POINT OF CARE TESTING: HIV-1 VIRAL LOAD

VLAD NOVITSKY
The risk of HIV-1 transmission is associated with levels of HIV-1 RNA load in blood and genital tract secretions.

- Dyer et al., J Infect Dis 1998
- Hisada et al., J Infect Dis 2000
- Fideli et al., AIDS Res Hum Retroviruses 2001
- Celum et al., J Infect Dis 2001
- Tovanabutra et al., J Acquir Immune Defic Syndr 2002
- Wawer et al., J Infect Dis 2005
- Lingappa et al., PLoS One 2010
- Beaten et al., Sci Transl Med 2011

Extended high viremics: high proportion of individuals maintaining high plasma HIV-1 RNA load after acute infection.

- Novitsky et al., PLoS One 2010
- Novitsky et al., AIDS 2011
- Novitsky & Essex, Curr Opin HIV AIDS 2012
- Serna-Bolea et al., PLoS One 2012
- Campbell et al., J Infect Dis 2013
- Armbruster et al., Health Care Manag Sci 2013
Viral load is more informative than CD4

Running with Scissors: Using Antiretroviral Therapy without Monitoring Viral Load

Davey M. Smith and Robert T. Schooley
Division of Infectious Diseases, University of California, San Diego

Clinical Infectious Diseases 2008;46:1598–1600

“If a choice must be made between monitoring viral load or CD4 cell count during HAART, we believe that it would be more useful to monitor viral load than CD4 cell count”.

“HAART has a direct effect on viral replication, not on CD4 cell count”.

“Failing to use laboratory tools that monitor treatment success is like running with scissors; it is all quick and easy until someone falls down”.
Viral load is more informative than CD4

“CD4+ T cell count … poor surrogate markers for treatment failure”

“When to switch therapy”.
“When not to switch therapy”. 

TREATMENT AS PREVENTION: HIV-1 VIRAL LOAD
# TREATMENT AS PREVENTION: HIV-1 VIRAL LOAD

**Genital tract viral load in HIV-1 subtype C**

<table>
<thead>
<tr>
<th>Country</th>
<th>n (M71 / F129)</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>36 / 82</td>
<td>4.0</td>
<td>5.1</td>
</tr>
<tr>
<td>S. Africa</td>
<td>11 / 27</td>
<td>4.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>5 / 11</td>
<td>4.8</td>
<td>5.0</td>
</tr>
<tr>
<td>India</td>
<td>19 / 9</td>
<td>4.1</td>
<td>5.4</td>
</tr>
</tbody>
</table>

**Screening CD4+ cells/mm³**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median</th>
<th>Q1, Q3</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>196</td>
<td>90, 259</td>
<td>.9002^a</td>
</tr>
<tr>
<td>Plasma HIV-1 viral load, log₁₀ copies/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>5.0</td>
<td>4.5, 5.4</td>
<td></td>
</tr>
<tr>
<td>Q1, Q3</td>
<td>4.5, 5.4</td>
<td>4.5, 5.3</td>
<td>.1722^a</td>
</tr>
</tbody>
</table>

**Genital secretion HIV-1 viral load, log₁₀ copies/mL**

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Q1, Q3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.8</td>
<td>2.7, 4.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.0</td>
<td>3.0, 4.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.0</td>
<td>3.2, 4.9</td>
<td></td>
</tr>
</tbody>
</table>

[^a]: Significant at the 0.05 level.
HIV-1 RNA LOAD

Monitoring of ART efficacy
Acute HIV infection
Early infant diagnosis

Clinical trials/Public health interventions:

Initiation of ART

Monitoring of intervention efficacy:

Community viral load
Proportion of individuals with suppressed viral load
HIV-1 RNA LOAD

Monitoring of ART efficacy
Acute HIV infection
Early infant diagnosis

Clinical trials/Public health interventions:

- Initiation of ART
- Monitoring of intervention efficacy:
  - Community viral load
  - Proportion of individuals with suppressed viral load
### HIV-1 RNA LOAD: CENTRALIZED VS. DE-CENTRALIZED TESTING

Centralized viral load testing:

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accurate results</td>
<td>Sending the sample / Receiving the result</td>
</tr>
<tr>
<td>Reproducible</td>
<td>Waiting time – delays</td>
</tr>
<tr>
<td>Feasible</td>
<td>Lab: delicate instruments</td>
</tr>
<tr>
<td></td>
<td>Cold chain</td>
</tr>
<tr>
<td></td>
<td>Missing results</td>
</tr>
</tbody>
</table>
**POCT SCREENING**

- **HIV status**
  - **RHT**
    - If HIV+: CD4 test
  - If HIV-:

- **CD4 test**
  - **350**
    - If <350: ART
    - If >350: VL test

- **HIV-1 VL**
  - **10K**
    - If >10K: ART
    - If <10K: Monitor
POCT SCREENING

HIV status

- RHT
  - If HIV+: VL test

HIV-1 VL

- 1K-?
  - If >1K: ART
  - If <1K: Monitor

Missing population (VL vs. CD4 – Mochudi data):
1.6% of individuals CD4 <350 vs. 37.3% of individuals with VL > 1,000 cp/mL
POC HIV VIRAL LOAD TECHNOLOGIES

Alere NAT system: Alere Q (Alere Inc.)

