**Application number/Title:** 27412 - Boosting the power of GWAS using novel statistical tools

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**Keywords provided by the Applicant PI to describe the research project:**

Bayesian statistical genetics, complex traits disorders

**Application Lay Summary:**

1a: This proposal seeks to apply UK Biobank data to study the genetic architecture of human traits using novel statistical tools. We aim to investigate the relationship between mental disorders and co-morbid diseases such as cardiovascular disease, cancer and metabolic disease (as well as protective phenotypes). Genome-wide association studies (GWAS) have successfully identified many genetic variants influencing complex human traits. However, the identified genetic variants only explain a small portion of the heritability of these traits. To improve discovery of genetic variants in complex human traits, we have developed statistical tools building on a Bayesian statistical framework.

1b: This proposal seeks to increase discovery of genetic loci influencing a range of human traits and disorders. Identifying genetic factors that confer risk or protect against health-related traits is critical for understanding the causal mechanisms underlying disease, and the causal relationship shared between clinical conditions. Improved gene discovery might inform the development of genetic prediction tools and ultimately improve treatment strategies for large patient groups. Hence, the proposed research is entirely congruent with the stated aim of UK Biobank “to improve the prevention, diagnosis and treatment of illness and the promotion of health throughout society”.

1c: We will analyze the GWAS data on complex traits in the UK Biobank cohort using novel statistical methodology. Using software and computational tools we are able to enhance gene discovery by integrating GWAS data with additional

knowledge about genetic variants, including their association in related traits or their genomic position. To assess the replicability (i.e. the robustness of the results) of the identified variants, we will evaluate their association in independent GWAS cohorts. Finally, the results may inform the development of novel genetic prediction tools.

1d: We would wish to study the full UK Biobank cohort.

Project extension:

This proposal seeks to apply UK Biobank data to study the genetic architecture of human traits using novel statistical tools. We aim to investigate the relationship between mental disorders and co-morbid diseases such as cardiovascular disease, cancer and metabolic disease (as well as protective phenotypes). Genome-wide association studies (GWAS) have successfully identified many genetic variants influencing complex human traits. However, the identified genetic variants only explain a small portion of the heritability of these traits. To improve discovery of genetic variants in complex human traits, we have developed statistical tools building on a Bayesian statistical framework. Furthermore, the statistical framework also takes into account of genetic relationships across multiple traits, trying to find a more succinct and objective definition of mental disorders. To maximize the available information, we intend to extract phenotypic information from the raw bulk data, which novel phenotypic features can be derived given our statistical framework. In particular, we will derived genetically orthogonal features from biometric measurements, similar to what have been performed in the neuroimaging field and metabolomic studies. Novel derived phenotypic variables will be generated and shared with the research community to facilitate clinical translations.