Project Details	
Project Code	MRCNMH25Ex Tyrrell
Title	Metabolic psychiatry – Understanding ethnic and global differences in the inter-relationships between obesity and mental health
Research Theme	Neuroscience & Mental Health
Summary	Many people live with multiple health conditions, but research still tends to focus on individual diseases. This project, focuses on two global health problems with a complex relationship: obesity and mental health. The student will become an expert in metabolic psychiatry, training at 3 world leading centres. They will utilise global studies, with genetic and life course approaches to understand complex relationships between obesity and mental health.
Description	This exciting interdisciplinary global health PhD will provide the student with an excellent underpinning in metabolic psychiatry, a new and exciting area focusing on the shared aetiology of metabolic and mental health. There is growing interest in the causes and consequences of multimorbidity, but huge research gaps remain, especially in diverse ethnic groups. This PhD addresses these issues, focusing on the inter-relationships between obesity and the mood-psychosis spectrum of severe mental illness (SMI; schizophrenia, bipolar disorder and severe depression). This topic represents an area of high priority for patients and their families because people with SMI have very high rates of obesity, type 2 diabetes and increased mortality from cardiovascular disease. There is some evidence to support shared causal and/or bi-directional mechanisms between metabolic dysfunction (e.g. obesity, type 2 diabetes) and psychopathology. However, many unanswered questions remain, for example it is not clear if these relationships are consistent globally nor whether lifestyle and diet partially explain the causal relationships. The student will use cutting-edge methods for causal inference, and for interrogating causal effects in ethnically diverse populations – both across the UK and across multiple global settings. The focus on diverse populations is a key priority area for genetic epidemiology, which has historically been biased towards white European populations.
	The student will use large cohort studies and genetic summary statistics in 100,000s of people to address several questions:
	1. Is there a bidirectional causal relationship between the SMIs and obesity, and does this relationship vary by ethnic group in the UK and global settings?
	2. What modifiable risk factors (e.g. physical activity, diet, smoking, medications) explain or mediate the relationship between SMIs and obesity, and do causal pathways differ across ethnic groups?
	3. Which factors mitigate against the negative impacts of SMIs on obesity and vice versa, and do these resilience-promoting factors differ across ethnic groups?
	Identifying causal associations in populations with diverse ancestries will provide important information about the complex and potentially setting-specific relationships between obesity and SMIs, thereby informing global decisions on medical management and public health strategies for both conditions over the life course. This builds on work led by the supervisory team members in Exeter, Bristol and Cardiff

exploring the role of genetic and environmental factors in higher BMI on depression in Europeans and South and East Asians and in considering mental-metabolic multimorbidity across the life course.

The student will have the opportunity to develop skills in several cutting-edge methodologies, including genetic (e.g. Mendelian randomisation (MR) and copy number variants (CNVs)) and epidemiological approaches in several datasets (e.g. UK Biobank, China Kadoorie Biobank). The student will gain skills in:

1. Statistical analyses: Regression models; mediation analysis; lifecourse epidemiology approaches.
2. Genetic analyses: One- and two-sample MR; MR for mediation; MR in populations with diverse ancestry; within-family MR; analysis of CNVs.
3. Data science: handing large datasets including electronic health records.
4. Clinical science: psychiatric assessments and cardiometabolic health.

The student will be able to tailor their PhD based on areas of interest, for example, focusing on a specific SMI. They will work across disciplinary boundaries, with their supervisors and external collaborators coming from molecular/genetic, epidemiological, psychiatric and physical health and advanced biostatistical backgrounds. We believe this PhD will provide an excellent platform for a successful scientific career, focusing on two high priority research areas, multimorbidity and diverse populations.

Supervisory Team	
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