Point-of-care and near patient testing for STIs in remote Australia

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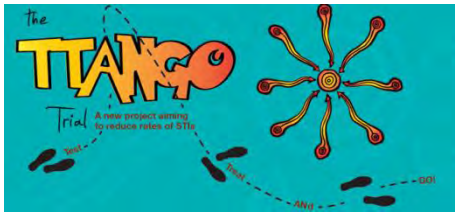
Viruses in May Conference

17 May, 2018

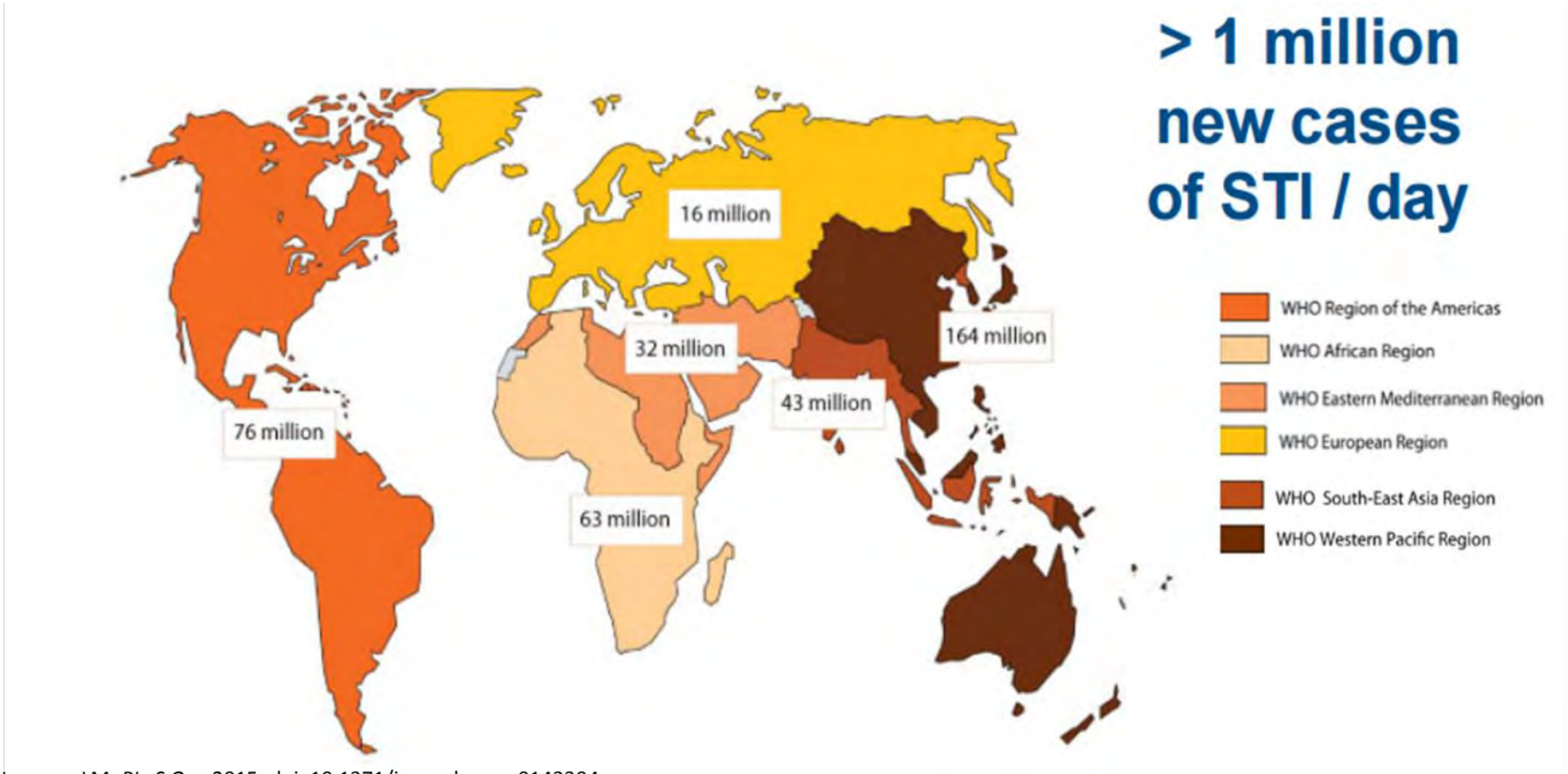


Outline

- Burden of STIs globally and in Australia
- POC testing for STIs in Australia
- STI POC test research in Australia
- Future directions

Global STI burden

- 357 million new cases of curable STIs in 2012
- Syphilis, chlamydia (CT), gonorrhoea (NG), trichomoniasis (TV)

