PROTOCOL Indoor Air Quality in Respiratory Disease

A Mixed Methods Observational Study to Determine the Sources and Impact of Indoor Air Pollution in Patients with Chronic Airways Disease

Study acronym: IndoorAirVG

Protocol version 6.3, 13th May 2022

Research Reference Numbers

IRAS Number	301897
Sponsor reference number	RG_21-096
ISRCTN number	ISRCTN17279929
REC reference number	22/LO/0259

This protocol has regard for the HRA guidance

Signature Page

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to adhere to the signed University of Birmingham's Sponsorship CI declaration.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Chief Investigator:

Name: Professor Alice M Turner

Sponsor statement:

Where the University of Birmingham takes on the sponsor role for protocol development oversight, the signing of the IRAS form by the sponsor will serve as confirmation of approval of this protocol.

Table of Contents

PROTOCOL Indoor Air Quality in Respiratory Disease

Key Study Contacts

Chief Investigator: Prof Alice M Turner
a.m.turner@bham.ac.uk, 01214148590

Study Co-ordinator: Miss Eleanor Holt
e.holt@bham.ac.uk

Sponsor: University of Birmingham, Dr Birgit Whitman
researchgovernance@contacts.bham.ac.uk, 01214158011

Funder(s): NERC (Natural Environment Research Council)
Polaris House, North Star Avenue, Swindon, SN2 1EU, United Kingdom
01793 411500 researchgrants@nerc.ukri.org.
Funder award number NE/V002414/1

Key Protocol Contributors: Prof Alice M Turner, Prof Neil Thomas, Dr Christian Pfrang

Medical Oversight (if applicable): Prof Alice M Turner

Study Summary

Study Title: A Mixed Methods Observational Study to Determine the Sources and Impact of Indoor Air Pollution in Patients with Chronic Respiratory Disease.

Internal ref. no. and short title: RG_21-096; IndoorAirVG

Study Design: Mixed methods study with 3 parts

Part 1: qualitative research exploring patient perceptions and sources of indoor air pollution/poor indoor air quality.

Part 2: questionnaire study to independent group of patients regarding findings of part 1.

Part 3: observational cohort study, distributing indoor air monitors to patients, and gathering symptom and indoor air quality data over a period of 2 weeks.

Study Participants: Subjects with any pre-existing respiratory disease, as determined by their clinician

Planned Size of recruitment target: Part 1: 20-30 patients, Part 2: ≥100 patients, Part 3: 60 patients. There may be overlap between parts 1 or 2 and 3, such that a patient may participate in any one or all three parts of the study.

Follow up duration: Parts 1 and 2: nil. Part 3: 2 weeks

Planned Study Period: 1 year

Research Question/Aim(s): To Determine the Sources and Impact of Indoor Air Pollution in Patients with Respiratory Disease.

Funding and Support in Kind

FUNDER(S)	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
NERC, Natural Environment Research Council, Polaris House, North Star Avenue, Swindon, SN2 1EU United Kingdom. Funder award number NE/V002414/1	Overall value of award: £504644

Role of Study Sponsor and Funder

The Sponsor is the Institution assuming overall responsibility for the initiation and management of the study and is not the main funder. The funder provides the budget for the work but does not have responsibility for its conduct. They will monitor progress with the project overall, of which this study is one work package, and will be recognised on publications arising from the work, but do not control decision to publish.

