adults globally. To help mitigate this catastrophe, HIV prevention and treatment services are being enhanced through major global initiatives.
- To achieve the ambitious goals of these initiatives, millions of persons will require HIV testing in order to appropriately target HIV prevention interventions and to identify individuals who need HIV care. Yet the availability of HIV testing services is limited in many countries due to a lack of laboratory facilities and trained personnel.
- The potential reach of HIV testing has been greatly extended by the development of rapid HIV tests that require minimal equipment, can be performed with minimal training, and provide HIV test results within 30 minutes.
- The World Health Organization recommends a three-phase approach to the evaluation and implementation of rapid HIV testing (Figure 1). To date, there are limited data describing the success of this approach and the success of rapid test implementation.
- Our objectives are to:
  - Determine the utility of country-based evaluations as vehicles for rapid test implementation; and
  - Assess the performance of rapid HIV tests during evaluations and after implementation.

Figure 1: Process for country-based evaluation and implementation of rapid HIV tests *



* Adapted from Guidelines for Appropriate Evaluations of HIV Testing Technologies in Africa (WHO / CDC / APHL, 2003)

Methods

- We conducted a retrospective review of rapid HIV test evaluations conducted in 11 countries.
- First, we identified countries in which evaluations of commercially available rapid HIV tests had been conducted within the past 5 years and in which the Global AIDS Program (GAP) has a country-based program. In each country, a questionnaire regarding evaluation and implementation of rapid HIV tests was completed by personnel in ministries of health, reference laboratories, GAP country programs, and other partner organizations. Additional information was obtained from country reports and presentations. Performance results for each rapid test were aggregated among evaluations. The analysis was subdivided into the three evaluation phases recommended by WHO (Figure 1).

Results

Reference laboratory evaluations (Phase 1)

- Rapid HIV tests were evaluated in reference laboratories in Angola, Ethiopia, Ivory Coast, Kenya, Mozambique, Namibia, Rwanda, Senegal, Tanzania, and Zimbabwe.
- Half of the evalutations used previously collected and stored sera, and half used prospectively collected whole blood, serium or plasma specimens. 'Gold standard' testing algorithms consisted of enzyme immunoassay (EIA) tests only, EIA tests with Western Blot, or Western Blot only. Each evaluation lasted a median of 6 months (range 2-26)
- Rapid test performance (Table 1)
  - The median sensitivity of 10 of the 15 rapid tests was above 99% (range 92.5% to 100%).
  - The median specificity of 13 of the 15 rapid tests was above 99% (range 97.4% to 100%).
- Evaluations findings were used to recommend rapid tests or testing algorithms for field evaluation (8 countries) or for implementation at point-of-service sites (3 countries).

Table 1: Performance of 15 rapid HIV tests evaluated in reference laboratories in ten countries, 2001 - 2003

Rapid test	Number of evaluations	Median sample size (range)		Median sensitivity (range)		Median specificity (range)	
Determine	11	600	(100 - 1422)	100.0	(98.5 - 100)	100.0	(97.1 - 100)
OraQuick	11	775	(298 - 2000)	99.8	(97.8 - 100)	100.0	(99.7 - 100)
UniGold	10	528	(80 - 1422)	99.8	(97.6 - 100)	100.0	(98.4 - 100)
HemaStrip	10	528	(100 - 1422)	98.7	(95.2 - 100)	100.0	(98.7 - 100)
Capillus	6	528	(298 - 1422)	100.0	(98.0 - 100)	100.0	(99.3 - 100)
Genie II	3	533	(524 - 600)	99.3	(99.1 - 100)	99.6	(99.3 - 100)
HIV-Spot	3	600	(524 - 775)	98.7	(98.0 - 100)	99.0	(96.5 - 99.4)
BiSpot	2	566	(533 - 600)	99.8	(99.5 - 100)	99.6	(99.3 - 100)
InstantCHEK	2	502	(472 - 533)	98.3	(97.5 - 99.1)	97.4	(95.3 - 99.6)
DoubleCheck	1	533		92.5		97.5	
Hexagon	1	503		100.0		100.0	
Instant Screen	1	51		100.0		100.0	
MultiSpot	1	600		100.0		99.7	
SeroStrip	1	775		98.7		100.0	
StatPak	1	508		100.0		100.0	

Field evaluations (Phase 2)

- Field evaluations were conducted in Ethiopia, Ivory Coast, Mozambique, Namibia, and Zimbabwe.
- Evaluation sites included VCT centers, blood donation centers, hospitals, or clinics. Two to three evaluation sites were used in each country. Each field evaluation involved 2 to 5 rapid tests (median 3). Rapid testing was performed by trained laboratory technicians using whole blood in the majority of evaluations. Including phases 1 and 2, the evaluation process lasted at least one year (median 29 months).
- The median sensitivities of the 4 tests ranged from 99.4% to 100%. Their median specificities ranged from 99.5% to 100%.

