MRC
Centre for
Environment and Health

2020/21 Annual Report

MRC
Centre for Environment & Health
Medical Research Council
Imperial College London

NIHR | Health Protection Research Unit in Environmental Exposures and Health at Imperial College London

NIHR | Health Protection Research Unit in Chemical and Radiation Threats and Hazards at Imperial College London

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1. OVERVIEW

1.1 Mission and vision

The mission of the MRC Centre for Environment and Health is to undertake the highest quality research to advance understanding of the effects of key environmental hazards with a significant impact on human health and wellbeing. The Centre's research aims to: i) identify novel associations between environmental exposures and adverse health outcomes, ii) quantify the risk of environmental exposures on health at both the individual (*exposome*) and population level, iii) produce new insights into possible mechanisms and causal associations, iv) provide high-quality, multidisciplinary training in quantitative sciences to form the next generation of research leaders in environment and health; and i) inform the development and targeting of interventions and policies to protect public health.

Since its creation in 2009, the MRC Centre has established itself as the *de facto* 'go to' unit in the UK for research, training and policy advice on environment and health, with a focus on air pollution, noise, non-ionising radiation, small-area health studies, and the '*exposome*'. In 2019 the Centre was awarded funding by the MRC for a third quinquennium (01 July 2019 to 30 June 2024). At the same time Imperial College has invested heavily in the Centre, with provision of dedicated new office and laboratory space on the new White City campus and transfer of Prof. Kelly's Environmental Research Group (ERG) from King's College London to Imperial College in July 2020. This equates to £19.5M to date in capital investment with a further £53.4M committed for completion of the School of Public Health Building, including from philanthropic donations, and approximately £4M in staffing and support costs to end June 2024.

We have also brought the MRC Centre together with two major new investments at Imperial College from the National Institute for Health Research (NIHR) for the Health Protection Research Units (HPRUs) in Environmental Exposures and Health (Director: Kelly) and Chemical and Radiation Threats and Hazards (Director: Elliott).

Our vision for this third quinquennium of the Centre is therefore to consolidate the expertise across the Centre and the two associated HPRUs to become the leading research centre in Europe on the study of the health effects of ubiquitous environmental challenges in urban environments by: i) continuing to grow the range and depth of cross-disciplinary research in our areas of expertise ii) expand the scope of our research to cover new and emerging environmental threats (e.g. microplastics, nanomaterials, highly toxic chemical agents), iii) develop and apply innovative advanced methods in exposure science, omics, epidemiology, biostatistics and data sciences, iv) develop our network of collaborations (including with PHE, with the MRC Toxicology Unit in Cambridge and others) to complement our expertise and enhance the impact of our research, iv) further strengthen and develop our training programme.

1.2 Strategy and objectives

The Centre's research combines advanced quantitative methods in exposure monitoring and modelling, omics, toxicology, epidemiology, biostatistics and computational biology, with the collection of large environmental and health datasets and the curation of large cohorts with deep phenotyping and biological sample collections. It incorporates the UK Small Area Health Statistics Unit (SAHSU) combining expertise in spatial epidemiology and access to routinely collected health and population data for high-resolution disease mapping and risk analyses.

This combination of multi-disciplinary expertise and access to extensive data resources underpins the Centre's distinctive research strategy, working both forward and backward from the molecular to the individual and to the population level to strengthen causal inference.

The Centre's training programme is a critical element of its strategy The Centre provides a high-quality, cross-disciplinary, working and training environment to attract, motivate and provide the necessary skills and expertise, to produce the next generation of research and policy leaders. It comprises our PhD programme, early career researcher fellowship programme, and associated programmes such as the collaborative fellowships developed with the MRC Toxicology Unit.

The Centre's objectives for the current quinquennium are to:

i) build upon our successful training programme, with a focus on multi- disciplinary and transferable skills in the quantitative sciences;
ii) advance knowledge of specific environmental pollutants, including effects of air and noise pollution, and non-ionising radiation, on individuals and urban populations;
iii) through use of advanced omic technologies, gain improved understanding of mechanistic pathways underlying such effects, to strengthen causal inference;
iv) improve the quality, accuracy and scope of exposure metrics, thereby helping to establish a more robust and targeted link between environmental exposures and health;
v) develop the underlying methods in biostatistics, data science, computational biology and related disciplines to advance the field;
vi) develop and enhance the Centre's core resources and cohorts, with a focus on deep phenotyping and biobanking;
vii) provide expert input to government and international agencies to inform environment and health policy at a national and international level.

1.3 Structure of the MRC Centre

The Centre currently comprises 37 investigators and their teams (see Centre's website for details), including over 150 students and early career researchers.

The work of the Centre is structured into three research programmes, reflecting the main areas of focus of our research (*Environmental exposures*, *Molecular signatures and disease pathways* and *Healthy cities, healthy people*), and two cross-cutting themes focussing on the development and application of methodologies and resources enabling the research (*Biostatistics and data science, Cohorts and data resources*) (see Figure 1).

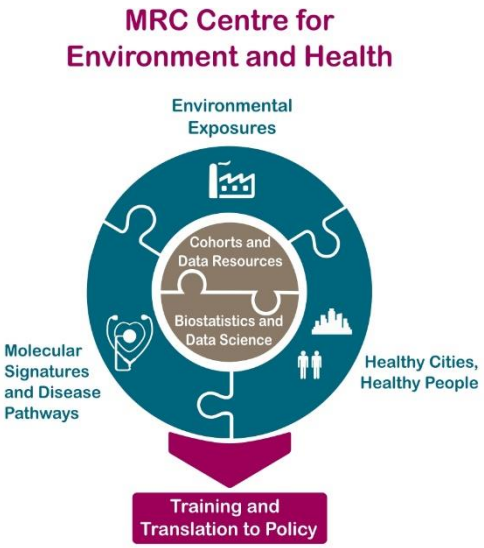

Fig. 1: MRC Centre research programmes and themes.

1.4 Progress/achievements

This report covers the period from 01 July 2019 to 30 June 2021. Despite the challenges resulting from the COVID-19 pandemic, and the move of the ERG to Imperial College, the Centre has made good progress in meeting the commitments set out in its renewal application.

A selection of the Centre's key research outputs and impacts in each of its programmes and themes are outlined in Section 2 of this report. In the first two years since renewal Centre members have published close to 400 papers in peer-reviewed journals (see Annex 4) and successfully leveraged approximately £36.3M in research funding (see Annex 5). Centre members currently hold four competitively obtained MRC programme grant awards. The achievements in underpinning activities including training, public engagement and knowledge translations are described in Section 2.

1.5 Future plans

The move of the ERG to Imperial College in 2020 together with the successful leveraging of funding from NIHR for two environmental HPRUs and the relocation of the three entities to one site on the new campus at White City, has created a highly integrated research hub under one roof, with a coherent and comprehensive research programme on environment and health. Overall, the MRC Centre and the two HPRUs form the largest concentration of researchers working on environment and health in the UK and one of the largest groups working in this area internationally. This new research hub represents a step-change in our ability to address major environment and health challenges, providing state-of-the art facilities and the critical mass with which to deliver our objectives.

The ambition for the MRC Centre is to be at the forefront of the MRC's proposed strategy to establish Centres of Excellence, with significantly increased funding and duration beyond the standard Centre

model. We have already initiated discussions with the MRC concerning this possibility as we approach the Centre's mid-term review. This expanded scope, together with the continued development of the collaborations with partners in the HPRUs, presents a unique opportunity to build on our successes to date and further develop and consolidate our leading position as a research and training hub addressing some of the major environment and health challenges of our time.

2. RESEARCH PROGRAMMES AND THEMES

2.1 Environmental Exposures

Programme Lead – Professor Frank Kelly (ICL)
Programme Teams – please see the MRC Centre website

2.1.1 Overview and programme strategy

Accurate and detailed exposure metrics are essential to establish robust links between environmental exposures and health outcomes. Improved exposure estimates can also provide more targeted evidence for control of harmful sources, more targeted evidence for the protection of sensitive population subgroups and more engaging and relevant evidence for raising public awareness and understanding. Thus, by improving our methods and tools for assessing environmental exposure, we can have a direct influence on policy, public health improvement and behavioural change.

The Environmental Exposures programme utilises its broad expertise in measurement sciences, analytical sciences, mechanistic modelling, source characterisation and behavioural sciences to deliver greater insight into how, where and when individuals, communities and populations are exposed to known and emerging environmental contaminants. This insight is utilised across the Centre for linkage to toxicological and epidemiological health outcomes to identify possible causal pathways and mechanisms and develop evidence-based recommendations for health improvement.

2.1.2 Progress and research highlights

Measurement sciences – utilising personal sensors for exposure assessment

We remain at the forefront of advancements in sensor technologies, delivering a range of research activities using mobile and static environmental sensors to assess hyperlocal and individual environmental exposures [1]. The *Breathe London Wearables* study assessed the exposure of 258 children and 30 teachers across five London primary schools to air pollution levels for a week, utilising 80 sensor backpacks provided by our industrial partners Dyson. The high accuracy and time resolution of the resulting data allowed us to link individual child activities, such as mode of transport, walking route, home and school environment, to the quality of air they were breathing. This information was presented to the children, their parents, teachers and Mayor of London to highlight how exposure could be reduced [2]. The backpacks are now being used in the NIHR "*Children's Air Pollution Profiles in Africa* (*CAPPA*)" study linking air pollution exposure to childhood asthma management. They will also be given to pregnant women in London as part of the GSTT Charity funded "*Mother and Baby Interventions to Lower Exposure to Air Pollution* (*MoBILE Air*)" pilot study, which will gather evidence for a future randomised-controlled trial designed to improve birth outcomes in high-risk pregnant women, commencing in late 2021.

In addition to characterisation and engagement, we have extended our use of personal monitoring for health studies. Initial results from the MRC "*COPE: Characterisation of COPD exacerbations using environmental exposure modelling*" study have recently been published, finding that, when considering total personal exposure to air pollutants, mainly the gaseous pollutants affect COPD patients' health. No association was observed between particulate matter and any respiratory outcome [3] - further analysis is ongoing. Personal environmental exposure monitoring is now being used in rural and peri-urban regions of sub-Saharan Africa to improve our understanding of the sources, behaviour and health impacts of air pollution as part of the Wellcome "*PRECISE-DYAD: linking maternal and infant health trajectories in sub-Saharan Africa*" study. Importantly, this study will assess the impact of ambient and household sources individually and in combination, on maternal and infant health in a large cohort.

