O233
1-hour Oral Session
Modelling and metaanalyses of antimicrobial stewardship efficacy

Quantifying where selection occurs: a mathematical modelling approach to better inform antimicrobial resistance control

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Background: Antibiotic resistant bacteria are selected via the use of antibiotics. In the face of increasing rates of antibiotic resistance, we must consider how and where to decrease this selective pressure. In the UK, although the majority of clinically used antibiotics are prescribed in the community, the problems with resistant pathogens are mostly faced in the hospital environment. In this work we investigated whether selection within the community or the hospital environment was a more significant driver of antibiotic resistance by using a mathematical model of selection and transmission. Our aim was to provide the first estimate of relative selection in these two interacting environments and determine the key parameters that need to be further investigated.

Material/methods: A mathematical modeling framework was created to explore the selection of antibiotic resistance in the community vs. in the hospital, by considering differences in antibiotic exposure and bacterial transmission as patients move between the two environments. Resistance in an individual could arise via selection or transmission of bacteria. Patients with resistant bacteria were tracked in order to record whether their resistance carriage was due to acquisition in the hospital or community setting. Due to the uncertainty in parameters, we explored large areas of likely parameter space and considered whether selection for resistant bacteria was stronger in hospitals or the community. These results were compared against UK data on beta-lactam resistance within the most common causative agent (>60%) of bacteraemias: *Escherichia coli*. We performed sensitivity analysis to explore which parameters had the biggest impact on this selection.

Results: Our modeling framework suggests that the majority of antibiotic resistance selection may be occurring in the community rather than in the hospital environment. This held true under a wide range of parameter combinations. For example, for parameters corresponding to beta-lactam resistant *E. coli,* less than 30% of resistance was likely to be generated in the hospital setting. Our sensitivity analysis suggested that the key parameters driving the difference in selection were levels of transmission of bacteria and levels of antimicrobial exposure, as well as time to clearance of resistance carriage in the community.

Conclusions: This novel modeling framework suggests that societal interventions to decrease antimicrobial resistance could have a greater impact if they decrease antimicrobial use in the community rather than in hospital settings. This is likely to be specifically true for beta-lactam resistant *E. coli.* Mathematical modeling approaches such as this allow us to identify future research needs in order to determine optimal intervention design. By including further model complexity, we can explore selection in further different environments and in different bacteria to improve our quantitative understanding of where resistance is acquired.