HIPTOX Study:

Hazard Identification Platform to Assess the Health Impacts from Indoor and Outdoor Air Pollutant Exposures, through Mechanistic Toxicology; Human Studies

Participant Information Sheet (PIS)

You are being invited to take part in a research study looking at the effect of common air pollutants on brain health and the ability to carry out tasks that test the brain. This is study is part of a wider group of studies looking at how air pollutants affect health and whether some pollutants affect health more than others do. Before you decide whether to take part, it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following information carefully before deciding whether to take part and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Thank you for taking the time to read this.

About the research

- **Who will conduct the research?**

The study is be carried out by a team of researchers under the supervision of Professor Jacky Smith from the University of Manchester School Of Biological Sciences. A mix of University of Manchester researchers and staff from Manchester NHS Foundation Trust will be working on the study.

- **What is the purpose of the research?**

We are studying the effects of common indoor and outdoor pollutants on health, in particular the effect of diesel fumes, wood smoke, cleaning products, cooking fumes and mixed pollutants on health. We are looking to see if being exposed to air pollutants at the same level as those in the environment affects the brain's ability to complete certain tasks and whether there is a difference between the pollutants. We are also studying the effect of these pollutants on the cells involved in the immune system and DNA.

We are inviting healthy volunteers from the public who have close family members (parents/brothers/sisters) with a diagnosis of dementia or Alzheimer's disease to take part. We intend to recruit 45 volunteers.

- **Am I suitable to take part?**

We are looking for healthy people i.e. no current medical problems aged 50 years or over and are not any regular medications. You must have a close family relative with a diagnosis of dementia or Alzheimer's disease in order to be able to take part in the study.

- **Will the outcomes of the research be published?**

The results of the study will be published in scientific journals, conferences, the University of Manchester and the Manchester University NHS Trust website. All volunteers taking part in the study will be provided with the results. All the data published will be anonymised.

- **Who has reviewed the research project?**

The study has been reviewed by the UK Research and Innovation agency, the University of Manchester Ethics Committee (UREC ID: 2022-14762-26354) and the Health Research Authority (IRAS ID: 314890).

- **Who is funding the research project?**

The Natural Environment Research Council is funding this research, which is a branch of the UK Research and Innovation agency.

What would my involvement be?

- **What would I be asked to do if I took part?**

We are asking volunteers to attend 15 visits over 10-12 months period. Seven of the visits will be long visits and require the volunteers to be in the department for 8 hours. The other 8 visits will be no longer than 2hours in duration. All the visits will occur at the NIHR/Wellcome Trust Clinical Research Facility, Grafton Street Manchester, M13 9WL. For part of the visit, a researcher will accompany the volunteers to the Manchester Aerosol Chamber based in the Simon Building, University of Manchester, Brunswick Street.

Prior to taking part in the study a screening consultation will take place with one of the research team. We will confirm that you have received this participant information sheet and answer any questions that you may have. If you are agreeable to take part we will ask you to sign a consent form and we will check that you have no medical or other reasons to prevent you from taking part in the study.

Due to the current COVID-19 pandemic, we have made some adjustments to the way in which this research study will be conducted that ensures we are adhering to the latest government advice in relation to social distancing as well as taking all reasonable precautions in terms of limiting the spread of the virus. You should carefully consider all the information provided below before deciding if you still want to take part in this research study. If you choose not to take part, you need to inform the research team. If you have any additional queries about any of the information provided, please speak with a member of the research team.

Are there any additional considerations that I need to know about before deciding whether I should take part?

If you agree to take part in this study, you will need to attend the Wellcome/NIHR clinical research facility and therefore may have contact with patients or research participants and members of staff. However, social distancing is still being practiced on site and several processes are in place to minimise the risk of infection to all individuals.

What additional steps will you take to keep me safe while I take part?

There are processes and procedures in place at the site to minimise the risk of coronavirus transmission. Both you and all staff members will be wearing appropriate PPE, provided by the NIHR CRF. The number of people permitted in any room in the CRF, room ventilation and study procedures have all been risk assessed to minimise risk. Only adequately ventilated rooms will be used for study visits. Adequate time will be left in between participant visits to allow for cleaning of all equipment and surfaces.

Is there any additional information that I need to know?

We will contact you within the 24 hours before your visit to ensure that you or anyone in your household are not suffering from any symptoms of COVID-19. If you are, the visit will be rearranged. Lateral flow tests will be required pre visits based on local risk assessment.

What if I have additional queries?

If you have any queries specific to COVID-19 then please contact the researcher(s) Cough Research Team on 0161 2091 5031 or cough.research@manchester.ac.uk.

Visit Schedule

The study comprises of 15 visits in total. Below is an overview of the visits

Screening Visit

This visit will last approximately 1.5 hours.

