Project Details	
Project Code	PHS27Br AFraser
Title	The placenta and lifelong health of mothers and their offspring
Research Theme	Population Health Sciences
Project Type	Dry lab
Summary	The placenta is critical to a healthy pregnancy yet is often described as the least understood human organ. This project will investigate the genetic and environmental determinants and long term health consequences of placental impairment using newly generated, globally unique placental pathology data. Placentas were collected >30 years ago as part of the Avon Longitudinal Study of Parents and Children. Mothers and offspring have been followed-up ever since. You will be supported to tailor the project to your interests: e.g focus on a specific type of pathology and/or health outcomes such as preeclampsia, cardiovascular disease or offspring neurodevelopment.
Description	The great obstetrical syndromes such as pre-eclampsia, preterm birth and fetal growth restriction are associated with significant maternal and neonatal morbidity and mortality as well as a two-fold increased risk of maternal cardiovascular disease later in life. Whilst the exact causes of these syndromes are not well-understood, impaired placentation and placental function are implicated. Despite the placenta's critical role in supporting a healthy pregnancy, it is one of the least studied human organs.[2] Pathological findings are more common in placentas from complicated pregnancies compared with placentas from healthy pregnancies; but even placentas from healthy pregnancies can present with pathology. This may be due to the placenta's ability to compensate for some level of impairment. In many settings, placentas from complicated pregnancies are routinely examined by expert placental pathologists to inform neonatal care, risk stratification (of neonates and future pregnancies), and counselling. However much less is known about the frequency and long term consequences of placental pathology in uncomplicated pregnancies. This is due to a lack of population-based collections of placentas and the absence of longitudinal studies that include placental pathology and information on long-term health in mothers and offspring. The current project will leverage globally unique data on 2,000 placentas collected as part of the Avon Longitudinal Study of Parents and Children (ALSPAC), a world-leading pregnancy cohort initiated in the early 1990s. Placentas have been examined by an expert placental pathologist who was blinded to clinical information (other than gestational age which is needed for some diagnoses). Pathology reporting follows the Amsterdam Consensus Statement on the reporting of placental findings.[3] ALPSAC mothers and offspring have been followed-up for over three decades and a wealth of health-related information, including genetics, is available on both generations. This PhD will be the first to use this unique resource to address knowledge gaps regarding the causes – both genetic and environmental – and long term sequalae of placental pathology in both mothers and their offspring. Key research question:

	What are the determinants and long-term health consequences of placental pathology in mothers and/or their offspring. Specific objectives: The student will be encouraged to develop the project according to their research interests and particular gaps that they wish to explore. The following are potential projects that will provide the student with experience using a range of analytical methods and data types. 1. To identify causal risk factors for placental pathology. Here the student could focus on a single or multiple pathologies such as vascular malperfusion, inflammation and/or umbilical cord morphology. Potential analytical approaches include multivariable regression adjusting for confounders, exposure negative control analysis using paternal data and Mendelian randomization. 2. To identify maternal and fetal genetic variation associated with placental pathology. This objective will provide the student with experience in genetic epidemiology, including common and rare variation through genome wide association studies (GWAS) and the analysis of polygenic risk scores. 3. To investigate shared genetic architecture of clinical pregnancy complications e.g. pre-eclampsia, preterm birth, placental pathology and CVD. Here the student will gain skills in colocalization analysis. , global and local genetic correlation estimation, and genomic structural equation modelling. 4. To investigate the long-term health consequences of placental pathology in mothers and/or offspring. The student will be supported to focus on outcome of interest to them, e.g. cardiovascular health, developmental health (offspring). Potential analytical approaches include multivariable regression and Mendelian randomization using results from project 2. 5. To determine whether placental pathology can improve CVD risk stratification in mothers. Here the student will gain skills in prediction modelling.
Can be completed part time?	Yes
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