

## **Principal Investigator**

Professor Sarah Parish

## **Address**

University of Oxford, CTSU, Old Road Campus, Headington, Oxford  
OX3 7LF

## **Summary of research**

Key words: Cognition, vascular risk factors, genetics, causality

**1a:** Various vascular risk factors, such as, blood pressure, diabetes and obesity, have been associated with cognitive decline and dementia in observational studies. Elevated blood pressure is a strong risk factor for stroke, which can cause cognitive impairment. However, whether vascular risk factors have a causal impact on cognitive decline, other than through risk of stroke, remains unclear. Many genetic variants produce lifelong differences in specific vascular risk factors and can be used to form scores for the genetic elevation of each factor. The association of the genetic scores with cognitive function will be investigated to assess causality.

**1b:** Dementia care is a major burden on health resources. Establishing the impact of modifiable vascular risk factors on dementia could contribute importantly to cost-benefit assessments guiding the use of vascular disease therapies and to lifestyle advice. In addition, a validation of the bespoke cognitive function measures used in UK Biobank will be undertaken through

comparison of the associations for age, stroke and the APOE genotype with those from analyses of the established TICS-M score in ~50K participants entered into three randomised trials of vascular therapies. This validation will enhance interpretation of the UK Biobank resource in future use.

**1c:** More than 300 genetic variants have now been robustly identified as associated with various vascular risk factors and can be used to form genetic risk scores for the separate vascular risk factors. The associations of cognitive function with each genetic score will provide tests for causal associations between lifelong differences in the factors and cognitive function. The analyses will be repeated in older and higher vascular risk subsets of UK Biobank. When sufficient hospital episodes involving dementia and/or brain imaging markers of dementia become available we will repeat such analysis for these indicators of dementia.

**1d:** Full cohort