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Amsterdam

## Test of cure for ano-genital gonorrhoea using modern RNA- and DNA-based nucleic acid amplification tests - a prospective cohort study

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## Disclosures

- **Funding:** Public Health Service Amsterdam
- **Disclosures:**
  - Hologic provided Aptima products in-kind
  - Roche provided Cobas products in-kind
- Neither Hologic nor Roche had any role in the design, analysis or interpretation of the data

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## Introduction

- Increasing antimicrobial resistance (AMR) in *Neisseria gonorrhoeae*
- Culture replaced by nucleic acid amplification test (NAAT)
  - AMR testing using NAAT still limited
  - Many infections are asymptomatic
- Use test of cure (TOC) to monitor treatment outcome
  - Previously based on culture
  - Evidence for timing with modern NAATs limited

• Unemo et al. Clin Microbiol Rev 2014  
• Bachmann et al. J Clin Microb 2002  
• Hjeltnes et al. Acta Derm Venereol 2012  
• Beymer et al. Sex Transm Dis 2014  
• Blasse et al. Clin Infect Dis 2014

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## Study design

- **Aim:** assess timing of TOC using modern RNA- and DNA-based NAATs
- **Design:** prospective cohort study
- **Patients** STI Clinic Amsterdam; March-October 2014
  - Ano-genital gonorrhoea
  - Receiving routine treatment:
    - Ceftriaxone 500 mg intramuscular
    - Chlamydia: plus azithromycin or doxycycline
- **Required sample size:** 80 patients
  - Similar numbers of urethral, vaginal and rectal infections

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## Study procedure

- Self-collection of swabs or urine
  1. RNA-based NAAT: Aptima Combo 2 assay
  2. DNA-based NAAT: Cobas 4800 NG/CT assay
- **Samples collected:**
  - Pre-treatment
  - Daily for 28 days following treatment
- **Study diary:**
  - Sexual contact and condom use
  - Intra-vaginal or rectal douching
- **Return visit** within 35 days

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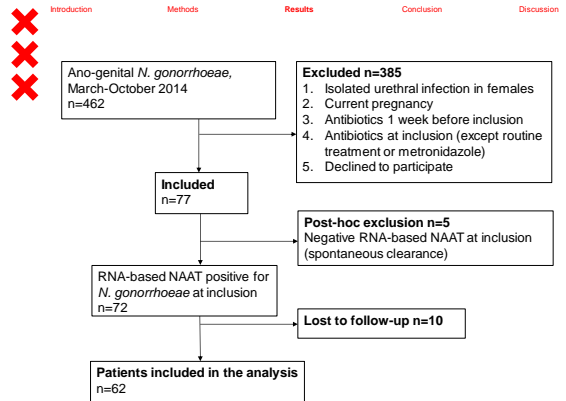
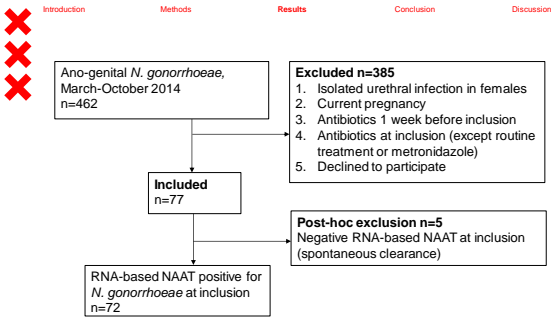
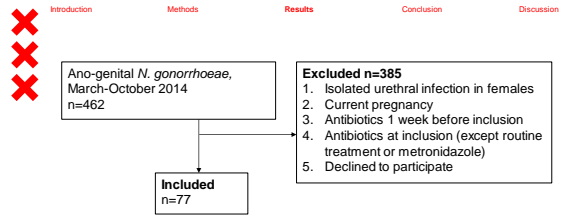
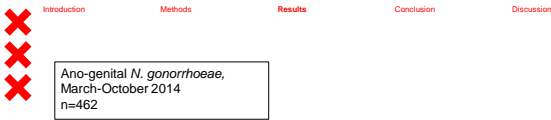
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## Definitions

- **Clearance:** 3 consecutive negative test results
- **Reinfection:**
  - ≥ 3 consecutive positive test results after clearance
  - AND
  - At least one sample positive for both RNA and DNA
- **Intermittent positive results ("Blips"):**
  - Positive test result after clearance
  - AND
  - Not meeting criteria for reinfection

• Bachmann et al. J Clin Microb 2002



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**Table 1 – Baseline characteristics (n=62)**

Characteristics	N (%)
Anatomical site	
Urethra	20 (32%)
Rectum	21 (34%)
Vagina	21 (34%)
Sexual risk group	
MSM	35 (56%)
Hetero male	6 (10%)
Female	21 (34%)

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Median age, in years (IQR)	25 (22-35)
<i>C. trachomatis</i>	23 (37%)
Symptoms or signs	37 (60%)

