

Evaluation of HIV testing Algorithms in Ethiopia:
The role of the tie-breaker algorithm and
weakly reacting test lines in contributing to a high
rate of false positive HIV diagnoses.

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Background

- Well known risk of false positive HIV results using RDT algorithm (choice in RLS)
- Tie-breaker algorithms often used instead of instead of WHO recommended serial or parallel algorithms*
- Evidence for high rate false positives (Ethiopia Amhara/Tigray region) – identified with confirmation using + **Immunocomb Combfirm®**
- Growing evidence of poor specificity of weakly reactive test lines

Aims

1. Evaluation of HIV RDT algorithm performance in Amhara region of Ethiopia.
- 2.a Assess the positive predictive value (PPV) of weakly reactive test lines;
- 2.b Value of simple confirmation test

Methods

- Two sites: Humera and Abdurafi
- 200 positive samples (and every n^{th} negative to reach 200), from VCT results {WHO nrs}
- Re-tested in laboratory with 3 RDTs (KHB, HIV 1/2 STAT-PAK®, Uni-Gold™ HIV)
- Reference methods: Western Blot (MP Diagnostics HIV Blot 2.2); Indeterminate results resolved by PCR (Cobas TaqMan HIV-1 Qual)



Summary of results

- 2620 subjects included, HIV prevalence 7.7%
- Tiebreaker algorithm (KHB, HIV 1/2 STAT-PAK®, Uni-Gold™ HIV) had 16 false positive results (PPV 92.7%)
- Serial algorithm (KHB, HIV 1/2 STAT-PAK®) had 1 false positive result (PPV 99.5%)
- Adding of ImmunoComb eliminated false positives
- All false positive results had at least one “weakly reactive test line” in the algorithm.

SE, SP, PPV and NPV of algorithms (N=2620)

Algorithm	Results (95% Confidence interval)			
	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Serial KHB/STAT-PAK	100% (98.2-100)	100% (99.8-100)	99.5%(97.3-100)	100% (98.4-100)
Serial KHB/STAT-PAK-OIC	100% (98.2-100)	100% (98.4-100)	100%(98.2-100)	100% (98.4-100)
Tiebreaker KHB/STAT-PAK/Unigold	100% (98.2-100)	99.3 % (98.9-99.6)	92.7% (88.4-95.8)	100% (98.3-100)

SE, SP, PPV and NPV of individual RDTs (N=2620)

	Results (95% Confidence interval)			
	Sensitivity	Specificity	Positive predictive value	Negative predictive value
KHB	100% (98.2-100)	99.15 (98.6-99.4)	89.8% (85.1-93.4)	100% (99.8-100)
Unigold	99.0% (96.5-99.9)	99.0% (98.5-99.4)	89.3% (84.5-93.0)	99.9% (99.7-100)
STAT-PAK	100% (98.2-100)	99.9% (99.7-100)	98.5% (95.8-99.7)	99.8% (99.9-100)

SE, SP, PPV and NPV of algorithms - after excluding weak positives

Algorithm	(95% Confidence interval)				
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	HIV prevalence
Serial KHB/STAT-PAK	100% (98.2-100)	100% (98.4-100)	100% (98.2-100)	100% (98.4-100)	7.59%
Tiebreaker KHB/STAT-PAK/Unigold	100% (98.2-100)	100% (98.3-100)	100% (98.2-100)	100% (98.3-100)	7.59%

Main conclusions

- Unacceptable risk of false positive with tie-breaker
- Weakly reactive test lines have poor specificity/PPV
- The confirmation test eliminated all false positive results

Recommendations

- Abandon tie-breaker algorithm in favour of WHO recommended algorithms
- Add confirmation tests to RDT algorithm
- Interpret weak positive RDT results as 'indeterminate'. Operational research is urgently needed on how to implement?

Thank you!



Suppl. 1 Demographics of study participants

		Humera Site N(%)	Abdurafi Site N(%)	Total N(%)
Number		230	198	428
Age	Mean [range] in years	31.3[10-65]	28.0 [10-67]	29.7 [10-67]
Sex	Male	140 (61.1)	119 (60.1)	259(61.0)
Residential status	Resident	122 (53.3)	101 (51.0)	223 (52.3)
	Migrant	47 (20.5)	68 (34.3)	115 (26.9)
	Settler	11 (4.8)	19 (9.6)	30 (7.0)
	Other	49 (21.4)	10 (5.1)	59 (13.8)
Reason for testing	Diagnostic testing	65 (28.4)	56 (28.3)	121 (28.3)
	Symptomatic	80 (35.0)	16 (8.1)	96 (22.5)
	Curious about status	8 (3.5)	63 (31.8)	71 (16.6)
	Pre-marriage	15 (6.6)	22 (11.1)	37 (8.7)
	Other	61 (26.6)	41 (20.7)	102 (23.9)

Suppl. 2 Variation of Specificity of HIV test over time and place

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1

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Variation in Specificity of HIV Rapid Diagnostic Tests over Place and Time: An Analysis of Discordancy Data Using a Bayesian Approach

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