“Investigating the Feasibility of a multi-disciplinary POC laboratory in an Active HIV treatment Clinic”

and

“Determining the impact of POC testing on Patient Outcome”

Wendy Stevens

Department of Molecular Medicine and Haematology, University of the Witwatersrand and National Priority Programs, NHLS, Johannesburg, South Africa

Personal view, not endorsing any particular supplier or policy

On behalf of the GCC Team
HOT TOPICS
in massive scale-up of ART/TB treatment

• Integration of HIV and TB services
• New treatment guidelines
  Drugs, CD4<500, populations started on rapid test alone
  CD4: beginning of the end?
• Global viral load scale-up required is massive
• Linkage to Care and algorithm reviews
• Re-visiting old and new rapid tests, their QA & data collection
• Continuous Monitoring of Quality (CMQ)
• Inter-operability of data systems
• Clinic Performance Monitoring using laboratory data
• Total Coverage Model vs. Total de-centralization
## Trends in HIV & TB management that will result in major changes in laboratory practice

### Clinical drivers
- Massive scale-up required; additional 2.4 million; de-centralised care
- **Rapid tests** have a more important role to play in treatment initiation and alternative approaches being considered: self-testing, opt out implementation, more convenient sites
- Universal screening of TB to accompany all HCT; and the reverse
- Initiation without CD4 for a large number of patients: pregnant women, TB patients, children<5, sero-discordant couples
- Lifelong treatment for pregnant mothers
- Treatment simplification: FDC drugs and massive price reductions
- CD4: Gatekeeper for initiation, cryptococcal meningitis, TB urinary LAM?
- Viral load more important in measuring treatment success
- The need for routine HIV drug resistant testing (2nd line)
- ARV treatment as prevention, or Test and Treat: New drugs

### Technology drivers
- Move towards same technology able to test for HIV and TB
- Catalyzation of POC assays for HIV and TB
- Analyzers with Massive automation
- Highly sensitive assays; earlier diagnosis
- Improvement in DBS results for VL and EID
- Random access and multiplexing

### Improved laboratory data collection tools
- Integration and co-ordination, e-Health and m-Health solutions
- Need for BIG data collection: e.g. Next gen Sequencing
- Integration to clinical data with a unique number is essential
A perspective on South Africa’s Testing volumes

Total Population 52 Million at last census
Estimated 6.4 million HIV infected individuals of which 2.4 million are receiving ARV therapy. HIV continues to drive these testing needs.
Currently Conduct approximately ~ 4 million CD4 tests annually, 2 million viral loads and currently 360 000 EID assays (2013)
3rd highest TB cases, 20% worlds reported HIV-associated TB cases and 4th largest reported numbers of MDR.
over 4 million GeneXpert tests (July2014); MTB 16-12%; Rif Resistance: 7%.
30-40% of all public health sector laboratory expenditure for HIV and TB

Universal testing for HIV and screening for TB – the primary objectives being to ensure that all citizens know their HIV and TB status, and to prevent new HIV and TB infections (NSP: 2012/2013-2016/2017). Increase testing requirements

Largely centralized PCR (HIV), CD4, TB (GeneXpert) laboratory footprint

CD4 labs
The NHLS enumerates CD4 for the public sector at 62 labs – current footprint for >3.8m test. Beckman Coulter, PLG CD4

HIV viral load labs
17 laboratories
8 sites with Abbott m2000 system
9 sites with Roche CAP/CTM
Current instrument capacity (8 hour shift)
6888 samples/day = 1,818,432/annum

GeneXpert TB testing labs
National policy
Roll out March 2011, testing at smear microscopy labs >4.2 million tests to date.
Gx at POC: NTCM=too costly

Testing centres: 207
Analysers: 286
Clinic placements: 20
Gx4: 95
Gx16-8: 1
Gx16: 186
GX80-48: 1
GX80: 4

Scott, L.E; Stevens, W et al. Comparison of Xpert MTB/RIF with other Nucleic acid technologies for diagnosing pulmonary tuberculosis in a high HIV prevalence setting: A prospective study. PLoS Medicine, July 2011 8:(7) e1001061
Game-changer volumes for SA and other countries

Predicted VL scale up will not meet the need at the current laboratory growth with the technology available. A global push to build laboratory capacity to achieve the 90–90–90 targets.
Volumes... moving towards consolidation
Significant effort on work flow efficiency: increase 1 million tests without adding additional equipment

Currently 17 functioning laboratories
  8 sites using the Abbott m2000 system
  9 sites using the Roche Cobas Ampliprep/ Cobas TaqMan system

Current instrument capacity (8 hour shift)
  6888 samples per day = 151,536 per month = 1,818,432 per annum

Currently 2 HIV viral load systems as per tender agreement:
  Abbott m2000
  Roche Cobas Ampliprep/Cobas TaqMan

Version 2.0

Primary Tube Pipetting

Specimen Preparation, Amplification & Detection
### Rapid Rate of Scale up Scenario: Eligibility at 500 CD4 cells/microl + PMTCT Option B+

#### Capacity Utilisation Analysis

<table>
<thead>
<tr>
<th>Year</th>
<th>CD4 Vols</th>
<th>Current Adjusted Capacity*</th>
<th>Capacity Utilisation</th>
<th>VL Vols</th>
<th>Current Capacity</th>
<th>Capacity Utilisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014/2015</td>
<td>3,484,757</td>
<td>5,665,248</td>
<td>62%</td>
<td>3,589,938</td>
<td>3,047,676</td>
<td>118%</td>
</tr>
<tr>
<td>2015/2016</td>
<td>1,502,379</td>
<td>5,665,248</td>
<td>27%</td>
<td>3,833,688</td>
<td>3,047,676</td>
<td>126%</td>
</tr>
<tr>
<td>2016/2017</td>
<td>1,109,244</td>
<td>5,665,248</td>
<td>20%</td>
<td>4,056,075</td>
<td>3,047,676</td>
<td>133%</td>
</tr>
<tr>
<td>2017/2018</td>
<td>983,484</td>
<td>5,665,248</td>
<td>17%</td>
<td>4,315,781</td>
<td>3,047,676</td>
<td>142%</td>
</tr>
</tbody>
</table>

