Are clinical facilities ready for POC beyond HCT?

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Representing the Grand Challenges Canada funded team

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NATIONAL HEALTH LABORATORY SERVICE

Unmet needs for POC

(Peeling,R, Clin Microbial Infect 2010)

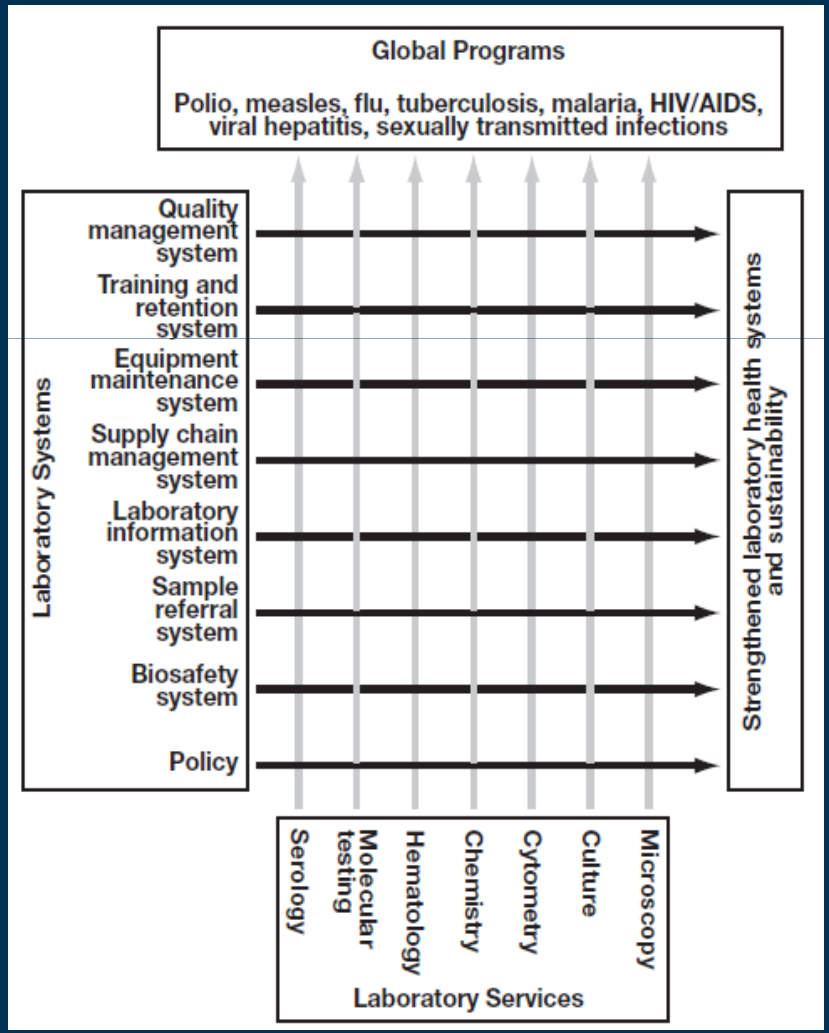
- Infectious diseases in the developing world:
  - Appropriate clinical management of sick patients presenting at PHC is a global health challenge.
  - Lack of accessibility to services and poor integration (HIV/TB) is one reason why health services fail.

	Unmet needs for POC
Acute lower respiratory infectious	Need to distinguish bacterial/viral pneumonia
Febrile illness in children	Multiplex test for causes of fever
STI (incl HIV)	Genital chlamydia/gonococcal, peadiatric HIV diagnosis, CD4 and viral load
Antenatal care	Multiplex screening HIV, malaria, syphilis, anaemia
Diseases (malaria, TB, Human African Trypanosomiasis, Visceral leishmaniasis)	Some rapids exist, still need active TB diagnosis, staging disease, cure, antimicrobial susceptibility.

Laboratory systems and services are critical in global health: *time to end the neglect*

(Nkengasong,J, Am J Clin Pathol 2010)

- Frameworks exist for strengthening laboratory core elements
- Point of Care has a place and should follow this framework….



Definition of Point of care (POC)

A test performed that has immediate impact on patient outcome

The purpose of POC is to provide timely test results that clinically and cost effectively contribute to immediate patient management decisions.
Clinical Laboratory Standards Institute

The description is outpatient clinic, ER, theatre, mobile clinics, PHC clinics, or even small laboratories:

- Small bench top analysers (blood gas machines or full blood count analyzers), portable hand held devices (glucometers, strip based assays). **(***Warsinke, 2009; Plebani,20009)*




Multiple POCT for *HIV*e

POCT requirements

- Quality, quality, quality!!!

POC checklist
Clinical need
Type of test and equipment
Testing infrastructure
Personnel
Connectivity
Impact and cost benefit

ISO/FDIS 22870: Point-of-care testing (POCT) —Requirements for quality and competence; NIH guidelines; National Academy of Clinical; Biochemistry (Clinica Chimica Acta, 2007); British Society of Haematology (BJH, 2008)

POC implementation checklist

(snapshot Gous,N, 2012)

Requirements for POC implementation		
Space requirements	POC room	✓ Workbench with allocated areas for sample receiving, sample preparation/ incubation
		Space for POC instruments ✓ GX4: H: 50cm W: 40cm D: 40cm ✓ PIMA: H16cm W13cm L22cm ✓ Reflotron: H21cm W30cm I35cm ✓ Hemocue: H4.3cm W8.5cm L16cm
		✓ Storage space (cupboards)
		✓ Power outlet
POC Equipment	POC instruments	✓ GeneXpert instrument, computer, barcode scanner, UPS, printer
		✓ Pima instrument and printer
		✓ Reflotron instrument and keyboard
		✓ HemoCue instrument and power adapter
	POC accessories	✓ Multi-plug Adaptor
		✓ Fridge 4°
		✓ Kensington lock (optional)
		✓ Memory stick/RW-CD's
Safety requirements		✓ Secure room that can be locked
		✓ Limited access
		✓ Good ventilation – windows/aircon
		✓ Basin with running water and soap dispenser
		✓ Biohazard medical waste bin
POC reagents and Consumables	GeneXpert	GeneXpert Kit induding: Xpert cartridges, sterile disposable transfer pipettes, Sample Reagent (SR) buffer
		Sterile screw capped specimen collection containers
		Stopwatch
		IDP 700 (ultraseptin)
	PIMA	PIMA CD4 cartridges
		Alcohol wipes/paper towel
		X3 Nalgene wash bottles or equivalent
		Fine tip permanent marker pens
		Printer paper
Miscellaneous	Training	Standard operating procedures

