Poster number: THUPDC056

Considerations on the accuracy and reliability of HIV self-testing: a literature review

Carmen Figueroa[1], Cheryl Johnson[1], Thilagawathi Deivanayagam[2], Annette Verster[1], Rachel Baggaley[1]

[1]Department of HIV, World Health Organization, Geneva [2] Newcastle University, Faculty of Medical Sciences, Newcastle-upon-Tyne, United Kingdom

INTRODUCTION

HIV self-testing (HIVST) provides an opportunity for people to test themselves discreetly and conveniently, but it does not provide an HIV diagnosis. Several countries have already introduced or are considering the introduction of HIVST but there are question as to how accurate rapid diagnostic tests (RDTs) adapted for self-testing will be, particularly in the hands of untrained users. This review compiles existing evidence and reports on the accuracy of HIV RDTs used for self-testing.

METHODOLOGY

- We systematically searched electronic databases (PubMed, PopLine, EMBASE and BHIVA/CROI/EACS/IAS/NHPC conferences databases) to identify original studies reporting on the accuracy of HIV RDTS used for self-testing by intended users published between January 1995 to October 2015. References were manually searched and experts were contacted to identify other studies.
- Primary measurements of accuracy included: specificity, sensitivity, and concordance or agreement, in comparison with a reference standard testing strategy. Sensitivity and specificity were recalculated using number of true positive, false positive, false negative and true negative results, as reported by authors. We also extracted the reference standard testing strategy used and assessed its alignment with WHO recommended HIV testing strategies.
- All extracted data was analyzed by type of specimen collection (oral fluid or fingerstick/whole blood), type of approach (supervised or unsupervised) and the HIV prevalence among study participants.

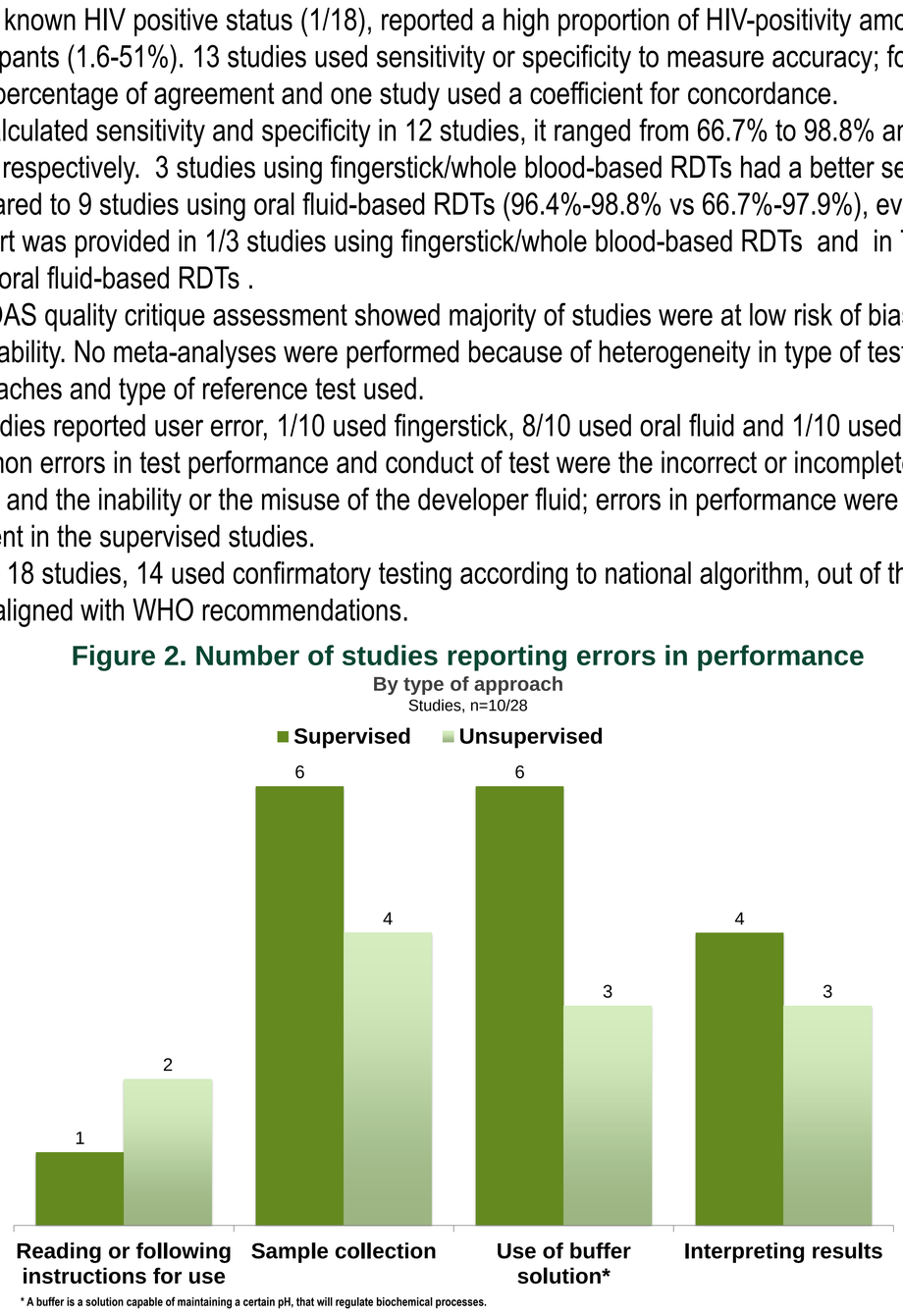
Table 1. Study characteristics (n=18)

