Clinical rationale for viral load testing

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Wits Reproductive Health & HIV Institute
Caveats

• I’m a believer in VLs
• My talk looks at resource poor environments
Why do we need a rationale???

• Its SO obvious!
Why should we do it?

- **Best** possible way to determine adherence
- Early prevention of resistance – may even re-suppress
- Prevention of unnecessary switch to second line – See R Hamers
- **Objective quality** measure of the programme - % suppression
- **Objective quantity** measure of the programme – how many are suppressed at 1 year is a superb M&E tool
Clinical Failure is Just the Tip of the Iceberg

VIROLOGIC FAILURE can lead to
IMMUNOLOGIC FAILURE which can lead to
CLINICAL FAILURE

Losina E et al, 15th CROI 2008, #823
Viral load monitoring in resource-limited settings: a medical and public health priority

Nathan Ford\textsuperscript{a, b}, Teri Roberts\textsuperscript{a} and Alexandra Calmy\textsuperscript{a, c}

\textit{AIDS} 2012, 26:1719–1720

There is little debate about the value of viral load in guiding clinical decisions for people on ART. However, the relative importance of viral load in resource-limited
### Evolution of WHO ART Guidelines in Adults

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</thead>
<tbody>
<tr>
<td><strong>When to start</strong></td>
<td>CD4 ≤200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 350</td>
<td>CD4 ≤ 500</td>
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<tr>
<td></td>
<td>- Consider 350</td>
<td>- Irrespective CD4 for TB</td>
<td>- Irrespective CD4 for TB and HBV</td>
<td></td>
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<tr>
<td></td>
<td>- CD4 ≤ 350</td>
<td>- CD4 ≤ 500</td>
<td>- CD4 ≤ 350</td>
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<tr>
<td>1st Line</td>
<td>8 options</td>
<td>4 options</td>
<td>8 options</td>
<td>6 options &amp; FDCs</td>
<td>2 options &amp; FDCs</td>
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<tr>
<td></td>
<td>- AZT preferred</td>
<td>- AZT preferred</td>
<td>- AZT or TDF preferred</td>
<td>- AZT or TDF preferred</td>
<td>- TDF and EFV preferred across all populations</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- d4T dose reduction</td>
<td>- d4T phase out</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3rd Line</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>DRV/r, RAL, ETV</td>
<td>DRV/r, RAL, ETV</td>
</tr>
<tr>
<td>Viral Load Testing</td>
<td>No</td>
<td>No (Desirable)</td>
<td>Yes (Tertiary centers)</td>
<td>Yes (Phase in approach)</td>
<td>Yes (preferred for monitoring, use of PoC, DBS)</td>
</tr>
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**Earliest initiation**

- Earlier initiation
- Simpler treatment
- Less toxic, more robust regimens
- Better monitoring

**HIV/AIDS Department**

**RHI**
Emergence of Mutations During Persistent Viremia on a NRTI/NNRTI Regimen

- 3727 patients in South Africa, CD4 and VL monitoring every 6 months
- 1007 (27%) patients developed viremia (VL >1000c/ml)
- Of 815 subjects with subsequent VL measured, 331 (41%) resuppressed on their own

Hoffmann CJ, et al. CROI 2009, Montreal, Canada. #656
Viral load monitoring in resource-limited settings: a medical and public health priority

Nathan Ford\textsuperscript{a,b}, Teri Roberts\textsuperscript{a} and Alexandra Calmy\textsuperscript{a,c}

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Regarding clinical decisions for people on ART. However, the relative importance of viral load in resource-limited settings continues to be contested. Costing studies have concluded that viral-load monitoring is not cost-effective compared with CD4 monitoring \cite{13} or clinical monitoring alone \cite{14}. To date, however, these studies have only considered the value of adding viral load to clinical and immunological monitoring.

The study by Hamers et al. \cite{4} offers an important alternative perspective by assessing the cost effectiveness of viral load as an alternative to CD4 monitoring following ART initiation. The study found that viral load monitoring could save costs in two ways; first, by identifying the right people to switch onto more expensive second-line regimens, and second, by switching patients to second-line treatment more quickly before they were at higher risk of clinical disease progression and death. The proposal to abandon CD4 following treatment
Reflections...

