TTANGO:
a molecular-based POCT program for
chlamydia and gonorrhoea in remote
Aboriginal communities in Australia

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AACB POCT SES
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**Chlamydia & Gonorrhoea**

- Sexually transmissible infections
- Cured with single dose antibiotics
- If left untreated, can lead to serious complications, pelvic inflammatory disease, infertility, ectopic pregnancy and adverse pregnancy outcomes
Why do we need a POC test for CT/NG in Australia?

- First and second most commonly reported STIs
- Disproportionately affect Australian Indigenous peoples
- Rates highest in remote areas

Trial (Guy 2015)
- 68 remote communities
- 13 480 patients
- Prevalence: 33% women, 21% men

Kirby ASR 2013
Why do we need a POC test for CT/NG in Australia?

• Management of STIs in remote communities through primary health care services

• Syndromic management in patients with symptoms, but most cases asymptomatic
  – Diagnostic testing and timely treatment essential

• Remote areas, delays between lab testing and treatment lengthy
  – Average time to treat 21 days
  – 20% untreated (Guy 2012)
Why do we need a POC test for CT/NG in Australia?

- Mathematical models suggest that the use of POCT may:
  - Increase timeliness of treatment
  - Increase treatment uptake
  - Reduce prevalence (Hui 2013)
Lateral Flow CT/NG POC Tests

- >20 lateral flow POC tests
- Inexpensive
- Simple to use
- Results <30 minutes

- But...specimen preparation
- Generally poor sensitivity (<80%)
  - Higher LOD
  - Trade off between sensitivity and speed
  - Less sensitive detecting antigen than antibody

Source: Natoli et al. 2016
Molecular-based POC Tests

- Rapid tests based on NAAT now available
- GeneXpert CT/NG (Cepheid)
- Dual detection of CT & NG
- 90 minutes to result
- Two targets for NG
- High analytical sensitivity/specificity (Tabrizi 2013)
- Suited for use at POC (Peeling 2011)
How does the GeneXpert Test work?

Hands on time: <2 minutes

OR

Results in 90 minutes

Sample Purification

Nucleic Acid Extraction

Reagent Reconstitution

Amplification

Result Interpretation and Reporting

TTANGO: Test, Treat ANd Go
To assess test performance using characterised samples
Laboratory Evaluation

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

**Laboratory evaluation**

*To assess test performance using characterised samples*

**Field study**

*To confirm test performance using fresh samples & assess feasibility*
Field Evaluation

- Evaluated 3 POC tests in field conditions using fresh specimens
- Two remote health services
- Trained researchers conducted testing
- Compared to reference lab NAAT results
Field Evaluation

CT POC tests

- GeneXpert (N=198): 100% Sensitivity, 99.5% Specificity
- Diaquick CT (N=104): 27.3% Sensitivity, 98.5% Specificity

NG POC tests

- GeneXpert (N=198): 100% Sensitivity, 100% Specificity
- Gonorrhea Card Test (N=29): 66.7% Sensitivity, 76.9% Specificity
**Evaluation Pathway**

1. **Laboratory evaluation**
   - To assess test performance using characterised samples

2. **Field study**
   - To confirm test performance using fresh samples & assess feasibility

3. **RCT, TTANGO**
   - To assess operational performance as well as individual and health service benefits, challenges, acceptability

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**Extensive consultation**
TTANGO

• TTANGO: Test, Treat ANd Go
• AIM: measure the cultural, operational and cost-effectiveness of POCT for CT/NG in remote Aboriginal communities
• GeneXpert (Cepheid)
  – Automated sample purification and PCR detection of CT/NG & TV
  – Single-use disposable cartridges
  – First phase of research demonstrates 100% sensitivity (NG and CT) and 100% specificity (NG only) vs. lab
  – Results available in 90 minutes
  – Sample type: urine or swab
TTANGO Study Design

Objectives

• Whether the addition of POC testing
  – Is acceptable to patients and staff?
  – Impacts on client flow?
  – Increase treatment rate?
  – Decrease time to treatment?
  – Is cost-effective?

• Determine the GeneXpert performance in a field setting

• Implement a model for quality management
TTANGO Training & Support

- Training – flexible
- Remote login learning
- Resources: training manual, step-by-step posters, standard operation procedures
TTANGO Quality Framework

- Standard Operating Procedures
- Internal Quality Control
  - Urine, provided by UQCCR lab
  - tested monthly
- External Quality Assurance
  - Swab, provided by NRL
  - tested twice yearly
TTANGO Quality Framework

- GeneXpert In-Built Quality Checks
  - Sample Adequacy Control: ensures sample contains human cells
  - Sample Processing Control: 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
TTANGO Preliminary Results

- Conducted 2013 to 2015
- Over 3000 POC tests conducted
- Most tests conducted by Aboriginal health workers and nurses
- GeneXpert CT/NG test
  - Highly acceptable to patients and health service staff
  - Health services indicated a strong desire to have access to GeneXpert CT/NG test after TTANGO completion
TTANGO Preliminary Results
Client Satisfaction (n=68)

