SYSTEMATIC REVIEW ON HIV SELF-TESTING (HIVST) PERFORMANCE AND ACCURACY OF RESULTS

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INTRODUCTION

HIVST has potential to increase access to and uptake of HIV testing, particularly among key populations. Many countries have already or are planning to introduce HIVST. However, some concerns about the usability and performance of HIV rapid diagnostic tests (RDTs) in the hands of self-testers have been raised. To address this issue and to inform WHO guidelines for release in December 2016, we summarize the available evidence.

METHODOLOGY

We searched three databases and five HIV conferences for abstracts (January 1995-November 2015) on studies assessing diagnostic accuracy and performance of RDTs used for HIVST. Review was restricted to studies reporting true/false-positive and true/false-negative results. This data was used to calculate the sensitivity and specificity estimates in comparison with reported reference standard testing strategy. Reference testing strategies were classified in accordance with the WHO HIV testing strategies which consider the most recent national HIV prevalence. Sensitivity and specificity estimates from studies using the same RDT for HIVST were pooled.

All extracted data was then analyzed by type of specimen collection (oral fluid or fingerstick/blood), the HIV seropositivity among study participants and type of approach (direct assistance or unassisted). We also described the errors in performance and the number of invalids when using an HIV self-test. Quality of studies was assessed with QUADAS-2.

Definitions:

- **Direct assistance:** studies providing direct face-to-face information or support before, during or after HIVST, in addition to instructions, package inserts and support tools included in the kit
- **Unassisted:** studies where self-testers were only provided an HIVST kit information in the test kit box (e.g. instructions, package inserts) and provided numbers or links to support tool (e.g. hotline or multimedia instructions).
- HIV counselling, linkage to care and referral information were not considered as HIVST assistance.

Figure 1. General characteristics of included studies (n=14)

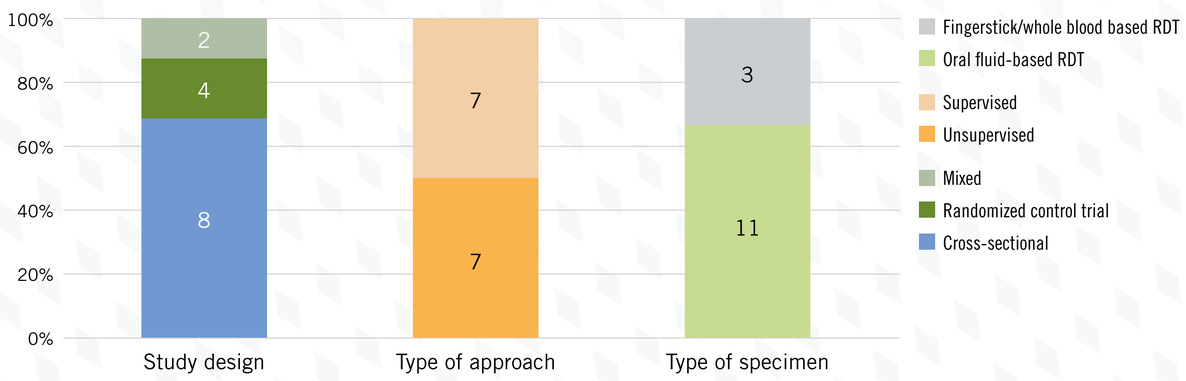
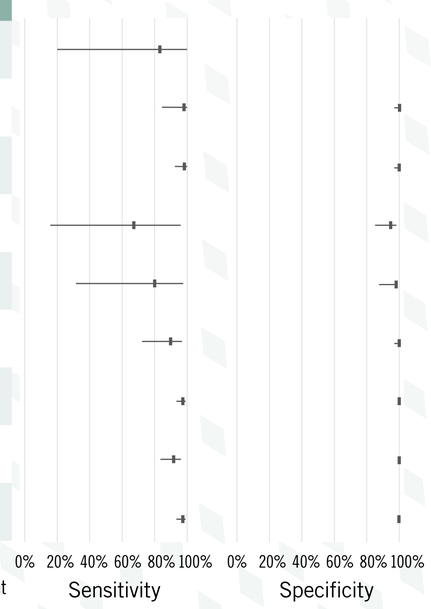


Figure 2. Sensitivity and specificity of RDTs used for self-testing with direct assistance (n=7)