* CD4 capacity adjusted due to labs planned for consolidation

# ART volumes from NACM model, Pre-ART numbers using a factor of 1.3 (G Rath)

### Analysis of additional systems required

<table>
<thead>
<tr>
<th>Year</th>
<th>CD4 Capacity Gap</th>
<th>CD4 System Capacity (BHR 2+2)</th>
<th>Additional Systems Required</th>
<th>VL Capacity Gap</th>
<th>VL System Capacity (24HR)*</th>
<th>Additional Systems Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014/2015</td>
<td>-2,180,491</td>
<td>259,200</td>
<td>None</td>
<td>342,262</td>
<td>86,184</td>
<td>6</td>
</tr>
<tr>
<td>2015/2016</td>
<td>-4,162,869</td>
<td>259,200</td>
<td>None</td>
<td>786,012</td>
<td>86,184</td>
<td>9</td>
</tr>
<tr>
<td>2016/2017</td>
<td>-4,356,004</td>
<td>259,200</td>
<td>None</td>
<td>1,008,399</td>
<td>86,184</td>
<td>12</td>
</tr>
<tr>
<td>2017/2018</td>
<td>-4,681,764</td>
<td>259,200</td>
<td>None</td>
<td>1,268,106</td>
<td>86,184</td>
<td>15</td>
</tr>
</tbody>
</table>

* Based on Roche capacity, minimal difference at 24 hours between Roche and Abbott

### Total Number of Instruments required (High capacity CD4 system and 24 hour Viral Load laboratories)

<table>
<thead>
<tr>
<th>Year</th>
<th>CD4 Vols</th>
<th>CD4 System Capacity (BHR 2+2)</th>
<th>No of Systems required</th>
<th>VL Vols</th>
<th>VL System Capacity (24HR)*</th>
<th>No of Systems required</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014/2015</td>
<td>3,484,757</td>
<td>259,200</td>
<td>13</td>
<td>3,589,938</td>
<td>86,184</td>
<td>42</td>
</tr>
<tr>
<td>2015/2016</td>
<td>1,502,379</td>
<td>259,200</td>
<td>6</td>
<td>3,833,688</td>
<td>86,184</td>
<td>44</td>
</tr>
<tr>
<td>2016/2017</td>
<td>1,109,244</td>
<td>259,200</td>
<td>4</td>
<td>4,056,075</td>
<td>86,184</td>
<td>47</td>
</tr>
<tr>
<td>2017/2018</td>
<td>983,484</td>
<td>259,200</td>
<td>4</td>
<td>4,315,781</td>
<td>86,184</td>
<td>50</td>
</tr>
</tbody>
</table>

* Based on Roche capacity, minimal difference at 24 hours between Roche and Abbott
cobas® HIV-1 correlation to TaqMan® HIV-1 v2

Method comparison (local HIV-1 cohort)

Data under analysis

Courtesy of Roche and Sergio Carmona
Large - connected
Reduce hands-on time to a minimum

Challenges addressed
- Higher throughput
- Predictable TAT
- Full sample traceability
The Liat™ HIV Quantitative VL (low volume POCT)

- Quantitative POC instrument
- Fully automated
- Lab in a tube technology
  - Sample extraction by magnetic silica beads
  - Multiplex amplification of what region???
  - Real-time detection
- **LOD**: 81 cp/ml in plasma,
- **Dynamic Range**: $10^2$ - $1.5 \times 10^6$ c/ml
- Sample types:
  - Blood – 75ul
  - Plasma – 150ul
- **TAT**:
  - Blood – 35 minutes
  - Plasma – 30 minutes

- Plasma testing as good as lab (<1000 c/ml) **but** requires phlebotomy and centrifugation: ?POC.
- Whole blood uses finger stick, but is TNA so threshold becomes 5000c/ml. ?clinical interpretation and second plasma follow up. Same as DBS.

Increased detection by LIAT in lower VL ranges: good for diagnostic assay using whole blood, but needs interpretation with finger stick.
Do we go BIG or SMALL or both?

Selection based on volumes and level of healthcare, technical skill and cost

UNITAID LANDSCAPE DOCUMENTS for HIV and TB in packs
South Africa:

- Evaluate in HIV/TB setting
- NTCM / Gx to smear microscopy centres
- Develop SOP’s, EQA
- Implement rapidly/high burden districts then 100% coverage
- Clinical + Lab algorithm and training
- Remote connectivity/calibration
- EPTB
- Paediatrics
- Surveillance

- A cartridge for INH, 2nd line?
- New markers

- Value of the Ct
- Monitoring?

- Difficult: is solution stool testing?
- New studies on urine

- WHO recommends

- 1 sputum only (except WC)
- Started March 2011, completed September 2013
- Trained: 1035 lab and 5332 clinic staff
- Novel EQA developed
- POC too costly

- Expansion: mines, correctional services

- WHO recommends

- Expansion: mines, correctional services

- Expansion: mines, correctional services

- Expansion: mines, correctional services
100% Coverage as per NDoH plan in public sector.