SAMBA: Simple AMplification Based Assay (Diagnostics for the Real World, Ltd.)

Liat™ NAT system (IQuum, Inc. -> Roche)

EOSCAPE-HIV™ (Wave 80 Biosciences)

Truelab Real Time micro PCR system (Molbio Diagnostics Pvt. Ltd.)
POC HIV VIRAL LOAD TECHNOLOGIES

ALERE Q (ALERE INC.)

Commercially available - ?
Pricing - ?
POC HIV VIRAL LOAD TECHNOLOGIES

**SAMBA** *(DIAGNOSTICS FOR THE REAL WORLD, LTD.)*

Simple AMplification Based Assay

![SAMBAprep](image1.png)

![SAMBAamp](image2.png)
POC HIV VIRAL LOAD TECHNOLOGIES

SAMBA:

HIV-1 subtype

<table>
<thead>
<tr>
<th></th>
<th>SAMBA test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
</tr>
<tr>
<td>J</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td></td>
</tr>
<tr>
<td>CRF01_AE</td>
<td></td>
</tr>
<tr>
<td>CRF02_AG</td>
<td></td>
</tr>
<tr>
<td>HIV-neg</td>
<td></td>
</tr>
<tr>
<td>HIV IC</td>
<td></td>
</tr>
</tbody>
</table>

Simple Amplification-Based Assay: A Nucleic Acid-Based Point-of-Care Platform for HIV-1 Testing

Helen H. Lee,1 Magda A. Dineva,1 Yui Leng Chua,1 Allyson V. Ritchie,1 Ines Ushiro-Lumb,2 and Craig A. Wisniewski3

1Diagnostics Development Unit, Department of Haematology, University of Cambridge, Cambridge, and 2Department of Virology, Barts and The London NHS Trust, London, United Kingdom

Samba machine at Namitambo health centre, in Chiradzulu, Malawi. Photograph: Giulio Donini/UNITAID
POC HIV VIRAL LOAD TECHNOLOGIES

LIAT™ ANALYSER (IQUUM, INC.):
Closed automated NAT system: Nucleic acid extraction, purification, reverse transcription, PCR amplification, and real-time detection to detect and/or quantify pathogens;

Pathogens: Influenza, Denge virus, TB, and HIV-1.
POC HIV VIRAL LOAD TECHNOLOGIES

EOSCAPE-HIV™ HIV RAPID RNA ASSAY SYSTEM
(WAVE 80 BIOSCIENCES)

Disposable cartridge with reagents (no cold chain);
A small, low cost, battery-powered processing unit;
A small, portable reader with touchscreen display (8 h battery).
POC HIV VIRAL LOAD TECHNOLOGIES

TRUELAB REAL TIME MICRO PCR SYSTEM
(MOLBIO DIAGNOSTICS PVT. LTD. [A TULIP GROUP BIGTEC LABS PARTNERSHIP])

Pathogens: MTB, HBV, dengue fever, Chikungunya, H1N1 and malaria. HIV is in development.

Blood, or plasma.
Extraction: 20-25 min/sample;
Micro PCR chip: 6 uL of NA;
Real Time PCR micro analyzer: results in 30 min.
POC viral load & EID products: available and pipeline*

2013
SAMBA VL**
DDU/Cambridge

2014
SAMBA EID
DDU/Cambridge

Liat™ Analyser
IQum

2015
EOSCAPE HIV™ Rapid RNA Assay System
Wave 80 Biosciences

Gene Xpert
Cepheid

LYNX HIV p24 Antigen
NWWGHF

Truelab PCR
Molbio/bigTec

Cavidi AMP
Cavidi

2016
RT CPA HIV-1 Viral Load
Ustar

Gene-RADAR
Nanobiosym

Micronics

Viral Load Assay with BART
Lumora
**HIV POCT VIRAL LOAD**

Scientific impact?

Public health impact:
- HIV incidence / HIV prevalence?
- Efficiency of the system? Missing results?

Clinical - Cascade of HIV Care:
- Screening for ART initiation?
- Monitoring of ART?

Technical:
- Available?
- Reliable/Standardized?

Economic aspects:
- Viable? Good investment?
- Affordable?