Full title of trial	Assessing effectiveness of **A**rtificial **I**ntelligence air **Sa**fety **Tool** (**AISaT)** recommendations in outpatient, day-case rooms, and wards to reduce risks of airborne disease transmission
Short title	**A**rtificial **I**ntelligence air **Sa**fety **Tool** (**AISaT)**
Version and date of protocol	Version 1.1, 17/JUL/2025
Sponsor:	University College London (UCL)
Sponsor reference number:	179418
Funder (s):	National Institute for Health and Care Research (NIHR)
IRAS Number:	353916
ISRCTN no:	TBC
UCL Data Protection Number:	Z6364106/2025/02/142 medical research
Intervention:	RCT

Chief investigator:

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PROTOCOL VERSION HISTORY

Version Stage	Versions Number	Version Date	Protocol updated & finalised by;	Reasons for Update
Current	1.1	17-JUL-2025	Anna Byrne (NIHR Air Safety Programme Manager)	Edited versions and dates of documents in document list, as per changes requested by REC
Outdated (original submitted to REC)	1.0	19-JUN-2025	Anna Byrne (NIHR Air Safety Programme Manager) Rossana Capitano (NIHR Air Safety Programme Administrator)	JRO approved sponsorship and corrected errors in document list
Outdated (draft)	0.2	05-JUN-2025	Anna Byrne (NIHR Air Safety Programme Manager) Rossana Capitano (NIHR Air Safety Programme Administrator)	Initial Feedback from JRO
Outdated (draft)	0.1	21-FEB-2025	Laurence Lovat (Chief Investigator Sharon Cheung (Clinical Trial Coordinator) Anna Byrne (NIHR Air Safety Programme Manager)	N/A

DECLARATIONS

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the U.K. Policy Framework for Health and Social Care Research 2017 (3rd edition) (as amended thereafter), the EU General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018), Sponsor SOPs and applicable Trust policies and legal frameworks.

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

I (investigator) agree to ensure that no research activity or recruitment will commence at participating research sites until the appropriate regulatory approvals and NHS confirmations of Capacity and Capability have been issued, and Sponsor green light confirmed.

I (investigator) 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. Any deviations from the study as planned in this protocol will be explained and reported accordingly.

Chief Investigator:

Signature: .....  **..... Date: 05/JUN/2025**

Print Name (in full): Prof Laurence Lovat.....

Position: ....Professor of Gastroenterology and Biophotonics.....

On behalf of the Study Sponsor:

Signature: ..... Date...../...../.....

Print Name (in full): .....

Position: .....

STUDY SUMMARY

IDENTIFIERS	
IRAS Number	353916
REC Reference No.	
Sponsor Reference No.	179418 University College London Joint Research Office, UCLH/UCL Joint Research Office, part of the Research Directorate, 4th Floor, West, 250 Euston Road, London, NW1 2PG
Other research reference number(s) (if applicable)	Z6364106/2025/02/142
Full (Scientific) title	Assessing relative effectiveness of **A**rtificial **I**ntelligence air **Sa**fety **Tool** (**AISaT)** recommendations in outpatient, day-case rooms, and wards to reduce risks of airborne disease transmission
Health condition(s) or problem(s) studied	Airborne disease transmission in hospitals
Study Type i.e. Cohort etc	A series of Randomised Controlled Trials
Aim(s):	To assess relative effectiveness of recommendations made by the **AI**r **Sa**fety artificial intelligence **T**ool (AISaT) to reduce risks of airborne disease transmission
Objectives:	These trials are to investigate: **A)** whether placing mitigations for airborne disease transmission according to the recommendations of the AISaT software tool reduces airborne disease transmission risks in outpatient consulting rooms, aerosol generating procedure rooms and hospital wards. **B)** Whether it is feasible to implement these mitigations at different hospital sites (and identify any variation in implementation). **C)** whether patients and hospital staff find the AISaT recommendations acceptable **Primary Objective:** To determine in hospital consulting rooms, aerosol generating procedure rooms and wards, when using mitigations for airborne disease transmission according to recommendations of the AISaT software tool, the reduction in the relative number of airborne aerosol droplets per standard time period breathed by any staff member present compared to when no mitigations are used or when mitigations are used as decided by the clinician using the relevant space.