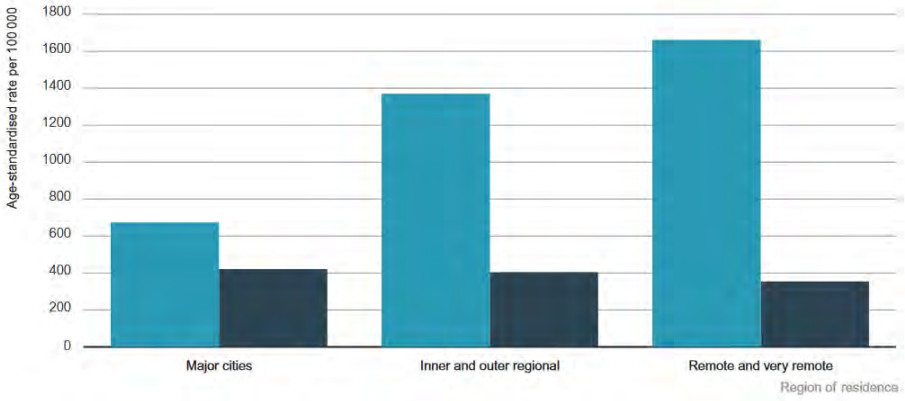


Newman LM. *PLoS One* 2015. doi: 10.1371/journal.pone.0143304

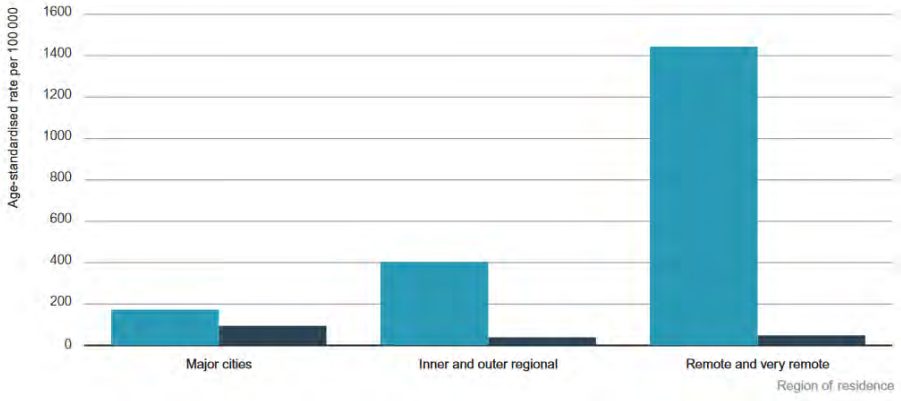
STIs in Australia

STI notifications per 100,000 population*

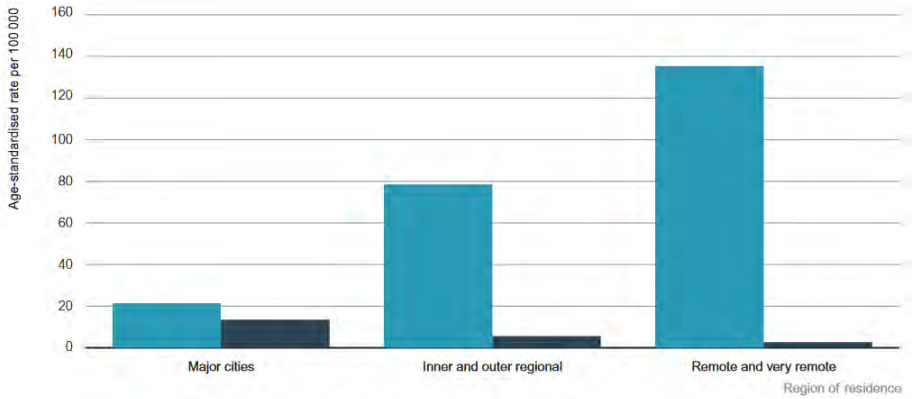
Chlamydia

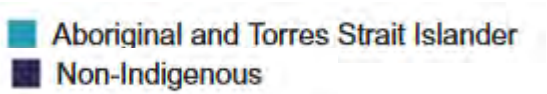


Gonorrhoea



Infectious syphilis





**Aboriginal Surveillance Report on HUIV, viral hepatitis and STIs 2017 (Kirby Institute, UNSW Sydney)*

https://kirby.unsw.edu.au/sites/default/files/kirby/report/KirbyInst_Indigenous_ASR2017-compressed.pdf

STIs in remote Australia

- Accurate laboratory-based diagnostic tests and effective treatments are available
- Prevalences of STIs are high
  - 33% women & 21% men have CT, NG or TV (Guy 2015)
  - Rates of co-infection are also high
  - Highest prevalences in the world for a young general population
- Sequelae of STIs
  - High rates of PID
  - Disseminated NG cases
  - Congenital syphilis cases

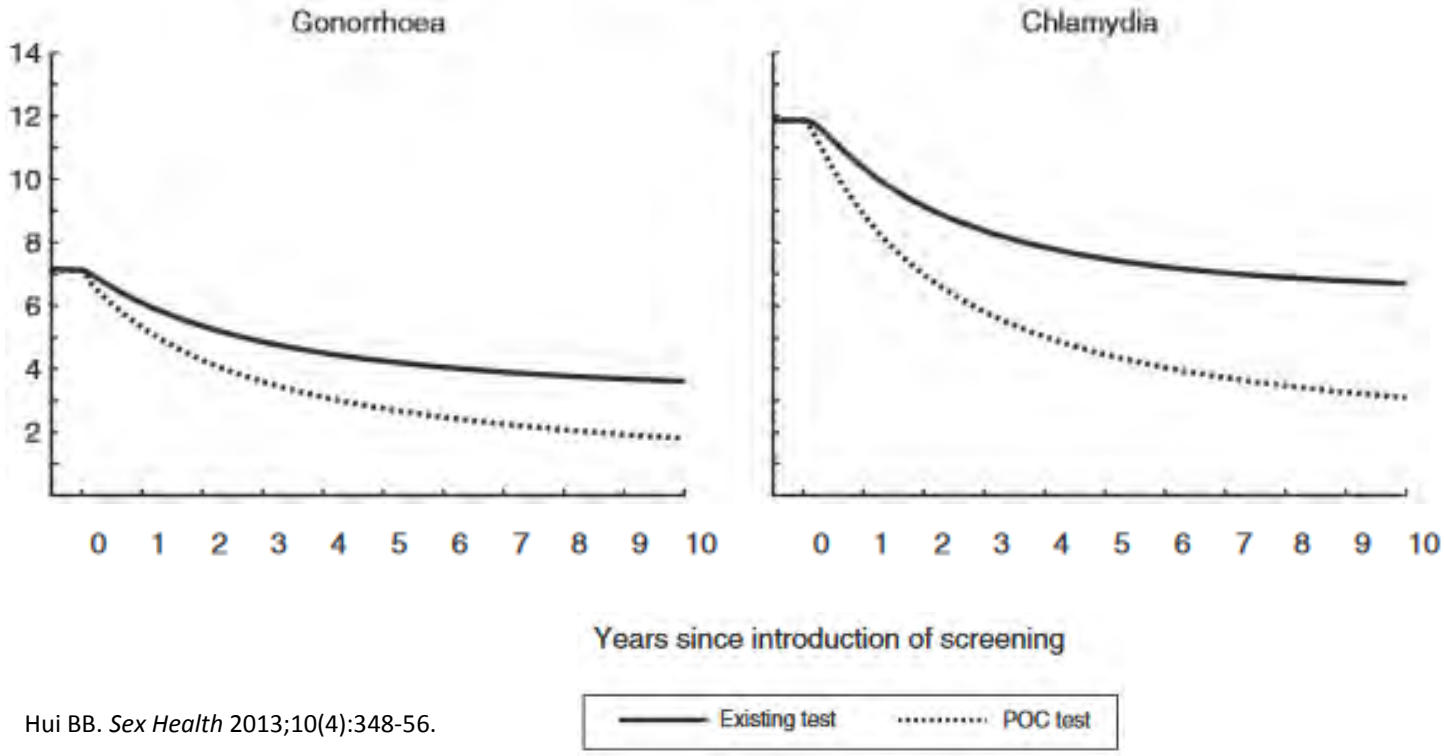
Guy R. *Sex Transm Infect* 2015;91:201–206. Guy R. *Sex Health* 2012;9(3):205-12. Kildea S. *Aust N Z J Public Health* 2000; 24:382-6. Tuttle CS. *Sex Transm Infect* 2015;91(7):497-501.

Diagnosis and management of STIs in remote Australia

- Management of STIs in remote communities mainly through primary health
- Patients with symptoms treated presumptively ('syndromic management')
- Asymptomatic patients have specimen sent to laboratory
  - Around 20% untreated
  - Average time to treatment 21 days (Guy 2012)
- Barriers to timely treatment include service and people factors (Hengel 2015)
  - Distance of services from laboratories
  - Under-utilisation of recall systems
  - Patient mobility
  - Poor community knowledge

STI prevalence and POC testing

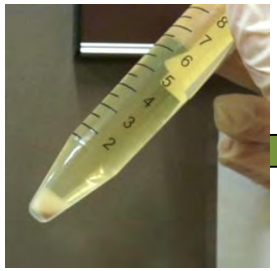
- Point-of-care tests for STIs may improve treatment uptake and timeliness
- Mathematical modelling suggests accurate point-of-care tests used at high coverage can reduce prevalence beyond that acheiveable by increasing testing coverage alone

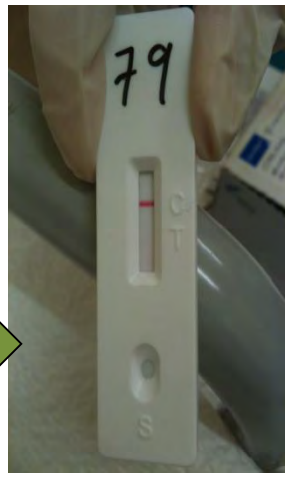


Hui BB. *Sex Health* 2013;10(4):348-56.

