Farr@Aberdeen Funded Research Theme: Fetal growth patterning, early life development and health in later life

Linkage of antenatal fetal measurements to SMR and PIS data to look at chronic conditions including asthma, diabetes, epilepsy and attention deficit hyperactivity disorder

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The aim of this study is to describe the relationship between growth during antenatal life and four common non-communicable diseases (NCD; asthma, diabetes, epilepsy and attention deficit hyperactivity disorder), and how this is modified by growth in the first five years. This study links four data sets which hold the following details: fetal ultrasound measurements, maternal details during pregnancy, child weight at 5 years, dispensed prescriptions data and hospital admission data. A first linkage has been completed and some amendments are required. Whilst the linkage has been taking place a PhD student designed two items of software; the first describes the appropriateness of using imputation to address data missingness and the second takes a computational/clustering approach to a large dataset. The software has been validated and tested in dummy datasets and also in a small data set from a cohort study (Study of Eczema and Asthma To Observe the effects of Nutrition - SEATON). The results from the cluster analysis are highly consistent with already published results from the SEATON study but provide an additional novel insight. The software will be applied to the linked dataset shortly. We anticipate that this approach will give a novel perspective to the management of missing data in large datasets and also provide a significant advance in our understanding of the relationship between fetal growth and NCD and how post-natal growth modifies this. In the next 12 months we will prepare papers for submission which describe the computational approach to the SEATON and linked databases.

This is a collaboration between health data scientists and computing scientists.

Linkage of antenatal fetal measurements to childhood obesity data in the Grampian Study of Trends in Obesity in North East Scotland (STONES) dataset

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The aim of this study is to describe the relationship between fetal size and fetal growth and childhood obesity. The Aberdeen Maternity and Neonatal Databank (this holds fetal ultrasound measurements and maternal details during pregnancy) has been linked to the STONES database (this holds height and weight in five year olds). We have data for over 20,000 mother-child pairs, which is comfortably the largest in the world to date. We have seen that increased size in the second and third, but not the first, trimester was associated with increased risk for obesity at five years and that increasing size between the three trimesters is associated with increased risk for obesity. These findings suggest that the origins of childhood obesity are apparent in the first half of pregnancy but the magnitude of effect was modest indicating that post-natal factors are more important determinants of childhood obesity. Based on observations seen in our main analysis, we have undertaken a sibling comparison study to describe how changing maternal smoking status between pregnancies is associated with offspring risk for obesity; we have seen that new onset or persistent smoking are associated with increased risk for obesity in younger offspring. A second sibling comparison study failed to demonstrate an association between changing maternal weight category or socioeconomic status and fetal ultrasound measurements. Collectively these findings suggest that the antenatal environment is relevant to the development of childhood obesity, perhaps by determining predisposition, and that some antenatal interventions, e.g. maternal smoking cessation, may be effective in reducing childhood obesity. Abstracts have been presented, one paper is being revised and resubmitted and at least one more paper is being drafted.

Linkage of antenatal fetal measurements to maternal exposure to poor quality outdoor air during pregnancy

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The aim of this study is to link maternal ambient air exposures with a focus on fine particles called PM2.5. PM2.5 are known to enter the blood stream from inhaled air and also to cross from mother's blood into the fetus. PM2.5 are also known to cause damage to the inside of blood vessels and might affect the growth of the developing fetus, particularly the brain which is growing very rapidly. The team from Universities of Aberdeen and Edinburgh linked the Aberdeen Maternity and Neonatal Databank (this holds fetal ultrasound measurements and maternal details during pregnancy) to ambient air exposures during pregnancy data provided by the UK Department for the Environment, Food and Rural Affairs. Linkage was achieved for over 25,000 pregnancies. Despite the relatively low PM2.5 exposures in North East Scotland we observed an association between maternal exposure to increasing PM2.5 concentrations and reduced fetal head size in the second half of pregnancy. We also observed that the association was predominantly seen among non-smoking mothers and the reduction in fetal head size seen in non-smoking mothers exposed to higher PM2.5 exposures was similar to that seen in fetuses whose mothers smoked. Fetal head growth was reduced in all those whose mothers smoked regardless of the PM2.5 exposure. The potential impact of this study is that it challenges the current understanding of what a "low" PM2.5 exposure is and also adds to our understanding of the harm from maternal smoking. A paper describing the findings is in submission. These findings were discussed at the FARR Frontiers *Environmental determinants of child cognitive function* meeting in January 2017 and future collaborations are planned.

This is a multidisciplinary, cross Farr Scotland collaboration.