- Implementation in all original smear microscopy centres: in a 3 phased approach, HBD first
- 207 centers across the 9 provinces
- Phased implementation started March 24th, 2011
- To date ~4.0 mill tests performed to date; 60% of global cartridges procured
- **289 analyzers**: GX4 (95); GX16(186);GX48(1)
- 7 GX 80’s have been purchased and 5 installed to improve capacity, but also assist with increased no's expected for high risk populations
- **4th phase: High risk populations**: correctional services, mines and peri-mining communities and MDR/XDR

Project framework

- Determine principal components for an HIV/TB POCT (diagnosis and monitoring) implementation model.
- Determine the feasibility of performing multiple POCT in SA and scalability to RLS.
- Determine the impact of POCT for ART initiation (and at what cost)
- Develop policy framework for POCT for ART initiation.
Summary of Project components

Develop principal components for multiple POC implementation:
- Assay selection
- Laboratory method verification
- Training and SOP material and infection control
- IT and data management system
- Quality assurance Plan
  EQA material

Perform pilot field evaluation (urban setting):
- Site preparation, employ, train
- Field evaluation (HCW POC vs. Lab testing)
- Clinic workflow, feasibility
  Acceptability questionnaire, biohazard risk

POC feasibility testing and diagnostic algorithm and scalability:
- Randomized clinical trial and observational study
- Expansion to rural sites, prepare sites and staff, deploy EQA
- Data analysis:
  - Safety
  - Cost-effectiveness
  - Clinical effectiveness

Develop and propose policy regulatory framework:
- National Policy Guideline development
- Knowledge dissemination
  Publications
  Presentations
- Reimbursement strategies
- Supply chain procurement
1. Components for POC Best Practice

- Suitable POC platforms and assays are available (CD4, Hb, ALT, Cr, TB and now VL).
  - A checklist and validation protocol is unique to POCT and a “starter kit” required to ensure safe GCLP.
  - Selected POCT are as accurate as laboratory tests.
  - Sample throughput must be matched to testing arena
  - Support laboratory
- Clinic staff and infrastructure:
  - GIS mapping of POCT/integrated existing lab services is valuable to determine gaps and ensure NSP for universal testing/screening HIV/TB).
  - Infrastructure is lacking in several clinic sites – and temperature fluctuations are a reality.
1. POC nurse-based venepuncture testing performed adequately compared to gold standard laboratory testing

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Average</th>
<th>Mean difference</th>
<th>Percentage similarity CV</th>
<th>Allowable (RCPA) differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4</td>
<td>101</td>
<td>347cells/µl</td>
<td>12cells/µl</td>
<td>6.9%</td>
<td>~20cells/µl</td>
</tr>
<tr>
<td>Hb</td>
<td>105</td>
<td>13.8g/dl</td>
<td>-0.23g/dl</td>
<td>3.63%</td>
<td>±0.5&lt;10 g/dl</td>
</tr>
<tr>
<td>ALT</td>
<td>96</td>
<td>30.5U/l</td>
<td>9.59U/l</td>
<td>13.5%</td>
<td>±8&lt;60U/l</td>
</tr>
<tr>
<td>Creatinine</td>
<td>97</td>
<td>68µmol/l</td>
<td>2.0µmol/l</td>
<td>11.4%</td>
<td>±10&lt;100µmol/l</td>
</tr>
<tr>
<td>Lactate</td>
<td>26</td>
<td>2.1mmol/l</td>
<td>0.1mmol/l</td>
<td>10.3%</td>
<td>±0.5&lt;5.0mmol/l</td>
</tr>
</tbody>
</table>

Study has been duplicated at Tshwane district hospital: n=276
Role of CD4 testing questioned

- Under scrutiny beyond role of establishing patient wellness and gatekeeper for resources
- Guideline changes: <200 (2002); <350 (2010) and <500 (2013)
- Change in SA: August 2014
- Starting high risk patients: pregnant women, TB, hepatitis B, sero-discordant couples, children <5 years. (greater emphasis needed on HIV rapid test; hepatitis B?)
- Use CD4 <100 cells/ul to screen for meningitis with cryptococcal antigen (11%)
- 2013/2014 fiscal year: >6 million tests-not feasible
- Treatment not changed based on poor sensitivity of CD4 for treatment failure
- Testing after year 1 only if patient ill or not virologically suppressed
- Savings of over 167 million rand (K.Schnippel)

- Stevens. W, Ford, N. SAMJ. 2014. CD4 testing for the management of ART in HIV infected individuals: is it the beginning of the end.
Nurse operated evaluation of Epoc® Blood Gas Analyser for Cr and Hb

- Reflotron (Alt and Cr) being discontinued.
- Potential alternative: Epoc® Blood Gas Analyser (Alere)
  - Multi-Analyte card incorporates 9 analytes and 6 calculated values including Creat and cHgb
  - 92 uL sample, fresh whole blood
  - Result in 30 seconds
- Performance evaluation: EPOC testing performed by a nurse was evaluated against Laboratory testing for Cr and Hb on venipuncture
- N=125 patients (N=5 used for precision testing (intra and Inter-variability), N=125 for accuracy testing on each of two instruments (250 measurements)

<table>
<thead>
<tr>
<th></th>
<th>EPOC1 vs Lab (n=125)</th>
<th>EPOC2 2 vs Lab (n=124*)</th>
<th>Reflotron vs Lab (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6.7</td>
<td>2.5</td>
<td>18.5</td>
</tr>
<tr>
<td>SD</td>
<td>15</td>
<td>13.5</td>
<td>9.3</td>
</tr>
<tr>
<td>CV</td>
<td>12.4</td>
<td>10.4</td>
<td>6.3</td>
</tr>
<tr>
<td></td>
<td>EPOC1 vs Lab (n=124*)</td>
<td>EPOC2 2 vs Lab (n=124*)</td>
<td></td>
</tr>
<tr>
<td>HB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>-1.5</td>
<td>-1.6</td>
<td>-1.5</td>
</tr>
<tr>
<td>SD</td>
<td>-1.5</td>
<td>0.8</td>
<td>3.2</td>
</tr>
<tr>
<td>CV</td>
<td>3.6</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>

*18 QC failures/all but one repeated
† one sample no routine lab result

Other technologies under validation

HIV/Syphilis Duo
CD4 BD Presto, Mbio, Omega
CD4 dipstick
Gene Xpert Stool in children
HIV VL
Transport media (Longhorn)
DBS – Hemophore, large DBS
DNAGenotek – sputum sample
viable bacteria medium
2. Feasibility of performing multiple POCT for HIV/TB ART initiation

- **POC operators: 2 sites, with previous research experience**
  - Nurses are “easily trained” and can accurately perform multiple POCT (n=364 validation study) and carry out QC/EQA, but are too busy to add an extra 22 POCT duties to their hectic schedule.
  - 2 ½ staff required for GeneXpert POCT to ensure 15 patients have same day treatment.
  - Hb POCT placement in hospital wards did not reduce lab testing volumes

- **Patients and POCT**
  - >69% patients require 3 or more POCT per visit.
  - Patients prefer finger stick to venous puncture blood draw and 150ul can be obtained from a single finger stick for accurate multiple POCT.
  - Patient flow is not randomly distributed over the day – puts pressure on HCW and POCT design: Majority POCT performed before midday. (re-engineering)

- **Existing lab testing environment**
  - 75% specimens collected from clinic and received in the lab same day
  - 72% results received back in clinic within 1 day.