	Outcome Measure: Number of aerosol droplets on average per minute per clinical encounter as measured by an air particle counter (APC) installed next to the clinician and at up to 4 other fixed locations in the room or ward bay. **Secondary Objective:** Mixed methods evaluation of staff experiences of using the tool and the mitigation approaches that are recommended (based on analysis of acceptability by staff and feasibility of implementation). **Outcome Measures:** **1.** Normalisation Measure Development Questionnaire (NoMAD) **2.** Ethnographic observations using formal and informal interviews to explore hospital staffs' views on the importance of AISaT, usability and management of the AISaT software and challenges to fidelity in implementation, and how team members can work together effectively to support implementation **3.** An estimation of the cost efficiency of AISaT
Type of trial:	A two-site 3*3 cross-over randomised controlled trial
Trial design and methods:	The trial will be run as a staged series of randomised control trials (RCTs), each one in a different clinical location. They will each be preceded by a pilot phase. The locations are in increasingly complex areas. The first location will be an outpatient consulting room. The second will be in a room where aerosol generating procedures (AGP) are performed, e.g. in endoscopy or in ENT, and the third will be an inpatient ward bay with approximately 6 beds. Before the RCTs commence, a **pilot phase** will identify the optimal settings to use (see trial design section). Each **RCT stage** will then be run in a cross-over format with aerosol droplet generation determined by outcomes of the pilot phase. The first two RCT stages will involve hospital clinicians running a weekly session in the same clinic or AGP room. There will be different configurations each week, which will be allocated randomly, to allow direct comparison. **Configuration 1:** The AISaT will be turned on and air quality safety measures will be implemented. These may include the use of air filters, fans, screens etc. **Configuration 2:** AISaT will be turned off completely with no extra air quality safety measures and **Configuration 3**: Air quality safety measures will be offered to the clinician to use and place as they see fit. The order of these 3 different configurations will be randomised. 54 clinicians (and their patients) will be invited to join, equating to roughly 27 clinicians per hospital. All patients attending either their outpatient clinic appointment or their AGP will be invited to join. A small aerosol-producing device(s) will be installed within the room to generate saline aerosol droplets and air particle counters (APCs) will be installed next to participating clinicians to measure the primary outcome, which is the average number of aerosol droplets per minute

	per clinical encounter as measured by an air particle counter (APC) installed next to the clinician and at up to 4 other fixed locations in the room or ward bay. In **Stage 3 of the RCT**, the same three configurations described above will be arranged in 12 ward bays (6 in each hospital), each for one day, in random order. Here, the clinician making the decision for configuration 3 will be the senior nurse for the ward. Running alongside all stages of the trial will be a mixed methods evaluation. This will include usability testing and exploratory research interviews with a subset of clinicians, patients and other relevant hospital staff such as nurses, estates staff and infection prevention and control (IPC) staff in the pilot phase, and a process evaluation during the main RCT stages.
Trial duration per participant:	Clinicians: 3 weeks Patients in outpatient clinic/ having an AGP: 1 day Ward patients and clinicians: 3 days For those patients or staff involved in the mixed methods evaluation, trial duration will last no more than 4 months.
Key Study milestones:	Each trial is due to complete within 6 months, with 3 months as a buffer to deal with any unforeseen issues. **Month 3:** Completion of first pilot phase **Month 9:** Completion of first clinical trial in outpatient consulting rooms **Month 12:** Completion of second pilot phase **Month 18:** Completion of 2nd clinical trial in AGP rooms **Month 21:** Completion of third pilot phase **Month 27:** Completion of 3rd clinical trial in ward bays/ Data envelope analysis completed Qualitative and quantitative data collection for the process evaluation will run alongside the clinical trials and will also be complete by month 27.
Estimated total trial duration:	Anticipated start date: 1st July 2025 Anticipated end date: 30th September 2027
Planned trial sites:	Multi-site: 1. UCL Hospitals NHS Foundation Trust 2. Lister Hospital (East and North Hertfordshire NHS Trust)
Total number of participants planned:	**Stage 1 Pilot: Outpatient clinic rooms** **12 sessions** Up to 12 clinicians

