DIRECT AND SPECIFIC DETECTION OF *NEISSERIA GONORRHOEAE* CIPROFLOXACIN SUSCEPTIBILITY—TOWARDS INDIVIDUALISED TREATMENT.

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Introduction: *Neisseria gonorrhoeae* antimicrobial resistance (AMR) is a major global concern; there are limited new treatment options and a lack of reliable AMR data in many settings. A proposed strategy to combat resistance is the recycling of previously effective antibiotics via the use of molecular methods to predict susceptibility and inform treatment. Ciprofloxacin is considered an ideal candidate for this purpose. However, until now, there has been insufficient data to inform its use.

Methods: As a part of a large nationwide study, we examined the molecular basis of ciprofloxacin AMR in 3,028 *N. gonorrhoeae* isolates from throughout Australia (years 2012 to 2014). Mutation profiles were correlated with minimum inhibitory concentrations. Through this screening we identified candidate sequences that predict ciprofloxacin susceptibility. We then developed and validated a real-time PCR method to predict ciprofloxacin susceptibility directly from clinical samples (Cipro-NAAT), and trialed it using *N. gonorrhoeae*-positive clinical samples (n=1,630; year 2014) from the Northern Territory (NT) of Australia.

Results: Based on the 3,028 tested isolates, the gyrA S91F provided 99% accuracy for predicting ciprofloxacin susceptibility and was used as the sequence target for the Cipro-NAAT. When the Cipro-NAAT was applied to the 1,630 NT clinical samples, 75.4% (1,229/1,630) were successfully characterised; of these, only 5.7% were indicated to be ciprofloxacin resistant. This was notably lower than culture-based testing at 13.5% from this time period.

Conclusion: This study represents the largest molecular assessment of gonorrhoea ciprofloxacin AMR. It is now evident that ciprofloxacin resistance is being overestimated in the NT where surveillance is based solely on bacterial culture data. Overall these data highlight the feasibility of recycling ciprofloxacin for treatment of gonorrhoea in Australia.

We propose that the Cipro-NAAT could be used to inform individualised treatment and are now progressing towards a clinical trial.

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