Sub-study: Assess clinic workflow for HIV/TB integration

- **AIM:** Assess standard clinical workflow and patient waiting times in a ARV treatment clinic
- **Method:**
  - One clinic site (Botshabelo) over a one month period; October 2012 (pre-POC implementation).
  - Patients were given a form when they entered the clinic to be handed to healthcare providers to fill out times.
  - This allowed capture of the waiting times for each phase of their clinic visit - time to first contact, time to see a nurse, time spent with nurse. We then calculated the average time spent in the clinic

<table>
<thead>
<tr>
<th>Before POC (H:M:S)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average time in clinic</strong></td>
</tr>
<tr>
<td><strong>Average time to see a nurse</strong></td>
</tr>
<tr>
<td><strong>Average time to first contact</strong></td>
</tr>
<tr>
<td><strong>Average visit time with health provider</strong></td>
</tr>
<tr>
<td><strong>Longest time in clinic</strong></td>
</tr>
<tr>
<td><strong>Shortest time in clinic</strong></td>
</tr>
</tbody>
</table>
Flexibility required for hurdles encountered

Challenges experienced throughout study at 3 clinical sites

Key:
- **Clinic issues**: HR shortages/stock shortages/infrastructure problems
- **National policy changes**: Change in guidelines /no eligible patients/campaigns
- **POC issues**: instrument downtime/errors/invalids/QC failures

2010, 2013 treatment guidelines/FDC: shift away from CD4 for initiation and VL for monitoring but not yet available at POC
EQA

- Not available for all POC tests
- Or not available in a format that can easily be used at the POC setting.
- Novel approach: the Dried culture spot program for TB including web based result management.
- New concern: HIV rapid testing


Scott LE, Stevens W, Kana B. 2013. GeneXpert TB EQA. Special Achievements WITS and Top Award for Innovation: National Innovation Annual Awards, NHLS


Dried Culture Spot (DCS) technology has been developed into a quality management program for molecular Mycobacterium tuberculosis (M.TB) diagnostic platforms like the GeneXpert® (Cepheid, Sunnyvale, CA). DCS are manufactured using M.TB cultures grown in single cell format, followed by chemical and heat inactivation, quantification and spotted onto Munkeli TIN filter cards (LabMate, Cape Town, SA). The DCS cards are barcoded and shipped by air at room temperature. Processing of the DCS on-site follows the Xpert MTB/RIF manufacturer’s testing protocol. The program involves two components: (1) verification (results unblinded) and (2) external quality assessment (EQA) (results blinded).

New concern: HIV rapid testing


US patent 8,709,712.
DCS coverage and performance

- Verification (1 DCS per module)
- Tested on instrument installation, relocation, maintenance, module replacement/failure.
- 4317 DCS performed globally (tbgxmonitor® reported on 4067), 97.4% modules functioning correctly.

Map = 18 countries for EQA
2014 EQA
- 282 sites globally
- 350 panels
- 363 GeneXpert instruments

Results from SA NPP

The SA program EQA results 2014

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>n= 1016</td>
<td></td>
</tr>
<tr>
<td>Correct results</td>
<td>998 (98.2%)</td>
</tr>
<tr>
<td>Errors</td>
<td>6 (0.6%)</td>
</tr>
<tr>
<td>Incorrect result</td>
<td>12 (1.2%)</td>
</tr>
</tbody>
</table>

Impact in SA of not verifying Gx before clinical testing.
~78 000 tests (of 3mil) could have been in error from 105 dysfunctional modules.

DCS EQA for alternative technologies.

<table>
<thead>
<tr>
<th>MTBDRplus v2</th>
<th>n</th>
<th>Observed result</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIF resistant DCS</td>
<td>70</td>
<td>100% MTB positive RIF resistant/INH sensitive</td>
</tr>
<tr>
<td>RIF susceptible DCS</td>
<td>36</td>
<td>100% MTB positive RIF sensitive/INH sensitive (including verification spots)</td>
</tr>
<tr>
<td>NTM DCS</td>
<td>46</td>
<td>93% (n=43) MTB negative</td>
</tr>
<tr>
<td>M. kansasii</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.intracellulare</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.fortuitum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NTM DCS</td>
<td>46</td>
<td>93% (n=43) MTB negative</td>
</tr>
<tr>
<td>CM assay (when performed)</td>
<td>24</td>
<td>96% (n=23) correct speciation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 incorrect, <em>M. avium</em></td>
</tr>
</tbody>
</table>

Abbott, MTB, using the *m2000* platform n=8 DCS, reported as MTB positive or negative, **100%** correct results.

