

Pima in South Africa, and experience at Point of Care (case studies)

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On behalf of the GCC and R&D team

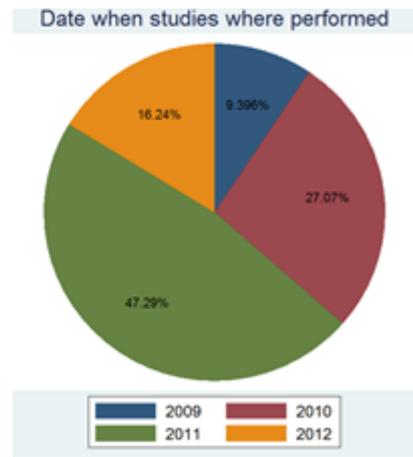
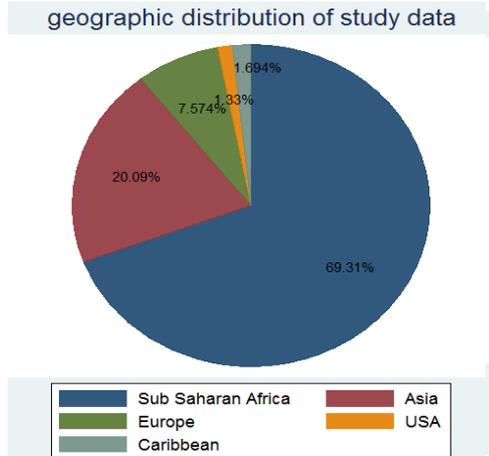
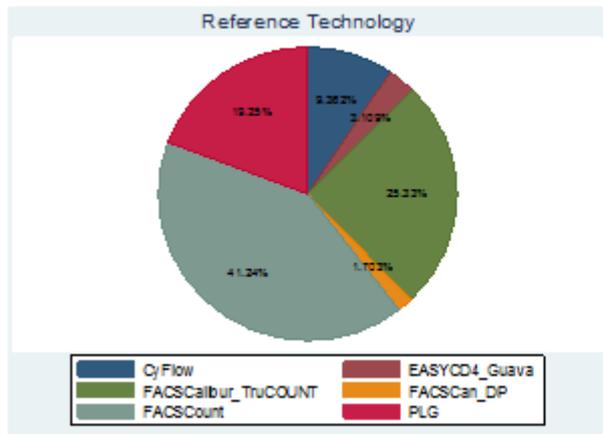
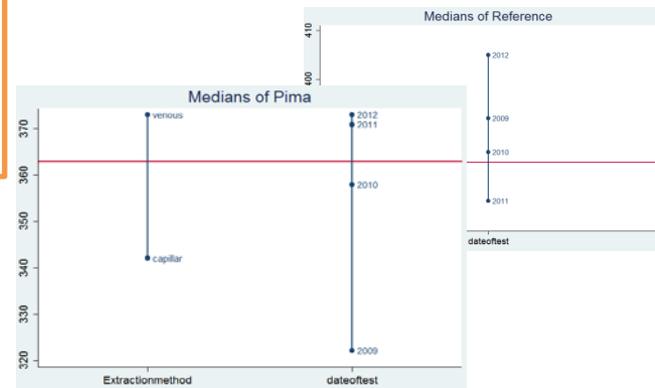
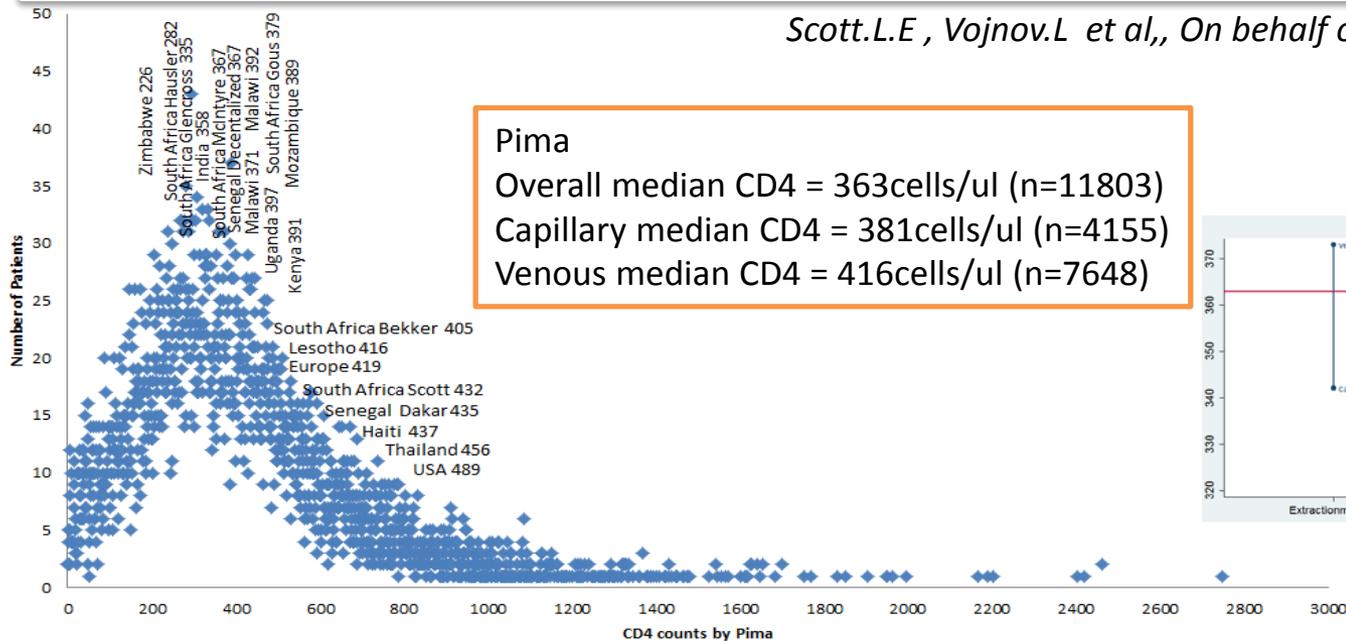


