

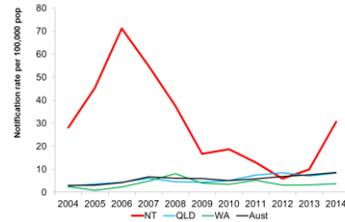
## Are Rapid Point-of-care Tests for Syphilis Useful in Outbreak Settings in Remote Australia? – Experience from the Northern Territory, Australia?

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On behalf of the Outbreak Response Team

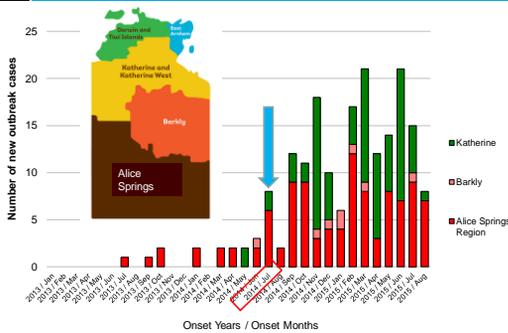
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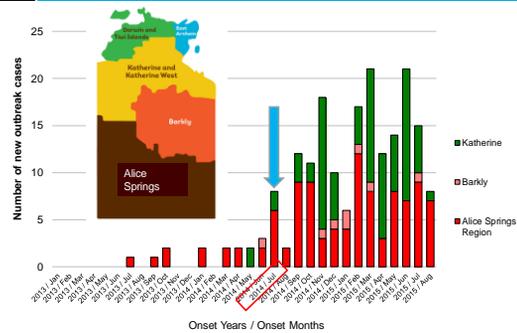
- Resurgence of syphilis in remote Indigenous communities (outbreaks in north QLD, NT and WA)



## The 2014/2015 syphilis outbreak in the NT



## The 2014/2015 syphilis outbreak in the NT



## Background – Serological diagnosis of syphilis

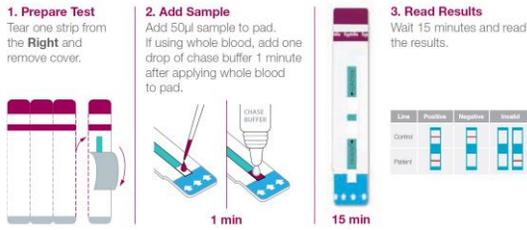
- 2 types of antibodies to detect:
  - Non-treponemal: RPR, VDRL
  - Treponemal: FTA-abs, TPPA, EIA/CMIA (PoCT available)
- Both test types have imperfect specificity
- False +ve possible for both
- Reactive treponemal test remain positive post treatment – cannot differentiate active infections from inactive ones
- Need trained technicians, controlled laboratory environment and equipment
  - Usually located in urban centres, far away from the location of outbreak; long transportation time; delayed diagnosis

## Background – PoCT for syphilis

- Mostly only treponemal test
- Targeting Anti-*T. pallidum* IgG, IgM, IgA
- Form: test strip, cassette
- Clear and easy-to-interpret results
- Specimen type: whole blood (finger prick), serum or plasma
- Room temperature storage
- Simple steps involved in the test: usually 2-3 steps
- No additional equipment required



**PoCT in the form of a test strip: Alere Determine**



Source: www.alere.com

**Background – Advantages of PoCT for syphilis**

- Advantages of PoCT
  - High specificity and adequate sensitivity (need to bear in mind)
  - Compared with traditional blood testing: easier to perform, less painful, without taking blood—better acceptability
  - Can be performed by clinical staff without lab training, with minimal training
  - Facilitating prompt clinical decision making
  - Can be used outside of labs and clinics (e.g. outreach or remote clinics, screening stations, etc.)

**Background – Criteria for Ideal PoCT**

- The ideal rapid test for STIs: ‘ASSURED’ criteria (WHO)\*
  - A= Affordable
  - S= Sensitive (few false negatives)
  - S= Specific (few false positives)
  - U= User-friendly (simple to perform, minimal training)
  - R= Robust and rapid (results available in <30 min)
  - E= Equipment free
  - D= Deliverable to those who need them
- We assessed the usefulness and suitability of using PoCT for community-wide screening in the current syphilis outbreak using these criteria.

