Does fatty liver disease predict cardiovascular outcomes independently of other known cardiovascular risk factors? An analysis of data in the UK biobank.

Section 1 – Project Details:

Maximum 800 words, using the following headings

Rationale:
It is well recognised that non-alcoholic fatty liver disease (NAFLD) occurs more commonly in a number of groups at high risk of cardiovascular disease, and it has been suggested that NAFLD is therefore a component of the so called metabolic syndrome which predisposes to IHD. This may be of importance in a number of ways, both in suggesting populations at risk of liver disease, but also potentially in identifying those at greater risk of IHD. To date there is no good evidence that NAFLD is an independent predictor of cardiovascular outcomes primarily as the assessment of its existence has been based on poor biomarkers (AST/ALT levels), or because the association has been made to proximate end points. If NAFLD is an independent risk factor for CVS disease it could potentially enhance existing cardiovascular risk prediction models such as Framingham and QRisk through its inclusion, leading to more efficient and cost-effective approaches to disease prevention.

Aims and methodology:
Within the UK biobank 4949 subjects have had MRIs of their livers within which fat has been measured, and of these 96.4% had successful measurements made. This gives an excellent assessment of NAFLD. This same resource provides also for highly valid prospective recordings of cardiovascular outcomes including MI, CVA and cardiovascular death. Further the UK biobank contains enough haematological and by Autumn of 2017 biochemical data to allow the calculation of potentially more reliable composite markers of NAFLD from simple blood tests than have previously been used to study prediction of IHD, and the necessary data to calculate conventional risk scores for IHD.

We therefore propose a PhD in which UK biobank data will be obtained and analysed in a series of cohort and cross sectional studies to answer the following questions

1. Does liver fat content measured by MRI independently predict cardiovascular outcomes?
2. Do the available composite blood predictors of NAFLD correlated with liver fat as measured by MRI?
3. Do the available composite blood predictors of NAFLD (from point 2) independently predict cardiovascular outcomes?
4. How does the addition of measures of NAFLD in the general population alter the existing cardiovascular risk prediction algorithms?

Benefits and suitability as a PhD project:
This PhD studentship offers a unique opportunity to work at the interface of clinical practice and public health. Whilst developing essential research skills the student will be delivering research with direct clinical impact and the potential to influence positive changes in policy and practice. Chronic liver disease has been identified as a national priority for research; as such this work is both crucial and timely. That such a PhD should be offered in
Nottingham is especially appropriate as the University has strengths in MRI (a cross cutting theme of the BRC), database epidemiology and academic hepatology (also a subtheme of the BRC).

For the student this project will place them in an optimal position for a future research career both due to the prioritisation of this area of healthcare and research, but also because of the particular skills provided. Making use the UK Biobank resource for this work will give experience of a data source increasing exponentially in its scope and importance, and therefore will position the student very well to maximise its use in future. Beyond academia recent PhD students supervised by members of the supervisory team have gone on to positions in the pharmaceutical industry, the NHS and the WHO.

**Key References:**


**Section 2 – Training Provision:**

Maximum of 250 words. Please detail the training provision that will be made available to the student.

This project will train the candidate to become an expert in the use of routinely collected healthcare data, epidemiological and statistical design and analysis, and risk prediction
modelling. The student will receive training in epidemiology and the management and analysis of electronic data sets via modules of the EPH master’s program (DOME, Basic statistics and epidemiology, Advanced Statistics). They will additionally complete appropriate training from the courses dedicated to the Nottingham PhD program, and will have close direct supervision to ensure their ability to complete the work. Two of the supervisors (TC and JW) have extensive experience of successful supervision of similar projects, and a 100% record of completion of their PhD students (n=13).

Beyond this direct training we will be able to provide an excellent general environment for the student’s learning. They would work alongside our current team of Post-Doc’s and PhD students and gain the help and support of their peers and we will also support the candidate in obtaining a mentor through the University of Nottingham Mentor scheme. They will contribute to the EPH PhD group meetings and also to the seminar series conducted in both EPH and the NDDC, and thereby have the opportunity to learn about ongoing research in both epidemiology and public health and hepatology, and to present their own data to both of these in house audiences in preparation for external presentations.