3 year PhD studentship in Health Sciences, commencing in September 2017

Comparative effectiveness of sodium-glucose co-transporter-2 inhibitors and glucagon-like peptide-1 receptor agonists in type 2 diabetes mellitus: randomized and real-word evidence

Available to UK/EU applicants only

Supervisors:
Dr N Dhalwani nnd2@le.ac.uk (Department of Health Sciences) and Prof K Khunti kk22@le.ac.uk (Diabetes Research Centre)

Project Description:
This PhD project will aim to examine the clinical effectiveness of GLP-1RAs and SGLT-2is combining RCTs and “real-word” evidence. Specific objectives are:

1. To conduct a network meta-analysis to assess the comparative effectiveness of GLP-1RAs and SGLT2is using information from RCTs
2. Conduct a longitudinal study using routinely collected primary care data to assess the effectiveness of SGLT2is and GLP-1RAs in type 2 diabetes in the real world
3. Synthesise the evidence from RCTs and real world studies together
4. Assess the comparative cost-effectiveness of SGLT2is and GLP-1RAs

Brief outline plan of research over the 3-7 years:
The project will involve the use of published aggregate-level data and available large existing datasets such as the Clinical Practice Research Datalink,

Assuming an intake of a full-time PhD student the following table describes a tentative research plan for the course of the PhD.

<table>
<thead>
<tr>
<th>Time</th>
<th>Task</th>
<th>Objective</th>
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<tbody>
<tr>
<td>Months 1-10</td>
<td>Network Meta-analysis</td>
<td>Evidence of the effectiveness of drugs from the trial</td>
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<tr>
<td>Months 10-20</td>
<td>Longitudinal studies</td>
<td>Real World Evidence of the effectiveness of the drugs</td>
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<tr>
<td>Months 20-24</td>
<td>Evidence synthesis</td>
<td>Combining RCT and observational evidence</td>
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<tr>
<td>Months 24-32</td>
<td>Health economic analysis</td>
<td>one of the selected two data sources) Health care utilisation and health care costs, benefits of healthy lifestyle</td>
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<td>Months 33 onwards</td>
<td>Thesis writing</td>
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Methodology to be used:
1. Systematic literature review
2. Synthesis of available RCTs evidence with a network meta-analytical approach
3. Data management and manipulation of large primary care datasets
4. Combination of randomised and observational evidence
5. Health economic analysis

**Background to Project:**

A range of glucose-lowering medications are currently available for the treatment of hyperglycaemia in patients with type 2 diabetes. In the last few years, two new classes of glucose-lowering drugs have been introduced and widely used [1]: glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium-glucose co-transporter-2 inhibitors (SGLT-2i). The efficacy and safety of different formulations of GLP-1RAs and SGLT-2i have been extensively compared to other glucose-lowering therapies in several randomised clinical trials (RCTs) [2-3]. Very limited, on the other hand, is the evidence from direct comparisons between GLP-1RAs and SGLT-2i.

Current ADA/EASD guidelines suggest either GLP-1RAs or SGLT-2i as add-on to metformin (alone or in combination with other treatments) if glucose control is not achieved; however, no specific suggestions are given about which agent should be preferred [4]. In this view, it would be relevant to know which medication performs better and is associated with a lower risk of side effects to help decision makers in an informed choice.

When direct ‘head-to-head’ data are unavailable or limited, network meta-analysis (NMA) is considered the methodology of choice to estimate the comparative effectiveness of multiple treatments [5]. Recently, softwares to perform NMA have been made available in widely-used statistical softwares (i.e., Stata and R), widening their applications. Data from published RCTs can therefore be synthesised using NMA to evaluate differences across treatments and rank them according to a specific outcome.

For a better and wider understanding of treatment efficacy, however, data from RCTs should be considered along with “real-word” evidence (RWE). RWE supplements the knowledge obtained from RCTs, whose limitations are the generalisability to larger, more inclusive populations of patients [6]. Large primary care databases (i.e., Clinical Practice Research Datalink) have been used to evaluate the effects of treatments in “real-world” patients although the evidence about glucose-lowering effects of GLP-1RAs or SGLT-2i is very limited. Furthermore, recent methodological advancements make possible to “combine” evidence from RCT and RWE accounting for their differences [7].

A more precise estimate of GLP-1RAs or SGLT-2i effects obtained from RCTs and RWE data can also allow performing a health economics analysis to compare these new classes of treatments with other available glucose-lowering drugs.

**Funding Notes:**

The studentship is funded by East Midlands CLAHRC which is a collaboration of University of Leicester and associated partners.

The award will pay full-time University UK/EU tuition fees for three years and include a tax-free annual maintenance grant worth at least £14,553 a year.

**References:**

Endocrinol 2012;8: 495-502

How to Apply:
Please submit your application using our online application system. In order to apply please select Health Sciences Research for a September 2017 intake. In the Funding section of the online application indicate Health Sciences Studentship.

Please indicate the name of the project supervisor(s) and the project title in the space provided within the application.

Application enquiries to pgradmissions@le.ac.uk

Project enquiries to Dr N Dhalwani nnd2@le.ac.uk (Health Sciences) and Prof K Khunti kk22@le.ac.uk (Diabetes Research Centre)

Closing date: Monday 15th May, 2017