Mohlabeng R, Gous N, Stevens W, Scott L E, Laboratory validation of Ustar EasyNAT™ Diagnostic test compared to GeneXpert MTB/RIF for qualitative detection of *Mycobacterium tuberculosis* using Dried Culture Spots. Accepted ASLM Dec 2014
## RE-thinking QA for rapid tests: Existing Mobile-based Rapid Strip Readers

<table>
<thead>
<tr>
<th>Name</th>
<th>Number of tests</th>
<th>Platform</th>
<th>Additional Hardware</th>
<th>Central Repository</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fio Corp.</td>
<td>‘near universal’</td>
<td>Mobile, Android</td>
<td>Deki Reader</td>
<td>Yes</td>
</tr>
<tr>
<td>Holomic LLC</td>
<td>‘near universal’</td>
<td>Mobile</td>
<td>RDT Reader</td>
<td>Yes</td>
</tr>
<tr>
<td>MobileAssay™</td>
<td>‘near universal’</td>
<td>Mobile &amp; Tablet Apple, Android, Windows</td>
<td>None required</td>
<td>Yes</td>
</tr>
<tr>
<td>Global Solutions for Infectious Disease (GSID)</td>
<td>‘near universal’</td>
<td>Mobile</td>
<td>Phone stand</td>
<td>Yes</td>
</tr>
<tr>
<td>BBI Solutions and Albagaia</td>
<td>Custom per test</td>
<td>Mobile Apple, Android, Windows</td>
<td>None</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Not entire list of available devices*
Smart Phone: data and graphic uploaded to cloud for analysis

61 million active sim cards in SA

14 million smart phones

Capture sample
- Manual Entry
- Take picture of barcode

Take picture of rapid test

Enter result

Automatic upload to Cloud Server for analysis and Verification of result
Rapid HIV Test

1. Detect Presence of Control Line
2. Detect Presence/Absence of Target

HIV Rapid Tests

Other Rapid Tests (Crag)
Potential value

- QC/QA of rapid testing nationally: strategy being developed.
- Centralised reporting and operational data.
- Monitoring of operator performance and identification of individuals/clinics which require (re)training.
- Automatic resulting of strips (no operator interpretation required).
- EQA sample processing, resulting and reporting.
- Configuration of system to be able to identify:
  - Multiple control lines
  - Multiple target lines
  - Multiplex Rapid Tests
- Support Home based self testing

- New thinking: Incentivized based activities in the continuum of care. Eg. Testing, adherence, DOTS, service delivery....
2. POCT principal components

• Connectivity: critical to POCT
  • A universal bi-directional multi-functional (clinic and lab) connectivity solution for POCT is lacking but “cloud-based” SaaS promising (eg PIMA data point – Dashboard and novel approach: Cepheid Remote monitoring).
  • Some areas require signal boosting and internet policing is essential.
  • Computer literacy is currently lacking by many staff.
  • Novel approaches: SMS printers shown to extend services and shorten TAT and being modified to encompass “linkage to care” and modified for bidirectional communication and expanded test repertoire.

Connectivity Data Analysis

- Automated results:
  - GeneXpert
  - Hemocue
  - PIMA
- Manual entry for Reflotron (Creatinine and ALT) - AegisPOC
- Analysis performed on manual entry
  - Transcription error of results
  - Incorrect patient ID used
  - Duplicate entry
  - Results not captured

62% of overall results captured correctly
LIS extended to the clinic: SMS printers

- SMS printers to **improve turn-around-time** of results back to facilities from the labs
- Beneficial in remote, far-reaching areas where no internet access is available
- SMS is automatically generated from the lab’s LIS
- *Result printed on paper* and to be stored in patient’s file
- Initial roll-out in 2009 (1990 SMS printers in the field nationwide (~4500 DoH facilities)
  - Services available for: CD4 Count, HIV VL, EID, GeneXpert TB and TB Microscopy.
  - Training on installation (uses a manual and with regional coordinators to train)
  - Monitor and follow up with dashboard
- In 2013: 2096 new bi-directional printer purchased by NHLS for implementation.

Connectivity = service expansion, quality and training maintenance.
Linkage to care: our plan for MTB-DR TB

3. Existing NHLS LIS Connection

4. NHLS CDW / LIS

5. MDR Patient Table

6. Secure, bi-directional web service interface

EMOCHA

2. Lab-based GeneXpert

- National Coordinators
- Provincial Coordinators
- District Coordinators

Reported mHealth Weekly Report

Real-Time mHealth
- District Trace Team Coordinators
- NIMDR Leaders

Integrating mHealth
- ETR.net & EDR.net

MDR Treatment Facility

Healthcare worker at clinic

Tracer Team
3: Impact (and cost) of multiple POCT on ART initiation

- 13 sites visited, 3 sites in North West Province identified for the RCT.
- Criteria
  - Clinical partner presence (enrol, recruit, follow up – record review, approval)
  - Moderate infrastructure
  - Defined as clinics (PHC, CHC)
  - ART/TB treatment initiation
  - Similar HIV/TB prevalence
  - Similar region for connectivity evaluations
  - No laboratory testing on site (CD4 testing turnaround time >2days),

Average Feb 2014, Botshebelo clinic, PHC

- Chronic & Minor elements, 607.25, 71%
- TB, 41, 5%
- Maternity, 7.75, 1%
- HIV Counselling & Testing, 43.5, 5%
- Immunisation, 48, 5%
- Emergency Treatment, 49.25, 6%
- Post Natal, 5.25, 1%
- ANC 1st visit, 6.5, 1%
- ANC Subsequent visit, 1.75, 0%
3. Outcome measures

Primary:
- Proportion of patients retained in care at 6 months

Secondary:
- Proportion of patients retained in care at 12 months
- Time from HCT to ART initiation
- Proportion of patients in each arm experiencing an OI (including TB) in the follow-up period
- Proportion of patients experiencing treatment interruptions in each group
- Cost effectiveness of POC testing vs Standard of Care (SOC)

Enrolment criteria:
- >18yrs, HIV+, presenting for ART.

Outcomes:
- Time to HIV ART initiation
- Cost of HIV ART initiation
- Short and medium term outcomes with respect to death, illness, loss to follow-up
- Follow up at 6 and 12 months
- Measure of effect of POC on clinic flow

Randomized controlled trial to determine if POCT is better than centralized laboratory testing for HIV ART initiation.
Study progress.

- 717 patients enrolled in study from May 2012 to September 2013.
- 23 patients currently on active follow-up that will end in September 2014.
- Study database entry complete as of August 13, 2014.