A researcher will talk through the study again with you and check that you understand the study and give you an opportunity to answer any further questions. If you are still happy to take part, you will be asked to sign a consent form. With your permission, your GP will be informed of your participation in the study.

After giving consent you will be asked about any medical history, lifestyle, and details of any medications that you are taking. Your height and weight will be measured and then you will be asked to perform a simple breathing test called spirometry. This involves inhaling as much air as you can and then blowing into a machine called a spirometer as fast as you can until your lungs are empty. You will be asked to wear a nose clip during the test to ensure that all the air you blow out is captured. These questions and the breathing tests will determine if you are eligible to take part in the study. It maybe that you are unable to proceed with the study at this stage. If there are concerns that the spirometry readings are abnormal and may indicate an undiagnosed disease/disorder, then we will forward the information onto your GP.

If you are eligible to continue with the study, the researcher will go through some brain or cognitive tasks/ challenges with you. These involve answering questions or carrying out tasks as quickly as possible to check how quickly your brain can process information. These same tasks will be used again when you attend for the following visits.

Visit 1a

This visit will last approximately 8-9 hours and occur a minimum of 24 hours after the screening visit, but no longer than 3 weeks after the screening visit.

A researcher will confirm again that you are willing to continue to take part in the study and that no changes have occurred in your medical history since the screening visit. You will have a repeat of the spirometry, blowing tests that you had in the screening visit. You will then undergo blood tests (further details described below), a nasal wash (described below) and a repeat of the brain/ cognitive challenges of tasks that you had in the screening visit.

Blood tests: a blood sample will be collected to look for cells that are part of the body's immune response. These, blood samples will be stored for up to 2 years as part of this study to complete any further testing needed. The total amount of blood drawn will be approximately 2 tablespoons of blood. The blood samples will be collected by the research team involved in this study. The analysis of the samples will take place at Imperial College London by the specialist researchers we are working with.

Optional blood tests:

An additional 2 tablespoons of the blood will be sent for DNA analysis looking at the effect of pollutants on parts of the DNA. These samples can be stored for up to 25 years. Other researchers at the University of Manchester, the Manchester University Foundation NHS trust and the Christie Hospital NHS Foundation Trust who are not directly involved in this study will be able to analyse the stored samples if you agree to this. You can choose to opt out of having these blood sample taken and still be able to take part in the study.

None of these blood tests are used to diagnose any medical conditions.

Nasal wash: this is a process where we collect a sample of the cells in the nasal area. Participants will squirt 10 sprays of warm, sterile, salty water into each nostril whilst the other is closed. This will be repeated five times and the fluid collected in a glass beaker. The whole process will then be repeated for the other nostril. The sample will then be processed and sent to the laboratory at Imperial College London for analysis.

Brain or "cognitive" tasks; participants will complete a series of 6 cognitive tasks some written some verbal to assess attention, memory, and other aspects of higher brain function. You will also be asked to complete a mood questionnaire.

Once you have completed these tests, a researcher will then escort you to the aerosol chamber building. There you will wear a mask attached to a large chamber containing either an air pollutant (Diesel fumes, wood smoke, cleaning products, cooking emissions, clean air with nitrous oxide, wood-smoke with nitrous oxide) or clean air. Neither you nor the researcher administering the tests will know what the mixture is at the time. You will wear a facemask covering your nose and mouth and be encouraged to breath in the air from the chamber. This will take 1hour. You will then be escorted back to the NIHR clinical facility and will have a lunch and rest break for approximately 3 and a half hours. You will then repeat the breathing tests, nasal washout, brain tasks/ tests and mood questionnaire carried out earlier in the day. If the breathing test (spirometry) becomes abnormal after the pollution exposure it will need to be repeated in visit b.

Visit 1b

This will occur 24hours after visit 1a and will take approximately 1 hour.

You will attend the NIHR clinical research facility as in visit 1a. A researcher will check that you are still willing to take part in the study and check that you are still eligible for the study. You will then

undergo the same blood tests as in the previous visit. If the breathing test was abnormal after the pollution exposure, this will be repeated at this visit to ensure that it has returned to normal. There will then be a period of up to 5 weeks "washout", where no further study procedures will be carried out.

Visits 2a-7b

You will then repeat visits 1a and 1b six times each in order for you to have undertaken all pollutant exposures. Thus, in total there will be 15 visits in the study, taking place over 10-12 months. Those visits are named 2a, 2b, 3a,3b,4a,4b,5a,5b,6a,6b,7a and 7b.