Table 2: Performance of 4 rapid HIV tests in field evaluations in five countries, 2000 - 2004

Rapid test	Number of evaluations	Median sample size (range)		Median sensitivity (range)		Median specificity (range)	
Determine	7	566	(209 - 1320)	100.0	(98.5 - 100)	99.5	(98.6 - 100)
UniGold	5	514	(209 - 837)	99.6	(96.8 - 100)	99.7	(98.6 - 100)
Capillus	4	540	(365 - 837)	100.0	(98.5 - 100)	99.8	(98.6 - 100)
OraQuick	3	1320	(209 - 1320)	99.4	(99.4 - 100)	100.0	(100)

Implementation and monitoring of test performance (Phase 3)

- Based on the evaluation results, ten countries developed a standard rapid HIV testing algorithm that was recommended for use at point-of-service sites (Table 3). Both serial and parallel algorithms are used, and seven countries use a third "tiebreaker" test to resolve discordant results.
- The rapid testing algorithms have been implemented in over 350 VCT centers and 120 PMTCT sites. The algorithms are also used for clinical HIV diagnosis, screening blood donors, testing prisoners, testing needle stick injury victims in hospitals, and HIV surveillance

Table 3: Recommended rapid HIV testing algorithms and implementation of rapid HIV testing in ten countries

	Country	Screening tests	Additional test	Testing venues	Number of persons tested, 2003
Serial algorithms	Angola	1. Determine 2. UniGold	None [a]	VCT sites (13), TB hospitals (3), various other centers	15,000 (VCT)
	Ethiopia	1. Determine 2. Capillus	UniGold	VCT sites, blood donation centers	Unknown
	Ivory Coast	1. Determine 2. Genie II	Capillus	PMTCT sites (27), VCT sites (6), hospitals (2)	93,000
	Mozambique	1. Determine 2. UniGold	None [a]	Blood donation centers (85), VCT sites (66), Integrated VCT/PMTCT sites (14)	130,000
	Rwanda	1. Determine 2. UniGold	Capillus	VCT sites, PMTCT sites, clinics (60 sites total)	132,000
	Senegal	1. Determine or OraQuick 2. BiSpot or MultiSpot	None [b]	VCT sites (6)	4,700
Parallel algorithms	Botswana	Determine & UniGold	OraQuick	VCT sites (16)	51,000
	Kenya	Determine & UniGold	InstantScreen	VCT sites (200), PMTCT sites with blood donation services (50)	315,000
	Namibia	Determine & UniGold	HemaStrip	None [d]	None [d]
	Zimbabwe	Determine & UniGold	Capillus [c]	Hospitals, PMTCT sites, VCT sites (300 sites total)	100,000

[a] Clients with discordant results are asked to return in 1 month for retesting
[b] Discordant specimens are sent to the national reference laboratory
[c] Oraquick is used if Capillus is unavailable
[d] Algorithm is not yet implemented

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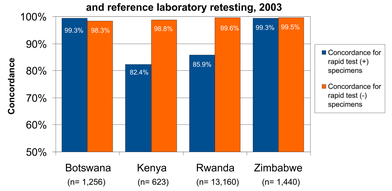
Figure 2: Concordance between on-site rapid testing and reference laboratory retesting, 2003



- In Botswana, Kenya, Rwanda, and Zimbabwe, 5-10% of all HIV-positive and HIV-negative specimens are retested at a reference laboratory for external quality assurance (EQA) (Figure 2). The causes of incorrect rapid test results included specimen mix-up, transcription errors, an inconsistent supply of test kits, and difficulty interpreting rapid tests.
- The most comprehensive EQA programs involved training, site visits, competency assessment of personnel who perform the tests, and retesting a proportion of specimens.
- In Botswana, Kenya, and Mozambique, the two screening tests in the rapid testing algorithm were discordant for fewer than one percent of specimens tested (range 0.4% - 0.9%). However, in one country, the discordance rate increased from 0.1% to 0.9% over a period of 4 years as testing was scaled up.

Conclusions

- Rapid HIV tests can provide reliable results in Africa, even in settings with limited laboratory infrastructure. The sensitivity and specificity of rapid tests in most of the evaluations were equivalent to or higher than published results from independent evaluations. Performance in field evaluations and reference laboratory evaluations was very similar.
- Country-based evaluations are an essential step in rapid test implementation. Evaluations served to overcome skepticism regarding rapid test performance, build familiarity and expertise with rapid tests, and establish methods and specimen panels for evaluating new rapid tests in the future. Nonetheless, evaluations are resource- and time-intensive.
- Rapid HIV tests can be performed by non-laboratorians. Quality assurance programs in 4 countries demonstrated 98.0% accuracy of rapid testing at point-of-service sites, including VCT centers.
- A robust quality assurance program will help to assure high quality test results as countries scale up the number of testing sites. Rapid testing errors can be minimized through training, on-site monitoring, and retesting specimens.