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<i>C. trachomatis</i>	23 (37%)
Symptoms or signs	37 (60%)
Mean RLU value (range)	1227 (567-1350)
Mean CT value (range)	29 (24-38)
<b>Treatment at inclusion</b>	
Ceftriaxone mono-therapy	23 (37%)
Ceftriaxone + azithromycin	27 (44%)
Ceftriaxone + doxycycline	12 (19%)

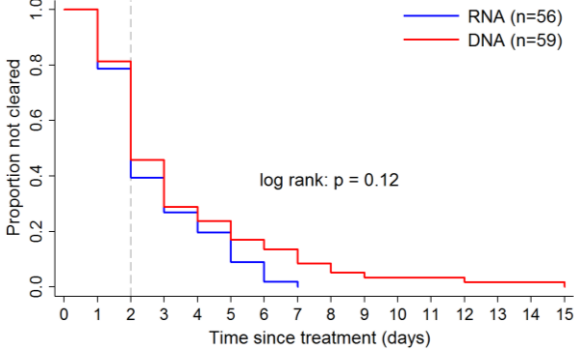
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## Behaviour after inclusion

**Table 2 – Behaviour after inclusion**

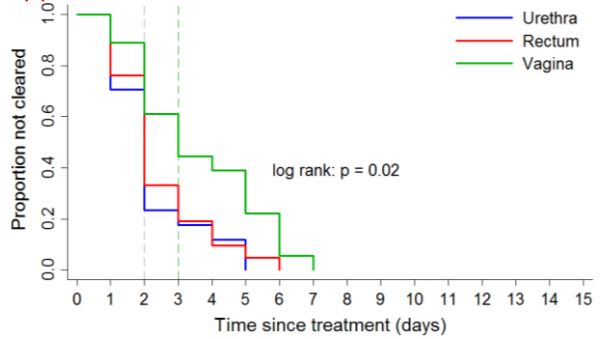
Characteristics	Total n (%)	Urethra n (%)	Rectum n (%)	Vagina n (%)	P
Patients	62	20	21	21	
Median no. of samples (range)	27 (20-28)	28 (25-28)	28 (20-28)	27 (20-28)	0.01
Rectal/vaginal douching	11 (26%)	-	7 (33%)	4 (19%)	0.29
Unprotected sexual contact	17 (27%)	4 (20%)	5 (24%)	8 (38%)	0.39

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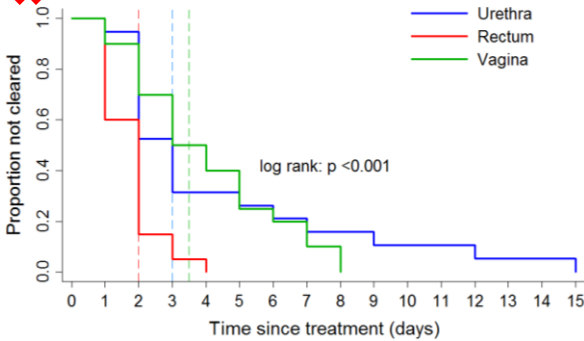
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## RNA clearance



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## DNA clearance



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## Blips

**Table 2 – Behaviour after inclusion and clearance of *N. gonorrhoeae***

Characteristics	RNA (n=61)	DNA (n=61)
	n (%)	n (%)
Patients with blips	6 (10%)	10 (16%)
Samples at risk for blip	1308	1285
Number of blips	11 (0.8%)	19 (1.5%)
Mean RLU/CT-value (range)	221 (91-463)	38 (35-40)
Unprotected sex <48 hours	0 (0%)	2 (3%)

- Logistic regression analysis: no association sex and blips
- Univariate association with:
  - *Chlamydia trachomatis* co-infection (RNA only)
  - Ceftriaxone MICs >0.016 mg/L



## Conclusions

- Median time to clearance: 2 days
- 100% clearance
  - RNA: 7 days
  - DNA: 15 days
- Associated: Sexual risk group / anatomical site / treatment
- Blips after clearance occur
  - RNA: 0.8% of samples
  - DNA: 1.5% of samples
- No association with sexual contact



## Discussion

- Time to clearance similar to previous research
  - Different molecular tests
- Limitations:
  - Single centre study
  - No pharyngeal samples
  - Limited power for associations clearance and blips
- Interpretation of blips unclear: viable organism?
  - Significant difference RLU/CT-value pre-treatment

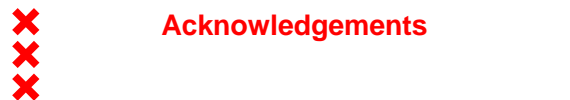
• Bachmann et al. J Clin Microb 2002  
 • Hjeltnes et al. Acta Derm Venereol 2012  
 • Beymer et al. Sex Transm Dis 2014  
 • Bissessor et al. Clin Infect Dis 2014



## Clinical recommendation

### Timing for TOC in ano-genital gonorrhoea

RNA (Aptima Combo 2):	after 7 days
DNA (Cobas 4800):	after 14 days



## Acknowledgements

- All participants of the study
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