Modelling – personalised exposure modelling approaches

While measurements can deliver detailed insight into individual exposures, models are required to increase the scope and breadth of assessments. At city level, we have brought together disparate data sources and advanced modelling techniques to better understand the complex interactions between the urban environment, human activity and health. The London Hybrid Exposure Model (LHEM) is capable of modelling exposures within the home, at work/school and while travelling, at high spatial and temporal resolution. The LHEM has been further enhanced to cover the whole of the UK. It also has an updated emissions inventory and there are additional annual time periods. Personal exposure measurements from Centre studies are now being used to validate components of the model, including indoor cooking sources, ambient pollutant infiltration and transport microenvironments. The NERC funded "*APEx: An Air Pollution Exposure model to integrate protection of vulnerable groups into the UK Clean Air Programme*" study is further augmenting the LHEM to incorporate agent-based models and qualitative surveys to formulate and test policy scenarios that incorporate behavioural change and specifically target vulnerable subgroups.

The capabilities of the LHEM were well demonstrated during the various lockdowns associated with the COVID-19 pandemic. We found that, in exposure terms, improvements in ambient air quality arising from reduced transport and industrial emissions were offset by increased time at home and exposure to indoor cooking emissions for some sectors of the population. These data underpinned a subsequent Rapid Evidence Review report to Defra [4]. The LHEM is also being utilised in the MRC "*Cognitive DeveLopment in the Urban Environment* (*CLUE*)" study, which addresses adolescent health and behaviours, with a particular focus on cognitive development, with biosamples available for analyses of exposure biomarkers including those related to noise.

Mechanistic models such as the LHEM require extensive input data, which can be scarce in less developed regions of the world. Funded by the European Space Agency the *Satellite Air Quality Modelling Demonstration Project* (*SAQM*) is developing methods to use high resolution satellite imaging to create spatially resolved transport emissions in regions without extensive traffic data.

Exposure misclassification

Reducing exposure misclassification and increasing specificity of exposure metrics are key goals for the Centre. Commencing in 2020, "*MELONS - Investigating the consequences of measurement error of gradually more sophisticated long-term personal exposure models in assessing health effects*" is a Health Effects Institute funded study that utilises our extensive measurement datasets and advanced modelling methods to evaluate whether increasingly detailed estimates of long-term individual exposure to pollutants for large scale studies are useful and effective in yielding better estimates of the health effects of exposure to outdoor air pollution [5-7]. We have developed methods to separate personal exposure measurements into components relating to outdoor sources and indoor sources. This important methodological development allows us to directly compare the health impacts of each source type in parallel, allowing prioritisation for distinct sections of the population. Future work will assess the impact of measurement error of several exposure assessment methods on effect estimates using simulated data sets and then apply them to UK Biobank participants.

Characterising pollution sources – evaluating known and emerging environmental contaminants

Transport microenvironments can produce extreme exposures to vehicle emissions, including both combustion and non-combustion sources. We have recently completed studies characterising exposure to particulate and gaseous pollutant in rail and urban commercial transport (e.g., IOSH "*DEMiSt – The driver Diesel Exposure Mitigation Study*") [8]. This work will be extended via the MRC "*Exposure to particulate matter on the London Underground in healthy subjects and patients with chronic respiratory disease*" study, which will link detailed chemical particulate components to acute health outcomes. Fieldwork is ongoing.

Centre research has identified airborne microplastics as a potential environmental hazard. There is concern that human exposure could lead to health effects, especially if they are present in inhalable size ranges. Methods, however, were not available to identify the presence of such small microplastics until Centre research developed these [9]. Ongoing work is now being extended via the NERC

"*Understanding UK airborne microplastic pollution: sources, pathways and fate*" study, which will provide a robust foundation for future assessments of the toxicological and health impact of this emerging issue.

2.1.3 Future direction and objectives

The indoor:outdoor exposure continuum

While we have previously focused much of our research on ambient environmental exposures, our progress in increasing the specificity of environmental exposure assessments now allows us to consider the indoor:outdoor exposure continuum as a whole. This activity will make a major step forward with the recently launched UKRI SPF "*West London Healthy Home and Environment Study* (*WellHome*)". The programme of research in *WellHome* creates an innovative long-term research and information resource within an engaged urban community to advance knowledge and awareness of residential air quality, its health impacts and methods to ensure reduced exposure to harmful agents. We will combine an intensive monitoring approach, toxicological assessments of chemical and biological particulate matter (PM) with activity/time linked health data, with a focus on homes with asthmatic children in areas of relatively low socio-economic status and high ambient air pollution concentrations.

The impacts of the COVID-19 pandemic on environmental exposure

While the COVID-19 pandemic has impacted much of our fieldwork, it has also presented opportunities and driven adaptations to research programmes. Originally designed to evaluate UK Clean Air Zones, the MRC "*Public Health Impacts of UK's Clean Air Zones* (*PHICAZ*)" study is being adapted to evaluate the combined impact of the London Ultra Low Emission Zone and pandemic lockdowns on population exposures and health impacts. This will necessitate modelling changes in local emissions, regional atmospheric chemistry, population behaviours and health vulnerabilities.

Forecast modelling - net-zero climate policies

Tackling climate change could offer the greatest global health opportunity of the 21st century. Integrating the costs and benefits of reduced air pollution into the health and economic benefits of net-zero policies may allow a more complete justification of early actions. We recently started the NIHR study "*The air quality health and economic costs and benefits of a zero carbon UK*", utilising our modelling tools to predict air pollution concentrations, health and economic impacts at baseline in 2017, and for 12 Climate Change Committee policy scenarios in 2030, 2040 and 2050. It is our intention that this project will instigate a series of future studies integrating net-zero issues into our environmental exposure research.

2.1.4 Selected papers

1. Chatzidiakou L, Krause A, Han Y, Chen W, Yan L, Popoola OAM, et al. Using low-cost sensor technologies and advanced computational methods to improve dose estimations in health panel studies: results of the AIRLESS project. J Expo Sci Environ Epidemiol. 2020;30(6):981-9. https://doi.org/10.1038/s41370-020-0259-6.
2. Varaden D, Leidland E, Lim S, Barratt B. "I am an air quality scientist"- Using citizen science to characterise school children's exposure to air pollution. Environ Res. 2021;201:111536. https://doi.org/10.1016/j.envres.2021.111536.
3. Evangelopoulos D, Chatzidiakou L, Walton H, Katsouyanni K, Kelly FJ, Quint JK, et al. Personal exposure to air pollution and respiratory health of COPD patients in London. Eur Respir J. 2021;58(1). https://doi.org/10.1183/13993003.03432-2020.
4. Defra (2020). Estimation of changes in air pollution during COVID-19 outbreak in the UK. Accessed Sept 2021.
5. Butland BK, Samoli E, Atkinson RW, Barratt B, Beevers SD, Kitwiroon N, et al. Comparing the performance of air pollution models for nitrogen dioxide and ozone in the context of a multilevel epidemiological analysis. Environ Epidemiol. 2020;4(3):e093. https://doi.org/10.1097/EE9.0000000000000093.
6. Samoli E, Butland BK, Rodopoulou S, Atkinson RW, Barratt B, Beevers SD, et al. The impact of measurement error in modeled ambient particles exposures on health effect estimates in multilevel analysis: A simulation study. Environ Epidemiol. 2020;4(3):e094. https://doi.org/10.1097/EE9.0000000000000094.

7. Evangelopoulos D, Katsouyanni K, Keogh RH, Samoli E, Schwartz J, Barratt B, et al. PM2.5 and NO2 exposure errors using proxy measures, including derived personal exposure from outdoor sources: A systematic review and meta-analysis. Environ Int. 2020;137:105500. https://doi.org/10.1016/j.envint.2020.105500.
8. Lim S, Barratt B, Holliday L, Griffiths CJ, Mudway IS. Characterising professional drivers' exposure to traffic-related air pollution: Evidence for reduction strategies from in-vehicle personal exposure monitoring. Environ Int. 2021;153:106532. https://doi.org/10.1016/j.envint.2021.106532.
9. Levermore JM, Smith TEL, Kelly FJ, Wright SL. Detection of Microplastics in Ambient Particulate Matter Using Raman Spectral Imaging and Chemometric Analysis. Anal Chem. 2020;92(13):8732-40. https://doi.org/10.1021/acs.analchem.9b05445.

2.2 Molecular Signatures and Disease Pathways

Programme Lead – Professor Paolo Vineis (ICL)
Programme Teams – please see the MRC Centre website

2.2.1 Overview and programme strategy

The Molecular Signatures and Disease Pathways programme aims to improve understanding of the causal links between exposures to environmental contaminants and disease, by characterizing the individuals' external and internal *exposome* (i.e. the sum of all exposures from conception onwards) particularly during critical periods of life, such as in utero or childhood. Our research in this area involves large population studies with collections of biological samples, using novel study designs and advanced multi-omic technologies to identify biomarkers of exposure and/or disease.

The goal of this research is to reduce uncertainties in assessing the risk related to environmental contaminants, by characterizing the molecular signatures (biomarkers) of these exposures and identifying plausible pathways or networks through which they lead to disease initiation or progression. We also explore new approaches to measuring external exposures, including the use of silicone wristbands and other sensors. A stream of research is devoted to social inequalities and how they interact with exposures (including behavioural) in modulating disease risk across the lifecourse.

2.2.2 Progress and research highlights

Through our leadership of EU programmes including *Lifepath, Expanse* and *ALEC* we are applying multi-omic technologies, including epigenetics, transcriptomics, proteomics and metabolomics, to decipher environmental signals and their biological signatures and interactions. Specifically, the *Lifepath* study investigated the molecular signatures associated with socioeconomic and lifestyle exposures in order to understand the biological pathways leading to poor health in mid- to later life, as well as to identify key influences on healthy aging. In this way we aim to identify the mechanisms through which the upstream and social determinants of health operate, with a view to identifying interventions that will improve individual and population health. This research is now being extended to the urban *exposome* (*Expanse* consortium), the external and internal *exposome* of childhood obesity (*STOP* H2020 grant) and the internal *exposome* of gig economy workers (COLT grant).

Development of epigenetic and metabolomic clocks

Building upon *Lifepath*, we established a research stream based on DNA-methylation clocks (using four epigenetic age acceleration indicators, Horvath DNAm age, Hannum DNAm age, Pheno DNAm age and DNAm GrimAge, and data on DNAm Telomere length) and metabolomic clocks in relation to multiple exposures and multiple outcomes. So far, we have explored socio-economic inequalities and mortality in relation to clocks, with several papers from the *Lifepath* H2020 consortium [10-12]. We are now extending this research to air pollution and to unstable jobs, the latter mimicking characteristics of the gig economy. We are also exploring newer clocks such as the Dunedin Pace of Aging in younger cohorts including children. We have developed a novel "metabolomic clock" selected from over 100,000 molecular features using untargeted metabolomics, that appears complementary to the established epigenetic clocks [12].