Traditional POC tests for CT and NG

- Traditional lateral flow tests
  - Antigen detection
  - Rapid (<20 minutes), low cost
  - Multiple steps



- Sub-optimal performance
- Not widely used

New molecular-based STI POC tests

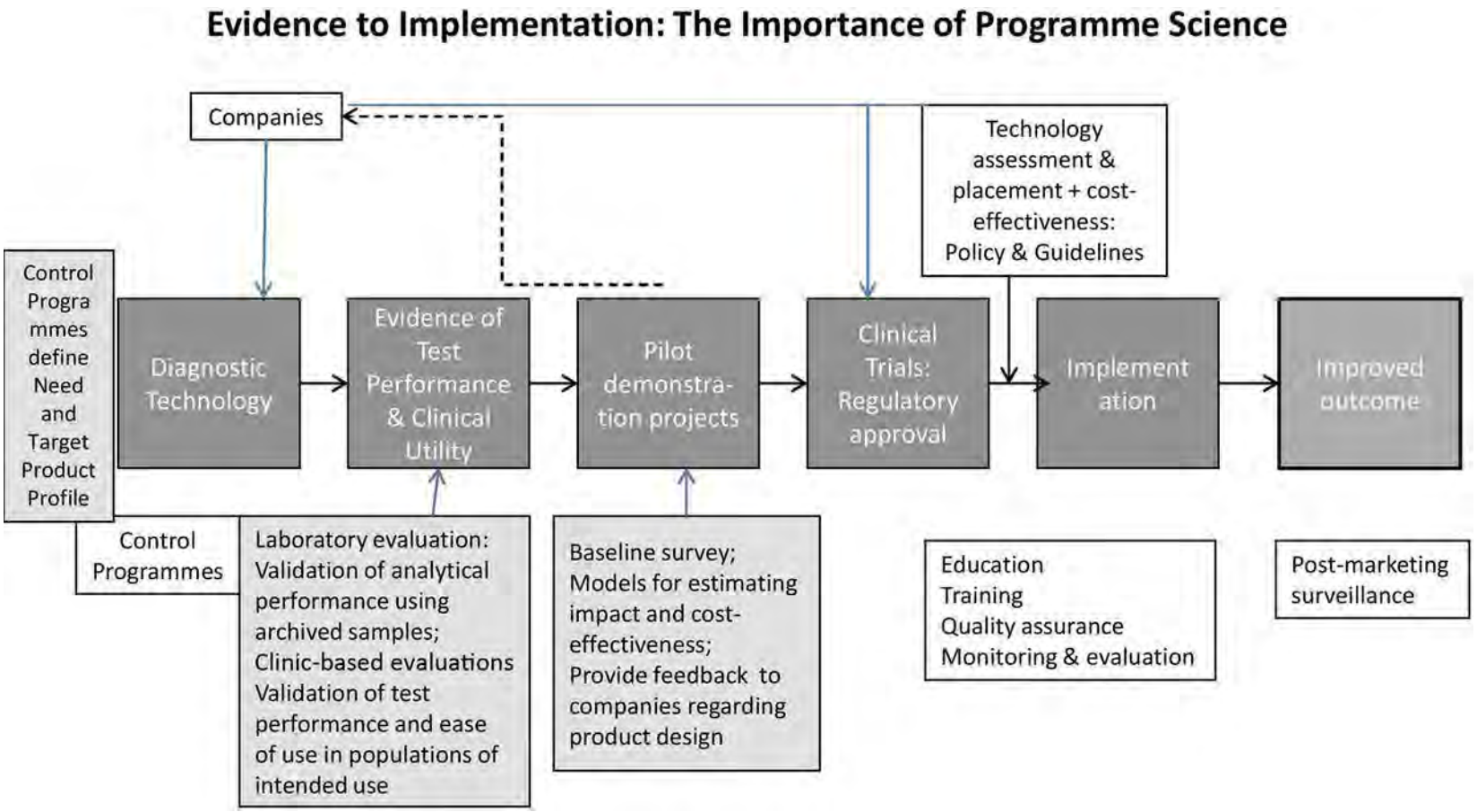
- GeneXpert (Cepheid)
- Portable, self contained molecular-based test
- Internal controls and calibration
- Dual CT and NG detection
- Two targets for NG (screen and confirm)
- Highly accurate
- Connectivity enabled
- Permanent electronic record of result
- Potentially suited to POC use

- Requires electricity
- Basic computer literacy
- 90 minutes to result
- More expensive

STI POC testing in Australia

- Might these new tests be suitable for use in Australia?
- Are these new tests feasible to use in remote primary health care settings in Australia?
- Are these tests accurate when performed by non-technical staff (AHW, nurses) working in a busy clinic setting?
- Will these new POC tests improve clinical outcomes at an individual and population level (and at what scale)?
- What are the elements, barriers and facilitators to scale-up of a POC testing strategy in order to maximise the clinical benefits?
- What are the costs associate with this testing strategy? Is it cost effective?
- What is needed to ensure an STI POC testing program is sustainable and at what cost?

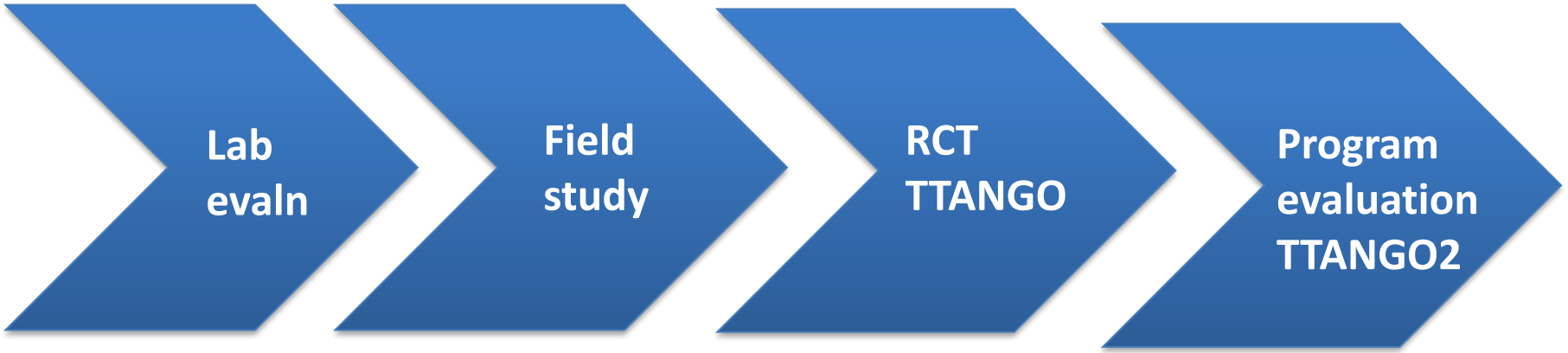
Translation of evidence of acceptable diagnostic performance to policy and implementation: importance of programme science.



Rosanna W Peeling et al. Sex Transm Infect 2013;89:115-119

STI

TTANGO STI POC Evaluation Pathway



To assess test performance using characterised samples

To compare and confirm test performances using fresh samples & assess feasibility

To assess operational performance as well as individual and health service benefits, challenges, acceptability, cost

To assess program-level implementation, challenges, acceptability, impact on STI prevalence

Laboratory evaluation

Journal of Clinical Microbiology

Analytical Evaluation of GeneXpert CT/NG, the First Genetic Point-of-Care Assay for Simultaneous Detection of Neisseria gonorrhoeae and Chlamydia trachomatis

Sepehr N. Tabrizi, Magnus Unemo, Daniel Golparian, Jimmy Twin, Athena E. Limnios, Monica Lahra and Rebecca Guy
J. Clin. Microbiol. 2013, 51(6):1945. DOI: 10.1128/JCM.00806-13.
Published Ahead of Print 3 April 2013.

