

Operational performance of a new molecular-based point-of-care test for diagnosis of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection: concordance with conventional laboratory testing

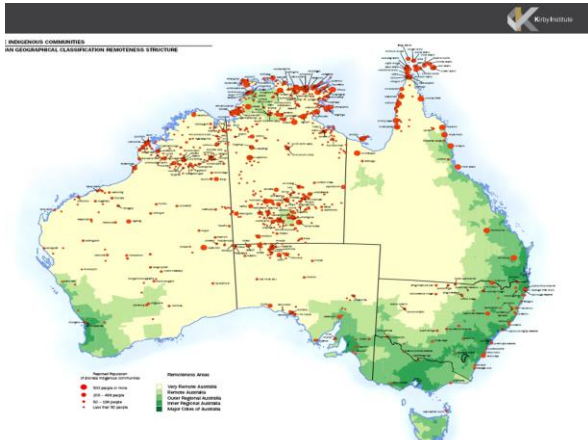
LM Causer, A Tangey, SG Badman, B Hengel, L Natoli, D Speers, SN Tabrizi, D Whiley, DA Anderson, J Ward, JM Kaldor, RJ Guy, on behalf of the TTANGO investigators

World STI & HIV 2015 Congress
Brisbane, Australia
13-16 September



Australian context

- Population ~ 23, 625, 600 (www.abs.gov.au)
- Indigenous Australians represent ~3% population
- ~ 25% of Indigenous Australian population live in areas classified as remote
- Communities spread across vast geographic area

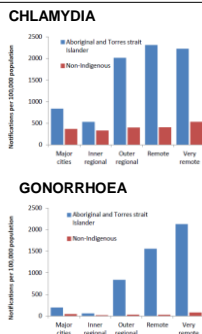


Health services in remote Australia

- Health care in remote Australia is provided through Government and Aboriginal controlled primary health services
- Minimal staff – nurse(s), Aboriginal health worker, doctor
- Pathology providers are located in major towns and cities
- Specimen transport depends on flights (e.g. weekly)

STIs in remote Australia

- High rates of chlamydia and gonorrhoea in remote Aboriginal communities
- Prevalence of any STI in 16-19 years old (Silver et al. *Sex Transm Infect*, 2014)
 - Males 33.4%
 - Females 48.9%



STI management

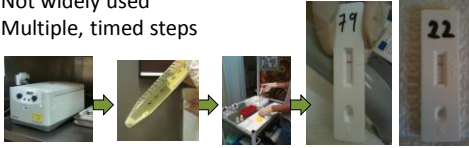
- Symptomatic infections treated presumptively
- Specimens sent to laboratories for testing
- Long delays to treatment
 - 3 weeks for asymptomatic patients (Guy et al. *Sexual Health*, 2012)
- Frequent loss to follow-up
 - up to 20% remain untreated (Guy et al. *Sexual Health*, 2012)
- Point-of-care (POC) tests may
 - Reduce time to treatment
 - Reduce onward transmission
 - Reduce complications of infection





Lateral flow POC tests for CT/NG

- Commercially available
- Rapid, low cost
- Not widely used
- Multiple, timed steps



- Performance extremely unreliable (*Dommelen et al. Sex Transm Infect 2010; Watchirs-Smith et al. Sex Transm Infect, 2013*)



New molecular-based POC tests

- GeneXpert CT/NG assay (Cepheid)
- Dual organism (CT +NG) detection
- Two targets for NG
- 90 minutes to result
- High analytical sensitivity/specificity (*Tabrizi et al. J Clin Micro, 2013*)
- Excellent performance in pilot field evaluation (*Causser et al, Sex Health 2014*)
- Suited to use at the point-of-care (*Peeling, STI, 2011*)



GeneXpert platform

- Already available and used for
 - Critical infectious diseases (MTB/RIF and Flu)
 - Other select health care associated infections (MRSA, *C. difficile*, Norovirus)
 - Primarily used in hospital laboratory or specialist clinical settings
- For STIs
 - CT/NG assay: approved by Australian Therapeutic Goods Administration in 2013



Aim

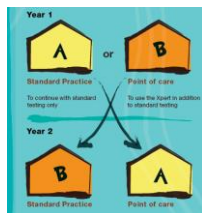
- To evaluate the operational performance of GeneXpert CT/NG assay when incorporated into routine use and performed by clinical staff at remote primary health services across Australia