This work is being extended to multiple cohorts (~45,000 participants) as part of the *METAGE* project which aims to: i) develop reproducible markers of biological age using metabolomics; ii) determine the utility of metabolomic age as a prediction tool of morbidity and mortality in adults; iii) determine the developmental impact of accelerated biological ageing in children; iv) describe the biological processes underlying biological ageing; and v) understand the social drivers and determinants of accelerated biological ageing in both children and adults. Predictive models of biological age are being developed using targeted NMR metabolomics in around 35,000 people (45,000 samples) across multiple cohorts, untargeted liquid chromatography-mass spectrometry (LC-MS) metabolomics in around 9000 adults alongside annotation work of new molecules, and in children using metabolomic, epigenetic and other data in three birth cohorts. Downstream epidemiological analysis will explore the social drivers of accelerated biological aging and the mediating behavioural, environmental and psychological pathways.

Alternative measures of the biological clocks are associated with a huge range of diseases and risk factors, but they weakly correlate among themselves suggesting that they capture different aspects of the ageing process [11, 12]. In one cohort (*Understanding Society*), the unemployed had an average age acceleration of 3.36 years, while permanently employed workers had a deceleration of 0.16 years and self-employed workers had a deceleration of 0.32 years. The effect of unemployment was comparable to that of current smoking (unpublished observations).

Ageing of the lungs

The *ALEC* study (Ageing Lungs in European Cohorts) is funded by the Horizon 2020 European Commission (EC) programme. This study aims to improve our understanding of risk factors for low lung function, respiratory disability and the development of chronic obstructive pulmonary disease (COPD), by using information held within existing cohort studies. Even though COPD has long been viewed as a predominantly smoking-related disease, there is increasing awareness that lifestyle and environment contribute to disease even from very early in life, including before birth. COPD is a major cause of disease, disability and death in European adults and lung function is a critical objective marker of good lung health, strongly associated with other major chronic diseases (for example, cardiovascular disease) and is a major independent determinant of overall health status. Elements of the *ALEC* initiative included examination of molecular signatures of disease. We showed smoking related DNA methylation changes were associated with lung function and found a relationship between epigenetic ageing and lung function [13, 14].

2.2.3 Future direction and objectives

Urban exposome

EXPANSE (*Exposome* Powered tools for healthy living in urbAN Settings) is a consortium on the urban *exposome* funded by H2020 and led by the Institute for Risk Assessment Sciences (IRAS), Utrecht. By 2030 more than 80% of Europe's population will live in and interact with a complex urban environment. The *EXPANSE* project will study the impact of the urban *exposome* on the two major contributors to Europe's burden of disease: cardio-metabolic and pulmonary disease. *EXPANSE* will bring together *exposome* and health data of more than 55 million adult Europeans; in-depth *exposome*, phenotype, and OMICs information for more than 2 million Europeans; personalized *exposome* assessment for 5,000 individuals in five cities across Europe; applying a novel approach to use ultra-high-resolution mass-spectrometry to agnostically screen for exogenous chemicals in 10,000 blood samples of cohort study members; studying the evolution of the *exposome* and health through the life course using both (matured) birth and adult cohorts; and evaluating the impact of changes in the urban *exposome* on the burden of cardio-metabolic and pulmonary disease. *EXPANSE* will translate its insights and innovations into research and dissemination tools that will be openly accessible via the EXPANSE toolbox.

Air pollution

We build on our leading expertise in metabolomics (including Elliott's leadership role in the MRC National Phenome Centre) to interrogate the plasma and urinary metabolome with regard to air pollution and other exposures. Given that the metabolome is close to the clinical and exposure phenotype, this will give valuable insights as to the mechanisms linking air pollutants with cardiorespiratory ill-health. As an example, funded by MRC, we are analysing data from a range of experimental chamber studies in which healthy volunteers were exposed on two separate occasions, at least six weeks apart, to either

a pollutant challenge (diesel, biodiesel or wood smoke) or clean air, in randomised order. This experimental approach has the advantage that the results are unconfounded by other environmental and lifestyle exposures.

We will also interrogate blood samples obtained from the *AIRLESS* population panel study in inner and outer Beijing, where air pollution concentrations are particularly high. *AIRLESS* involved individual personal exposure monitoring of PM2.5, NO2/NOx, ozone (O_3) over a 7-day period in both winter and summer seasons. We have already detected in the randomised *Oxford Street II* study numerous associations of MS-measured metabolites with NO2 exposures, indicating proof-of-principle of the approach, based on the EC-funded *Exposomics* network. We also have extensive availability of genetic data (e.g. from genome-wide association studies, GWAS) which will help to anchor our findings in a biological context.

The interactions between air pollutants and the physiological response are complex and the usual practice of reducing these to a single pollutant model is overly simplistic. We are interested in mechanistic pathways in relation to 'real-world' multi-pollutant exposures as this is what is required for future policy. To unravel the effects of different components of the pollutant mix we will construct a matrix of pollutant concentrations against metabolic signatures to identify common and disparate signals. We have already made some progress in this regard. In a recent pilot study, we used variants of partial least squares (PLS) algorithms to model the metabolomic response to a multivariate set of exposures. More formal modelling will also be implemented using counterfactual models and mediation analyses which will quantitatively assess the relative (direct or indirect) contribution of each of the pollutants to the overall metabolic response.

Cognitive impairment

Another direction of our work is to investigate the metabolomics signatures associated with mild cognitive impairment, cognitive decline and frank dementia as part of our foundation programme (Elliott) in the UK Dementia Research Institute at Imperial College. We will use our cohort resources to follow-up cognitive performance over time (e.g. *Airwave* study) and to monitor progression from mild cognitive impairment to dementia using a range of national and international cohorts, in relation to baseline metabolomic profiles. These untargeted metabolomic data were generated by the MRC National Phenome Centre both by proton magnetic resonance (^{1}H NMR) and ultra- performance liquid chromatography mass spectrometry (UPLC-MS). The results of these studies will give new insights into the metabolic processes and environmental triggers involved in cognitive decline and transition to dementia, providing improved understanding of the environmental risk factors and causes leading to dementia, and thus help inform strategies for prevention.

Water exposome

Identification and monitoring of potentially hundreds of new highly toxic agents (HTAs) in drinking water arising from by-products of chemical treatment processes (e.g. disinfection) or contamination with chemical substances (pharmaceuticals, pesticides, organometallics, plastic-related compounds, etc.) remains a significant challenge. In the "Detection of Highly Toxic Agents in Water" study, analytical methods involving ion chromatography, liquid chromatography and comprehensive gas chromatography coupled to full-scan high resolution mass spectrometry (HRMS) instruments will be developed and validated for several main classes of currently known compounds including plasticisers, disinfectant by-products (haloacetic acids, oxyhalides, trihalomethanes), pesticides (herbicides, insecticides, rodenticides, etc.), pharmaceuticals and illicit drugs (focussing on those which survive wastewater treatment). Full-scan measurement data for these 'model' compounds will then be used to construct machine learning-based prediction models to assist in identification of new HTA substances.

This study will characterise and classify new chemical HTAs in UK municipal, well and bottled drinking waters and assess their potential risks for human exposure. The objectives of the project are to i) develop AI-assisted high resolution analytical methods for screening of large numbers of suspect neurotoxins and HTA markers, ii) conduct a temporal survey of drinking water sources across the UK; iii) analyse urine samples to assess individual-level exposure and analyse wastewater from the corresponding city to extrapolate to both human population and environmental exposure; iv) evaluate public health and environmental risk of HTAs from drinking water sources.

2.2.4 Selected publications

10. Fiorito G, McCrory C, Robinson O, Carmeli C, Ochoa-Rosales C, Zhang Y, et al. Socioeconomic position, lifestyle habits and biomarkers of epigenetic aging: a multi-cohort analysis. Aging (Albany NY). 2019;11(7):2045-70. https://doi.org/10.18632/aging.101900.
11. McCrory C, Fiorito G, Ni Cheallaigh C, Polidoro S, Karisola P, Alenius H, et al. How does socio-economic position (SEP) get biologically embedded? A comparison of allostatic load and the epigenetic clock(s). Psychoneuroendocrinology. 2019;104:64-73. https://doi.org/10.1016/j.psyneuen.2019.02.018.
12. Robinson O, Chadeau Hyam M, Karaman I, Climaco Pinto R, Ala-Korpela M, Handakas E, et al. Determinants of accelerated metabolomic and epigenetic aging in a UK cohort. Aging Cell. 2020;19(6):e13149. https://doi.org/10.1111/acel.13149.
13. Imboden M, Wielscher M, Rezwan FI, Amaral AFS, Schaffner E, Jeong A, et al. Epigenome-wide association study of lung function level and its change. Eur Respir J. 2019;54(1). https://doi.org/10.1183/13993003.00457-2019.
14. Rezwan FI, Imboden M, Amaral AFS, Wielscher M, Jeong A, Triebner K, et al. Association of adult lung function with accelerated biological aging. Aging (Albany NY). 2020;12(1):518-42. https://doi.org/10.18632/aging.102639.

Additional selected publications

15. Ponzi E, Vineis P, Chung KF, Blangiardo M. Accounting for measurement error to assess the effect of air pollution on omic signals. PLoS One. 2020;15(1):e0226102. https://doi.org/10.1371/journal.pone.0226102.
16. Dagnino S, Bodinier B, Grigoryan H, Rappaport SM, Karimi M, Guida F, et al. Agnostic Cys34-albumin adductomics and DNA methylation: Implication of N-acetylcysteine in lung carcinogenesis years before diagnosis. Int J Cancer. 2020;146(12):3294-303. https://doi.org/10.1002/ijc.32680.
17. Peters S, Broberg K, Gallo V, Levi M, Kippler M, Vineis P, et al. Blood Metal Levels and Amyotrophic Lateral Sclerosis Risk: A Prospective Cohort. Ann Neurol. 2021;89(1):125-33. https://doi.org/10.1002/ana.25932.
18. McCrory C, Fiorito G, Hernandez B, Polidoro S, O'Halloran AM, Hever A, et al. GrimAge Outperforms Other Epigenetic Clocks in the Prediction of Age-Related Clinical Phenotypes and All-Cause Mortality. J Gerontol A Biol Sci Med Sci. 2021;76(5):741-9. https://doi.org/10.1093/gerona/glaa286.
19. Merid SK, Novoloaca A, Sharp GC, Kupers LK, Kho AT, Roy R, et al. Epigenome-wide meta-analysis of blood DNA methylation in newborns and children identifies numerous loci related to gestational age. Genome Med. 2020;12(1):25. https://doi.org/10.1186/s13073-020-0716-9.
20. Kachuri L, Johansson M, Rashkin SR, Graff RE, Bosse Y, Manem V, et al. Immune-mediated genetic pathways resulting in pulmonary function impairment increase lung cancer susceptibility. Nat Commun. 2020;11(1):27. https://doi.org/10.1038/s41467-019-13855-2.
21. Vineis P, Demetriou CA, Probst-Hensch N. Long-term effects of air pollution: an exposome meet-in-the-middle approach. Int J Public Health. 2020;65(2):125-7. https://doi.org/10.1007/s00038-019-01329-7.
22. Laine JE, Bodinier B, Robinson O, Plusquin M, Scalbert A, Keski-Rahkonen P, et al. Prenatal Exposure to Multiple Air Pollutants, Mediating Molecular Mechanisms, and Shifts in Birthweight. Environ Sci Technol. 2020;54(22):14502-13. https://doi.org/10.1021/acs.est.0c02657.

