Performance of HIV-1 Rapid Tests to Identify Seroconverters in MTN 003 (VOICE)

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Introduction

- Accurate and efficient identification of seroconverters in antiretroviral-based HIV prevention trials is critical for minimizing emergence of resistance.

Objective

- We evaluated 150,125 HIV rapid tests performed in MTN 003 (VOICE) to assess the performance of the tests used in this detection algorithm.

Methods

- The VOICE study was a Phase 2B, five-arm, double-blinded, placebo-controlled, multi-site, randomized, controlled trial to evaluate the safety and effectiveness of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate Tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women.
- The study was conducted at the following clinical research sites: MU-JHU, Kampala, Uganda; MRC (7 sites) Isipingo, Chatsworth, Overport, Tongaat, Umkomaas , Verulam, Botha's Hill, Durban and vicinity South Africa; CAPRISA eThekwini, Durban South Africa; CAPRISA Aurum, Klerksdorp, South Africa; PHRU Soweto South Africa; WRHI Johannesburg South Africa; UZ-UCSF (3 sites) Seke South, Spilhaus, Zengeza, Harare Zimbabwe.

Figure 1 Study Visit Scheme

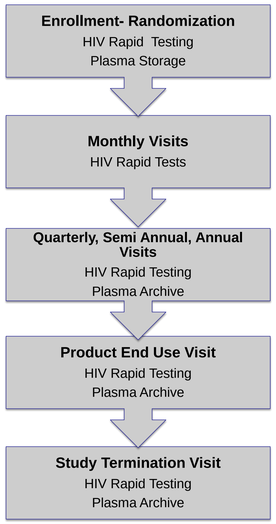
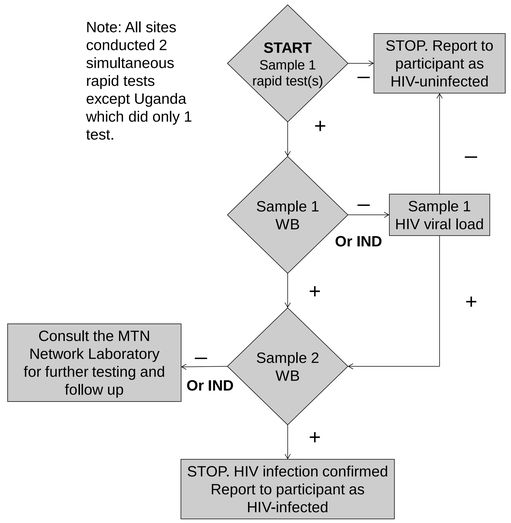


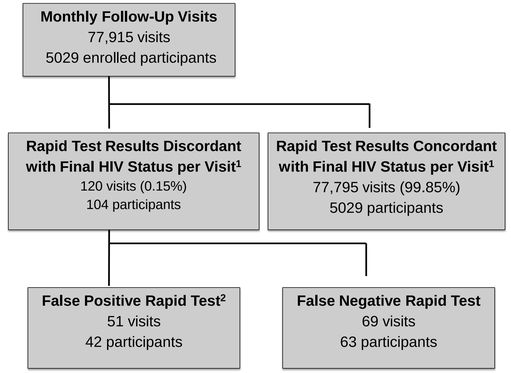
Figure 2 Follow up and Primary Endpoint HIV Testing Algorithm



Results

- Rapid testing correctly identified HIV infection status (positive or negative) at 77,795/77,915 (99.85%) follow-up visits in VOICE.

Figure 3: Overall Performance of Rapid Testing in VOICE by Study Visit and Number of Participants



1. As determined by confirmation with Western blot or HIV-1 RNA

2. 161 rapid tests 120 visits had results discordant with the final HIV status at the visit.

- 51/161(32%) were due to a false positive rapid
- 48/51 false-positive cases had rapid test results for subsequent visits
- 14/48 (29%) cases (from 7 participants) resolved by switching the falsely positive rapid kit to a different rapid kit

Table 1: Performance of Rapid Testing in VOICE by Test Kit
(Based on 72,169 Visits with Dual Rapids)

Rapid Kits Used			Total # of Specimens	Final Status				
				POSITIVE		NEGATIVE		
				WB[3]	RNA[4]	WB[3]	RNA[4]	No further testing
Concordant	Unigold/ Determine	+/+	322	296	26	0	0	-
		-/-	54969	4	31	-	-	54934
	OraQuick/ Determine	+/+	14	13	1	0	0	-
		-/-	16791	5	1	-	-	16785
Discordant	Unigold/Determine	+/-	19	0	2	10	7	-
		-/+	36	9	6	17	4	-
	OraQuick / Determine	+/-	3	2	0	0	1	-
		-/+	15	3	1	7	4	-

3. Participant was seropositive – WB used to resolve status

4. Participant was seronegative – HIV RNA needed to determine status due to negative or indeterminate WB

Table 2: Aggregate Sensitivity, Specificity, Positive and Negative Predictive Values of each Rapid Test Kit Based on all 150,125 Rapid Test Results. (95% Confidence Interval)

	Sensitivity	Specificity	PPV	NPV
Abbott Determine	88.78% (85.27, 91.70)	99.96% (99.94, 99.97)	91.75% (88.56, 94.29)	99.94% (99.92, 99.95)
OraSure OraQuick	61.54% (40.57, 79.77)	99.99% (99.97, 100.00)	94.12% (71.31, 99.85)	99.94% (99.89, 99.97)
Uni-Gold Recombigen	85.86% (82.00, 89.17)	99.97% (99.95, 99.98)	94.89% (92.04, 96.94)	99.91% (99.88, 99.93)

Table 3: Regional Sensitivity and Specificity of Each Rapid Test Kit Based on all 150,125 Rapid Test Results. (95% Confidence Interval)

		South Africa	Uganda	Zimbabwe
Determine	Sens	88.78% (85.23, 91.72)	--	87.50% (47.35, 99.68)
	Spec	99.96% (99.94, 99.98)	100% (99.43, 100.00)	99.92% (99.85, 99.96)
OraQuick	Sens	66.67% (40.99, 86.66)	--	50.00% (15.70, 84.30)
	Spec	100% (99.92, 100.00)	--	99.99% (99.95, 100.00)
Unigold	Sens	86.63% (82.76, 89.91)	66.67% (38.38, 88.18)	--
	Spec	99.97% (99.95, 99.98)	99.98% (99.91, 100.00)	100% (69.15, 100.00)

Conclusions

- The combination of Determine, Unigold and OraQuick accurately (99.85%) characterized HIV infection status in VOICE.
- Because of the design of the study, many participants were tested in acute seroconversion, resulting in a limited sensitivity (61-88%).
- The use of newer antigen/antibody rapid tests could improve current HIV testing algorithms by reducing the time from infection to detection.

VOICE
VAGINAL + ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC

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MTN microbicide trials network