Chlamydia trachomatis
Testing, Treatment and Prevention

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Blood Safety, Hepatitis, HIV & STI Division
National Infection Service
Public Health England
Testing is easy

Self-sampling possible; tests are highly acceptable and highly sensitive

Simple treatment

Doxycycline first line, well tolerated, inexpensive and efficacious

Very common

In 2018 there were approximately 218,000 diagnoses of chlamydia made in England
Testing is easy
Chlamydia as a stealth pathogen

Simple treatment
Optimising care pathways

Very common
Prophylaxis for prevention
Testing

New variant chlamydia
Early 2019

Heterosexual woman
Chlamydia detected
• Abbott RealTime

24th April
EPIS-STI Alert
February
Symptomatic male contact
Chlamydia negative
• Aptima Combo 2

24th April
EPIS-STI Alert
February
Symptomatic male contact
Chlamydia negative
• Aptima Combo 2

Chlamydia detected
• Allplex
• Aptima CT

24th April
EPIS-STI Alert
Rapid Communication

Chlamydia trachomatis samples testing falsely negative in the Aptima Combo 2 test in Finland, 2019

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9. Fimalab, Lahti, Finland
10. Fimalab Laboratories, TAMPERE, Finland

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### Table 2
Samples re-analysed with Aptima CT test in HUSLAB, Finland, 6 March–30 April 2019 (n=757)

<table>
<thead>
<tr>
<th>Qualitative result in the original AC2 test according to the instrument display</th>
<th>RLU in the original AC2 test</th>
<th>Number of samples tested by ACT test</th>
<th>Positive in the ACT in %</th>
<th>The AC2 test RLU values in the ACT positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative or equivocal for CT and negative for GC</td>
<td>≤10</td>
<td>330</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>11–15</td>
<td>266</td>
<td>7</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>16–19</td>
<td>71</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>20–84</td>
<td>73</td>
<td>68</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>85–250</td>
<td>3</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>Negative for CT and positive for GC</td>
<td>48–1,492</td>
<td>14</td>
<td>1</td>
<td>7.1</td>
</tr>
</tbody>
</table>

AC2: Aptima Combo 2; ACT: Aptima CT; CT: Chlamydia trachomatis; GC: Neisseria gonorrhoeae; RLU: relative light units.

a) Of 50 samples ≤25 RLU, one sample was flagged as equivocal in the original AC2 test.

b) Of three samples with RLU between 85 and 99, three samples were flagged as equivocal in the original AC2 test.

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10 AC2-/ACT+ sequenced
Single nt change in 23S rRNA

C1515T

Proportion of positive cases that may have been missed

6-10%
<table>
<thead>
<tr>
<th>Target/s</th>
<th>Real-time</th>
<th>Artus</th>
<th>GeneXpert</th>
<th>Cobas 4800/6800/8800</th>
<th>BD Viper/probetec</th>
<th>BD Max</th>
<th>Aptima Combo 2 (AC2)</th>
<th>Aptima CT mono</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 targets on cryptic plasmid &amp; 2nd target on genome</td>
<td>Abbott</td>
<td>Qiagen</td>
<td>Cepheid</td>
<td>Roche</td>
<td>Becton Dickinson</td>
<td>Becton Dickinson</td>
<td>Hologic</td>
<td>Hologic</td>
</tr>
<tr>
<td>Technology</td>
<td>RT-PCR</td>
<td>RT-PCR</td>
<td>PCR</td>
<td>PCR</td>
<td>SDA</td>
<td>RT-PCR</td>
<td>TMA</td>
<td>TMA</td>
</tr>
</tbody>
</table>

Acknowledgement: Dr Michelle Cole
4th June
PHE briefing note to Labs in England
7th June
Hologic Field Safety Notice
14th June
Alert to BASHH Clinicians

