Project Details	
Project Code	MRC22PHSEx Beaumont
Title	Using genetics to understand the links between preterm birth and lung disease in childhood
Research Theme	Population Health Sciences
Summary	Babies who are born prematurely are more likely to develop lung disease, but the underlying mechanisms are poorly understood. This project will combine world-class training in genetics, epidemiology and data science to test the hypothesis that genes and intrauterine exposures which lead to prematurity also lead to reduced future lung function.
Description	Babies born prematurely often have increased respiratory symptoms and reduced lung function in childhood and beyond. It is increasingly recognised that they are at a greater risk of prematurely developing chronic obstructive pulmonary disease (COPD). However, the underlying reasons of their developing poor respiratory health are unknown. Using well-established cohorts including RHiNO and ALSPAC the student will explore the role of genetic and intrauterine factors in preterm birth and childhood respiratory dysfunction. Improved understanding of the mechanisms linking prematurity to lung function are crucial to improve treatment for these vulnerable babies. The successful student will apply state-of-the-art quantitative methods to available large datasets to examine the links between preterm birth and childhood lung function. Specifically, the student will: 1. Examine the relative contributions that environmental and intrauterine factors make to poor childhood lung function in babies born preterm. The student will learn about clinical aspects of the problems faced by a premature baby and about lung function as they grow up. They will also learn the use of (i) linear regression techniques to identify intrauterine and environmental factors (from the intrauterine and wider environment) associated with lung function in preterm infants, and (ii) the principles of Mendelian Randomisation, which uses genetics to test for causal relationships between environmental factors and lung function in childhood. The student will have access to a range of datasets with detailed phenotype data and parent and offspring genotype information available locally including RHiNO (Cardiff), ALSPAC and MCS (Exeter/Bristol), as well as through collaborations (Norwegian MoBa cohort) to disentangle maternal and fetal genetic effects. 2. Examine genetic links between preterm birth and lung function. The student will investigate genetic links by identifying common and rare genetic variants that have established associations with preterm birth and/or lung function. They will then investigate the associations of the identified variants with lung function and preterm birth in publicly available datasets, such as the UK Biobank which has detailed phenotype data as well as common and rare genetic data on 500,000 individuals. 3. Test the hypothesis that babies whose birthweight and gestational age deviates from that predicted by their genetics have higher risk of poor lung function in childhood than those whose birthweight is as predicted by their genetics. The student will learn the principles of calculating genetic scores, and will test using different machine learning techniques to define individuals who do and do not deviate from their genetically predicted birthweight or

	gestational age. 4. Explore prediction models to identify preterm babies who are at risk of poor lung function using phenotypic and genetic data, building on the results of 1-3 above. The student will learn approaches to prediction modelling, and examine whether such an approach could potentially be useful in predicting which babies are likely to develop poor lung function. The studies and analysis techniques are diverse, so the student will gain a valuable range of experiences and skills. The student will be encouraged and supported to present their results at national and international conferences and publish in peer-reviewed journals.
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