1. PIMA CD4 Metanalysis: what do we know about performance.
2. PIMA at POC in SA: GCC project- what have we learnt?
3. Realistic PIMA testing in the context of SA: Free-State study vs NHLS (volumes vs task shifting)
4. Impact of PIMA on ART guidelines: GCC RCT
 - RCT (preliminary outcomes) in NW province – the “PIMA effect” and what it means.

1. A multi-data analysis of the performance of the PIMA CD4 from twenty two studies across four continents compared to six existing CD4 technologies.

N=11803

Scott.L.E , Vojnov.L et al,, On behalf of the PIMA CD4 consortium



Clinical questions	Venous derived specimen testing	Capillary derived specimen testing
<p>Is Pima suitable for screening for reflex testing of CryAg testing at the <u>100cells/μl</u> threshold?</p>	<p>Suitable: 88% sensitive, negative bias of 34cells/μl, <u>1.8%</u> expect total misclassification</p>	<p>Not suitable: 79% sensitivity, negative bias of 73cells/μl, <u>3.5%</u> total misclassification</p>
<p>Good specificity >97%</p>		
<p>Is Pima suitable for identifying patients eligible for ART initiation at <u>350cell/μl</u> (WHO 2010 guidelines)?</p>	<p>Suitable: >91% sensitive, negative bias 38-51cells/μl</p>	
<p>Is Pima suitable for identifying patients eligible for ART initiation at <u>500cell/μl</u> (WHO 2013 guidelines)?</p>	<p>Expect <u>9.2%</u> (6.3% false positive) total misclassification with specificity of 89%</p>	<p>Expect <u>13.8%</u> (9.3% false positive) total misclassification with specificity of 82%, will increase treatment costs significantly more than venous testing.</p>
<p>Is Pima suitable for identifying patients eligible for ART initiation at <u>500cell/μl</u> (WHO 2013 guidelines)?</p>	<p>Suitable: >95% sensitive, negative bias 53-79cells/μl</p>	
	<p>Expect <u>8.3%</u> (6.3% false positive) total misclassification with 81% specificity</p>	<p>Expect <u>11%</u> (7.5% false positive) total misclassification with 74% specificity which will increase treatment costs significantly more than venous testing.</p>