17th June
ECDC Rapid Risk Assessment published

21st June
Labs start reporting discrepant results to PHE

4th June
PHE briefing note to Labs in England

7th June
Hologic Field Safety Notice
Chlamydia tests in England, 2018 ~3.8 million
Chlamydia tests in England, 2018

~3.8 million

~40% tested on AC2 platform

~1.6 million

- 1 lab in Scotland
- None in Wales or Northern Ireland
Chlamydia tests in England, 2018

~3.8 million

~40% tested on AC2 platform

~1.6 million

~90% negative test result

~1.4 million
Chlamydia tests in England, 2018

~3.8 million

~40% tested on AC2 platform

~1.6 million

~90% negative test result

~1.4 million

~1.5% within affected RLU range

~2,000 a month
AC2

- CT Negative and RLU <15
- CT Positive

~99%
AC2

• CT Negative and RLU <15
• CT Positive

~99%

• CT Negative and RLU ≥15
• CT Negative and GC equivocal/positive
• CT equivocal
• Equivocal

~1.5%
AC2

- CT Negative and RLU <15
- CT Positive

~99%

- CT Negative and RLU ≥15
- CT Negative and GC equivocal/positive
- CT equivocal
- Equivocal

~1.5%

Alternative target

Negative
- True Negative
- No further action

Positive
- Discrepant Result
- Refer to PHE
AC2

- CT Negative and RLU <15
- CT Positive ~99%

- CT Negative and RLU ≥15
- CT Negative and GC equivocal/positive
- CT equivocal
- Equivocal ~1.5%

Alternative target

Negative
True Negative
No further action

Positive
Discrepant Result
Refer to PHE

Sequencing

Wild Type
AC2 False Negative
No further action

C1515T
nv-CT
**Sensitivity**

The fraction of those with chlamydia correctly identified as positive by the test

**Specificity**

The fraction of those without chlamydia correctly identified as negative by the test

Alternative target

- **Negative**
  - True Negative
  - No further action
- **Positive**
  - Discrepant Result
  - Refer to PHE

Sequencing

- **Wild Type**
  - AC2 False Negative
  - No further action
- **C1515T**
  - nv-CT
Sensitivity
96.7%

Specificity
99.2%

Assuming 10% prevalence
For every 1000 tests:
3-4 false negatives

Sequencing

Wild Type
AC2 False Negative
No further action

C1515T
nv-CT

ECDC Laboratory Guidelines on Bacterial STIs, 2012
Current situation

- Two confirmed C1515T nvCT outside of Finland (Sweden)
- All labs in England using AC2 following field safety notice and reporting results weekly to PHE
- Preliminary data do not show any sign of nvCT
- Membership of National Management Team includes BASHH
- Aim to update BASHH membership at End of July
Treatment

Optimising online clinical care pathways
Chlamydia tests among 15 to 24 year olds by test setting 2014-2018, England

eSHS

>200,000 tests
54% increase (2017 to 2018)
17% of all tests
14% of all diagnoses
Chlamydia negative

Chlamydia positive

Clinical assessment & Treatment
Chlamydia negative

Chlamydia positive

Clinical assessment & Treatment
eSexual Health Clinic System

Slide acknowledgement:
Dr Jo Gibbs, UCL
Exploratory studies

• 221 people with chlamydia (GUM & NCSP), nearly 2000 negatives
• 97% GUM patients received treatment
  • 74 exclusively online, in median 1 day
• 89% NCSP patients received treatment
  • 60 exclusively online in median 1 day
• High user satisfaction
• Partner treatment feasible online
• ~ 25% of patients used the clinical helpline
The eSexual Health Clinic system for management, prevention, and control of sexually transmitted infections: exploratory studies in people testing for Chlamydia trachomatis

Claudia S Estcourt, Jo Gibbs, Lorna J Sutcliffe, Voula Gkatziou, Laura Tickle, Kate Hone, Catherine Aicken, Catherine M Lowndes, Emma M Hurding-Esch, Sue Eaton, Pippa Oakeshott, Ali Szczepura, Richard E Ashcroft, Andrew Copas, Anthony Netteship, S Taniq Sadig, Pam Sannenberg

