P643 ADVERSE PREGNANCY AND NEONATAL OUTCOMES ASSOCIATED WITH *NEISSERIA GONORRHOEAE:* A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background *Neisseria gonorrhoeae* (NG) infections during pregnancy have been reported to be associated with a range of adverse pregnancy outcomes, but systematic information is lacking. The objective of this study was to systematically review data about associations between NG and: preterm birth (PTB); low birth weight (LBW); premature rupture of membranes; spontaneous abortion; perinatal mortality; and ophthalmia neonatorum.

Methods We searched Medline, Excerpta Medica, Cochrane Library and the Cumulative Index to Nursing and Allied Health Literature databases up to October 2017. Two researchers selected studies, extracted data and assessed risk of bias independently. We used meta-analysis to calculate summary odds ratios (OR with 95% confidence intervals, CI) separately for unadjusted and adjusted results, stratified by study design. We assessed heterogeneity using the I^2 statistic.

Results We screened 2,290 articles and included 15 studies, published from 1976–2017, of which seven were from low or lower-middle income countries. For PTB, the summary unadjusted OR was 1.47 (95% CI 1.17–1.78, I^2=0%) in four case-control studies, 1.93 (1.24–2.63, I^2=86%) in two cross-sectional studies and 0.78 (0.49–1.06, I^2=0%) in three cohort studies. Adjusted ORs were only available in three case-control studies, summary OR 1.14 (0.85–1.44, I^2=16%). For LBW, the summary unadjusted OR was 1.57 (1.15–1.99, I^2=53%) in three case-control studies, 1.20 (0.30–4.30) in one cross-sectional study and 0.99 (0.73–1.25, I^2=47%) in two cohort studies. The adjusted summary OR was 1.33 (0.96–1.71, I^2=0%) in the case-control studies. For other outcomes, unadjusted summary ORs varied, generally being lower for cohort than cross-sectional or case-control studies.

Conclusion In this systematic review of observational studies, the strength of associations between NG and adverse pregnancy outcomes were weaker than expected and, where data were available, attenuated after adjusting for confounding. Ongoing randomised controlled trials will now determine whether screening and treatment of NG in pregnancy reduces adverse outcomes.

Disclosure No significant relationships.

P644 ANALYZING THE GENOMES OF *NEISSERIA GONORRHOEAE* ISOLATES USING A NOVEL INTEGRATED BIOINFORMATIC PIPELINE: GEN2EPI

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Background Whole genome sequencing (WGS) is a high-resolution approach for tracking the transmission and antimicrobial susceptibility (AMS) of *Neisseria gonorrhoeae* (Ng). Multiple bioinformatics tools currently used for the analysis of WGS data for Ng complicate their application in clinical settings. We determined the genomic epidemiology and AMS of Ng from Saskatchewan (SK) using our integrated pipeline, Gen2-Epi, previously validated on 1484 publicly available Ng genome datasets.

Methods WGS was performed on 99 Ng isolates (2017–2018) from SK submitted to the Roy Romanow Provincial Laboratory. Genomic DNA was isolated using the DNAeasy mini kit (QIAGEN) and sequenced using MiSeq (Illumina). MICs were determined by agar dilution. Gen2Epi includes read assembly, scaffolding, strain typing (ST) by MLST and NG-MAST, plasmid identification, and, identification of mutations in antibiotic resistance genes by NG-STAR.

Results Nine MLST/NG-MAST/NG-STAR (M/M/S) STs comprised 75.6% (75/99) of the isolates; other M/M/S STs (24.3%, 24/99) comprised single isolates. M/M/S ST 1901/10451/90 predominated (21.3%, 21/99), carrying mosaic *penA* type 34.001 and mutations in *mtrR*/*porB*/*ponA*/*gyrA*/*parC*. These isolates were chromosomally resistant to penicillin (38%, 8/21), tetracycline (95.2%, 20/21), and ciprofloxacin (90%, 19/21); they were susceptible to ceftriaxone and 38% (8/21) had cefixime MICs of 0.125 mg/L. The second-most prevalent ST was 1584/7638/160 (18/99); most of these isolates (16/18) were susceptible to all antibiotics. Overall, 57.6% (57/99) of the isolates were tetracycline resistant; 29.8% (17/57) of these were from Regina and carried a *tetM* gene (M/M/S ST 12462/5985/42). One sporadic isolate was azithromycin resistant (23S rRNA-A2059G), carried *tetM* and was M/M/S ST 7822/304/515.

Conclusion Gen2Epi is a one-stop pipeline that both assembles and annotates raw reads and simplifies the analysis of transmission markers and AMS in Ng. We showed the emergence of M/M/S ST 1901/10451/90 as the predominant ST in SK. NG-MAST ST 10451 is similar (≤2bp) to ST 1407 which is implicated in reduced susceptibility to cefixime.

Disclosure No significant relationships.

P645 PERUVIAN GONOCOCCAL STRAINS REVEAL NOVEL NG-MAST TYPES AND FALSE-POSITIVE β-LACTAMASE ISOLATES WITH BLA_{TEM} GENE MUTATIONS

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Background The Global Emerging Infectious Surveillance Program of the U.S. Department of Defense, Armed Forces Health Surveillance Branch supports a repository for *Neisseria gonorrhoeae* (GC) clinical isolates recovered from routine care at U.S. Military Treatment Facilities in the continental US (CONUS) and at several overseas (OCONUS) labs though collaborative surveillance projects. Here we report the use of phenotypic data in conjunction with molecular typing and whole genome sequencing (WGS) of GC to describe the antimicrobial resistance trends from isolates collected from three geographically different clinics in Lima, Callao and Iquitos, Peru.