Roles and responsibilities of study management committees/groups and individuals

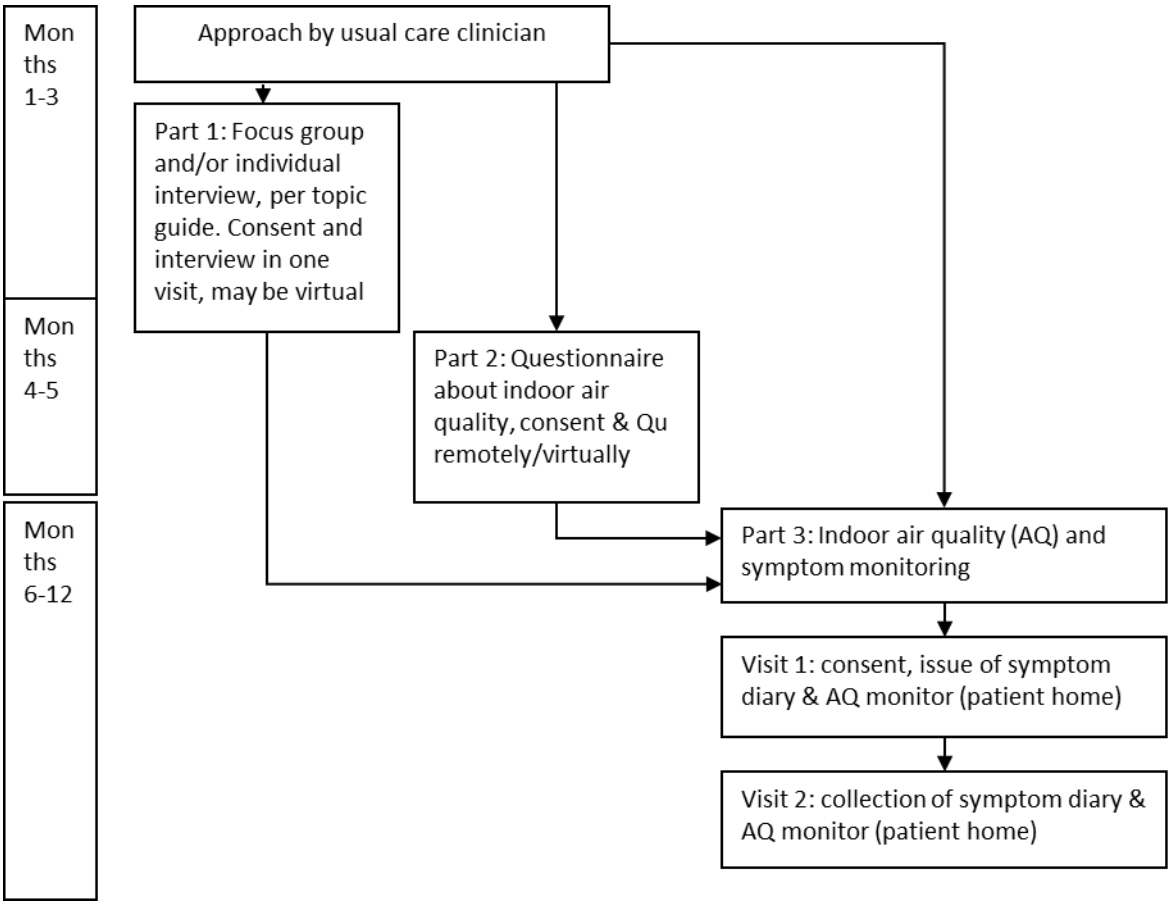
There are no study specific committees, however the University of Birmingham Respiratory Patient Advisory Group have been consulted about the overall aims of the project and content of the topic guide, as well as the structure of the patient information sheets. They will also be approached to aid recruitment to part 2 of the study, and for dissemination of results about the project. The wider grant within this project sits also engages the public and other stakeholders through a series of events that inquire about indoor air quality.

Protocol Contributors

The general study design was determined by Profs Turner, Shi and Thomas, and Dr Pfrang, equally. Prof Turner was responsible for specific protocol content, and Miss Holt for formatting of the document and liaison with the sponsor. Final responsibility for the protocol lies with the Chief Investigator. Protocol authors are jointly responsible for drafting and publishing work arising from the study, with Dr Pfrang taking the lead in the parent project grant, and thus having oversight of the full publication strategy. Patients have commented on the draft proposal.