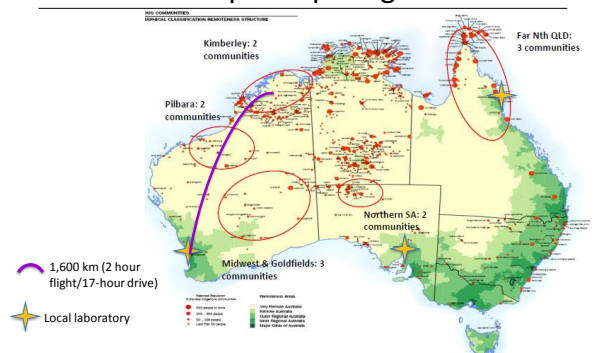
TTANGO



- TTANGO = Test, Treat And GO
- Cluster-randomised, cross-over control trial
- Comparing standard care for management of STI vs standard care PLUS POC testing for CT/NG
- First use of GeneXpert POC test incorporated into routine clinical setting



TTANGO – 12 participating sites



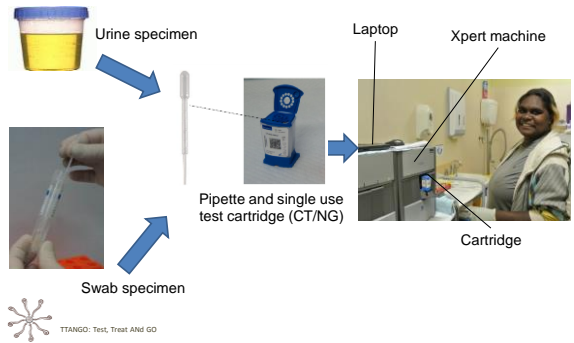


TTANGO implementation

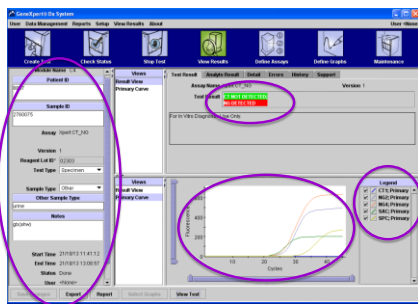
- Commencing mid-2013
- Study coordinators visited service to
 - set up GeneXpert
 - train designated clinical staff
 - assess competency in POC testing
- Quality assurance (QA) program established
 - External QA at commencement and 3 months
 - monthly quality control component
- Urine/swabs specimens collected as usual



GeneXpert® (Cepheid) CT/NG



GeneXpert results



- Patient ID
- Specimen ID
- Test information
- CT and NG result
- Cycle threshold
- Internal controls



STI testing

- POC test results guided STI management as per standard guidelines at each service
- Specimens sent to local laboratories for routine STI testing (NAAT)*
- *Concordance*: POC test result compared with local laboratory NAAT result
- *Discordant result*: POC result differed from laboratory NAAT result as reported by health service
 - additional testing at reference laboratory
 - cycle threshold analysis

*NAAT = nucleic acid amplification testing (by local laboratory)



Laboratory results (positivity)

NAAT*	N	CT positive n (%)	NG positive n (%)
APTIMA	724	20 (2.8)	38 (5.3)
COBAS	878	99 (11.3)	24 (2.7)
In-house	883	93 (10.5)	83 (9.4)
TOTAL	2486	212 (8.5)	145 (5.8)

*NAAT = Nucleic acid amplification test



POC test concordance for CT

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



POC test concordance for CT

- Positive concordance = 98.6% (94.9 – 99.6)

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



POC test concordance for CT

- Positive concordance = 98.6% (94.9 – 99.6)
- Negative concordance = 99.5% (99.0 – 99.8)

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



POC test concordance for CT

- Positive concordance = 98.6% (94.9 – 99.6)
- Negative concordance = 99.5% (99.0 – 99.8)
- Overall concordance = 99.4% (99.0 – 99.8)

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



POC test concordance for NG

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



POC test concordance for NG

- Positive concordance = 100% (96.3 – 100.0)

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



POC test concordance for NG

- Positive concordance = 100% (96.3 – 100.0)
- Negative concordance = 99.9% (99.6 – 100.0)

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



POC test concordance for NG

- Positive concordance = 100% (96.3 – 100.0)
- Negative concordance = 99.9% (99.6 – 100.0)
- Overall concordance = 99.9% (99.6 – 100.0)

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



Discordant results

- 16 discordant results (0.6%)
- 14 CT results
- 2 NG results
- 10 urines, 6 lower vaginal swabs
- 8 services & 5 laboratories (3 NAAT tests)

