R12

Hub: Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU)	Host University: University of Oxford
Supervisor: Martin J Landray martin.landray@ndph.ox.ac.uk	Co-supervisors: Colin Baigent, Will Herrington Natalie Staplin
Is the project clinical or non-clinical? Non-clinical or clinical	
Title of PhD project: Can routine healthcare data be used to efficiently and reliably follow-up participants in renal trials: analyses using linked data from 2 large renal trials	

Background to the project: Evidence from randomized clinical trials is essential for the reliable evaluation of the safety and efficacy of medical interventions, yet nephrology as a speciality generates the least number of trials, despite chronic kidney disease affecting around 5-10% of the middle- and old-aged Western population and accounting for £1.6 billion of UK healthcare costs per year. In this high risk and neglected population, considerable uncertainty remains about the safety and efficacy of many old drugs which no longer attract industry funding for trials. In such a situation, radical changes are required to lower the cost of running trials. In contrast, nephrology is advanced in its development of registries, which now record detailed information on all renal replacement therapy patients and can collect laboratory data real-time from all renal units (>65) in the UK. Developing trials which solely rely on registry and routine hospital admission data for follow-up could transform the evidence base that underpins renal care. The results of the proposed work on trial methodology in this PhD will impact directly on trials currently under development in Oxford and other UK trials units, including the NIHR-funded SIMPLIFIED trial of 4000 dialysis patients being run by Cambridge Clinical Trials Unit.

What the studentship will encompass: The studentship will focus on data from two large renal trials: (a) the Study of Heart and Renal Protection (SHARP) which is the largest trial in a renal disease population, randomizing 9438 patients (including 1987 from the UK) and following them for an average of 5 years during 2003-2010 (Lancet 2011; 377(9784):2181-92); (b) the 3C trial of 852 kidney transplant patients followed since 2010 (Lancet 384(9955):1684-1690). During both trials, participants were followed directly in nurse-led clinics with supporting evidence, in the form of hospital notes, collected for all major study outcomes. These were subject to clinician adjudication blind to treatment allocation and according to standard definitions. This methodology PhD is proposed to include the following:

1. A systematic review of previous published work assessing the validity of using routinely collected hospital admission data in the UK for cardiovascular, renal and infective outcomes, with an emphasis on data specific to renal populations.
2. Assessment of the completeness and reliability of Hospital Episode Statistics (HES) and Welsh/Scottish equivalents, for outcomes of interest in renal trials, by comparing these with the nurse-reported events for SHARP and 3C, and the separately with the 'gold standard' clinician adjudicated outcome datasets. Outcomes will include major cardiac events (including heart failure), stroke and its subtypes, revascularisation procedures, end-stage renal disease events, admissions with acute kidney injury, and a range of infections.
3. Collaborating with the PhD candidate Graham Powell at the North West MRC Trials Methodology Hub to disseminate findings to other Hubs and to the renal community via the UK Kidney Research Consortium Clinical Trials Network.
4. Should HES data be sufficiently reliable, the candidate will propose methods on how HES data is handled alongside other sources of outcome data, assess whether current CDISC standards are for fit for this purpose.

Detail of supervision: Lead supervisor is Prof Martin Landray, who is co-Principal Investigator (PI) for SHARP and 3C, Deputy Director of the Big Data Institute, and responsible for the UK Biobank health informatics hub (including use of hospital admissions data for the 500,000 participants in England, Wales and Scotland). He will be supported by Prof Colin Baigent (SHARP/3C co-PI, Director MRC Population Health Research Unit); Dr Will Herrington (renal clinician epidemiologist who performed much of SHARP adjudication); and Dr Natalie Staplin (senior statistician, Renal Studies Group, CTSU).

Planned secondments: None planned but opportunities may arise to work with other Hubs on similar projects (see item 2 above) or to work with the UK Renal Registry.

R12

Supplementary information

1. Describe the alignment of the project with the HTMR Network strategy

This PhD project has the potential to have a major effect on the efficiency of future renal trials and also includes reporting long-term SHARP/3C follow-up results. It therefore fits nicely with the Network's strategy of 'Improving Health by Improving Trials'. The project also has the potential to support a trial run at the Cambridge Clinical Trial's Unit - the NIHR-funded SIMPLIFIED trial of 4000 dialysis patients which relying solely on routinely collect healthcare data for all follow-up.

2. Does this project align with the work of a HTMR Working Group; if so, which?

This PhD aligns most closely with the work of the HTMR Trial Conduct group as the main aim of this project is to make substantial improvements in efficiency of future trials and long-term follow-up. It is proposed that a successful candidate would join this group. The Outcomes research working group will also find the results of this work of interest.

3. Describe how this project aligns with the host Hub strategy

This fits well into the CTSU Hub strategy to achieve reliable results through supporting streamlined approaches to conducting large cost-effective randomized trials of relevance to public health. The successful candidate will be able to draw on CTSU's expertise in large-scale clinical trials, experience of using routine healthcare data (hospital admissions, death, cancer) for other trials and for UK Biobank, and integral role in data analytics capacity of the Big Data Institute.

4. Detail of any Project specific training offered in the studentship

The project will provide a range of opportunities and training in the design and conduct of clinical trials as well as statistical aspects of trials methodology research. By the end of the project students would be expected to be fluent in all aspects of late phase clinical trial design, conduct and analysis. There will be opportunities to be involved in collaborations across the MRC HTMR network, learn to write project proposals, to attend relevant training courses and to present your research findings at relevant meetings. The project will be based in the Clinical Trial Service Unit and Epidemiological Studies Unit which has excellent facilities, and a world-class community of clinical scientists, trialists, and statisticians.

5. Are there any prerequisite qualifications or experience for this studentship?

Candidates for an MRC-funded studentship must meet residence eligibility and hold qualifications in a relevant subject at the level of, or equivalent to, a good honours degree from a UK academic institution (see methodology website for more details- www.methodologyhubs.mrc.ac.uk).

For this project: The successful applicant is expected to have a good grounding in data processing and statistical analysis, and will work closely with experienced clinicians, statisticians, data analysts and computer programmers.

A PhD candidate at the Nuffield Department of Population Health needs to demonstrate:
1. Proven academic excellence (ie, 1st class or upper second-class undergraduate degree; or international equivalent)
2. Proficiency in English
3. Research or employment experience relevant to population health