**Recruitment progress**: variable due to clinic renovations, campaigns, stock out, staff shortages and changes in guidelines (no longer enrolling pregnant women/critically sick/TB)
Baseline clinical and demographic characteristics of persons in RCT

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>currently</td>
<td>20%</td>
</tr>
<tr>
<td>previously</td>
<td>68%</td>
</tr>
<tr>
<td>Ever received PMTCT</td>
<td>9.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Employment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Full time</td>
<td>17.7%</td>
</tr>
<tr>
<td>none</td>
<td>72%</td>
</tr>
<tr>
<td>occasional</td>
<td>2.6%</td>
</tr>
<tr>
<td>Part time</td>
<td>7.3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode transport</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>bike</td>
<td>1.7%</td>
</tr>
<tr>
<td>Taxi</td>
<td>3.3%</td>
</tr>
<tr>
<td>Private car</td>
<td>19%</td>
</tr>
<tr>
<td>walking</td>
<td>77%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>35.7yrs</td>
</tr>
<tr>
<td>% male</td>
<td>33%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>2.4%</td>
</tr>
<tr>
<td>primary</td>
<td>27%</td>
</tr>
<tr>
<td>secondary</td>
<td>65%</td>
</tr>
<tr>
<td>tertiary</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distance from clinic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10mins</td>
<td>22%</td>
</tr>
<tr>
<td>10-30mins</td>
<td>59%</td>
</tr>
<tr>
<td>30-60mins</td>
<td>18%</td>
</tr>
</tbody>
</table>

All four clinics within 35km from Tshepong District hospital

TB positivity rate: 12% (23/189), n=2 MDR
Baseline CD4

Mean CD4 for POC = 337.0 c/mm$^3$, slightly higher than SOC = 332.3 c/mm$^3$
Proportion Patients with CD4 less than 350 cells/mm$^3$: higher in arm POC (63% (226/360)) than SOC (56% (189/337))

CD4 Results by Branch of Care

The PIMA effect: over estimate at 350c/ul, underestimate at 500c/ul

PIMA CD4 metanalysis, n=11803 data pairs, 22 studies, ScottL.E et al (under submission)

<table>
<thead>
<tr>
<th>@350c/ul</th>
<th>Total misclassification</th>
<th>False positive</th>
<th>False Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=8945</td>
<td>12%</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>n=5368 (venous)</td>
<td>10%</td>
<td>7.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>n=3577 (capillary)</td>
<td>14%</td>
<td>9.3%</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

More patients eligible at POC due to technology variability!
Enrollment
(Mid August 2014)

**Total HCT** 9495
**HIV positive** 1367
**Enrolled** 717
**Branch of care**
- **CD4 <350 ART eligible**
  - 368 (POC) 51.3%
  - 349 (SOC) 48.6%
- **Initiated on ART**
  - 226 (61.4%)
  - 189 (56.1%)
**Initiated on ART**
- 196 (86%)
- 136 (72%)
**Median days to initiation**
- 1 day
- 16 days

Difference due to misclassification of PIMA CD4 (over classify up to 8%)

- More patients identified as eligible for ART initiation by “Pima effect”.
- Significantly more patients initiated using POC
- But increased LTFU in POC arm (?adherence)

**Initiated on ART**
- 196 (86%)
- 136 (72%)
**Completed 6 months**
- 108 (47.8%)
- 88 (46.6%)
**LTFU**
- 80 (35%)
- 44 (23%)

1.21 (95% CI (1.09-1.34))
1.03 (95% CI (0.84-1.26))
What do we know from the literature?

**Jani.I. (2011, the Lancet)**
- Prior to POC CD4, loss before completion of staging = 57%, post POC CD4 = 20%
- ART initiation rates improved from 12 – 22%
- Days to ART initiation decreased from 48 – 20 days

### POC CD4: impact on misclassification and ART initiation

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Initiation Rate in Facilities</th>
<th>ART Initiation Rate Before POC</th>
<th>ART Initiation Rate After POC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muchedzi, IAS, 2012</td>
<td>43 high-volume PMTCT sites, Zimbabwe</td>
<td>Proportion initiated on ART before CD4 POC = 9%</td>
<td>ART initiation rate in facilities was 15.3% in 2010 (before POC)</td>
<td>ART initiation rate in facilities was 30.4% in 2011 (after POC)</td>
</tr>
<tr>
<td>Schacht, XIX IAS, 2012, Washington</td>
<td>Pregnant women in Gaza Province, Mozambique, eight health facilities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Matambo et al, IAS, 2012</td>
<td>Mobile HIV/TB service for migrant workers on six farms in Musina District, SA</td>
<td>Before the mobile service, 51% eligible for ART based on CD4 testing, were initiated</td>
<td>After introduction of mobile services of those eligible for ART, 83% were initiated</td>
<td></td>
</tr>
</tbody>
</table>
Evaluations of POC CD4 Count Within Comprehensive Interventions

• Recently completed pilot evaluations (no comparison arms):
  - HBCT-Plus (Home based counseling and testing, POC CD4 count, facilitated referrals, and follow up home visits)
    ▪ 86% initiated ART ≤ 3months in rural KZN
  - RAP (“Rapid Initiation of Antiretroviral Therapy in Pregnancy”)
    ▪ 97% initiated ART (91% on same day) in Cape Town
  - PIMA performance during pregnancy (CD4 rate of ART misclassification linked to gestation age (Myer. L et al 2013, JIAS)

• Randomized controlled trials now underway
  - Grand Challenges Canada RCT (“Investigating the feasibility of implementation of multi-disciplinary point-of-care testing in an HIV treatment clinic using a randomised controlled trial”)
  - RapIT (“Rapid Initiation of Antiretroviral Therapy to Promote Early HIV/AIDS Treatment in South Africa”)

• Others?
POCT cost analysis - ongoing

- Context matters
- Key cost drivers
  - Labour
  - Consumables (e.g. cartridges)
  - Volume of tests
- Systems and roll-out costs

How to Estimate the Cost of Point-of-Care CD4 Testing in Program Settings: An Example Using the Alere Pima™ Analyzer in South Africa

Bruce Larson1,4, Kathryn Schnippel2, Buyiswa Ndibongo2, Lawrence Long2, Matthew P. Fox1,2,3, Sydney Rosen1,2
April 2012 | Volume 7 | Issue 4 | e35444

