O230
1-hour Oral Session
Modelling and metaanalyses of antimicrobial stewardship efficacy

Intelligent mixing of antibiotics: modelling the impact of informed prescribing on the development of resistance among Enterobacteriaceae

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Background: Extended spectrum beta-lactamase (ESBL)-producing and carbapenem-resistant (CR) *Enterobacteriaceae* are emerging globally. Reduction of inappropriate empiric prescribing could enhance individual patient outcomes, but might also aid in reducing the development and spread of resistance. This study aimed to perform a model-based evaluation of the effectiveness informed empiric prescribing through rapid diagnostic testing (RDT) in terms of emergence of ESBL-producing and carbapenem resistant bacterial subtypes.

Material/methods: Hospital-wide screening and clinical sample data were used to inform a deterministic compartmental model of *Klebsiella pneumoniae* acquisition in a 500-bed hospital, incorporating both colonisation and clinical infection (i.e. bacteraemia). Different antibiotic usage policies were simulated and evaluated, namely: 1) Current empiric prescribing guidelines for bacteraemia; 2) RDT informed prescribing; 3) Cycling (30 day intervals); 4) Mixing. Relative effectiveness was investigated under four levels of cross-transmission.

Results: Employing current empiric prescribing practice resulted in inappropriate treatment of 56% of infections caused by ESBL-producing subtypes and 100% of CR subtypes. In the base case scenario (i.e. 3 days delay until appropriate treatment and low transmission (net-reproduction number (Rn)=0.23), RDT informed prescribing reduced overall inappropriate prescribing by 10%. This was reduced to only 1% for the cycling regime, and, perhaps counter-intuitively, a minor increase in inappropriate prescribing (>1%) was observed for the mixing regime. As a result, RDT reduced ESBL prevalence (colonisation and clinical infection) by 2%, and CR prevalence by 5%, while cycling saw a smaller reduction in prevalence of resistant subtypes. Mixing yielded, albeit limited, ESBL and CR-emergence. The effects were stronger when levels of cross-transmission were high.

Conclusions: In settings of low transmission, RDT informed empiric prescribing would have minimal effect on the emergence of resistance. Studies on the measured impact of inappropriate treatment on excess mortality have been inconclusive to date. Reliable estimates of this impact are needed to allow assessment of the impact of RDT on individual patient outcomes, and this is an important area for further research. Random allocation of antibiotic treatment types through cycling regimes has proven effective in theory. However, the higher likelihood of inappropriately treated resistant subtypes caused

these to spread under mixing regimes, especially when transmission levels were high. Further understanding of resistance mechanisms in Gram-negative rods is needed, to allow realistic incorporation of within-host dynamics and the relative importance of transmission vs. selection under antimicrobial pressure in the potential impact of reducing inappropriate treatment.