QUANTIFYING THE FITNESS BENEFITS AND COST OF CEFIXIME-RESISTANCE IN NEISSERIA GONORRHOEAE

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Introduction Gonorrhoea is among the most common bacterial sexually-transmitted infections in the UK, over 41,000 cases were recorded in 2015, with over half in men who have sex with men (MSM). As the bacterium has developed resistance to each first-line antibiotic in turn, we need improved quantification of fitness-benefits and costs of antibiotic resistance to inform control policy. Cefixime was recommended as a single-dose treatment for gonorrhoea from 2005–2010, during which time resistance increased, and then subsequently declined. We hypothesise that there is a net fitness-benefit to cefixime-resistance when cefixime is widely-prescribed and a net fitness-cost when cefixime-prescriptions decline.

Methods We developed a stochastic compartmental model representing the natural history and transmission of cefixime-sensitive and -resistant strains of gonorrhoea in UK MSM, which was fitted to data on diagnoses and prescriptions over 2008-2015 using particle Markov Chain Monte Carlo (pMCMC) methods.

Results The model replicated the observed data and indicated that the fitness-benefit of cefixime-resistance exceeds its cost when cefixime is prescribed for >31% (95% CI [26%, 36%]) of gonorrhoea diagnoses, and that the resistant strain is fitter than the cefixime-susceptible strain when cefixime is prescribed for >51% (95% CI [43%, 62%]) of diagnoses.

Discussion The use of state-of-the-art pMCMC methods provided significant evidence in favour of our hypothesis and insights into the dynamics of cefixime-resistance in gonorrhoea. Our findings have important implications for antibiotic-stewardship and public health policies, such as targeted prescriptions and combination therapy; as well as emerging resistance through similar mechanisms to the current first-line treatment, ceftriaxone.

CLINICAL EVALUATION OF THE RESISTANCEPLUS™ MG KIT, FOR DETECTION OF MYCOPLASMA GENITALIUM AND SCREENING FOR MACROLIDE RESISTANCE

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Introduction European guidelines on *Mycoplasma genitalium* (MG) infections and on the mangement of non-gonococcal urethritis strongly recommend NAAT testing for MG and screening for macrolide resistance. The ResistancePlus™ MG kit has been developed for the simultaneous detection of MG and five mutations in the 23S rRNA gene associated with azithromycin resistance.

Methods The ResistancePlus™ MG kit (SpeeDx) was evaluated in a prospective-restrospective study on 182 urogenital samples from patients routinely tested for Chlamydia and gonorrhoea.

The ResistancePlus™ MG (550) kit was performed using the 7500 Fast (Applied Biosystems), after sample extraction on the MagNA Pure 96 Instrument (Roche) using the DNA and Viral NA Small Volume Kit following the Universal Pathogen 200 protocol. Results were analysed using the FastFinder ResistancePlus™ MG (7500) analysis software. Results were compared with an in-house qPCR test for MG detection with positives subsequently sequenced to determine 23S rRNA mutation status.

Results The ResistancePlus™ MG kit showed high clinical performance compared with the reference methods with sensitivity and specificity for MG detection of 98% and 100%, and 23S rRNA mutation detection of 92.5% and 100%, respectively. The ResistancePlus™ assay has an analytical sensitivity of 10-15 copies for all targets, and no cross-reactivity was seen in a wide range of non-target organisms.

Discussion The ResistancePlus™ MG kit demonstrated excellent clinical performance for the simultaneous detection of MG and mutations associated with macrolide resistance. Detection of MG with resistance information is capable of guiding personalised treatment at the first health-care visit, reducing clinical-care costs and reducing the spread of antimicrobial resistance.

EFFECTIVE CLINICAL DESIGNS OF MULTIPLEX POINT-OF-CARE-TESTS FOR GENITAL DISCHARGE SYNDROME MANAGEMENT IN WOMEN: WHICH PATHOGEN COMBINATIONS AND TESTING PROTOCOLS DELIVER THE BEST OUTCOMES?

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Introduction Syndromic management of sexually transmitted infections (STIs) is common practice in sexual health clinics (SHC). Implementation of multi-pathogen point-of-care-tests (POCTs) can improve patient management by providing same day diagnoses and treatment. We assessed the potential impact of five POCT protocols consisting of tests for different combinations of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), *Mycoplasma genitalium* (MG) and *Trichomonas vaginalis* (TV) infections, on a standard care pathway (SCP), for 81 symptomatic female patients.

Methods 5 virtual POCT protocols (assuming 100% sensitivity and specificity) were analysed against diagnoses and laboratory results. Reflex tests (i.e. tests used dependent on the result of another test) were incorporated into protocols to investigate utility of testing for certain pathogens separately. McNemar's test was used to compare proportions of correct diagnoses from each protocol against each other and establish which is most effective. P values were adjusted using Holm-Bonferroni correction.

Results Protocol P1 was statistically the most effective at providing the correct diagnosis (p=0.000). P5 was also statistically more effective than the SCP (p=0.001). No significant differences were found between other protocols. Although P4 and P5 diagnosed equal proportions of patients, P5 had better performance (p=0.001) compared with P4 (p=0.0012).