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## AZITHROMYCIN PHARMACOKINETICS AND IMPLICATIONS FOR EXTENDED DOSES FOR CHLAMYDIA TRACHOMATIS AND OTHER SEXUALLY TRANSMITTED INFECTIONS

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Introduction Chlamydia treatment failure remains concerning with high repeat positive diagnoses of up to 14% in women and 22% for rectal infections in men. Meta-analysis estimates of rectal chlamydia treatment efficacy suggests azithromycin may be 20% less efficacious than doxycycline, but this is based on observational data only – with no RCTs evaluating rectal chlamydia treatment nor any pharmacokinetic data for azithromycin in rectal mucosa. This systematic review will examine the dose-related pharmacokinetics of azithromycin in blood and tissues with discussions on possible considerations of extended regimens to improve efficacy for anorectal infections should a 1 g dose prove suboptimal from RCTs.

Methods Medline and Embase were searched from 1946 to February 2015. Inclusion criteria were: English language, adults and reported pharmacokinetics after any oral dose of azithromycin. Studies of urogenital and rectal tissue were the primary focus but other tissues (excluding eyes) were included. Dose administered and pharmacokinetic parameters such as peak concentration and area under the concentration-time curve (AUC) were extracted.

Results Studies reported high concentrations of azithromycin in cervical, urological, gynaecological, pulmonary, prostatic and oral tissue/fluid after total doses of 500 mg to >2 g. No studies of rectal tissue were reported, however studies of gastric tissue/fluid (a proxy for rectal tissue) showed high concentrations being rapidly attained and sustained for >7 days. Increasing doses results in greater tissue concentrations, which are sustained longer above chlamydia minimum inhibitory concentration (MIC) but with only modest increases in peak blood levels between high and low doses. Similar tissue concentrations were obtained whether the total dose was given over short versus longer duration, suggesting regimens beyond (e.g. >3 days) do not have absorption advantages.

Conclusion Azithromycin concentrations above the MIC are rapidly attained and sustained following treatment. While no data are available in rectal tissue, studies in gastric tissue/fluid suggest adequate rectal concentrations should be obtained. Azithromycin pharmacokinetics also suggest that total doses >1 g given over a few days can be effective in delivering high concentrations to tissues susceptible to chlamydia infections.

Disclosure of interest statement None.

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## NUMBER OF SEX ACTS MATTERS FOR HETEROSEXUAL TRANSMISSION AND CONTROL OF CHLAMYDIA TRACHOMATIS

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Introduction Mathematical models are frequently used to assess the impact of control interventions for *Chlamydia trachomatis* and other sexually transmitted infections (STIs). Modelling approaches that stratify the population by the number of sex partners often assume the transmission risk per partner to be constant. However, sexual behaviour data suggests that people with many partners share less sex acts per partner than people with fewer partners. This should lower the risk of transmission per partner for highly sexually active individuals and could have important epidemiological consequences for STI transmission.

Methods We devised a new epidemiological model that we fitted to chlamydia prevalence data from Natsal-2 and CSF, two population-based probability sample surveys of sexual behaviour in Britain and France.

Results Compared to a standard model where the transmission risk per partner is constant, a model with realistic numbers of sex acts per partner provided a better fit to the data. The improved model provided evidence for strong assortative mixing ( $\epsilon = 0.83$ ; 95% CI 0.46–0.96) among individuals with different numbers of sex partners. The basic reproduction number ( $R_0$ ) exceeds the threshold of one for all individuals with one or more new heterosexual partners in the last year, and saturates around three for higher number of partners.

Conclusion Our results suggest that all chlamydia infected individuals with one or more new heterosexual partners per year contribute significantly to ongoing transmission, underlining that control interventions should be aimed towards all sexually active young adults.

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CLUSTER ANALYSIS OF CHLAMYDIA TRACHOMATIS
STRAINS USING TWO MULTILOCUS SEQUENCE TYPING
SCHEMES SHOWS DIFFERENCES IN DISCRIMINATION OF
MSM STRAINS VERSUS THOSE OF HETEROSEXUALS

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Introduction Despite intensive efforts Chlamydia trachomatis (Ct) remains the most common bacterial sexually transmitted infection worldwide. Therefore, to gain more insight into the epidemiology and transmission of Ct, multilocus sequence typing (MLST) schemes have been developed. However, there is no consensus regarding the use of an MLST scheme for epidemiological studies. Therefore, the objective of this study was to investigate the clustering of Ct strains using two MLST schemes with differing discriminatory capacities.

