Project Details	
Project Code	MRC23PHSBr Borges
Title	Using multi-omics to improve prediction and early diagnosis of pregnancy complications
Research Theme	Population Health Sciences
Summary	Pregnant women are among the most neglected populations in medical (and genomics) research. This PhD will aim to address this research gap by promoting innovation in risk stratification and early diagnosis of APOs. This is key to inform tailored antenatal care and reduce unnecessary interventions and costs to health services, leading to improvements in equitable and sustainable health.
Description	More than a third of pregnant women will have complications during pregnancy, such as miscarriage, pre-eclampsia, gestational diabetes, perinatal depression, preterm birth, and fetal growth restriction. These pregnancy-related complications carry a heavy burden to the health and wellbeing of mothers and their babies. Therefore, identifying women at high risk is essential to provide them with effective and timely treatment to prevent such complications. Currently, the UK National Institute of Health and Care Excellence (NICE) guidelines recommend screening women with certain risk factors (e.g., maternal age, parity, BMI, ethnicity) for some pregnancy complications, such as gestational diabetes and gestational hypertension. However, many women without these risk factors go on to develop such complications, emphasising the need for better prediction tools. 'Omics refers to scientific fields that comprehensively measure and characterise molecular phenotypes or modifications (e.g. gene expression, DNA methylation, proteins, and metabolites). High dimensional 'omics data have the potential of providing a comprehensive approach to identifying new predictive biomarkers for diseases and using 'omics technologies in large scale population studies has now become possible owing to recent technological advancements. However, most of the current studies investigating the clinical utility of using 'omics to improve prediction of pregnancy-related disorders are small and have not validated their models or used appropriate methods to assess prediction performance. This project offers the exciting opportunity of exploring, for the first time, the potential of multi-omics for prediction of pregnancy complications at scale using rigorous methods. It is particularly timely due to (i) the recent availability of large-scale genetic and clinical data (N > 500,000 women) from the MR-PREG collaboration, led by Dr. Borges and Prof. Lawlor; (ii) the unprecedented generation and compilation of molecular data collected during pregnancy or at delivery as part of Prof. Lawlor's MRC research programme; (iii) the rigorous methodological framework led and proposed by Dr McBride (1, 2); and (iv) the expertise of Prof. Murray and Prof. Lawlor on reproductive genomics. In addition, the student will engage with other epidemiologists, biologists, obstetricians, and statisticians based in Bristol and Exeter ensuring she/he is aware of the latest methodological developments in the field, and maximising impact and knowledge transfer across disciplines. Specific objectives The student will lead on projects to address the specific objectives detailed below: 1) Assess the potential of polygenic scores to improve prediction of pregnancy complications using data from

	> 500,000 pregnancies by (i) deriving and validating polygenic scores for multiple pregnancy complications, and (ii) assessing the transportability of polygenic scores across ancestries 2) Investigate the prediction utility for pregnancy complications of high-dimensional omics data measured in maternal blood samples routinely collected during antenatal care (i.e. DNA methylation, proteomics, and metabolomics) using rigorous protocols for feature selection (e.g. via machine learning), performance assessment and performance metrics selection as outlined in recent publications (1-3). This will include comparing discrimination of molecular models at different gestational times and among women from different socioeconomic backgrounds and ancestries 3) Explore the potential of using placenta transcriptomics to discover new candidate circulating biomarkers for prediction of pregnancy complications Potential differences between ethnic and socioeconomic groups will be key feature of the work. References 1. McBride et al. BMC Med. 2020;18(1):366. 2. McBride et al. Metabolites. 2021;11(8). 3. Yousefi et al. Nat Rev Genet. 2022.
Supervisory Team	
Lead Supervisor	
Name	Dr Maria Carolina Borges
Affiliation	Bristol
College/Faculty	Bristol Medical School
Department/School	Population Health Sciences
Email Address	m.c.borges@bristol.ac.uk
Co-Supervisor 1	
Name	Professor Deborah Lawlor
Affiliation	Bristol
College/Faculty	Bristol Medical School
Department/School	Population Health Sciences
Co-Supervisor 2	
Name	Dr Anna Murray
Affiliation	Exeter
College/Faculty	Medical School
Department/School	
Co-Supervisor 3	
Name	Dr Nancy McBride
Affiliation	Bristol
College/Faculty	Bristol Medical School
Department/School	Population Health Sciences