Neisseria gonorrhoeae antimicrobial co-resistances: implications for the utility of rapid molecular antimicrobial resistance assays and informing antimicrobial use

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Background:
Neisseria gonorrhoeae antimicrobial resistance (AMR) is an escalating problem and new approaches, including improved antimicrobial stewardship, are needed. The WHO recommends increasing the availability of molecular AMR tests, given the challenges associated with phenotypic testing, however, molecular AMR assay development is challenging. We investigated associations of *N. gonorrhoeae* co-resistances in New South Wales, Australia, to evaluate the potential utility of theoretical molecular AMR assays to reduce ceftriaxone use and inform priorities for assay development.

Methods:
N. gonorrhoeae AMR data from the Australian Gonococcal Surveillance Program (2008-2019) were analysed for associations between year of acquisition and resistances/decreased susceptibility to ceftriaxone, azithromycin, ciprofloxacin, and penicillin. Theoretical molecular assay-guided treatment strategies were then assessed based on the observed associations. For these experiments, we considered strategies to be more favourable if they (1) utilized fewer assays, (2) limited ceftriaxone consumption, and (3) limited use of ceftriaxone on isolates exhibiting ceftriaxone decreased susceptibility.

Results:
Based on data from 23,089 *N. gonorrhoeae* isolates, 22.8% (5,266) exhibited co-resistances, ranging between 13.7% (year 2018) and 54.3% (year 2008). All theoretical assay testing strategies significantly decreased ceftriaxone use ($p<0.001$) compared to an empiric ceftriaxone treatment strategy. The optimal testing strategy incorporated a single assay for ciprofloxacin susceptibility, predicting reduction of ceftriaxone use by 64.7%. However, most strategies did very little to reduce use of ceftriaxone on isolates with ceftriaxone decreased susceptibility as these isolates typically exhibit co-resistance to penicillin and ciprofloxacin.

Conclusion:
Molecular AMR assays, ideally for use at the point-of-care, present opportunities to reduce ceftriaxone use through individualised resistance-guided treatment over empiric treatment strategies. However, the non-random effect of co-resistances amongst circulating *N. gonorrhoeae* strains may curb benefits. Rapid molecular AMR assays, coupled with robust surveillance systems, integrating pathogen susceptibility

and antimicrobial use, are essential to strengthen antimicrobial stewardship activities.

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