Methods We selected and tested samples from Ct infected men having sex with man (MSM) and heterosexual women using two existing MLST schemes. One MLST scheme was based on 6 highly variable targets in the chlamydial genome, also referred to as high-resolution MLST (hr-MLST-6) and the other scheme was based on 7 housekeeping genes (MLST-7). For this study, the existing MLST-7 scheme was modified to a nested PCR enabling to test clinical samples. Sequences obtained from both MLST schemes were analysed for cluster analysis and phylogenetic relationships.

Results Full profiles were obtained for 175 samples; 84 (48%) were from MSM and 91 (52%) from heterosexuals. We detected 32 sequence types (STs) using the MLST-7scheme and 78 STs using the hr-MLST-6scheme. Cluster analysis using hr-MLST-6data showed segregation between isolates from MSM and heterosexuals. However, cluster analysis using the MLST-7 data did not show this segregation between isolates from MSM and heterosexuals.

Conclusion The MLST-7 scheme was not able to discern closely related Ct strains over a small time-frame confirming that it is more suitable for evolutionary studies. For short-term cluster analysis the hr-MLST-6scheme is considered more suitable to study the epidemiology and transmission of Ct in various populations.

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## P08.36 CHLAMYDIA TRACHOMATIS INFECTION IN WOMEN IN GERMANY, 2008–2014

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Background Chlamydia trachomatis (CT) infections are not reportable in Germany and limited data on CT-prevalence among women is available. In 2008 an opportunistic CT-screening programme for women <25 years (OCS) was introduced. We assessed positivity rate of CT-infection among women and coverage of the OCS in order to develop recommendations for prevention.

Methods In September 2010 voluntary laboratory-based sentinel surveillance system was implemented and is collecting retrospective (from 2008) and prospective data on CT-tests together with information on age and test reason (TR). We calculated positivity rates (PR) by age-group and TR over years. We used Chi2 and two-sample t-test, accordingly. We estimated coverage of OCS by extrapolating the proportion of CT-tests attributable to OCS to the respective German population.

**Results** As of 10.04.2015 data from 24 laboratories were available for analysis. Overall 93% (3,440,131) of all tests (3,701,288) were among women. Among those 24% were

attributable to OCS, 36% to screening in pregnancy, 25% to diagnostic testing, and in 15% the TR was unknown. The coverage of OCS increased over time from 8% in 2008 to 11% in 2009, and 12% in 2014.

PR was highest in age-groups 15-19 (6.75%) and 20-24 (5.93%) years compared to age-groups <15 (3.38%), 25-29 (3.26%), and  $\geq 30$  (1.42%) years, p-value <0.001. PR gradually decreased from 2008 to 2014 in age-groups 15-19 (7.44% to 6.51%) and 20-24 (6.64% to 5.71%) years, p-value <0.001.

Conclusion The proportion of young women testing positive for CT is high despite gradual but slight decrease in PR among 15–24 years old women. OCS coverage in Germany is low and did not increase substantially in the last years. OCS should be promoted among the target population and physicians. Awareness campaigns for young women should be implemented. Respective regulations should be expanded and remuneration for counselling to physicians for OCS offered.

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## EPIDEMIOLOGICAL TRENDS IN CHLAMYDIA TESTING IN DENMARK 1991 TO 2011 AND FORMATION OF A RETROSPECTIVE, POPULATION-BASED COHORT: THE DANISH CHLAMYDIA STUDY

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Background Despite widespread, sustained testing for chlamydia in high income countries, there remain questions about the population impact of chlamydia screening. We analyse the epidemiological trends in chlamydia testing and chlamydia diagnoses in Denmark (1991 to 2011) and describe cases and controls for The Danish Chlamydia Study.

Methods We describe the Danish Chlamydia Study; a unique database of individuals involving linkage of administrative health data, chlamydia tests and hospital records. We analyse trends in testing and diagnosed incidence of chlamydia and selected reproductive outcomes in men and women in Denmark. The laboratory dataset contained 4,150,498 test records from 1,348,058 individuals (1/1/1991 to 2/11/2011). Cases: individuals with a positive chlamydia diagnosis; controls: age and gender matched, selected from Danish population register. The proportion ever tested and test positivity were calculated by age, gender and calendar year.

Results The cleaned laboratory dataset (1 confirmed test result per person, per day) consists of 3,298,104 test records with 264,410 (8%) positive chlamydia diagnoses. 1,277,463 individuals were tested (346,235 men and 904,587 women). Nearly all women and almost half of men in Denmark have been tested for chlamydia by age 30. Most individuals had only negative tests: 80% of men and 86% of women. Test coverage has increased and been sustained since 2008 but there has been no decline in positivity over time.

Individuals included in the Danish Chlamydia Study dataset: