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Performance of Determine Combo and other Point-of-Care HIV Tests Among Seattle MSM

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ABSTRACT

Objective:
The Rapid Test Study was a real-time comparison of point-of-care (POC) HIV tests designed to determine their relative abilities to detect early HIV infection.

Methods:
HIV-negative MSM and transgender persons were recruited at the Public Health - Seattle & King County STD Clinic, Gay City Health Project, and University of Washington Primary Infection Clinic. Study procedures included one POC test performed on oral fluids (OraQuick) and POC tests performed on fingerstick whole blood specimens: OraQuick, Uni-Gold Recombigen HIV Test, Determine HIV-1/2 Ag/Ab Combo, and INSTI HIV-1/HIV-2 Rapid Antibody Test. Serum specimens from subjects with negative POC results were sent for EIA and pooled NAAT. McNemar's exact tests were used to compare the numbers of HIV-infected subjects detected by the different tests.

Results:
Between February 2010 and August 2014, 3438 subjects were enrolled (Table). Twenty-four subjects had discordant POC results with at least one reactive and one non-reactive POC test, including one subject with a reactive Determine p24 antigen and an HIV RNA level of 5.8 million copies/mL. This subject represented 9% of the 11 cases of acute (RNA+) and early (EIA+) HIV infection diagnosed at the three sites who were screened prospectively by Determine. OraQuick performed on oral fluids identified fewer men with discordant results compared to all fingerstick tests. OraQuick performed on fingerstick also identified significantly fewer men with discordant results compared to the Determine antibody test component (p=.008) and the overall Combo (p=.004), and there was a trend when compared to INSTI (p=.06).

There were 21 (1.0%) false-positive test results in 2121 visits among HIV-negative persons screened at the STD Clinic. False-positive results were obtained for three participants tested by OraQuick performed on oral fluids (specificity 99.9%), six participants on the Determine Combo antigen and nine on the antibody (combined specificity 99.0%), and four by EIA (specificity 99.8%).

Conclusion:
As reported by others, Determine underperforms compared to laboratory-based testing for acute HIV infection, but it detected more persons with early HIV infection compared to other one commonly used fingerstick test. The lower specificity of Determine may limit its usefulness in populations with lower HIV incidence.

BACKGROUND

2003: • Public Health – Seattle & King County (PHSKC) starts pooled nucleic acid amplification testing (NAAT) program for MSM
2009: • OraQuick detects ~80% of HIV-infected MSM tested
• repeat testing of frozen specimens differs from real time results
• unclear if other POC tests better able to detect early infection

OBJECTIVE

To compare point-of-care HIV tests and determine their relative abilities to detect early HIV infection in real time.

METHODS

Study population
MSM and transgender persons recruited when seeking HIV testing at:
PHSKC STD Clinic
Gay City Health Project Wellness Center (GC)
Or when referred to University of Washington Primary Infection Clinic (PIC)

HIV tests
Point of care tests
OraQuick (oral fluids, OraSure Technologies, Inc)
OraQuick (fingerstick)
Uni-Gold (fingerstick, Trinity Biotech) until 5/2013
INSTI (fingerstick, BioLytical) after 5/2013
Determine HIV-1/2 Ag/Ab Combo (fingerstick, Alere Inc.)
EIA
PHSKC: 3rd gen Genetic Systems HIV-1/HIV-2 Plus O EIA Bio-Rad
PIC: 3rd gen GS assay until May 2011, then
4th gen Abbott ARCHITECT HIV Ag/Ab Combo assay
NAAT
PHSKC: 27-specimen master pools (3x3x3 matrix)
Abbott RealTime HIV-1 RNA assay (lower limit 40 copies/mL)

METHODS (continued)

Data collection and statistical analyses
- Each test performed on separate fingersticks
- Quarterly participation allowed, longitudinal participation allowed at PIC
- $20 compensation
- Approved by UW Human Subject Division and all subjects gave verbal informed consent
- Chart reviews conducted for all participants with discordant results
- McNemar's exact tests used to compare numbers of cases detected
- Sensitivity and specificity calculated for STD participants only
- Fiebig staging characterized for PIC subjects only

HIV TEST RESULTS

Overall HIV Test Results among 3438 MSM and transgender persons, 2/2010 – 8/2014

	STD Clinic n=2189	Gay City n=1215	PIC n=34	Total n=3438
HIV-Negative	2121	1176	1	3298
Total HIV Positive	68 (3.2%)	39 (3.2%)	33	140
Concordant Reactive POC Tests	51 (75.0%)	31 (79.5%)	18	100
Discordant POC AntibodyTests	7 (10.3%)	3 (7.6%)	13	23
All POC Tests Negative / EIA Positive	2 (2.9%)	4 (17.9%)	0	6[1]
Acute (EIA Neg / NAAT Pos)	8 (11.9%)	1 (2.6%)	2	11[2]

[1]Includes 5 persons tested by Determine Combo
[2]Includes 1 person with reactive p24 Ag on Determine (#1 below) among 6 persons tested

Sensitivity and specificity of screening HIV tests at the PHSKC STD Clinic

	Number of tests	Sensitivity (95% CI)	Specificity (95% CI)
OraQuick (oral fluid)	2180	51/68 = 75.0% (63.0-84.7)	2109/2112 = 99.86% (99.59-99.97)
OraQuick (fingerstick)	2175	53/68 = 77.9% (66.2-87.1)	2107/2107 = 100% (99.82-100)
Uni-Gold	1614	45/53 = 84.9% (72.4-93.3)	1561/1561 = 100% (99.76-100)
INSTI	559	11/15 = 73.3% (44.9-92.2)	543/544 = 99.82% (98.98-100)
Determine Combo	1523	34/40 = 84.6% (70.2-94.3)	1468/1483 = 98.99% (98.34-99.43)
GS HIV-1/HIV-2 Plus O Ab (EIA)	2161	58/66 = 87.9% (77.5-94.6)	2091/2095 = 99.81% (99.51-99.95)

