Performance evaluation of four point-of-care HIV tests using unprocessed specimens: baseline data from Project DETECT

Pollyanna Chavez, PhD[a], Heather Bradley PhD[a], Laura Wesolowski, PhD[a], Lauren Violette, MPH[b], David Katz[b], PhD, Lisa Niemann, MSW, MPH[b], Vanessa McMahan MS[b], Andy Cornelius-Hudson[b], George Ure II [b], Steve Ethridge BS MT (ASCP)[a], Joanne Stekler, MD, MPH[b], Kevin Delaney, PhD[a]
[a] Centers for Disease Control and Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention, Atlanta, GA. [b] University of Washington, Seattle, WA.

Background

Point-of-care (POC) HIV tests are useful to improve receipt of results and in settings where more sensitive laboratory testing is not possible. Recently approved POC HIV tests that aim to identify infection earlier are in need of performance evaluations using unprocessed specimens.

We analyzed baseline data from "Diagnostic Evaluation to Expand Critical Testing Technologies" (Project DETECT), to evaluate the performance of POC HIV tests using venous whole blood (WB) and oral fluid (OF).

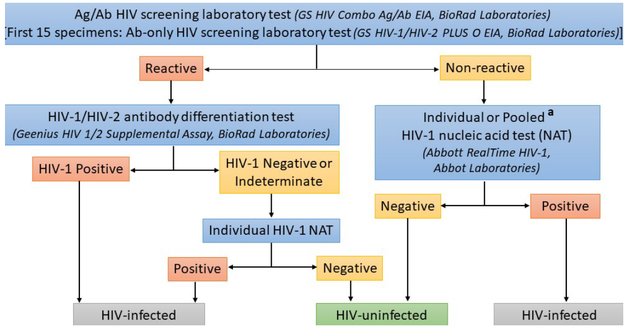
Methods

From 9/2015- 9/2017, we invited into Project DETECT: (1) Persons at-risk for HIV infection seeking HIV testing at a public health STD clinic in Seattle; (2) Persons with recent HIV diagnosis, including persons with acute HIV infection (AHI), or on antiretroviral therapy (ART) at referral sites.

Baseline visit: Participants' ART and pre-exposure prophylaxis (PrEP) use was recorded. They were tested with 4 POC tests using WB and 2 tests using OF (Table 1). Additional plasma/serum were processed for lab testing (Fig.)

- HIV-uninfected participants were allowed to re-enroll every 3 months.
- Sensitivity and specificity of the POC tests with exact 95% confidence intervals (CI) were calculated based on participant's HIV status (Fig).

Figure. Algorithm used to determine participant's HIV status at time of visit



Abbreviations: Ag/Ab, antigen/antibody; Ab, antibody; NAT, nucleic acid test.
Footnotes: [a] Individual NAT performed when there was a recorded positive HIV test result. Pooled NAT was done on 27–member pools and after 10/12/2015 on 10-member pools.
Exceptions: 3 specimens with non-reactive Ag/Ab result, missing NAT → HIV-uninfected.
1 specimen missing screening test and with negative pooled NAT → HIV-uninfected.
1 specimen missing screening test and with positive Geenius → HIV-infected.

Results

Table 1. Sensitivity and specificity of POC screening HIV tests, Project DETECT, September 2015 – September 2017