- POC instrument space and room requirements
- POC equipment
- Safety requirements
- POC reagents and consumables
- Miscellaneous items needed

Quality in POCT

(Nichols Expert Rev Mol Diagn 2003); Cvitkovic, Crit care nurs Q, 2011)

- Site-neutral philosophy of CLIA* "control over the entire process"
  - Pre-analytical (patient ID, sample quality, aseptic technique, collection devise/tube, draw, label)
  - Analytical (device operation, ID, mix, analysis, maintenance, operator competency)
  - Post-analytical (sample disposal, result interpretation, audit trail, EQA, reporting)
- CLSI# for standardised best practices of patient testing

**clinical improvement amendments*
#clinical and laboratory standards institute

CAP (College of American Pathologists) POCT requirements
Perform under direction of doctor/scientist
Site enrolled in proficiency program
Quality control and quality improvement program
Written procedures manual (patient identification – result reporting – action errors)
Personnel are trained
Results are reported with normal ranges
Critical test limits established
Appropriate person available for troubleshooting
Procedures and records maintained ~2yrs
Reagents, calibrations expiry dates recorded
New lots verified
Two levels of controls evaluated daily and corrective action documented
A system to regularly check maintenance

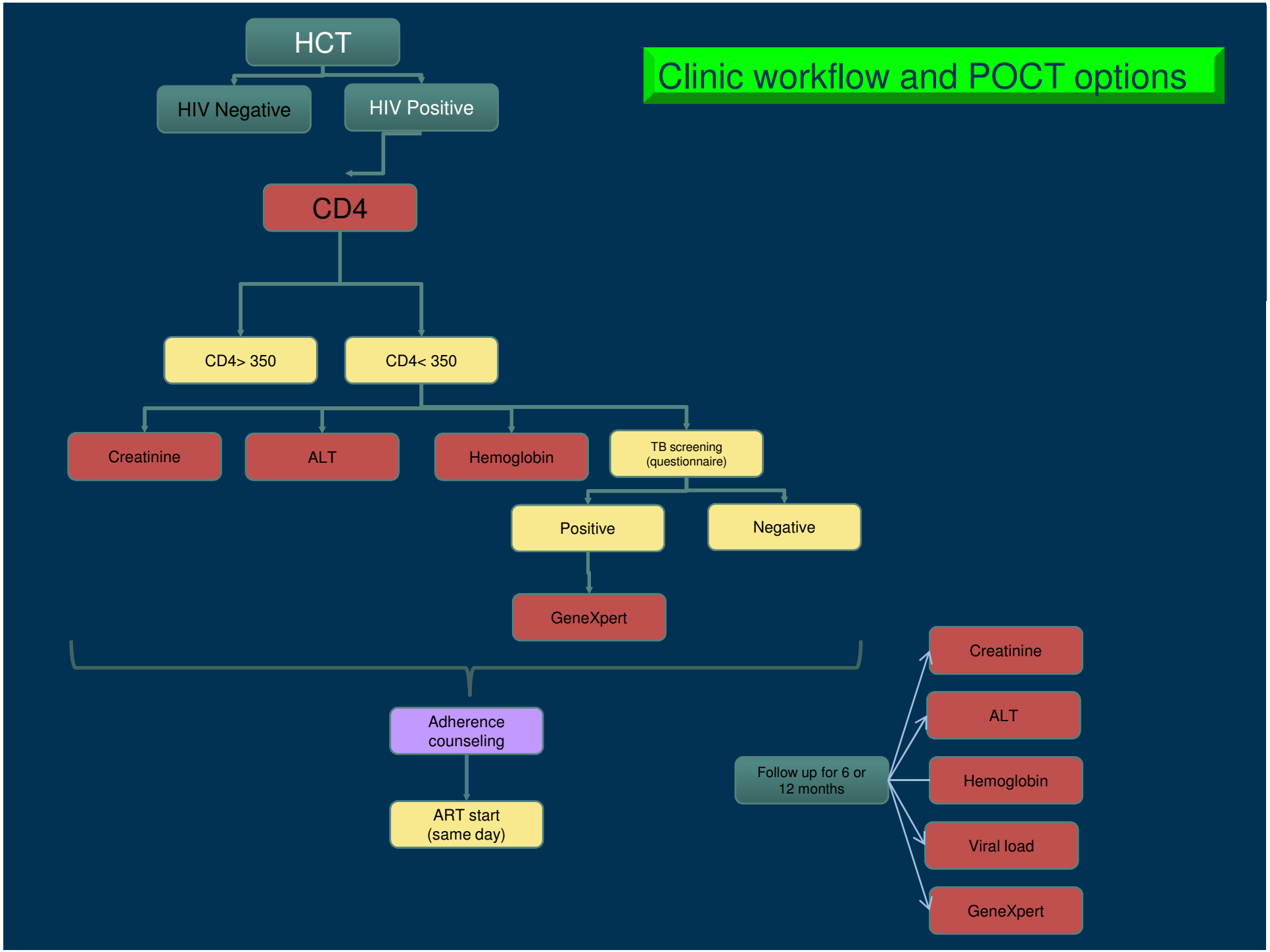
So are we ready for POC post HCT?