- 372 characterised strains
- 100% sensitivity and specificity for NG
- 100% sensitivity for CT (specificity not assessed)

Pilot Evaluation

- Evaluate
  - Feasibility and logistics
  - Performance
  - Training materials and data collection processes
- 2 remote health services
- Routinely collected specimens (urine)
- Evaluated 3 STI POC tests
  - 2 lateral flow tests (Gonorrhea Card Test, Diaquick CT)

  - 1 molecular based (GeneXpert)

- POC tests performed by trained but non-lab technician
- Parallel laboratory-based reference testing for CT and NG

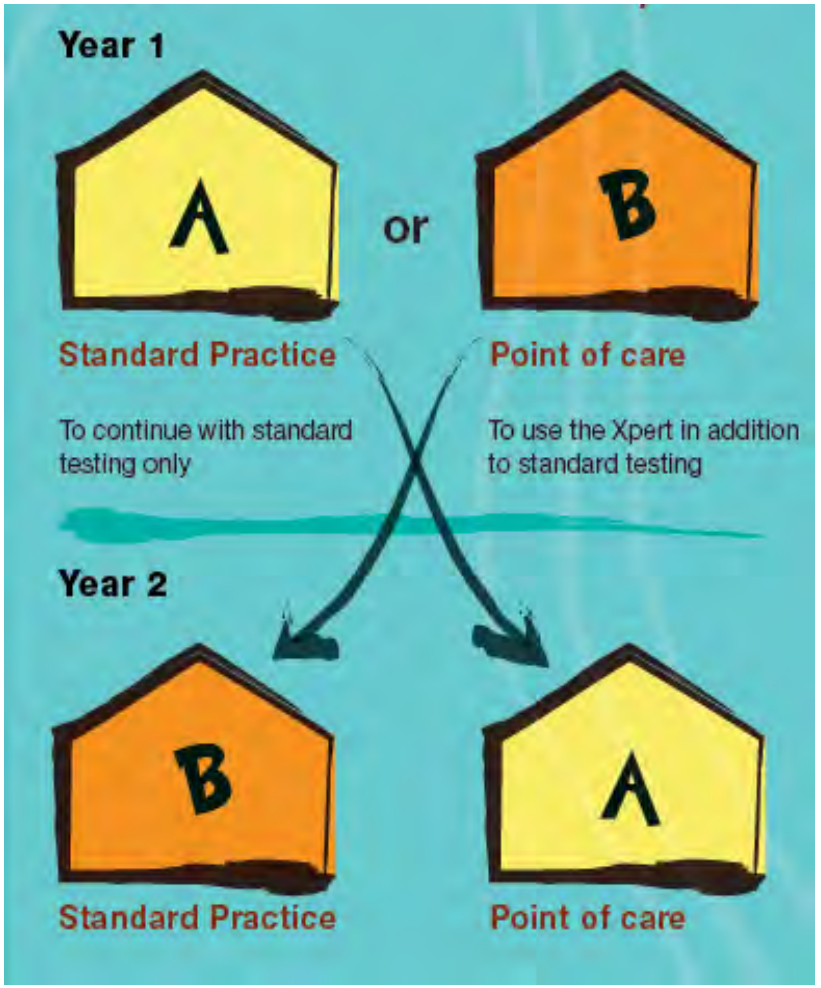
Pilot Evaluation Findings

- Lateral flow tests performed relatively poorly
- Xpert CT/NG test
  - Performance was similar to reference laboratory tests
  - Simple to perform
  - Minimal specimen volume and preparation time
  - Suitable for larger RCT

Causer LM, Hengel B, Natoli L, Tangey A, Badman SG, Tabrizi SN, et al. A field evaluation of a new molecular-based point-of-care test for chlamydia and gonorrhoea in remote Aboriginal health services in Australia. Sex Health 2014.

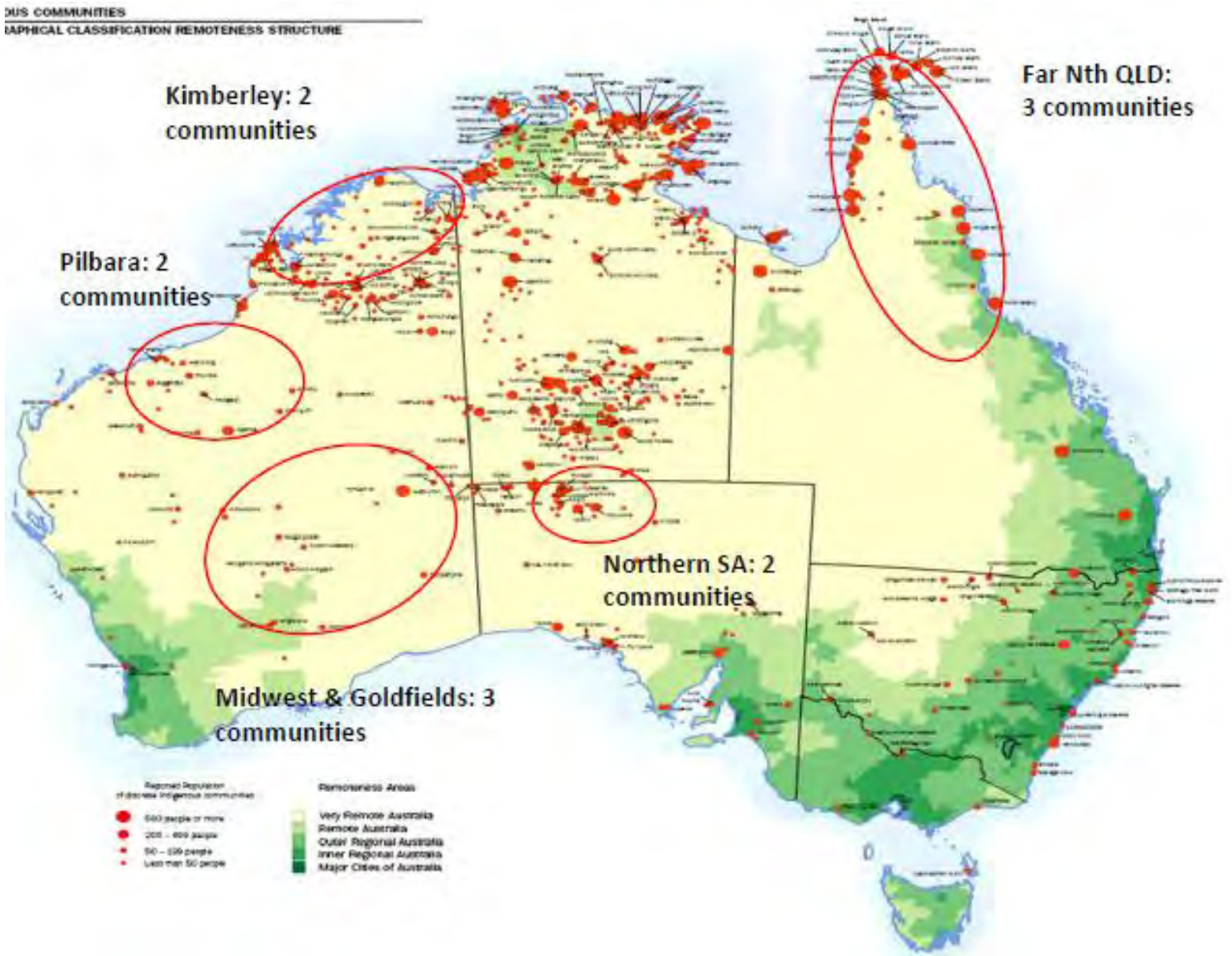
TTANGO: Test, Treat ANd Go

- **Cluster cross-over RCT**
- **Outcomes**
  - Re-infection
  - Treatment uptake and timeliness
  - Acceptability
  - Cost-effectiveness
  - Operational performance



Tabrizi SN. *J Clin Microbiol* 2013;51(6):1945-7.
Causer LM, Sex Health 2015; 12(1):27-33.