KEY WORDS: asthma; chronic obstructive pulmonary disease; air pollution, indoor; quality of life; signs and symptoms, respiratory

Study Flow Chart



Study Protocol

1. Background

Air pollution causes 29,000 pre-mature deaths and costs the economy £20 billion per year in the UK alone. The majority of these impacts are associated with Vulnerable Groups (VGs), who are most strongly affected by air pollution with up to ca. 12 life years lost for the individual. People with pre-existing medical conditions, in particular those where the lung is affected, are of particular concern in terms of long-term health, societal and economic impacts. Despite this, most of the efforts in air quality improvement focusses on the general population and outdoor exposure. This potentially promotes inequalities and leads to major gaps in understanding exposure to key air pollutants (particularly PM1, ultrafine particles and VOCs), health risks and economic consequences, and the key challenges and mitigation options for these Vulnerable Groups. The CleanAir4VG project grant to which this specific project contributes aims to build a self-sustaining and interdisciplinary network of academics, stakeholders and industry capable to deliver co-designed research and innovation to develop robust solutions that reduce the impact of pollution on VGs; and to cross-link to UK and international expertise to establish research gaps, effective behaviour and technology intervention opportunities and catalyse future cross-disciplinary research capability.

This patient centred work package aims to understand the sources of poor air quality (AQ) indoors for people with respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD). A systematic review of 56 studies (3 from the UK) has shown an association between short term exposure to pollutants (NO2, PM2.5, CO and PM10) and acute exacerbations (AE) of respiratory disease, in particular AECOPD [1]. The attributable fraction for hospital admissions for COPD was 9.7% for the 6 pollutants considered [1], thus of the 140,000 admissions/year for COPD[2], outdoor pollutants account for around 13,594 admissions/year. Hence we anticipate that hospital admissions will be a key outcome for VGs, however long term decline of lung function in adults has also been identified in our prior research as a potential outcome of interest [3]. However, day to day symptoms may be a more feasible outcome for interventional studies arising from the parent grant, being shorter and thus less expensive in nature. They are also relevant to the types of pollutant likely to be present indoors, such as small particulates (E.g. PM2.5). Air purifiers may reduce PM2.5 by up to 57%[4], and have been associated with improvement in peak expiratory flow rate (PEFR) variability in asthma[5] as well as reductions in exhaled nitric oxide (FeNO)[4], a measure of eosinophilic inflammation linked to asthma control. Short term change in PM2.5 has potential to improve symptoms from COPD[6] and has been shown to reduce arterial stiffness[7], which relates to COPD severity[8] and risk of death[9]. We will therefore explore association of indoor pollutants with symptoms in one part of our study.

2. Rationale

We have systematically reviewed published work on indoor air quality and its health effects, and found an evidence gap relating to respiratory patients. As such a focus onto this group is required.

Indoor Air Quality VG is a mixed methods study recruiting respiratory patients from within the NHS, and collecting research data remotely/virtually (parts 1 and 2) or in person (part 3). Patients will be managed for their respiratory disease according to their local procedures and policies with no interference from the study team. Patients will give informed consent to participate to each part of the study independently, and will be able to participate in either part 1, 2, and part 3, or one part alone. The key outputs are expected to be (i) A prioritised list of areas in which indoor air quality or indoor/outdoor interfaces (IOIs) contribute to perceptions of respiratory and general health (ii) A list of health outcomes which would be most important to assess in studies of psychological and/or technological interventions identified by other groups working within the parent grant. We anticipate challenges related to the diversity of patients' lives and environments, their understanding of what is possible in short-medium term interventional studies, such as those which may stem from our initial work, and the potential for off target deleterious effects – for example avoiding poor air quality could result in lower physical activity if patients stay in one area, and this is known to be harmful to health[10, 11]. For this reason, we have chosen a mixed method design where we can fully explore views in an initial qualitative package, before refining our inquiry in a questionnaire to a larger group of patients, independent of those participating in the qualitative work. We will then test the potential for indoor air to influence day to day symptoms by way of a short-term monitoring study.