• Viral loads are expensive
A widening menu of ARV use for treatment and prevention

Despite immediate increase from currently 17 million to 26 million people eligible for ART, the preventive effect will lead to decrease of number eligible after 2020.
A widening menu of ARV use for treatment and prevention

Despite immediate increase from currently 17 million to 26 million people eligible for ART, the preventive effect will lead to decrease of number eligible after 2020.

26 million x $20 – over $1/2 billion annually

Cost effectiveness questioned...
And we know the result in >90% in well performing clinics...

- Will be undetectable.
- How often should we test?
Clinics do not respond timeously

- PoC not available – so “call-backs” the only way to go
- Health care systems notoriously bad at contacting patients
- Anecdote: almost no large scale programmes showing consistent success
- ?make detectable viral loads ‘notifiable’ – need urgency
And in places WITH VL testing?
Impact of Community Groups on ART Delivery and Retention in Mozambique

Distribution of Antiretroviral Treatment Through Self-Forming Groups of Patients in Tete Province, Mozambique

Tom Decrooc, MD, *Barbara Telfer, MPH, *Marc Biot, MD, MSc, *Jacob Maiké, MD, MSc, PhD, †
Sergio Dezembro, *Luisa Isabel Cumbo, MD, ‡Carla das Dores, MD, §
Kathryn Chu, MD, MSc, ¶ and Nathan Ford, MPH, PhD

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Median Follow up time</td>
<td>12.9 months</td>
<td></td>
</tr>
<tr>
<td># Patients remained on care</td>
<td>1269 (97.5%)</td>
<td></td>
</tr>
<tr>
<td># Patients transferred out</td>
<td>83 (6%)</td>
<td></td>
</tr>
<tr>
<td># Deaths</td>
<td>30 (2%)</td>
<td></td>
</tr>
<tr>
<td># LFU</td>
<td>2 (0.2%)</td>
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Approximately 4-fold reduction in medical consultations among patients receiving CAG-based care.
Monitoring of HIV viral loads, CD4 cell counts, and clinical assessments versus clinical monitoring alone for antiretroviral therapy in rural district hospitals in Cameroon (Stratall ANRS 12110/ESTHER): a randomised non-inferiority trial


received antiretroviral therapy, and were followed-up for 2 years by health-care workers in routine activities. We randomly assigned participants (1:1) to CLIN or LAB (counts of HIV viral load and CD4 cell every 6 months) groups with a computer-generated list. The primary outcome was non-inferiority of CLIN to LAB in terms of increase in

Interpretation Our findings support WHO’s recommendation for laboratory monitoring of antiretroviral therapy. However, the small differences that we noted between the strategies suggest that clinical monitoring alone could be used, at least temporarily, to expand antiretroviral therapy in low-resource settings.
And as for ‘accumulation of resistance mutations’...

• Does it matter, if we have a PI in second line?
Virologic Response to Second-Line Therapy with LPV/r in South Africa

- 3365 patients initiating ART since 2004 in Durban, 192 (6%) have required LPV/r-based 2nd-line ART, majority (72%) due to virologic failure of 1st line
- Median CD4 count at switch = 143/mm³
- NRTI backbone: AZT/DDI (47%), AZT/3TC (29%), d4T/3tC (15%)
- After 6 months, 82% achieved virologic suppression (<50 copies/ml):
  - No significant difference by:
    - NRTI backbone used
    - Indication for 2nd-line ART
    - Number of prior 1st-line regimens
    - Concurrent TB therapy
  - Significant differences were found by gender:
    - Women (89%) vs. men (71%); p = 0.01

R. Murphy et al, 15th CROI 2008, #831
Finally...

• This is NOT a minor addition to laboratory infrastructure
HIV VL in KZN: 2006-2011

Year | No. of HIV VL
--- | ---
2006 | 96,000
2007 | 162,414
2008 | 206,000
2009 | 192,000
2010 | 218,466
Conclusions

• Viral load testing adds to programmes, but at considerable expense, and benefits are small - other interventions may be less sexy, but more effective
• Far more attention needed to chasing detectable results and improving systems
• Affordable PoC VL has ability to be transformative
SAVE THE DATE
24 – 27 SEPTEMBER 2014

- Excellent local and international speakers
- Lively debates
- Skills building sessions
- Presentations on the latest on treatment, prevention, basic science and ethics to mention a few

www.sahivsoc2014.co.za