\* Peeling et al. (2006). Rapid tests for sexually transmitted infections (STIs): the way forward. STI, 82 Suppl 5, v1–6.

**Assessment: A=Affordable**

- Cost per test kit:
  - OnSite Ab Combo: \$2.0-2.5
  - SD Bioline: \$3.5-4.0
  - Determine: \$3.5-4.0
- The population of 12-30 year olds in most remote communities affected by the current outbreak: ≈250-300
- Material cost for PoCT per screen ≈\$1000-\$1200

**Assessment: S= Sensitive S= Specific**

	Clinic whole blood		Lab whole blood		Lab serum	
	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)
Tanzania	59.6 (12.7)	99.4 (0.7)	80.7 (10.2)	99.4 (0.7)	91.2 (7.3)	97.9 (1.3)
Brazil	88.5 (8.7)	97.9 (2.0)			88.5 (8.7)	97.9 (2.0)
China	81.9 (8.3)	99.4 (0.8)	77.1 (9.0)	100 (n=362)	100 (n=83)	98.9 (1.1)
Haiti	72.5 (13.8)	98.5 (0.9)	100 (n=40)	95.7 (1.5)	100 (n=40)	95.7 (1.5)

	Clinic whole blood		Lab whole blood		Lab serum	
	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)
Tanzania	85.7 (8.4)	98.1 (1.2)	90.9 (6.9)	96.1 (1.6)	90.9 (6.9)	95.5 (1.8)
Brazil	88.2 (8.9)	99.4 (0.7)			90.2 (8.2)	99.4 (0.7)
China	87.6 (6.8)	99.4 (0.8)	87.6 (6.8)	99.4 (0.8)	95.5 (4.3)	97.9 (1.4)
Haiti	100 (n=30)	98.3 (1.2)	100 (n=30)	98.5 (1.1)	100 (n=30)	98.5 (1.1)

Mabey et al. (2006). Prospective, multi-centre clinic-based evaluation of four rapid diagnostic tests for syphilis. STI, 82 Suppl 5, v13–16.

**Assessment: S= Sensitive S= Specific**

N	Determine		Onsite		DPP (Trep)		Bioline	
	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec
(IA+IA-)*	(95% CI)							
1203	97.3	96.4	92.5	97.0	89.8	98.3	87.8	98.5
(736/467)	(95.8-98.3)	(94.1-97.8)	(90.3-94.3)	(94.9-98.3)	(87.3-91.9)	(96.5-99.2)	(85.1-90.0)	(96.8-99.3)

Causser et al. (2014). A laboratory-based evaluation of four rapid point-of-care tests for syphilis. PLOS ONE, 9(3):e91504. (n=1203, urban, Sydney/Melbourne, stored sera)

SD Bioline: performance :  
 Specificity: 100%  
 Sensitivity: 81.5% (95%CI: 76.6-86.4%)

Robertson et al. (2014) The utility of syphilis point of care testing in remote Queensland communities. Pathology 46(4):367-8 (n=240, remote, Mt Isa of north Queensland, sera)

**Assessment: U, R, E**

- U= User-friendly
- R= Robust and rapid (results available in <30 min)
- E= Equipment free



**Assessment: D= Deliverable to those who need them**



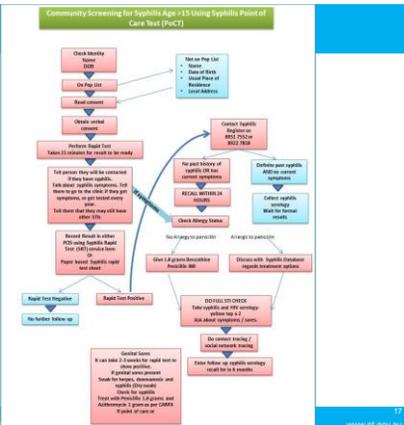
**Syphilis outbreak response**

- Forming a multi-disciplinary outbreak response team; weekly team meetings
- Alerting clinicians with public health alerts and surveillance newsletters, with updates
- Surveillance and monitoring with testing and treatment data (Syphilis Register; PCIS; lab testing data)
- Education and promoting opportunistic testing at PHC clinics; repeat every 3 months (remote sexual health team)
- Enhanced case management (incl. contact tracing)
- Enhancing awareness in government and non-government key stakeholders and community representatives