3. Research question/aims

The study objectives are:

1. To identify the environments and/or locations that VGs considered to be important in their exposure to poor air quality indoors. This will be achieved by a combination of qualitative research and questionnaires

2. To identify symptom-based health outcomes driven by air quality based on symptoms and indoor air quality monitoring. This will be achieved using a daily symptom diary and an air quality monitor, used over a period of minimum 2 weeks, maximum 6 weeks.

4. Study design and methods of data collection and data analysis

Part 1: Understanding VGs perceptions on indoor AQ

This part of the project will recruit 20-30 people, which is likely to be the amount required to reach data saturation. All will give informed consent.

Focus groups of up to 6 people, or individual interviews, according to patient preference, will be conducted using the topic guide, which will inquire about sources and impacts of indoor air pollutants, and about IOIs. The interviews will be conducted by a trained researcher, recorded and transcribed verbatim. Where possible interactions will take place virtually, to ensure a degree of robustness to any future Covid related disruptions, and to provide greater convenience to participants. Interactions will be recorded using the technology available on the virtual meeting platform Zoom, both recording and transcription will occur on a University owned computer. Where a participant feels they cannot use a virtual medium or telephone, face to face will be offered as an alternative. Should face to face be required this will occur either on the University campus or in the patient's home. If a home visit is required the University lone worker policy will be adhered to. Data will be stored in an anonymised manner. Qualitative analysis using the Framework method [12], which is a systematic approach well suited to interdisciplinary health research and to working with clinical and lay collaborators.

Part 2: Understanding VGs perceptions on indoor AQ and interventions to improve AQ

This part of the study will recruit a minimum of 100 patients, however if more wish to participate this will be allowed, since costs and logistics of the study will not rise unduly with more participants. As this is an exploratory part of the study no formal power calculations are possible or required at this stage. Consent will be taken remotely only, and the questionnaire distributed as a link to an electronic survey provided by Microsoft Forms. Participants can also request a paper equivalent, which will be sent by post thereafter. The questionnaire will take approximately five minutes to complete for each participant.

Data from the thematic analysis will be used to design a questionnaire inquiring about sources and impacts of indoor AQ, especially at IOIs, and the impact of each on respiratory symptoms and overall health. This will verify the findings of part 1, and will go further by also inquiring about usability and acceptability of interventions possible to improve each potential source. Data will be stored in an anonymised manner electronically. Each question will use a binary yes/no response, or a numerical response (e.g. Likert scale) and data will be analysed using simple descriptive statistics only. Responses from those with asthma and those with COPD will also be sub-grouped and analysed separately.

Part 3: Quantifying indoor AQ and respiratory symptoms

This part of the study will recruit approximately 60 patients, aiming for an equal distribution of people with asthma and people with COPD. Any severity stage will be allowed. In a study of an air purifier in asthmatic children a 4% difference in PEFR variability was seen [5]; the study had power 80% and α=0.05, and it was possible to detect this with 30 patients in each arm of a study. Consequently, we feel that 30 is a reasonable target per condition in an exploratory study of this nature in adults.

<u>Visit 1: Screening and issue of monitoring device(s)</u>

The informed consent form is signed at this baseline visit. All available information will be collected according to a structured case record form (CRF). Baseline data will be collected including Date of Birth, Sex, Race and ethnicity, Height, Weight, Respiratory Diagnosis, Date of Diagnosis, Severity of disease (clinician defined), Exacerbations in last 12 months, Hospital admissions due to respiratory disease in last 12 months, smoking history, including years as a smoker, year of start and quitting and pack years, working status including relevant occupational exposures and type of agent. Current medication will also be recorded. Consent will be taken to extract from the medical record the latest values for lung function and any relevant radiological results. A symptom questionnaire will be distributed to collect data, and patients with asthma will also receive a peak expiratory flow monitor (if they do not already have one) for conducting daily peak expiratory flow rate (PEFR).