POC test and specimen type	HIV-infected participants				Specimens [b] from HIV-uninfected participants [c]					
	All (n=179)		Excluding those with AHI [a] (n=173)		All (n=1077)		Not on PrEP (n=872)		Currently on PrEP (n=155)	
	TP	Sensitivity % (95% CI)	TP	Sensitivity % (95% CI)	TN	Specificity % (95% CI)	TN	Specificity % (95% CI)	TN	Specificity % (95% CI)
DPP OF	161	89.94 (84.57- 93.93)	161	93.06 (88.20-96.36)	1077	100 (99.66-100.00)	872	100 (99.58-100.00)	155	100 (97.65-100.00)
DPP WB	171	95.53 (91.38-98.05)	171	98.84 (95.89-99.86)	1077	100 (99.66-100.00)	872	100 (99.58-100.00)	155	100 (97.65-100.00)
OQ OF	165	92.18 (87.23-95.66)	165	95.38 (91.09-97.98)	1076	99.91 (99.48-100.00)	871	99.89 (99.36-100.00)	155	100 (97.65-100.00)
OQ WB	172	96.09 (92.11-98.41)	172	99.42 (96.82-99.99)	1077	100 (99.66-100.00)	872	100 (99.58-100.00)	155	100 (97.65-100.00)
INSTI WB	173	96.65 (92.85-98.76)	172	99.42 (96.82-99.99)	1075	99.81 (99.33-99.98)	870	99.77 (99.17-99.97)	155	100 (97.65-100.00)
DET WB	174	97.21 (93.60-99.09)	172	99.42 (96.82-99.99)	1071	99.44 (98.79-99.80)	869	99.66 (99.00-99.93)	153	98.71 (95.42-99.84)

Abbreviations: POC, point of care; AHI, acute HIV infection; PrEP, pre-exposure prophylaxis; TP, true positive; TN, true negative; OF, oral fluid; WB, venous whole blood; DPP, DPP HIV1/2 Assay (Chembio Diagnostics System, Inc.); OQ, OraQuick Advance HIV-1/2 (OraSure Technologies); INSTI, INSTI HIV-1/HIV-2 Rapid Antibody Test (bioLytical Laboratories Inc.); DET, Determine HIV-1/2 Ag/Ab Combo (Abbott Laboratories).

Footnotes: [a] Reactive Ag/Ab + Negative or Indeterminate Geenius + positive NAT →AHI. Non-reactive or missing Ag/Ab results + positive individual or pooled NAT →AHI.
[b] HIV-uninfected participants could have provided more than one specimen. [c] 50 specimens were missing data about PrEP use.

Table 2. Comparison of the sensitivity of POC screening tests when used with OF versus WB among HIV-infected specimens by participant's ART status [a]

ART Status	POC test	OF specimens		WB specimens		p-value [b]
		TP	Sensitivity % (95% CI)	TP	Sensitivity % (95% CI)	
On ART (n=120)	DPP	109	90.83 (84.19-95.33)	118	98.33 (94.11-99.80)	**0.003**
	OQ	112	93.33 (87.29-97.08)	119	99.17 (95.44-99.98)	**0.008**
Not on ART (n=56)	DPP	49	87.50 (75.93-94.82)	50	89.29 (78.12-95.97)	0.32
	OQ	50	89.29 (78.12-95.97)	50	89.29 (78.12-95.97)	>0.99

Abbreviations Table 2 and 3: POC, point of care; ART, antiretroviral therapy; OF, oral fluid; WB, venous whole blood; TP, true positive; DPP, DPP HIV1/2 Assay; OQ, OraQuick Advance HIV-1/2; INSTI, INSTI HIV-1/HIV-2 Rapid Antibody Test; DET, Determine HIV-1/2 Ag/Ab Combo; PrEP, pre-exposure prophylaxis; N, Negative; P; Positive; Ag, Antigen; Ab, Antibody, AHI, acute HIV infection, EIA, Ag/Ab screening lab test; NAT, nucleic acid test.

Footnotes Table 2 and 3:
[a] Of the 179 HIV infected specimens, 31.3 % (56/179) were not in treatment, 67% (120/179) were in treatment, and 1.67% (3/179) were missing treatment data.
[b] Comparison between oral fluid and whole blood using McNemar's test.
[c] Overall result of Determine antigen and antibody lines. If either was reactive, the overall result was considered positive.

