Background to the project: Diabetes develops over a long period of time, has substantial costs and is associated with high morbidity and mortality. Randomised trials in diabetes provide key effectiveness data but are limited by short duration of a few years which is insufficient to estimate the long-term health gains and costs of interventions and guide healthcare reimbursement decisions. Computer simulation models of diabetes aim to support such evaluations and regular scientific meetings are organised to present advances in the area of diabetes modelling and compare model performance [1]. However, the model's suitability to simulate disease progression in target population/s is not guaranteed and the model/s might not be suited to evaluating effects of target intervention/s. Hence, new methods are often required. We would like to recruit and mentor a high-calibre graduate with interest in health to undertake doctoral research on the methods for assessment of long-term effects of aspirin in diabetes. The work will include reviews of current methods and data, evidence synthesis and methods/model development and validation. The rich individual participant data of the 15,000-patient ASCEND (A Study of Cardiovascular Events in Diabetes) trial (7.5 years mean follow up) [2] will be extensively used in the project together with external data.

What the studentship will encompass: Initial overview of existing modelling methods in diabetes will be followed by:

- Validation of the performance of UKPDS outcomes model[3] (based on 1977-2007 data on ~5000 patients with newly diagnosed type 2 diabetes), the recommended computer simulation model for diabetes by the National Institute for Health and Care Excellence, using the ASCEND trial data with particular focus on performance in predicting cause-specific mortality and morbidity overall and in different categories of participants in ASCEND.
- Development of a substantive adaptation to the UKPDS outcomes model or a novel diabetes simulation model using UKPDS outcomes model, data from the ASCEND trial and other published data. This may involve adapting the UKPDS outcomes model to allow for the direct effects of aspirin on different cardiovascular outcomes (eg on MI, ischaemic and haemorrhagic strokes), gastrointestinal bleeds, and (colorectal) cancer to be evaluated. Alternatively, if the UKPDS model is found to be unable to capture the disease progression observed in ASCEND, a new model will be developed.
- Development of quality of life and healthcare costs' evaluative frameworks that include all relevant disease and intervention outcomes for the evaluative question. For example, different cardiovascular outcomes, other serious bleeding events (well phenotyped in ASCEND) and cancers (eg, colorectal cancer) are of particular interest in the assessment of effects of aspirin and have not been concurrently evaluated previously.
- Evaluation of cost-effectiveness of aspirin and the value of collecting further data. The value of reducing decision uncertainty will be evaluated with respect to particular parameters, such as aspirin's effects on cancer.


Detail of supervision, including the roles of any named co-supervisors: Associate Professor Borislava Mihaylova will be the principal supervisor and will provide guidance on all aspects of project. Associate Professor Louise Bowman will provide guidance on epidemiology of diabetes, aspirin effects and ASCEND and other relevant data. Dr Jose Leal will provide guidance on the UK PDS outcomes model and the diabetes modelling aspects of the project.

Detail of any planned field work/ Secondments/industry placement: The UK PDS model validation work will be included at future Mount Hood Challenge meeting. The newly developed model framework will also be disseminated and included in the model-comparison challenge. Collaboration with other HTMR researchers in particular with respect of the value of information analysis component will be sought and is likely to benefit from short visits.
Supplementary information

1. Describe the alignment of the project with the HTMR Network strategy
The project will foster further collaboration within the MRC HTMR (see point 2) as well as with other internationally recognised researchers in the area of diabetes modelling. The UK PDS outcomes model, developed by researchers in Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford in collaboration with others is one of the core contributors to the Mount Hood diabetes modelling biennial challenge. The outputs from the projects will be widely disseminated and made available for external use. We are also well aware of shortage of suitably trained and experienced high quality researchers in this research area through our latest recruitment campaigns and are confident that this post will help alleviate this shortage. The project has a particular focus on enabling analysis of effects in categories of patient in order to support stratified decision making.

2. Does this project align with the work of a HTMR Working Group; if so, which?
Borislava Mihaylova is a member of the Evidence Synthesis and the Health Economics HTMR network working groups. The work aligns very well with both groups with respect to its data synthesis/ modelling/ VoI analytical approaches and its methods for costs/QoL parts, respectively. The successful student will be involved in both working groups and progress and emerging results from his/her DPhil project will be discussed within the relevant working groups and in more detail with relevant member experts from the networks.

3. Describe how this project aligns with the host Hub strategy
The Clinical Trial Service Unit Hub, Oxford specialises in the development, implementation and analysis of large clinical trials to address important policy questions in the area of chronic conditions including cardiovascular, kidney and diabetes disease. One area of work related to the trials is the development of the economic analyses to support the implementation of the study interventions in clinical practice. The proposed project is aligned to support development of the methods and researchers to support this area of work. The outputs of the programme of work are expected to contribute to the economic analyses of the ASCEND trial but the methods developed during the project will be of wider relevance to modelling disease and propagating intervention’s treatment effects in RCTs.

4. Detail of any Project specific training offered in the studentship
Further training (some through external courses) will be offered in the fields of Health Economics; Decision Analytic modelling; Advanced Survival Analysis; Systematic review and Meta-analysis and Value-of-Information analyses if not already covered in previous training by the successful candidate.

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: First-class or strong upper second-class undergraduate degree with honours (or equivalent international qualifications) is required. The project is quantitative in nature and a previous academic degree in a quantitative discipline (e.g., Statistics, Mathematics, Economics, Epidemiology, Operation Research) or, if in different discipline, the inclusion of substantial and well-graded quantitative component, is required. Applicants whose first language is not English are usually required to provide evidence of proficiency in English at the higher level as required by the University of Oxford.