



### **Principal Investigator**

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### **Applicant Institution**

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### **Application Number / Title**

10171 - Nutritional and lifestyle influences on neurocognitive and mental health: genetic epidemiological study on causal effects, mediating pathways and gene-environment interaction

### **Keywords**

Mendelian-randomisation; interaction; cognition; depression; lifestyles

### **Application Lay Summary**

**1a:** Nutrition and lifestyles are important for health, including neurocognitive diseases. However, evidence about the role of a particular factor is often weak, it is not known how the effects are modified by genes, or what are the pathways (metabolic, neurological, other) mediating the effects of lifestyles on health. We will examine causal effects and gene-environment interactions affecting the way obesity, diet or other lifestyles affect the risk of cognitive decline, dementia and mood disorders. This study will aim to establish new disease prevention strategies, and inform on the way we can overcome disease inducing genetic vulnerabilities by lifestyle choices.

**1b:** The proposed will further understanding of the role of nutrition and other environmental factors on neurocognitive and mental health. It will inform prevention and treatment strategies directly by demonstrating causal influences, and indirectly through establishing metabolic and vascular pathways through which these exposures influence our health. As we are largely focussing on modifiable lifestyles, this work will inform on public health messages which will empower individuals to improve their neurocognitive and mental health. This work may also lead to identification of pharmacological targets and the development of treatments, through novel insights into the mediating pathways, and gene discovery.

**1c:** In addition to observational analyses, we will utilise two genetic epidemiological approaches. We will use a Mendelian Randomisation approach to identify causal effects on neurocognitive and mental health. In MR genetic variants (SNPs) are used

to proxy for nutrition or other environmental exposures, allowing us to overcome some of the problems with other types of study. By gene-environment interaction analyses, we will look how common genetic variations (genomewide, and candidate gene SNP data) modify the effects that lifestyles or nutrition have on the outcomes. This can lead to novel gene discovery and tailored treatment strategies accounting for genetic background.

**1d:** Full cohort