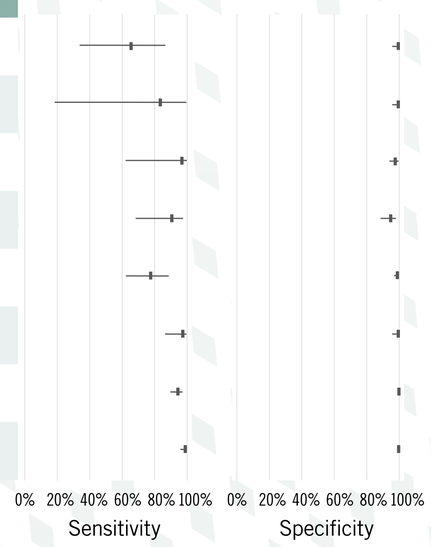
Studies	Sensitivity Estimate (CI 95%)	Specificity Estimate (CI 95%)	HIV seropositivity	Type of population	Invalids
Gras (2014)*	96.4% (84.1–99.3)	n/a	100% (40/40)	PLHIV (100%)	2/35
Dong (2014)*	97.7 (85.6–99.7)	99.5% (96.3–99.9)	18.9% (44/233)	GP (100%)	2/233
Lee (2007)*	98.8% (92.0–99.8)	99.6% (97.3–99.9)	25% (88/350)	GP (90%) and KP (10%)	197/350
Mavadzenge (2015) urban arm+	80.0% (30.9–97.3)	97.8% (86.1–99.7)	9% (16/172)	GP (100%)	5/172
Mavadzenge (2015) rural arm	66.7% (15.4–95.7)	94.7% (84.9–98.3)	8% (5/62)	GP (100%)	2/62
Kurth (2014)	89.7% (72.4–96.6)	99.4% (96.0–99.9)	14.6% (35/239)	GP (100%)	36/239
Ng (2012)	97.4% (93.9–98.9)	99.9% (99.1–99.8)	19.3% (192/994)	GP (63.7%), PLHIV (20%) and KP (16.3%)	3/983
Phase 3 OraQuick (2012)	91.7% (84.2–95.8)	100% (99.9–100)	2.12% (120/5662)	GP (86.9%) and KP (13.1%)	10/4999
Phase 2b OraQuick (2012)	97.9% (96.2–98.9)	99.8% (98.5–100)	51% (526/1031)	GP (42.,4%), PLHIV (51.3M) and KP (6.3%)	33/986



GP: general population; KP: key population (men who have sex with men, sex workers, transgender people, people who inject drug and people in prison or other closed settings); PLHIV: people living with HIV; n/a: non available; + 1 participant was on ART; All these studies are using Oral fluid-based RDT except * using Fingerstick/whole blood based RDT

Figure 3. Sensitivity and specificity of RDTs used for self-testing with unassisted approach (n=7)

Studies	Sensitivity Estimate (CI 95%)	Specificity Estimate (CI 95%)	HIV seropositivity	Type of population	Invalids
Pant Pai (2013)	65.% (33.6–89.2)	99.8% (96.8–100)	3.6% (9/249)	Health care workers (100%)	n/a
Sarkar (2015)	83.3 (19.4–99.0)	99.7% (96.1–100)	0.9% (2/202)	Pregnant women (100%)	3/202
Asiimwe (2014) arm A+	96.4% (61.6–99.8)	98.6% (93.6–99.7)	10.6% (13/123)	GP (100%)	1/123
Assimwe (2014) arm B+	90.0% (67.6–97.5)	95.1% (88.9–98.0)	16.3% (20/123)	GP (100%)	1/117
Marley (2014)	77.5% (62.1–87.9)	99.7% (97.7–100)	5.6% (13/229)	GP (29%)	n/a
Choko (2015)*	94.0% (8.9–96.6)	99.9% (99.5–100)	8.6% (141/1649)	GP (100%)	1/1649
Choko (2011)	96.9% (86.2–99.4)	99.8% (96.3–100)	16.9% (48/283)	GP (100%)	n/a
Mkwamba (2015)	99.1% (96.5–99.8)	99.9% (99.1–100)	21.9% (221/1005)	GP (100%)	n/a



GP: general population; n/a: non available; * 4 participants were on ART; + In arm A, participants were supervised by a health care worker while self-esting. In arm B, participants self-tested at home or in a convenient private location without supervision; All these studies are using Oral fluid-based RDT