- Proof of concept NHS & world first, showed preliminary evidence of effectiveness of online automated chlamydia pathway within an eSexual Health clinic
- Median time to treatment: 1 day & fastest 32 minutes!
- Next steps: RCT of cost-effectiveness, maximising digital inclusion
<table>
<thead>
<tr>
<th>Cost effectiveness</th>
<th>Clinical effectiveness</th>
<th>Health inequalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are online care pathways cost effective?</td>
<td>Are there differences in clinical outcomes?</td>
<td>Who is less likely to engage with online services?</td>
</tr>
<tr>
<td>Risk behaviour</td>
<td>PN and PrEP modules</td>
<td>Other infections</td>
</tr>
<tr>
<td>Are there missed opportunities for prevention?</td>
<td>Is it feasible to include additional modules?</td>
<td>Is it feasible to manage other infections online?</td>
</tr>
</tbody>
</table>
Prevention

Doxycycline prophylaxis for STIs
Antibiotic prophylaxis is not new.
Doxycycline prophylaxis also not new

1. Traveller’s diarrhoea
   - 100mg daily; 85% efficacy

2. Scrub typhus
   - 200mg weekly; 89% efficacy

3. Lyme disease
   - 200mg stat; 87% efficacy

4. Leptospirosis
   - 200mg weekly; 95% efficacy

References:
Current evidence for doxycycline prophylaxis for STIs

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model of sexual behaviour</td>
<td>~50% reduction in syphilis after 12 months if 50% uptake in gay men and 70% efficacy</td>
</tr>
<tr>
<td>Survey and focus groups</td>
<td>52.7% very or slightly likely to use chemoprophylaxis to reduce risk of syphilis</td>
</tr>
<tr>
<td>RCT of Doxy PrEP</td>
<td>30 MSM 100mg daily 73% reduction in any bacterial STI</td>
</tr>
<tr>
<td>RCT of Doxy PEP</td>
<td>232 HIV PrEP users 200mg within 72 hours 70% reduction in chlamydia</td>
</tr>
</tbody>
</table>

1. Doxy PEP for STIs is **not endorsed** by BASHH or PHE
2. Any potential benefits will be outweighed by the considerable potential to select resistance in STIs and other bacterial species
3. Further **studies are required** to measure the wider impact on AMR at an individual and population level
4. Recommend use of Abx as prescribed by HCP and as indicated by results of suitable diagnostic test in chlamydia

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**RCT of Doxy PEP**

- **302 HIV PEP users**
- **200mg within 72 hours**
- **no efficacy** in chlamydia
Planned and ongoing studies
**DuDHS**
Dual Daily HIV & Syphilis PrEP

- N=50 MSM on HIV PrEP
- Condomless sex in last 6 months
- Syphilis diagnosis in last 3 years

- Single blind RCT
- Immediate/ deferred initiation
- Daily doxycycline 100mg vs. delayed

- Adherence & tolerability
- STI incidence
- Change in sexual behaviour
- Tetracycline resistance
- Resistance in oral flora
- Rectal microbiome

**DaDHS**
Daily Doxycycline in HIV+ for Syphilis PrEP

- N=52
- MSM living with HIV

- Single blind RCT
- Daily doxycycline 100mg or placebo

- Adherence & tolerability
- STI incidence
- Change in sexual behaviour
- Tetracycline resistance
- Resistance in oral flora
- Rectal microbiome
ANRS Prevenir sub-study
Efficacy of meningococcal type B vaccine in preventing *Neisseria gonorrhoeae* and the use of Doxycycline Post Exposure Prophylaxis 200mg to prevent syphilis and chlamydia

