Assessing the impact of individualised treatment: an individual-based mathematical modelling study of antimicrobial resistant *Neisseria gonorrhoeae* transmission, diagnosis and treatment in men who have sex with men

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1. Antimicrobial resistant gonorrhoea

Antimicrobial resistant (AMR) gonorrhoea is a global public health threat. In London, diagnoses in men who have sex with men (MSM) have more than quadrupled from 2010 to 2015, with gonorrhoea being the most commonly diagnosed STI in MSM (**Figure 1**).

Last-line ceftriaxone is first-line treatment (plus azithromycin). However, over half of tested isolates are sensitive to older drugs, e.g. **ciprofloxacin**.

Discriminatory point-of-care tests (**POCT**) to detect drug sensitivity are in development. This would allow individualised treatment decisions and preserve last-line antibiotics and prolong their efficacy.

Here we assess the impact of POCT, and other individualised treatment strategies, by simulating multi-strain gonorrhoea transmission dynamics under different diagnostic and treatment scenarios.

2. Multi-strain individual based model

Model structure: Individual-based, SIS transmission model of gonorrhoea infection in MSM,

- ciprofloxacin-sensitive (I) and **resistant** (I_R) strains
- simultaneous co-infection with either strain
- scale-free sexual partnership networks using power-law degree distributions (MSM specific)

Dynamic sexual contact networks $A(t)$ and infection states $\Omega(t)$:

3. Treatment and recovery pathways

We explored different strategies to improve treatment selection including:

- (i) **Discriminatory POCT** all cases tested & treated with infection-specific drug on same day
- (ii) **Informed partner treatment based on index case susceptibility** individuals are treated as if infected with a resistant strain *unless* their index partner had a non-AMR strain
- (iii) **Delayed partner treatment & susceptibility testing** all individuals traced from an infected index case undergo susceptibility testing then given infection-specific treatment

Example pathway without POCT: 1-3 AMR infected individual develops symptoms, seeks advice and is treated as if non-AMR (Ciprofloxacin). 4-6 Lab tests indicate patient was misdiagnosed. Patient is notified and recalled, along with recent partners (assumed also to be AMR infected). 7-10 Index case recalled and treated with ceftriaxone (full cure).

Infection: Compute the ‘infection force’ of each strain on each individual due to their partners, given by:

$$F = 1 - (1 - \beta)^{A \times \Omega(t)} \in \mathbb{N}^{N \times 2}$$

F :- relative likelihood of becoming infected [0..1] β :- per day infection rate

Infection state $\Omega(t + 1)$ updated for each day (discrete-time) via *stochastic* process

Recovery: Individuals are treated with either **Ciprofloxacin** or **Ceftriaxone** (plus azithromycin), or recover spontaneously

e.g. Co-infected

• **Cipr./A** treats non-AMR strain only

• **Ceft./A** suitable for both strains.

4. Experiments and Results

We simulated London gonorrhoea transmission dynamics in MSM

Model calibrated to 2-10% prevalence, 10-50 daily diagnoses per 100,000 (London) MSM

Reference scenario (REF): 100% use of recommended first-line therapy (**Ceft/A**)

Treatment scenarios (1-4): POCT or strategies with either random or targeted use of **Cipr/A** or **Ceft/A**

Time horizon: 1 year

Treatment scenarios:	REF	100% <i>Ceft/A</i>	Reference scenario current UK guidelines – ceftriaxone & azithromycin <i>Ceft/A</i> combined therapy for all cases and traced partners
1	80% <i>Ceft/A</i> , 20% <i>Cipr/A</i> (random choice)	Current situation - recommendations not always followed e.g. where <i>Ceft/A</i> cannot be prescribed	
2	Point-of-care test	Same-day testing for <i>Cipr.</i> susceptibility with specific treatment administered on same day according to infection state	
3	‘Informed’ partner treatment	Individuals who have been screened or traced via partner notification prescribed <i>Cipr/A</i> if index partner was infected with a drug-sensitive strain	
4	Delayed partner treatment	Treatment is delayed for all notified partners who are screened for infection prior to either drug being prescribed

5. Conclusions

- Summary:**
- Overtreatment - Many infections could be treated with older drugs
 - Wastage – Many uninfected individuals are treated through partner notification
 - Random treatment with **Cipr/A** leads to increasing (7%) levels of treatment failure and increasing prevalence
 - POCT - Decreased all prescriptions – with apx. 73% fewer doses of Ceft/A,**
 - Decreased overall prevalence
 - No wastage or overtreatment

POCT could reduce reliance on ceftriaxone, but tests are not yet commercially available. In the UK, existing susceptibility test data could be used to target partner treatment. This new model framework addresses limitations of previous models and provides a flexible platform for exploring control options for AMR gonorrhoea.

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