Feasibility study:

Implementing multi-disciplinary POCT in an active HIV treatment clinic in South Africa

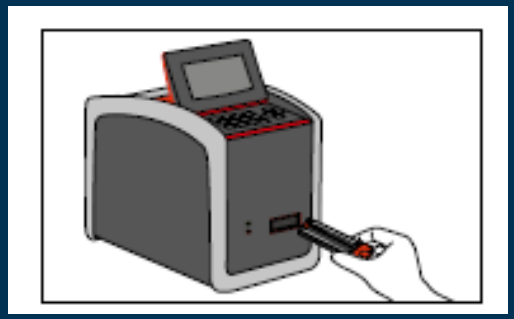
- Develop a Combined Clinical POC Laboratory Platform (CCPLP) model.
- Determine whether multi-disciplinary POC testing for HIV and TB can be performed in remote settings and is feasible, by non-laboratory personnel.
- Evaluate: cost effectiveness
- Recommend policy (including appropriate model of POCT placement in SA's health care

Clinic workflow and POCT options



CD4 count: PIMA (Alere)

- Portable bench-top flow cytometer
- A disposable test cartridge and PIMA analyzer
- Capillary or Venous whole blood
- Critical range is 350cells/ul
- Time to result: 20 minutes



ALT, Creatinine: Reflotron (Roche)

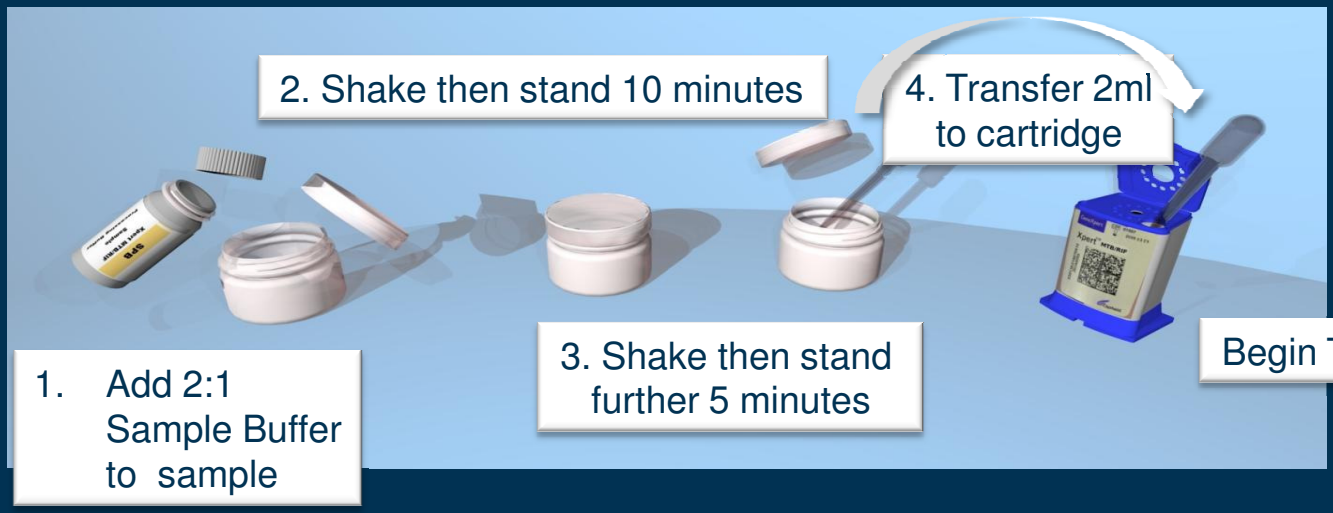
- Uses disposable test trips
- Enzymatic reaction measured by photometery
  - ALT - 5.00 – ~ 2000 U/l
  - Creatinine – 44.2 -884umol/l
- Direct from whole blood, serum or plasma
- Time to result: 3 minutes

Hemoglobin Hb: Hemocue Hb201

- Hand-held device
- Disposable cuvettes
- Quantitative determination of Hb
- Enzymatic reaction measured by photometery
- Capillary, venous or arterial blood
- The measuring range is 0-25.6 g/dL.
- Time to result: <1minute

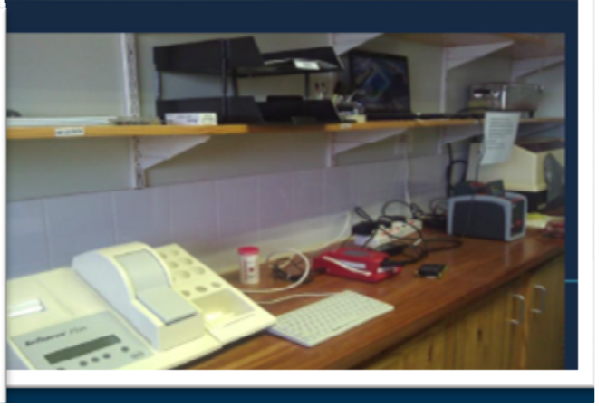
TB with Rif resistance: GeneXpert (Cepheid)

- **Closed platform for extraction, amplification and detection of *Mycobacterium tuberculosis* (*Mtb)* complex and Rif resistance**
- **Direct from unprocessed sputum (0.5 – 4ml)**
- **Time to result: 2 hours**



Findings: Space in clinics

- Multiple POC requires space (POC work flow: specimen, testing, reporting, disposal) security and place for computer for connectivity.
- Clinic space varied



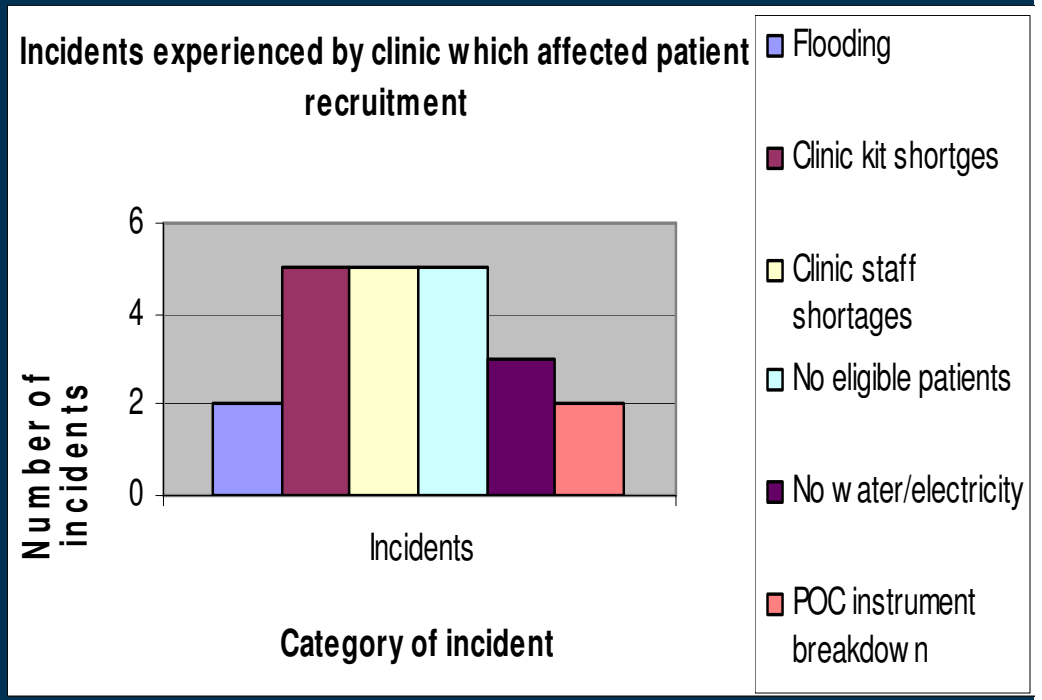

Wheelchair
Foundation

Clinic management

During the RCT the number of Incidents in the clinic which affected patient recruited and testing were noted:

Majority of incidents were due to:

- VCT kit shortages at the clinic,
- Clinic staff shortages (no counselors/nurses on duty to initiate) and high turnover
- Disruption in the clinic work flow: No eligible patients to recruit (patients being referred from other areas due to trials and community programs)



Training

Training for POCT in Australia: *(Shephard et al 2009, rural and remote health)*

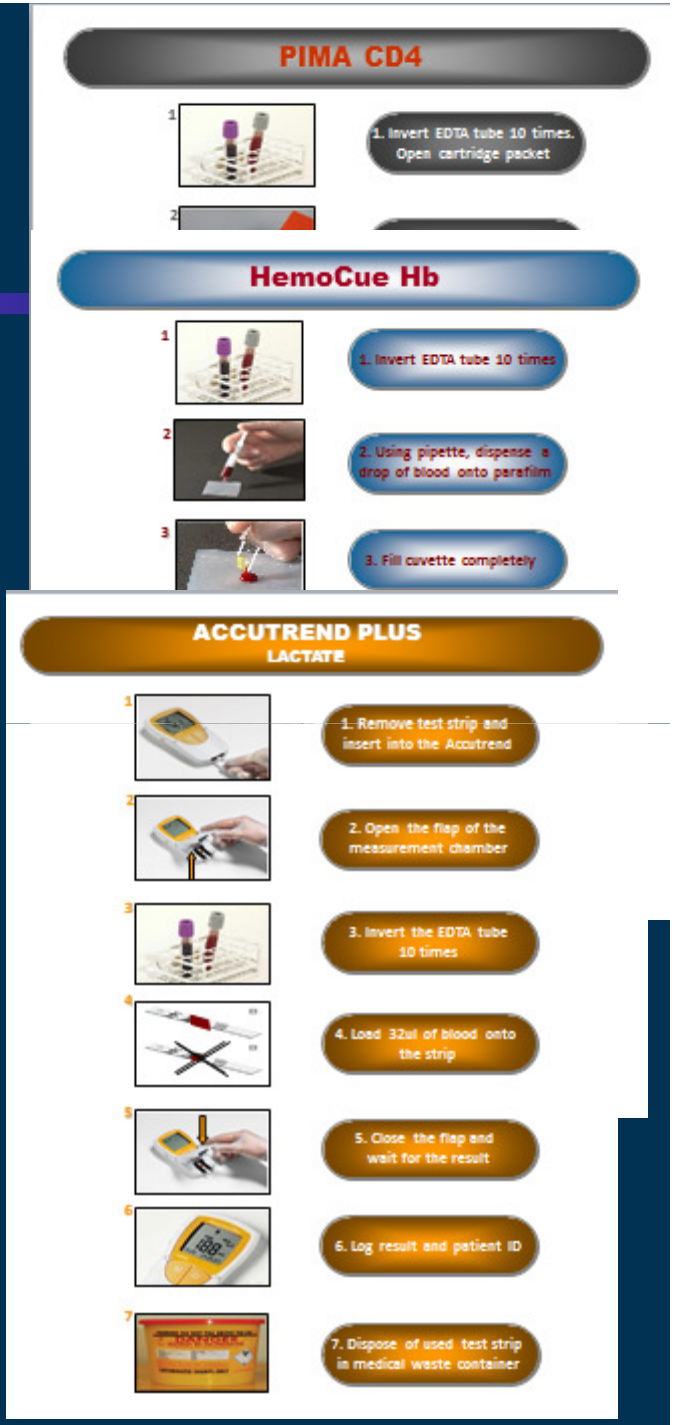
- Remote POCT users had a greater need for training and support to urban counterparts.
- Remote training requires flexible options to cater for much higher staff turnover.

South Africa *(SEAD report on assessment of POC HIV rapid testing, 2010)*

- Overall process compliance: 3.4% nationally: rural facilities (6.9%) performed better than urban (1.7%), higher workflow clinics performed better
- Recommendations: A system's approach is essential to address training, mentoring, responsibilities, on-going monitoring, effective and efficient procurement, on-going quality assurance, .

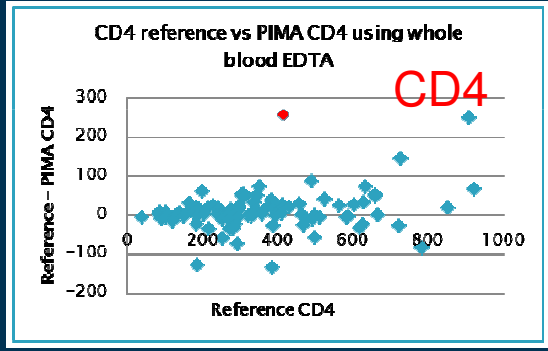
Training: our experience

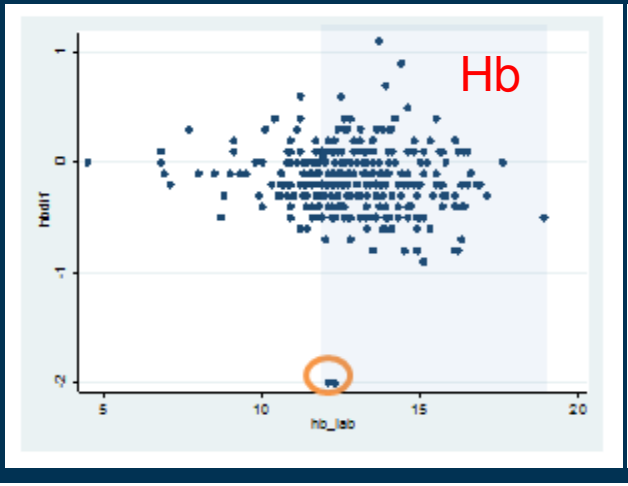
- Developed **SOP manuals** in POC-GCLP format
  - quick reference charts more effective
- Training: Centralised training
  - ½ day per platform (Pima, Hemocue, Reflotron, Accutrend)
  - Xpert MTB/RIF required 1 full day due to computer and software operation.
- On-site test witnessing
  - Xpert MTB/RIF required more intensified on-site training.
  - Measured also by QC testing
- Made use of pre and post training questionnaires
  - N=18 trainees (mostly for Xpert MTB/RIF)
  - Training yielded 8.3% increase in knowledge

