Principal Investigator

Prof Andrew Morris

Address

University of Liverpool, Department of Biostatistics, Duncan Building, Daulby Street, Liverpool L69 3GA, United Kingdom

Lead Collaborators: 1) Dr Cecilia Lindgren
2) Dr Reedik Mägi
3) Dr Rachel Freathy

Collaborating Institutions and Addresses:

1) University of Oxford, Wellcome Trust Centre for Human Genetics, Roosevelt Drive, Oxford OX3 7BN, United Kingdom
2) University of Tartu, Estonian Genome Centre, Riia 23B, Tartu 51010, Estonia
3) University of Exeter, Medical School St. Luke's Campus, Magdalen Road, Exeter EX1 2LU, United Kingdom

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Summary of research

Gestational Diabetes, Genome, Co-morbidities, Epidemiology

Application Lay Summary:

1a: Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy, and increases risk of prenatal and delivery complications. GDM also increases predisposition to long-term adverse health outcomes in both the mother and her offspring, including type 2 diabetes (T2D). Risk factors for GDM include polycystic ovary syndrome (PCOS), pre-pregnancy obesity, and family history of diabetes, but evidence from twin studies suggests that there is a major genetic component to predisposition. In this proposal, we will determine environmental, lifestyle and genetic risk factors for GDM in UK Biobank through epidemiological investigations and genome-wide

association analyses.

1b: GDM occurs in ~3-5% of all UK pregnancies. Glucose intolerance is usually resolved after delivery, but increases risk of adverse pregnancy outcome, including preterm labour, intensive neonatal care, and pre-eclampsia. GDM often recurs, and is associated with adverse health impacts including metabolic syndrome, T2D, and cardiovascular disease, in both the mother and her offspring. Most women with GDM are treated with lifestyle modifications, although insulin is required when these changes do not maintain glycaemic control. The identification of risk factors for GDM thus fits with the central aim of UK Biobank to improve the prevention, diagnosis and treatment of diseases.

1c: We will conduct epidemiological analyses to identify demographic, disease, environmental and lifestyle factors associated with increased risk of GDM. We will then perform genome-wide association analyses of DNA-genotyping data to identify genetic variants that increase the likelihood of GDM, after accounting for these "epidemiological" risk factors. We will also perform sub-phenotype analyses to investigate epidemiological and genetic risk factors for GDM-related adverse pregnancy outcomes and subsequent development of T2D and cardiovascular disease. We will also investigate the overlap of the genetic contribution to GDM with co-morbid traits, including T2D, obesity, and PCOS.

1d: For these analyses, we request access to data generated for all women in UK Biobank. We request information on relevant demographic, environmental and lifestyle factors that are potentially associated with GDM (such as anthropometric measures and diet summaries), co-morbidities and downstream adverse health outcomes (such as PCOS, T2D, and cardiovascular disease), family history of diabetes, and pregnancy complications (such as caesarean section, miscarriages, pre-eclampsia, and birth weight of first child). We also request genetic data (from direct genotyping and imputation) for all women in UK

Biobank to evaluate association of genetic variants with GDM after accounting for lifestyle factors.