"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"

Grand Challenges Canada
Grands Défis Canada
BOLD IDEAS FOR HUMANITY
DES IDÉES AUDACIEUSES POUR L'HUMANITÉ

Wendy Stevens

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Personal view, not endorsing any particular supplier or policy

On behalf of the GCC Team

NATIONAL HEALTH LABORATORY SERVICE
NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

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.

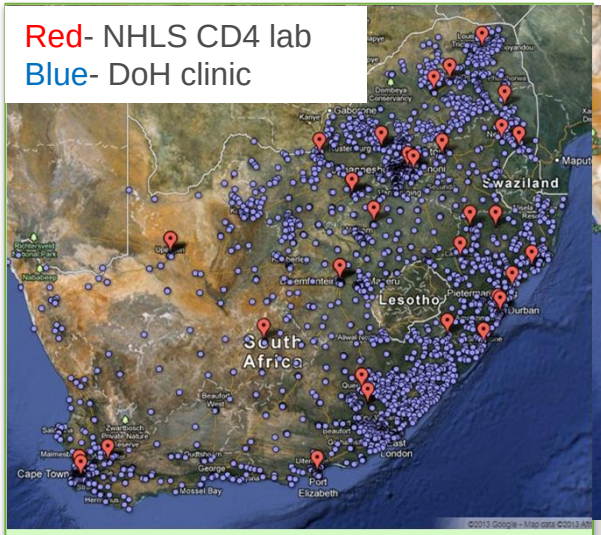
over 4 million GeneXpert tests (July2014); MTB 16-12%; Rif Resistance:7%.

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**

NSP, 2012 http://www.doh.gov.za/docs/stratdocs/2012/NSPsum.pdf

AS IS: 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 millionl 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

Scott.LE, Stevens,W et al .The diagnostic accuracy of Xpert MTB/RIF on extra pulmonary tuberculosis specimens: Establishing a laboratory testing algorithm for South Africa. J Clin Microbiol. 2014 Mar 12. [Epub ahead of print] PMC3951458

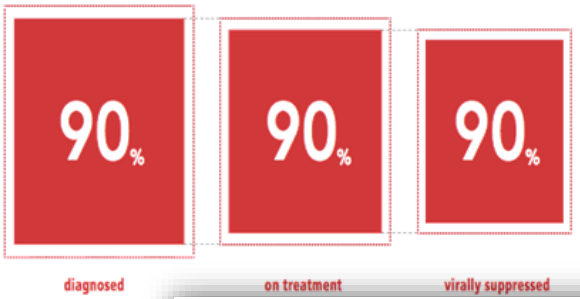
UNAIDS

Game-changer

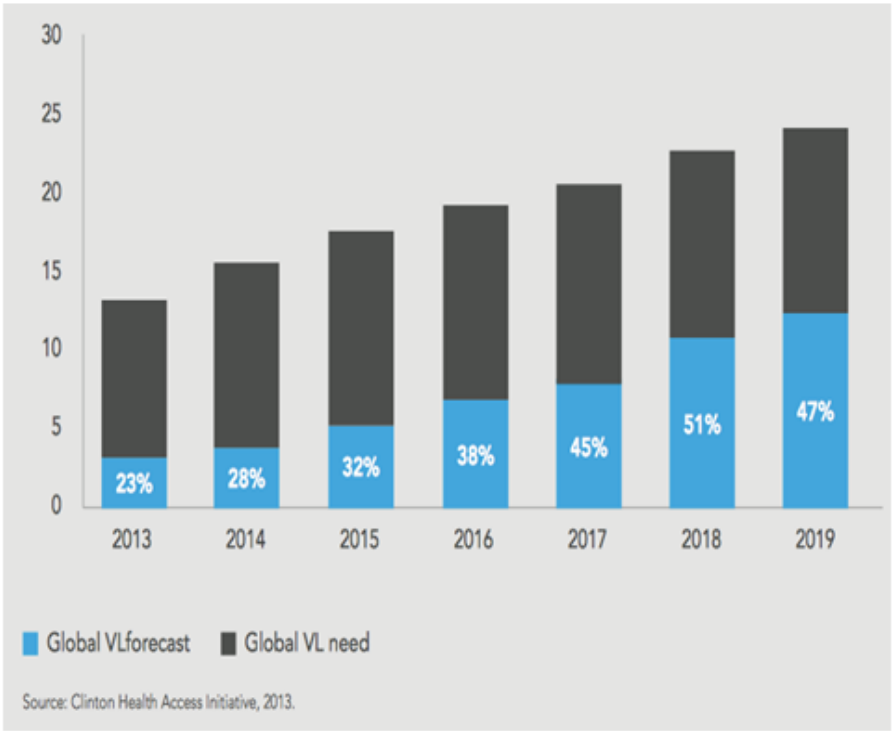
volumes for SA and other countries

AMBITIOUS TREATMENT TARGETS:

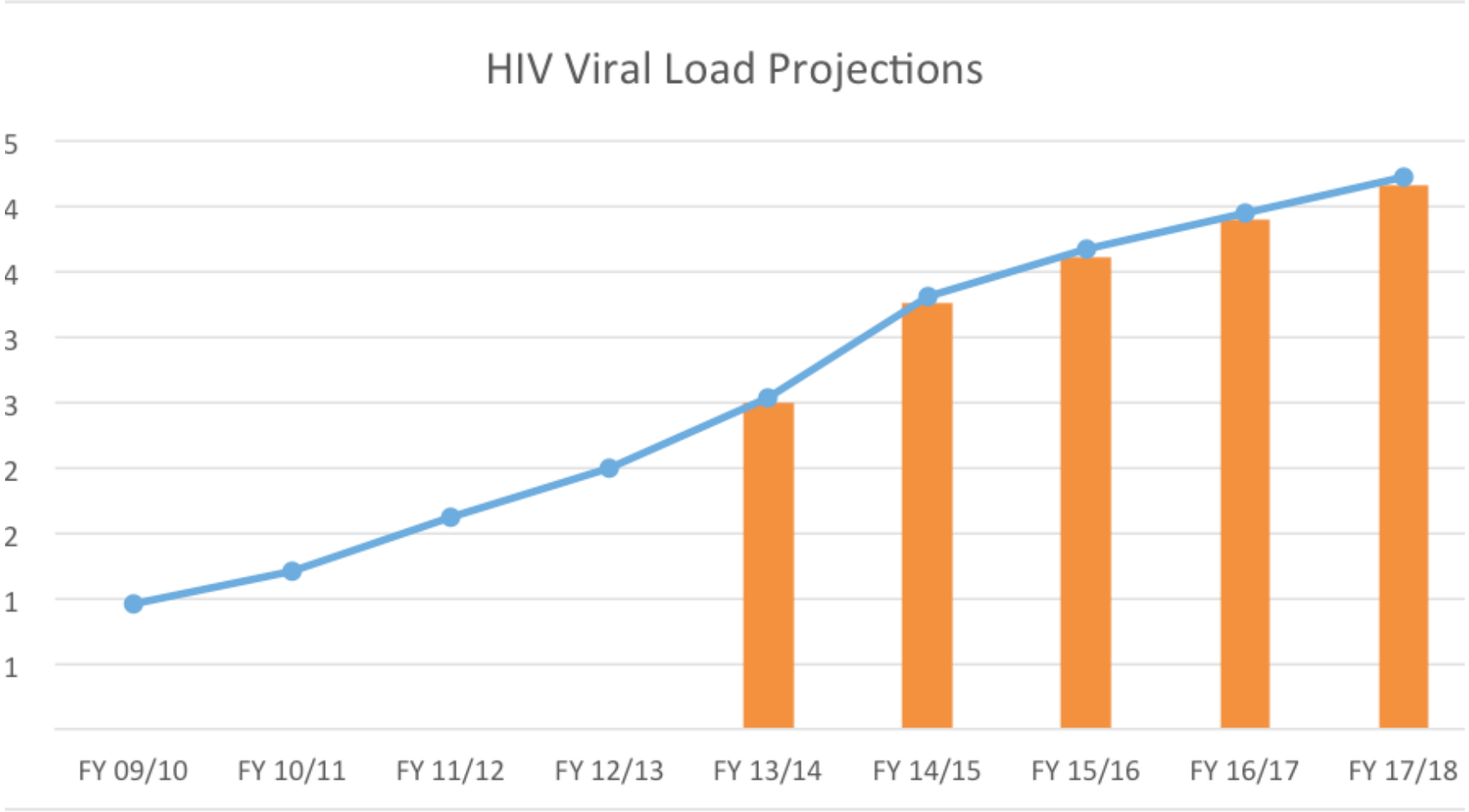
WRITING THE FINAL CHAPTER OF THE AIDS EPIDEMIC



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 *m*2000 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 *m*2000
- Roche Cobas Ampliprep/Cobas TaqMan

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

Year	CD4 Vols	Current Adjusted Capacity*	Capacity Utilisation	VL Vols	Current Capacity	Capacity Utilisation
2014/2015	3 484 757	5 665 248	62%	3 589 938	3 047 676	118%
2015/2016	1 502 379	5 665 248	27%	3 833 688	3 047 676	126%
2016/2017	1 109 244	5 665 248	20%	4 056 075	3 047 676	133%
2017/2018	983 484	5 665 248	17%	4 315 782	3 047 676	142%

* 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)

TRUE TRUE

Analysis of additional systems required

Year	CD4 Capacity Gap	CD4 System Capacity (8HR 2+2)	Additional Systems Required	VL Capacity Gap	VL System Capacity (24HR)*	Additional Systems Required
2014/2015	-2 180 491	259 200	None	342 262	86 184	6
2015/2016	-4 162 869	259 200	None	786 012	86 184	9
2016/2017	-4 556 004	259 200	None	1 008 399	86 184	12
2017/2018	-4 681 764	259 200	None	1 268 106	86 184	15

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

TRUE FALSE

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

Year	CD4 Vols	CD4 System Capacity (8HR 2+2)	No of Systems required	VL Vols	VL System Capacity (24HR)*	No of Systems required
2014/2015	3 484 757	259 200	13	3 589 938	86 184	42
2015/2016	1 502 379	259 200	6	3 833 688	86 184	44
2016/2017	1 109 244	259 200	4	4 056 075	86 184	47
2017/2018	983 484	259 200	4	4 315 782	86 184	50

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

TRUE TRUE

User Interaction

User Interaction

User Interaction

First 96 results
In less than 3.5 hrs

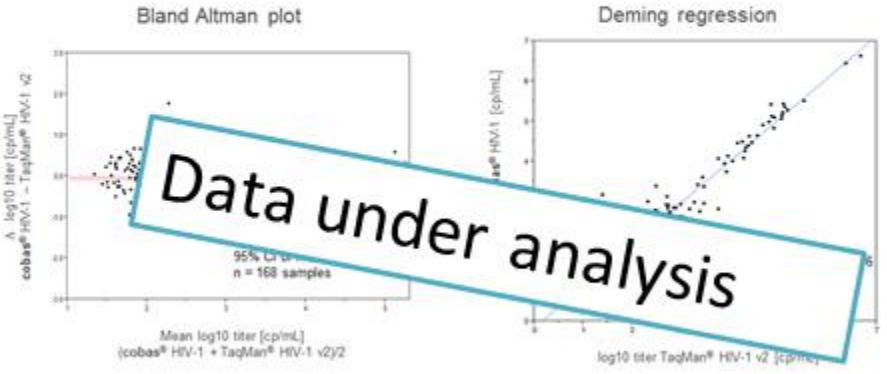
4 hours
Work-away time

The **cobas**® HIV-1 test is currently in development and not commercially available.

cobas® 8800 System

Method comparison (local HIV-1 cohort)

cobas® *HIV-1 correlation to TaqMan*® *HIV-1 v2*

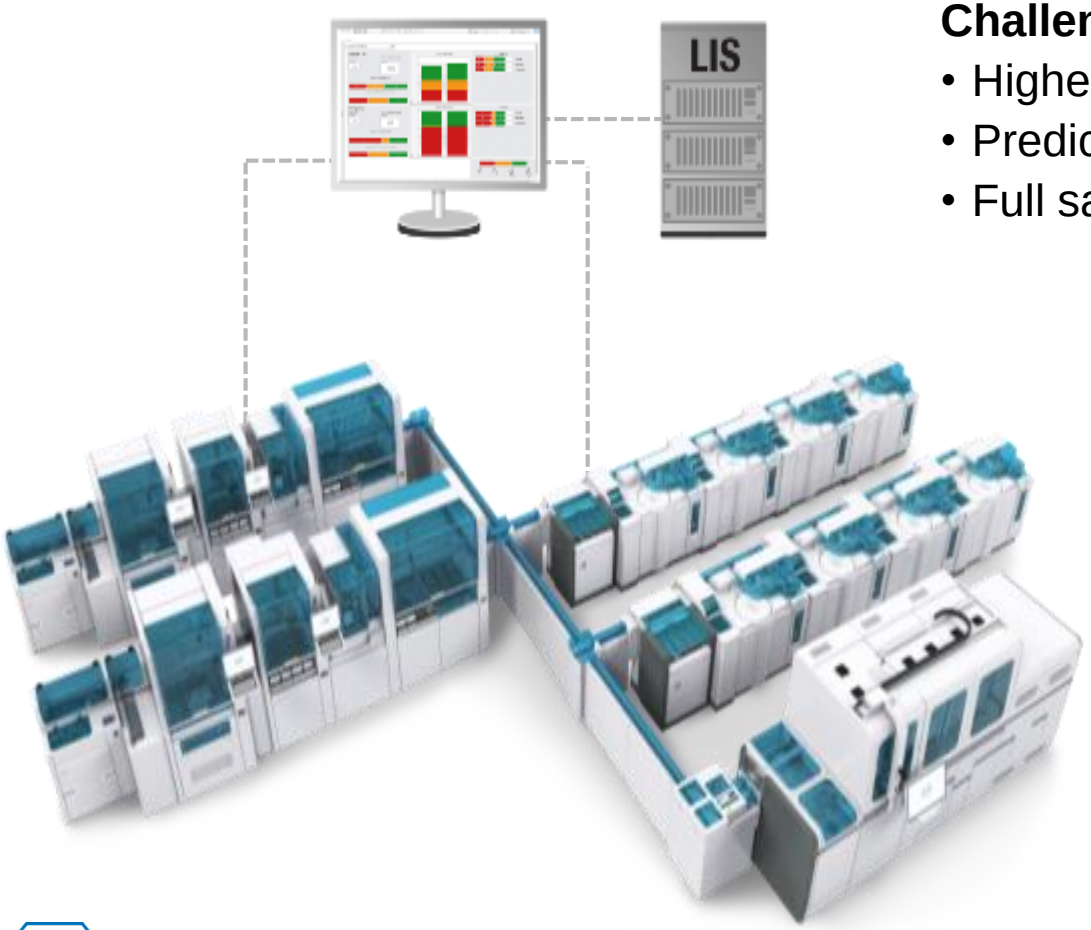


Data under analysis

Courtesy of Roche and Sergio Carmona

Large - connected

Reduce hands-on time to a minimum



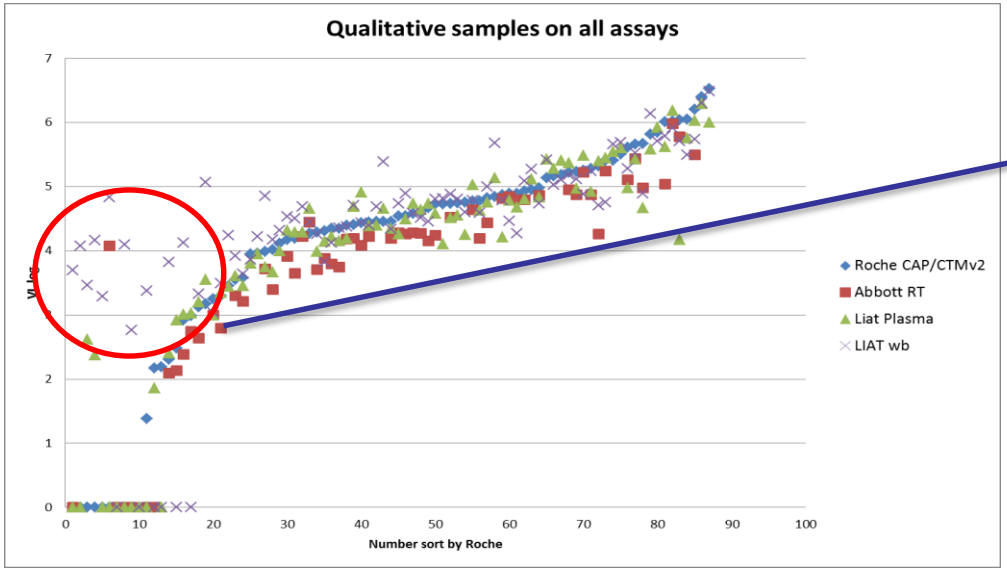
Challenges addressed

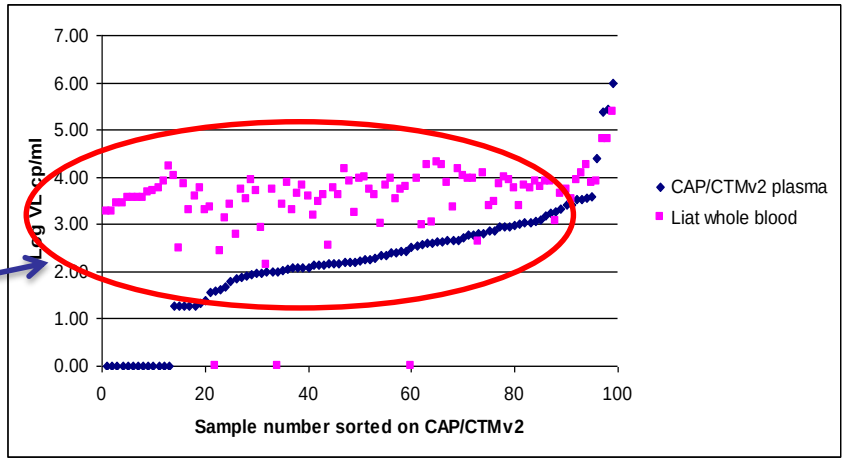
- Higher throughput
- Predictable TAT
- Full sample traceability

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 -1.5x10^6 c/ml
- Sample types:
  - Blood – 75ul
  - Plasma – 150ul
- TAT:
  - Blood – 35 minutes
  - Plasma – 30 minutes

- Plasma testing as good as lab (<1000c/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?