	10 patients + 5 accompanying persons each per clinic = 120 patients + 60 accompanying persons = 180 + 12 clinicians **Total = 192** **<u>Stage 1: Outpatient clinic rooms</u>** 27 clinicians x 2 hospitals = 54 clinicians 10 patients + 5 accompanying persons per clinic = 540 patients + 270 accompanying persons x 3 weeks = 2430: Total = **2484** **<u>Stage 2 Pilot: AGP Procedure Rooms</u>** **<u>9 sessions</u>** Up to 9 clinicians 10 patients per session per clinician = 90 patients Total = **99** **<u>Stage 2: AGP Procedure Rooms</u>** 27 clinicians x 2 hospitals = 54 clinicians 10 patients per session per clinician = 540 patients x 3 weeks = 1620 Total = **1674** **<u>Stage 3 Pilot: Wards</u>** **<u>3 days</u>** Approximately 6 beds in 1 bay. As days may not be consecutive, aim for up to 18 patients Day nurse & night nurse = 2 per day so **6** in 3 days Day HCA and night HCA = 2 per day so **6** in 3 days Up to 3 doctors per day = **9** in 3 days Total = 18+6+6+9 = **39** **<u>Stage 3: Wards</u>** Each of the 2 hospitals has 6 bays, each bay containing 6 beds. This gives a total of 72 beds. 25% patient turnover rate (72 x 1.25) = approximately **90** patients in 3 days. Day nurse & night nurse = 12 per 24 hour period, so **36** in 3 days Day HCA and night HCA = 12 per 24 hour period, so **36** in 3 days 6 doctors per day = **18** in 3 days Total = 90+36+36+18= **180** For each stage, we will also speak to **up to 30** other staff members including estates, infection prevention and control, managers and other relevant staff groups in each hospital. We will conduct

	ethnographic observations, and informal interviews with infection control leads, clinical and estates staff to consider use of ventilation devices, how they are deployed, how are they used, challenges and solutions to their use - and we will perform up to 15 *semi-structured interviews* with management leads, clinical and estates staff. With observations. Total = 30 x 2 hospitals x 3 stages = **180** Overall total = **192+2484+99+1674+39+180+180= <u>4848 participants</u>**
Inclusion criteria:	Clinicians working at relevant clinical testing environments (1st trial outpatient clinic room, 2nd trial AGP room, 3rd trial ward bay) All patients (and accompanying persons) attending in those relevant clinical testing environments The mixed method evaluation may include people working in estates teams, hospital managers and other healthcare staff.
Exclusion criteria:	Obstetric, psychiatric and paediatric clinical areas will be excluded, to minimise the risks of ethical complications involving children, pregnant women or patients with psychiatric illnesses that may have difficulty consenting. People under the age of 18 years old will be excluded

Statistical methodology and analysis:	**Clinical trials:** Data analysis will be linear mixed modelling controlling for confounding factors which may include number of people in the room, baseline ventilation, room size, room shape, temperature, humidity and various other factors (see full list of suggested confounding factors in study design section). **Process evaluation:** Descriptive statistics will be used to present the findings from the NoMAD questionnaire. Observations will be analysed using framework analysis, organised according to the core constructs of Normalisation Process Theory (NPT) using the format of context, mechanism, and action according to each observation. Based on these data a convergence coding matrix will be generated using normalisation process theory (NPT). **Pilot phase:**

	Semi-structured interviews will use framework analysis, guided by the core constructs of the NPT. Qualitative data analysis in the evaluation phase will be carried out using the RREAL Sheet for real-time analysis and framework analysis for in-depth analysis. **Health economics**: Data envelope analysis (DEA) to rank the efficiency of AISaT in removing air droplets in different settings. Cost-utility analysis to calculate the mean incremental cost of AISaT compared to current practice. This will be calculated using information from the DEA combined with data from the literature on the relationship between air droplets and common air born infections such as influenza.
FUNDING & OTHER	
Funding	This work is funded by the National Institute for Health and Care Research (NIHR) under its Programme Grants for Applied Research Programme (Ref: NIHR205439).
Other support	N/A
STORAGE of SAMPLES / DATA (if applicable)	
Human tissue samples	N/A
Data collected / Storage	Any personal data collected as part of the qualitative evaluation will be stored in a data safe haven, a technical solution for storing, handling and analysing identifiable data. The UCL Data Safe Haven has been certified to the ISO27001 information security standard and conforms to NHS Digital's Information Governance Toolkit.
KEY STUDY CONTACTS	
Committees	Name(s) of committees, full contact details including, phone and email. E.g. study steering groups. For each committee/group, the protocol should state their roles and responsibilities and degree of independence from the Sponsor and Investigators. The Trial Management Group (TMG) will have responsibility for day to day running of the trial. This will consist of the Chief Investigator, Professor Prof Laurence Lovat (l.lovat@ucl.ac.uk, Tel 020 7679 9083), the Air Safety Programme Manager, Anna Byrne (anna.byrne@ucl.ac.uk Tel: 020 7679 9060) and Senior Clinical Trials Coordinator Sharon Cheung (sharon.cheung@ucl.ac.uk, Tel: 020 7679 9060) and the Principle Investigator for the Lister Hospital, Dr Danielle Morris (danielle.morris@nhs.net), Tel: 07976702732. This group is not independent from the investigators.

