Application number/Title:  30592 - Vitamin D and Major Depression: understanding the causal relationship and shared genetic influences

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Keywords provided by the Applicant PI to describe the research project:
Depression, Vitamin D, Genetics

Application Lay Summary:

1a: Increasing evidence suggests that low circulating levels of 25-hydroxyvitamin D [25(OH)D] may play a role in the pathophysiology of depression. Using genetic epidemiology methods, we propose to investigate the causal relationship and shared genetic influences of serum 25(OH)D and major depression. Specifically, we aim to:
(1) Quantify the amount of genetic overlap between serum 25(OH)D and major depression
(2) Assess the causal directionality, if any, of the relationship between serum 25(OH)D and major depression

1b: The proposed study will provide further understanding of the role of vitamin D in major depression etiology. Investigating the genetic overlap between vitamin D levels and major depression may identify biological mechanisms that could eventually inform novel pharmacological targets. Moreover, elucidating the causal relationship between vitamin D and major depression could contribute to the development of prevention strategies and personalized medicine. Given the high prevalence and healthcare burden of major depression and vitamin D deficiency in the general population, this project is of significant public health interest, which aligns well with the purpose of the UK Biobank.

1c: We will perform a statistical analysis to determine the amount of genetic
covariation between vitamin D levels and depression. We will conduct an analysis, known as Mendelian Randomization, that allows us to examine the causal effects of vitamin D on depression and vice versa. Because genetic variants are randomly assorted to offspring, we can use genetic variants previously shown to influence vitamin D levels or depression to effectively randomize vitamin D levels and examine their effect on depression (and vice-versa). This will avoid many of the problems in inferring causality that have limited prior observational studies.

1d: We require access to data from the full cohort with individual level genetic data, serum 25(OH)D measures and baseline questionnaire data on demographics, health conditions, and lifestyle factors.