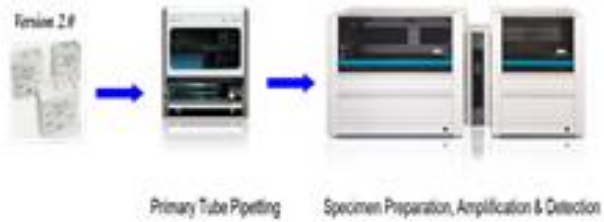
Trends in Technology and scale

SAMBA

LIAT

Simplified testing

Up to 1000 samples/8hrs



cobas® 8800 System

Complex Systems

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

UNITAID LANDSCAPE DOCUMENTS for HIV and TB in packs

South Africa:

POC too costly

Evaluate in HIV/TB setting

Expansion: mines, correctional services

NTCM / Gx to smear microscopy centres

A cartridge for INH, 2nd line?

Novel EQA developed

New markers

Develop SOP's, EQA

Surveillance

Implement rapidly/high burden districts then 100% coverage

Started March 2011, completed September 2013

Value of the Ct

Monitoring?

Clinical + Lab algorithm and training

1 sputum only (except WC)

Trained: 1035 lab and 5332 clinic staff

Paediatrics

Remote connectivity/ calibration

Difficult: is solution stool testing?

EPTB

Real time test monitoring

New studies on urine

WHO recommends

100% Coverage as per NDoH plan in public sector.

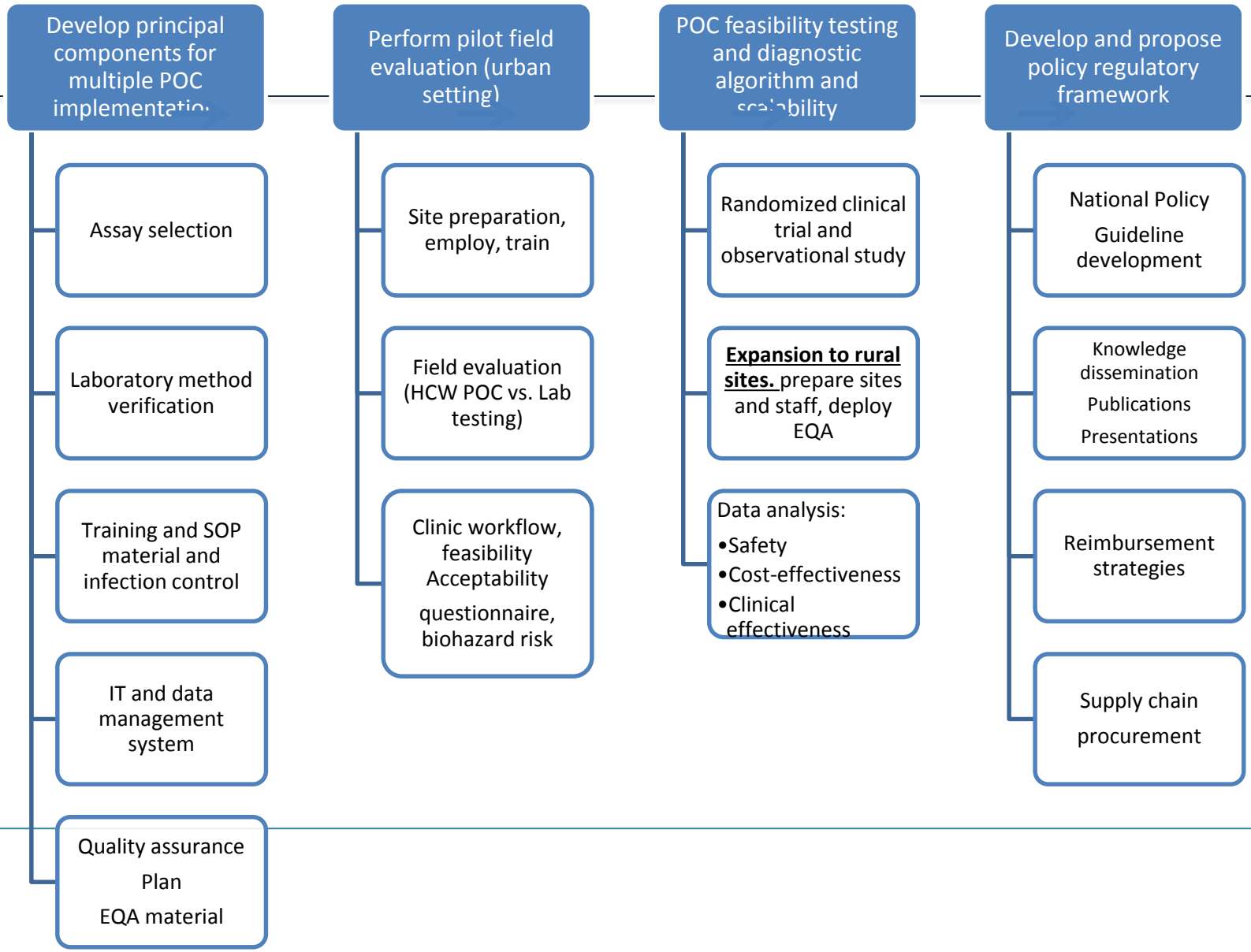
- Implementation in all original smear microscopy centres: in a 3 phased approach, HBD first
- 207 centers across the 9 provinces
- Phased implementation started March 24th, 2011
- To date ~4.0 mill tests performed to date; **60%** of global cartridges procured
- **289 analyzers**: GX4 (95); GX16(186);GX48(1)
- 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

- *Hanrahan, C, Scott.L.E, Van Rie. A, Stevens.W et al. Time to Treatment and Patient Outcomes among TB Suspects Screened by a Single Point-of-Care Xpert MTB/RIF at a Primary Care Clinic in Johannesburg, South Africa. PLoS One June 2013. PMC3686680*
- *Van Rie.A, Page-Shipp.L, Scott.L, Stevens.W, et al. Point-of-care Xpert® MTB/RIF for smear-negative tuberculosis suspects at a primary care clinic in South Africa, INT J TUBERC LUNG DIS 17(3):368–372, 2013*
- *Kate Clouse, Lesley Scott, Wendy Stevens, Annelies Van Rie et al. Implementation of Xpert MTB/RIF for routine point-of-care diagnosis of tuberculosis at the primary care level. S Afr Med J. 2012 Sep 7;102(10):805-7. doi: 10.7196/samj.5851*
- *Van Rie A, Scott L, et al. False-positive rifampicin resistance on Xpert® MTB/RIF: case report and clinical implications, Int J Tuberc Lung Dis. 2012 Feb;16(2):206-8.*
- *Clouse K, Scott L, Stevens WS, van Rie A. et al. Implementation of Xpert MTB/RIF for routine point-of-care diagnosis of tuberculosis at the primary care level. Accepted to PLOS Medicine, March 2012*
- Van Rie, A, Scott,L, Sanne,I, Stevens,W et al. Xpert MTB/RIF for point of care diagnosis of TB in high HIV burden, resources-limited countries: Hype or hope? Expert Review Mol Diagn 2010 Oct (7):937-46

Project framework

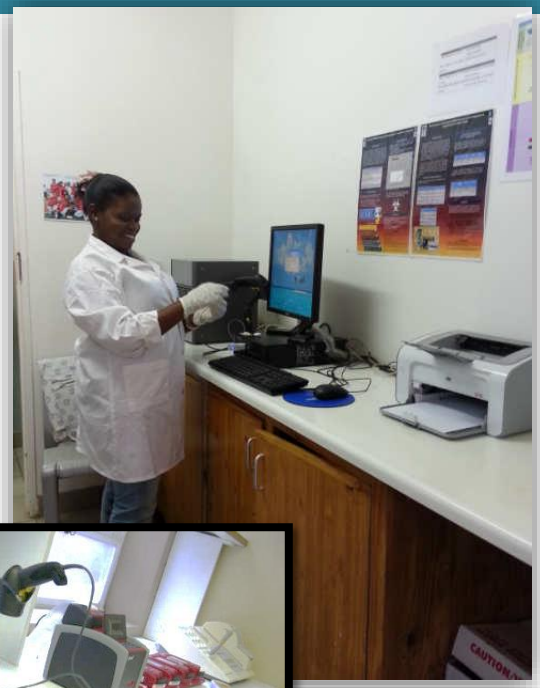
- Determine principal components for an HIV/TB POCT (diagnosis and monitoring) implementation model.
- Determine the feasibility of performing multiple POCT in SA and scalability to RLS.
- Determine the impact of POCT for ART initiation (and at what cost)
- Develop policy framework for POCT for ART initiation.

Summary of Project components



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.



Scott.L.E. A laboratorian’s experience of implementing multiple point-of-care testing in HIV antiretroviral treatment clinics in South Africa. December 2013, Vol. 103, No. 12 SAMJ

1.POC nurse- based venepuncture testing performed adequately compared to gold standard laboratory testing

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

Study has been duplicated at Tshwane district hospital: n=276

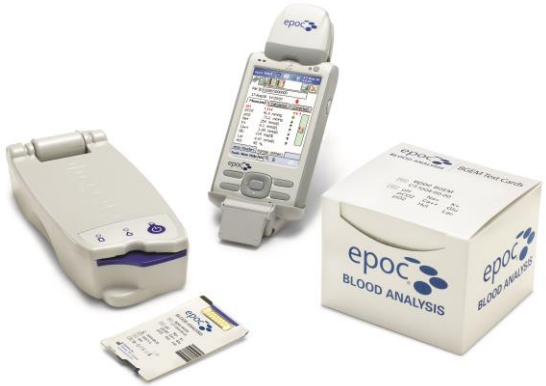
Role of CD4 testing questioned

- 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.*
- *Ford et al. Lancet 2014. The future role of CD4 cell count for monitoring ART.*

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



	EPOC1 vs Lab (n=125)		EPOC2 2 vs Lab (n=124*)		Reflotron vs Lab (n=125)	
Creat	**Difference**	**% Sim**	**Difference**	**% Sim**	**Difference**	**% Sim**
Mean	6.7	94.7	2.5	97.4	18.5	86.5
SD	15	11.8	13.5	10.7	9.3	5.5
CV		12.4		10.4		6.3
	EPOC1 vs Lab (n=124Ŧ)		**EPOC2 2 vs Lab (n=124Ŧ)**			
HB	**Difference**	**% Sim**	**Difference**	**% Sim**		
Mean	-1.5	105.4	-1.6	106.0		
SD	-1.5	105.4	0.8	3.2		
CV		3.6		3.0		

*18 QC failures/all but one repeated

Ŧ 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 form clinic and received in the lab same day
  - 72% results received back in clinic within 1 day.

Gous N, Scott.L,Stevens.W, et al. Feasibility of performing multiple Point of Care testing for HIV anti-retroviral treatment initiation and monitoring from multiple or single fingersticks. PLoS One, December 2013 | Volume 8 | Issue 12 | e85265

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

Grand Challenges Canada Study/ University of the Witwatersrand Department of Haematology and Molecular Medicine

udy Code: HREC 10333 Sub-Study: Investigating the effect of POC laboratory on Patient Flow

REGISTER FORM

Consent documented YES/NO Study Coordinator (sign)

Client number: 13 Date: 26.09.13 Time arrived: 9:05

Time departed: 10:00.

Sex: Male ___ Female ✓

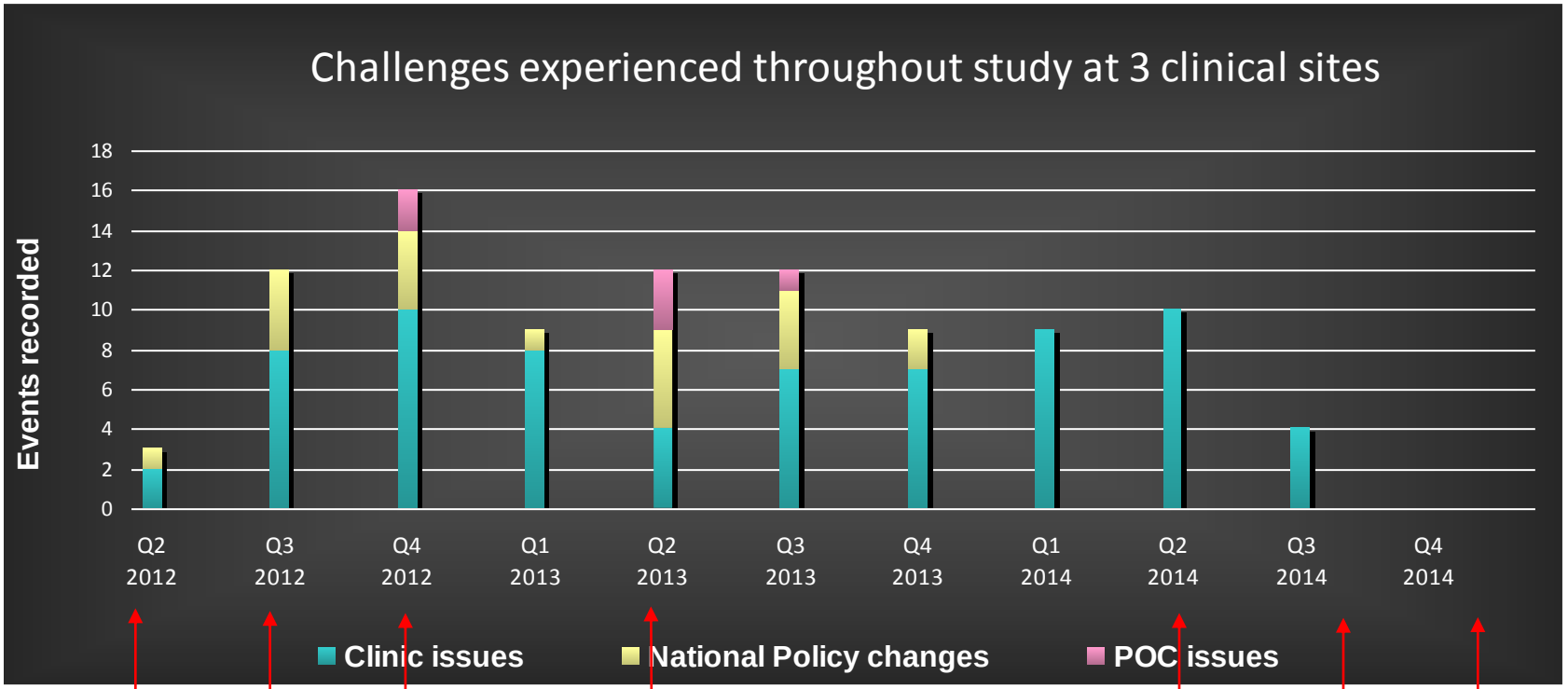
Primary reason for visit (see visit code below): F