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



GeneXpert cycle threshold

CT positive	N	Median Crossing point	Inter Quartile Range	Gx Crossing point >35
Discordant	11	35.7	31.6 – 37.4	63.6%
Concordant	209	29.0	26.3 – 32.6	6.2%

- Higher threshold = lower organism load
- Specimens with discordant results had higher cycle threshold than concordant results
- Discordants may have lower organism load, closer to the limit of test detection



Further testing of discordants

- 10/16 discordants investigated further at reference lab*

NAAT test	Specimen type	Local lab NAAT result	GeneX result	GeneX cycle threshold	Reference lab Result
Cobas	Urine	CT neg	CT pos	34.2	CT neg
Cobas	Urine	CT neg	CT pos	37.2	CT pos
In-house	Swab	CT pos	CT neg	0	CT neg
In-house	Urine	CT neg	CT pos	37.2	CT pos
In-house	Urine	CT neg	CT pos	31.6	CT neg
Cobas	Urine	CT neg	CT pos	30.3	CT pos
Cobas	Urine	CT neg	CT pos	35.5	CT pos
Cobas	Urine	CT neg	CT pos	35.7	CT pos
In-house	Urine	CT neg	CT pos	42.4	CT neg
Aptima	LVS	NG neg	NG pos	35.3/33.9	NG neg

*Royal Womens Hospital (Melbourne): Samples in Cobas transport media/urine retested by Cobas 4800 (for both CT and NG) and by In-house Omp CT assay, In-house PorA and Opa NG assays. Swab or Aptima samples were extracted and run on the in-house Omp CT assay, In house PorA and Opa NG assays only.



Further testing of discordants

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Cobas	Urine	CT neg	CT pos	34.2	CT neg
Cobas	Urine	CT neg	CT pos	37.2	CT pos
In-house	Swab	CT pos	CT neg	0	CT neg
In-house	Urine	CT neg	CT pos	37.2	CT pos
In-house	Urine	CT neg	CT pos	31.6	CT neg
Cobas	Urine	CT neg	CT pos	30.3	CT pos
Cobas	Urine	CT neg	CT pos	35.5	CT pos
Cobas	Urine	CT neg	CT pos	35.7	CT pos
In-house	Urine	CT neg	CT pos	42.4	CT neg
Aptima	LVS	NG neg	NG pos	35.3/33.9	NG neg

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Challenges

- Different comparator tests were used (depending on jurisdictional laboratory)
- Specimens not tested by POC and NAAT at same time - specimen degradation may have occurred between testing modalities



Conclusions

- Excellent concordance of GeneXpert CT/NG POC test when performed by trained health service staff
- GeneXpert testing is very suitable for routine detection of CT and NG in these settings
- GeneXpert POC testing for STIs has potential to transform current practice and significantly improve management of STIs in remote Australia



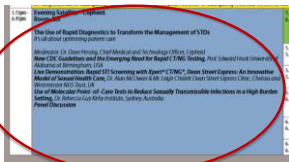
Acknowledgements

- TTANGO Investigators : Rebecca Guy, John Kaldor, Basil Donovan, David Wilson, Handan Wand, David Regan, Steven Badman, Louise Causer, James Ward, Belinda Hengel, Lisa Natoli, David Anderson, David Whaley, Sepehr Tabrizi, Mark Shephard and Christopher Fairley
- Participating health services & staff
 - Kirby Institute, UNSW
 - Baker IDI
 - Apunipima Cape York Health Council
 - Ngaanyatjarra Health Service
 - Burnet Institute
 - Royal Women's Hospital, Melbourne
 - QLD Paediatric Infectious Disease Laboratory
 - Flinders University
 - University of Melbourne
 - National Reference Laboratory
 - Medical Communication Associates
 - Cepheid
- Departments of Health WA, QLD, SA
- West Australian Country Health Service
- PathWest Laboratory Medicine
- Western Diagnostics Pathology
- Clinipath Pathology
- Queensland Health Pathology
- Sullivan Nicolaides Pathology
- SA Pathology
- Aboriginal Health Council of Western Australia
- Queensland Aboriginal and Islander Health Council
- Aboriginal Health Council of South Australia
- TTANGO Reference Group

TTANGO is Funded through the National Health and Medical Research Council



Monday 5.35pm, Room M3 Evening satellite: Use of Rapid Diagnostics to Transform Management of STDs



Tuesday, 2.40pm Room S12 Presentation: TTANGO