RESULTS

- 14 studies were included. HIV seropositivity among participants was high (median:14.6%).
- QUADAS-2 quality critique assessment showed majority of studies were at low risk of bias and applicability.
- Most studies (n=11/14) used oral fluid-based RDTs. While there is a wide range in sensitivity estimates, only 3 studies out of 14 had a sensitivity less or equal to 80%. Specificity estimates were consistently more than 94% across all studies. Studies using blood RDTs reported higher sensitivity (96.4%-98.8%) compared to those using oral fluid-based RDTs (65%-99.1%). Studies with lower sensitivity were generally among people with known HIV status and/or using ART, and rural populations with lower literacy.
- Estimates for studies using the same oral fluid test (n=10) were 94.3% (CI 95% 90.6-96.7) sensitivity and 99.4% (CI 95% 98.6-99.8) specificity, similar to manufacturer's indications, sensitivity of 91.7% and 99.9% specificity.
- 10 studies reported user error, 1/10 used fingerstick, 8/10 used oral fluid and 1/10 used both. Common errors in test performance and conduct of test were the incorrect or incomplete swab of gums, and the inability or the misuse of the buffer; errors in performance remain the same no matter the approach.
- Studies using blood RDTs (0.86%-5.71%) had a higher proportion of invalids, compared to studies using oral-fluid RDTs (0.06%-15.1%), except for a study in Singapore with 56.3% of invalids results, where participants were not able to use a capillary tube to transfer the blood to the device.

Table 1. RDTs used for HIV self-testing and reference standard testing strategy among studies (n=14)

	Author and year of publication	Setting	HIV RDT for self-testing	Reference test procedure	Confirmatory testing aligned with WHO
1	Lee (2007)*	Singapore	Determine HIV 1/2 Abbott Laboratories, Abbott Park, IL)	Retesting and verifying participant interpreted result by a HCW	No
2	Dong (2014)*	South Africa	iCARE OneStep HIV 1/2 (JAL Innovation, Singapore)	Retesting by a HCW	Yes
3	Gras (2014)	France	INSTI HIV-1/HIV-2 Antibody Test, (bioLytical, Richmond, BC Canada)	Known PLHIV	n/a
4	Kurth (2014)	Kenya	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
5	Mavedzenge (2015) urban arm	Zimbabwe	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	RDT oral-fluid by HCW	No
	Mavedzenge (2015) rural arm	Zimbabwe	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	RDT oral-fluid by HCW	No
6	Orasure phase IIb (2012)	USA	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
	Orasure phase III (2012)	USA	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
7	Ng (2012)	Singapore	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
8	Asiimwe (2014)	Uganda	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	No
9	Choko (2015)	Malawi	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
10	Choko (2011)	Malawi	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
11	Marley (2014)	China	Aware HIV-1/2 OMT (Calypte Biotech Co, Ltd, Petchaboon,Thailand)	Retesting by a HCW	Yes
12	Pant Pai (2013)	South Africa	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
13	Sarkar (2015)	India	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes
14	Mkwamba (2015)	South Africa	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA, USA)	Retesting by a HCW	Yes

*Study used modified kits, with components from other self-test kit (Dong 2014) or adapted an approved point-of-care RDT for self-testing (Lee 2007)

LIMITATIONS

- Heterogeneous study methodologies (variability in participants, different index tests and different reference standards) made comparisons across studies difficult;
- In some studies reference testing strategy was not aligned with WHO testing guidance;
- Few studies used finger-stick/whole blood-based RDTs;
- No study provided information on persons recently or acutely infected with HIV or disaggregated data associated with participants on ART;
- One study had a 100% background of HIV seropositivity;
- Data was not disaggregated by type of population.

CONCLUSIONS

A wide range of self-testers (key populations, pregnant women, general population) are able to achieve high sensitivity and specificity with minimal errors when either direct assistance or no assistance is provided. However, instructions for use and other support tools are important and can improve performance (particularly sensitivity), especially in rural populations with lower literacy levels.

Additionally, HIVST is not advised for people with HIV with known status – particularly as many will be on ART and this can result in false-negative results. Clear messages are needed in communities where HIVST is offered to emphasize this point.

Studies using blood-based RDTs for HIVST reported both higher sensitivity and higher levels of invalid results compared to studies using oral fluid-based RDTs. Few studies used blood-based RDTs and further research is needed on how to reduce invalid results.