Visit timing: First visit: ___ Follow up visit: ✓

	Staff code & initials	Waiting time	Time service started	Time service completed
First contact	A	30 min	9:10	9:15
Second contact	C	15 min	9:25	9:930
Third contact	E	20 min	9:45	10:00.
Fourth contact				

	Before POC (H:M:S)
Average time in clinic	02:47:12
Average time to see a nurse	02:11:07
Average time to first contact	01:00:00
Average visit time with health provider	00:09:30
Longest time in clinic	04:05:00
shortest time in clinic	01:45:00

Flexibility required for hurdles encountered



1st clinic site initiated

2nd clinic site initiated

3rd clinic site initiated

SA Treatment guidelines changed: 7days ART

SA Treatment guidelines changed: CD4 500c/ul

Patient follow up complete

Data analysis

Key:

Clinic issues: HR shortages/stock shortages/infrastructure problems

National policy changes: Change in guidelines /no eligible patients/campaigns

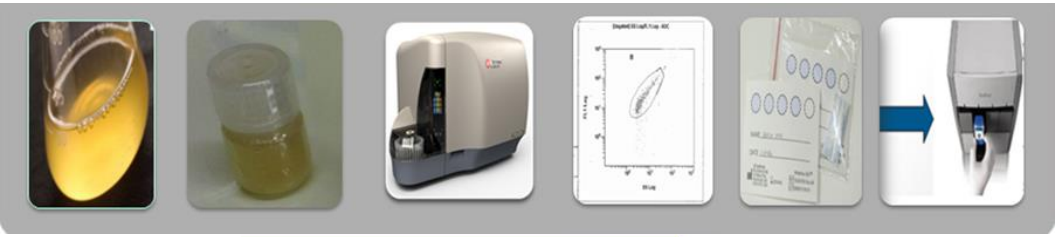
POC issues: instrument downtime/errors/invalids/QC failures

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

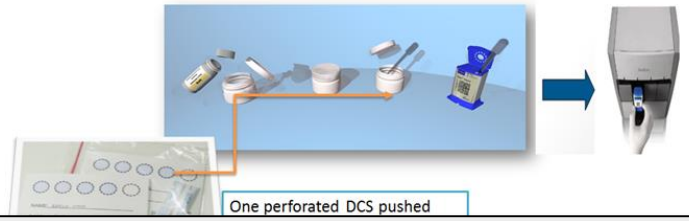
EQA

- Scott.L.E, Stevens. W, Kana.B, 2013. GeneXpert TB EQA. Special Achievements WITS and Top Award for Innovation: National Innovation Annual Awards, NHLS
- Scott.L.E. 2014. " International Inventor Certificate" from WITS Innovation/WITS Enterprise.

- 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*



The testing process



One perforated DCS pushed

Dried Culture Spot Program for External Quality Assessment (EQA)

Quality management of *Mycobacterium tuberculosis* molecular diagnostics

Dried Culture Spot (DCS) technology

US Patent Number 8,709,712

Dried culture spot (DCS) technology(1) 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 Munktell TFN filter cards (LabMate, Cape Town, SA). The DCS cards are barcoded and shipped by post 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). Re… manually by receiving laboratories or a…

DCS for EQA

1 EQA panel consisting of 4 DCS. Annual EQA program requires 3 panels.

EQA Result reporting

Department of Molecular … Johannesburg, South Afric…

Dried Culture Spot Program for Verification

Quality management of *Mycobacterium tuberculosis* molecular diagnostics

Dried Culture Spot (DCS) technology

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DCS are manufactured using *M.tb* cultures grown in single cell format, followed by chemical and heat inactivation, quantification and spotted onto Munktell TFN filter cards (LabMate, Cape Town, SA). The DCS cards are barcoded and shipped by post at room temperature. Processing of the DCS on-site follows the Xpert MTB/RIF manufacturers testing protocol. The program involves two components: (1) verification (results unblinded) and (2) external quality assessment (EQA) (results blinded). Result reporting is managed manually by receiving laboratories or automated through www.tbgxmonitor.com.

1. Scott L.E. et al., JCM 2011, 49(12): 4356-60.; 2. Scott L. et al. JCM 2014 Apr 30. [Epub ahead of print]; 3. Gous N. et al. JCM. 2013 Dec 51

DCS for Verification

Single verification card of 1 DCS.

Multiple verification card of 5 DCS.

Verification Result reporting

Instrument verification involves testing standardized material on a diagnostic instrument to ensure that it is 'fit-for-purpose' before clinical specimens can be tested. Verification should be performed on each GeneXpert® module upon instrument installation, module replacement and if an instrument is moved. The DCS product for verification is available in a 5 spot and 1 spot card format, as shown. Verification panels are provided free to end-users via Cepheid on installation of new GeneXpert® instrumentation.
*The **Global Laboratory Initiative** (GLI), working group, has endorsed the use of DCS technology in GeneXpert® instrument verification.*

A report form is included with the DCS verification product for manual result reporting if access to www.tbgxmonitor.com is not possible. Access to TBGxMonitor® is provided through enrolment and registration via info@tbgxmonitor.com.

…ent of Molecular Medicine and Haematology, University of …atersrand, Johannesburg, South Africa, also in collaboration …CDC and ACTG.

US patent 8,709,712.

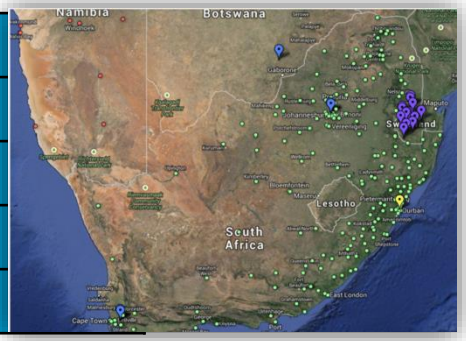
- Gous N, Cunningham B, Kana B, Stevens W, Scott LE. Performance Monitoring of M.tb Dried Culture Spots for use with the GeneXpert System within a National Program in South Africa. J Clin Microbiol. 2013 Dec;51(12):4018-21
- Scott LE, Gous N, Cunningham BE, Kana BD, Perovic O, Erasmus L, Coetzee GJ, Koornhof H, Stevens W. Dried Culture Spots for Xpert MTB/RIF External Quality Assessment: Results of phase 1 pilot study from South Africa. *J Clin Microbiology* 2011, 49(12):4356

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	
n= 1016	
Correct results	998 (98.2%)
Errors	6 (0.6%)
Incorrect result	12 (1.2%)



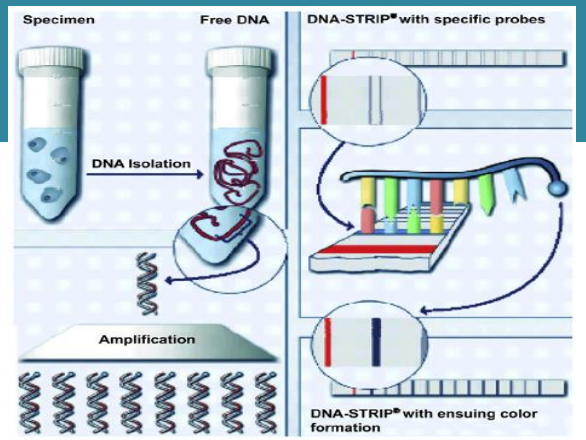
Impact in SA of not verifying Gx before clinical testing.
~78 000 tests (of 3mil) could have been in error from 105 dysfunctional modules.

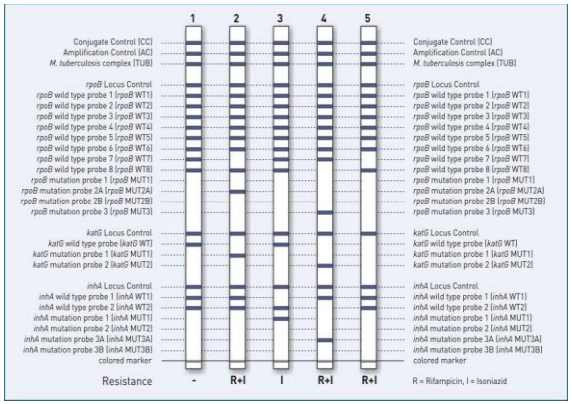
Scott.L.E, Albert. H, Gilpin.C, Alexander.H, DeGruy.K, Stevens,W. Multicenter Feasibility Study to assess external quality assessment panels for Xeprt MTB/RIF assay in South Africa.. *JCM, 2014doi:10.1128/JCM.03533-13*

DCS EQA for alternative technologies.

MTBDRplus v2	n	Observed result
RIF resistant DCS	70	100% MTB positive RIF resistant/INH sensitive
RIF susceptible DCS	36	100% MTB positive RIF sensitive/ INH sensitive (including verification spots)
NTM DCS M. kansasii M.intracellulare M.fortuitum	46	93% (n=43) MTB negative 3 MTB positive, inconclusive RIF/INH bands *)
CM assay (when performed)	24	96% (n=23) correct speciation 1 incorrect, *M.avium*

1





DCS EQA program	Ustar EasyNAT TB assay(Correctly identified)
MTB RIF susceptible DCS n=6	100% RIF susceptible
MTB RIF resistant DCS n=6	100% RIF resistant
NTM DCS n=6	100% negative

2

3

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

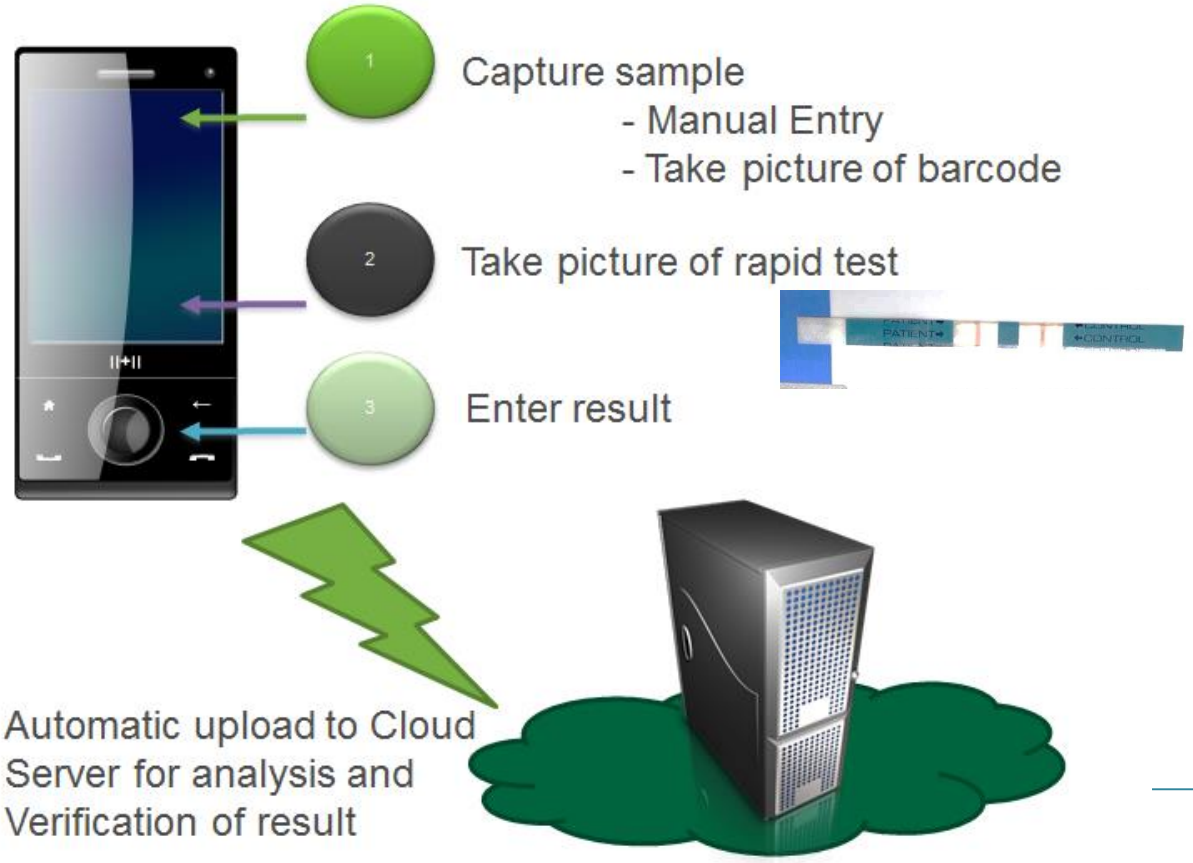
Name	Number of tests	Platform	Additional Hardware	Central Repository
Fio Corp.	'near universal'	Mobile, Android	Deki Reader	Yes
Holomic LLC	'near universal'	Mobile	RDT Reader	Yes
MobileAssay™	'near universal'	Mobile & Tablet Apple, Android, Windows	None required	Yes
Global Solutions for Infectious Disease (GSID)	'near universal'	Mobile	Phone stand	Yes
BBI Solutions and Albagaia	Custom per test	Mobile Apple, Android, Windows	None	Yes

Not entire list of available devices

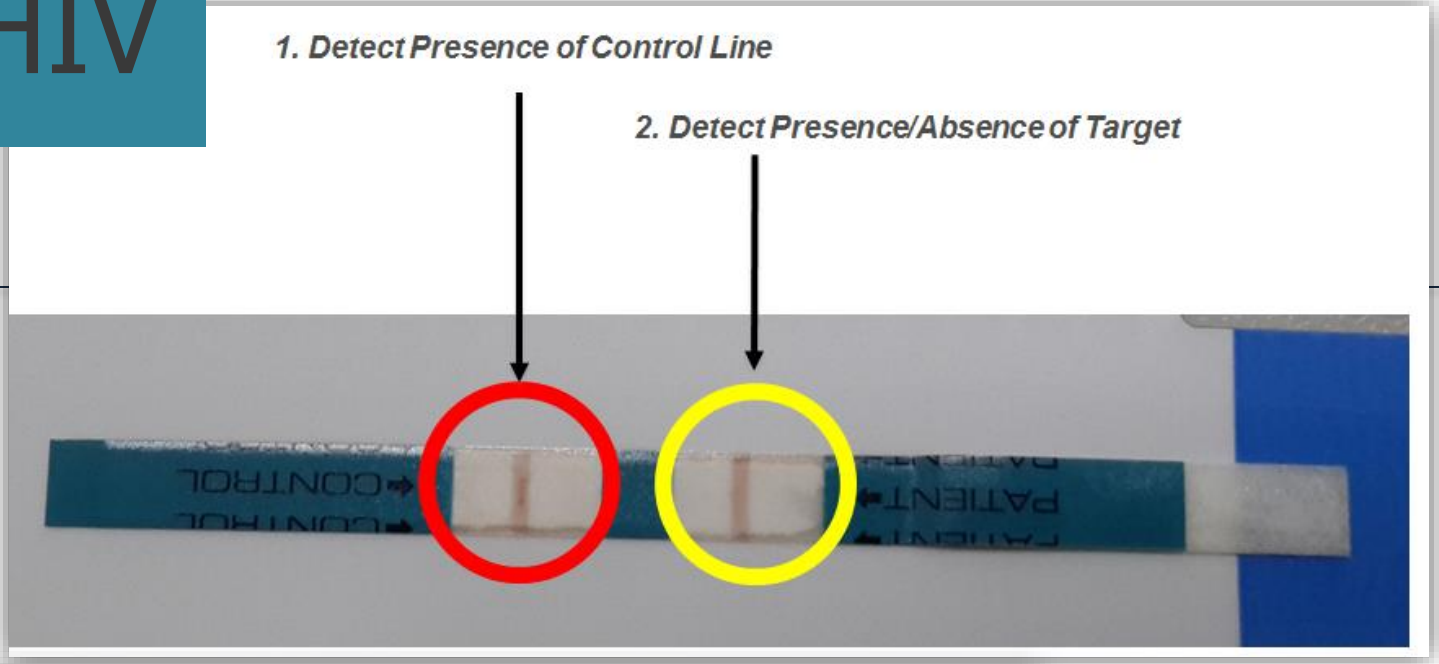
Smart Phone: data and graphic uploaded to cloud for analysis