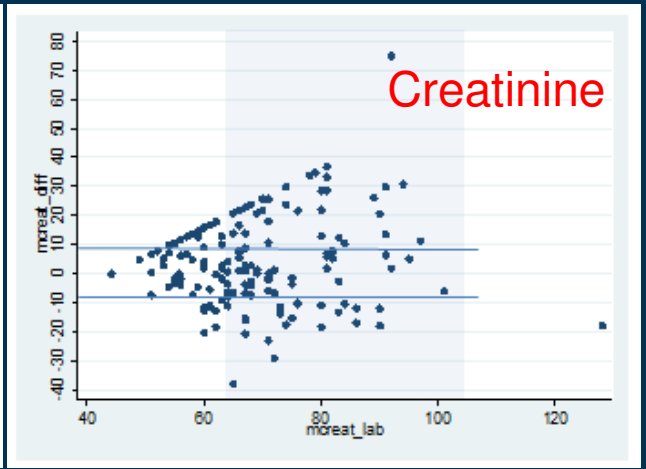


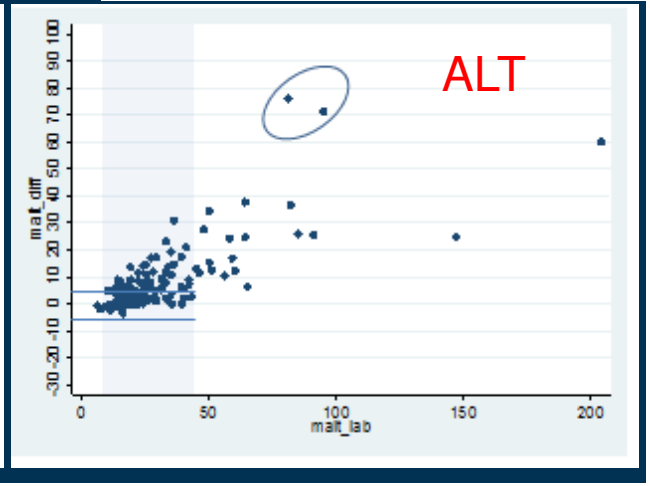
Assay performance:
Can nurses perform multiple POC as well as lab?

- Site 1: (HJH) n=160; site 2: TAH, n= 320
- Venepuncture POCT compared well with laboratory results:
  - mean differences: 24cells/µl CD4; 0.5g/dl Hb; 1.27µmol/l creatinine; 8.4IU/l ALT
  - 5.8% (9/155) CD4 tests required repeat testing



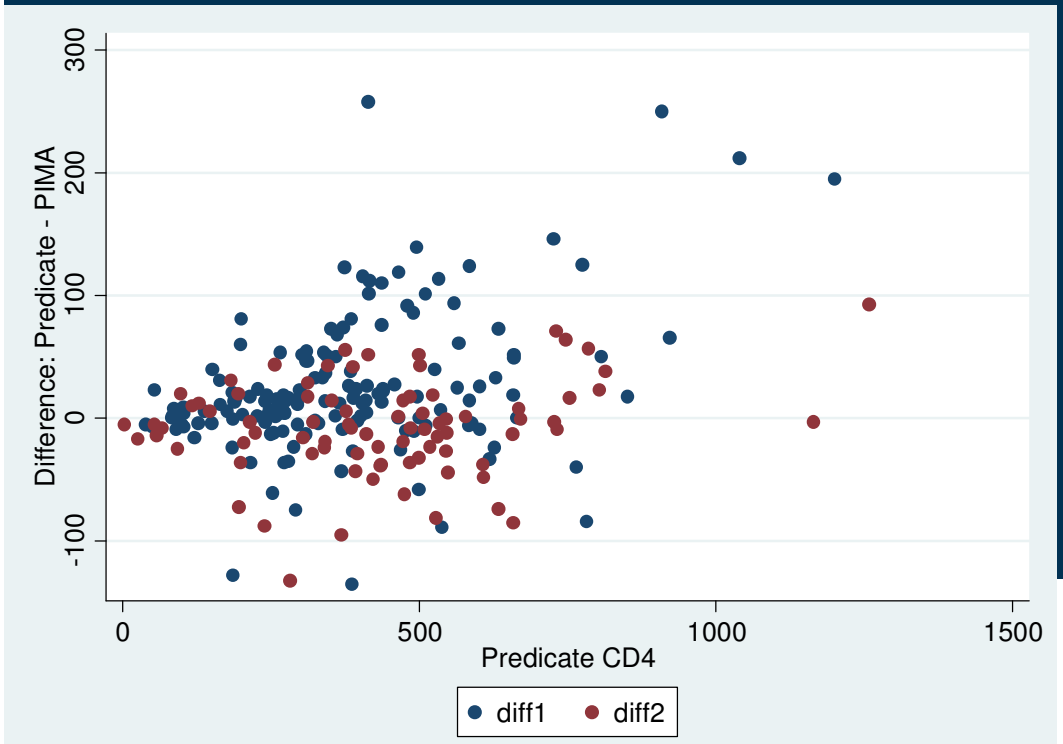




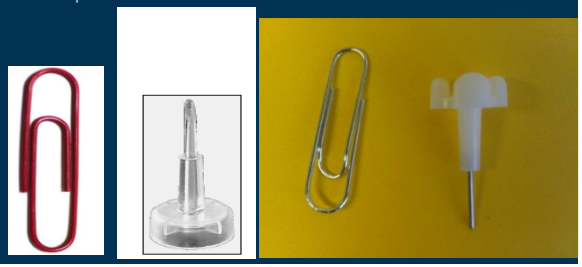


Sample collection: open tube vs finger-stick

- Increased variability with finger stick for CD4 PIMA testing *(Glencross et al, J int AIDS soc, 2012).*
- Alternative to finger-stick using a Vacuette VacuDrop



