

## **Principal Investigator**

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## **Summary of research**

Metabolically Healthy Obesity, Metabolically Obese Normal weight

## **Application Lay Summary:**

1a: In the proposed research we seek to leverage the large sample size of the UK Biobank data to study the etiology and disease risk of "Metabolically Healthy Obese" (MHO) and "Metabolically Obese Normal-Weight" (MONW) individuals accounting for their cardiometabolic heterogeneity. The large sample size will present an unparalleled opportunity to study the subtypes observed among the MHO and among the MONW by focusing on the separate cardiometabolic components (i.e. blood pressure, glycemic traits, lipid traits, markers of inflammation). We aim to study their prevalence, etiology and risk of disease and mortality.

1b: The proposed research is entirely congruent with the stated aim of UK Biobank to improve "the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses".

The characterization of MHO and MONW has high clinical relevance as their risk of disease and mortality will likely differ from the obese and normal-weight

group. Inferences derived from well-powered and well-designed epidemiological studies underpin efforts to offer improved strategies for prevention, diagnosis and treatment. Through focusing on MHO/MONW, we aim to gain insights in mechanisms that link obesity and cardiometabolic complications in the general population.

1c: Obesity is a major risk factor for cardiometabolic complications. However, some obese are protected from one or several of these complications, despite excess adiposity. Conversely, some normal-weight suffer from one or several cardiometabolic abnormalities, despite being lean. The reasons why some obese are protected and why some normal-weight are at risk are poorly understood. We propose to describe the prevalence of the “metabolically healthy obese” (MHO) and “metabolically obese normal-weight” (MONW). Subsequently, we will examine whether lifestyle or genetics contribute to being MHO/MONW. Finally, we will examine whether being MHO/MONW affects disease risk and mortality.

1d: We would like to include the maximum available number of participants.

Project extension:

“We have data on environmental data, such as physical activity and plan doing a GWAS on physical activity to examine whether it mediates the association with BMI.”