	The Programme Steering Committee is fully independent of both sponsor and investigators. It will act as the Trial Steering Committee (TSC) and will have responsibility for: • Participant safety oversight • Trial integrity to ensure compliance with regulatory and ethical standards • Review of interim data • Protecting scientific validity • Recommending trial continuation or termination • Assessment of benefit-risk balance • Guidance on unanticipated ethical or practical issues that arise • Support for Trial Adaptations 1, Anthony Fisher, Consultant Clinical Scientist, Seconded to the Chief Scientific Officer NHSE, Department of Physics, University of Liverpool. Email: A.C.Fisher@liverpool.ac.uk 2, Rachel Philips, Senior Lecturer in Medical Statistics and Clinical Trials, Imperial College London. Email: r.phillips@imperial.ac.uk 3, Epaminondas Mastorakos, Professor of Applied Thermodynamics, Hopkinson Lab, Department of Engineering, University of Cambridge. Email: em257@cam.ac.uk 4, Lesley Booth, Deputy Director, Cambridge Rare Disease Network. Email: lesleyboothmbe@gmail.com 5, Anika Singanayagam, Consultant Virologist, UK Health Security Agency (and Imperial College London). Email: Anika.Singanayagam@ukhsa.gov.uk 6, Alastair Denniston, Consultant / Honorary Lecturer / Professor of Regulatory Science and Innovation, University Hospitals Birmingham / Birmingham University. Email: a.denniston@bham.ac.uk 7, Georgia Black, Reader in Health Services Research, Centre for Prevention, Detection and Diagnosis, Wolfson Institute, QMUL. Email: g.black@qmul.ac.uk 8, Jamie Ross, Senior Lecturer in Primary Care Sciences, Wolfson Institute of Population Health, QMUL. Email: jamie.ross@qmul.ac.uk
Sub-contractors	None
Other relevant study personnel	The data controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

	This 'local' privacy notice sets out the information that applies to this particular study. Further information on how UCL uses participant information can be found in our 'general' privacy notice: For participants in health and care research studies, please visit this weblink for further information: https://www.ucl.ac.uk/legal-services/privacy/ucl-general-privacy-notice-participants-and-researchers-health-and-care-research-studies The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices.

KEY ROLES AND RESPONSIBILITIES

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also must be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR (CI): The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals and confirmations of NHS Capacity and Capability are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

The Chief Investigator is responsible for submission of annual reports as required. The Chief Investigator will notify the REC and JRO of the end of the study (including the reasons for premature termination, where applicable). Within one year after the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC and JRO.

PRINCIPLE INVESTIGATOR (PI): Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

TRIAL COORDINATOR: The trial coordinator is responsible for coordinating all trial activities across sites

TRIAL PERSONNEL

See protocol cover page for Chief Investigator and Sponsor contact details.

Study Coordinator: Name: Sharon Cheung (UCL)
E-mail: sharon.cheung@ucl.ac.uk
Tel: N/A

Statistician: Name: Hakim Dehbi (Clinical Trials Unit, UCL)
E-mail: h.dehbi@ucl.ac.uk
Tel: N/A

KEY WORDS

Artificial intelligence; airborne disease transmission; infective respiratory particles

LIST OF ABBREVIATIONS

AGP = Aerosol Generating Procedure
AI = Artificial Intelligence
AISaT = **A**rtificial **I**ntelligence air **Sa**fety **Tool**
APC = Air Particle Counter
CI = Chief Investigator
COVID-19 = Coronavirus Disease of 2019
CRF = Case Report Form
DEA = Data Envelope Analysis
DMU = Decision Making Units
ENT = Ear, Nose and Throat
NoMAD = Normalisation Measure Development Questionnaire
PI = Principal Investigator
PSC = Programme Steering Committee
RCT = Randomised Control Trial
TMG = Trial Management Group
TSC = Trial Steering Committee
UCL = University College London
UVC = Ultraviolet C

Contents

1. INTRODUCTION

This series of sequential clinical trials is part of the Air Safety programme grant, funded in July 2024 by National Institute for Health and Care Research (NIHR), led by Prof Laurence Lovat. The clinical trials are due to take place from year 2 of the 5-year programme.