Tropical Medicine and International Health

Scaling up Xpert MTB/RIF technology: the costs of laboratory-vs. clinic-based roll-out in South Africa

Kathryn Schnippel1, Gesine Meyer-Rath1,2, Lawrence Long1, William MacLeod1,2, Ian Sanne1,2, Wendy S. Stevens3,4 and Sydney Rosen1,2

$9.98 Xpert MTB/RIF cartridge

<table>
<thead>
<tr>
<th>Cost component:</th>
<th>Laboratory:</th>
<th>Clinic:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labor</td>
<td>20.40</td>
<td>37.70</td>
</tr>
<tr>
<td>Overhead</td>
<td>19.70</td>
<td>30.10</td>
</tr>
<tr>
<td>Transport</td>
<td>9.80</td>
<td>4.90</td>
</tr>
<tr>
<td>Calibration</td>
<td>4.20</td>
<td>10.40</td>
</tr>
<tr>
<td>Consumables</td>
<td>2.50</td>
<td>8.50</td>
</tr>
<tr>
<td>EQA &amp; training</td>
<td>1.00</td>
<td>27.20</td>
</tr>
<tr>
<td>GX instruments</td>
<td>16.50</td>
<td>35.50</td>
</tr>
<tr>
<td>Other equipment</td>
<td>1.10</td>
<td>8.80</td>
</tr>
<tr>
<td><strong>TOTAL cost / test</strong></td>
<td><strong>R195.10</strong></td>
<td><strong>R282.80</strong></td>
</tr>
</tbody>
</table>

Annual cost: R780 million 49% more

<table>
<thead>
<tr>
<th>Category</th>
<th>Expected Case</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Materials</td>
<td>150.21</td>
</tr>
<tr>
<td>Materials - Shared</td>
<td>1.83</td>
</tr>
<tr>
<td>Salaries / Activities</td>
<td>20.13</td>
</tr>
<tr>
<td>Salaries / Activities - Shared</td>
<td>3.51</td>
</tr>
<tr>
<td>Quality Control</td>
<td>61.82</td>
</tr>
<tr>
<td>Equipment</td>
<td>160.99</td>
</tr>
<tr>
<td>Equipment - Shared</td>
<td>1.17</td>
</tr>
<tr>
<td>Other</td>
<td>24.76</td>
</tr>
<tr>
<td>Other - Shared</td>
<td>10.83</td>
</tr>
<tr>
<td><strong>TOTAL: Cost per test</strong></td>
<td>435.23</td>
</tr>
</tbody>
</table>

The above uses actual testing volume (0.58 per working day)

| TOTAL: Cost per successful test | 439.58 | 42.39 |

The above uses high volume scenario (10 per working day)

| TOTAL: Cost per test          | 185.65 | 17.90 | 100% |
| TOTAL: Cost per successful test | 187.51 | 18.08 |
Expansion of an integrated tiered laboratory service for HIV and TB

**Level IV:** National/multi-country reference laboratories
**Staff:** Senior Health Specialist / lab management, research staff
**Dx:** HIV drug resistance testing, HIV viral load, EID PCR, ELISA, CD4 count, chemistry, haem, micro, histopathology

**Level III:** Regional provincial Laboratory
**Staff:** Lab specialists, senior techs, Programme officer
**Dx:** HIV Viral Load, qualitative EID PCR, ELISA, CD4 count, chem, haem, micro, histopathology

**Level II:** District lab
**Staff:** Lab specialists, senior techs, Programme officer
**Dx:** HIV serology by ELISA, other ELISA, CD4 count, basic chemistry, haematology & microbiology

**Level I:** Primary Health care laboratory testing
**Staff:** Doctors, Nurses, lab or Medical assistants, phlebotomists
**Dx:** HIV rapid tests, other point-of-care tests* and DBS collection

Modified from: http://www.who.int/hiv/amds/amds_cons Tech oper lab_test.pdf
Accurate GIS Mapping
Accurate volumes
Site and logistics

Figure 1
Figure 2: CD4 example: volumes
Figure 3

Turnaround time

Legend
- Current Community Labs
- Current District Labs
- Current Centralised Labs

% of reports with < 48-hour TAT

- 34
- 35 - 85
- 86 - 95
- 96 - 100
Figure 5

Legend:
- CHC Offering ART Services
- New POC Sites
- New Community Labs
- New District Labs
- Current District Labs
- Current Centralised Labs

Volumes
Distance
TAT
The tiered laboratory framework extended to ensure quality servicing to the community

Ref: http://www.who.int/hiv/amds/amds_cons_tech_oper_lab_test.pdf
Community involvement through incentivization

The Market: specific to South Africa

- Official unemployment is 25.5%,
- 69.2 million active sim cards
- 32.9 million people with some form of telephony
- 14.1 million smartphones (estimated)
- Data cost declining, free WIFI penetration increasing
- Advertising & market research on the decline
- Tougher legislation changing the landscape for marketers
- Social engagement continues to grow
- Chat based platforms: highest levels of engagement

Micro jobbing can be the game changer for Developing Markets

www.m4jam.com
Digitally Enabled **Micro Jobbing**

Breaks large projects into small tasks, empowering many geographically dispersed people to quickly and independently complete the tasks using their phones in exchange for payment.

**The Flow:**

- Many jobbers using m4jam aim to complete micro jobs to earn money and in-turn satisfy an overall client's business need.

1. **Enterprise (client): Project**
2. **Jobbers:** Grab a micro job
3. **Race against the clock to complete the micro job**
4. **Jobber gets paid**
5. **Submit the Job for client approval**
6. **Meet your Jobber and your new customer!**
2. POCT principal components

- Connectivity: critical to POCT
  - A universal bi-directional multi-functional (clinic and lab) connectivity solution for POCT is lacking but “cloud-based” SaaS promising (eg PIMA data point – Dashboard and novel approach: Cepheid Remote monitoring).
  - Some areas require signal boosting and internet policing is essential.
  - Computer literacy is currently lacking by many staff.
  - Novel approaches: SMS printers shown to extend services and shorten TAT and being modified to encompass “linkage to care” and modified for bidirectional communication and expanded test repertoire.