61 million active sim cards in SA

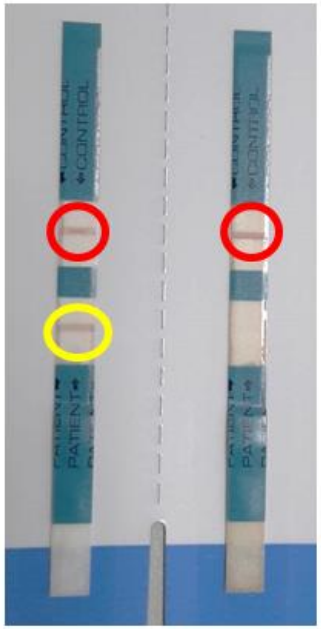
14 million smart phones



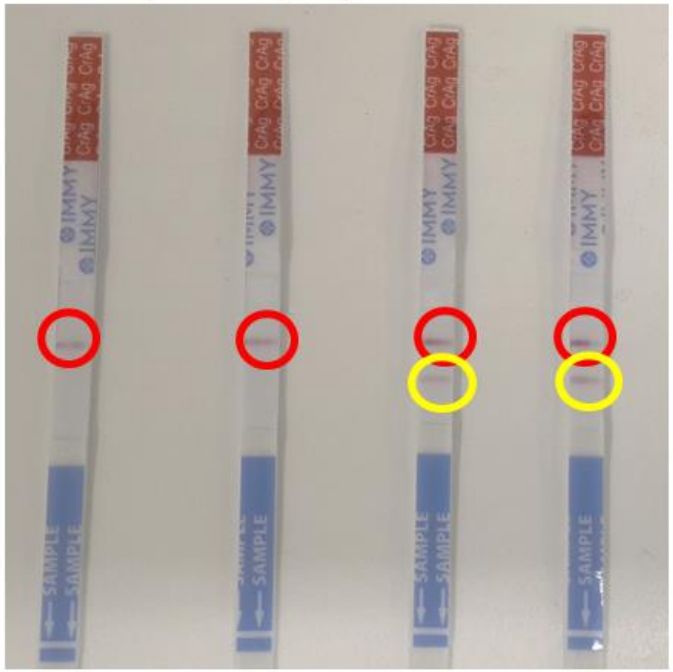
Rapid HIV Test



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

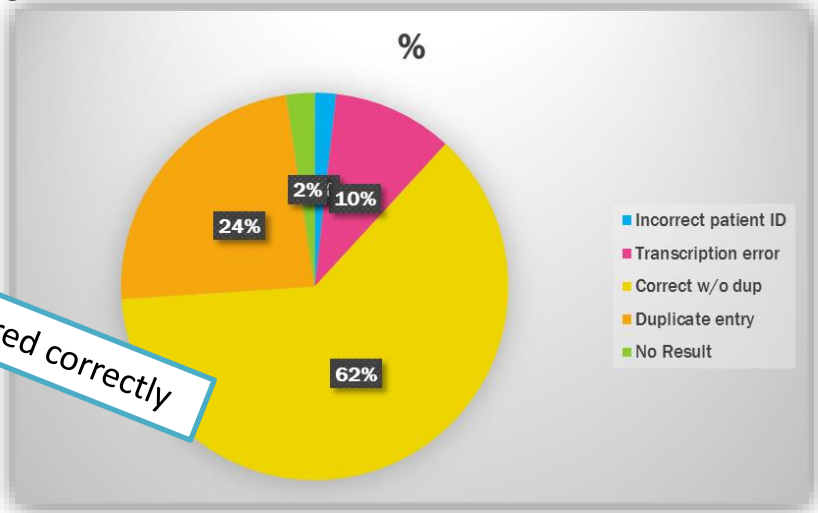
- Connectivity: critical to POCT
  - A universal bi-directional multi-functional (clinic and lab) connectivity solution for POCT is lacking but “cloud-based” SaaS promising (eg PIMA data point – Dashboard and novel approach: Cepheid Remote monitoring).
  - Some areas require signal boosting and internet 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.

Stevens. W, et al. Remote connectivity. Book Chapter under submission

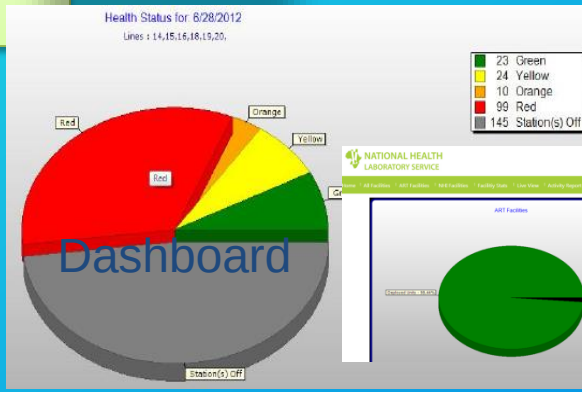
Connectivity Data Analysis

- 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



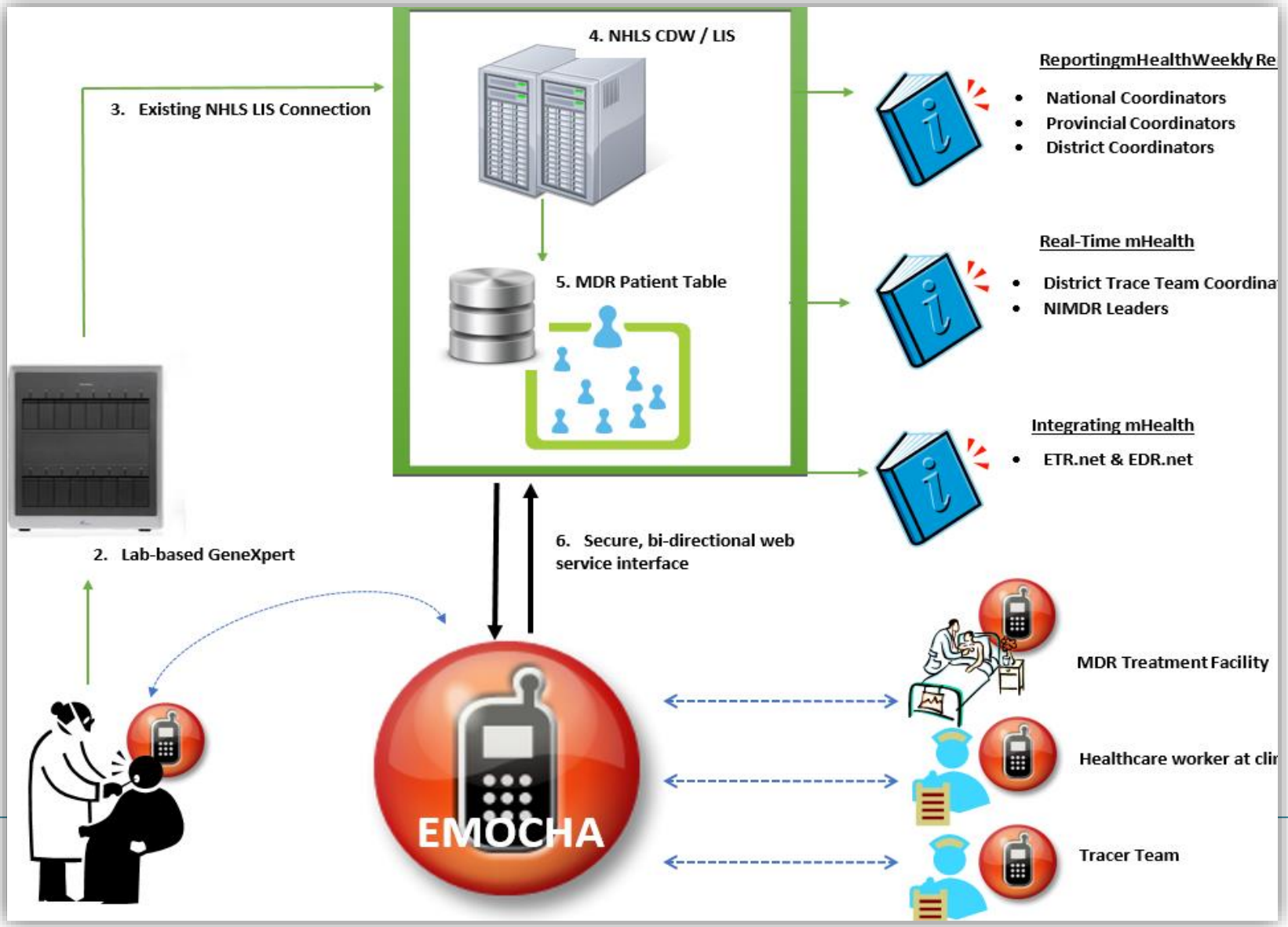
LIS extended to the clinic: SMS printers



- 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.

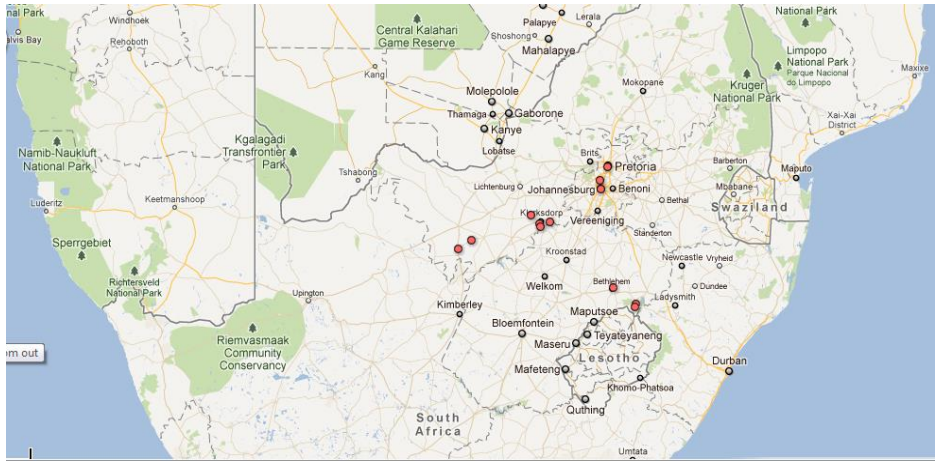
Connectivity = service expansion, quality and training maintenance.

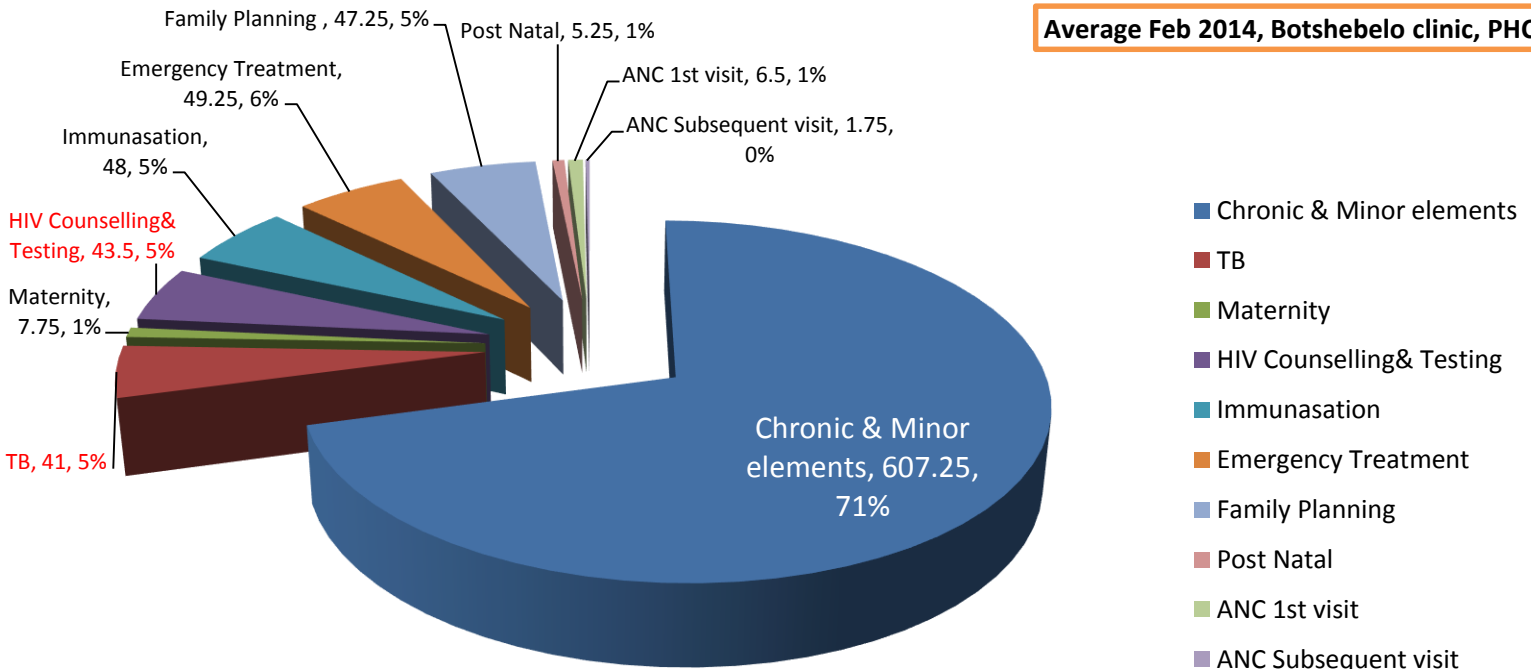
Linkage to care: our plan for MTB-DR TB



3: 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),





3. Outcome measures

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

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)

<u>Enrolment criteria</u>:

- >18yrs, HIV+, presenting for ART.

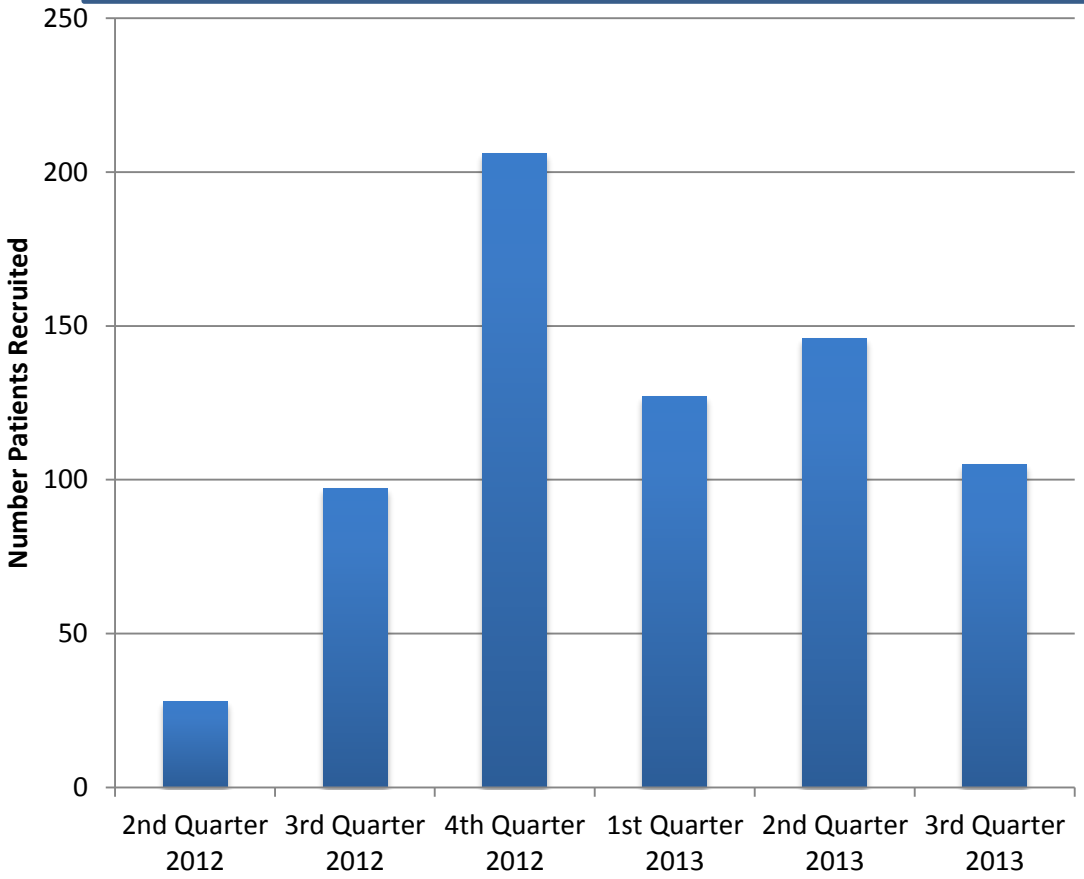
Outcomes:

- 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 12months
- Measure of effect of POC on clinic flow

