Viral load platforms for point-of-care testing and opportunities for TB/HIV integration

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World Health Organization
Access to ART worldwide has significantly increased but coverage still very heterogeneous...

Hill et al. CROI 2015 [abstr 1118]
Treatment initiation still late in the large majority of countries

Median CD4 count at start in 2012 (data for some countries extrapolated)
New global targets
From numbers on treatment to virological suppression

People receiving antiretroviral therapy, 2005 to June 2014, all countries

13.6 MILLION
People receiving antiretroviral therapy, June 2014

% diagnosed 90%
% on treatment 90%
% virally suppressed 90%

World Health Organization
Evolution of WHO recommendations for ART monitoring

- **2003**: 1) Clinical Monitoring
  2) CD4 monitoring if available
  
- **2006**: 1) Clinical monitoring,
  2) CD4 monitoring
  
- **2009**: 1) Clinical monitoring,
  2) CD4 monitoring
  3) VL monitoring to confirm suspected treatment failure
  4) Encourage expansion of viral load monitoring

- **2013**: 1) Routine VL monitoring recommended as preferred method to identify treatment failure

Viral load not recommended due to cost and complexity. Hope expressed that viral load will become more affordable.
Growing demand for Viral Load

Africa includes both SSA and North Africa; Asia and EE includes all of Asia and Eastern Europe, LAC includes all of Latin America and the Caribbean.
Growing demand for Viral Load

Data Projection

Demand for viral load tests will likely reach 15-30 million tests by 2018.

Africa includes both SSA and North Africa; Asia and EE includes all of Asia and Eastern Europe, LAC includes all of Latin America and the Caribbean.
Viral Load Implementation

Guidance for MoH
- Phase in, planning, lab network
- Overview of technologies
- DBS use, cutoff at 1000 cpm
- Quality

Phase I: Planning
- Policies and Leadership
- Harmonization Algorithm
- Mapping and Forecasting
- Assess Capacity
- Costing
- Specimen and Product Selection Equipment Procurement

Phase II: Scale Up
- Phase In
- Human Resources Training and Supervision
- Quality Management System

Phase III: Sustainability
- Partner Harmonization
- M&E Data Collection
- Operational Research
• WHO Prequalification of In Vitro Diagnostics Programme
• Viral load platforms for point-of-care testing
• And opportunities for TB/HIV integration
WHO Prequalification of IVDs Programme
Assuring the quality of IVDs

Why?
- IVD regulation is poorly understood and/or poorly enforced
- Risk-based regulation for different classes of IVDs
  - E.g. TB IVD regulated differently in different jurisdictions

What is PQ?
- PQDx assesses the safety, quality and performance of IVDs
  - Based on international best practice
  - Using a risk-based approach
  - Provides recommendations on quality, safety and performance
  - Increasing in-country capacity for regulation of IVDs

Customers
- WHO Member States
- UN agencies
- Funding and procurement agencies
Prequalification: process

- Current scope of WHO PQ
  - HIV, HCV, HBV, malaria
  - Multiplex, multi-analyte

- Emphasis on formats of IVDs most used in resource-limited settings
  - RDTs, EIAs, NAT

Pre-submission form

Priority product

Yes

Dossier screening

Dossier complete

Dossier review

Site inspection

Independent laboratory evaluation

Prequalification decision. UN procurement eligibility.
Some definitions

- **Multiplex testing**
  - Simultaneous detection of different analytes in a single specimen using one test procedure/test run
  - May/may not be discriminatory detection

- **Multi-analyte platforms (polyvalent)**
  - A platform that tests multiple analytes using same assay principle e.g. serology, NAT
Synergies with current PQed products

- Laboratory based assays only

- Abbott RealTime HIV-1 and HIV-1 Qualitative
  - Abbott RealTime MTB assay available on same platform

- COBAS AmpliPrep/COBAS TaqMan HIV-1 Test, version 2.0 (Roche)
  - COBAS® TaqMan®MTB available on same platform

- Many commonalities with PQed products, however, no stringent assessment by SRA
HIV NAT technologies for POC currently in the pipeline

- Alere Q
  - Alere™ q
  - HIV1/2 Detect
- Gene Xpert® System
  - Cepheid EID
  - and VL
- SAMBA EID
  - DRW
- SAMBA VL
  - DRW
- Truelab™ PCR
  - Molbio/bigTec
- RT CPA HIV-1
  - Viral Load
  - Ustar
- Gene-RADAR®
  - Nanobiosym
- LYNX Viral Load Platform
  - NWGHF
- Viral Load Assay with
  - BART
  - Lumora
- EOSCAPE HIV™ Rapid RNA Assay System
  - Wave 80 Biosciences
- Micronics
- ALL
- BioHelix
- World Health Organization
Efficiencies: laboratory

- Procurement
  - Harmonization and standardization of suppliers
  - Better negotiation power
  - Capital purchase vs. reagent rental vs lease

- Installation
  - Calibration

- Maintenance
  - Corrective and preventive
  - Reduce duplication, demand better customer service