2.3 Healthy Cities, Healthy People

Programme Lead – Professor Majid Ezzati (ICL)
Programme Teams – please see the MRC Centre website

2.3.1 Overview and programme strategy

The Healthy Cities, Healthy People programme aims to advance our understanding of the effects of the urban environment on health, and supports technical and policy interventions that create healthier and more equitable urban environments. The work covers the following areas: i) high-resolution measurement of urban environment and population health; ii) characterising complex urban environments and health

outcomes; and iii) policy modelling and evaluation. Associated with these areas are methodological advances in statistics and machine learning, and in environmental and epidemiological modelling. London, and other cities in the UK, continue to be a major focus of the research but there is also a significant body of work elsewhere in Europe, Africa, Asia and the Americas. The work involves using routine health and population data, collection of primary data and increasingly "big data" resources such as satellite and street images. Through its substantive focus, methodology and data sources, the programme interacts regularly with other programmes and themes at the Centre.

2.3.2 Progress and research highlights

Through our leadership of the Wellcome Trust-funded Pathways to Equitable Health Cities (*Pathways*) programme we are studying the urban environment and population health in a comparative manner in cities in Bangladesh (Dhaka), Canada (Vancouver), China (Beijing), Ghana (Accra) and the UK (London). Work in *Pathways* is organised along two inter-related frameworks, which allow us to cross-learn across cities in data, methods and policies: i) quality of housing and neighbourhood environment and ii) housing location, mobility, and access to services. This approach allows understanding of the linkages and trade-offs among housing cost, location and quality; transport mode, cost, duration and safety; and access to beneficial (e.g. education, healthcare, sports and play) and harmful (e.g. air and noise pollution, crime) urban features, and are being used for modelling the impacts of policies.

Other key funded activities which we lead or have a major role in include:

- Science and Solutions for a Changing Planet Doctoral Training Partnership – funded by NERC
- *Children's Places* project – funded by the Health Foundation
- Science and technology in childhood obesity policy (*STOP*) – funded by EC's H2020
- Public Health Impacts of UK's Clean Air Zones (*PHICAZ*) – funded by the MRC
- The Real-time Assessment of Community Transmission (*REACT*) programme that is tracking the spread of the SARS-CoV-2 virus across randomised samples of communities in England.

Specific research activities are summarised below.

High-resolution measurement of population health

We have developed and applied spatiotemporal models to geocoded civil registration and health service data to quantify relevant measures of health in different cities, at a higher resolution than attempted before. For example, in London, we have successfully quantified trends in life expectancy for 4,835 London Lower Layer Super Output Areas (LSOAs) the finest level ever analysed. This result shows that a significant proportion of inequalities in London are highly local, within local authority districts, and the local component of inequalities has increased over time. Work in London, Beijing and Vancouver is now focusing on cause-specific mortality across the life-course whereas in Accra, the initial focus has been on child mortality while evaluating the completeness of death registration for cause-specific analysis. Specifically, we have analysed spatial and socioeconomic inequalities in child mortality for 406 neighbourhoods in Greater Accra from the census and demographic methods. We have also obtained records of deaths registered in Accra and are evaluating the extent of (in)completeness of death registration to analyse age- and cause-specific mortality. In parallel to variations over space, we have begun to consider multiple health outcomes (see also Future direction), including changes in the composition of mortality in terms of causes of death.

Quality of the living environment – air and noise pollution and sources

As part of the Health Effects Institute-funded *ELAPSE* (Exposure to Low-level Air Pollution: a Study of European cohorts) project we are investigating differential impacts of air pollution on a wide range of health outcomes across different socio-demographic groups including individuals and communities of different socioeconomic status and by ethnicity. In the MRC-funded *PHICAZ* programme we are evaluating the public health impact of the introduction of the Ultra-Low Emissions Zone in London, using a time-series approach.

In Accra, we have collected the most granular data on spatial and temporal patterns of air and noise pollution and their sources of any city in Africa to understand the extent and contributors to inequalities in pollution. In Beijing, we have used atmospheric and land-use regression models to map PM2.5 concentration for all housing complexes.

We are working on two projects to evaluate the impact of aircraft noise on cardio-vascular hospitalisations and mortality at high spatial resolution. The NIHR-funded *RISTANCO* project is investigating short-term impact of aircraft noise around Heathrow airport using a case-crossover design. The MRC-funded *ANCO* project is assessing the long-term impact of aircraft noise around multiple airports in England using a spatio-temporal modelling framework.

Quality of the living environment – greenspace, walkability and play

The *Children's Places* project, funded by the Health Foundation, investigates how characteristics of the different places where children spend their time (including home, school and social networks) may generate impacts on education and skills development. We apply novel approaches, combining spatial databases on health-relevant place-based characteristics (e.g. air pollution, walkability, food environment, social hazards), advanced geospatial and mathematic models and routinely collected population-level educational attainment information from the Department for Education. We actively engage with teenagers throughout the project via focus groups and workshops. Outputs so far include a systematic review of the literature on built environment and educational attainment and development of methods to mine school Twitter accounts to construct social networks.

We have also mapped open and green space for all schools in London and are mapping traffic safety in areas around schools. We are conducting similar activities in Accra, Beijing and Dhaka with consideration of locally relevant features of children's environment.

In the work funded via the NERC Science and Solutions for a Changing Planet Doctoral Training Partnership we are probing the effect modifiers of the relationship between health and exposure to natural environments (i.e. urban greenspace), including biodiversity, green and blue space interactions, and the presence of traffic near natural environments. We are also studying the relationship between greenspace and cardiovascular health outcomes in *UK Biobank* participants. We developed novel pathway-specific exposure metrics including 'green walkability', and greenspace function and applied them to participants of this large, adult cohort. Using survival analyses, we examined the associations of greenspace with cardiovascular, respiratory, and non-injury mortality, adjusting for relevant individual- and area-level confounders.

Finally, beyond specific features, we are analysing variations in the urban form in African cities to understand the organisation of the city in relation to building numbers and density, roads and vegetation. Together with data on socioeconomic status from the census, which we have access to, this will allow us to answer an emerging question in urban expansion in Africa: whether the poor are being marginalised to outer parts of expanding cities, with limited access to essential services.

COVID-19 pandemic and population health

In parallel to the work of our colleagues in outbreak analysis, modelling the dynamics of outbreaks, we have focused on the impacts of the COVID-19 pandemic on population health in a data driven approach, also eliciting features of communities with higher/lower infection.

In the *REACT* programme we have been quantifying the effects of the pandemic on different socio-economic groups finding that more deprived communities, minority ethnic groups and people in some public-facing occupations were more at risk of infection. This higher infection risk together with higher morbidity (such as obesity) among people living in deprived areas help explain the greater propensity for such groups to be hospitalised with severe disease (also more recently reflecting lower vaccination rates in some of these groups).

We have also developed methodology to stochastically estimate the total mortality impacts of the pandemic and how it may be related to community socioeconomic and built environment characteristics such as overcrowding and air pollution. The work has been at difference scales, ranging from local to national. For example, we applied Bayesian spatial models to geocoded civil registration mortality data held by the UK Small Area Health Statistics Unit to quantify excess mortality during the first wave of the COVID-19 pandemic in England. The risk of excess mortality was related to greater social and environmental deprivation factors, such as poverty and overcrowded homes. This work is the highest-resolution analysis of excess mortality in England and is being extended with a cross-country comparison including high spatial resolution data from Italy and Sweden.

2.3.3 Future direction and objectives

We will continue empirical and methodological research on cities and population health in the areas described above. In addition, we are increasingly working in two cutting-edge areas that will help advance the field.

Digital surveillance of urban environment

We are leveraging traditional administrative and survey data sources as well as emerging big data sources, including street and satellite imagery and online data, to better measure urban environment and exposures. We are also advancing methodology for use of big data, for example transferability of deep learning networks trained in one city to other cities with limited outcome data for training. Examples of ongoing work include methods for combining street and satellite images, the use of images and audio clips to identify variations over space and time in air and noise pollution sources, and the use of street and satellite images to measure different dimensions of neighbourhood quality.

Multi-dimensional urban health and environmental phenotypes

Many features of the urban environment have shared social, historical and physical determinants – e.g. arise from poverty or distance to roads or city centre. Similarly, many health outcomes have shared determinants (e.g. smoking, obesity, air pollution, etc) and may share interventions or intervention delivery platforms (e.g. diseases addressed in primary care, diseases requiring surgery, etc). We are increasingly using unsupervised and supervised statistical and machine learning approaches to identify and understand multi-dimensional phenotypes of the urban environment and population health. The aim is to identify related features of the environment and diseases, based on their pattern's concordance and discordance, and identify places where these related exposures or outcomes may be important.