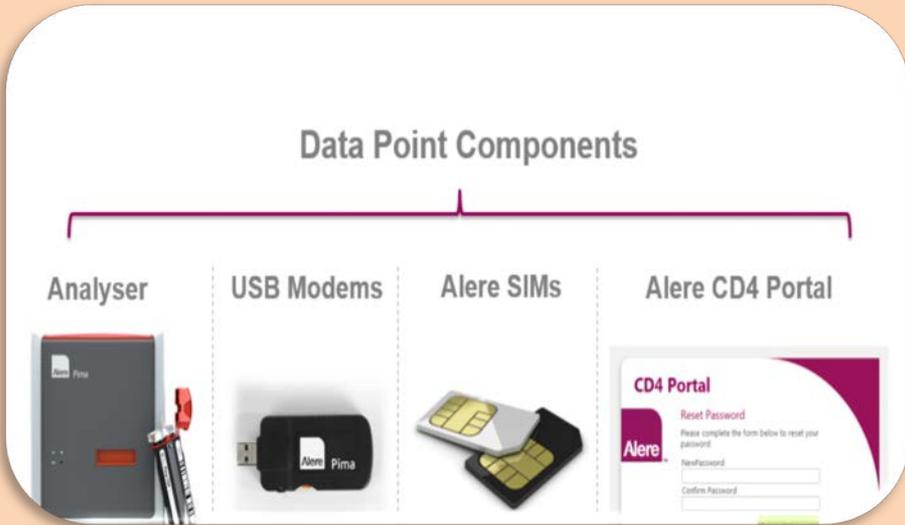
2. Nurse operated PIMA CD4 at POC

How long does it take to train HCW to operate the PIMA CD4?	<½ day training for operations. Computer literacy required for use with middleware.
Can verification and EQA be performed?	Yes and fixed whole blood material is available (NHLS-AFRIQAS). Maintenance and QC easy, and minimal “starter kit required”.
How well do nurses operate PIMA compared to lab on venous blood?	Nurses operated PIMA CD4 as good as Lab: within allowable cells/ul difference.
Are there issues with finger stick performance?	Increased variability in colder weather, 98% patients generate a result, 8% may require >1 finger-stick. Patients prefer finger stick and 150ul max volume
ART requires multiple tests (CD4, ALT, Cr, Hb): 69% patients need >3 tests.	Multiple POC can be performed, but 22 duties added to nurses and POCT/patient can take up to 1hr47mins incl. CD4.
What are the issues with data?	

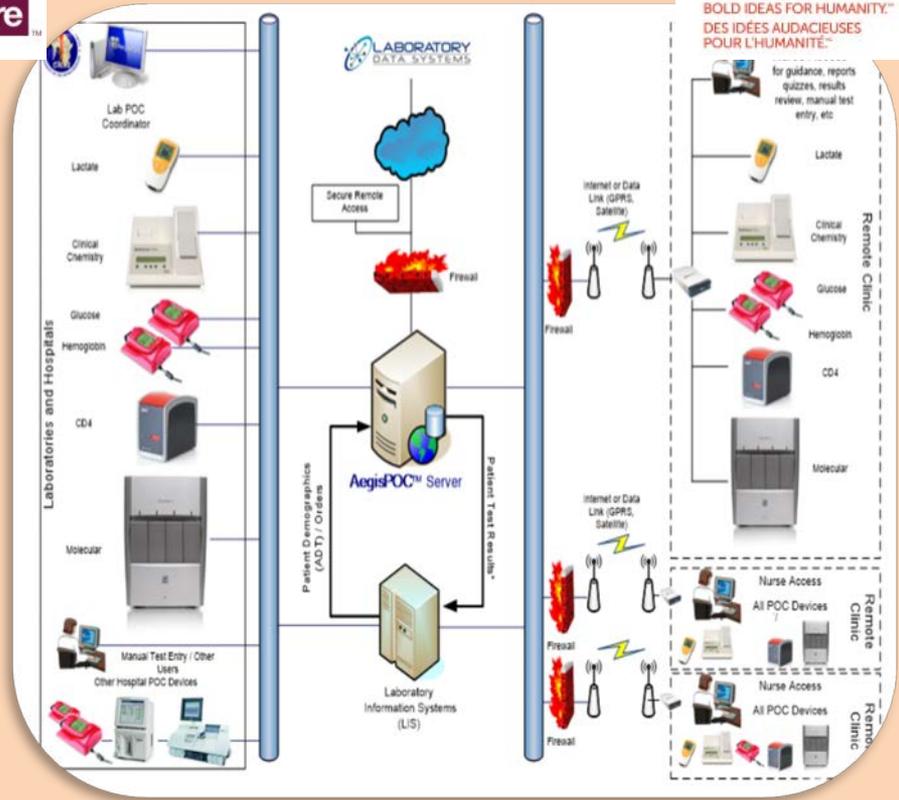


- Gous.N, et g for HIV Anti-Retroviral Treatment Initiation and Monitoring from Multiple or Single Fingersticks. PlosOne 2013 | e85265
- Maier.T, et al An Investigation of Fingerstick Blood Collection for Point-of-Care HIV-1 Viral Load Monitoring in South Africa, under submission.

