Point-of-Care CD4 Testing in Low & Middle Income Countries: Current and Future perspectives

Minh Pham
Burnet Institute
Monash University, school of Public health and Preventive medicine
Melbourne, Australia

Burnet Institute   MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

---

Introduction

- HIV epidemics
- HIV diagnosis & HIV continuum of care
  - Availability
  - Cost
  - Accessibility
- HIV point-of-care (POC) Tests
  - HIV antibody
  - Early Infant Diagnosis (EID)
  - CD4
  - Viral load

Burnet Institute   MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

---

Why CD4 Point-of-care Test

- Treatment eligibility assessment
- Treatment monitoring
- Patient benefit
  - Increased accessibility
  - Same day result
  - One stop services of testing, counseling and initiation of therapy => Reduce loss-to-follow up
- Service provider benefit:
  - Decentralizing HIV related testing to clinic level =>
  - No need for specialized laboratories and highly skilled laboratory staff

Burnet Institute   MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

---
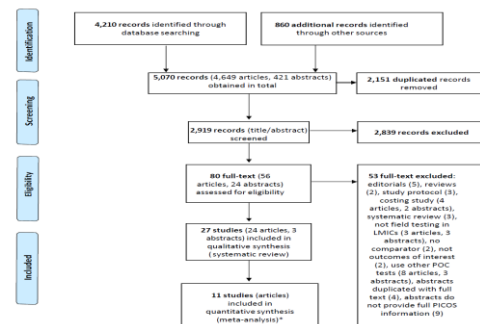
Research question

- Implementation of POC CD4 tests in resource-constrained settings (LMICs)?
  - In-field diagnostic performance
  - Acceptability
  - Feasibility
  - Impact on continuum of care

Burnet Institute   MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

---

Systematic review

- In-field studies/evaluation of POC CD4 technologies in LMICs (Jan 2005 – Jan 2015)

Burnet Institute   MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

---

Figure 1: Selection process of included studies

Result – Study characteristics

- Three out of six reportedly available POC CD4 tests have published data from field studies in LMICs: Pima™ CD4, PoinCare NOW™, MyT4™ CD4
- Pima: ~ 90% (24/27) of included studies
- Test operators: non-lab technician
- Quality of studies: "moderate" to "strong"

Burnet Institute | MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

Result – Acceptability & Feasibility

- No studies have *assessment of* acceptability/feasibility in field settings as primary objective
- High acceptance: 90-100%
- Service provider perspectives:
  - *"Efficient in resources used" "user friendly" "easy to use by non-lab person" "responded well to patient need"* (Galiwango, R.M., et al., 2014; van Rooyen, H., et all., 2013; Manabe, Y. C., et al., 2012; Thakar, M., et al., 2012)
- Patient perspectives:
  - Having POC CD4 test on site *"We now receive our result there and then"* (Mtapuri-Zinyowera, S., et all., 2013)

Burnet Institute | MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

Result – Impact on continuum of care

- Increased access to CD4 testing (ART eligibility assessment)
  - Clinical setting: 90% vs 67% RR: 2.4, p<0.001
  - Home based care & treatment: 96% vs 52%
- Reduced loss to follow-up by 50%
  - HIV confirmation and ART eligibility assessment
  - No/little effect between ART eligibility assessment and ART initiation

Burnet Institute | MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine
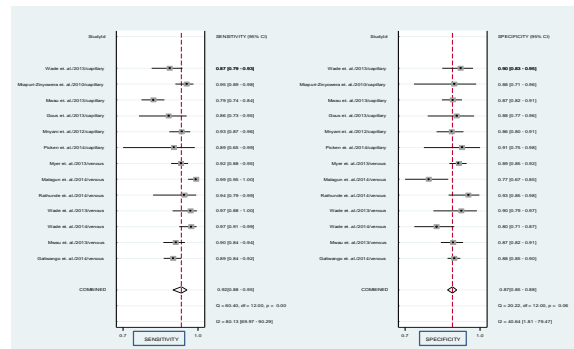
Result – Diagnostic performance

- Across studies…
  - Strong performance: sensitivity: 80-100%; specificity: 79-99% (CD4 threshold of 350 cells/μl)
  - Differences in test performance: Venous vs Capillary blood
  - Failure rate: 5% - 23%

Burnet Institute | MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine
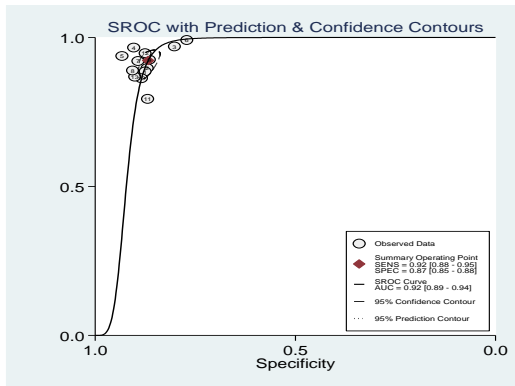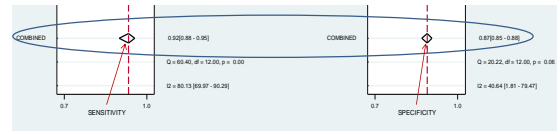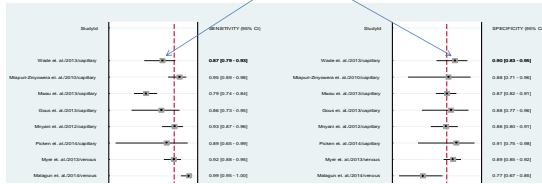
Result – Meta analysis