The questionnaire will be delivered in an electronic format compatible with all major phone operating systems, and will utilize validated questionnaires, namely the Bronkotest® questionnaire for patients with COPD and the asthma control test (ACT) for patients with asthma. Those with asthma will also enter their PEFR. Importantly the Bronkotest® system has already been developed for use in an e-diary for another study running locally (a clinical trial, Colour-COPD, funded by NIHR). Adaptation to use ACT is required, but not challenging, and is included in the budget. The Bronkotest® questionnaire will take approximately two minutes to complete each day, while the ACT questionnaire will take around one minute to complete. Self-reported symptoms will be gathered every day over a minimum 2-week period, but if the data in parts 1 and 2 suggests it is required an extension to a period of up to 6-weeks will be considered. If this is required the PIS will be amended with the new timeframe and approval sought for this from ethics. E-diary collection has been shown to result in more complete data than paper forms and be less expensive overall as a result, thus is commonly used in modern respiratory trials. A paper version of the e-diary will be made available for those without a suitable device on which to collect data electronically.

The indoor air quality device will be a Plume Labs Flow 2. This air quality device has previously been used in research by the sponsor. If there is not an adequate amount of Flow 2 devices available an AirBeam or Purple Air PA-I-Indoor device may be used. All of these devices will collect data on PM10 and PM2.5 mass concentrations which will be stored on clouds and which are easily accessible for the research team. It will be installed in the location deemed most appropriate for gathering of data on exposure to indoor air, which we anticipate being their home, but will emerge from parts 1 and 2 of the study. However, the device is portable to allow collection of data in multiple locations, and if the patient is moving between locations information on their location will be gathered by self-reporting. The research team will have a contact number set up for any device issues, and will arrange any repairs needed during the study.

As an example, our preferred device, the Flow 2, is 12.5cm in height, 4 cm width, depth 3.5cm and a weight of 70g; with manufacture estimated median coefficient of correlation with static reference monitors at 96% for NO_2 experiments, 69% for VOC experiments, 93% for PM1, 92% for PM2.5, and 88% for PM10 experiments [13]. The growth in development in low cost sensors has been rapid over the last decade, with the quality assurance (QA) and validation processes for low cost sensors also rapidly evolving [14]. The latest advice on QA for low cost sensors provided from the dedicated DEFRA webpage [14] and in related literature will be followed at the time of the study. The chosen low-cost sensor at the time of the study will be the one which provides the best accuracy and precision of those available.

Visit 2: Follow up

This visit will include collection of the monitor and symptom questionnaire, if applicable (paper only).

Analysis

Simple descriptive statistics will be used to delineate characteristics of the cohort, and the correlation between each pollutant measured by the indoor monitor and day to day symptoms, as determined by the total score on Bronkotest® or ACT. In addition, daily puffs of inhaled short acting treatment (salbutamol) and (asthma only) PEFR will also be examined for relationship to indoor AQ, using a similar correlation analysis. Other factors relating to indoor AQ within collected demographic and medical history data will also be reported using simple comparative statistics.

Participant Recruitment

Eligibility Criteria

The in-/exclusion criteria are deliberately broad to allow the inclusion of a large and varied population representative of “real-life” respiratory patients. We are targeting asthma and COPD as they are the most common problems, with validated symptom questionnaires.

Inclusion criteria

Either COPD or asthma, as defined by their referring/usual care clinician in the medical record. The same inclusion criteria apply across all 3 parts of the study. Participants in this study need to be over the age of 16 and able to give informed consent.

Exclusion criteria

Patients unwilling or unable to participate in the study; again, this applies across all 3 parts of the study.

