Automated Oral Fluid-Based HIV Testing in Screening Programmes: *Automatic for the People?*

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Oral fluid based HIV testing: The global perspective

- First commercial oral fluid based kits available from 2004
- Only FDA licensed product: Orasure Oraquick Advance® (POCT)
- Oral fluid based HIV testing has been used in several settings, particularly in non-specialist, community and other settings
- Highly acceptable to patients

Performance of OraSure®

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Sensitivity of Five Rapid HIV Tests on Oral Fluid or Finger-Stick Whole Blood: A Real-Time Comparison in a Healthcare Setting

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Abstract

Background: Health authorities in several countries recently recommended the expansion of human immunodeficiency virus (HIV) antibody testing, including the use of rapid tests. Several HIV rapid tests are now licensed in Europe but their sensitivity on total blood and/or oral fluid in routine healthcare settings is not known.

Methods and Findings: 200 adults with documented HIV-1 (n = 194) or HIV-2 infection (n = 6) were prospectively screened with five HIV rapid tests using either oral fluid (OF) or finger-stick whole blood (FSB). The OraQuick Advance rapid HIV1/2® was first applied to OF and then to FSB, while the other tests were applied to FSB, in the following order: Vikia HIV 1/2®, Determine HIV 1–2®, Determine® HIV-1/2 Ag/Ab Combo® and INSTI HIV-1/HIV-2®. Tests negative on FSB were repeated on paired serum samples. Twenty randomly selected HIV-seronegative subjects served as controls, and the results were read blindly. Most patients had HIV-1 subtype B infection (63.3%) and most were on antiretroviral therapy (68.5%). Sensitivity was 86.5%, 94.5%, 98.5%, 94.9%, 95.8% and 99% respectively, with OraQuick OF, OraQuick FSB, Vikia, Determine, Determine Ag/Ab Combo and INSTI ($p<0.0001$). OraQuick was less sensitive on OF than on FSB ($p = 0.008$). Among the six patients with three or more negative tests, two had recent HIV infection and four patients on antiretroviral therapy had undetectable plasma viral load. When patients positive in all the tests were compared with patients who had at least one negative test, only a plasma HIV RNA level <200 cp/ml was significantly associated with a false-negative result ($p = 0.009$). When the 33 rapid tests negative on FSB were repeated on serum, all but six (5 negative with OraQuick, 1 with INSTI) were positive. The sensitivity of OraQuick, Determine and Determine Ag/Ab Combo was significantly better on serum than on FSB (97.5%, $p = 0.04$; 100%, $p = 0.004$; and 100%, $p = 0.02$, respectively).

Conclusion: When evaluated in a healthcare setting, rapid HIV tests were less sensitive on oral fluid than on finger-stick whole blood and less sensitive on finger-stick whole blood than on serum.

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Introduction

Late diagnosis of human immunodeficiency virus (HIV) infection, resulting in delayed patient management, is associated with poorer survival [1]. About one-third of new diagnoses in industrialized countries are made when the patient is already severely immunosuppressed [2,3], while in developing countries more than 80% of patients are diagnosed at an advanced clinical stage [4,5]. In the United States, the Centers for Diseases Control and Prevention have recommended extending HIV antibody testing to people aged 13–64 years [6]. Such a program would be implemented in a variety of healthcare settings, such as hospital emergency departments, and could involve disposable rapid HIV diagnostic tests, the patient receiving the necessary information at the same site [6]. Such HIV rapid tests use finger-stick capillary whole blood (FSB) or oral fluid (OF), thus avoiding the need for venous blood sampling and centrifugation.

Medical laboratories have been using these rapid tests for more than two decades to test serum and plasma, particularly in developing countries and for emergency diagnosis [7]. They are simple to use but lack sensitivity relative to reference enzyme immunoassays (EIA), particularly during primary HIV infection and infection by variant strains [8].

In the EU, these tests must first undergo validation studies of sensitivity and specificity against panels of frozen sera or plasma

Pavie, *PLoS One*, 2010

Head-to-head comparison of accuracy of a rapid point-of-care HIV test with oral versus whole-blood specimens: a systematic review and meta-analysis

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Summary

Background The focus on prevention strategies aimed at curbing the HIV epidemic is growing, and therefore screening for HIV has again taken centre stage. Our aim was to establish whether a convenient, non-invasive, HIV test that uses oral fluid was accurate by comparison with the same test with blood-based specimens.

Methods We did a systematic review and meta-analysis to compare the diagnostic accuracy of a rapid HIV-antibody-based point-of-care test (Oraquick advance rapid HIV-1/2, OraSure Technologies Inc, PA, USA) when used with oral versus blood-based specimens in adults. We searched five databases of published work and databases of five key HIV conferences. Studies we deemed eligible were those focused on adults at risk of HIV; we excluded studies in children, in co-infected populations, with self-reported inferior reference standards, and with incomplete reporting of key data items. We assessed the diagnostic accuracy of testing with oral and blood-based specimens with bivariate regression analysis. We computed positive predictive values (PPVs) in high-prevalence and low-prevalence settings with Bayesian methods.

Findings In a direct head-to-head comparison of studies, we identified a pooled sensitivity about 2% lower in oral (98·03%, 95% CI 95·85–99·08) than in blood-based specimens (99·68%, 97·31–99·96), but similar specificity (oral 99·74%, 99·47–99·88; blood 99·91%, 99·84–99·95). Negative likelihood ratios were small and similar (oral 0·019, 0·009–0·040; blood 0·003, 0·001–0·034), but positive likelihood ratios differed (oral 383·37, 183·87–799·31; blood 1105·16, 633·14–2004·37). Although in high-prevalence settings PPVs were similar (oral 98·65%, 95% credible interval 85·71–99·94; blood 98·50, 93·10–99·79), in low-prevalence settings PPVs were lower for oral (88·55%, 77·31–95·87) than blood (97·65%, 95·48–99·09) specimens.