2.3.4 Selected publications

23. Davies B, Parkes BL, Bennett J, Fecht D, Blangiardo M, Ezzati M, et al. Community factors and excess mortality in first wave of the COVID-19 pandemic in England. Nat Commun. 2021;12(1):3755. https://doi.org/10.1038/s41467-021-23935-x.
24. Kontis V, Bennett JE, Rashid T, Parks RM, Pearson-Stuttard J, Guillot M, et al. Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries. Nat Med. 2020;26(12):1919-28. https://doi.org/10.1038/s41591-020-1112-0.
25. Collaboration NCDRF. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. Nature. 2019;569(7755):260-4. https://doi.org/10.1038/s41586-019-1171-x.
26. Clark SN, Alli AS, Nathvani R, Hughes A, Ezzati M, Brauer M, et al. Space-time characterization of community noise and sound sources in Accra, Ghana. Sci Rep. 2021;11(1):11113. https://doi.org/10.1038/s41598-021-90454-6.
27. Alli AS, Clark SN, Hughes A, Nimo J, Bedford-Moses J, Baah S, et al. Spatial-temporal patterns of ambient fine particulate matter (PM2.5) and black carbon (BC) pollution in Accra. Environ Res Lett. 2021;16(7):074013. https://doi.org/10.1088/1748-9326/ac074a.
28. Sheridan CE, Roscoe CJ, Gulliver J, de Preux L, Fecht D. Inequalities in Exposure to Nitrogen Dioxide in Parks and Playgrounds in Greater London. Int J Environ Res Public Health. 2019;16(17). https://doi.org/10.3390/ijerph16173194.
29. Shoari N, Ezzati M, Baumgartner J, Malacarne D, Fecht D. Accessibility and allocation of public parks and gardens in England and Wales: A COVID-19 social distancing perspective. PLoS One. 2020;15(10):e0241102. https://doi.org/10.1371/journal.pone.0241102.
30. Clark SN, Alli AS, Brauer M, Ezzati M, Baumgartner J, Toledano MB, et al. High-resolution spatiotemporal measurement of air and environmental noise pollution in Sub-Saharan African cities: Pathways to Equitable Health Cities Study protocol for Accra, Ghana. BMJ Open. 2020;10(8):e035798. https://doi.org/10.1136/bmjopen-2019-035798.
31. Shoari N, Ezzati M, Doyle YG, Wolfe I, Brauer M, Bennett J, et al. Nowhere to Play: Available Open and Green Space in Greater London Schools. J Urban Health. 2021;98(3):375-84. https://doi.org/10.1007/s11524-021-00527-0.
32. Suel E, Bhatt S, Brauer M, Flaxman S, Ezzati M. Multimodal deep learning from satellite and street-level imagery for measuring income, overcrowding, and environmental deprivation in urban areas. Remote Sens Environ. 2021;257:112339. https://doi.org/10.1016/j.rse.2021.112339.

33. Riley S, Ainslie KEC, Eales O, Walters CE, Wang H, Atchison C, et al. Resurgence of SARS-CoV-2: Detection by community viral surveillance. Science. 2021;372(6545):990-5. https://doi.org/10.1126/science.abf0874.
34. Ward H, Atchison C, Whitaker M, Ainslie KEC, Elliott J, Okell L, et al. SARS-CoV-2 antibody prevalence in England following the first peak of the pandemic. Nat Commun. 2021;12(1):905. https://doi.org/10.1038/s41467-021-21237-w.

Selected submitted manuscripts

Rashid T, Bennett JE, Paciorek CJ, Doyle Y, Pearson-Stuttard J, Flaxman S, et al. Life expectancy and risk of death in 6,791 English communities from 2002 to 2019: high-resolution spatiotemporal analysis of civil registration data. [in press] The Lancet Public Health

Nathvani R, Clark SN, Muller E, Alli AS, Bennett JE, Nimo J, et al. Spatiotemporal characterisation of urban environment and activity with street-level imagery and deep learning – data, analytics and application to Accra, Ghana. [submitted]

2.4 Biostatistics and Data Science

Theme Lead – Professor Marta Blangiardo (ICL)
Theme Teams – please see the MRC Centre website

2.4.1 Overview and theme strategy

The Biostatistics and Data Science theme develops statistical methodology and innovative data analytics, anchored in the Bayesian hierarchical modelling paradigm and machine learning, to improve statistical inference in environment and health studies. We employ flexible, spatio-temporal semi- and nonparametric models for large complex data from environmental and epidemiological studies, and we work on multi-omic high-throughput platforms and develop strategies to address the computational challenges of high-dimensional estimation applied to biomarker discovery and the identification of metabolic pathways supporting causal inference.

The theme aims to provide statistical support and quantitative methods development to enable Centre researchers to probe the available rich data resources in new and flexible ways, to tease out complex interactions and pathways linking predictors and outcomes, and to analyse and integrate multiple data sources linked in space and time in a coherent and robust manner.

2.4.2 Research highlights

In spatio-temporal modelling we have worked on augmenting population-based registries via cohorts/surveys to improve confounder adjustment of the association between exposures/risk factors and health outcomes, dealing at the same time with missing data via propensity score adjustment (MRC Methodology grant - PI Blangiardo) [35] and have developed a modelling approach to identify geographical areas characterised by unusual temporal trends in life expectancy (MRC Centre fellowship, Boulieri). Additionally, we are currently working on scalable, reproducible and generalizable spatio-temporal models for evaluating the impact of climate and local socio-environmental conditions on joint population health outcomes (Wellcome Trust Seed Award on Science - PI Pirani; paper in preparation).

We have proposed the first algorithm that uses genetic information as causal anchors to select exposures increasing disease risk from a high-dimensional set of candidate exposures [36] which has been applied to identify lipid traits causing cardiovascular and peripheral artery disease (in collaboration with the Million Veteran Program - PI Scott Damrauer - funded by the US Department of Veterans Affairs) [37].

In line with the two EU-funded next generation *exposome* projects (*EXPANSE* and *LongITools*) where we lead the statistical work packages, we have developed, as part of our complexity reduction approach, the Biological Health Score (BHS), a composite score which showed strong social gradient in the Understanding Society study. This score was further investigated in relation to cancer and CVD mortality and incidence in the *UK Biobank* study, showing a similar social gradient and a predictive

ability that complemented established risk factors and behaviours for the prediction of CVD incidence [38]. Ongoing work is looking at the molecular determinants of the BHS in the *UK Biobank* cohort and in the Northern Finland Birth Cohort (NFBC) and shows promising results at the metabolome level.

We have developed an automated procedure for the calibration of conditional independence networks based on an in-house stability score, which can accommodate multiple blocks (i.e. multi-omic) of correlated features. Based on simulated data, our approach outperformed existing calibration methods, and its pilot application to smoking related DNA methylation and gene expression revealed biological and functional relevance of the network topology. The approach is currently being applied to the multi-omic profiling of future lung cancer cases.

We continue to work on metabolomics, developing a new approach to correct for multiple testing in metabolome-wide association studies and comparing several methods for metabolomic time series data [39]. We have also applied these new methods to epidemiological cohorts (*Airwave*, *MESA*, *Rotterdam Study*) to enable discovery of novel biomarkers of atherosclerosis [40].

We developed and applied complex statistical models at small area level i) to evaluate the impact of air pollution on COVID-19 mortality accounting for misalignment between exposure and health data and ii) to assess the impact of community level characteristics on total excess mortality during the first wave of the COVID-19 pandemic in England [23]. We have also leveraged genetic data on COVID-19 severity to demonstrate the likely causal role of obesity, diabetes and smoking, increasing the risk of severe COVID-19 outcomes [41]. Moreover, we have shown that angiotensin-converting-enzyme (ACE) inhibitors, a commonly used class of anti-hypertensive drugs, is unlikely to increase risk of severe COVID-19. Finally, we provided evidence that genetic susceptibility to severe COVID-19 outcomes is associated with increased risk of ischemic stroke supporting calls for better monitoring of COVID-19 patients for neurological symptoms. We have also developed a stability-based calibration procedure to be applied to penalized regression or graphical models (paper under review at JRSS-C). This has been applied in a penalized regression context to analyse the drivers of COVID-19 positivity [42], COVID-19 mortality, COVID-19 symptomatology.

We continued to actively collaborate and methodologically supported the work of other research teams within the Centre for developing cutting edge research revealing new complex interactions between environmental exposures and outcomes [43].

2.4.3 Future directions and objectives

A key area of development in this Theme will continue to be data integration. We will develop scalable methods of analysis to combine environmental exposure information from satellites and *in-situ* observations, allowing for uncertainty, measurement error, bias and spatio-temporal misalignment. We will extend the framework to estimate multi-pollutant concentrations and to link these with health outcomes. We will further develop network analysis to integrate multi-omic data, and methods for large scale pre-processing and analysis of multi-cohort metabolomics data.

We will continue our focus on methodology as well as substantive applications of our work in support of the Centre programmes. For instance, we will develop disease surveillance methods for multi-morbidity studies (as part of Health Data Research UK) aiming at the discovery of common risk factors underpinning clusters of health conditions. We will build a flexible, comprehensible and generalisable statistical modelling framework to evaluate the individual and cumulative impact of “shocks” (e.g. government policies or unpredictable events) on health outcomes over time. We will use this approach to quantify the impact of changes in air pollution during the COVID-19 pandemic on health outcomes across the life-course in an urban setting (Wellcome Trust Collaborative award - PI: Blangiardo; PHICAZ programme - PI: Elliott).

We will develop machine learning approaches to reconstruct source determination from particulate matter components and at the same time model the links with health outcomes (MRC Methodology award - PI Blangiardo). We will also propose a modelling framework that captures how synchronised changes in environmental and meteorological conditions over space and time affect human health, for example, exacerbations of chronic conditions such as asthma and COPD (MRC SDF Fellowship - Konstantinoudis; Centre PhD student - Riley).

We will develop models to integrate personal, residential and ambient exposures using data from the *COPE* and *AIRLESS* studies. Our aim is to interpolate data from defined periods of intensive personal monitoring, both indoors and outdoors, to provide annual mean personal exposure estimates for both PM and gaseous pollutants.

Our exposome research requires clustering approaches to identify "Expo-types", clusters of individuals experiencing similar sets of exposures to behavioural, psychosocial and environmental factors. Evidence of potential intermediate effects of these exposure sets is sought for by investigating the molecular and biological signatures of these "Expo-types". In a final step, the relevance of these "Expo-types" for health outcomes will be investigated by means of risk prediction models where blocks of variables are selected (via stability selection) such that they complement each other. To ensure reproducibility, we are currently extending our stability-based calibration approach to i) unsupervised dimensionality reduction techniques, ii) penalised regression [44], iii) penalized partial least square models, and iv) clustering approaches. These extensions are currently being compiled in an R package and accompanying note to be submitted to the Journal of Statistical Software.

Preliminary results from the *UK Biobank* study using this approach are promising and identify several "Expo-types", each associated with specific biomarkers, and possibly intermediate health outcomes. Future development of this work involves the generation of the "Expo-types" by using (semi)-supervised clustering approaches, ensuring that clusters are defined such that they maximise the contrast across cluster for a given set of variables (e.g. prevalence/incidence of sub-clinical phenotypes).

We will continue the implementation of dynamic models for the natural history of disease progression using multi-state models. We have developed a reversible jump sampler and a hierarchical model, first selecting the variables contributing to each transition probabilities, and conditional on inclusion, estimate the effect of the covariate. These two approaches perform variable selection ensuring we optimize the reconstruction of individual pathological trajectories. These approaches offer a refined modelling of disease natural history and identify key factors driving the dynamic of disease progression. Current applications investigate drivers of the dynamic of lung carcinogenesis (using lifestyle, demographic and genetic factors).

We will make R or C++ code available (via R-packages and/or GitHub repositories) for all the above approaches, together with detailed documentation to ensure their utility outside the scope of the projects they stemmed from.

