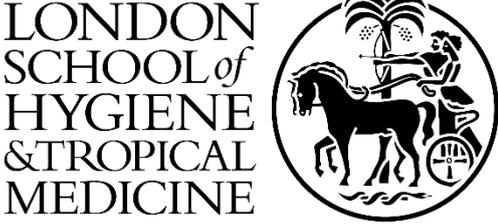


MRC LID Studentships: 2023-24 Research Project

	
<p>TITLE OF PROJECT</p>	
<p>Antimicrobial Resistance Diversity: quantification, evolution, and importance for public health</p>	
<p>SUPERVISORY TEAM</p>	
<p>Supervisor</p>	<p>Dr Gwen Knight Email: Gwen.Knight@lshtm.ac.uk</p>
<p>Co-Supervisor</p>	<p>Professor Jodi Lindsay Email: jlindsay@sgul.ac.uk</p>
<p>PROJECT SUMMARY</p>	
<p>Project summary</p>	<p>Antimicrobial resistance (AMR) is a growing global problem, that requires innovative, cross-disciplinary solutions. However, the dynamics that underpin the transfer and stability of resistance genes within bacterial populations and how this affects the diversity in AMR in a host population is poorly understood.</p> <p>In this project, we will use mathematical modelling and data analysis to quantify the distributions of resistance in the clinically important bacteria methicillin resistant <i>Staphylococcus aureus</i> (MRSA). The evolution of AMR diversity will then be dynamically modelled by fitting to experimental data on gene transfer. From this, the effect of AMR diversity on AMR surveillance and intervention impacts will be quantified to support improvements in control of this public health priority.</p>
<p>Project key words</p>	<p>Antimicrobial resistance Mathematical modelling MRSA Resistance diversity Intervention impact</p>
<p>MRC LID themes</p>	<p>Infectious Disease Health Data Science Global Health Translational and Implementation Research</p>
<p>MRC Core Skills developed through this project</p>	<p>Quantitative skills Interdisciplinary skills</p>

Skills we expect a student to develop/acquire whilst pursuing this project	Antimicrobial resistance, microbiology, mathematical modelling	
Is this project available for students applying for the 1+4 route? And possible Master's options identified by supervisory team	Route	1+4 = Yes +4 = Yes
	Suitable Master's programmes	LSHTM – MSc Epidemiology
Particular <u>prior</u> educational requirements for a student undertaking this project		
PROJECT IN MORE DETAIL		
Scientific description of this research project	<p>Methicillin resistant <i>Staphylococcus aureus</i> (MRSA) is one of the biggest contributors to infections with, and deaths due, to antimicrobial resistant bacteria globally. Many MRSA infections can still be treated, but as successful clones spread, they accumulate additional antibiotic resistances. Resistance in MRSA is due partly due to mutations, but most is driven by genes carried on mobile genetic elements (MGEs) that transfer frequently. This rapid rate of transfer and the variance in antibiotic exposure means that high levels of diversity have been seen in the antibiotic resistance profile of bacterial isolates isolated from hospitals and even within individual patients.</p> <p>The objectives of this project are:</p> <ul style="list-style-type: none"> - To quantify the distribution of resistance diversity within patient samples and hence hospitals - To determine the evolution and rates of MGE shuffling and hence resistance diversity maintenance within clinical populations of MRSA - To explore the impact that this diversity has interventions to tackle antibiotic resistance such as screening and antibiotic stewardship. <p>The techniques to be used will be:</p> <ul style="list-style-type: none"> - Data analysis and model fitting to determine parametric distributions for resistance diversity in different settings - Evolutionary mathematical models fit to existing and newly generated data from resistance transfer experiments - Develop transfer assays to explore stability and resistance diversity levels under different competition - Dynamic transmission models to explore bacterial transmission within hospital settings fit to data on within host populations <p>Resources</p> <ul style="list-style-type: none"> - Several active hospital collaborations will provide patient level information on resistance diversity in hospitals 	

	<ul style="list-style-type: none"> - A comprehensive set of clinical MRSA isolates from the UK and Europe are already available and characterised with whole genome sequencing (WGS). - Mathematical modelling training and support within the Centre for Mathematical Modelling of Infectious Diseases (CMMID) at LSHTM - MRSA laboratory with all assays and resources for studying and characterising resistance available at St George's as well as data from past experiments <p>Potential risks Common surveillance methods do not sample more than one bacterial isolate so data on the diversity within patients may be limited. However, this is (a) important to understand and quantify and (b) could be tackled as has been done in previous work through collaboration with the hospital microbiology service at St George's.</p>
<p>Further reading (Relevant preprints and/or open access articles)</p>	<p>https://pubmed.ncbi.nlm.nih.gov/25957384/</p>
<p>Additional information from the supervisory team</p>	<p>The supervisory team has provided a recording for prospective applicants who are interested in their project. This recording should be watched before any discussions begin with the supervisory team. To access the recording please see MRC LID Project – Knight & Lindsay.</p>