TTANGO sites



TTANGO intervention

- Self-collected vaginal swabs or urines
- Test sample at beginning of the consultation when doing health checks
- Ask patient to wait locally for result
- Offer treatment if positive
- Lab testing in parallel

Bega Garnbirringu Health Service worker Henry Dalgetty tests a sample with the new STI machine. Picture: Paul Braven

Remote Aboriginal communities get sexual health boost

GeneXpert CT/NG test

Urine specimen

Swab specimen

Single use test cartridge

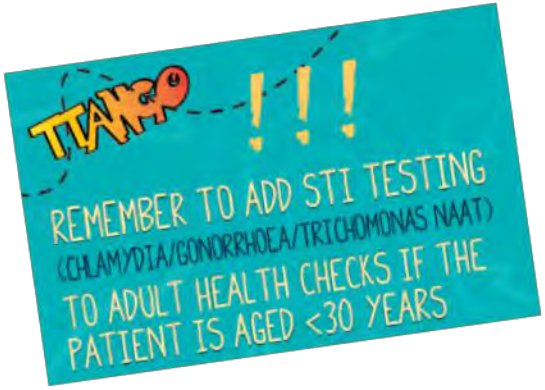
Laptop

GeneXpert machine

Xpert cartridge

TTANGO training and resources

- Formal training package
  - Flexible
  - Competency assessment
  - Training manual, wall charts, SOPs, posters
- Remote login learning and system support



TTANGO Quality Framework

- Standard Operating Procedures
- Internal Quality Control
  - Dried, heat inactivated
  - provided by UQCCR lab
  - tested monthly
- External Quality Assurance
  - Swab, provided by NRL
  - tested twice yearly

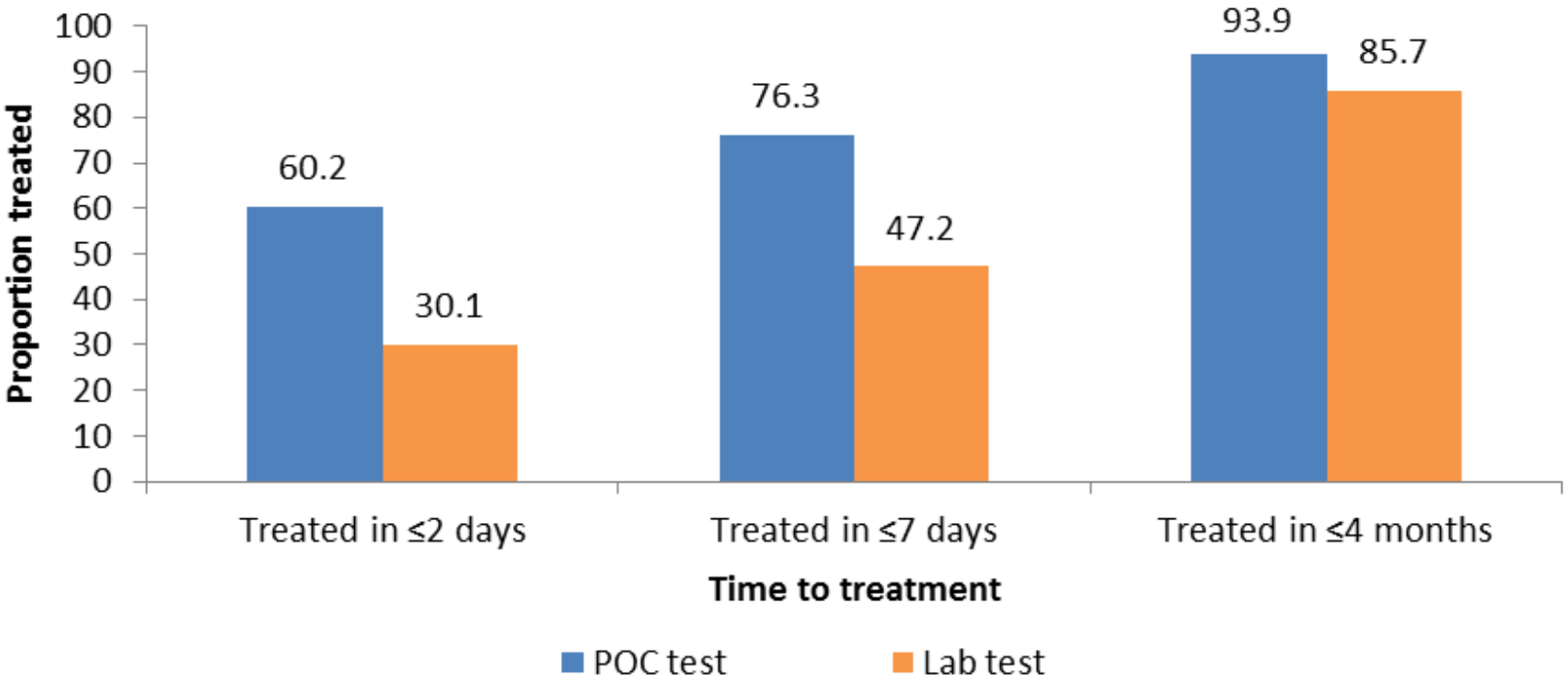
Internal Quality Control

External Quality Assessment

TTANGO Quality Framework

- GeneXpert In-Built Quality Checks
  - Sample Adequacy Control (SAC): ensures sample contains human cells
  - Sample Processing Control (SPC): ensures sample correctly processed
  - Probe Check Control: checks the probe integrity and dye stability
- All three controls must pass for the GeneXpert to give a valid result

Treatment uptake and interval



Treatment intervals among target population (16-29 year olds), by study arm

*Lab test = standard nucleic acid amplification test for CT and NG conducted in reference lab

Duration infection free

- Median time to treatment
  - POC =0 days
  - Lab =7 days

- 1000 positive tests

- 7 days x 1000=7,000 days, **19 years**

Xpert operational performance

- 2486 tests
- GeneXpert compared with laboratory NAATs*

  Positive and negative concordance of the GeneXpert
  - 98.4% and 99.5% for CT
  - 100% and 99.9% for NG

CT	NAAT+	NAAT-	Total
Gx +	209	11	220
Gx -	3	2263	2266
Total	212	2274	2486

NG	NAAT+	NAAT-	Total
Gx +	145	2	147
Gx -	0	2339	2339
Total	145	2341	2468

*(Aptima, Cobas, in-house)

Causer LM, Guy RJ, Tabrizi SN, et al. Molecular test for chlamydia and gonorrhoea used at point of care in remote primary healthcare settings: a diagnostic test evaluation. *Sex Transm Infect* 2018.

Acceptability

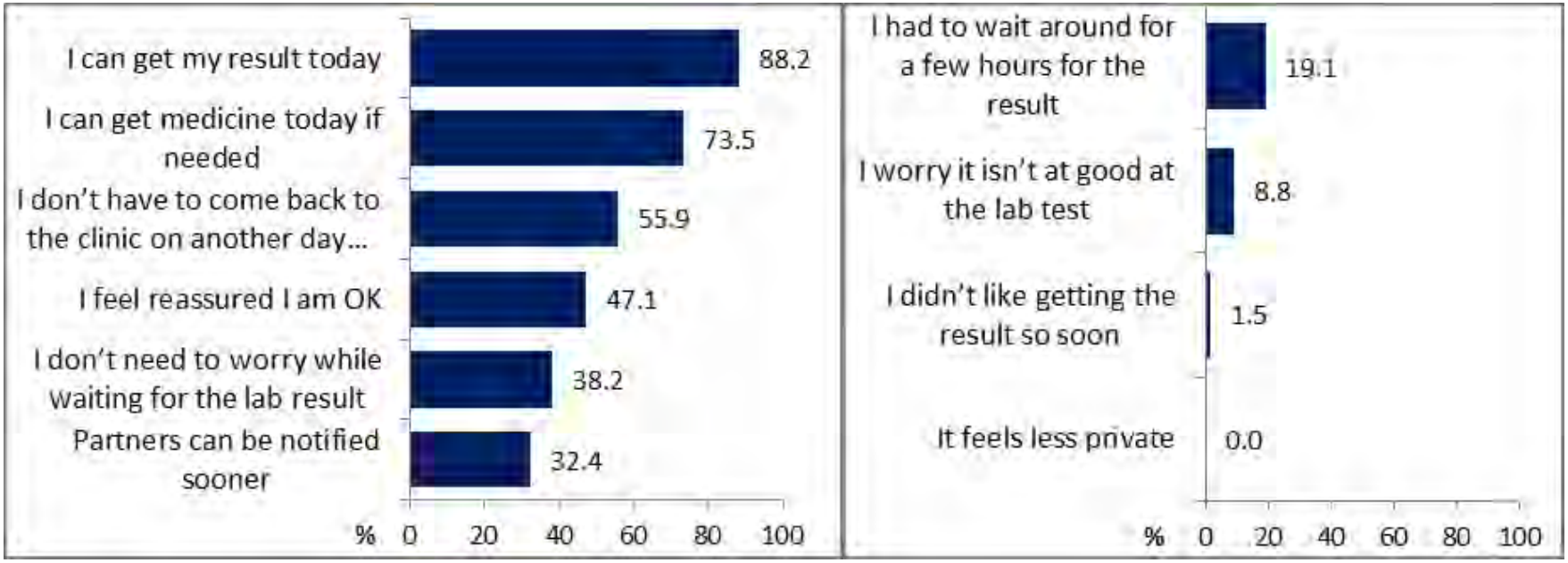
- In-depth interviews conducted with 16 staff (registered or enrolled nurses and Aboriginal Health Workers/Practitioners)