Recruitment target

Size of recruitment target

The target sample size is based on experiences with similar projects, with 30 likely to be sufficient to reach data saturation, and 100 likely to give sufficient pilot data to design onward studies of interventions (parts 1 and 2 respectively). The number of patients who can have home monitoring is a pragmatic choice made from availability of monitors and knowledge of sample size in other interventional studies; without data on the extent to which indoor AQ relates to symptoms in COPD and asthma it is impossible to conduct a robust power calculation. Notably the data from part 3 of the study would be used to aid power calculations for onward interventional studies.

Participant identification and recruitment technique

Potential participants will be identified from existing databases of subjects with known respiratory conditions who have previously indicated that they are willing to take part in research. Participants will be identified by practitioners who have access to these databases from their own previous research or as part of their role as a practitioner of respiratory medicine. These practitioners will approach potential participants and discuss the study with them.

Both follow-up and new patients referred to specialist NHS respiratory clinics at the research site will also be approached about the study by members of the research team.

The study will also be advertised via respiratory patient advocacy and support groups.

If patients are interested in the research, the team will then contact them to consent to the study and conduct study related procedures (for example provide the PIS and other documents).

In addition, we will advertise publicly for participants using a poster which can be put up in participating NHS sites and will also be put onto the CleanAir4V study website and social media.

Consent

Informed consent will be taken by an appropriately trained individual in accordance with GCP who has been delegated to do so by the CI. Consent will be taken and documented fully prior to any study related procedures being performed, and will be separate for each part of the study.

Safety reporting

This is an observational study therefore adverse and serious adverse events are not expected, however procedures will be place in case of an event. Adverse events (AE), defined as any untoward medical occurrence in a study participant, which does not necessarily have a causal relationship with the study, can be any unfavourable and unintended sign (including abnormal laboratory finding), symptom, or disease. All adverse events reported spontaneously by the participant or observed by the Chief Investigator or their staff will be recorded.

A serious adverse event (SAE) is any untoward medical occurrence or effect that:

- results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing in patients' hospitalisation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect;
- is a new event of the trial likely to affect the safety of the participants, such as an unexpected outcome of an adverse reaction, lack of efficacy of an IMP used for the treatment of a life-threatening disease, major safety finding from a newly completed animal study, etc.

Any Serious Adverse Event, with a possible relation to the study will be reported by the Chief Investigator to the National Co-ordinating Centre within 24 hours of being made aware of the event, who will then forward on to

the Research Ethics Committee and University of Birmingham Research Governance team within 15 days. Any SAE not, or unlikely to be related to the study, will be reported to the Funder of the Network (NERC) and the National Institute for Health Research (NIHR) by the Chief Investigator within 24 hours.

All adverse events will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist.

Ethical and regulatory considerations

This study does not contain any major ethical issues since it is observational in nature and does not ask intrusive questions. It will be made clear to participants that benefit is likely to be others and not to them personally, with the possible exception of part 3, which may benefit patients by giving them a greater understanding of their own personal indoor AQ, and its impact on their respiratory symptoms. All routine ethical procedures for research in the NHS will be followed, specifically: *REC and HRA.*

Before the start of the study, approval will be sought from a REC and the HRA for the trial protocol, informed consent forms and other relevant documents e.g. advertisements and GP information letters. Substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the study. All correspondence with the REC will be retained in the Trial Master File/Investigator Site File. An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended. The CI (or delegate) will produce the annual reports as required and notify the REC of the end of the study. If the study is ended prematurely, the CI will notify the REC, including the reasons for the premature termination. The CI (or delegate) will submit a final report with the results, including any publications/abstracts, to the REC.

NHS permission

Before enrolling patients into the study, the CI or designee will apply for NHS permission from the site's Research & Development (R&D) department.

Registration of Trial

This trial will be registered to the ISRCTN, which is a primary clinical trial registry recognised by WHO and ICMJE that accepts all clinical research studies (whether proposed, ongoing or completed).