Ref: Pooled data re-analysis from 30 studies published on CD4 PIMA



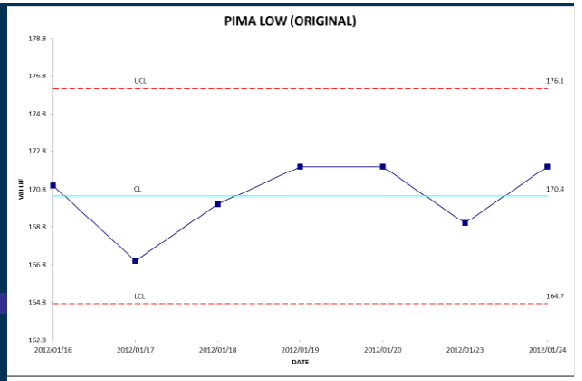
CE

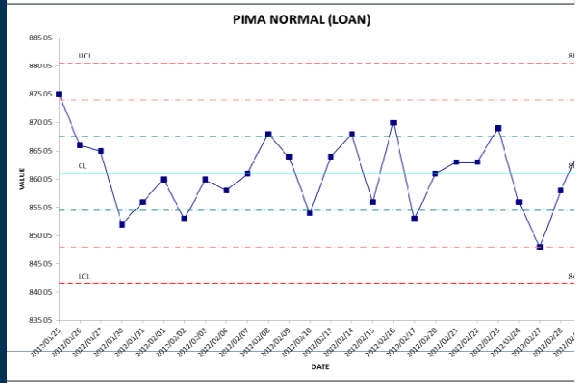
VACUETTE® VacuDrop
Instructions for Use

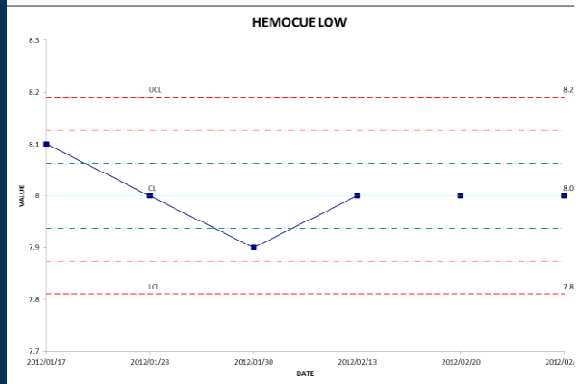
Intended Use: The VACUETTE® VacuDrop is a non-sterile plastic spike to be used together with VACUETTE® VACUETTE® Blood Collection Tubes as a system in routine venipuncture procedures. The VACUETTE® VacuDrop was specially designed for hematological laboratories, where differential blood smears are common practice. Previously the obtainment of a blood droplet was a process that required extra time as well as carrying the risk of contamination. This device is to be used by properly trained healthcare professionals only in accordance with these instructions.

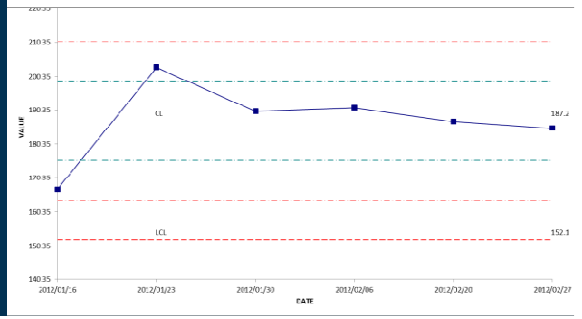
QC and EQA

- QC (Levy Jenning plots): good QC performance
- NHLS QAD can provide: EQA for CD4, Hb, (chemistry needs matrix validation)
- New “kid” = GeneXpert?
  - Novel verification and EQA developed.
  - DCS: *M.tb* single cell organisms, inactivated, quantified by flow cytometry, spotted onto filter cards, distributed to sites, tested.
  - Good performance on ~1500 DCS for verification
  - Good performance of DCS for EQA