- I can get my result today: 88.2%
- I can get medicine today if needed: 73.5%
- I don’t have to come back to the clinic on another day for medicine: 55.9%
- I feel reassured I am OK: 47.1%
- I don’t need to worry while waiting for the lab result: 38.2%
- Partners can be notified sooner: 32.4%
TTANGO Preliminary Results
POCT Operator Satisfaction (n=16)

- It was easy to transfer POCT results to PMS
- The machine is sturdy
- I trust the POCT results
- POCT has greatly reduced recall efforts
- Helps with clinical decision making
- I prefer giving results on the same day
- Results on the computer are easy to interpret
- It is easy to load the test cartridge

Agree  Neutral  Disagree  Missing

No. responses
TTANGO Preliminary Results
GeneXpert CT/NG Operational Performance

1995 tests: 182 (9.1%) CT positive: 127 (6.4%) NG positive

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>98.4</td>
<td>94.9 – 99.6</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.5</td>
<td>99.0 – 99.8</td>
</tr>
<tr>
<td>PPV</td>
<td>95.2</td>
<td>90.8 – 97.6</td>
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<tr>
<td>NPV</td>
<td>99.8</td>
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<td>NG</td>
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</tr>
<tr>
<td>Sensitivity</td>
<td>100.0</td>
<td>96.3 – 100.0</td>
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<td>Specificity</td>
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<tr>
<td>PPV</td>
<td>98.4</td>
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<td>100.0</td>
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TTANGO Preliminary Results
Treatment Outcomes

• Clinical audit for all those with positive test (CT and/or NG) by laboratory NAAT or POC test
• Time to treatment comparing POC test in POC year vs laboratory NAAT in standard care year
• Data collected
  – 541 positive tests
  – across 8 services
## TTANGO Preliminary Results
### Treatment Outcomes

<table>
<thead>
<tr>
<th>Overall</th>
<th>POC phase (n=225)</th>
<th>Standard phase (n=316)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment uptake</td>
<td>96%</td>
<td>88%</td>
</tr>
<tr>
<td>Time to treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (days)</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Median (days)</td>
<td>0</td>
<td>7</td>
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*Difference (range)*

- Treatment uptake: 36% (11 - 64%)
- Time to treatment: 25% (3 - 51%)
TTANGO Preliminary Results
Treatment Interval

Time to treatment (days)

- <3 days: 69% (POC test), 33% (Lab test*)
- <7 days: 85% (POC test), 50% (Lab test*)
- <120 days: 96% (POC test), 91% (Lab test*)

*NAAT for CT/NG performed during standard phase
TTANGO Summary and Looking Ahead

• Feasible
• Acceptable
• GeneXpert equal accuracy to lab
• Improved treatment timeliness
  • Reduced duration of infection

• Challenges
  – Staff turnover in remote settings
  – Cost of device and reagents
• NHMRC Partnership Grant and Australian Department of Health

• Scale up to 33 services, including TTANGO sites
  – 20 in WA
  – 4 SA
  – 3 QLD
  – 6 NT
TTANGO2 Translational Design

- Scaling up training and quality systems
- Training
  - E-learning available 24/7
  - Basic and advanced training
  - Mobile trainers
- Quality
  - Improved feedback reports
- Connectivity (with Medical Communications Associates)
- Integrating into sexual health CQI
- Trichomonas testing
TTANGO2 Timeline

• Implemented and evaluated over 5 years
  – 2015/16 (overlapping with TTANGO): consultation, preparation and transition
  – 2016-2019: POC test and CQI implementation; and data collection and monitoring
  – 2019-2020: final evaluation analysis and reporting
• All implementation and evaluation activities will be planned in consultation with the partner organisations and health service staff
Partnerships and Collaborations

• TTANGO2 Investigators and their institutions (Kirby Institute UNSW, Flinders University International Centre for Point-of-Care Testing, Royal Women’s Hospital, Burnet Institute, University of QLD Centre for Clinical Research, Deakin University, South Australian Health and Medical Research Institute, WA Department of Health, Cepheid, Apunipima Cape York Health Council, Ngaanyatjarra Health Service, PathWest Laboratory Medicine)

• In partnership with and support from
  ➢ WA: WA Health, AHCWA, NHS, KAMSC
  ➢ NT: AMSANT, NT Health
  ➢ SA: AHCSA, SA Health
  ➢ QLD: QAIHC, QLD Health, Apunipima
  ➢ Pathology providers: PathWest, ClinPath, Westerns, Pathology QLD, SA Pathology, SNP

• National Serology Reference Laboratory
• Monash University
• Medical Communications Associates
References

Thank you

For more information on TTANGO:

For more information on TTANGO2:

Our new book:
A Practical Guide to Global Point-of-Care Testing

Published November 2016