
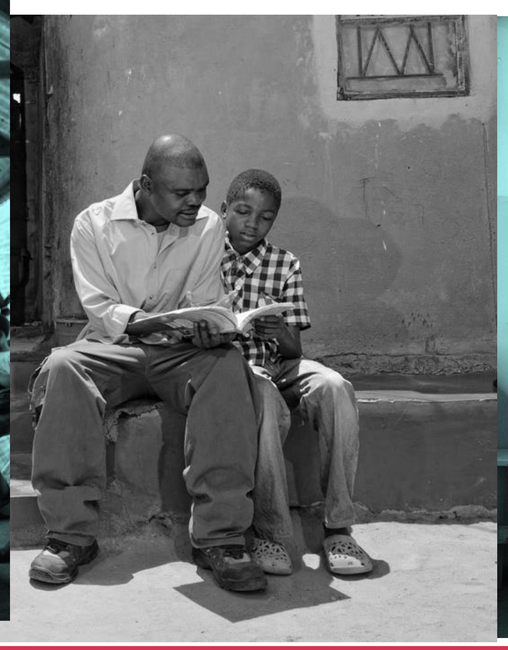

Is OraQuick® HIV-self-testing valid among intended users? Analysis from a clinical performance study in Lusaka, Zambia.

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BACKGROUND.

Self-testing for HIV (HIVST), where an individual performs, reads and interprets their own HIV test, offers a simple and private option for people wanting to screen themselves for HIV. HIVST is highly acceptable, increases coverage and frequency of HIV testing, and reaches first-time testers, men, and adolescents.

The OraQuick® HIV self-test kit is an oral fluid test (OFT) available for purchase in two versions: OraQuick In-Home HIV Test, (FDA approved), and OraQuick Advance Rapid HIV 1/2 Antibody Test with a double foil package containing an illustrated insert providing HIVST instructions for use (IFU).

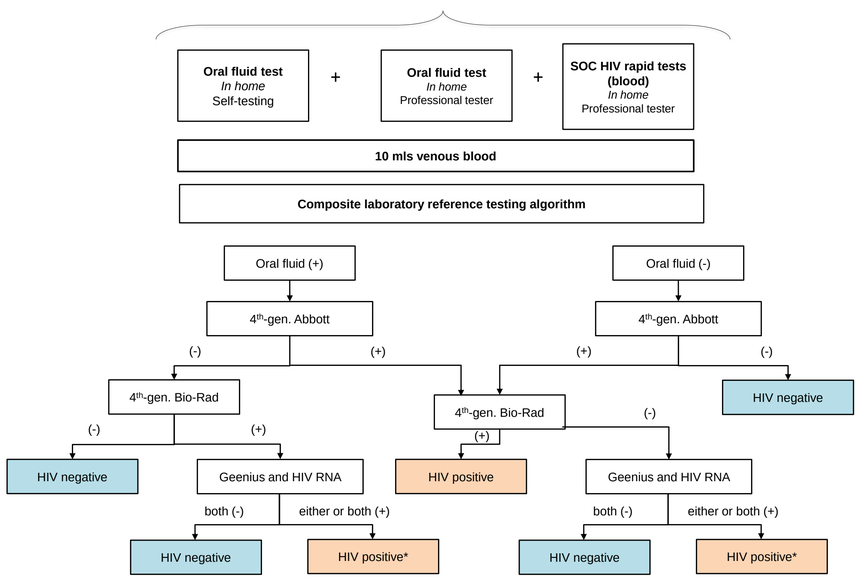
Previous diagnostic evaluation studies have compared OraQuick Advance HIVST with a reference standard of professionally-administered and -read finger-prick rapid diagnostic test (RDT) kits, as used in national algorithms. These have shown some loss of performance, mainly relating to a high frequency of user errors for HIVST, but with sensitivity and specificity remaining within acceptable performance in most populations. As with all RDTs, OraQuick Advance has an inherently limited clinical validity, especially early in the course of HIV infection.

Here we report the clinical performance of OraQuick® Advance HIVST assessed in a large cohort of intended users in Zambia using both laboratory and RDT reference standards .After pilot testing the IFU with video recording and cognitive interviewing (See Poster:MOPED1167) all participants in this study received the manufacturers IFU **AND** a standardized demonstration of the processes involved in self-testing.

METHODS

The study was conducted in an urban and a rural area in Lusaka, Zambia. Both communities were mapped and divided into smaller zones which were randomly selected. All individuals aged 18 years and above in the randomly selected zones were visited at home and invited to participate in the study. Participants provided written informed consent for inclusion. In the urban area, in addition to the random community sampling, consecutive individuals who attended the health facility for VCT services were also invited to participate.