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

All four clinics within 35km from Tshepong District hospital

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

Pregnancy	
currently	20%
previously	68%
Ever received PMTCT	9.7%

Characteristics	All subjects
Mean age	35.7yrs
% male	33%

Employment	
Full time	17.7%
none	72%
occasional	2.6%
Part time	7.3%

Education	
none	2.4%
primary	27%
secondary	65%
tertiary	2.8%

Mode transport	
bike	1.7%
Taxi	3.3%
Private car	19%
walking	77%

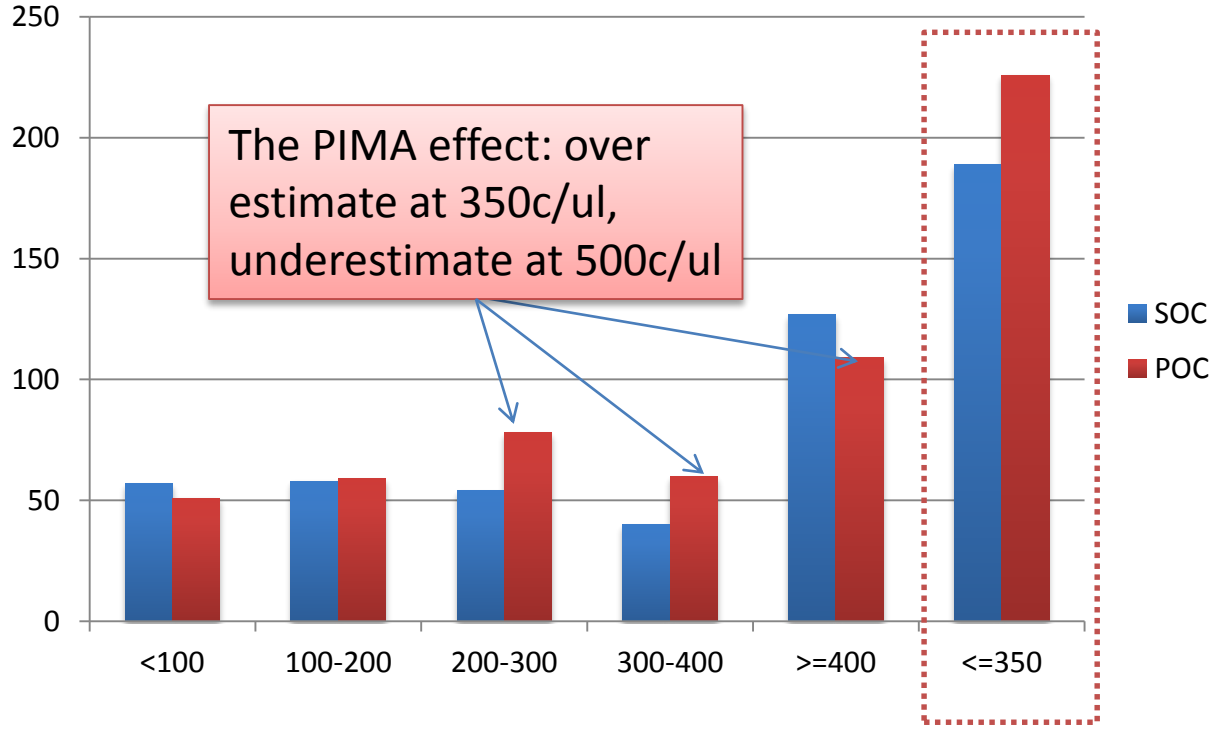
Distance from clinic	
<10mins	22%
10-30mins	59%
30-60mins	18%

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

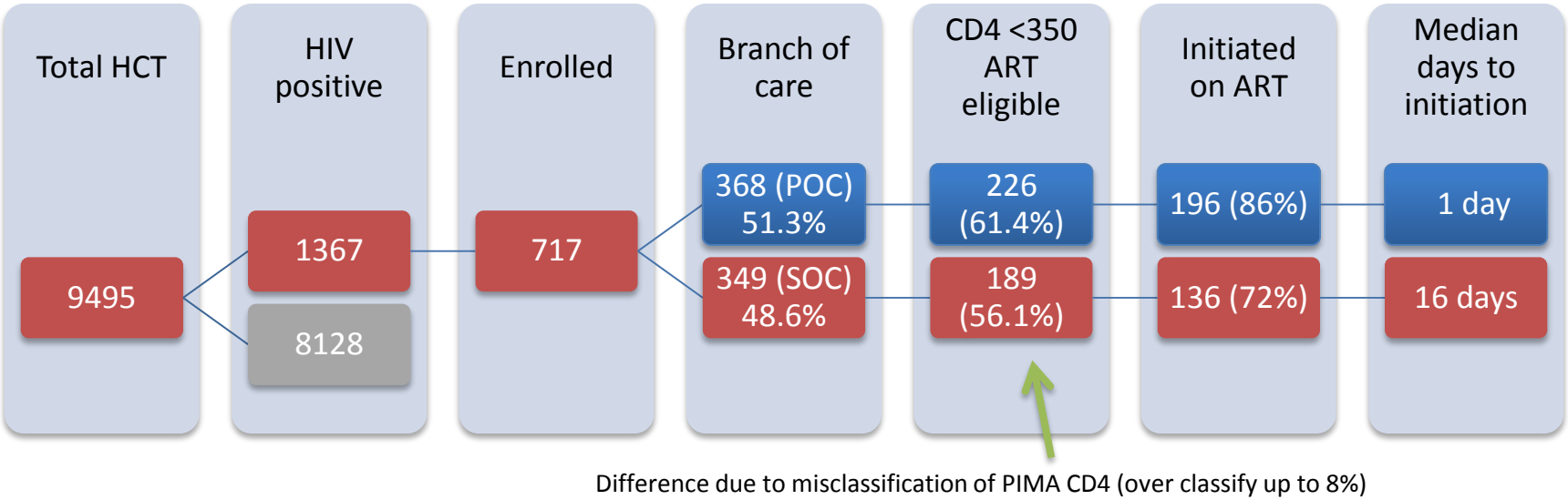


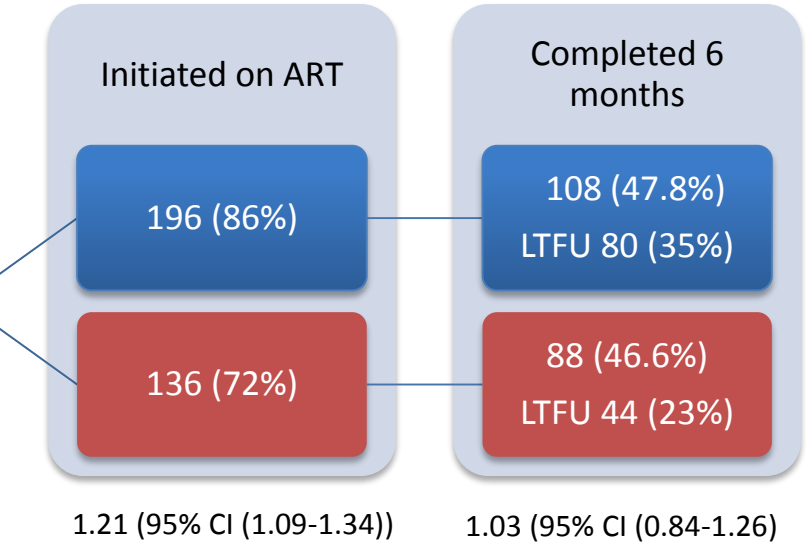
PIMA CD4 metanalysis, n=11803 data pairs, 22 studies, *ScottL.E et al (under submission)*

@350c/ul	Total misclassification	False positive	False Negative
n=8945	12%	8%	4%
n=5368 (venous)	10%	7.1%	3.3%
n=3577 (capillary)	14%	9.3%	5.1%

More patients eligible at POC due to technology variability!

Enrollment
(Mid August 2014)





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

Are patients being pressurised

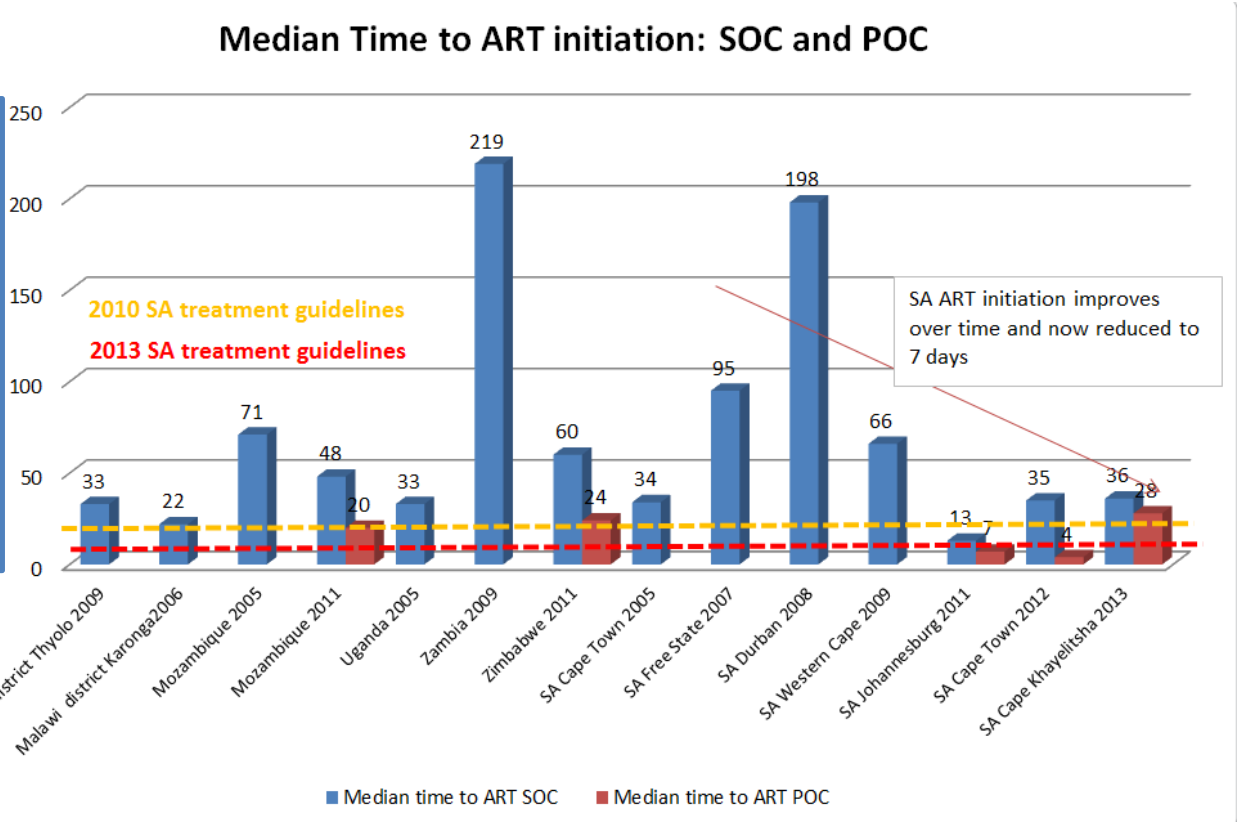
POC CD4: impact on misclassification and ART initiation

What do we know from the literature?

Initiation rates			
Muchedzi, IAS, 2012	43 high-volume PMTCT sites, Zimbabwe	Proportion initiated on ART before CD4 POC **=9%**	Proportion initiated on ART after CD4 POC **=25%**
Schacht , XIX IAS, 2012, Washington	Pregnant women in Gaza Province, Mozambique, eight health facilities	ART initiation rate in facilities was **15.3%** in 2010 (before POC)	ART initiation rate in facilities was **30.4%** in 2011(after POC)
Matambo et al, IAS, 2012	Mobile HIV/TB service for migrant workers on six farms in Musina District, SA	Before the mobile service, **51%** eligible for ART based on CD4 testing, were initiated	After introduction of mobile services of those eligible for ART, **83%** were initiated on ART.

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 – 20days



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

OPEN ACCESS Freely available online

PLoS one

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 Larson[1,4*], Kathryn Schnippel[2], Buyiswa Ndibongo[2], Lawrence Long[2], Matthew P. Fox[1,2,3], Sydney Rosen[1,2]

April 2012 | Volume 7 | Issue 4 | e35444

Tropical Medicine and International Health

doi:10.1111/j.1365-3156.2012.03028.x

VOLUME 17 NO 9 PP 1142–1151 SEPTEMBER 2012

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

Kathryn Schnippel[1], Gesine Meyer-Rath[1,2], Lawrence Long[1], William MacLeod[1,2], Ian Sanne[1,2], Wendy S. Stevens[3,4] and Sydney Rosen[1,2]

$9.98 Xpert MTB/RIF cartridge

Cost component:	Laboratory:		Clinic:
• Labor	• 20.40		• 37.70
• Overhead	• 19.70		• 30.10
• Transport	• 9.80		• 4.90
• Calibration	• 4.20	Annual cost:	• 10.40
• Consumables	• 2.50	R522 million	• 8.50
• EQA & training	• 1.00		• 27.20
• GX instruments	• 16.50		• 35.50
• Other equipment	• 1.10		• 8.80
TOTAL cost / test	R195.10		R282.80

Annual cost:
R780 million
49% more

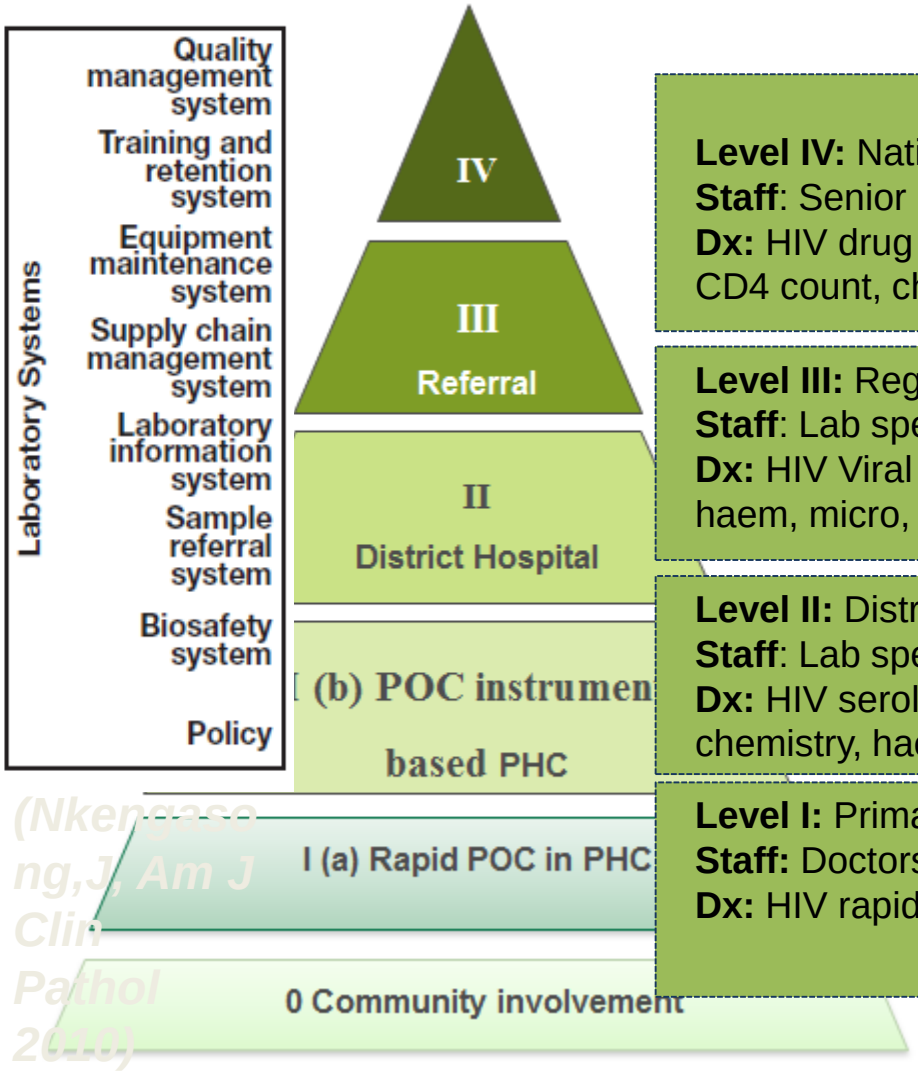
Category	Expected Case		
	R	$	%
Materials	150.21	14.48	35%
Materials - Shared	1.83	0.18	0%
Salaries / Activities	20.13	1.94	5%
Salaries / Activities - Shared	3.51	0.34	1%
Quality Control	61.82	5.96	14%
Equipment	160.99	15.52	37%
Equipment - Shared	1.17	0.11	0%
Other	24.76	2.39	6%
Other - Shared	10.83	1.04	2%
TOTAL: Cost per test	**435.23**	**41.97**	**100%**
TOTAL: Cost per successful test	**439.58**	**42.39**	