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

GCC experience with middleware solutions(AegisPOC, POCcelerator)

Limitation with connectivity required for multiple POCT:

- All systems require **permanent IT support**:
 - Configuration of test lots, expiration dates, user training, downtime support, result review, troubleshooting, but is **centrally located** and managed.
- **Loss, availability and stability** of internet connections
 - 3G, ADSL, satellite
 - Of 3 clinics, additional antennae installed (dual carrier 3G/internet router)
 - AegisPOC requires **constant connection for use**
 - Data remains on POC instruments until connection is restored
 - POCcelerator has **limited capabilities offline** (caching of data)
 - **Web based** (AegisPOC) vs **local installation** (POCcelerator) has significant IT support implications
 - Web based allows for simple computer swap-out, but requires constant access to web browsing (needs firewalling and restrictions)
 - Local installation requires on site maintenance, re-installation of software and configuration of client (requires IT personnel – can't be done by POC staff).
- IT policing required: viruses, excessive downloads.



62% of overall results captured correctly

3. Realistic PIMA testing in the context of SA: Free-State study vs NHLS (volumes vs task shifting).

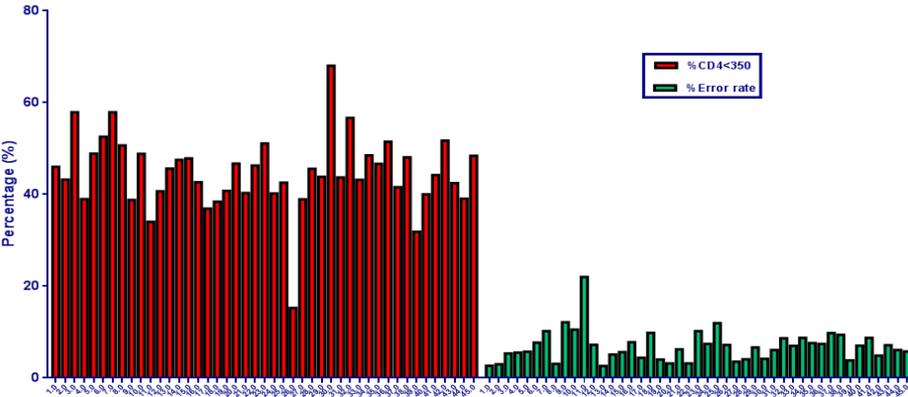
- Courtesy: Dr Lindi Coetzee (NHLS), Free State Department of Health and the University of Free State.
- 45 PIMA CD4 instruments
- 31 PIMA testing sites (clinics)
- 4 NHLS centralized CD4 labs
 - PLG CD4 (Beckman Coulter)
- Data collection and analysis
 - PIMA data manually retrieved via Usb and manually entered/sorted in MS[®]Excel.
 - NHLS data centrally collected CDW through interfaced instruments.



Current locations of PIMA Instruments in the Free State (according to data provided)