Statistical Comparisons:

OraQuick OF versus:	
OraQuick FS	p=.0002
Uni-Gold	p=.006
INSTI	p=.002
Determine Ag/Ab	p=.0001
OraQuick FS versus	
Uni-Gold	p=.7
INSTI	p=.06
Determine Ab	p=.008
Determine Ag/Ab	p=.004
Determine Ag/Ab versus 3rd gen EIA	p=.2

Test results of PIC subjects[1] by Fiebig stage

Fiebig stage		n (%) with positive test				
		OraQuick OF n=38	OraQuick FS n=41	Uni-Gold n=24	INSTI n=13	Determine Combo n=33
I/II[2]	n=5	0/4 (0)	0/5 (0)	0/2 (0)	0/2 (0)	0/3 (0)
II	n=1	0/1 (0)	0/1 (0)	0/1 (0)	-	0/1 (0)
III	n=4	0/3 (0)	1/4 (25)	-	1/2 (50)	1/3 (33)
IV	n=4	0/3 (0)	2/4 (50)	0/1 (0)	2/2 (100)	3/3 (100)
V	n=17	9/17 (53)	15/17 (88)	11/11 (100)	6/6 (100)	16/16 (100)
VI	n=10	9/10 (90)	10/10 (100)	9/9 (100)	1/1 (100)	7/7 (100)

[1]Includes research test results for 5 persons seen initially at other sites and clinical test results of 3 additional persons later seen as PIC subjects.
[2]Specimen not available for discriminatory testing.

HIV tests results among 24 HIV-positive participants with discordant results

	Last neg HIV test	OraQuick OF	OraQuick FS	Uni-Gold	INSTI	Determine Ag/Ab	3rd or 4th gen EIA	WB results	HIV RNA (copies/mL)
1	2mo	—	—	—	ND	+/—	3rd —	negative	5.8 million
2	4yr	+	+	—	ND	ND	3rd +	24, 31, 40, 55, 120	141,000
3	2yr	—	+	+	ND	ND	3rd +	24, 31, 40, 55, 160	128,000
4	2yr	—	+	+	ND	ND	3rd +	18, 24, 31, 40, 51, 55, 120, 160	25,000
5	NA	—	—	+	ND	ND	3rd +	24, 51, 55, 160	12.8 million
6	NA	—	—	+	ND	—/+	3rd +	24, 40, 55, 160	21,000
7	1yr	—	+	—	ND	—/+	4th Ab+	24, 51, 55	719,000
8	1yr	—	+	+	ND	—/+	4th Ab+	24, 31, 55, 160	436,000
9	6mo	—	+	+	ND	—/+	4th Ab+	24, 55, 160	33,000
10	2mo	—	+	+	ND	—/+	4th Ab+	24, 55, 160	9000
11	3mo	—	+	+	ND	—/+	4th Ab+	18, 24, 55, 160	32,000
12	2mo	—	+	+	ND	—/+	4th Ab+	24, 160	94,000
13	2mo	—	—	+	ND	—/+	3rd +	18, 24, 31, 41, 51, 55, 65, 120, 160	ND
14	2yr	—	—	+	ND	—/+	3rd +	18, 24, 31, 40, 51, 55, 65, 120, 160	ND
15	4mo	—	—	ND	+	—/+	3rd +	24, 55, 160	ND
16	3mo	—	—	ND	+	—/+	3rd +	24, 51, 55, 160	347,000
17	7mo	—	—	ND	+	—/+	3rd +	18, 24, 65, 160	110,000
18	5mo	—	—	ND	+	—/+	3rd +	24, 51, 55, 160	62,000
19	4mo	—	+	ND	+	—/+	3rd +	18, 24, 31, 41, 51, 55, 65, 120, 160	7000
20	8mo	—	+	ND	+	—/+	4th Ab+	24, 51, 55, 65, 120, 160	70,000
21	NA	—	+	ND	+	—/+	4th Ab+	24, 55, 160	7000
22	2mo	—	+	ND	+	—/+	4th Ab+	negative	323,000
23	2mo	—	+	ND	+	—/+	4th Ab+	160	316,000
24	NA	—	—	ND	+	—/+	4th Ag+	24	4.4 million

ND: not done; NA: results not available

LIMITATIONS

- Findings may not be generalizable to populations with lower HIV prevalence and incidence and less frequent HIV testing.
- Participants were not all tested with the same array of tests.
- Tests are not independently read and may overestimate sensitivity.

CONCLUSIONS

1) Oral fluid testing, although preferred as a specimen collection method, is less trusted among tested MSM, is significantly less sensitive than fingerstick tests, and should be the test method of choice only in rare circumstances.
2) Determine Combo underperforms compared to laboratory-based testing but did detect one acute infection. If these results are validated, the lower specificity may limit its usefulness in populations with lower incidence.
3) In high HIV incidence populations like ours, currently approved point-of-care tests are not sufficient and must be supplemented with pooled NAAT or 4th generation assays.
4) This HIV testing program for MSM is one example of a setting that could benefit from FDA approval of POC NAAT.

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Determine Combo was not FDA-approved at the start of this study and was provided by the manufacturer for investigational use beginning 10 months after the start of enrollment. During the course of this study, the manufacturer changed their production procedures for devices distributed in the U.S.