Amendments

If amendments are made these will be approved by the sponsor prior to submission to the REC and HRA. For any amendment that will potentially affect a site's NHS permission, the CI or designee will confirm with that site's R&D department that NHS permission is ongoing (note that both substantial amendments, and amendments considered to be non-substantial for the purposes of REC and/or HRA may still need to be notified to NHS R&D).

Protocol compliance

The procedures and assessments detailed in the study protocol should be followed at all times, however, accidental protocol deviations can happen and they must be adequately documented on the relevant forms and reported to the sponsor immediately. Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

A "serious breach" is a breach which is likely to effect to a significant degree –

a) the safety or physical or mental integrity of the subjects of the trial; or
b) the scientific value of the trial

The sponsor will be notified immediately of any case where the above definition applies during the trial study.

Data protection and patient confidentiality

All investigators and study site staff will comply with the requirements of the Data Protection Act 2018 and GDPR 2018 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. All data will be de-identified before being stored electronically on secure University servers. All source documents will be stored according to University of Birmingham SOPs and the Trial Master File (TMF) and Investigator Site File (ISF) will be stored in a secure office location by the study co-ordinator.

Indemnity

This study is covered by the standard University of Birmingham clinical trials insurance (see https://intranet.birmingham.ac.uk/finance/insurance/Clinical-Trials.aspx). In addition, any process occurring at an NHS site will have additional NHS indemnity.

End of study and archiving

After the final report has been sent, study documents will be archived for 10 years from the end of the study, as per the University of Birmingham guidelines

Access to the final study dataset

All those involved in developing the protocol will have access to the final study dataset. All participants will also be given the option to receive a lay summary of the results of the study when they are published. This information will be collected as part of the consent form at the beginning of the study.

Dissemination policy

The sponsor owns the data arising from the study and on completion of the study, the data will be analysed and tabulated and a Final Study Report prepared. This will be available via academic publications arising from the work and from the lead researcher for the parent project (Dr Pfrang) or the sponsor on request. It is anticipated that all protocol authors will be authors on publications arising, assuming they meet the guidance for authorship in each individual part of the work.

References

1. Li, J., et al., *Major air pollutants and risk of COPD exacerbations: a systematic review and meta-analysis.* Int J Chron Obstruct Pulmon Dis, 2016. **11**: p. 3079-3091.
2. The battle for breath - the impact of lung disease in the UK, 2016, British Lung Foundation: London.
3. Wood, A.M., et al., Outdoor air pollution is associated with rapid decline of lung function in alpha-1-antitrypsin deficiency. Occup Environ Med, 2010. **67**(8): p. 556-61.
4. Chen, R., et al., Cardiopulmonary benefits of reducing indoor particles of outdoor origin: a randomized, double-blind crossover trial of air purifiers. J Am Coll Cardiol, 2015. **65**(21): p. 2279-87.
5. Noonan, C.W., et al., Randomized Trial of Interventions to Improve Childhood Asthma in Homes with Wood-burning Stoves. Environ Health Perspect, 2017. **125**(9): p. 097010.
6. Wu, S., et al., Short-term exposure to high ambient air pollution increases airway inflammation and respiratory symptoms in chronic obstructive pulmonary disease patients in Beijing, China. Environ Int, 2016. **94**: p. 76-82.
7. Mehta, A.J., et al., Associations between short-term changes in air pollution and correlates of arterial stiffness: The Veterans Affairs Normative Aging Study, 2007-2011. Am J Epidemiol, 2014. **179**(2): p. 192-9.
8. McAllister, D.A., et al., Arterial stiffness is independently associated with emphysema severity in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med, 2007. **176**(12): p. 1208-14.
9. Vlachopoulos, C., K. Aznaouridis, and C. Stefanadis, Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol, 2010. **55**(13): p. 1318-27.
10. Luke, A., et al., Assessing Physical Activity and its Relationship to Cardiovascular Risk Factors: NHANES 2003-2006. BMC Public Health, 2011. **11**(1): p. 387.
11. Vaes, A.W., et al., *Changes in physical activity and all-cause mortality in COPD.* Eur Respir J, 2014. **44**(5): p. 1199-209.
12. Gale, N.K., et al., Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol, 2013. **13**: p. 117.
13. plumelabs.zendesk.com/. 2019. How Accurate is Flow?. [online] Available at: https://plumelabs.zendesk.com/hc/en-us/articles/360025092554-How-Accurate-is-Flow- [Accessed 7 July 2021].
14. Uk-air.defra.gov.uk. n.d. AQEG advice on the use of 'low-cost' pollution sensors. [online] Available at: https://uk-air.defra.gov.uk/research/aqeg/pollution-sensors.php [Accessed 7 July 2021].