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

TOTAL: Cost per test	**185.65**	**17.90**	**100%**
TOTAL: Cost per successful test	**187.51**	**18.08**	

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

Expansion of an integrated tiered laboratory service for HIV and TB



(Nkengasong, J, Am J Clin Pathol 2010)

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

NATIONAL HEALTH LABORATORY SERVICE
NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

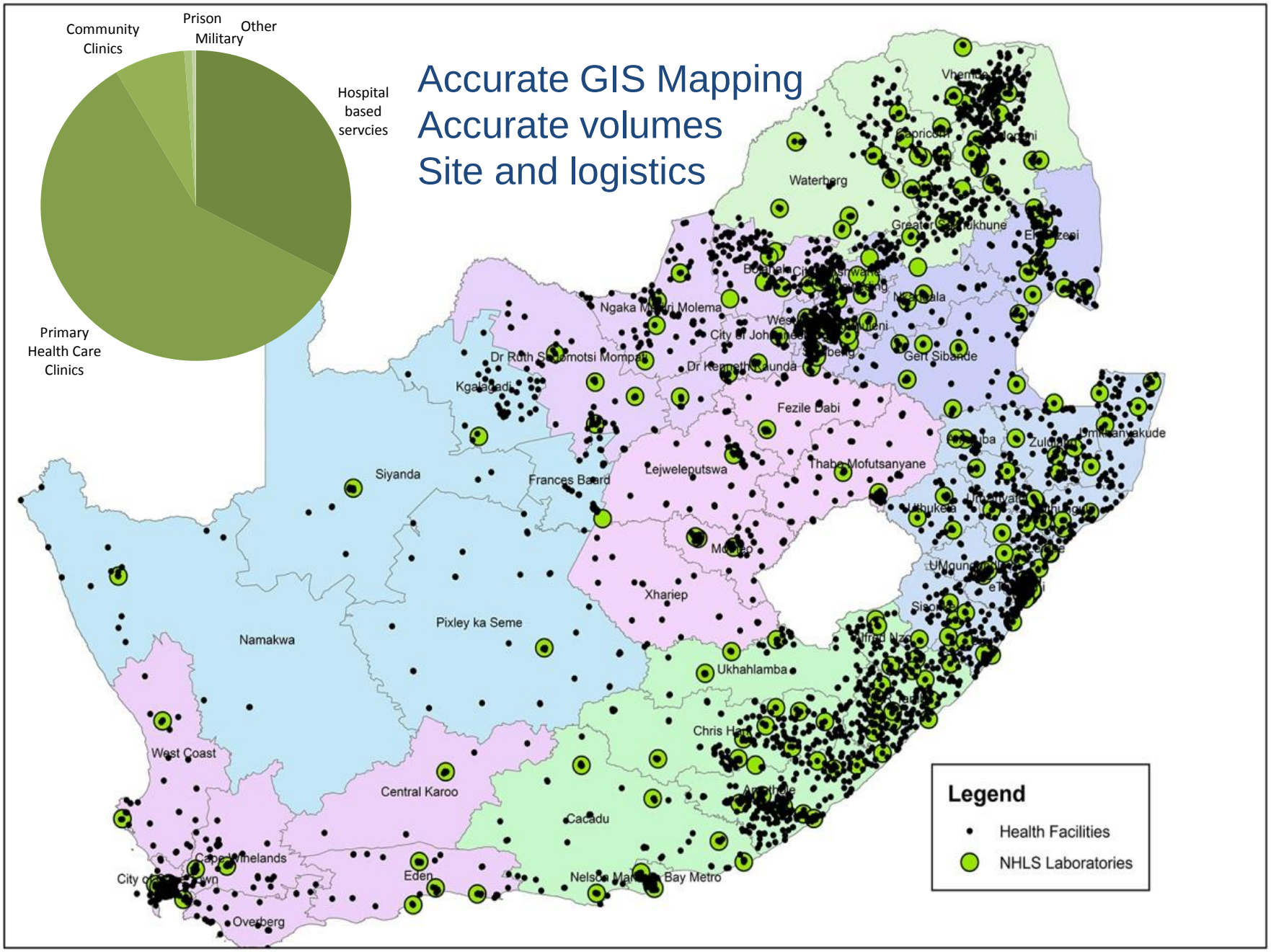

Community Clinics
Prison
Military
Other
Hospital based servcies
Primary Health Care Clinics
Accurate GIS Mapping
Accurate volumes
Site and logistics
Waterberg
Ngaka Modiri Molema
Dr Ruth Segomotsi Mompati
Kgalagadi
Siyanda
Frances Baard
Lejweleputswa
Fezile Dabi
Thabo Mofutsanyane
Gert Sibande
Xhariep
Pixley ka Seme
Namakwa
Ukhahlamba
West Coast
Central Karoo
Cacadu
Eden
Overberg
Legend
Health Facilities
NHLS Laboratories

Figure 1

CD4 example: volumes

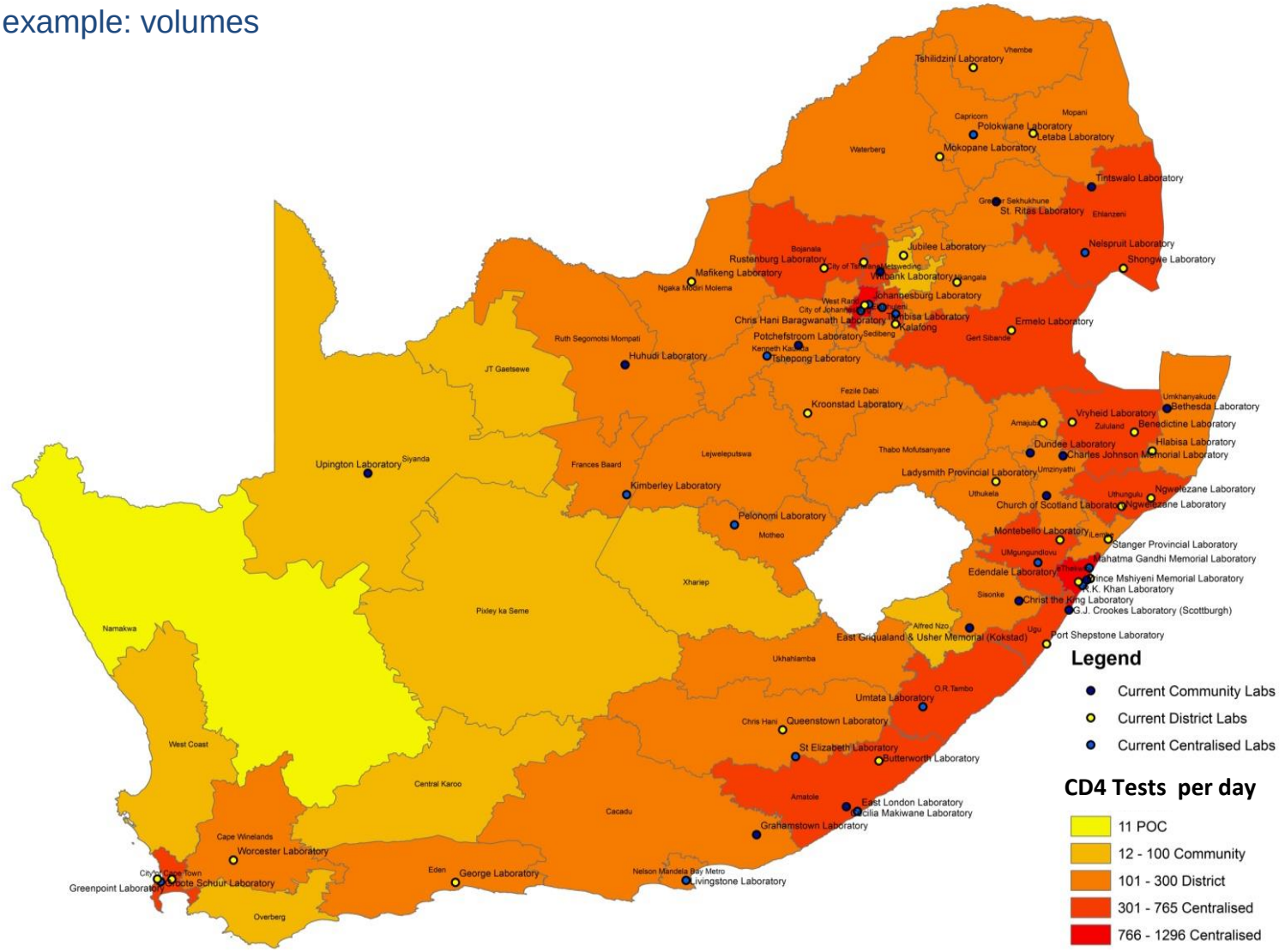


Figure 2

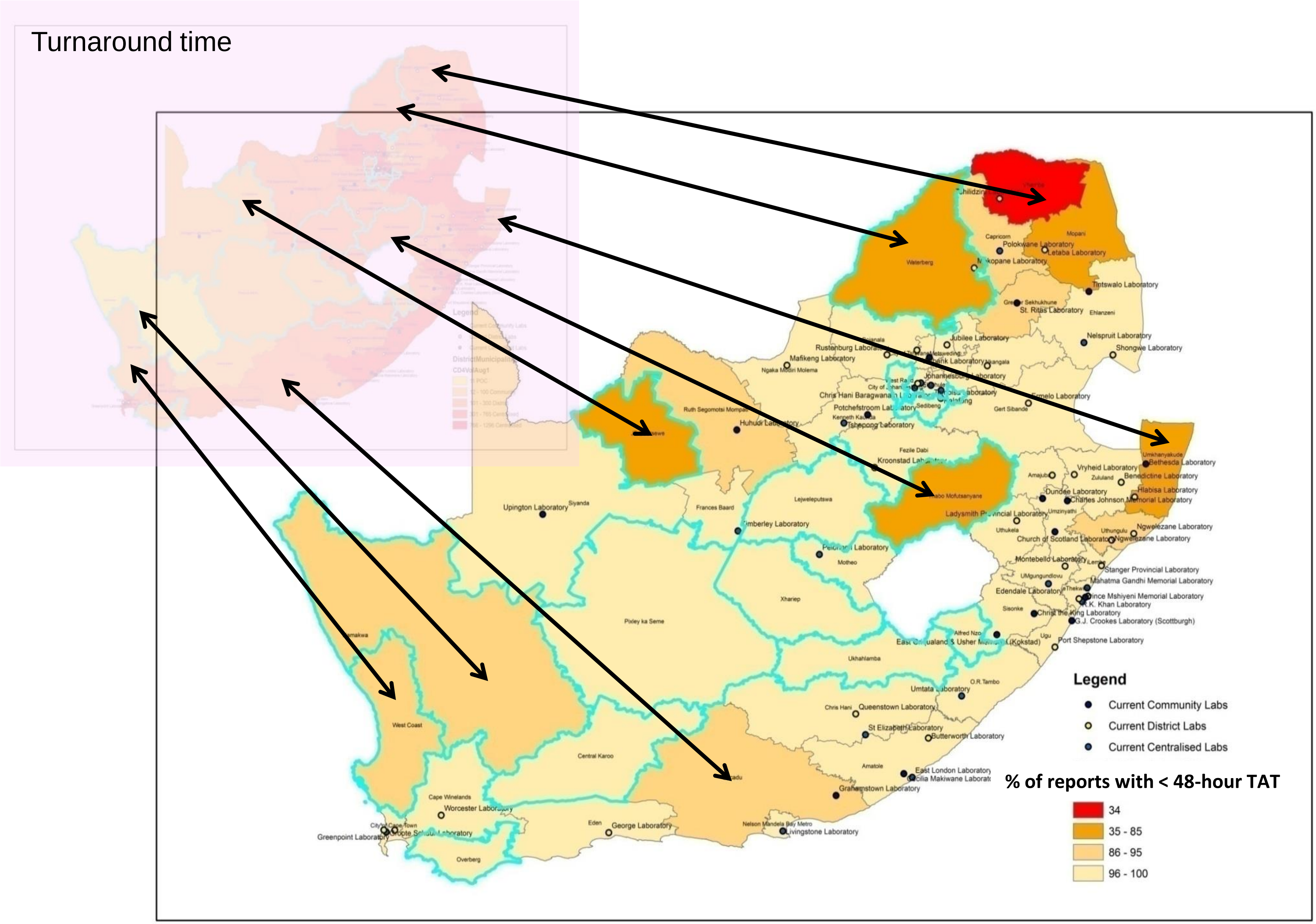

Turnaround time
Legend
Current Community Labs
Current District Labs
Current Centralised Labs
% of reports with < 48-hour TAT
34
35 - 85
86 - 95
96 - 100

