Application number/Title: 30921 - Methods development for improved inference from meta-GWAS summary statistics

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Keywords provided by the Applicant PI to describe the research project: statistical-methods-development

Application Lay Summary:
Fine-mapping of GWAS results is an important post-discovery step, and an area of active statistical development by our groups. Previously we developed ‘JAM’, which enables fine-mapping from GWAS summaries by imputing genetic correlations from a reference dataset. We would like to explore using the UK Biobank as a reference dataset for summary data methods such as JAM. The large number of participants will provide detailed correlation structure, which should allow more accurate fine-mapping of much denser regions. In addition to methodological development, planned applications within the project include Prostate Cancer, Cardiovascular Disease and Autoimmune Disease. The availability of enhanced methods for more accurate genetic fine-mapping from publically available disease and disease trait meta-GWAS results are clearly in the public interest. Initially we will use the UK Biobank genotype data in realistic and large-scale simulation studies to support a range of methodological extensions to JAM, including computational improvements to handle a much larger reference dataset, the use of JAM to generate genome-wide causal instruments, and an extension to leverage variant-specific functional annotation. Subsequently, genetic correlations from the UK Biobank data will be used in the application of the resulting methods to fine-map publically available meta-GWAS summary statistics for a range of diseases and disease traits; including prostate cancer and autoimmune disease. Called and imputed genotypes for the full cohort please.