Researchers demonstrated how to use the OFT and provided manufacturer's instructions for use (IFU) before participants conducted the test in privacy and recorded their results by themselves on a self-completed questionnaire (SCQ), which included symbols for those with lower literacy level. The participant placed SCQ and the used HIV-ST kit in an opaque envelope and returned it to the researcher who repeated the OFT using standard procedures and re-read the participant's test strip. A nurse, blinded to OFT results, performed rapid HIV diagnostic test (RDT) by finger prick according to the Zambian national HIV testing algorithm. 10 mls venous blood was collected into EDTA bottle, which was sent to the laboratory within 8 hours to prepare plasma aliquots which were used for all laboratory-based reference testing. The blood was processed in the laboratory and a corresponding amount of plasma harvested and stored at -80 degrees for testing according to the algorithm shown in fig1. Demographic data and information on HIV testing prior to HIV-ST was collected and entered in electronic data capture devices. The study was conducted between 22 June, 2016 – 30 June 2017.



Assays: Oral fluid: OraQuick HIV test; 4th-gen. Abbott: Architect HIV Ag/Ab Combo assay; 4th-gen. Bio-Rad: GS HIV Combo Ag/Ab EIA assay; Geenius: Geenius HIV 1/2 Supplemental Assay; HIV RNA: Abbott Real Time HIV assay.
(+) indicates reactive/positive; (-) indicates non-reactive/negative.
*If HIV RNA is undetectable, samples may be tested for the presence of antiretroviral drugs.

Figure 1: Field and laboratory testing algorithm

RESULTS

A total of 2,572 participants were recruited, table 1. Overall 59.4% were women and 85.6% had previously tested for HIV. Literacy levels were higher in the urban community and facility based testers than in the rural community testers.

	Rural community		Urban community		Urban facility		Total	
	No.	%	No.	%	No.	%	No.	%
Total participants	613	100	1038	100	921	100	2572	100
Female (No./% testers)	289	47.1	744	71.7	494	53.6	1527	59.4
Age (median/IQR)	31	(22, 43)	25	(20, 32)	25	(21, 32)	26	(21, 35)
Age (years) (No./% testers)								
15-17 years	30	4.9	66	6.4	11	1.2	107	4.2
18-24 years	164	26.8	438	42.2	424	46	1026	39.9
25-34 years	166	27.1	307	29.6	309	33.6	782	30.4
35-44 years	113	18.4	125	12	135	14.7	373	14.5
45-54 years	55	9	52	5	32	3.5	139	5.4
55 years and older	85	13.9	50	4.8	10	1.1	145	5.6
Educational attainment (No./% testers)								
Incomplete primary education	90	15.7	75	7.3	44	4.8	209	8.3
Complete primary education	178	31.1	182	17.8	111	12.1	471	18.8
Secondary or higher education	303	52.9	765	74.9	762	83.1	1830	72.9
Literacy: able to read a newspaper or letter (No./% testers)	514	83.8	993	95.7	904	98.2	2411	93.7
Previously tested for HIV (No./% testers)	502	81.9	882	85	817	88.7	2201	85.6
Self-reported HIV+ (No./% previous testers)	17	3.5	11	1.3	17	2.1	45	2.1
Current ART use (No./% HIV+)	2	14.3	1	10	3	17.6	6	14.6
HIV positive (based on rapid diagnostic test)*	40	6.5	82	7.9	124	13.5	246	9.6

The flow of participants through the processes of the study is shown in figure 2.
There was good agreement between participant conducted and read OFT-ST and the researcher reading of the same test as well as between the participant conducted and read OFT-ST and researcher conducted OFT, Table 2.