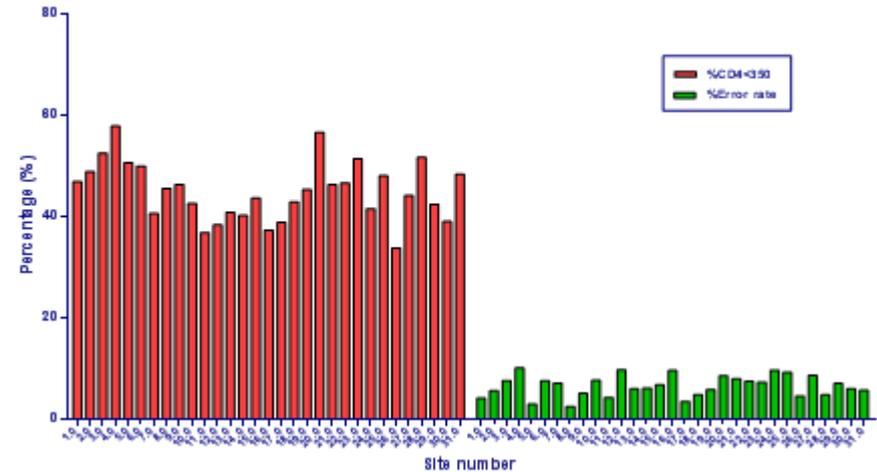
Per instrument

CD4 data summary
PIMA instruments FState per instrument



Per clinic site

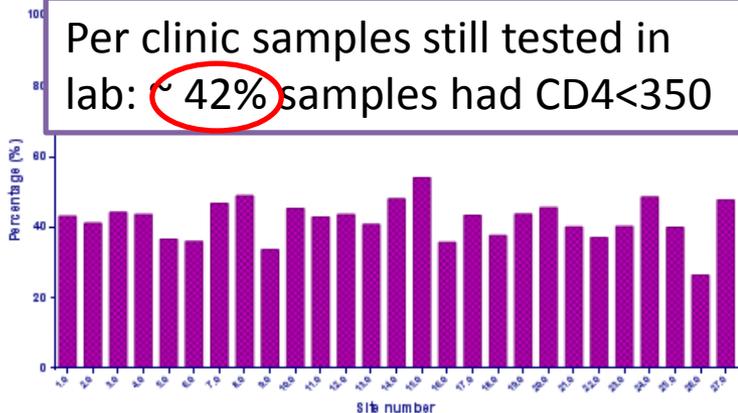
CD4 data summary
PIMA instruments FState Per Site



Per instrument/per site: **~ 45%** of samples tested had a CD4 < 350
Error rate per instrument/site averaged at < 7%

Comparative CDW/Lab tested data: period 2011-2014 Per Clinic Site with CDW CD4

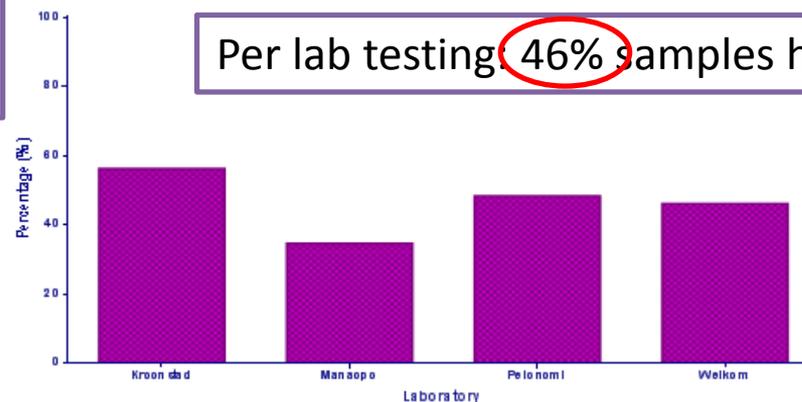
CD4 data summary
CDW Data for PIMA clinics 2011 to 2014
CD4 < 350



Per clinic samples still tested in lab: **~ 42%** samples had CD4 < 350

Per NHLS CD4 lab CDW CD4

CD4 data summary
NHLS LABS FState
March 2011 to March 2014
CD4 < 350



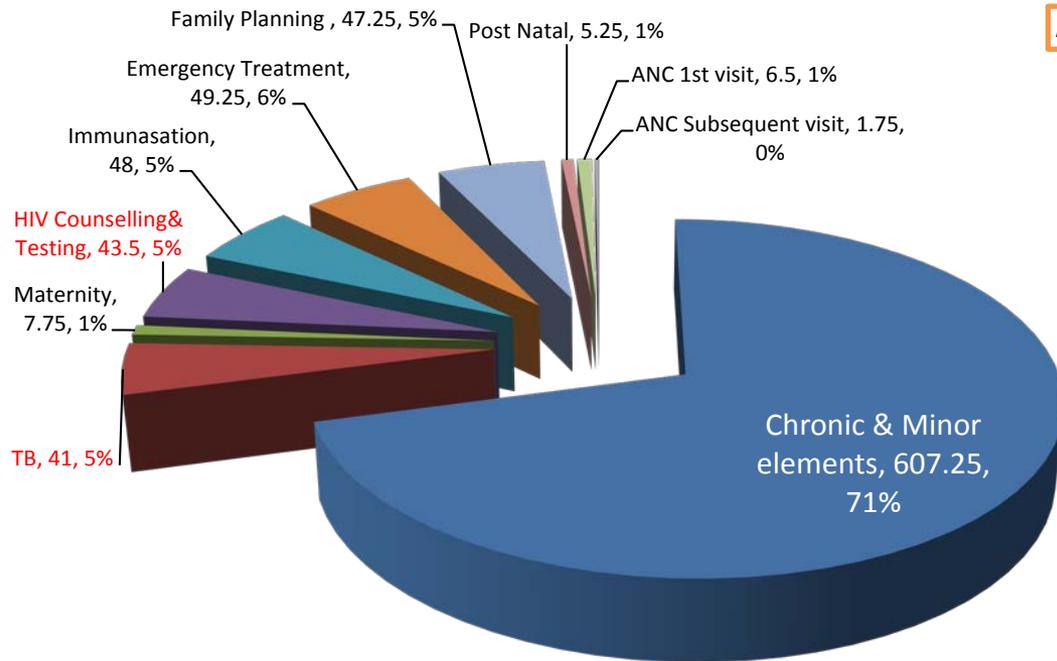
Per lab testing **46%** samples had CD4 < 350