- Training
  - Reduce duplication, demand better customer service

- EQAS
  - Inter-laboratory comparison
Challenges

- Instrument downtime will affect both HIV and TB services
- Different specimen types for different analytes
  - e.g. plasma for HIV Quant, whole blood for HIV Qual, sputum for TB
- Epidemiology driven or programmatically driven?
- Creating monopolies, reduces incentive for good customer service
Efficiencies: service delivery

● Service delivery efficiencies
  – Integrating service delivery through availability of platforms capable of testing than one analyte
  – Moving towards a 1-stop shop
  – Costs to the patient may be reduced with integration

● Optimal placement of multi-analyte platforms
  • Quantitative (viral load)
    – HIV services provide ART and monitor response to ART including OI (may diagnosis and treatment of TB and other co-infections)
  • Qualitative (infant/adults)
    – PMTCT clinics provide diagnosis for infants and mothers
TB continues to be a leading case of HIV-related mortality

<table>
<thead>
<tr>
<th>Region</th>
<th>Proportion (95% CI)</th>
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<tbody>
<tr>
<td>Adults</td>
<td>23.91 (18.40, 29.42)</td>
</tr>
<tr>
<td>AFRO</td>
<td>26.98 (16.93, 37.02)</td>
</tr>
<tr>
<td>SEARO</td>
<td>33.11 (14.42, 51.81)</td>
</tr>
<tr>
<td>WPRO</td>
<td>27.83 (21.95, 33.70)</td>
</tr>
<tr>
<td>EMRO</td>
<td>7.21 (3.15, 11.27)</td>
</tr>
<tr>
<td>EURO</td>
<td>20.00 (3.17, 36.83)</td>
</tr>
<tr>
<td>AMRO N</td>
<td>12.02 (8.50, 15.54)</td>
</tr>
<tr>
<td>AMRO S</td>
<td>18.03 (15.47, 20.59)</td>
</tr>
<tr>
<td>Overall</td>
<td>15.08 (8.31, 21.85)</td>
</tr>
<tr>
<td>Children *</td>
<td>4.44 (1.40, 7.49)</td>
</tr>
<tr>
<td>Overall</td>
<td>6.71 (2.77, 10.65)</td>
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<tr>
<td></td>
<td>10.77 (7.61, 13.94)</td>
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</tbody>
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* data not reported for all regions

Ford et al, submitted
Service integration is critical for further scale up

**The Effect of Complete Integration of HIV and TB Services on Time to Initiation of Antiretroviral Therapy: A Before-After Study**

Bernhard Kerschberger, Katherine Hildbrand, Andrew M. Boulle, David Coetzee, Eric Goemaere, Virginia De Acevedo, Gilles Van Cutsem

**Abstract**

Background: Studies have shown that early ART initiation in TB/HIV co-infected patients lowers mortality. One way to implement optimal ART commencement could be through integration of TB and HIV services, a more efficient model of care than separate, vertical programs. We present a model of full TB/HIV integration and estimate its effect on time to initiation of ART.

Methodology/Principal Findings: We prospectively reviewed TB registers and clinical notes of 205 TB/HIV co-infected adults with a CD4 count <500 cells/µl and registered for TB treatment at primary care clinic in a South African township between June 2008 and May 2009. Using Kaplan-Meier and Cox proportional hazards analysis, we compared time between initiation of TB treatment and ART for the periods before and after full, "one-stop shop" integration of TB and HIV services (in December 2009). Potential confounders were determined a priori through directed acyclic graphs. Reliability of assumptions was investigated by sensitivity analyses. The analysis included 188 patients (97.1% pre- and 98% post-integration) yielding 165 person-years of observation. Baseline characteristics of the two groups were similar. Median time to ART initiation decreased from 147 days (95% confidence interval [CI] 85-188) before integration of services to 73 days (95% CI 32-110) post-integration. In adjusted analyses, patients attending the clinic post-integration were 1.60 times (95% CI 1.21-2.12) more likely to have started ART relative to the pre-integration period. Sensitivity analyses supported these findings.

**Conclusions:** Full TB/HIV care integration is feasible and led to a 69% increase in chance of co-infected patients starting ART while reducing time to ART initiation by an average of 72 days. Although these estimates should be confirmed through larger studies, they suggest that scale-up of full TB/HIV service integration in high TB/HIV prevalence settings may shorten time to ART initiation, which might reduce excess mortality and morbidity.

**WHO 2013 Recommendations:**

ART should be initiated and maintained in: TB programmes, maternal & child health programmes, opioid substitution programmes ... ...Hepatitis C? Sexual and Reproductive Health?
Conclusions

- Access to viral load a key priority for HIV programmes

- Point-of-care viral load offers significant potential for increasing VL capacity
  - Need for centralized and decentralized platforms
  - Choice will depend on context

- The need to integrate HIV treatment into other key disease programmes underscores the utility of multi (analyte) platforms
More information

- For more details on the WHO Prequalification of IVDs

WHO Prequalification of Diagnostics programme website:

http://www.who.int/diagnostics_laboratory/evaluations/en/

- Contact us by email!

diagnostics@who.int