MRC LID Project Proposal

Background

In the last decades, antibiotics have greatly reduced the public health threat posed by bacteria. Nevertheless, antimicrobial resistance (AMR) is now becoming a global issue that must be dealt with urgently, as highlighted in the Review on Antimicrobial Resistance. In this review commissioned by the UK government in 2014, AMR is predicted to cause 10 million deaths worldwide per year by 2050 if we fail to implement key interventions (Review on Antimicrobial Resistance, 2016).

Amongst the microorganisms which have successfully acquired various resistances, methicillin-resistant staphylococcus aureus (MRSA) is one of the key threats. It represents at least 25% of all S. aureus isolates in a third of European countries (European Centre for Disease Prevention and Control, 2017). In addition, patients infected with MRSA have a 42% higher risk of dying compared to patients infected with regular S. aureus (Cosgrove et al., 2003). This data clearly underlines that MRSA is already an important public health issue, and it is crucial to prevent it from becoming an even greater one.

MRSA is now a well characterized organism, therefore the focus has shifted from understanding it to developing new interventions against it. However, while real-life studies are ultimately the most reliable source of scientific evidence, their results can be hard to generalize and apply to different contexts. Mathematical modelling is often the tool relied upon to generate predictions, used in turn to formulate public health strategies. In addition, it is already commonly employed to study AMR (van Kleef et al., 2013). For this reason, I believe that mathematical modelling of MRSA is a field where much research is needed, and one where I could make a meaningful contribution.

My desire to work on this topic has led me to select the project “What drives antibiotic resistance diversity? Modelling for MRSA control” offered by Dr Gwenan Knight (Department of Infectious Disease Epidemiology, LSHTM) as part of the MRC LID programme. I have had the opportunity to meet with Dr Knight to discuss potential research questions regarding MRSA. This pathogen is usually restricted to the hospital setting, but has the potential to spread and thrive in the community (Fridkin et al., 2005). However, there is limited data available to prepare for this scenario. Consequently, understanding the impact of interventions in the hospital and being able to apply the results to the community would undeniably be valuable. We believe that mathematical modelling could be a useful method to do this by representing the transmission dynamics of MRSA, and extrapolating data from one location to facilitate the design of interventions in another. My research question would therefore be “How can we generalize the effects of interventions against MRSA using mathematical modelling?”.

Research Methodology

The first step of this project will be to design new mathematical transmission dynamics models to study the impact of multiple interventions (hand hygiene, screening, antibiotic stewardship…). I am already familiar with complex mathematical modelling through my Undergraduate Final Year project, where I worked with [removed]. The focus of this research was to modify an existing transmission dynamics mathematical model of malaria to visualise the community impact of insecticide-treated nets, and assess the importance of this phenomenon for controlling the disease. This opportunity allowed me to develop my modelling skills, since I worked on a complex model simulating the effects of various interventions in a heterogeneous human population exposed to a dynamic mosquito population in the Berkeley-Madonna modelling software. In addition, I have independently

learned to use the “odin” package in the R software to develop models. It is my personal interest to explore new modelling tools to be flexible when answering a specific research question, since relying on a single framework is often not enough. Overall, this has provided me with a solid base of knowledge in mathematical modelling, and I feel that the research I would undertake in this PhD would perfectly build up on those skills.

In parallel to the design of the models, we will gather new data on MRSA transmission and prevalence. Based on discussions with Dr Knight, we hope to obtain access to data from specific wards in hospitals. This would allow me to precisely parameterize the models developed during my research, and improve their accuracy compared to traditional models which typically rely on regional or local data. In particular, this data would provide information on the impact of local S. aureus strains heterogeneity on the incidence of MRSA, a feature not yet fully understood. In addition, further data will be collected from laboratory experiments in a parallel project directed by Professor Jodi Lindsay (Institute of Infection and Immunity, St George’s University of London). I believe that my BSc degree in Microbiology has provided me with the necessary background laboratory knowledge for this research. I am confident that I will be able to fully understand the experiments taking place in the lab, and the data obtained from these and from hospitals. This will allow me to be more efficient in my own modelling work, without requiring additional assistance to guide me through the data.

Impact of the results

As explained previously, I believe that this research would lead to the design of well-parameterized models of the impact of interventions on the transmission of MRSA. These predictive tools have the potential to assist the design of intervention strategies in other areas where local research is lacking. The environment that would benefit the most from this research would naturally be the hospital, which is where our data will have originated from. However, if I am able to parameterize the model with more precise individual-level data compared to the standard regional data, the conclusions could be extended to MRSA in the community.

Finally, the results of this research could be relevant to other cases of AMR. For example, hand hygiene would also reduce the transmission of many other microorganisms, such as E. coli. Consequently, the results of this research could be generalized to other pathogens to some extent, or used as a basis for further research into different microorganisms.

Conclusion

Methicillin-resistant staphylococcus aureus is a model organism for studying antimicrobial resistance. I believe that research on MRSA modelling incorporating new data from hospitals and the lab would allow us to create effective predictive tools to guide the design of interventions in various locations. In addition, the results could be generalized to prepare against an eventual spread of the pathogen in the community. Finally, the conclusions we would reach on the efficacy of interventions could be generalized to other organisms displaying AMR, thereby increasing the usefulness of this research.

After having spent the past 4 years at [removed], I now wish to change my working environment while remaining in London. The LSHTM is a world-renowned institution in terms of public health research, and is therefore the most relevant place for me to study at since it aligns with my own research interests. I visited the university last year during an open day, and greatly appreciated the facilities and the staff there. For these reasons, I feel that I would fit at the LSHTM perfectly to work on the research I am most interested in, and that it is the ideal institution to enable the environment change I seek.

Upon completing my MSc in Epidemiology degree, I am certain that I will have finally acquired the necessary skills to confidently undertake a PhD in MRSA modelling. I believe that the MRC LID Studentship would place me in an optimal position to provide the best quality of work possible; I am persuaded that the LSHTM is the best institution for me to study at, especially in this field. I therefore hope that you will consider my application for this studentship, which would grant me the opportunity to join a world class institution while contributing to the research on a topic I am passionate about and which could greatly contribute to improving global public health.

References:

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