Benefits	Challenges
• Useful	• Management support
• Easy to use and interpret	• Staff turnover
• Improved management	• Connectivity, public health surveillance
• Reduced follow-up efforts	• Adapting clinic practice – no more presumptive treatment?
• Confidence in results	• Cost/sustainability
• Greater job satisfaction	

Natoli L, Guy RJ, Shephard M, et al. "I Do Feel Like a Scientist at Times": A Qualitative Study of the Acceptability of Molecular Point-Of-Care Testing for Chlamydia and Gonorrhoea to Primary Care Professionals in a Remote High STI Burden Setting. PLoS One. 2015

Acceptability

- Brief acceptability surveys completed by patients (n=80) who experienced the POC testing process
- Overall, most patients liked the new POC test and didn't mind waiting for the result



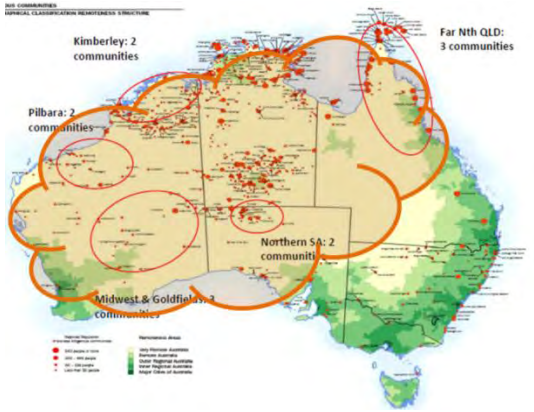
TTANGO Summary

- Molecular POC test incorporated into routine clinical setting
  - Highly accurate
  - Increased uptake of treatment
  - Reduced time to treatment
  - Highly acceptable to patients and staff

- Other findings
  - Flexible training essential
  - Coordinator support valuable
  - Quality assurance program feasible
  - Connectivity and integration with patient management systems highly desirable

TTANGO2

- TTANGO findings → additional funding (NHMRC, DOHA, WA Heath) and support
- Programmatic scale up of POC testing for STIs
- Planned implementation over 5 years
  - At 33 remote and regional services in 4 jurisdictions
  - Includes original 12 TTANGO health services
  - Regional and remote locations
  - With high rates of CT and NG
- Strategy components
  - Implementation
  - Continuous quality improvement (CQI)
  - Evaluation

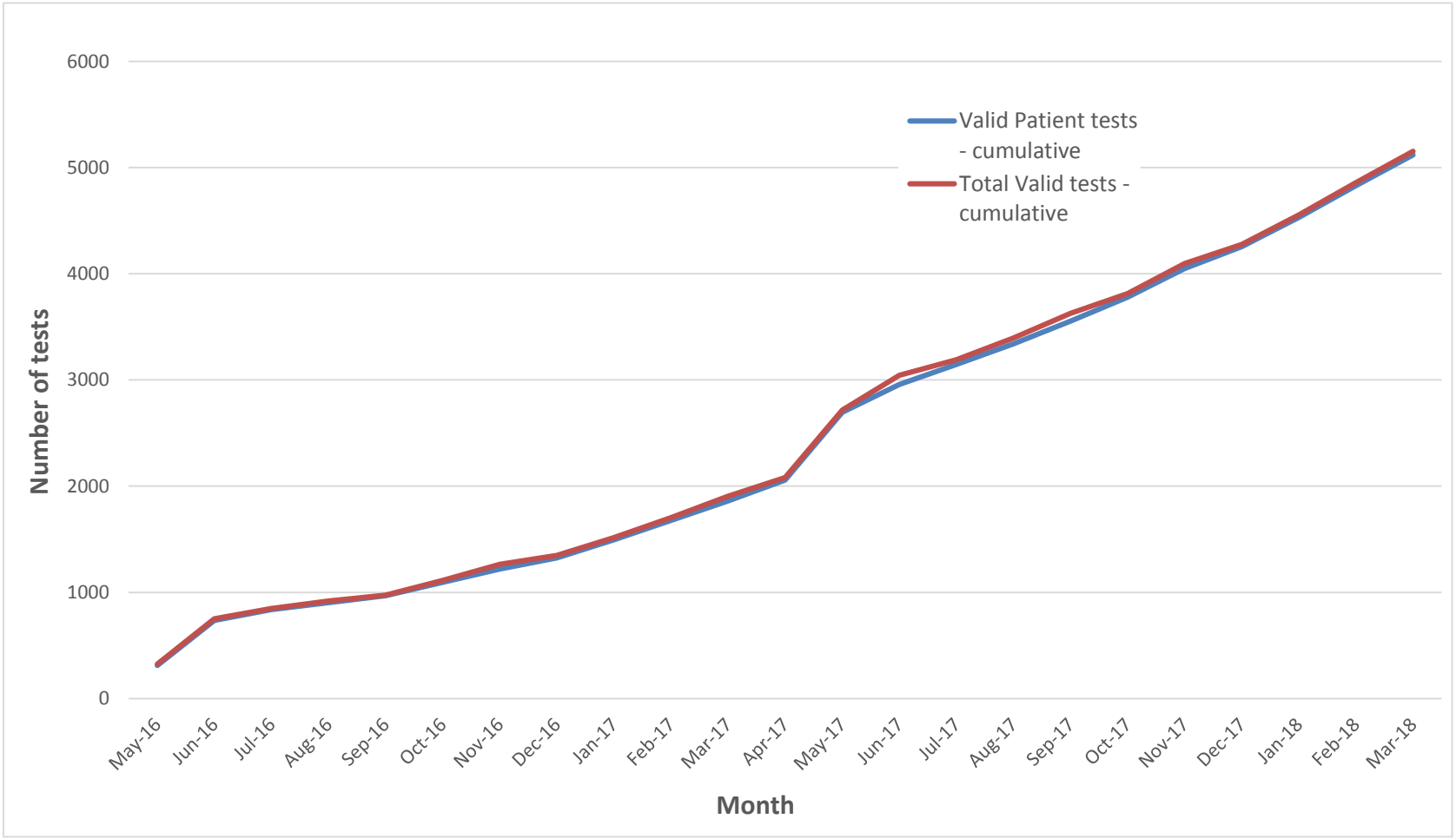


TTANGO2 implementation

- Standardised, flexible training program
  - face-to-face & remote/web-based
  - telephone and online support
- Quality assurance (QA) program
  - Internal and external QA programs
  - Regular monthly QA reports back to services
- CQI program:
  - 6 monthly reports to services to improve and increase testing uptake
  - routinely collected data from patient management systems to report on sexual health KPIs