2.4.4 Selected publications

35. Pirani M, Mason AJ, Hansell AL, Richardson S, Blangiardo M. A flexible hierarchical framework for improving inference in area-referenced environmental health studies. Biom J. 2020;62(7):1650-69. https://doi.org/10.1002/bimj.201900241.
36. Zuber V, Colijn JM, Klaver C, Burgess S. Selecting likely causal risk factors from high-throughput experiments using multivariable Mendelian randomization. Nat Commun. 2020;11(1):29. https://doi.org/10.1038/s41467-019-13870-3.
37. Levin MG, Zuber V, Walker VM, Klarin D, Lynch J, Malik R, et al. Prioritizing the Role of Major Lipoproteins and Subfractions as Risk Factors for Peripheral Artery Disease. Circulation. 2021;144(5):353-64. https://doi.org/10.1161/CIRCULATIONAHA.121.053797.
38. Chadeau-Hyam M, Bodinier B, Vermeulen R, Karimi M, Zuber V, Castagne R, et al. Education, biological ageing, all-cause and cause-specific mortality and morbidity: UK biobank cohort study. EClinicalMedicine. 2020;29-30:100658. https://doi.org/10.1016/j.eclinm.2020.100658.
39. Jendoubi T, Ebbels TMD. Integrative analysis of time course metabolic data and biomarker discovery. BMC Bioinformatics. 2020;21(1):11. https://doi.org/10.1186/s12859-019-3333-0.
40. Tzoulaki I, Castagne R, Boulange CL, Karaman I, Chekmeneva E, Evangelou E, et al. Serum metabolic signatures of coronary and carotid atherosclerosis and subsequent cardiovascular disease. Eur Heart J. 2019;40(34):2883-96. https://doi.org/10.1093/eurheartj/ehz235.
41. Ponsford MJ, Gkatzionis A, Walker VM, Grant AJ, Wootton RE, Moore LSP, et al. Cardiometabolic Traits, Sepsis, and Severe COVID-19: A Mendelian Randomization Investigation. Circulation. 2020;142(18):1791-3. https://doi.org/10.1161/CIRCULATIONAHA.120.050753.

42. Chadeau-Hyam M, Bodinier B, Elliott J, Whitaker MD, Tzoulaki I, Vermeulen R, et al. Risk factors for positive and negative COVID-19 tests: a cautious and in-depth analysis of UK biobank data. Int J Epidemiol. 2020;49(5):1454-67. https://doi.org/10.1093/ije/dyaa134.
43. Maes M, Pirani M, Booth E, Shen C, Milligan B, Jones K, Toledano M. Benefit of woodland and other natural environments for adolescents' cognition and mental health. Nat Sustain (2021). https://doi.org/10.1038/s41893-021-00751-1
44. Dagnino S, Bodinier B, Guida F, Smith-Byrne K, Petrovic D, Whitaker MD, et al. Prospective Identification of Elevated Circulating CDCP1 in Patients Years before Onset of Lung Cancer. Cancer Res. 2021;81(13):3738-48. https://doi.org/10.1158/0008-5472.CAN-20-3454.

2.5 Cohorts and Data Resources

Theme Lead – Professor Debbie Jarvis (ICL)
Theme Teams – please see the MRC Centre website

2.5.1 Overview and theme strategy

The Centre's mission to examine environment/health associations is predicated on access to information from cohorts large enough to detect effects and with sufficient detail to adjust for confounding and examine effect modification by other environmental or lifestyle factors. Cohorts and data resources are integral to much of the work of the three major themes of the Centre which have been detailed earlier in this report.

The theme promotes the inception, maintenance, enrichment and linkage of longitudinal cohorts that have appropriate detailed information on phenotypes, relevant confounders and environmental exposures. Application of Centre expertise in personal exposure assessment, geocoding, biomarkers and exposure assignment and in data linkage of cohorts with environmental and health utilisation record databases (including activities through collaboration with HDR UK) ensures that the contribution of our in-house and affiliated cohorts to environmental research is maximised.

All cohorts have made progress in extending information on phenotype and exposure information over the last years and expanded biological collections and molecular profiling. However, over the last 18 months during the COVID-19 pandemic clinically based follow-up within most cohorts has been severely limited by restrictions on face-to-face assessments and competing priorities for the clinical research units where such assessments may take place.

2.5.2 Research highlights

SCAMP

SCAMP, a study of about 7000 children recruited at ages 11-12 to evaluate associations of mobile phone usage with cognitive and behavioural development has received programme-level MRC funding for a second wave of data collection (participants now aged 17-18). This funding supports a greater focus on mental health and includes genotyping. Assessments will include of cognitive function (an online assessment platform has been developed), mental health, technology use, health, lifestyle, and social and physical environments. There has already been biological sampling from about 2,000 cohort members at baseline and the study has been extended to include lung function testing and exposure assessment of cohort members to individual air pollutants, pollutant mixtures, 'greenness' and noise through geographical information systems (GIS) techniques. A mobile app is under development for further follow-up of *SCAMP* participants after they have left school. Two papers about markers of puberty are drafted/under preparation. The study biobank will be used to assess whether cognitive deficits are linked with systemic oxidative stress and neuro-inflammation and whether pro-oxidant components of the urban airshed (e.g. transition metals, oxidative gases) may drive associations (the sub-study *CLUE* study).

SCAMP has obtained data linkage to educational outcome data (Department for Education). *SCAMP* with other databases of cohorts established for examination of radiofrequency radiation and health (UK-*COSMOS*, *Airwave*) have obtained data linkage or are in the process of making data linkage of health outcomes through NHS Digital, NHS Scotland and the UK Longitudinal Linkage Collaboration (LLC).

SCAMP researchers have developed fruitful collaboration with *CVEDA* an adolescent cohort in India with detailed information on mental health. This has led to development of harmonised protocols for assessment of environmental exposures and to joint work on associations of puberty and mental health.

Airwave

The *Airwave* study is a cohort study of the health of the British police forces, involving over 50,000 participants. It has a focus on possible health effects associated with use of the police radio system (TETRA), and also has established a multi-omic resource for exposome studies. Face-to-face follow-up, funded by the Imperial NIHR Biomedical Research Centre and programme-grant funding from the MRC was halted by the COVID-19 pandemic in March 2020. However, the cohort was re-purposed for COVID-19 related research and over 5,000 participants attended for a clinic visit during 2020 to test antibody response to the SARS-CoV-2 virus as well as testing for the virus using different media. The opportunity was taken to collect additional blood samples for analysis and long-term storage to augment the *Airwave* bioresource.

SAHSU

The UK Small Area Health Statistics Unit (SAHSU) contributes national-level data and expertise across the MRC Centre with a programme of studies that address the health impact of environmental exposures, socio-demographic and geographic inequalities. Recent developments include the MRC programme-funded Public Health Impacts of Clean Air Zones (*PHICAZ*), a collaboration with the *CHILL* study (see below) where the impact of a large-scale ultra low emission zone (uLEZ), recently implemented in London, on a range of health outcomes including respiratory function in children and hospital admissions will be analysed. SAHSU collaborates with PHE/UKHSA to undertake small-area analyses of the health impacts of residential proximity to current or former industrial sites, within projects bringing together environmental monitoring, human exposure biomonitoring and health data. In addition, SAHSU has linked population-level data on health from people living near Heathrow airport to modelled airport noise contours. SAHSU is contributing to studies within the CRTH HPRU on nuclear installations and brownfield sites.

Response to the pandemic

Inevitably the COVID-19 pandemic has impacted in multiple ways the work of the cohorts and data resource teams. Although it has created some difficulties for cohorts it has also provided opportunities to develop new COVID-19 cohorts and enrich the information within some established cohorts.

Centre investigators have been involved in high profile repeat cross-sectional studies to assess the prevalence of SARS-CoV-2 virus and antibody positivity within the population of England during the pandemic, with over 2 million participants ages 5 years and above having taken part to date (the *REACT* studies). People participating in these studies will be followed up long term and information already collected includes sociodemographic, COVID-19 history, symptoms, and vaccination data (from January 2021), co-morbidities and behaviour. Biological samples are available from over 10,000 participants who have been recalled for further investigation through the *REACT-Genomics England* (*REACT-GE*) and *REACT-Long Covid* (*REACT-LC*) studies funded by UKRI and NIHR. These studies will provide a platform for environmental research including impact of environment on short- and long-term effects of COVID-19 over the coming years.

Participants in some centre-led cohorts (e.g. *Airwave*, see above) have been recruited into COVID-related studies. The *SCAMP* study has also been exploited for assessing the impact of COVID-19 on adolescent mental health.

SAHSU has conducted a programme of studies to understand the role of the environment in vulnerability and resilience to the health impacts of the COVID-19 pandemic. publishing an analysis of the community factors associated with excess mortality during the first wave of the pandemic in England.

Research in China

There are longstanding links with China through the *INTERSALT* and *INTERMAP* studies developed over 20 years ago. These platforms continue to be developed to provide insights into environmental health effects. The *INTERLIPID* study is an epidemiological investigation of relationships between micro- and macronutrients on cardio-metabolic health and has received additional funding for NMR and UPLC MS profiling of about 1,200 participants. The centre-led *INTERMAP* China Prospective (ICP) Study has worked with the exposure science theme to assign air pollution exposure (two 24-hr timed personal exposure data) along with detailed fuel use data of about 800 adults. The AIRLESS study, a panel study of over 250 adults in urban and peri-urban areas of Beijing assessing the relationships between short term pollutant exposures and a range of health outcomes (including inflammatory and metabolomic markers) has included participants from *INTERMAP*. This means that some participants in this intensively monitored *AIRLESS* study group have extensive longitudinal information collected over the last 20 years that can be incorporated into future analyses

Work with low- and middle-income countries (LMICs)

The cohort work programme has extended further into LMICs. Centre investigators are leading the environmental component of a new mother and baby cohort in sub-Saharan Africa funded by the Wellcome Trust (von Dadelszen, King's College London, 2020-23). They will exploit the detailed pregnancy information and samples gathered in the *PRECISE* cohort (von Dadelszen, King's College London, https://precisenetwork.org/), following up a cohort of 4800 women in The Gambia and Kenya, and their children. Environmental data will be combined with clinical, geographical and social data. The overarching aim is to investigate environmental determinants and mechanisms that underpin optimal maternal and child health trajectories.

Centre investigators also work with a consortium of researchers in the UK and Africa to understand and improve the health of young people with asthma in Africa - *ACACIA* (Achieving Control of Asthma in Children in Africa) (NIHR, Grigg, Queen Mary University of London -QMUL). In collaboration with urban schools in Ghana, Malawi, Nigeria, South Africa, Uganda and Zimbabwe, teams from local universities are collecting data from 3000 children on respiratory symptoms, medication, healthcare, and lung health. This has been extended to incorporate a strong environmental component through *CAPPA* (Children's Air Pollution Profiles in Africa) (Grigg, QMUL, 2021-22), which will describe the burden of personal air pollution exposure in urban children with asthma symptoms in sub-Saharan Africa, its geographic, and temporal variability, the role of transport, indoor and outdoor microenvironments and activity profiles, and the effect of socioeconomic variables.

