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

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**Australian context**

- Population ~ 23,625,600
  - 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)

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**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%

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**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 (Causer 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

1,400 km (2 hour flight/17 hour drive)
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

- Urine specimen
- Swab specimen
- Pipette and single use test cartridge (CT/NG)
- Xpert machine
- Laptop

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)

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

*NAAT = Nucleic acid amplification test

POC test concordance for CT

<table>
<thead>
<tr>
<th>POC test</th>
<th>NAAT+</th>
<th>NAAT-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gx CT +</td>
<td>209</td>
<td>11</td>
<td>220</td>
</tr>
<tr>
<td>Gx CT -</td>
<td>3</td>
<td>2263</td>
<td>2266</td>
</tr>
<tr>
<td>Total</td>
<td>212</td>
<td>2274</td>
<td>2486</td>
</tr>
</tbody>
</table>
### POC test concordance for CT

- Positive concordance = 98.6% (94.9 – 99.6)

<table>
<thead>
<tr>
<th>POC test</th>
<th>NAAT+</th>
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<td>Total</td>
<td>212</td>
<td>2274</td>
<td>2486</td>
</tr>
</tbody>
</table>

- Negative concordance = 99.5% (99.0 – 99.8)

<table>
<thead>
<tr>
<th>POC test</th>
<th>NAAT+</th>
<th>NAAT-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gx CT +</td>
<td>209</td>
<td>11</td>
<td>220</td>
</tr>
<tr>
<td>Gx CT -</td>
<td>3</td>
<td>2263</td>
<td>2266</td>
</tr>
<tr>
<td>Total</td>
<td>212</td>
<td>2274</td>
<td>2486</td>
</tr>
</tbody>
</table>

- Overall concordance = 99.4% (99.0 – 99.8)

### POC test concordance for NG

- Positive concordance = 100% (96.3 – 100.0)

<table>
<thead>
<tr>
<th>POC test</th>
<th>NAAT+</th>
<th>NAAT-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gx NG +</td>
<td>145</td>
<td>2</td>
<td>147</td>
</tr>
<tr>
<td>Gx NG -</td>
<td>0</td>
<td>2339</td>
<td>2339</td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>2341</td>
<td>2468</td>
</tr>
</tbody>
</table>

- Negative concordance = 99.9% (99.6 – 100.0)
**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)

<table>
<thead>
<tr>
<th>POC test</th>
<th>NAAT+</th>
<th>NAAT-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gx NG +</td>
<td>145</td>
<td>2</td>
<td>147</td>
</tr>
<tr>
<td>Gx NG -</td>
<td>0</td>
<td>2339</td>
<td>2339</td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>2341</td>
<td>2468</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>NAAT+</th>
<th>NAAT-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gx +</td>
<td>209</td>
<td>11</td>
<td>220</td>
</tr>
<tr>
<td>Gx -</td>
<td>3</td>
<td>2266</td>
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</tr>
<tr>
<td>Total</td>
<td>212</td>
<td>2274</td>
<td>2486</td>
</tr>
</tbody>
</table>

**GeneXpert cycle threshold**

<table>
<thead>
<tr>
<th>CT positive</th>
<th>N</th>
<th>Median Crossing point</th>
<th>Inter Quartile Range</th>
<th>Gx Crossing point &gt;35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discordant</td>
<td>11</td>
<td>35.7</td>
<td>31.6 – 37.4</td>
<td>63.6%</td>
</tr>
<tr>
<td>Concordant</td>
<td>209</td>
<td>29.0</td>
<td>26.3 – 32.6</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

- 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*

<table>
<thead>
<tr>
<th>NAAT test</th>
<th>specimen type</th>
<th>Local lab NAAT result</th>
<th>GeneX result</th>
<th>GeneX cycle threshold</th>
<th>Reference lab Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobas</td>
<td>Urine</td>
<td>CT neg</td>
<td>CT pos</td>
<td>34.2</td>
<td>CT neg</td>
</tr>
<tr>
<td>Cobas</td>
<td>Urine</td>
<td>CT neg</td>
<td>CT pos</td>
<td>37.2</td>
<td>CT pos</td>
</tr>
<tr>
<td>In-house</td>
<td>Swab</td>
<td>CT neg</td>
<td>CT pos</td>
<td>31.6</td>
<td>CT neg</td>
</tr>
<tr>
<td>In-house</td>
<td>Urine</td>
<td>CT neg</td>
<td>CT pos</td>
<td>31.6</td>
<td>CT neg</td>
</tr>
<tr>
<td>In-house</td>
<td>Urine</td>
<td>CT neg</td>
<td>CT pos</td>
<td>35.5</td>
<td>CT pos</td>
</tr>
<tr>
<td>In-house</td>
<td>Urine</td>
<td>CT neg</td>
<td>CT pos</td>
<td>42.4</td>
<td>CT pos</td>
</tr>
<tr>
<td>Aptima</td>
<td>LVS</td>
<td>NG neg</td>
<td>NG pos</td>
<td>35.2/33.9</td>
<td>NG neg</td>
</tr>
</tbody>
</table>

*Royal Women's Hospital (Melbourne): Samples in Cobas transport medium were retested by Cobas 4800 (for both CT and NG) and by In-house Omp CT assay. In-house PorA and Opa NG assays. Swabs 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**

- 10/16 discordants investigated further at reference lab*

- 10/16 discordants investigated further at reference lab*

**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

- Participating health services & staff
- Departments of Health WA, QLD, SA
- PathWest Laboratory Medicine
- Western Diagnostics Pathology
- Clinipath 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
- 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

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

Tuesday, 2.40pm Room S12
Presentation: TTANGO