**Community-wide screening using PoCT**

- Deemed required due to high numbers of cases and untraced contacts in 3 communities
- As an additional outbreak control strategy
- NT Guidelines on the conduction of community-wide screening for syphilis in outbreak situations
- Using PoCT to facilitate the screening, and enable prompt treatment and contact tracing
- Devising screening protocol (flow chart)
- Producing updated population list with status of past infection (blood test for those with past infection)
- Staff training (administering and interpreting PoCT, learning screening protocol)
- Support by Syphilis Register (e.g. for visitors not on the list)

**Screen Protocol Flow Chart**



**Further considerations**

- Less than ideal sensitivity of the PoCT
  - Some cases might be missed (false neg)
  - But it is to be expected that some early cases might be missed
- The outbreak response will keep promoting repeat testing in 3 months and opportunistic testing at clinics.
- Community-wide screen- deemed as an additional outbreak response measure, complementing other measures
- Rescreens are planned
- Feasibility of using PoCT in community-wide screening for outbreak control
  - Low background seropositivity in the targeted age group (12-30 year olds) → lower possibility of overtreatment
  - Syphilis Register provided information on past infection → further reduced possibility of overtreatment
  - Expected high prevalence (during outbreak) → higher PPV

## Results of community-wide screening (PoCT part only)

- ❑ 2 communities with high numbers of cases (>5 cases) and untraced contacts (>5 cases)
- ❑ Community-wide screens conducted in September-December 2014
- ❑ Staff of Remote Sexual Health Team of NT CDC conducted the screens with local clinic staff
- ❑ Age-range targeted : 12-30 years (based on early cases)

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## Results of community-wide screening (PoCT part only)

Category	Male	Female	Total
<b>Resident population</b>	359	417	776
<b>Resident tested, n</b>	189	232	421
<b>(%)</b>	(52.6%)	(55.6%)	(54.3%)
<b>Visitors tested</b>	35	38	73
<b>Total tested</b>	224	270	494
<b>Among all tested</b>			
<b>Median age</b>	19	21	20
<b>IQR</b>	15-24	16-26	15-25
<b>PoCT positive</b>			
all	24	28	52
no past infection	19	20	39
<b>Prevalence among those tested</b>			
	8.5%	7.4%	7.9%

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## Results of community-wide screening (PoCT part only)

- ❑ All PoCT positive individuals were treated on site and blood taken for serology according to protocol; contact tracing initiated immediately.
- ❑ All PoCT positive results (n=52) were confirmed to be positive by treponemal test.
- ❑ 13 (25.0%) were found to be not active infection (positive due to past treated infection)
- ❑ 39 (75.0%) were confirmed active infection and notified.
- ❑ The overall prevalence: 7.9% (95%CI: 5.7-10.6%)
- ❑ Of 442 negative by PoCT, 5 (1.1%) were false negative (having history of past infection)

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## Discussion

- ❑ Great acceptability and compliance (no one refused the test)
- ❑ Screening protocol ensured the screening ran smoothly.
- ❑ Many residents not found in relevant communities for testing (low coverage, ~60% among residents)
- ❑ High number of visitors tested (transient population) May need synchronised whole-of-region screening to achieve high overall coverage. Currently will need repeat community testing.

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## Discussion-cont'd

- ❑ Need to emphasise repeat testing in 3 months required (as less than ideal sensitivity of PoCT; early cases may be missed)
- ❑ Re-screens yielded poorer coverage, despite same method (the PoCT was still very accepted)
- ❑ Conducting screening outside clinic deemed culturally inappropriate in some communities – further communication and engagement needed
- ❑ Problem: no PoCT available for purchase from 1 Jul 2015 as needing TGA approval for sale in Australia.

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## Conclusion

- ❑ PoCT for syphilis is useful for case detection in an outbreak setting in remote Indigenous communities in Australia, with
  - ❑ prior community engagement,
  - ❑ updated population lists with sero-status,
  - ❑ clear screening protocols, and
  - ❑ staff training.
- ❑ However, given the less than ideal sensitivity, community-wide screening with PoCT
  - ❑ can only be used as an additional/supplementary outbreak response measure, and
  - ❑ retesting in 3 months is important.

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## Acknowledgements

- The NT Syphilis Outbreak Response Team
- All staff participating in the community-wide screens for their hard work