With funding from the Wellcome Trust we are collaborating to establish the South Asia Biobank on the Indian sub-continent (100,000 individuals) and to extend the *LOLIPOP* study of South Asians living in West London to 100,000 people. This will provide a rich resource for multi-omic studies among South Asians.

Other

Lifepath is a H2020-funded consortium that has combined information from multiple cohorts with good characterization of socio-economic position, mortality and functional outcomes of ageing, and a range of biomarkers (e.g. allostatic load) and omic measurements, has continued to publish extensively on the intermediate pathways linking risk factors for non-communicable disease, adverse childhood environment and events, molecular mechanisms and health outcomes.

The Centre-led respiratory/allergy focused adult inception European Community Respiratory Health Survey (*ECRHS*) has developed protocols for the fourth wave of data collection (participants will be aged 50-75 years) and continues to contribute to major international consortia and joint analyses. The Centre-led cardiovascular/metabolic focussed birth cohorts *Northern Finnish Birth Cohorts*, have expanded testing of their associated biobanks, including omics measures, to assess the role of environmental factors in growth, ageing and multi-morbidity.

The *CHILL* study, a five-year study to determine whether reducing air pollution from traffic (uLEZ intervention in London) improves lung function growth trajectories and respiratory health in primary school children. This will be achieved by linking high resolution models to detailed longitudinal assessments of lung function over a five year period in London and Luton, but in Luton will also include

linkage to primary care records. Since 2020 both DNA collection for epigenetics and cognitive function testing have been added and the team will add bloodspot collection in the final year to permit proteomic, metallomic and metabolomic assessment of exposure and response biomarkers.

The exposure modelling teams continue to provide air pollution exposure to external cohorts – for example to *UK Biobank* using an extension of CMAC-Urban applied to the whole of the UK.

2.5.3 Future direction and objectives

The Cohorts and Data Resources groups major focus over the coming year will be to continue to work with Centre themes, including the biostatics and data science theme, to ensure that cohorts provide relevant phenotype, and confounder information, appropriate information on lifestyle and behaviours and biobanking. This ensures all cohorts can be used for environmental research even if their original aims were more wide ranging. With the challenge of climate change cohorts will need to identify relevant information on behaviours for assessment of temperature related threats.

Within the theme there is rapidly expanding expertise in the use of mobile and web-based technologies for collection of information on health, lifestyle, occupational exposures, and environmental exposure assignment. Development of these will continue.

Within HDR UK we will be developing a demonstrator project on social and environmental determinants of health, building on our expertise in SAHSU, cohorts and exposure assessment including GIS and use of remote sensing data.

2.5.4 Selected publications

45. de Matteis S, Jarvis D, Darnton A, Hutchings S, Sadhra S, Fishwick D, et al. The occupations at increased risk of COPD: Analysis of lifetime job-histories in the population-based UK Biobank Cohort. European Respiratory Journal. 2019;54(1). https://doi.org/10.1183/13993003.00186-2019.
46. Burte E, Leynaert B, Marcon A, Bousquet J, Benmerad M, Bono R, et al. Long-term air pollution exposure is associated with increased severity of rhinitis in 2 European cohorts. Journal of Allergy and Clinical Immunology. 2020;145(3):834-42.e6. https://doi.org/10.1016/j.jaci.2019.11.040.
47. Cai Y, Hansell AL, Granell R, Blangiardo M, Zottoli M, Fecht D, et al. Prenatal, early-life, and childhood exposure to air pollution and lung function: The alspac cohort. American Journal of Respiratory and Critical Care Medicine. 2020;202(1):112-23. https://doi.org/10.1164/rccm.201902-0286OC.
48. Elliott J, Bodinier B, Bond TA, Chadeau-Hyam M, Evangelou E, Moons KGM, et al. Predictive Accuracy of a Polygenic Risk Score-Enhanced Prediction Model vs a Clinical Risk Score for Coronary Artery Disease. JAMA - Journal of the American Medical Association. 2020;323(7):636-45. https://doi.org/10.1001/jama.2019.22241.
49. Fecht D, Garwood K, Butters O, Henderson J, Elliott P, Hansell AL, et al. Automation of cleaning and reconstructing residential address histories to assign environmental exposures in longitudinal studies. International Journal of Epidemiology. 2020;49:I49-I56. https://doi.org/10.1093/ije/dyz180.
50. Han Y, Chen W, Chatzidiakou L, Krause A, Yan L, Zhang H, et al. Effects of AIR pollution on cardiopuLmonary disEaSe in urban and peri-urban reSidents in Beijing: Protocol for the AIRLESS study. Atmospheric Chemistry and Physics. 2020;20(24):15775-92. https://doi.org/10.5194/acp-20-15775-2020.
51. Riley S, Ainslie KEC, Eales O, Walters CE, Wang H, Atchison C, et al. Resurgence of SARS-CoV-2: Detection by community viral surveillance. Science. 2021;372(6545):990-5. https://doi.org/10.1126/science.abf0874
52. Wielscher M, Amaral AFS, van der Plaat D, Wain LV, Sebert S, Mosen-Ansorena D, et al. Genetic correlation and causal relationships between cardio-metabolic traits and lung function impairment. Genome Medicine. 2021;13(1). https://doi.org/10.1186/s13073-021-00914-x.
53. Zhang Y, Vaidya N, Iyengar U, Sharma E, Holla B, Ahuja CK, et al. The Consortium on Vulnerability to Externalizing Disorders and Addictions (c-VEDA): an accelerated longitudinal cohort of children and adolescents in India. Molecular Psychiatry. 2020;25(8):1618-30. https://doi.org/10.1038/s41380-020-0656-1.

3. TRAINING PROGRAMME

Joint Academic Career Development Programme Director – D Frédéric Piel
Joint Academic Career Development Programme Deputy Director – Dr Stephanie Wright

3.1 Overview and Mission

The MRC Centre Training Programme was established in 2009 with the mission of providing first-class training and career development opportunities for students and early career researchers (ECRs) in the environment and health sciences. From 2020 the training programmes of the MRC Centre and the two NIHR HPRUs were merged, forming the Joint Academic Career Development Programme (JACD), with the aim of expanding and diversifying the range of activities on offer while optimising the use of the resources available in the three units, and to give our students and ECRs the opportunity to have more applied experiences through the close collaboration with PHE (for more information see Annex 2).

The vision for the JACD is to be the leading European programme for training of a new generation of research and policy leaders in environment and health sciences. This involves providing training for PhD and early postdoctoral scientists i) across a range of disciplines, especially those involving quantitative and computational science, ii) of both dry- and wet lab scientists providing them with the quantitative skills needed to analyse and use the outputs of large-scale omics analyses, and iii) to apply the outputs of modern epidemiological, toxicological and omic analyses within a public health context, and in relation to policy development.

Currently the JACD hosts **79 PhD students** (62 PhD students in the MRC Centre) of whom 44 are 'core' students, funded directly from the MRC and NIHR awards or from studentships contributed by the universities (27 'core' students in the MRC Centre), and **76 ECRs** (57 Fellows, Post-doctoral Research Associates and Research Assistants in the MRC Centre).

3.2 Recruitment and appointments

Our approach to recruitment is based on identifying excellent PhD and early career fellowship candidates through consistent and inclusive processes encouraging diversity and equality. Since the renewal of MRC funding in 2019, we ran five competitive rounds of PhD recruitment, the last three jointly with the two HPRUs. In total we received applications from 264 candidates, interviewed 52, and offers were made to 21 candidates (3 declined - 8% success rate). Of the **18 studentships awarded** 13 were in the MRC Centre and the remainder in the HPRUs. Ten students in the current MRC Centre cohort directly address the MRC strategic skill priority area of quantitative skills, reflecting the expertise within the Centre in biostatistics, data science and computational biology.

The recruitment process for the Centre's innovative MRC Early Career Research Fellowship Programme was modelled on the Imperial College Research Fellowships and similar MRC schemes. Over four rounds of recruitment since July 2019, a total of 27 applications were received. The applications covered the range of research areas within the Centre and came from both the UK and overseas. Nine candidates were interviewed, and **6 MRC Early Career Research Fellows** have been appointed, covering a broad range of Centre research: They are:

- Dr Holly Lam (Sept 2019-Feb 2021): *Seasonality of food-related anaphylaxis hospitalizations and its association with pollen.*
- Dr Niloofar Shoari (Sept 2020-present): *School neighbourhood and compliance with WHO-recommended levels of air pollution - A case study of Greater London.*
- Dr Timothy Lucas (July 2020-June 2021): *Combining human movement and disease data because not all exposure to air pollution occurs at home.*
- Dr Hanbin Zhang (Starting Dec 2021): *Evaluation of the combined effects of dietary intervention and environmental changes on cardiovascular health in rural Northern China.*
- Dr Dimitris Evangelopoulos (start date TBC): ***M**ulti-**D**imensional assessment of the **I**mpact of Measurement **E**rror on the health effect estimates of long-term exposure to air pollution (M-DIME study*).
- Dr Ricky Nathvani (start date TBC): *Characterising climate-change resilience of the built environment in Accra with high resolution satellite imagery and deep learning.*

In addition, we host a large cohort of research fellows within the Centre funded from other awards, currently with 12 competitive fellowships awarded to Centre PIs, providing a unique environment for ECRs to interact and develop skills in environment and health research.

3.3 Training activities

The training programme covers three main areas: training and personal development, networking and collaboration, and support and pastoral care.

The COVID pandemic and the change to working remotely created additional challenges in maintaining contact with the students and ECRs. A series of online resources were specifically created to continue to engage with and support this important group through this period including: i) a Training Portal in MS-Teams, providing a single point of access to a collection of remote training resources and information on news, events and career opportunities available across all partners in the Centre and HPRUs; ii) one-to-one online sessions with the JACD Leads to provide additional confidential support on any problems students and ECRs may have been facing, as well as fortnightly wellbeing online coffee mornings in conjunction with the Researchers' Society, providing an online space to connect with peers; iii) a new series of workshops focused on strategic skills areas, such as molecular epidemiology, omics, health analytics, machine learning, Bayesian statistics and coding (see more below); iv) a fortnightly online journal club organized by a committee of Centre students and ECRs, providing regular opportunities for the students and ECRs in the Centre to discuss new studies in their field or to present their own research, providing exposure to diverse topics.