PIMA FS province summary (based on data analysis)

- Between March 2011 – March 2014:
 - PLG (Lab testing) = 705 799 tests
 - PIMA (Clinic testing) = 38 275 (5%)
- **CD4 Testing demands in SA is high: POC vs total coverage.**
- Overall PIMA identified more (45%) patients with CD4 <350 in the clinic than the lab (42%), but overall FS province needs, the lab identified more (46%)/region: **PIMA coverage limited.**
- Data collection by manual means is problematic, and no clear evidence of QC being performed or monitored at all sites.
- Some variation in instrument performance (error rates on PIMA on average <7%, though as high as 10% per site and 22% per instrument.

4. Impact (and cost) of multiple POCT on ART initiation

- 13 sites visited, 3 sites in North West Province identified for the RCT.



Average Feb 2014, Botshebelo clinic, PHC



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

RCT: determine if POCT is better than centralized lab testing for HIV ART initiation.

Primary outcome: Proportion of patients retained in care at 6 and 12 months.

717 patients enrolled in study from May 2012 to September 2013.

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%

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

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

Characteristics	All subjects
Mean age	35.7yrs
% male	33%

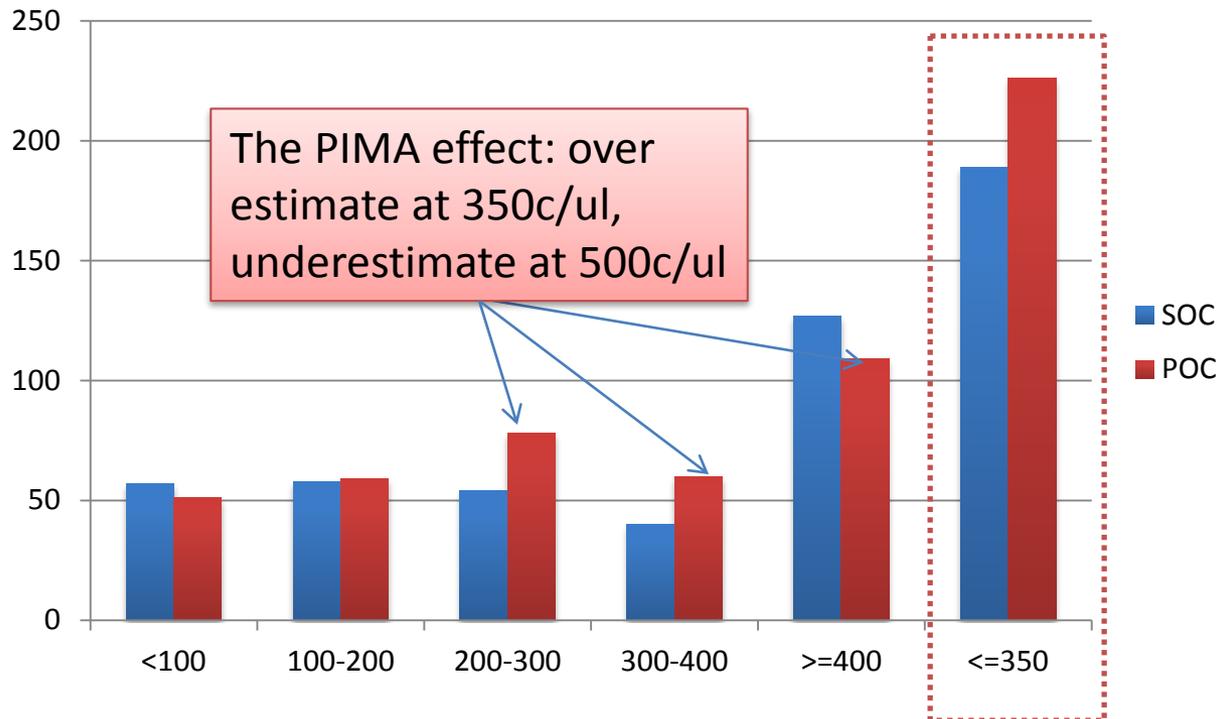
Education	
none	2.4%
primary	27%
secondary	65%
tertiary	2.8%