Appendices

Appendix 1- Required documentation

- CVs of research team members
- Patient information sheet (parts 1, 2 and 3)
- Consent form
- GP information letter
- Bronkotest® questionnaire
- ACT questionnaire
- Representative screenshots from the electronic form of the questionnaire

Appendix 2 – Schedule of Procedures

Study part	Visit 1	Daily participation	Visit 2
1	Consent, interview	-	-
2	Consent, questionnaire	-	-
3	Consent, demographics, medical history, issue of AQ monitor	Daily symptoms	Collection of AQ monitor

Appendix 3 – Amendment History

Amendment No.	Protocol Version No.	Date Issued	Author(s) of Changes	Details of Changes
1	6.1	14.04.2022	Miss Eleanor Holt	Edits to Part 4 – Study Design and methods of data collection and data analysis: - Minor grammatical changes - Addition of timescales for questionnaires Addition of information about AQ devices
2	6.1	14.04.2022	Miss Eleanor Holt	Edits to Participant Recruitment: - Removal of children from the eligibility criteria.
3	6.1	14.04.2022	Miss Eleanor Holt	Edits to Registration of Trial: -Trial will be registered with the ISRCTN
4	6.1	14.04.2022	Miss Eleanor Holt	Edits to Appendix: -Addition of Appendix 4 (Information about Air Quality Sensors)
5	6.2	28.04.2022	Miss Eleanor Holt	Grammar check to document and images added to Appendix 4.

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.

Appendix 4 – Information about Air Quality Devices, in preferred order.

Name of Air Quality Device	Basic Information	Preference of Use	Additional Information	Image
Plume Labs Flow 2 Plume Labs - Flow 2 (aqmd.gov)	**Pollutants Measured:** PM1, PM2.5, PM10, NO2, VOCs **Size:** 125mm x 40mm x 35mm **Weight:** 70g **Power Supply:** USB Cable **Sampling Mechanism:** Fan, Laser Particle Counter (Particle Matter), Heated Metal Oxide Sensor (Gases) **Price:** £151.50 (14.04.2022)	First	- Not Weatherproof. - Data is transferred via Bluetooth (no data stored internally. - 24-hour battery life.	
AirBeam AirBeam2 Technical Specifications, Operation & Performance (habitatmap.org)	**Pollutants Measured:** PM1, PM2.5, PM10 **Size:** 132mm x 98mm x 28mm **Weight:** 142g **Power Supply:** USB C Cable **Sampling Mechanism:** Sensing Chamber **Price:** £189.50 (14.04.2022)	Second	- Temperature and Relative Humidity can also be measured. - Data is transferred via Wi-Fi (no data stored internally). - 10-hour battery life.	
Purple Air PA-I-Indoor PurpleAir PA-I-Indoor Air Quality Sensor - PM2.5 Detector	**Pollutants Measured:** PM2.5 **Size:** 108mm x 67mm x 57mm **Weight:** N/A **Power Supply:** USB A Cable **Sampling Mechanism:** Laser Particle Counter **Price:** £151.50 (14.04.2022)	Third	- Pressure, Temperature and Relative Humidity can also be measured. - Indoor Use Only. - Data is transferred via wi-fi (no data is stored (internally).