Connectivity Data Analysis

- Automated results:
  - GeneXpert
  - Hemocue
  - PIMA
- Manual entry for Reflotron (Creatinine and ALT) - AegisPOC
- Analysis performed on manual entry
  - Transcription error of results
  - Incorrect patient ID used
  - Duplicate entry
  - Results not captured

62% of overall results captured correctly
Operational Dashboard

- Interface single instrument type/s from a specific vendor
- Limited, more basic reports
- Non-patient identifiable
- Unlinked

Free (generally)

Middleware

- Interfaces 100’s of instruments and types – vendor neutral
- Flexible, extensive reporting
- Patient Identifiable
- Linked to LIS & HIS

High cost – but high cost saving
Challenges, barriers and opportunities

- Poor infrastructure.
- Costs of maintenance to systems and instrumentation.
- No incentive schemes to invest in electronic capture of data.
- Fragmentation of systems; SA full of legacy systems.
- Limited use of standards (Some Well-established systems. e.g. SNOMED).
- Systems are often complex and require vendor support (*No access to proprietary communication standards making interfacing difficult*).
- No standardized physical connectivity (infra-red, serial, direct network etc.)
- Bi-directional communications support with DMS or host LIS is not supported by all devices (especially for POC).
- IN SA, a unique identifier is needed and connection to EMR is essential.
- Numerous based technical standards (*CIC 1999 – communication protocols*) to ensure stability e.g. HL7 (health), CLIA etc.
- Many are adding **SLAMs** (stand alone add on modules (apps)) to LIS; specific modules with specific functions e.g.web portals, management, QA/QC, telepathology etc to fill the LIS functionality gap.
- Software delivery has a thin client application; remote server, frequently accessed by web browser. **Service investment rather hardware investment** (*SaaS = software as a service*)
Cloud computing

- **Cloud computing** is emerging as a new paradigm in healthcare.
- simple means of the delivery of a service rather than a product.
- The main enabling technology Virtualisation is the ability to allow the system to operate independently of the hardware.
- From the Cloud via the internet, one can provide information to other users of hardware or software
- resources can be shared within and between organisations to improve economies of scale. Data can be transferred in a computer network that is able to compartmentalise your needs.
- Advantages cited include increased speed, flexibility and a reduction in costs and labour.
- New work suggests the use of the “mobile cloud” which combines the use of mobile devices and the cloud (PDA’s, smart phones etc.).
- The cloud provides an affordable outsourcing model for whoever has dynamic needs for scalable computing.
- Cloud computing could facilitate global disease surveillance
A new Era in Lab services: “the cloud”

Gx verification (on installation, module maintenance) and EQA 3 x per year, but third quality monitoring component = real time monitoring.

- Operational dashboard for real-time monitoring of results, errors, resistance and positivity rates
- Pre-configured on all newly installed GeneXperts

Alpha and beta testing completed, National Priority Program
Appropriate, controlled placement is required

1. **Total Coverage model**: where Point of Care added to ensure complete coverage of laboratory services in a tiered laboratory service, focussing on remote, low volume sites. Equipment selection: based on volumes largely and gaps.

2. **Point of Treatment (total decentralized)**
   - Disease specific e.g. HIV treatment initiation, TB diagnosis, diagnosis of diarrhea, non-communicable e.g. glucose, HbA1c
   - Assay specific e.g. Hb, or GeneXpert, cryptococcal antigen or POC CD4 for wellness testing

3. **Product niching**: VL/EID maternity wards,

**Needs**
Accreditation of sites: staff, quality and connectivity with appropriate checklists.
An extension of the existing laboratory infrastructure/footprint.

---

Trends in “supplier business models”: Partnering is essential.

Multiple suppliers with Single platform solution for POCT. Numerous examples in UNITAID development pipeline documents 2014 (HIV and TB).

Single supplier with multiple separate platform solution for POCT eg Alere (HIV Determine, PIMA CD4 and now EID/VL, ePOC for Hb and Cr).

Single supplier with high/ultra throughput analysers, with extension to low throughput at POC, eg. Roche (8800 to the “LIAT” and/or DBS).

Single supplier with high throughput analysers with multiplexing of assays (HIV, TB, HPV, HBV…..Roche, Abbott).

Single supplier with modular approach (single cartridge across all volume testing) and multiplex, Eg. Cepheid.

Now there is an increase in options which facilitates competition and innovation.
Future work

- **HIV rapid tests: Quality concerns**
  - HIV misclassification study (impact on test and treat - CD4 to 500c/ul): pilot underway
  - Reader/smartphone use for quality
  - EQA needed for national program: protocol design to include whole blood material and result capture managed by SaaS (SMS printers and/or cell phone technology).
  - Community involvement for expanded access

- **Linkage to Care**
  - MDR TB project (Gates funded)
    - Principles likely to apply to HIV

- Complete CD4 and viral load validations.

- Draft policy: difficult as guidelines, technology and regulatory changes.

- Investigation of new cadres of staff with official training and registration and “implementation science” course,

- Role of Incentivization: previously absolute refusal via ethics: more open to approaches

- Pilot project: investigation of solutions such as m4JAM and expand connectivity applications
Acknowledgements

- Ministery of Health: Dr Motsoaledi, Drs Mametje, Pillay, Mvusi, Barron, Mabope
- The National Health Laboratory Service and the NHLS POC working group and NPP.
- The GCC team: Lesley Scott, Johan Potgieter, Natasha Gous, Brad Cunningham, Matilda Nduna, Regina Osih, Charlotte Jansen van Rensburg, nurses and counsellors
- Funders (GCC, PEPFAR (CDC, USAID), FIND, Bill and Melinda Gates foundation
- Clinical partners (CHRU/RTC, WRHI, PHRU)
- Patients and participants
- Suppliers (hardware and software)
- Centre for Excellence for Biomedical TB Research
- CHAI team, Trevor Peter, Jonathan Lehe