Author and year of publication	Setting	Type of approach	Type of specimen	HIV RDT for self-testing	Reference test strategy	Confirmatory testing aligned with WHO
Choko (2011)	Malawi	Supervised	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA)	RDT blood by HCW/trained personnel	No
Choko (2015)	Malawi	Supervised	Oral fluid-based	OraQuick Advance HIV ½ (Orasure Technologies, Bethlehem, PA)	RDT blood by HCW/trained personnel	No
Marley (2014)	China	Supervised	Oral fluid-based	Aware HIV-1/2 OMT (Calypte Biotech Co., Ltd, Petchaboon,Thailand)	ELISA and Western blot	Yes
Napierala (2015)	Zimbabwe	Supervised	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA)	RDT blood by HCW/trained personnel	No
Ng (2012)	Singapore	Supervised	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA)	RDT oral-fluid by HCW	No
Phase II FDA (2012)	USA	Supervised	Oral fluid-based	OraQuick Advance HIV 1/2(Orasure Technologies, Bethlehem, PA)	RDT oral-fluid by HCW	No
Wang (2015)	China	Supervised	Oral fluid-based	Aware HIV-1/2 OMT (Calypte Biotech Co., Ltd, Petchaboon,Thailand)	ELISA and Western blot	Yes
Lee (2007)	Singapore	Supervised	Blood-based	Determine HIV 1/2 Ag/Ab Combo (Alere Medical, Matsudo-shi, Japan): specially adapted for the study	RDT blood by HCW/trained personnel	No
Prazuck (Under review)	France	Supervised	Blood-based	Autotest VIH finger stick-whole blood HIV test, (AAZ-LMB, Cedex France)	n/a	n/a
Kurth (2014)	Kenya	Unsupervised	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA)	ELISA and RDT blood	Yes
Nour (2012)	USA	Unsupervised	Oral fluid-based	OraQuick Advance HIV 1/2(Orasure Technologies, Bethlehem, PA)	RDT oral-fluid by HCW	No
Pant Pai (2014)	Canada	Unsupervised	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA), before FDA approval	n/a	n/a
Phase III FDA (2012)	USA	Unsupervised	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure, Bethlehem, PA)	Western-Blot and EIA	Yes
Gaydos (2011)	USA	Unsupervised	Both	OraQuick Advance HIV 1/2 (Orasure Technologies, Bethlehem, PA) or Uni-Gold Recombigen HIV-1/2 (Trinity Biotech, Wicklow, Ireland)	RDT oral-fluid by HCW	No
Dong (2014)	South Africa	Unsupervised	Blood-based	iCARE OneStep HIV1/2 (JAL Innovation, Singapore): specially adapted for the study	ELISA and RDT blood	Yes
Gras (2014)	France	Unsupervised	Blood-based	INSTI HIV 1/2 Test, (Bio Lytical, Richmond, BC Canada)	n/a	n/a
Asiimwe (2014)	Uganda	Both	Oral fluid-based	OraQuick Advance HIV 1/2 (Orasure, Bethlehem, PA)	RDT blood by HCW/trained personnel	No
de la Fuente (2012)	Spain	Both	Blood-based	Determine HIV 1/2 Ag/Ab Combo (Alere Medical, Matsudo-shi, Japan)	n/a	n/a

RESULTS

- We included 18 studies; 12 studies used oral fluid-based RDTs, five studies used fingerstick/whole blood-based RDTs and one used both. Most studies (12/18), excluding those among participants with a known HIV positive status (1/18), reported a high proportion of HIV-positivity among study participants (1.6-51%). 13 studies used sensitivity or specificity to measure accuracy; four studies used percentage of agreement and one study used a coefficient for concordance.
- We calculated sensitivity and specificity in 12 studies, it ranged from 66.7% to 98.8% and 94.7% to 100% respectively. 3 studies using fingerstick/whole blood-based RDTs had a better sensitivity compared to 9 studies using oral fluid-based RDTs (96.4%-98.8% vs 66.7%-97.9%), even when support was provided in 1/3 studies using fingerstick/whole blood-based RDTs and in 7/9 studies using oral fluid-based RDTs .
- QUADAS quality critique assessment showed majority of studies were at low risk of bias and applicability. No meta-analyses were performed because of heterogeneity in type of tests, type of approaches and type of reference test used.
- 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 developer fluid; errors in performance were more frequent in the supervised studies.
- Of the 18 studies, 14 used confirmatory testing according to national algorithm, out of this, only five were aligned with WHO recommendations.

