Project Details	
Project Code	MRC23PHSBr von Hinke
Title	Impacts of air pollution on neurodevelopment and neurodegeneration
Research Theme	Population Health Sciences
Summary	There is increasing evidence that air pollution affects neurodevelopment and neurodegeneration. However, the mechanisms that mediate these relationships are unclear. This project will exploit large-scale data on air pollution and clinical and educational outcomes, and explore the role of genetic, epigenetic and brain imaging traits in this association. Results will provide new insights into how the environment shapes outcomes both early and later in life.
Description	Air pollution is a ubiquitous pollutant, implicated in neurodevelopment and educational attainment, neurodegeneration, cognitive decline as well as dementia and Alzheimer's disease.1–3 Air pollution includes fine particulate matter (PM2.5 and PM10), ozone, sulphur dioxide, carbon monoxide, and nitrogen dioxide. There are two major challenges to studying the effects of air pollution. First, there is very little high-quality historical pollution data, meaning that most of the literature exploring the consequences of pollution focuses on short-term effects, rather than longer term effects. Second, more advantaged areas are in general less polluted than more disadvantaged areas. We can overcome these two issues, first, by exploiting newly digitised historical pollution from 1954 onwards. Second, we will employ causal inference methods and natural experiments to estimate the causal effects of pollution. Aim: to study the impact of air pollution on neurodevelopment and neurodegeneration Research questions: 1. What is the impact of air pollution on neurodevelopment? 2. What is the impact of air pollution on neurodegeneration? 3. Are there causal factors impacting susceptibility to neurodevelopment and neurodegeneration in a high pollution environment? Data Exposure: Linked air pollution data, geographic linkage, genetics, epigenetics Outcome: Questionnaire data on mental health, linked educational attainment data, neuroimaging data, medical records diagnosis of neurodegenerative diseases The main data sources that will be exploited include the UK Biobank and ALSPAC. We have already digitized and merged data on pollution from 1954 onwards. We can use this to relate individuals' exposure to pollution early in life to their later life health and educational outcomes. We have detailed health and educational outcomes via questionnaires and linked admin data, neuroimaging data on sub-samples of both ALSPAC and UK Biobank. This can provide a high-quality measure of brain development in early life (ALSPAC), and atrophy in later life (UK Biobank). We also have extensive longitudinal epigenetic data from blood in ALSPAC, which can be used both as proxy exposures, and to interrogate causation.4,5 Methods We will use natural experiments for causal inference, such as exploiting the sudden occurrence of fogs (e.g. the London smog),6 as well as the introduction of (local) government policy (e.g. the Clean Air Act)7 and within-sibling and spousal designs.8,9 For example, investigating known neurodegenerative disease susceptibility loci (e.g., APOE e4 for Alzheimer's) and exposure to pollution, plus exome sequencing to model the effect of rare variation. Student ownership: The student can adapt

	the project in line with their current research interests and focus on epigenetic, neuroimaging or linked geographical air pollution data. All three research questions are: - exceptionally significant, due to a focus on health across the life course, a core MRC priority area - challenging, being based on state-of-the-art health and biomedical data science methods, geographic information systems (GIS), and causal inference; - feasible, as data for all three objectives has already been collected; - original due to the interdisciplinary character, combining population health, environmental science, data science, economics, epidemiology, and epigenetics Added-value features: This project will implement cutting-edge statistical methods in health data science. 1. Fu & Yung JAD 77, 701–714 (2020). 2. Mizen et al. Health & Place 63, 102355 (2020). 3. Aguilar-Gomez et al. doi:10.3386/w29848. 4. Richardson et al IJE 48, 887–898 (2019). 5. Relton & Davey Smith IJE 41, 161–176 (2012). 6. von Hinke & Sørensen (2022) doi:10.48550/ARXIV.2202.11785. 7. Davies et al. Nat Hum Behav 2, 117–125 (2018). 8. Howe et al PLoS Genet 17, e1009883 (2021).
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