Visit procedures and duration

	Duration (hrs)	Procedures
Screen	1.5	Written informed consent, medical history, breathing tests, cognitive tests
Visit 1a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 1) followed by repeat breathing tests, nasal washout and cognitive tasks
Visit 1b	1	Blood tests, breathing tests if abnormal from the previous day.
Visit 2a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 2) followed by repeat breathing tests, nasal washout and cognitive tasks
Visit 2b	1	Blood tests, breathing tests if abnormal from the previous day.
Visit 3a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 3) followed by repeat breathing tests, nasal washout and cognitive tasks.
Visit 3b	1	Blood tests, breathing tests if abnormal from the previous day.
Visit 4a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 4) followed by repeat breathing tests, nasal washout and cognitive tasks.
Visit 4b	1	Blood tests, breathing tests if abnormal from the previous day.
Visit 5a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 5) followed by repeat breathing tests, nasal washout and cognitive tasks.
Visit 5b	1	Blood tests, breathing tests if abnormal from the previous day.
Visit 6a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 6) followed by repeat breathing tests, nasal washout and cognitive tasks.

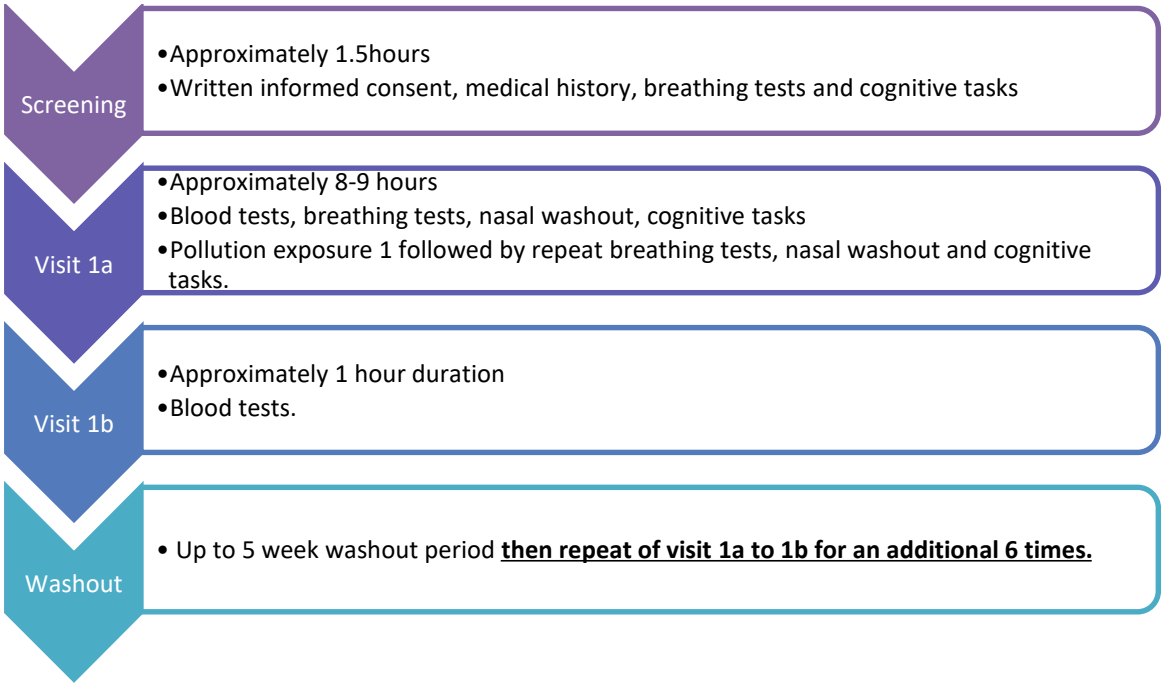
Visit 6b	1	Blood tests, breathing tests if abnormal from the previous day.
Visit 7a	8-9	Blood tests, breathing tests, nasal washout, cognitive tasks, pollutant exposure (number 7) followed by repeat breathing tests, nasal washout and cognitive tasks.
Visit 7b	1	Blood tests, breathing tests if abnormal from the previous day.
Total duration over 12 months	**70 hrs**	

Benefits and risks

There are no direct benefits in taking part in this study. Indirect benefits include the further advancement of the understanding of how pollution exposures affect us all.

This is a relatively safe study. The main risk will be from exposure to pollutants. Some studies have shown that pollution exposure can be associated with cardiovascular conditions. However, the levels of pollutants we are using in this study are all within the same levels that we are exposed to in normal day-to-day life. As part of the safety mechanisms of the study, we will carry out breathing test and check the medical history from you to ensure that anyone who is at an increased risk of a side effect from pollutant exposure will be NOT included in the study. We will also be continuously monitoring the levels of the pollutants during the exposure.

Figure 1: Study Schedule



- **Will I be compensated for taking part?**

You will be compensated £140 per exposure visit attendance or at total of £980 for the whole study, via bank transfer. In addition to this, refreshments will be provided for the long day visits.