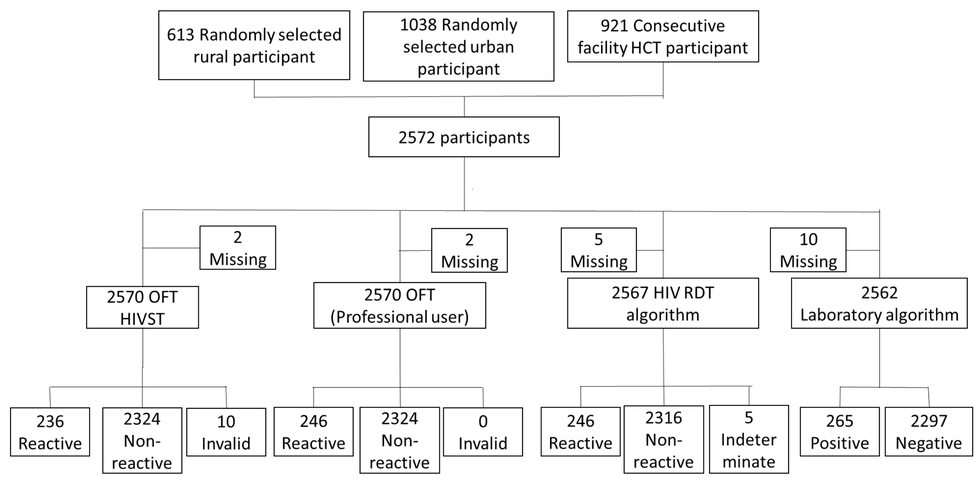


Figure 2: Participant Flow through study protocol

Interrater agreement between participant and researcher read of OFT result

	Researcher-read reactive	Researcher-read non-reactive	Sub-total*
Participant-read reactive	229	7	236
Participant-read non-reactive	9	2314	2323
Sub-total	238	2321	2559

% Agreement	99.37	
Cohen's kappa	0.9628	p<0.0001

* Excludes 11 OFT results read as invalid by either participant, or researcher, or both; and 2 clients missing OFT results (13 total)

Agreement between participant-administered and read and researcher-administered and read OFT result

	Researcher-conducted reactive	Researcher-conducted non-reactive	Sub-total*
Participant-read reactive	229	7	236
Participant-read non-reactive	11	2313	2324
Sub-total	240	2320	2560

% Agreement	99.3	
Cohen's kappa	0.9583	p<0.0001

* Excludes 10 OFT results read as invalid by participant and 2 clients missing OFT results (12 total)

Table 2: Comparisons of OFT between intended users and professional users

SENSITIVITY

The sensitivity of OFT-ST was 94.2% (95%CI 90.4-96.8) when compared to RDT, with a specificity of 99.7% (95%CI 99.3-99.9) and fell to 87.6% (95%CI 83.0-91.4) when compared to the gold standard of the laboratory algorithm, specificity was 99.7% (95%CI 99.4-99.9). Self-testers from the rural community achieved a lower sensitivity (76.6%, 95%CI 62.0-87.7) compared to the urban community (88%, 95%CI 79.0-94.1), when compared to the gold standard

Agreement between participant-administered and read OFT result and rapid diagnostic blood test

	RDT positive	RDT negative	Sub-total*
Participant-read reactive	226	8	234
Participant-read non-reactive	14	2304	2318
Sub-total	240	2312	2552

Agreement (%)	99.14	
Cohen's kappa	0.9488	p<0.0001
Sensitivity (%, 95% CI)	94.2	90.4-96.8
Specificity (%, 95% CI)	99.7	99.3-99.9

* Excludes 10 OFT results read as invalid by participant , 5 clients with indeterminate RDT results, 3 participant missing RDT results, and 2 participants missing OFT results (20 total)

Agreement between participant-administered and read OFT result and laboratory test algorithm

	Laboratory positive	Laboratory negative	Sub-total*
Participant-read reactive	227	7	234
Participant-read non-reactive	32	2286	2318
Sub-total	259	2293	2552

Agreement (%)	98.47	
Cohen's kappa	0.9125	p<0.001
Sensitivity (%, 95% CI)	87.6	83.0-91.4
Specificity (%, 95% CI)	99.7	99.4-99.9

* Excludes 10 OFT results read as invalid by participant , 8 participants missing laboratory results, and 2 clients missing laboratory and OFT results (20 total)

CONCLUSION

This study provides robust evidence of the sensitivity and specificity of the OraQuick® HIV self-test kit, with prior demonstration, in the hands of intended users in urban and rural Zambia, and is likely to be generalizable to other similar settings. Pilot studies of this test kit being used with manufacturers instructions for use only showed poor sensitivity and further analysis of this (shown on poster MOPED1167) showed that, for populations with variable literacy levels and limited exposure to self testing in general, additional support in the form of demonstration will be needed, at least until widespread familiarity with the test develops, in order to obtain reasonable results.

When compared to the standard of care in this setting, the RDT algorithm, the performance of the OFT-ST provided a reasonable sensitivity (94.2%) and excellent specificity. However, when compared to a laboratory reference standard the sensitivity decreases, though the specificity remains constant. The oral fluid test is inherently less sensitive than the laboratory standard due to it being an antibody-alone test and also possibly due to lower levels of antibody in oral fluid. This result may have important implications in the utility of the test, however, as a means to increasing access to testing and reaching the target of 90% of PLHIV knowing their status, lower sensitivity will need to be weighed against the increased number of individuals who will use the test to learn their HIV status.

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