The first training workshop took place in December 2020 and January 2021 on "Machine learning methods in Environment and Health Research". It was coordinated and led by one of the MRC ECR Fellows and combined theory and practical sessions, with presentations of case studies by other students and ECRs. This workshop had to be run twice due to high demand, and was highly successful both in terms of attendance (38 participants in the two practical sessions and an average of 53 attending the case study presentations) and the feedback received (over 85% of participants rated the training received very-useful or useful). The specific content of the training programme is dynamic, shaped by input from the Centre students through regular surveys, and recently, statistics, data visualisation and coding were identified as key areas for future workshops. A second workshop in "Data Visualisation Principles and Methods" is being planned in early 2022.

The first Annual Training Event took place in December 2019: MRC Centre students and ECRs presented their work in a poster session and in plenary oral presentations and had the opportunity to co-chair sessions and network with their peers and Centre members. The second Annual Training Event was held online over two half-days in March 2021: students and ECRs from the MRC Centre and the HPRUs had the opportunity to present their research projects as posters, flash oral presentations, or plenary oral presentations. In total over the two half-days the programme included 9 presentations in plenary from students and Fellows/ECRs and 24 poster presentations from students in three breakout rooms. This was a highly successful meeting, measured by both the number of participants (approximately 100 on each of the two days) and feedback received.

To provide training and support for our ECRs, we will be offering a pump-priming grant package, within which our ECRs will be mentored through a series of workshops focused around the proposal writing and project delivery process, culminating in the opportunity to bid for seed funding from the MRC Centres, with impact and PPI embedded.

Finally, the Centre hosts the Researchers' Society, run by and for students and ECRs of the MRC Centre, which aims to promote the welfare and career development of all students and ECRs across the Centre and the HPRUs. Many events in the Centre training programme, namely external seminars and networking and social events, are initiated and organised by the Researchers' Society. Recent activities have included i) a series of online presentations and panel discussions, open to internal and external participants, on air pollution, plastic pollution, diet and health and on women in science, ii) podcast interviews with the Centre's staff and ECRs iii) a variety of social and cohort building activities such as the online coffee mornings mentioned above, a wellness and mental health week, a book club and regular cook-alongs. The Researchers' Society has taken the lead in promoting sustainable transitions in Imperial College and more widely, establishing a Sustainability Working Group in 2020 and organising activities for students and staff raising awareness and promoting the adoption of

sustainable practices to reduce environmental impact at work and in daily life.

3.4 Future strategy

Our vision for the Centre's training programme is to focus particularly on quantitative skills training, to extend collaborative training with other organisations, and to offer focused support for fellows, building on our success in training at both PhD and post-doctoral levels. We will introduce initiatives related to mentoring and mental health support, and will continue to support networking events, including an "alumni" meeting (e.g. during Year 3) inviting former and current PhD students to present their current research. This will provide a unique opportunity to showcase their successful career paths.

4. PUBLIC AND COMMUNITY INVOLVEMENT, ENGAGEMENT AND PARTICIPATION

PCIEP Lead – Dr Ian Mudway

The pandemic restrictions presented significant challenges for public engagement and involvement activities, for example, we were unable to participate in our usual major public engagement events: New Scientist Live, the Imperial Festival and the MRC Festival of Science. During this challenging period, we have sought to build on our previous successes in public and community involvement, engagement and participation (PCIEP) investing time in refreshing our governance structures, innovating online communication tools and activities, focused on maintaining our continued relationship with our longitudinal cohorts (e.g. *SCAMP* and *CHILL*), as well as planning for events post-August 2021. As a substantial part of our research activity over the last year has focused on COVID-19, PCEIP effort has focused in this area to support disease surveillance and public communication, especially in hard-to-reach groups, through collaboration with Imperial's Patient Experience Research Centre (PERC). Each of these areas are summarised below.

Following the funding of the new NIHR HPRUs and reflecting areas of intersection with Centre core and cross cutting themes, we have instigated a refresh of the Centre PCEIP strategy, identified new theme PCIEP leads and established an extended Public Community Oversight Group (PCOG) - Oct. 2020 (for more information see Annex 3. The inaugural PCOG meeting was held on 26th November 2020 and in February 2021 we appointed Phil Taverner as the non-professional Chair of the PCOG. We have worked collaboratively with PCOG members to develop an updated Public and Community Involvement Engagement and Participation (PCIEP) strategy, incorporating the NIHR INVOLVE National Standards for Public Involvement in Research (March 2021). Our second meeting with the full PCOG committee took place on the 1st September 2021 and included presentations on aircraft noise and adverse cardiovascular outcomes (from the Environmental Exposures and Healthy Cities, Healthy People programmes), how to communicate new findings on the neurological impacts of air pollution to the public and recent funding to support enhanced mechanistic work in this area (Molecular Signature and Disease Pathways) and our engagement plans in the run-up to COP26, including our contribution to the Parliamentary NetZero meeting in October 2021. The consolidation of our strategy and governance across the two HPRUs and the Centre reflects our commitment to embed PCIEP across all themes, with active consultation, collaboration, monitoring, reporting, evaluation, and exchange of learning from the activities undertaken.

To support these wider aims we have sought to increase PCIEP capacity and expertise across all themes, regularly identifying opportunities for training and learning (internally and externally) to share with our researchers. We have achieved this through close collaboration with the JACD programme, with bespoke sessions designed for PhD students and ECRs focusing on the principles and practice of public engagement, highlighting the benefits and rewards of doing public engagement and mechanisms for evaluation. In September 2020, we delivered a session for PhD students and ECRs on how to engage with school children to communicate research, and in April 2021 we held an online seminar on the JACD & Public Engagement Programmes to highlight how we could support Centre PCIEP activities. These sessions, together with an NIHR online interactive training course aimed at members of the public on reviewing research documents were also offered to PCOG members.

We have been capturing the impact of our activities using post event feedback forms. The feedback gathered from the evaluation forms has provided the opportunity for reflection and learning to drive improvement in our future work. We have also developed a public engagement logging tool for recording activities and reporting PCIEP metrics as well as to identify thematic areas that need additional support in public involvement and engagement activities. We are also continually identifying ways to increase diversity and inclusion through links with various networks and online platforms to engage with difficult to reach groups, e.g., the VOICE Digital Platform and The Young Persons' Advisory Network (YPAN).

PCIEP highlights

- Clean Air Day activities in October 2020 and June 2021;
- Establishing the Breathe London network, supported by the GLA, Bloomberg Philanthropies and Clarity, with active public consultation (see also press release);
- Dissemination of the findings of the Diesel Exhaust Mitigation study (DEMiSt), with the Institution of Occupational Safety and Health to professional drivers and business stakeholders (see also YouTube video);
- Active engagement with the White City community in the planning and design of the recent NERC UKRI funded WELLHOME study;
- The Garriott award for recognition for the development of online tools and activities to support continued engagement with children and parents within the CHILL study;
- Participation in the London festival of Architecture (June 2020) focusing on collecting perceptions on the urban built environment;
- July 2021 – Online Educational lecture and Q&A session on "Airports and public health" aimed at Year 11 school students (14–16-year-olds) as part of Imperial College Outreach Y11 STEM Challenge Summer School 2021.
- We have worked closely with the digital and print media to disseminate findings to the general public, summarised on the MRC Centre website.

5. RESEARCH TRANSLATION AND COMMUNICATION

The Centre's research is driven by the aim of having an impact on improving public health. Our members actively engage with a wide range of stakeholders to translate and apply the findings from our research, as well as the broader scientific knowledge in our areas of expertise, to inform the debate and decision-making on priority environmental health issues. A key aspect of this work involves the participation of Centre members in a variety of advisory and policy roles, providing expert input to industry, government and public health agencies at national and international level, promoting the development of science-based policies on environment and health.

Policy support

We focus our policy-related work in three overlapping strategic areas:

i) Air pollution sources and health impacts - contribution to consultations and providing evidence at local, national, European and global level.
ii) Disease and risk factor surveillance – development and application of methods for documenting geographical patterns and time trends of major health risks and outcomes, globally as well as in the UK.
iii) Risk assessment – application of our expertise in exposure science and modelling, epidemiology, and population health to provide quantitative estimates of the health effects of environmental risks, or of policies that address them.

Our scientists both lead and serve on several expert advisory committees through which we have important input into shaping national environment and health policies, including:

- Committee on the Medical Effects of Air Pollutants (COMEAP) - Kelly (Chair, 2011-2021)
- Committee on the Medical Effects of Air Pollutants (COMEAP) - Walton
- Committee on Medical Aspects of Radiation in the Environment (COMARE) - Toledano
- Committee on Toxicity (COT) – Toledano
- Defra's Air Quality Expert Group – Fuller

- UKRI and Met Office Strategic Priority Fund Clean Air Programme 'Air Quality Champions' - Fuller

The Centre has a long-standing partnership with PHE, which has been enhanced with the renewal/ award of the two NIHR HPRUs, providing a direct channel for translation of research findings into health protection policy and practice in the UK. At local level the Centre continues to foster strong partnerships providing advice and support on air quality to the Greater London Authority, Transport for London and the 33 London Boroughs.

Internationally, our scientists engage extensively with health agencies and national governments, playing a prominent role in several WHO and EU advisory committees, including:

- WHO Expert Consultation Panel on Air Pollution Risk Communication - Barratt
- WHO Expert Consultation Panel on Outcomes and Exposure Response function - Katsouyanni, Walton
- WHO Expert Consultation Panel on Methodology - Walton (Chair)
- WHO Expert Consultation Panel on Desert Dust - Fussell
- WHO Expert Consultation of Health Impacts Assessment of NO2 in the European Region - Beevers
- WHO Review of evidence on health aspects of air pollution – Kelly, Mudway, Walton
- WHO Reference Group on Health Statistics Task Force on Risk Factors – Ezzati
- WHO Advisory Group on Classification of Diabetes Complications – Gregg
- European Commission Microplastics Working Group - Wright

The Centre also hosts the Non-Communicable Disease Risk Factor Collaboration (NCD-RisC, led by Ezzati) in close collaboration with WHO, providing data on NCD risk factors from high-quality population-based surveys from 193 counties.

Communications

The new Centre website was launched in November 2020. The website was completely redesigned and updated to give it an engaging design, that is easy to navigate and is a good vehicle to disseminate and promote the work at the MRC Centre. The content was updated to make it accessible to a general audience and the new content management system enabled the website to be more responsive, allowing the regular updates of news, events, publications, and job vacancies to be done in-house, and for the website to be inclusive of users with special needs and facilitate use on tablets and smartphones.

The Centre Twitter feed continues to be updated regularly, and our followers are steadily increasing. Twitter is a particularly valuable tool for promoting public engagement events and recent publications.

The Centre's research again featured prominently in the media in 2019/20. Our media strategy is based around:

- promoting awareness of the health effects of air and other pollutants by general media appearances to highlight the research and issues in the field and/or providing commentary on topical news items;
- to promote specific Centre publications that may be of public interest.

Highlights of media reports on the Centre's research can be found on our Twitter feed.