Table 3. Line list of participants with false-negative or false-positive POC results

HIV Infection	ART/PrEP status	DPP OF	DPP WB	OQ OF	OQ WB	INSTI	DET[c]	*DET Ag*	*DET Ab*	*EIA*	*NAT*
Infected, AHI	Currently on ART	N	N	N	N	P	N	*N*	*N*	P	P
Infected, AHI	Not on ART	N	N	N	N	N	N	*N*	*N*	N	P
Infected, AHI	Not on ART	N	N	N	N	N	N	*N*	*N*	P	P
Infected, AHI	Not on ART	N	N	N	N	N	N	*N*	*N*	N	P
Infected, AHI	Not on ART	N	N	N	N	N	P	*P*	*N*	-	P
Infected, AHI	Not on ART	N	N	N	N	N	P	*P*	*P*	P	P
Infected	Currently on ART	N	P	N	P	P	P	*N*	*P*	P	P
Infected	Currently on ART	N	P	N	P	P	P	*N*	*P*	P	P
Infected	Currently on ART	N	P	P	P	P	P	*N*	*P*	P	P
Infected	Not on ART	N	P	N	P	P	P	*P*	*P*	P	P
Infected	Currently on ART	N	P	N	P	P	P	*N*	*P*	P	P
Infected	Currently on ART	N	P	N	P	P	P	*N*	*P*	P	N
Infected	Currently on ART	N	P	N	P	P	P	*N*	*P*	P	N
Infected	Currently on ART	N	P	N	P	P	P	*N*	*P*	P	N
Infected	Currently on ART	N	N	N	P	P	P	*N*	*P*	P	P
Infected	Currently on ART	N	P	P	P	P	P	*N*	*P*	P	N
Infected	Currently on ART	N	P	P	P	P	P	*N*	*P*	P	P
Infected	Not on ART	N	N	P	N	N	N	*N*	*N*	P	P
Uninfected	Missing	N	N	N	N	N	P	*N*	*P*	-	N
Uninfected	Not on PrEP	N	N	N	N	N	P	*N*	*P*	N	N
Uninfected	Currently on PrEP	N	N	N	N	N	P	*P*	*N*	N	N
Uninfected	Not on PrEP	N	N	N	N	N	P	*P*	*N*	N	N
Uninfected	Currently on PrEP	N	N	N	N	N	P	*P*	*N*	N	N
Uninfected	Not on PrEP	N	N	N	N	N	P	*P*	*N*	N	N
Uninfected	Not on PrEP	N	N	N	N	P	N	*N*	*N*	N	N
Uninfected	Not on PrEP	N	N	N	N	P	N	*N*	*N*	N	N
Uninfected	Not on PrEP	N	N	P	N	N	N	*N*	*N*	N	N

Results

Four participants missing WB POC tests → excluded from analysis.

Analytic sample: 1,004 participants contributed 1,256 visits.

Sensitivity:

- 179 HIV-infected participants: six with AHI and 120 on ART.
- Sensitivity of POC WB tests was high (>95%) and similar (>0.05).
- Sensitivity was significantly higher when using WB compared to using OF for DPP (p=0.0016) and OQ (p=0.0196).
- For all tests, sensitivity point estimates were higher when excluding specimens from participants with AHI. (Table 1)
- ART did not lower the sensitivity of the WB POC tests (p>0.3; data not shown). However, sensitivity was lower when using OF than WB among persons on ART. (Table 2)
- DET and INSTI were able to identify AHI (2 and 1, respectively) missed by other POC tests. (Table 3)

Specificity

- 826 HIV-uninfected participants contributed 1077 visits.
- Specificity was high (>99%) for all tests. DET had a significantly lower specificity than DPP OF, DPP WB, and OQ WB (all p values = 0.014).
- PrEP use did not seem to affect the specificity of the tests (p>0.05).
- No specimen tested false-positive on > 1 test (Table 3).

Conclusions

These POC HIV tests displayed high sensitivity and specificity when conducted with unprocessed specimens, including when used with participants taking PrEP, supporting their effectiveness in identifying infections in settings where laboratory–based testing is not feasible.

However the possibility of missed acute infections or false results indicates the need to address their occurrence, including resolving false-negative results by reviewing exposure risk and retesting or resolving false-positive results with additional HIV testing onsite (using a different rapid HIV test) or confirmatory laboratory testing.

Contact Info

Pollyanna Chavez, PhD
geo5@cdc.gov
404.639.1742