STI POC testing scale up – TTANGO2

- >200 staff trained
- 26 services successfully implementing POC testing (CT/NG)
- TV POC testing is being rolled out



Program implementation challenges

- IT connectivity, support and integration into patient management systems
  - Electronic pathology requests are not routine
  - Risk of data entry and errors (@ test and result record)
  - ONDAS middleware adapted (request and result)
  - De-identified copy available for evaluation
- Staff turnover
  - Flexible training and re-training options
  - Face-2-Face, web based, hotline, other resources
- Case notifications
  - Currently reported from labs to public health units
  - Process must be developed to ensure maintenance of notifications
- NG antimicrobial resistance surveillance

Evaluation

- To determine whether POC testing in addition to increased testing is a effective and sustainable strategy for STI control in remote communities
- Routinely collected data at health service extracted from patient management systems
- Key performance indicators developed
  - Testing coverage and testing rate
  - Positivity
  - Completeness of testing
  - Time to treatment
  - Retesting and repeat positivity
  - POC test uptake

TTANGO 2 - Still to come

- Cost study and cost effectiveness anaylsis
- Application to Medicare for a rebate
- Determine robust case notification processess
- Determine process to support and enhance AMR surveillance for NG
- Final program evaluation

Syphilis and POC testing

- Syphilis POC testing is promoted globally as a cost effective way to improve testing coverage and treatment, especially among pregnant women
- POC testing among pregnant women attending ANCs is a cornerstone of the global strategy to eliminate congenital syphilis
- Now combined with the goal of elimination of MTCT of HIV
- Primary focus is LMIC where burden is highest

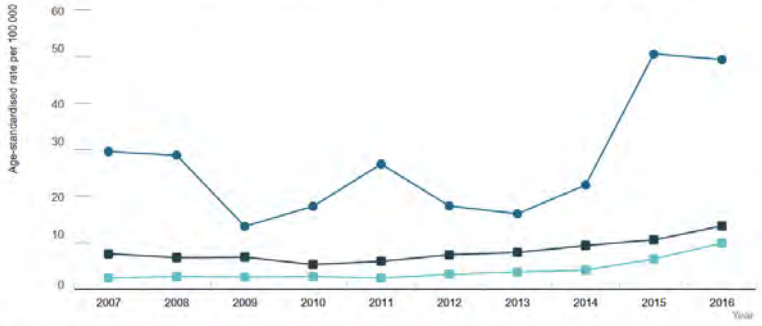
Rapid Syphilis POC tests

- Syphilis POC tests
  - detect treponemal (TP) antibody
  - Blood sample or serum
  - Easy to use, rapid (15 -20 mins)
  - Relatively inexpensive
  - High accuracy
  - Limitation: unable to distinguish current from past infection

- Newer platforms
  - detect Tp and non-TP antibody
  - dual test detect TP and HIV

Syphilis

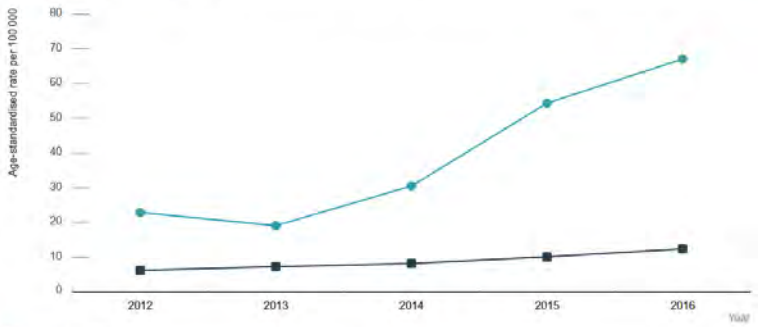
Figure 3.3.6 Infectious syphilis notifications per 100 000 population, 2007–2016, by region of residence



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Major cities	7.6	6.8	6.9	5.3	6.0	7.4	7.9	9.4	10.6	13.6
Inner and outer regional	2.4	2.7	2.6	2.7	2.4	3.2	3.7	4.1	6.5	9.9
Remote and very remote	29.6	28.8	13.5	17.8	26.9	17.9	16.2	22.4	50.6	49.4

Source: Australian National Notifiable Diseases Surveillance System.

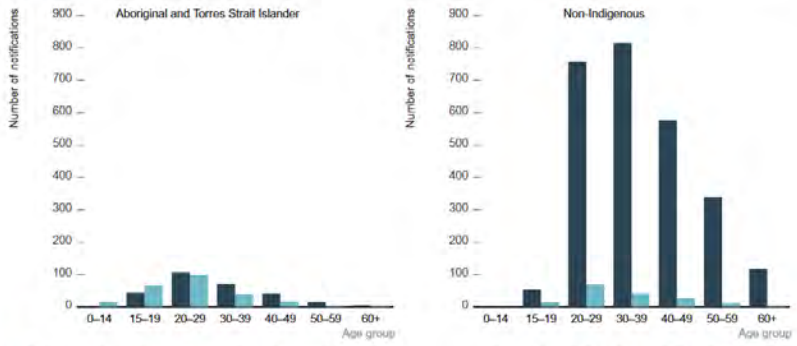
Figure 3.3.8 Infectious syphilis notification rate per 100 000, 2012–2016, Aboriginal and Torres Strait Islander status



	2012	2013	2014	2015	2016
Non-Indigenous	6.2	7.3	8.2	10.1	12.4
Aboriginal and Torres Strait Islander	22.9	19.1	30.5	54.4	67.1

Source: Australian National Notifiable Diseases Surveillance System. Includes all jurisdictions, as Aboriginal and Torres Strait Islander status was reported for ≥50% of diagnoses for each year.

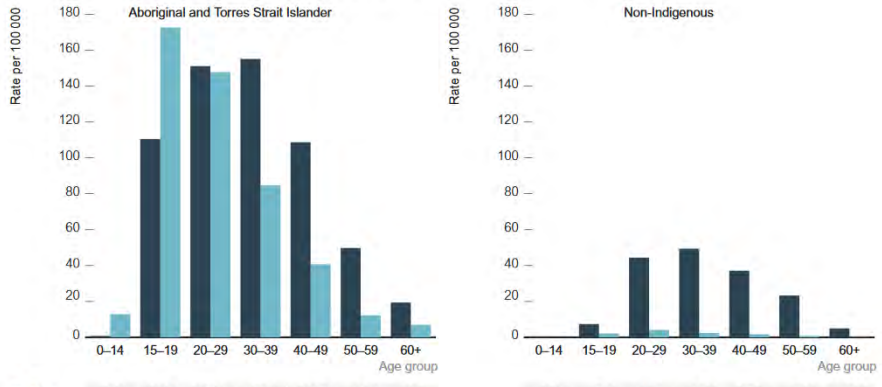
Figure 3.3.3 Number of infectious syphilis notifications, 2016, by Aboriginal and Torres Strait Islander status, sex and age group



	0–14	15–19	20–29	30–39	40–49	50–59	60+
Aboriginal and Torres Strait Islander – Men	1	44	107	72	42	15	5
Aboriginal and Torres Strait Islander – Women	16	66	99	40	17	4	2
Non-Indigenous – Men	0	53	757	815	577	340	117
Non-Indigenous – Women	0	14	70	42	27	12	3

Source: Australian National Notifiable Disease Surveillance System; includes all jurisdictions as Aboriginal and Torres Strait Islander status was ≥50% in 2016.