- Pima™ CD4: 11 studies (2 studies report both capillary & venous sample results)
- Multi-level bivariate random-effect modeling
- Covariate for blood sample type (venous/capillary)
- Adjusted standard error for multiple sets of diagnostic data taken from single studies
- Diagnostic statistics & sensitivity analysis on effect of outlier bias

Burnet Institute | MONASH University — Medicine, Nursing and Health Sciences — School of Public Health and Preventive Medicine

Meta analysis

Meta analysis

SROC with Prediction & Confidence Contours

Capillary vs. Venous…

Blood types	No of point estimates	Sensitivity	Specificity
Pooled estimate (Meta-analysis)	13	0.92 (0.88-0.95)	0.87 (0.85-0.88)
Capillary	6	0.89 (0.83-0.93)	0.87 (0.86-0.89)
Venous	7	0.94 (0.89-0.97)	0.86 (0.82-0.89)

Wald χ^2 (2)= 4.77; p= 0.09

Key findings

- Acceptable diagnostic accuracy
- Increased accessibility & improved retention
- High acceptance
- Feasible in primary health & community settings

Issues & Questions

- Data scarcity…
- Differences in performance by blood types?
- Failure rate: technology failure vs. test operator error? Venous vs. capillary?
- Influencing factors?
  - Training for test operators & supervisors: Impact of blood sampling on test performance
  - External Quality Assurance
  - Staff workload/incentive
  - POC test throughput vs. patient volume
  - Service delivery organization: POC testing at ART-initiation site

Future of CD4 testing?

- Early initiation of ART: New evidences from START & TEMPRANO
- WHO guidelines on ART: ART initiation independence of CD4 count?
- Health system capacity
- Feasibility and sustainability of ART programs
- Financial & resource constraints in LMICs
- "90-90-90" Goal: priority given to PLWHA CD4 less than 350 cells/µl

Burnet Institute

MONASH University
Medicine, Nursing and Health Sciences
School of Public Health and Preventive Medicine

References

- Mtapuri-Zinyowera, S., et al., PIMA Point of Care CD4+ Cell Count Machines in Remote MNCH Settings: Lessons Learned from Seven Districts in Zimbabwe. Infect Dis (Auckl), 2013. 6: p. 51-60
- van Rooyen, H., et al., High HIV testing uptake and linkage to care in a novel program of home-based HIV counseling and testing with facilitated referral in KwaZulu-Natal, South Africa. J Acquir Immune Defic Syndr, 2013. 64(1): p. e1-8
- Manabe, Y.C., et al., Evaluation of portable point-of-care CD4 counter with high sensitivity for detecting patients eligible for antiretroviral therapy. PLoS One, 2012. 7(4): p. e34319
- Galiwango, R.M., et al., Field evaluation of PIMA point-of-care CD4 testing in Rakai, Uganda. PLoS One, 2014. 9(3): p. e88928
- Thakar, M., et al., Utility of the point of care CD4 analyzer, PIMA, to enumerate CD4 counts in the field settings in India. AIDS Res Ther, 2012. 9(1): p. 26
- Glencross, D.K., et al., Performance evaluation of the Pima™ point-of-care CD4 analyser using capillary blood sampling in field tests in South Africa. J Int AIDS Soc, 2012. 15(1): p. 3
- Mwau, M., et al., Evaluation of PIMA™® point of care technology for CD4 T cell enumeration in Kenya. PLoS One, 2013. 8(6): p. e67612.
- Scott, L.E., et al., A meta-analysis of the performance of the Pima(TM) CD4 for point of care testing. BMC Med, 2015. 13: p. 168
- Wade, D., et al., CD4 T-cell enumeration in a field setting: evaluation of CyFlow counter using the CD4 easy count kit-dry and Pima CD4 systems. PLoS ONE [Electronic Resource], 2013. 8(9): p. e75484
- Picken, S., et al., The routine paediatric human immunodeficiency virus visit as an intervention opportunity for failed maternal care, and use of point-of-care CD4 testing as an adjunct in determining antiretroviral therapy eligibility. Southern African Journal of Epidemiology and Infection, 2014. 29(2): p. 70-74.
- Myer, L., et al., Comparison of point-of-care versus laboratory-based CD4 cell enumeration in HIV-positive pregnant women. J Int AIDS Soc, 2013. 16(1): p. 18649.

Acknowledgements