MRC LID Studentships: 2023-24 Research Project

TITLE OF PROJECT		
Comparing drug-resistant tuberculosis empirical treatment choices		
SUPERVISORY TEAM		
Supervisor	Dr Finn McQuaid Email: Finn.Mcquaid@lshtm.ac.uk	LSHTM
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PROJECT SUMMARY		
Project summary	With an estimated 30% of AMR-related deaths a result of drug-resistant TB globally, the choice of drugs used for treatment of TB disease is of the utmost importance. However, many cases of TB disease are treated without a complete knowledge of the resistance profile of the underlying bacteria, due to a lack of availability of diagnostic tests. The aim of this project will be to improve the decision-making around such empiric therapy, by using mathematical modelling and quantitative methods to balance and assess the factors contributing to the decision-making process. The intention will be to inform development of treatment guidelines, to ensure that treatment decisions are based on a comprehensive consideration of evidence.	
Project key words	Tuberculosis Drug-resistance Modelling Health economics	
MRC LID themes	Infectious Disease Global Health Health Data Science	
MRC Core Skills developed through this project	Quantitative skills Interdisciplinary skills	
Skills we expect a student to develop/acquire whilst pursuing this project	Mathematical modelling skills, including coding. Economic evaluation skills, including costing and integration of approaches into transmission modelling.	

	Public health knowledge and communication skills, including with country-level decision-makers and technical assistance organisations.	
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	Undergraduate and/or graduate degree in biological sciences, with evidence of additional quantitative skills OR Undergraduate and/or graduate degree in epidemiology, biostatistics, mathematics, physics, health economics or other quantitative science	
PROJECT IN MORE DETAIL		
Scientific description of this research project	With an estimated 30% of AMR-related deaths a result of drug-resistant TB globally, the choice of drugs used for treatment of TB disease is of the utmost importance. Currently, most cases of TB disease are treated without any knowledge of the resistance profile of the underlying bacteria due to a lack of availability of diagnostic tests. This project will aim to improve the decision making around such empiric therapy by using quantitative methods to balance and assess the factors contributing to the decision making process. In particular, testing for resistance to second-line drugs such as fluoroquinolones has low coverage (median ~40%) and can take weeks. However, clinicians faced with results demonstrating multidrug (resistance to rifampicin and isoniazid) or rifampicin resistance (MDR/RR) have a clear incentive to start a patient on treatment; this is likely to increase the chances of successful treatment, as well as decrease morbidity and onward transmission. In 2019 alone, roughly 165,000 patients were faced with this decision, of whom ~20% likely had TB resistant to fluoroquinolones. National TB programmes are then faced with a choice on how to proceed in the absence of (or while waiting for results from) a fluoroquinolone DST. They could recommend starting treatment with either a regimen that assumes fluoroquinolone susceptibility, or one that assumes fluoroquinolone resistance. Each option has risks that vary by the population, in particular the prevailing fluoroquinolone resistance. These include the risk of treatment failure and onward transmission if an ineffective regimen is prescribed, the risk of resistance amplification, the risk of adverse events associated with more toxic regimens, and costs associated with more expensive regimens. As a result, there is the potential for TB programmes to be treating a large number of people with suboptimal regimens.	

	1. Project objectives: The aim of this project will be to develop evidence to assist in decision-making for treatment guideline development when only an MDR/RR DST result is available in a given setting. In addition, the work will serve to highlight the value of rapid fluoroquinolone DST; as availability of DST increases, further information is required on its added value in different settings. The objectives will be • To evaluate the evidence for empiric prescribing for treatment with different levels of drug resistance prevalence • To develop models of MDR/RR-TB treatment outcomes in different settings, including mortality, the incursion of adverse events, amplification of resistance and cost associated with all of the above. • To evaluate treatment regimen choice under different circumstances for a given set of values. • To explore how such models could inform empiric treatment more generally. 2. Techniques to be used: Mathematical modelling and epidemiology and/or economic evaluation 3. Confirmed availability of databases No databases will be required as publicly available data will be used. 4. Risks to the project These include insufficient data on treatment regimen outcomes (mitigated by the exploration of parameter space), and insufficient data linking TB treatment outcomes to value (mitigated by simplifying our assumptions here, at the expense of a more detailed understanding of the issue).
Further reading (Relevant preprints and/or open access articles)	https://doi.org/10.5588/ijtld.20.0330
Additional information from the supervisory team	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 – McQuaid & Knight.