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

Baseline CD4

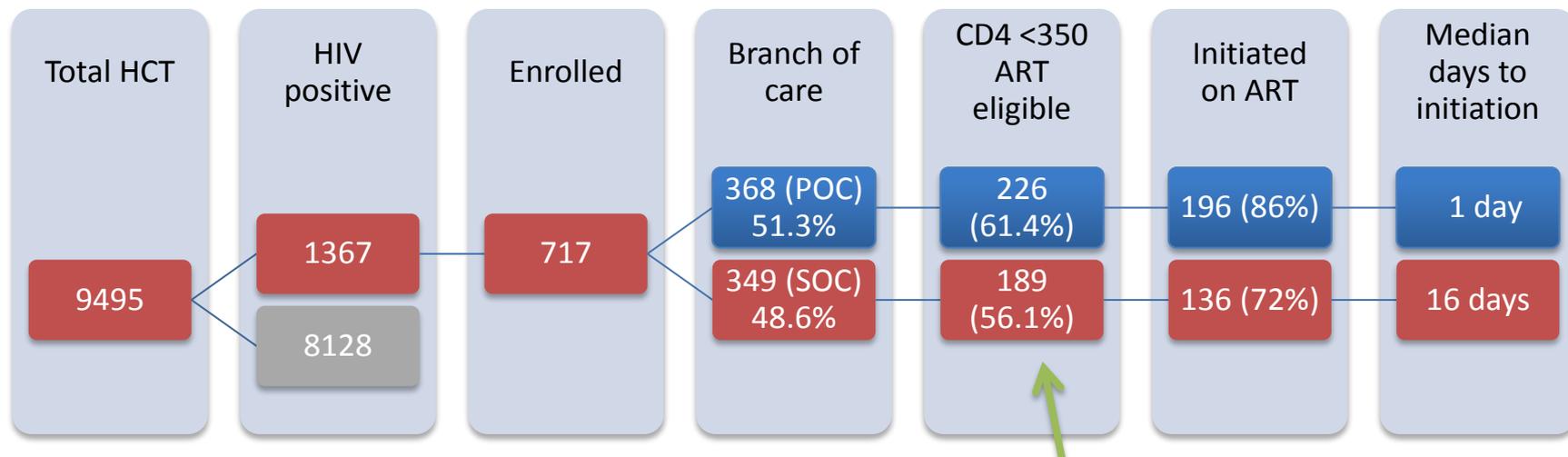
Mean CD4 for POC = 337c/ul, slightly higher than SOC = 332c/ul.
Proportion Patients with CD4 less than 350 cells/mm³: higher in arm POC (63% (226/360)) than SOC (56% (189/337))

CD4 Results by Branch of Care

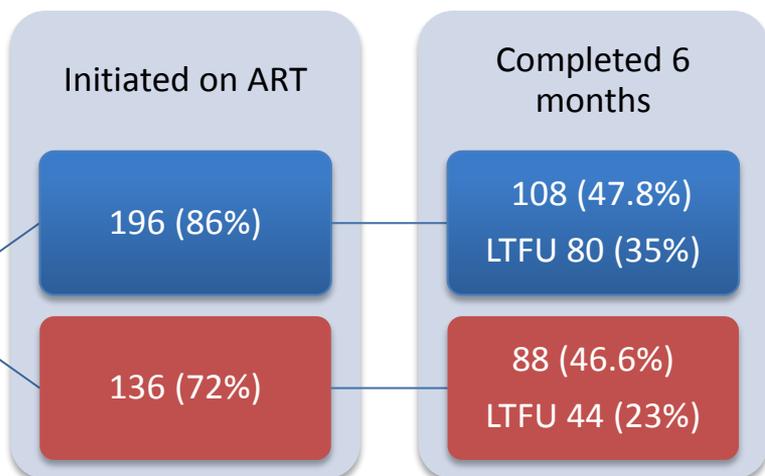


More patients eligible at POC due to technology variability!

Enrollment (Mid August 2014)



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



1.21 (95% CI (1.09-1.34))

1.03 (95% CI (0.84-1.26))

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

Are patients being pressurised

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



Great Challenges Canada Study/ University of the Witwatersrand Department of Epidemiology and Molecular Medicine
Study Code: HREC 10331 Sub-study: Investigating the effect of POC laboratory in Patient Flow

REGISTER FORM

Consent documented YES/NO _____ Study Coordinator (sign) *[Signature]*

Client number: 13 Date: 26.07.12 Time arrived: 9:05
Time departed: 10:00

Sex: Male Female

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

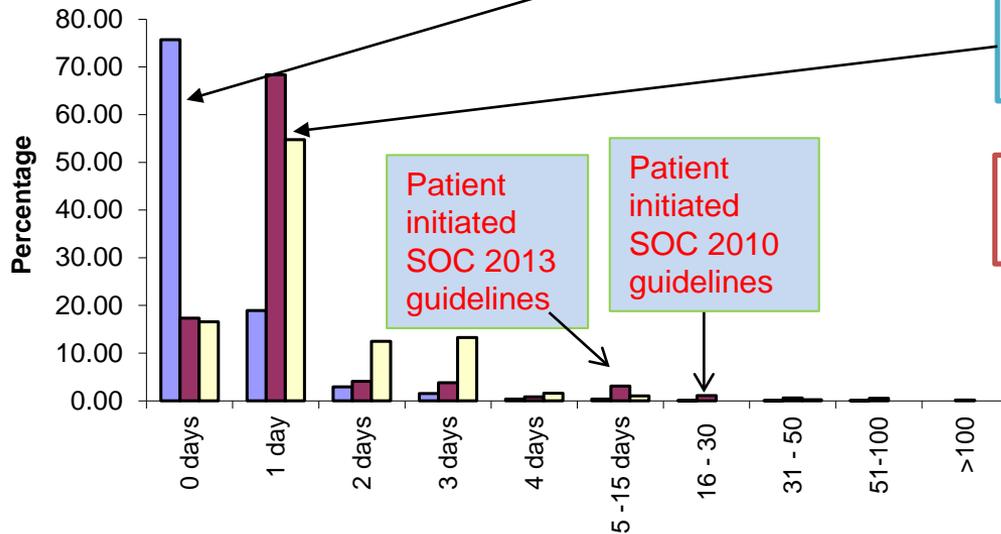
Visit timing: First visit Follow up visit

	Staff code & initials	Waiting time	Time service started	Time service completed
First contact	<u>A</u>	<u>30 min</u>	<u>9:10</u>	<u>9:15</u>
Second contact	<u>C</u>	<u>15 min</u>	<u>9:25</u>	<u>9:40</u>
Third contact	<u>E</u>	<u>30 min</u>	<u>9:45</u>	<u>10:00</u>
Fourth contact				

Multiple POC: 22 duties added to nurses and if perform a PIMA CD4, Hb, ALT, Cr, can take up to 1hr47mins.

	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

Turnaround times



75% of specimens are collected from the clinic and received at laboratory within one day;

85% lab tests completed by lab within one day;

72% printed results stamped in the clinic within one day.

■ Sample collected from clinic to received at laboratory (n=1638)
■ Sample received at laboratory to result printed (n=1638)
■ Result printed at laboratory to stamped at clinic (n=1611)*

TAT: 3 clinics NW

- Patient initiated day 1 with POC , same day 72% lab results returned to clinic
- Question added benefit of POC placement with dedicated staff versus treatment guideline change to 7 day with lab results already in the clinic.

Summary

- PIMA CD4 has good performance on venous derived specimens at 100c/ul, 350c/ul and 500c/ul with maximum misclassification of 9%.
 - Capillary derived testing performance is suitable at 350c/ul and 500c/ul, but will increase treatment costs as misclassification increases to 14%.
- Nurse operated PIMA CD4 POC is good, time consuming and requires connectivity that can be challenging (dashboard vs middleware) and will require support.
- Sporadic error rates are still a concern (7%-20%) and QC/EQA is required.
- The “PIMA effect” (false positivity) leads to significant increase in ART initiation, but LTFU still a concern.
- Implementation requires training, connectivity (real time monitoring), ongoing quality and integration into existing laboratory framework.
- Need to take into account change in ART guidelines!

Acknowledgements

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