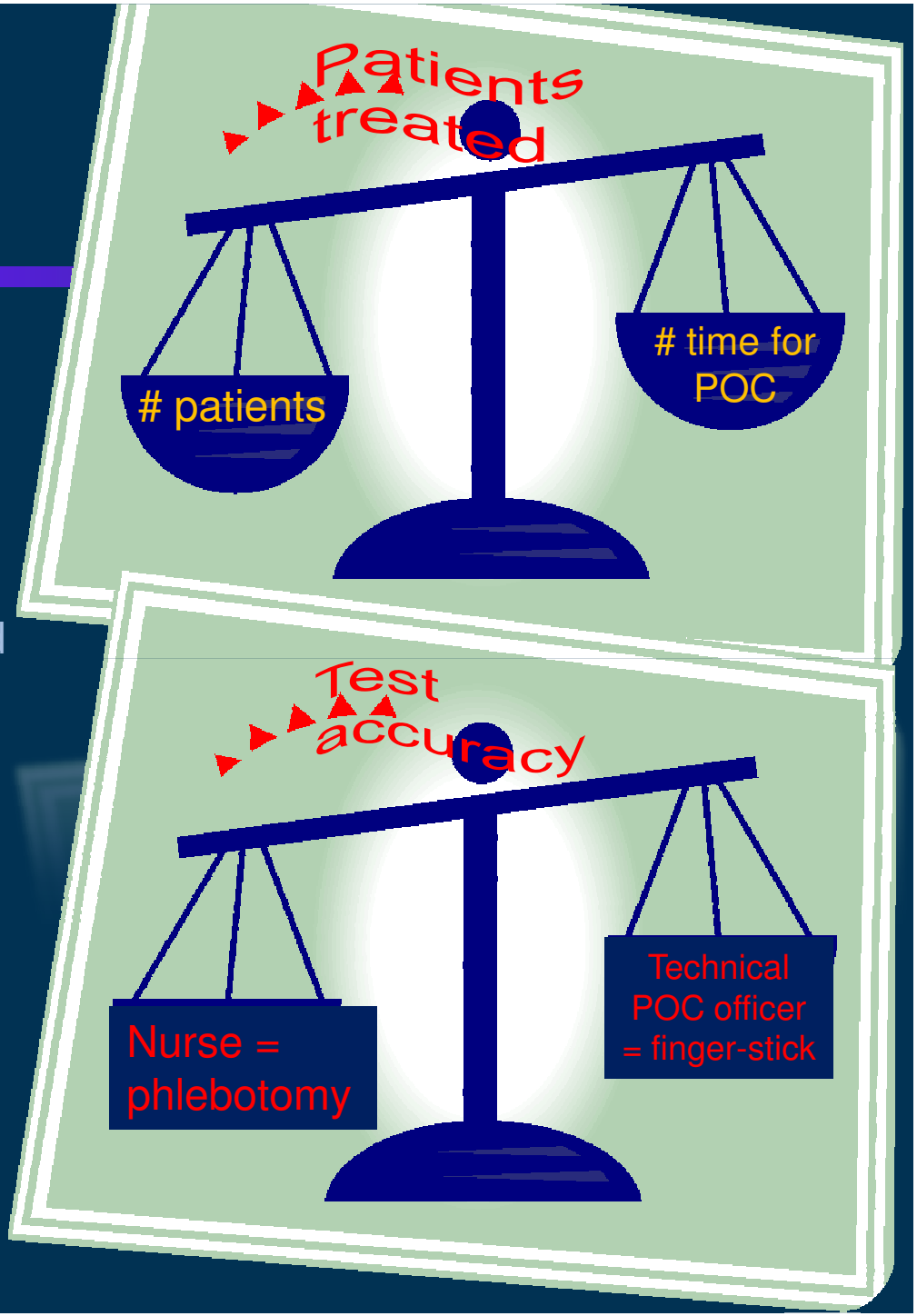




Human Resources

- Who will perform POCT?
- Task Shifting – management of task shifting from lab staff to clinical staff
- Regulation and certification around scope of work?

- Phlebotomy training need for non clinical staff!

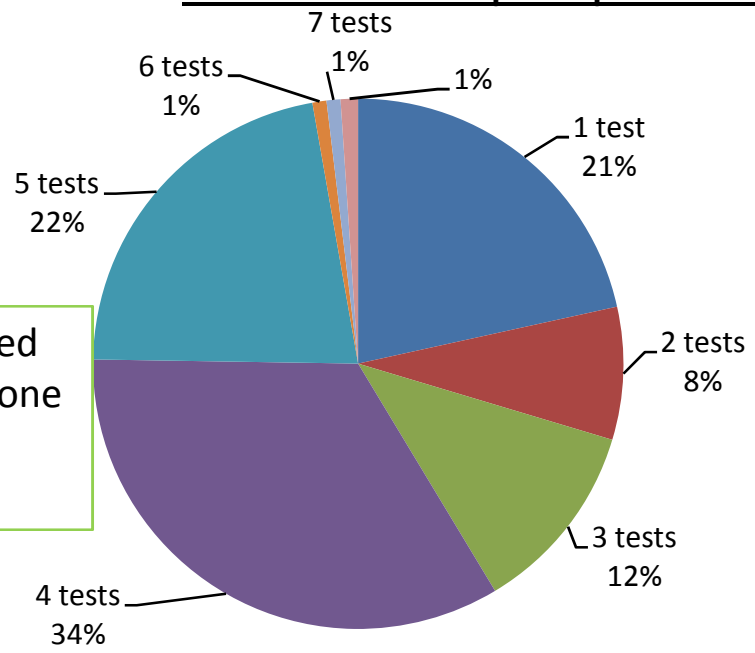


Number of tests a patient required / visit

Numbers of tests requested at any one time: HJH (site 1)

- 34% = 4 tests at one visit
- 25%=3 tests
- 21% = 2 tests
- 17.8%=1 test
- n=1 patient had 5 tests requested

Number of tests required per visit: TAH (site 2)



69% required >3 tests at one visit

Time taken to perform POCT

- HJH study:
- Earliest blood draw 8:15 (median time 9:55).
- Earliest **time a** POCT performed was 09:30, (median11:00 and the latest 12:24).
- Median time taken from the time the nurse started the first POCT to the time taken to start the last POCT varied depending on the number and type of tests requested.
  - When CD4 requested, tests took ~1hr47min,
  - CD4 not requested, ~6min - 14minutes. These time measurements did not include acting on result or any connectivity.

GeneXpert at POC >2hrs

- Gx placement (phased approach) currently at moderate to advanced infrastructure NHLS sites
- Collaboration with clinical partners to assess feasibility and impact of Gx at POC.
  - Concerns: Expanding Xpert to POC could result in important patient benefits but requires substantial strengthening of primary care facilities and investment in human resources (a minimum of two full-time staff required to supervise sputum collection, process sputum, perform assays, document and communicate results for an average of 15 TB suspects daily). Some patients did not receive same day treatment due to specimen preparation times. *(Clouse, K et al, SAMJ 2012)*

"Convenience comes with cost"

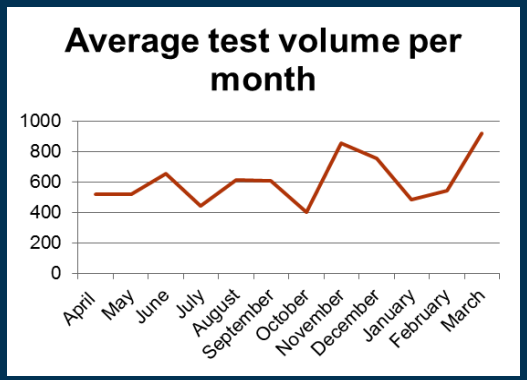
Overuse !

Study: Hospital POC placement of Hemocue (Hb201 DM)

Aim : to assess value of POC HB in wards where rapid result may alter care

- Lab Role
  - Training – 370 health care workers and laboratory staff trained
  - Quality control, maintenance of Hemocue instrument
  - Data management and stock control
- First outcome: No change in lab based FBC and Hb testing volumes before or after POC HB placed in specific wards
  - 12% increase in lab testing?
  - Awaiting clinical evaluation for impact.