Methods Putative GC collected from patients between 2012 and 2015 were confirmed as GC using standard biochemical and serological methods. Susceptibility to eight different antibiotics was determined by Etest. β-lactamase (ßL) activity was determined by nitrocefin hydrolysis. NG-MAST types were determined by standard methods and WGS analysis.
Results Sixty eight out of 90 isolates examined were confirmed as GC. Antimicrobial susceptibility testing showed a high level of resistance to ciprofloxacin (70%) and lower percentages of resistant strains to other common antibiotics. Although 63% percent of isolates were β-lactamase positive by the nitrocefin test, only 70% of these isolates were Pen^R. The other 30% had reduced susceptibility to Pen (Pen^{RS}). Whole Genome Sequencing (WGS) revealed mutations in the bla_{TEM-1B} gene for these Pen^{RS} isolates. These isolates were collected from different clinics, but showed genetic relatedness based on nucleotide polymorphism (SNP)-based analysis. Several novel NG-MAST types were detected among the isolates.
Conclusion These findings highlight the high prevalence of multidrug resistant GC in Peru. The identification of NG-MAST types not identified in surveillance reports from Europe or the United States is important. Further, WGS allowed us to discern false positive β-lactamase isolates by detecting mutations in the bla_{TEM} genes observed in Pen^{RS} isolates and showed the clonally relatedness of these isolates.
Disclosure No significant relationships.

P646 AGENT-BASED MODELLING STUDY OF ANTIMICROBIAL RESISTANT *NEISSERIA GONORRHOEAE* TRANSMISSION

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Background Antimicrobial resistant (AMR) gonorrhoea is a global public health threat. Diagnoses of gonorrhoea have increased in England over the last decade. Guidelines in UK now recommend single dose ceftriaxone, so preserving the efficacy of ceftriaxone is essential. In England, over half of tested isolates remain sensitive to previously recommended drugs, e.g. ciprofloxacin. We evaluate options for improving antibiotic stewardship, through better use of existing surveillance data or new diagnostic tests.
Methods We previously developed an agent-based stochastic network model of gonorrhoea transmission, including ciprofloxacin-sensitive and resistant strains for MSM. This has been modified, to add a heterosexual population and a full model including bridging between MSM and heterosexuals. A novel feature is the time-varying network which breaks and reforms connections within a fixed cumulative network to capture behavioural heterogeneity in duration and number of partnerships. We explored different strategies to facilitate individualised treatment selection, including discriminatory POCT, and selecting treatment based on either index case or partner susceptibility.
Results Our MSM model suggests, based on 50% resistance to ciprofloxacin at baseline, that using POCT to detect ciprofloxacin-sensitive infections could reduce ceftriaxone doses by 70%. If index case susceptibility information were to be used to determine partner treatment, ceftriaxone use could be reduced by 27%. In the heterosexual model, the prevalence is much lower and could only be maintained through assuming higher transmission probability or duration of infection or via bridging to the higher prevalence MSM group.
Conclusion Novel POCT which identify susceptible infections are likely to come to market soon, but are costly. Mathematical models can evaluate the trade-offs between increasing test costs and reduced time to treatment or between delaying treatment to confirm susceptibility and reduce use of ceftriaxone in partners. The flexible model structure will be used in future to implement evolution of resistance and the impact of vaccination.
Disclosure No significant relationships.

P647 EFFECTIVE MONOTHERAPY DUE TO HIGH RATE OF AZITHROMYCIN RESISTANCE IN *NEISSERIA GONORRHOEAE* INFECTION IN MEN IN SOUTH AFRICA

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Background *Neisseria gonorrhoeae* drug resistance has emerged worldwide. There is limited data about the situation in South Africa where syndromic management is used for sexually transmitted infections (STIs). We investigated the antimicrobial resistance profile of *Neisseria gonorrhoeae* infections in high-risk men.
Methods We conducted a cross-sectional study at three primary healthcare facilities in Johannesburg, South Africa. We recruited: (a) men with persistent or recurrent discharge following recent treatment, and b) men-who-have sex with men (MSM) presenting with urethral discharge. Urethral swab and urine were obtained for culture of *Neisseria gonorrhoeae* on New York city medium followed by drug susceptibility testing using E-test with minimum inhibitory concentration (MIC) as per EUCAST guidelines. Molecular diagnostics for STIs were performed using the TIB MOLBIOL Lightmix Kit 480 HT CT/NG assay and real-time PCR assays for *Trichomonas vaginalis* and *Mycoplasma genitalium*.
Results We recruited 48 men of which 30 (63%) had persistent or recurrent discharge and 18 (37%) were MSM. Urine PCR was positive for *Neisseria gonorrhoeae* in 36 men (75%); *Chlamydia trachomatis* was detected in 9 (19%), *Mycoplasma genitalium* in 13 (27%) and *Trichomonas vaginalis* in 6 (13%). Gonococcal cultures were positive for 25/36 men (69%) with *Neisseria gonorrhoeae* detected molecularly. Isolates showed resistance to ciprofloxacin in 60%, penicillin 32% and tetracycline 60%. Reduced susceptibility to azithromycin was identified in 11/25 (44%) isolates: 5 were resistant (MIC range 1–8 µg/ml) and another 6 showed intermediate resistance. All MIC values for the cephalosporins and spectinomycin were within the susceptible range.
Conclusion The observed high rate of azithromycin resistance in *Neisseria gonorrhoeae* infection in our high-risk population is of great concern as it effectively results in monotherapy. These findings add to the debate on the best regimen choice for syndromic management, and emphasize that the introduction of diagnostics is a priority in our setting.
Disclosure No significant relationships.