Figure 3

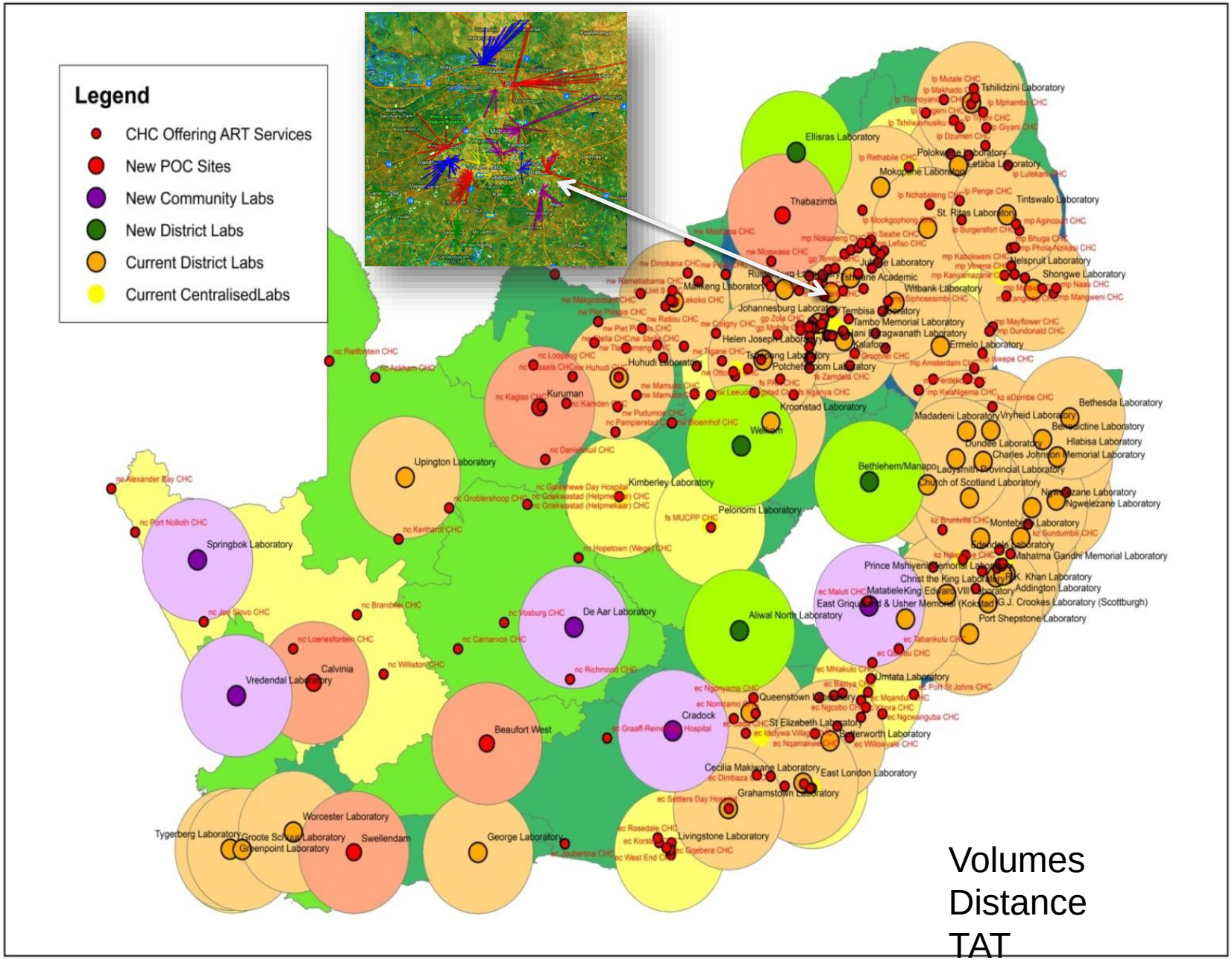
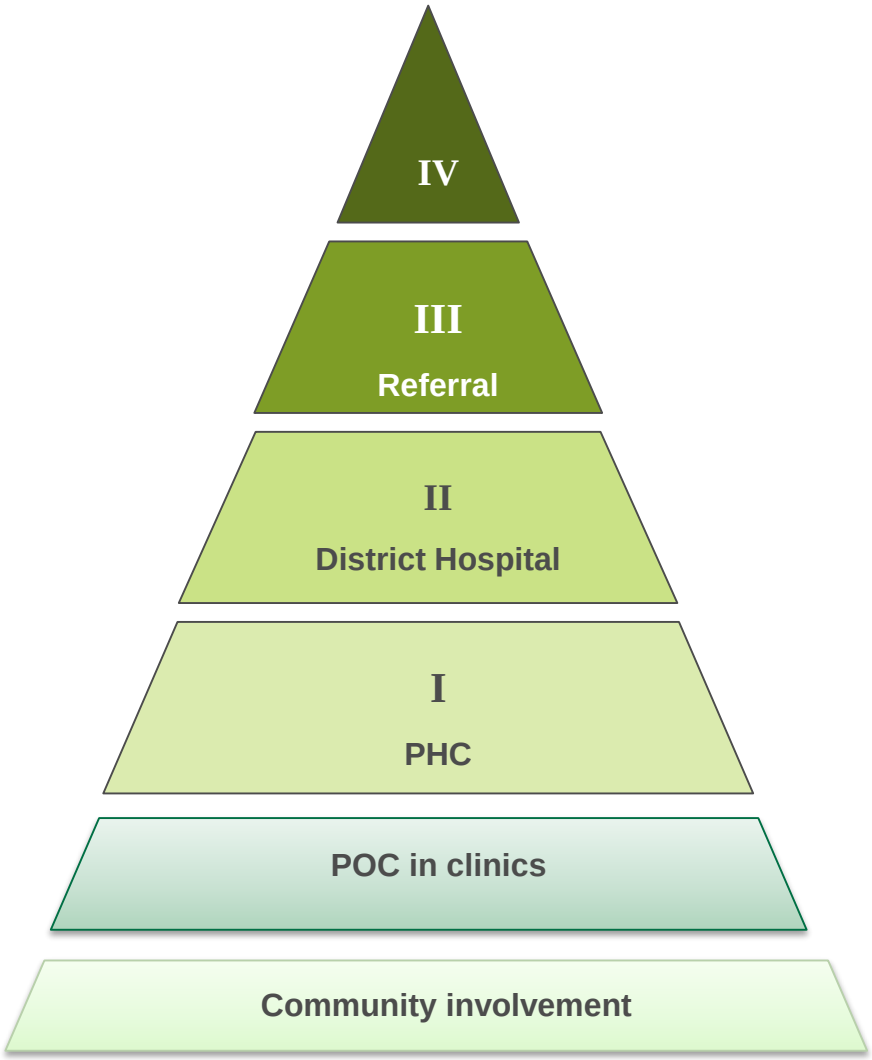
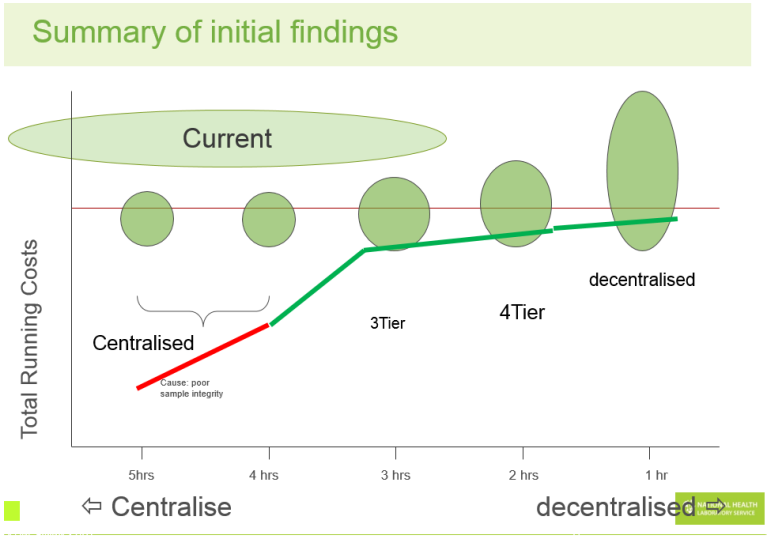

Legend
CHC Offering ART Services
New POC Sites
New Community Labs
New District Labs
Current District Labs
Current CentralisedLabs
Volumes
Distance
TAT

Figure 5

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

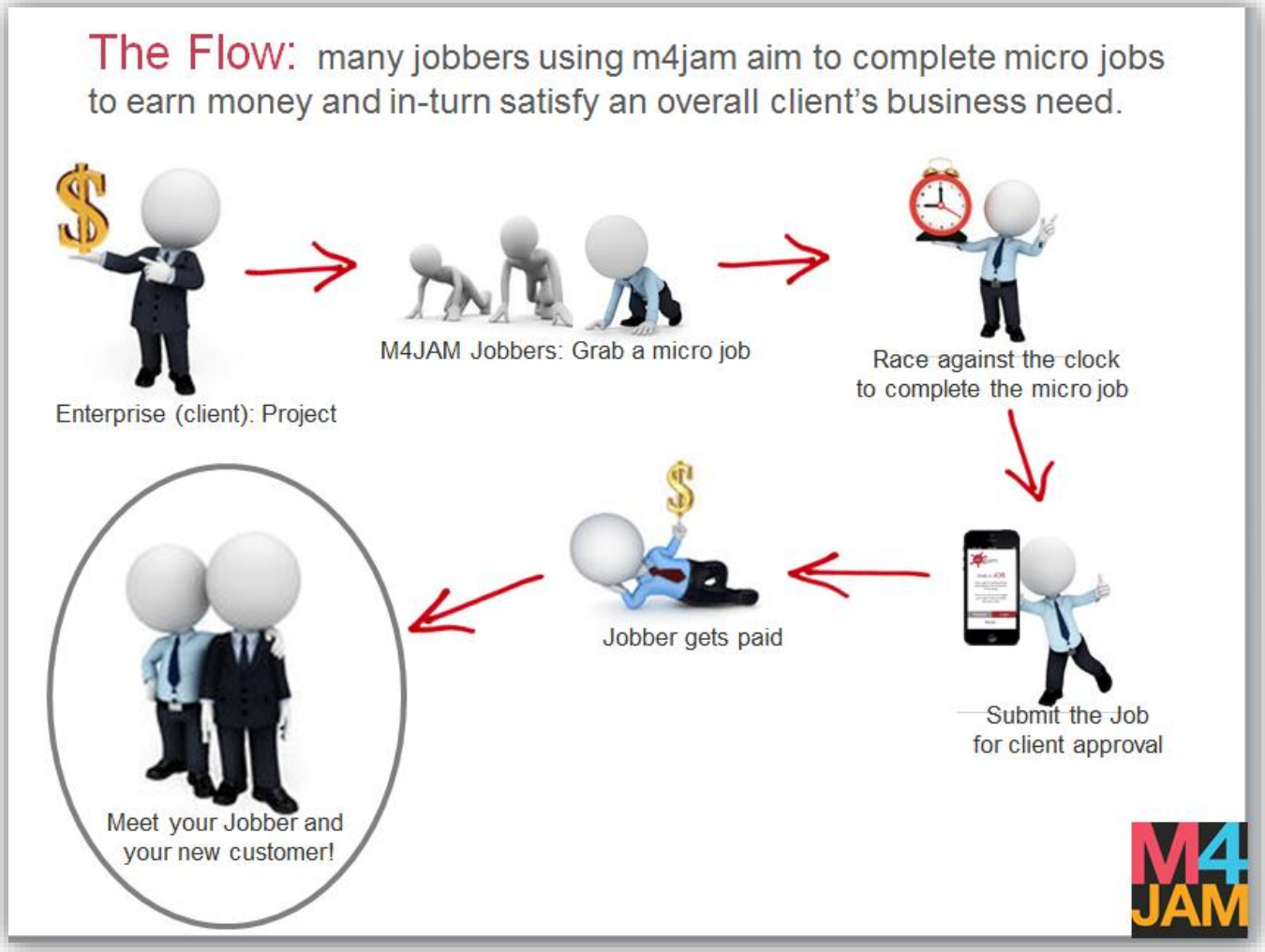
The Market: specific to South Africa

- Official unemployment is 25.5%,
- 69.2 million active sim cards
- 32.9 mill people with some form of telephony
- 14.1 mill 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

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.



2. POCT principal components

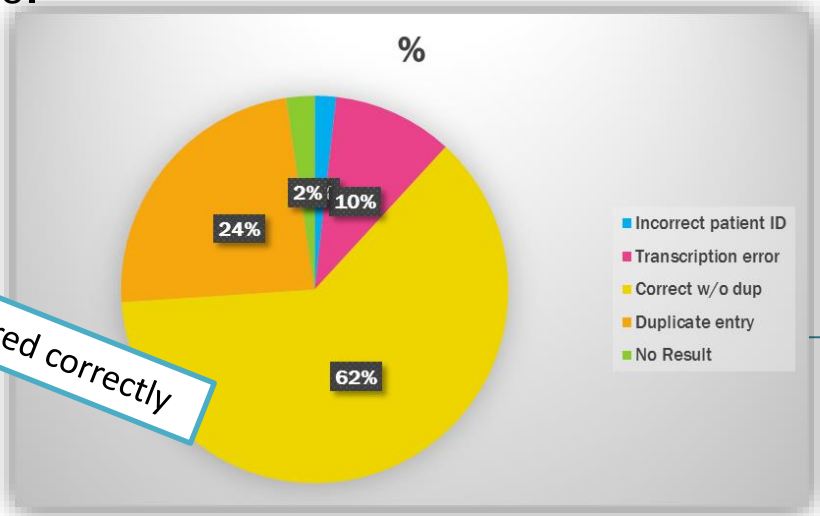
- Connectivity: critical to POCT
  - A universal bi-directional multi-functional (clinic and lab) connectivity solution for POCT is lacking but “cloud-based” SaaS promising (eg PIMA data point – Dashboard and novel approach: Cepheid Remote monitoring).
  - Some areas require signal boosting and internet 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.

Stevens. W, et al. Remote connectivity. Book Chapter under submission

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



NATIONAL HEALTH LABORATORY SERVICE

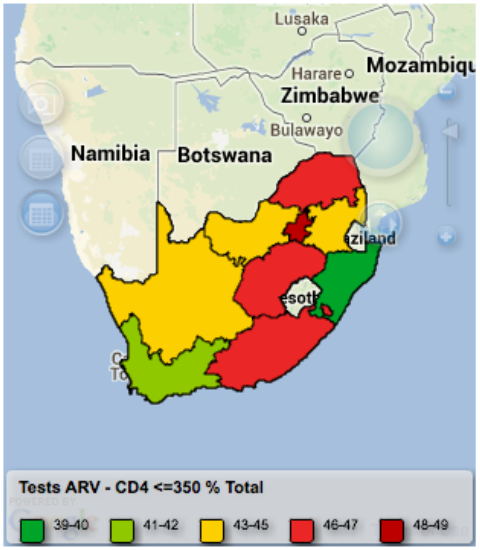
Year: 2014 | Quarter: Q1 2014 | Month: Jan 2014 | Age Range: All Ages

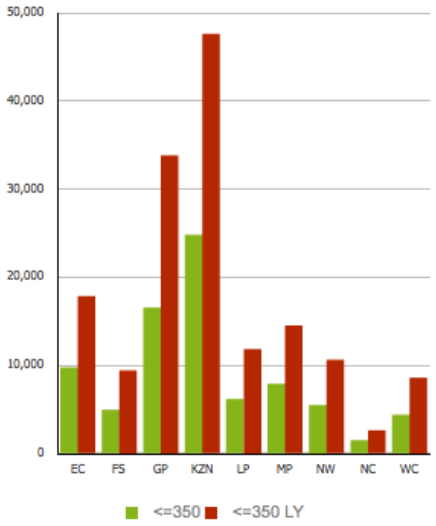
National | Provincial | NHI

M&E Geo Analysis

CD4

CD4 <= 100 (as % of Total) | CD4 <= 350 (as % of Total)

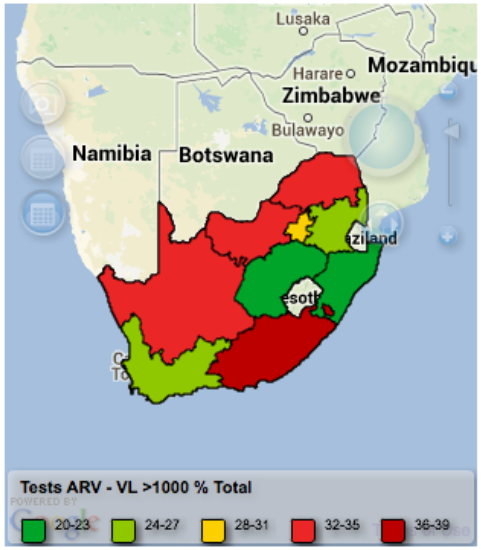


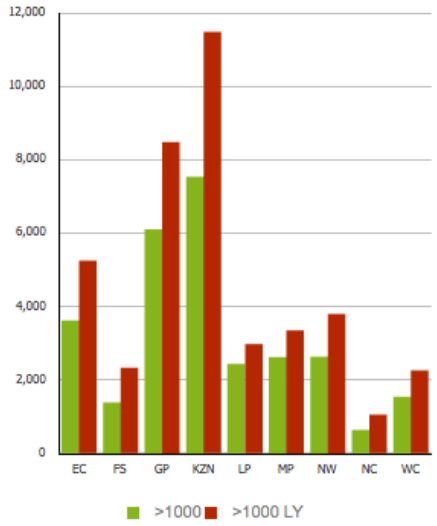


Province		Total Current	Total LY	<= 350 Current	<= 350 LY	Delta	%	% LY	
Eastern Cape	EC	20,659	37,253	9,741	17,844	(8,103)	47.2	47.9	↓
Free State	FS	10,548	19,471	4,947	9,413	(4,466)	46.9	48.3	↓
Gauteng	GP	33,613	68,753	16,551	33,823	(17,272)	49.2	49.2	↓
KwaZulu-Natal	KZN	62,563	108,538	24,790	47,604	(22,814)	39.6	43.9	↓
Limpopo	LP	13,436	23,829	6,145	11,848	(5,703)	45.7	49.7	↓
Mpumalanga	MP	17,722	31,239	7,894	14,508	(6,614)	44.5	46.4	↓
North West	NW	12,491	23,443	5,479	10,603	(5,124)	43.9	45.2	↓
Northern Cape	NC	3,343	5,873	1,486	2,594	(1,108)	44.5	44.2	↓
Western Cape	WC	10,223	20,173	4,378	8,596	(4,218)	42.8	42.6	↓
Total		184,598	338,572	81,411	156,833	(75,422)	44.1	46.3	

VL

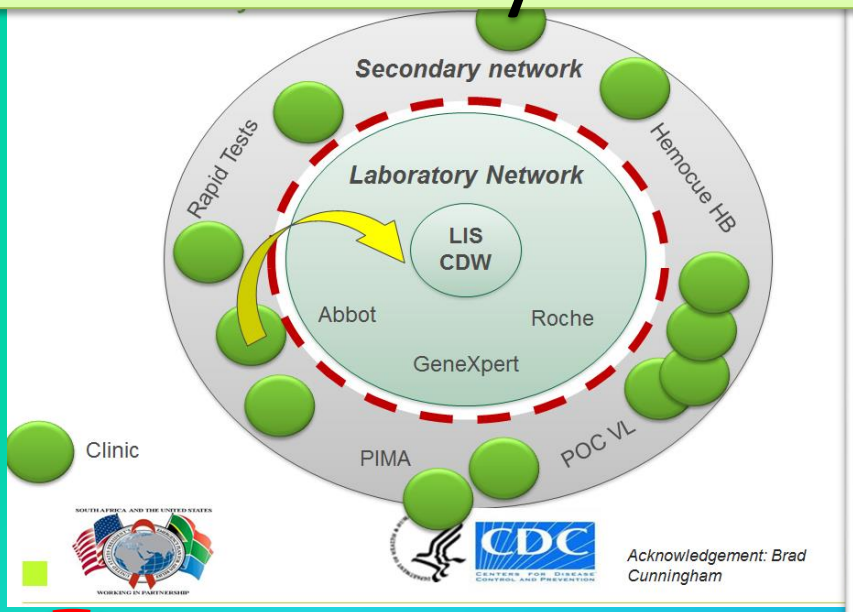
VL <= 1000 (as % of Total) | VL > 1000 (as % of Total)