Volunteers who attend for the screening visit and are unable to proceed with the study due to a medical or other issue will unfortunately not be compensated. However, if on subsequent visits they must withdraw they will be compensated for their time and given the opportunity to take part in a later part of the study if they wish. The compensation per visit is reflected below;

Study compensation

	Compensation £
Screen	none
Visit 1a	20
Visit 1b	90
Visit 2a	20
Visit 2b	90
Visit 3a	20
Visit 3b	90
Visit 4a	20
Visit 4b	100
Visit 5a	40
Visit 5b	100
Visit 6a	40
Visit 6b	155
Visit 7a	40
Visit 7b	155
Total duration over 12 months	**980**

What will happen to my samples at the end of the study?

The blood and nasal fluid samples will be stored for 2 years under the Human Tissue Authority License number 12275, at Imperial College Healthcare NHS Trust. After the 2 years these samples will be destroyed. The optional blood samples collected for storage in the biobank will be stored for up to 30 years and then destroyed.

What happens if I do not want to take part or if I change my mind?

It is up to you to decide whether to take part. If you do decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time without giving a reason and without detriment to yourself. However, it will not be possible to remove your data from the project once it has been anonymised as we will not be able to identify your specific data. This does not affect your data protection rights. If you decide not to take part, you do not need to do anything further.

Data Protection and Confidentiality

- **What information will you collect about me?**

In order to participate in this research project, we will need to collect information that could identify you, called "personal identifiable information". Specifically, we will need to collect your:

- Name
- Date of Birth
- Sex
- Address
- Ethnicity
- Record of Consent
- General Practitioner details

- **Under what legal basis are you collecting this information?**

We are collecting and storing this personal identifiable information in accordance with UK data protection law which protect your rights. These state that we must have a legal basis (specific reason) for collecting your data. For this study, the specific reason is that it is "a public interest task" and "a process necessary for research purposes". In this study this information will then be anonymised and thus you will not be directly identifiable. Your GP information is collected for us to be able to inform your GP (with your permission) that you are taking part in this study.

- **What are my rights in relation to the information you will collect about me?**

You have several rights under data protection law regarding your personal information. For example, you can request a copy of the information we hold about you.

If you would like to know more about your different rights or the way we use your personal information to ensure we follow the law, please consult our Privacy Notice for Research (attached at the end of this information sheet)

- **Will my participation in the study be confidential and my personal identifiable information be protected?**

In accordance with data protection law, The University of Manchester is the Data Controller for this project. This means that we are responsible for making sure your personal information is kept secure, confidential, and used only in the way you have been told it will be used. All researchers are trained with this in mind, and your data will be looked after in the following way:

- Volunteers will be assigned identification numbers only known to the research team this is known as pseudonymised data.
- Your data will be pseudonymised which means that there will be a key which would enable the research team directly involved in the study to identify the specific volunteer if needed. This information will NOT be available to researchers accessing the stored samples.

The study team at The University of Manchester will have access to your personal information and they will anonymise it as soon as possible. Your name and any other identifying information will be removed and replaced with a random ID number. The research team will have access to the key that links this ID number to your personal information. Your consent form will be retained for 5 years in a locked cabinet on UoM premises for audit purposes. With your consent, we would also like to retain your contact details for 5 years in order to provide you with a summary of the findings for this study and also to inform you about future studies that you may be interested in. If you provide consent for this, your details will be safely stored on UoM servers in a digital folder only accessible to the study team and used only for the purposes described above.

Please also note that individuals from The University of Manchester or regulatory authorities may need to look at the data collected for this study to make sure the project is being carried out as planned. This may involve looking at identifiable data. All individuals involved in auditing and monitoring the study will have a strict duty of confidentiality to you as a research participant.

Insurance and Indemnity for the study

The University of Manchester has insurance available in respect of research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students. The University also has insurance available that provides compensation for nonnegligent harm to research subjects occasioned in circumstances that are under the control of the University. Provision of this insurance cover in respect of a specific project may be subject to the acceptance of the project by the University's insurers and is conditional upon the project receiving approval from an appropriate ethics committee.

What if I have a complaint?

- **Contact details for complaints**

If you have a complaint that you wish to direct to members of the research team, please contact:

Prof Jacky Smith on 0161 291 5031 or cough.research@manchester.ac.uk

If you wish to make a formal complaint to someone independent of the research team or if you are not satisfied with the response you have gained from the researchers in the first instance, then please contact

The Research Ethics Manager, Research Office, Christie Building, The University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 306 8089.

If you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, The University of Manchester, Oxford Road, M13 9PL at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office about complaints relating to your personal identifiable information (See attached copy). Tel 0303 123 1113.

Contact Details

If you have any queries about the study or if you are interested in taking part, then please contact the researcher(s) **Cough Research Team on 0161 2091 5031 or cough.research@manchester.ac.uk**.