165	Casualty
276	Paeds ICU
296	Paeds Renal
376	Trauma ICU
377	Trauma high care
396	General surgery
394	General surgery
561	Adult renal transplant
576	General ICU
577	General high care



Duties

CLINIC DUTIES

- Patient registration
- History taking
- Physical exam
- Counselling
- Rapid testing (HIV, pregnancy)
- Phlebotomy – lab tests
- Treatment
- Return visit booking

+

POC DUTIES (pre-analytical, analytical, post-analytical)

- Additional finger stick/venepuncture
- Sample labelling
- Instrument QC testing
- Instrument maintenance
- Testing:
  - ALT, Creat, Hb: <2minutes
  - PIMA = 20 minutes
  - Xpert MTB/RIF =2 hours
- Result recording/printing/reporting
- External quality assessment (EQA)
- Infection control
- Spill cleaning
- Waste disposal
- Additional skills:
  - Phlebotomy
  - Testing performed from blood tubes (pipetting skills)
- Additional duties:
  - Operator certification and on-going monitoring
  - Managing test failures, instrument downtime
  - Stock control
  - Specimen storage

Automation through information technology

Manual result entry…..

<10% POCT managed by central LIS.

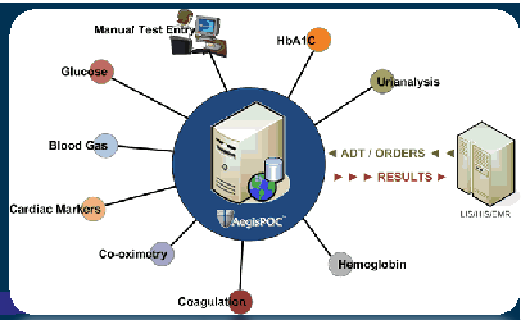
Billing and data management often handled manually
(Blick,K, Clin Chem Acta 2001)

Our experience:

Manual entry transcription errors

- Both clinic sites had transcription errors (1%; n=5/480):
  - Incorrect assay result recorded
  - Assay result recorded under incorrect test.

Solution is connectivity?



Level III and IV tertiary referral and reference laboratory: provincial hospitals

Level II laboratory: district hospital

Level I laboratory: health post/health center

NHLS LIS* and links to HIS* extends to here

Solutions beyond: sms printers, wireless networks

*laboratory information system
*Hospital information system

Connectivity standards *(Nichols Expert Rev Mol Diagn 2003)*

Results must be passed onto LIS and/or HIS:

- Permanent record of medical history
- Billing/reimbursement purposes
- Future reference

- CIC (Connectivity Industry Consortium) 1999:"*The vision: to expeditiously develop, pilot and transfer the foundation for set of seamless 'plug-and-play' POC communication standards :bidirectionality, device connection commonality, commercial software interoperability, security, and QC / regulatory compliance."*
- *The result was the POCT1-A international standard*

What is the situation with connectivity?

The good the bad and the non-conne

Ideal is a universal management system

Host LIS/HIS

HL7/ASTM

HL7/ASTM

HL7/POCT1-A

COBAS IT

GENEXPERT SOFTWARE

3rd PARTY APPLICATION

Proprietary

HL7/ASTM

N/A

POCT1-A

REFLOTRON

ACCUTREND

GENEXPERT

PIMA

HEMOCUE

POC Devic e #1

POC Devic e #2

POC Devic e #3

POC Devic e #4

POC Devic e #5

….off the shelf options don't satisfy all requirements

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

Instrument and Data Management

Patient Management

Are we ready?

Checklist	
Clinic infrastructure for dedicated POC space	Limited: needs reorganisation
	Follow pharmacy (dedicated space, well organised, security gate, some temperature controlled)
Instrument availability	Yes: CD4, ALT, Creat, Hb, Xpert, Viral load
Nurse operated POC accuracy	Yes: nurses as good as lab (venepuncture useful for multiple POCT)
Quality systems	Yes: for QC, not all for EQA (some need cold storage)
Staff	Nurses yes: time and workflow?
	Technical **no**: new cadre dedicated to POC? but need for phlebotomy!!!!! Also useful if want to reflect blood specimen for lab re-testing or POC repeat test.
Training and SOP	Yes: quick reference charts are effective, need large scale training (success story Xpert)
Data management and instrument connectivity	**No**: lose national data (no program performance or measure of interventions), reimbursement?, billing?
	Solution: (1) extend the LIS, (2) off the shelf products (included operator certification, EQA/QC, stock control etc
	Issue: instrument connectivity "the good, the bad and the not connectable", national coverage via wireless routers?

The question?

Questions	Answers
Does POC have a place post HCT?	Yes
Does it flow with clinic care	Reengineer
Who takes responsibility for the test?	A partnership
Who performs the POCT?	New cadre of technical POC officers?
Is a solution better logistics?	<4hr specimen transport to the lab (POC lab)
Is a solution better specimen preservation >6hrs?	DBS, ppt, Primestore (preservative material)
Is a solution faster TAT on reported result?	SMS printers, lab LIS terminals in each clinic – electronic era

Acknowledgements

- The National Health Laboratory Service and the NHLS POC working group and NPP
- The GCC team:.
- Wendy Stevens, Johan Potgieter, Lumka Ntabeni, Natasha Gous, Brad Cunningham, Elizabeth Prentice, Sebaka Molapo, Matilda Nduna, Regina Osih, Charlotte Jansen van Rensburg, nurses and counsellors
- Funders (USAID, GCC, CDC, Pepfar)
- Clinical Partners (WRHI, CHRU/RTC, PHRU)
- Patients and participants
- Suppliers forum/ working group (hardware and software suppliers) for technical support, platforms and reagents.

Advantages

- Quality and efficiency of care can be improved in certain scenarios
- Improved accessibility
- Improve patient compliance and LTFU
- Improved turnaround time
- Smaller sample volumes
- Economic benefits –
  - reduced length of stay
  - reduced complications and readmission
- Improved patient and clinician satisfaction

Disadvantages

- Difficulties with quality control/documentation
- Greater personnel requirements at clinic
- Longer patient wait times
- Data management/audit issues
- Slower sequential processing time/throughput in high clinics
- Over-servicing
- Higher unit of cost/reagent
- Poor regulatory control