



Title of PhD project	Use of novel negative control techniques: an application to cardiovascular and vaccine research	
Supervisor	Dr Angel Wong	LSHTM
Co-Supervisor	Dr Yingfen Hsia	SGUL
Co-Supervisor	Dr Elizabeth Williamson	LSHTM
Brief description of project	<p>This PhD project is an exciting opportunity to join the well-established Electronic Health Record Group at the London School of Hygiene and Tropical Medicine, and the paediatric infectious disease research group at St Georges' University London. The PhD candidate will analyse population-based routine health data (Clinical Practice Research datalink with several large linked datasets) to answer a range of outstanding cardiovascular and vaccine related research questions by applying cutting-edge negative control techniques in self-controlled studies, and cohort studies with propensity scores.</p> <p>Application to drug interaction with oral anticoagulants Warfarin has traditionally been used for the prevention of thrombotic events among people with atrial fibrillation but it is well known to interact with many medications. Newer direct oral anticoagulants (DOACs) have been perceived as safer and more convenient alternatives to warfarin but the understanding of drug interactions with DOACs is still insufficient. Therefore, this PhD project will utilise a modified case-crossover study design to investigate drug interactions with DOACs compared with warfarin. Outcomes include risk of ischaemic stroke, venous thromboembolism, cardiovascular mortality, bleeding and all-cause mortality.</p> <p>Application to effectiveness of pneumococcal vaccines There is an urgent need to understand the potential beneficial role of non-COVID-19 vaccines in preventing COVID-19 related outcomes. There have been limited studies investigating such association and their results might be biased due to confounding. Self-controlled case series (SCCS) was initially developed to investigate vaccine safety to eliminate time-invariant confounding. This PhD project will perform a modified self-controlled case series with an active</p>	

	<p>comparator to account for both time-varying and time-invariant confounding. Cohort studies with propensity scores will also be conducted and repeated using negative controls (with negative control calibration) to compare findings with self-controlled studies.</p> <p>There has been an increasing trend in harnessing big healthcare data to conduct timely and evidence-based research. Our group has established a strong track record of high-quality research regarding cardiovascular drugs and vaccines in electronic health record data.</p> <p>A skill set including conducting a systematic review, performing analysis of electronic health records, and utilising advanced epidemiological methods to investigate drug effects for both communicable and non-communicable diseases will be acquired after completing this PhD project.</p>
<p>Skills we expect a student to develop/acquire whilst pursuing this project</p>	<p>We expect the student to develop skills in:</p> <ol style="list-style-type: none"> 1) Systematically searching and identifying relevant literature; 2) Critically appraising the literature on the implementation of negative control; 3) Extracting, cleaning and analysing large-scale electronic health records (CPRD); 4) Conducting modified case-crossover studies and selecting suitable negative controls, with a specific focus on drug interactions with oral anticoagulants; 5) Applying the new method of using a negative control as a comparator in self-controlled case series study design and implementing negative control calibration in a cohort study design.
<p>Particular <u>prior</u> educational requirements for a student undertaking this project</p>	<p>Applicants must hold, or expect to obtain before the start of the PhD; a relevant MSc awarded with good grades, or have a combination of relevant qualifications and experience which demonstrates equivalent ability and attainment.</p> <p>This project can also be awarded as 1+4 (1-year MSc programme + 4-year PhD candidature). Through this route, a relevant BSc awarded with good grades is required.</p>
<p>Project key words</p>	<p>Electronic health records Negative control Pharmacoepidemiology Cardiovascular safety Oral anticoagulants Pneumococcal vaccine</p>
<p>Possible under 1+4 route? Master's options identified.</p>	<p>Yes</p>

	<p>LSHTM - MSc Health Data Science LSHTM - MSc Epidemiology LSHTM - MSc Medical Statistics</p>
MRC Core Skills developed through this project	Quantitative skills
MRC LID themes	Health Data Science
Further reading	<p><u>Negative Controls: A Tool for Detecting Confounding and Bias in Observational Studies</u></p> <p><u>The Case–Crossover Design for Drug–Drug Interactions: Considerations for Implementation</u></p>