Figure 2. Number of studies reporting errors in performance

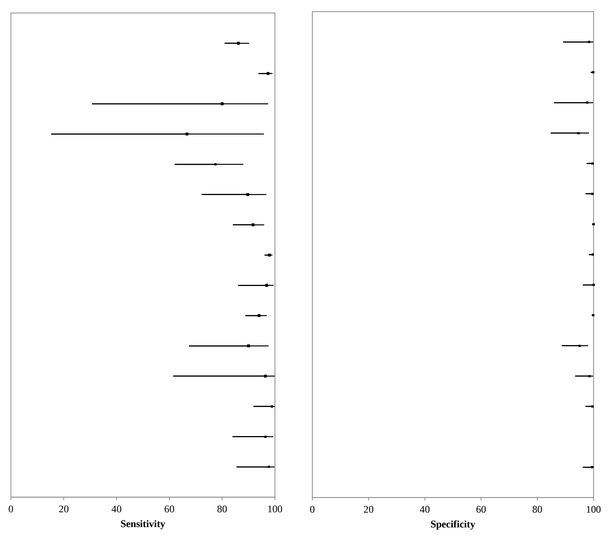


LIMITATIONS

- Heterogeneous study methodologies;
- Errors not affecting sensitivity or specificity, such as invalid test results, were not fully analyzed;
- Different reference standard testing strategies, settings and assays were used**—few of which aligned with WHO recommendations;**
- Few studies used finger-stick/whole blood-based RDTs; and
- HIV prevalence could not be assessed in real-world setting, as some studies were among only HIV-positive participants who knew their status.

Fig. 1. Forest plots of recalculated sensitivity and specificity of HIV RDTs for self-testing

	Studies	Sensitivity Estimate (CI 95%)	Specificity Estimate (CI 95%)	HIV Prevalence
Oral fluid-based	Wang (2015)*	86.0% (81.1 - 95.6)	98.2% (97.8 - 98.5)	n/a
	Ng (2012)	97.4% (93.9 - 98.9)	99.9% (99.1 - 100)	19.3% (192/994)
	Napierala-urban (2015)	80.0% (30.9 - 97.3)	97.8% (86.1 - 99.7)	9% (16/172)
	Napierala-rural (2015)	66.7% (15.4 - 95.7)	94.7% (84.9 - 98.3)	8% (5/62)
	Marley (2014)	77.5% (62.1 - 87.9)	99.7% (97.7 - 100)	5.6% (13/229)
	Kurth (2015)	89.7% (72.4 - 96.6)	99.4% (96.0 - 99.9)	14.6% (35/239)
	FDA III (2012)	91.7% (84.2 - 95.8)	100% (99.9 - 100)	2.12%(120/5662)
	FDA II (2012)	97.9% (96.2 - 98.9)	99.8% (98.5 - 100)	51% (526/1031)
	Choko (2011)	96.9% (86.2 - 99.4)	99.8% (96.3 - 100)	16.9% (48/283)
	Choko (2015)	94.0% (88.9 - 96.8)	99.9% (99.5 - 100)	8.6% (141/1649)
	Asiimwe-unsupervised (2014)	90.0% (67.6 - 97.5)	95.1% (88.9 - 98.0)	13.4% (33/246)
	Asiimwe-supervised (2014)	96.4% (61.6 - 99.8)	98.6% (93.6 - 99.7)	10.6% (13/123)
Finger-stick/whole blood-based	Lee (2007)	98.8% (92.0 - 99.8)	99.6% (97.3 - 99.9)	25% (88/350)
	Gras (2014)	96.4% (84.1 - 99.3)	n/a	100% (40/40)
	Dong (2014)	97.7% (85.6 - 99.7)	99.5% (96.3 - 99.9)	18.9% (44/233)



Sensitivity and specificity estimates may differ from what studies reported. * Sensitivity and specificity reported in the study. n/a: non available.

CONCLUSIONS

- Accuracy of HIV RDTs used for self-testing can be as high as 98.8% sensitivity and 100% specificity, but not always depending on RDT, population and setting.
- Inappropriate products, poor or no instructions for use can result in a poorer accuracy and a high level of user errors reported.
- Particular users, such as known HIV positives on ART and people with low literacy, might need more support and information when self-testing.