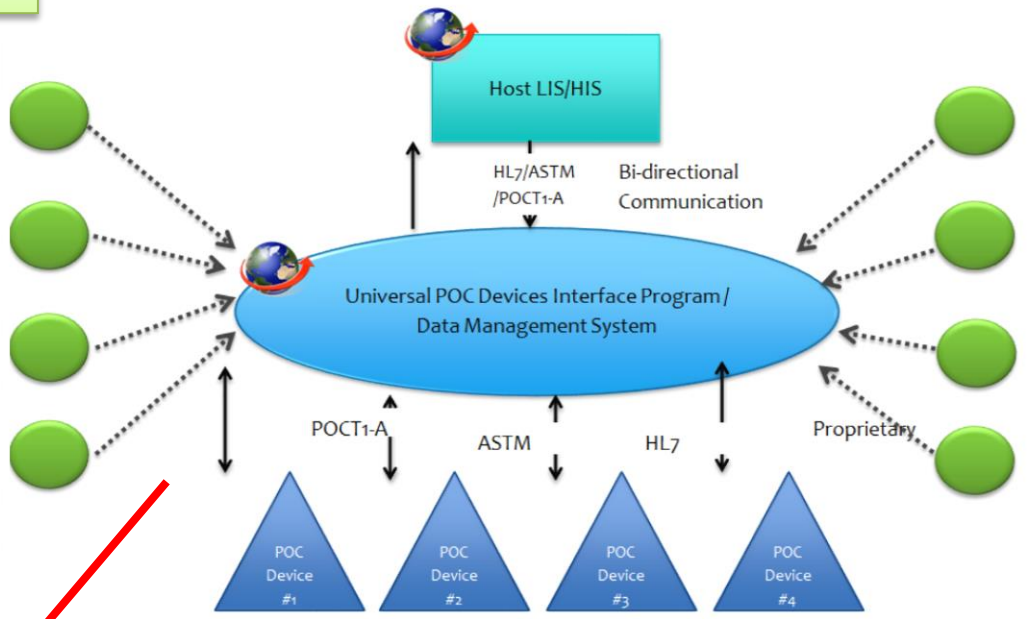


Province		Total Current	Total LY	> 1000 Current	> 1000 LY	Delta	%	% LY	
Eastern Cape	EC	10,013	16,089	3,618	5,246	(1,628)	36.1	32.6	↓
Free State	FS	6,324	9,584	1,388	2,330	(942)	21.9	24.3	↓
Gauteng	GP	21,348	34,751	6,103	8,482	(2,379)	28.6	24.4	↓
KwaZulu-Natal	KZN	34,133	53,167	7,538	11,480	(3,942)	22.1	21.6	↓
Limpopo	LP	7,579	10,375	2,429	2,974	(545)	32.0	28.7	↓
Mpumalanga	MP	9,478	13,772	2,625	3,352	(727)	27.7	24.3	↓
North West	NW	7,536	11,116	2,633	3,799	(1,166)	34.9	34.2	↓
Northern Cape	NC	1,830	2,606	634	1,051	(417)	34.6	40.3	↓
Western Cape	WC	6,423	10,864	1,542	2,253	(711)	24.0	20.7	↓
Total		104,664	162,324	28,510	40,967	(12,457)	27.2	25.2	

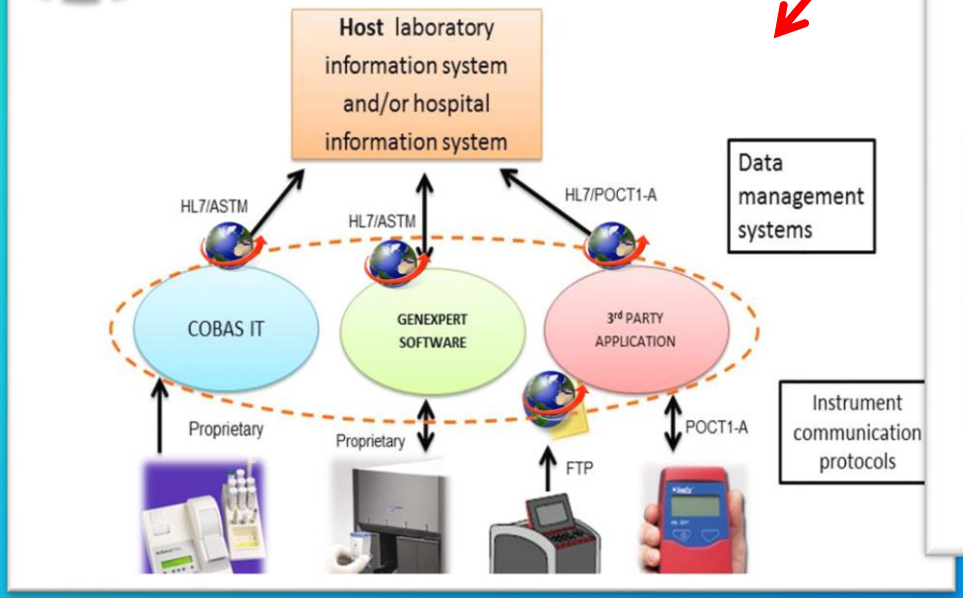
Connectivity at POC



Centralised data for decentralised testing



Reality of Connectivity for multi-disciplinary POCT



Available Options for POC Connectivity

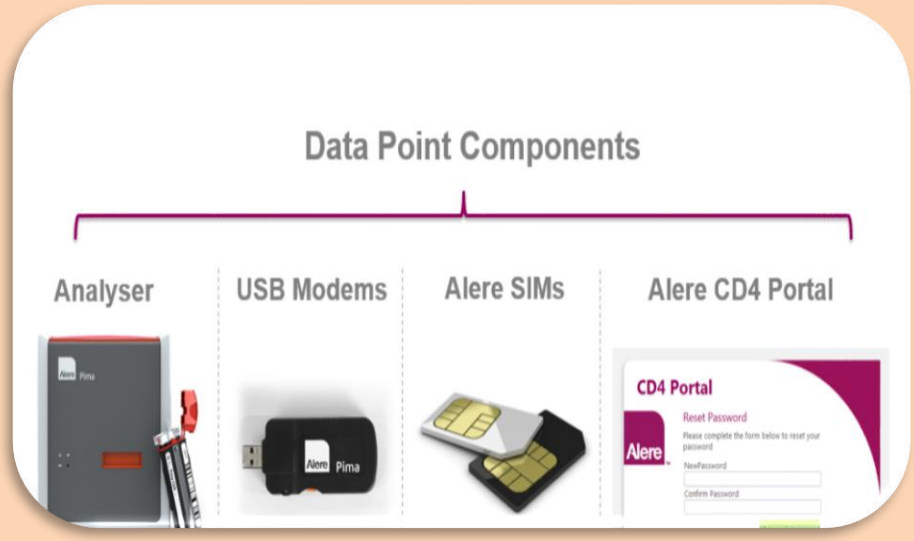
Product	Instrument Interfacing	Training and Certification	QC and instr. Management	Patient History	Result Management	Clinical Information	Visit Management
AegisPOC	Extensive	Yes	Yes	Yes	Yes	No	No
POCcelerator	Extensive	Yes	Yes	Yes	Yes	No	No
Cobas IT	Limited	Yes	Yes	No	Yes	No	No
Identicare	Development	No	No	Yes	Yes	No	Yes
Therapy Edge	None	No	No	Yes	Yes	Yes	Yes
eKAPA	None	No	No	Yes	Yes	Yes	Yes

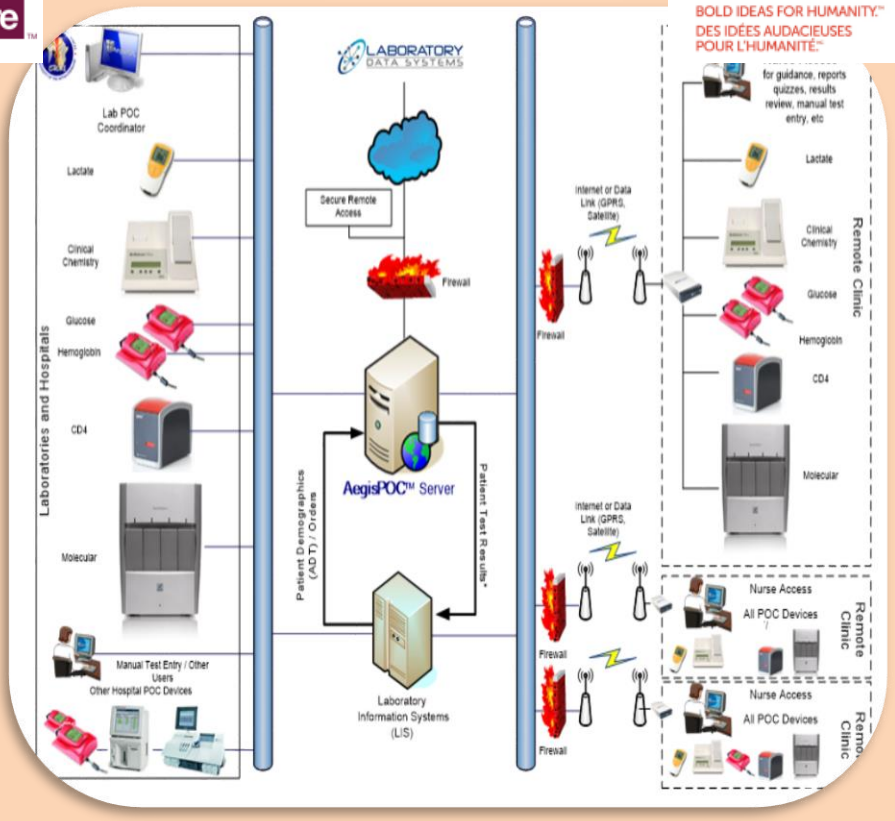
Instrument and Data Management

Patient Management

Dashboard

Middleware





PIMA connectivity:

Operational Dashboard	Middleware
Interface single instrument type/s from a specific vendor	Interfaces 100's of instruments and types – vendor neutral
Limited, more basic reports	Flexible, extensive reporting
Non-patient identifiable	Patient Identifiable
Unlinked	Linked to LIS & HIS
Free (generally)	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)

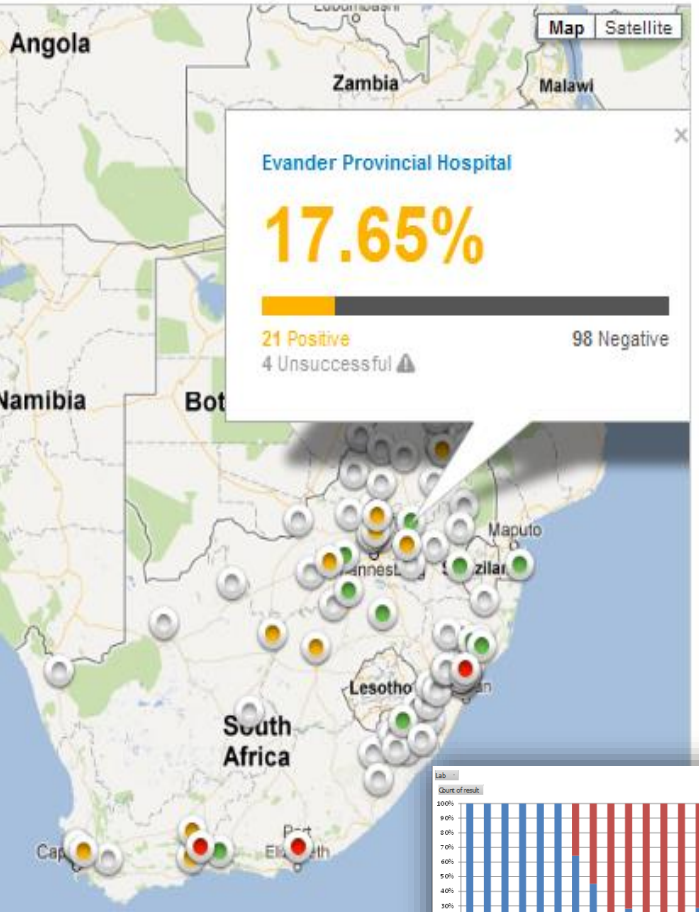
Cloud computing

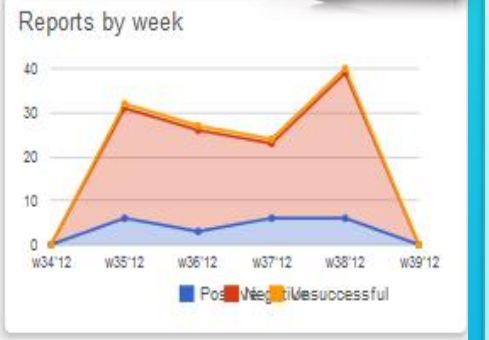
- **Cloud computing** is emerging as a new paradigm in healthcare.
- simple means of the **delivery of a service rather than a product**.
- The main enabling technology Virtualisation is the ability to allow the system to operate independently of the hardware.
- From the Cloud via the internet, one can 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

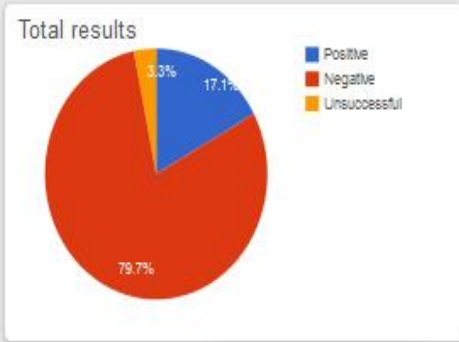
A new Era in Lab services:“the cloud”

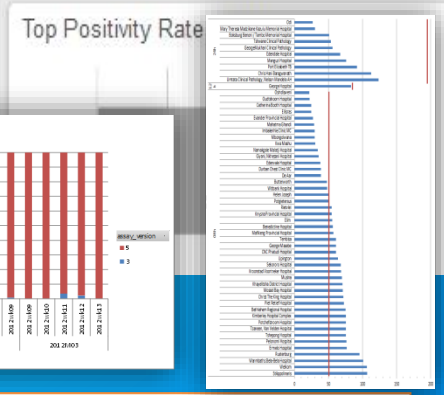
Gx verification (on installation, module maintenance) and EQA 3 x per year, but third quality monitoring component = real time monitoring.

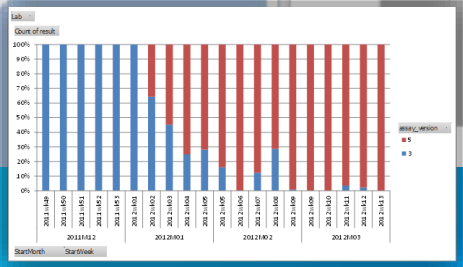
- Operational dashboard for real-time monitoring of results, errors, resistance and positivity rates
- Pre-configured on all newly installed GeneXperts



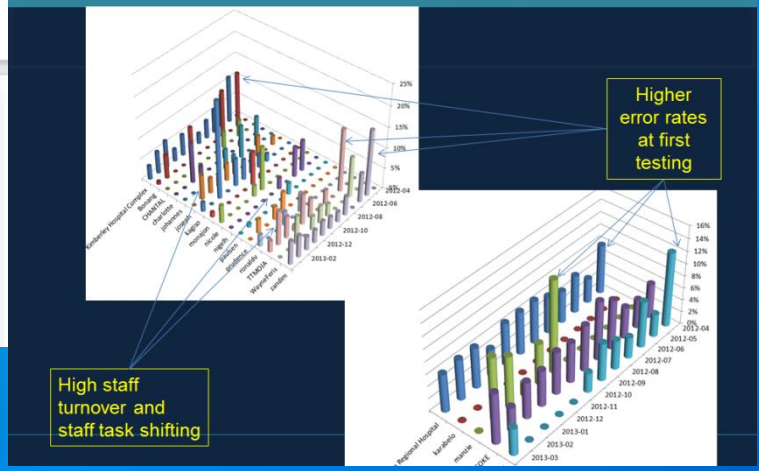








Training needs and managing staff turnover



Alpha and beta testing completed, National Priority Program

Models for POCT implementation in SA

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 diarrhoea, 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.

Stevens. W, Gous.N,Scott.L.E. Feasibility of HIV POCT for RLS: Challenges and solutions. BMC in press.
Stevens.W, et al. POCT: Policy document for SA. NDoH, NHLS and partners collaborative forum. Pretoria, July 2013

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
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- 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
- HERO team, G. Meyer –Rath, K. Bistline, Prof S.Rosen, Bill McLeod, Lawrence Long.
- CHAI team, Trevor Peter, Jonathan Lehe