Interpretation Although Oraquick had a high PPV in high-prevalence settings in oral specimens, the slightly lower sensitivity and PPV in low-prevalence settings in oral specimens should be carefully reviewed when planning worldwide expanded initiatives with this popular test.

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Introduction

In 2004, a rapid HIV-antibody-based point-of-care test (Oraquick advance rapid HIV-1/2, OraSure Technologies Inc, PA, USA), initially approved for finger-stick, whole-blood, and plasma specimens, was approved by the US Food and Drug Administration (FDA) as a Clinical Laboratory Improvement Amendments waived test for use with specimens of oral mucosal transudate. Since 2006, with the widespread expansion of HIV testing in the USA, and with the possible expansion of home-based and new supervised self-testing initiatives in sub-Saharan Africa, this HIV test has become one of the most popular point-of-care tests based on oral specimens.[1,3] It is more acceptable to patients because of its non-invasive and pain-free specimen collection and its rapid turnaround time.[4,5] In Kenya and Uganda, an increased acceptance and preference for this test has helped improve the uptake of home-based HIV-testing initiatives.[7,8] The Kenyan Government also announced an expansion of bold and controversial self-testing initiatives for HIV, and is reviewing the possible approval of oral tests. Self-testing initiatives are also relevant for southern Africa, a region that has remained the epidemiological locus of the epidemic; countries such as Botswana, Lesotho, Mozambique, South Africa, Swaziland, Zambia, and Zimbabwe are focused on scaling up alternative HIV-screening programmes.

Oraquick is also being considered for potential use as an over-the-counter test in the USA and in many sub-Saharan countries. This move might revolutionise HIV testing by offering a proactive testing option to people who, because of stigma, do not wish to attend public health centres for testing. Hopefully, offering a confidential testing option will bring an end to the stigmatisation associated with HIV testing.[9] Although performance data are available on this test from the USA, there has not been a review of its worldwide accuracy. With optimistic developments in HIV aimed at eradicating infection, worldwide expansion of HIV-testing programmes has taken centre stage because testing is the cornerstone of care and treatment.[10] With self-testing initiatives imminent, programme planners

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Pai, *Lancet Inf Dis*, 2012

Oral fluid based testing: local perspective

- Orasure® has been used in specialist settings in the UK
- Expansion of HIV testing to non-specialist settings in light of UK National Guidelines 2008
- HINTS Study – prospective study of routine HIV testing in non-specialist settings in high prevalence areas
- Operational barriers identified to use of POCT, in addition to staff and governance barriers
- **AIM:** Develop method of oral fluid field sampling with laboratory based testing

Initial phase

- Bio-Rad Genscreen Ultra HIV Ag-Ab test on Best 2000 platform
- Manufacturer performance: 99.95% specific on serum
- HPA validation: 100% sensitive at 3/12

- In-house validation of whole saliva tested against reference sample:
  - n=140 (120 known positives; 20 having contemporaneous serology) **100% agreement**

- Method rolled forward for use in pilot program

Initial phase (2)

- Labour intensive – manual aliquotting and processing
- Long turnaround time
  - Sample process time 4 hours;
  - Batching: mean collection to result time - 8 days
- Initial sample collection – whole saliva in sterile containers
- Moved to Oracol+ device (Malvern Medicals PLC, UK)
  - Higher quality samples with fewer re-tests

Initial phase (3)

- 3721 tests undertaken
- 11 reactive results
- 4 true positives
- **Specificity: 99.81%**
- **PPV: 36%**
- Prevalence of HIV in sample = 0.11%

Acceptability of HIV Testing Methods (n=1003)

"I would be happy providing the following sample for an HIV test"	Agree (%)
Blood test with result in one week	89%
Fingerprick blood test with immediate result	90%
Saliva (spitting) with result in one week	96%*
Mouth swab (like brushing teeth) with result in one week	95%*

*p<0.001

Automation: Validation on Abbott Architect

- **AIM:**
  - To ascertain whether automation of oral fluid testing was possible using the 4th generation test on the fully automated Abbott Architect platform
- **METHODS:**
  - Oral fluid collected from 143 patients (56 known HIV+ volunteers and 87 others having contemporaneous HIV serology)
  - Oracol+ collection device

Validation on Abbott Architect: Results

	Control Assay		Bio-Rad Genscreen Ultra HIV Ag-Ab test (manual handling on Best 2000 platform)		Abbott Architect 4th Generation Assay (automated)	
Sample type	**Serum**		**Oral fluid**		**Oral fluid**	
Assay result	**Reactive**	**Negative**	**Reactive**	**Negative**	**Reactive**	**Negative**
Known HIV-positive (n=56)	56	0	56	0	56	0
Unknown HIV status accepting standard of care HIV test (n=87)	1	86	1	86	1	86

Interpretation

- Laboratory testing of oral fluid requires less training of field staff
- Highly acceptable to patients
- Automation is feasible, reducing laboratory workload

Ongoing shop floor experience

- Use of testing in HEDsUP NW London program (Abstract PS1/O1)
- Full time use of Abbott Architect since 10/2011
- 430 tests to date
- Minimum volumes a problem: 11.6% insufficient rate
- 97.7% on Architect; 2.3% on BioRad
- Three reactives to date

For further information:

- Talk to us at Poster PS6/O1
- Email: *michaelrayment@nhs.net*