- N=700
- MSM on HIV PrEP
- Prior STI diagnosis in the past 18 months

- Open-label RCT
  - 2:1 Doxycycline PEP 200mg or no PEP and 1:1 vaccine or no vaccine

- NG, CT and syphilis diagnosis
- Culture and molecular based resistance testing
- Rectal and oral microbiome sub-study on antimicrobial resistance
Luetkemeyer & Celum
Evaluation of doxycycline Post Exposure Prophylaxis to reduce STIs in PrEP users and MSM living with HIV

N=780 MSM & TGW
390 living with HIV, 390 HIV PrEP users
≥1 bact. STI and ≥1 CSI with ≥1 male partner in 12m

- Open-label RCT 2:1 randomisation
  Doxycycline PEP 200mg versus standard of care
- Incidence of NG, CT or syphilis
- Culture and molecular based resistance testing
- Commensal flora and gut microbiome resistance testing
‘Syphilaxis’

N=350 MSM & TGW
Condomless SI with men, diagnosed with syphilis in prior 12 months, or any STI in last 12m and syphilis in last 24m and at least two episodes on STI screening in last 12m

Single-arm trial
Daily doxycycline 100mg

- NG, CT and syphilis diagnosis
- Use and acceptability
- Rectal and oropharynx microbiome sub-study on antimicrobial resistance (n=100)
Challenges and knowledge gaps
Challenges and knowledge gaps

1. Efficacy
   - Two studies show approx. 70% but samples small and underpowered
   - Precise estimate important to inform cost-effectiveness analyses, community education and patient counselling
Challenges and knowledge gaps

1. Efficacy

2. Target population
   - Modelling suggests targeting MSM with >20 partner/6m almost as effective as broader DoxyPrEP use¹
   - Controlling STIs in core HR populations important for reducing STIs in broader populations

Challenges and knowledge gaps

1. Efficacy

2. Target population

3. Community acceptability
   - Surveys suggest acceptable to MSM for personal health and community health\(^1\)
   - Some evidence that MSM already using Abx prophylaxis\(^2\)

8%

Of 106 had taken antibiotics to prevent STIs

Challenges and knowledge gaps

1. Efficacy
2. Target population
3. Community acceptability
4. Risk compensation
Challenges and knowledge gaps

1. Efficacy
2. Target population
3. Community acceptability
4. Risk compensation
5. **Dose, regimen and formulation**
   - Monohydrate or enteric coated hyclate (fewer GI SE), vs. uncoated hyclate
Challenges and knowledge gaps

1. Efficacy
2. Target population
3. Community acceptability
4. Risk compensation
5. Dose, regimen and formulation

6. Duration of use and long term safety
   • c.f. malaria, acne
Challenges and knowledge gaps

1. Efficacy
2. Target population
3. Community acceptability
4. Risk compensation
5. Dose, regimen and formulation
6. Duration of use and long term safety
7. Antimicrobial resistance

Sexually transmitted infections
• Chlamydia trachomatis
• Neisseria gonorrhoeae
• Mycoplasma genitalium
• Treponema pallidum

Other infections
• Respiratory infections (COPD/ CAP)
• Hospital acquired infections (MRSA)
  ➢ Relieve pressure on carbapenems
  ➢ Lower risk of C. difficile
Challenges and knowledge gaps

1. Efficacy
2. Target population
3. Community acceptability
4. Risk compensation
5. Dose, regimen and formulation
6. Duration of use and long term safety
7. Antimicrobial resistance
8. Risk/benefit and cost effectiveness
   - If risks a/w chlamydia are primarily borne by women then Doxy prophylaxis in MSM may have limited impact on serious health outcomes
Very common

Doxycycline prophylaxis already being used

Several ongoing & planned studies to address important unanswered questions

Simple treatment

Getting treatment to those who need it

Evidence gaps relating to optimal online pathways of care

Testing is easy

Not as simple as A, B, Pee..?

Health professionals central to identifying potential new variants
Acknowledgements

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