Figure 3.3.4 Infectious syphilis notification rate per 100 000 population, 2016, by Aboriginal and Torres Strait Islander status and age group

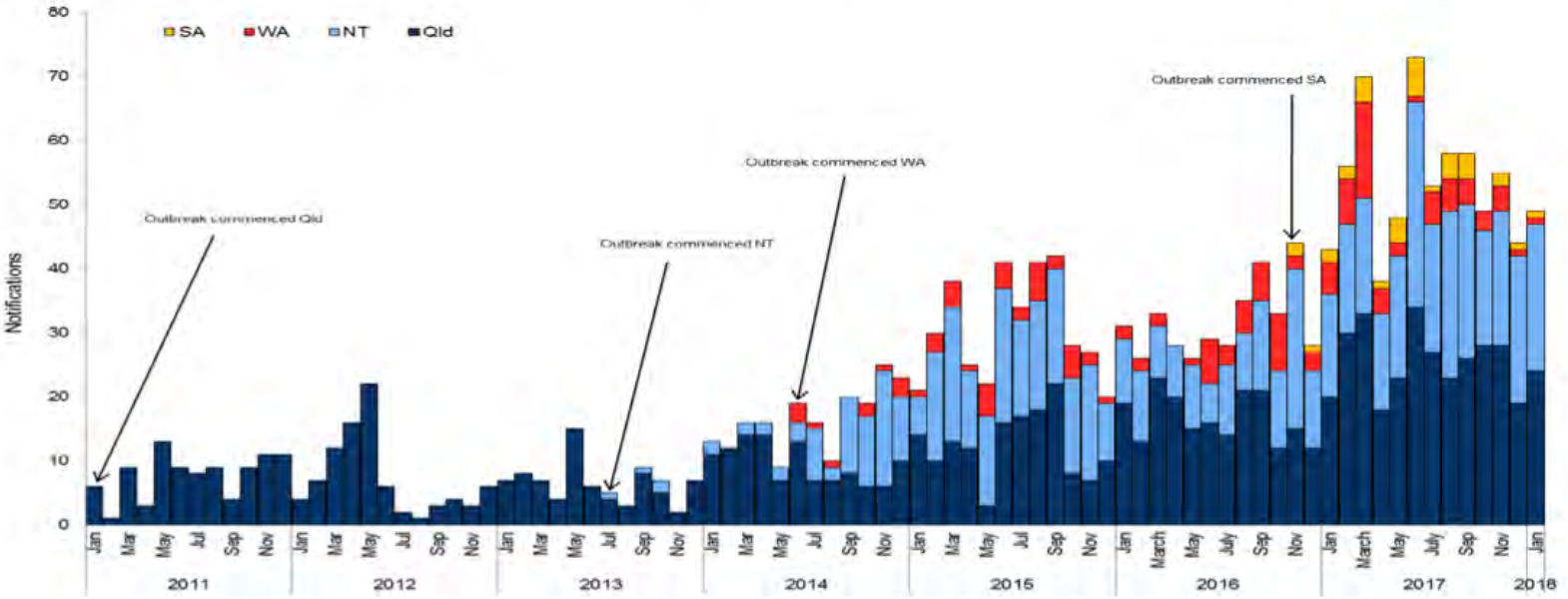


	0–14	15–19	20–29	30–39	40–49	50–59	60+
Aboriginal and Torres Strait Islander – Men	0.8	110.5	151.1	155.1	108.7	49.8	19.4
Aboriginal and Torres Strait Islander – Women	12.9	172.6	147.7	84.7	40.8	12.3	7.0
Non-Indigenous – Men	0.0	7.4	44.4	49.4	37.1	23.3	5.0
Non-Indigenous – Women	0.0	2.1	4.2	2.5	1.7	0.8	0.1

Source: Australian National Notifiable Disease Surveillance System; includes all jurisdictions as Aboriginal and Torres Strait Islander status was ≥50% in 2016.

Syphilis epidemic in Northern Australia

Figure 1. Epidemic curve showing outbreak cases of infectious syphilis[α] notified in affected regions[β] of Queensland, the Northern Territory, Western Australia and South Australia from commencement of the outbreak in each jurisdiction to 31 January 2018[γ].



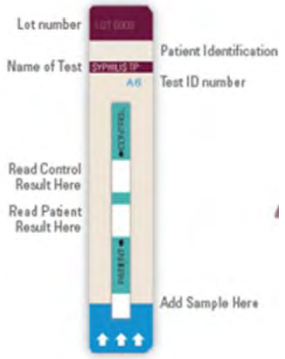
	North Qld (four HHSs[β])	NT (four regions[β])	WA (Kimberley region)	SA (three regions[β])
Situation to-date, 31 January 2018				
Outbreak commencement month/year	January 2011	July 2013	June 2014	November 2016
Total number of cases[α]	**1066**	**704**	**148**	**34**
Percent cases reported in 15-29 year age group	67%	66%	70%	47%
% Male / % Female	48% / 52%	47% / 53%	37% / 63%	44% /56%
Congenital cases, confirmed (probable)	4 (4)	2 (2)	0 (0)	1 (0)
-number of deaths in congenital cases	6	0	0	0

http://www.health.gov.au/internet/main/publishing.nsf/Content/71E8A32E7518E532CA25801A0009A217/$File/Feb-2018-communique.pdf

Syphilis POC test use in outbreak response

- SD Bioline chosen initially
  - Robust platform for field use
  - TGA approved at the time
  - Good sensitivity/specificity (88%/99%)
  - Finger prick blood (50 uL)

- Determine TP currently being used
  - Only TGA approved rapid test
  - Least expensive
  - Better sensitivity (98%)
  - Finger prick blood (20 uL)



- Syphilis register checked for any positive POC test prior to treatment

Syphilis POC test use in outbreak response

- 2 NT communities (2014)
- 326 of 545 population (12 -30 yo) tested
- Found a prevalence of 9% (M~=F)
- Key conditions for success
  - Prior community engagement
  - updated population lists
  - screening protocols (including register check for past history of syphilis)
  - staff training
- POCT for syphilis can be an effective for case detection in an outbreak setting in remote Indigenous communities in Australia
- 3 month follow up important

J-Y Su, L Garton et al. STI journal STI & HIV World Congress 2015, September 2015 - Volume 91 - Suppl 2

Syphilis National Guidelines

- Point of care rapid syphilis testing has been used with good effect in recent outbreaks in remote Australia, both in the context of community-wide testing and to increase opportunistic testing within primary care services. In the latter setting, the rapid test process must be embedded in work practices within the health service, to be effective

http://www.health.gov.au/internet/main/publishing.nsf/Content/B2ECD660086F7FCBCA257C94001BFB4B/$File/syphilis-SoNG-Aug2015.pdf

Enhanced syphilis response

- New funding available to support enhanced response
- Will include
  - Syphilis POC testing and treatment
  - Contact tracing/partner notification
  - Comprehensive training
  - Health promotion activities
  - Dedicated teams

Acknowledgements

- The Kirby Institute
- The Burnet Institute
- Flinders University International Centre for Point-of-Care Testing
- South Australian Health and Medical Research Institute
- Royal Women's Hospital, Melbourne
- University of Queensland Centre for Clinical Research
- Monash University
- National Reference Laboratory (NRL)
- Cepheid
- The WA Department of Health
- WA Country Health Service (WACHS)
- Ngaanyatjarra Health Service (NHS)
- Kimberley Aboriginal Medical Services Council (KAMSC)
- The Aboriginal Health Council of Western Australia (AHCWA)
- Pathwest
- Western Diagnostics Pathology
- Clinipath
- Queensland Health
- Queensland Aboriginal and Islander Health Council (QAIHC)
- Queensland Pathology
- Apunipima Cape York Health Council
- SA Health
- Aboriginal Health Council of SA (AHCSA)
- Medical Communications Associates (MCA)
- Department of Health, Northern Territory Government
- Aboriginal Medical Services Alliance of the Northern Territory (AMSANT)

Further information

- http://www.kirby.unsw.edu.au/projects/ttango-test-treat-and-go

- http://www.flinders.edu.au/medicine/sites/point-of-care/research/field-programs/ttango2.cfm

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