The Air Safety programme research team has developed an **A**rtificial **I**ntelligence air **Sa**fety **Tool** (**AISaT**). AISaT is computer software that guides users on how to best reduce airborne infection risks in hospitals, using cheap solutions like air filters, fans and screens etc. Our research programme is investigating whether AISaT works, is acceptable and cost-effective. We will also develop guidance on how to use AISaT across the NHS. These clinical trials in 2 hospitals (UCLH and Lister hospital) are a key part of our research programme, to assess the effectiveness of AISaT recommendations in outpatient, aerosol generating procedure rooms, and wards to demonstrate reduced infection risks.

Our AISaT tool could allow higher hospital patient throughput while reducing risks of spreading airborne transmitted diseases such as influenza, respiratory syncytial virus and COVID-19. To do this, we need to understand how a successful AISaT tool would be implemented and what the barriers to that implementation might be. Alongside the clinical trials, we will undertake a series of studies using validated instruments to explore issues such as usability and acceptability to key stakeholders.

2. BACKGROUND AND RATIONALE

When people breathe, speak or cough, they spray saliva into the air. The smallest droplets, (aerosols), can remain suspended in the air for hours and spread widely. Viruses in these droplets can infect others, particularly indoors. Indeed, early in the COVID-19 pandemic, there were some high profile cases of super-spreading events such as the Shincheonji Church of Jesus in South Korea and the Sri Petaling mass gathering in Malaysia, which at one point accounted for more than 60% and 35% of cases in their respective countries, and were the largest clusters of infection within each country[1, 2.] Adequate ventilation can effectively prevent accumulation.[3] Increasing room air flow lowers risk but usually needs expensive building work and/or high energy costs. Simple, low-cost techniques to reduce infection risks are urgently needed. Many UK hospitals were built at a time when the importance of preventing airborne disease transmission was not adequately recognised. They may rely on passive ventilation through use of windows or have no ventilation whatsoever. Even newer hospitals with air conditioning may have been built to maximise energy efficiency with an inevitable trade off against air safety as recycling air increases the risks of transmitting airborne diseases. It is impractical to retrofit entire hospitals.

Inadequate hospital room airflow drove nosocomial disease transmission during the COVID-19 pandemic. Safeguarding against future respiratory viruses with a rapidly deployable technology is a critical NHS need. During the COVID-19 pandemic, multiple retrofit solutions were tried including screens, fans, high efficiency particulate air (HEPA) filters and ultraviolet C (UVC) air cleaning among others. But national advice on implementation was lacking, because nobody knew the best way to implement them. Research has dramatically increased, and we now know that they can reduce the

numbers of infective respiratory particles in the air, although the best way to deploy mitigation devices currently remains beyond our grasp.

What we are now very clear about is that the performance of mitigation devices is heavily driven by their location within the space they are employed.[4] Airflow design and flow rates also have an important impact. Simulations of enclosed UVC air cleaning units suggest that positioning the device closest to the infectious source (if known) will provide the most benefit[5,6,] Ventilation rates and air mixing in the room determine interactions between airborne virus and the mitigation strategy. Computational modelling studies have shown that repositioning a mitigation device on the opposite side of the room could reduce effectiveness by more than 50%.[7] Several studies also show that room airflow mixing is important for UV systems located towards the roof of the room to perform effectively.[8] This can be enhanced in some settings using mixing fans,[9] although unexpected airflow patterns can result in diffusing a virus throughout a wider area.[10]

Studies on indoor aerosol transmission and air filtration in clinical settings pointed to a series of strategies to reduce the spread of COVID-19 in hospitals. The use of room air purifier units with HEPA filtration (free-standing or ceiling mounted) was one of the most widely recommended strategies[11]. In terms of the use of devices for air cleaning, recent studies showed that inexpensive portable air cleaning devices, particularly those with HEPA filters, should be considered for small and enclosed spaces in healthcare settings, such as inpatient rooms and personal protective equipment donning/doffing stations.[12–14] These portable air cleaning devices were identified as particularly important where there was limited ability to reduce aerosol transmission with building HVAC ventilation.[15] Although it has not been definitively proven that reducing infective respiratory particle density leads to lower rates of infection, small studies do point toward an approximately 20% reduction in risk of disease spread when mitigations are in put in place in environments akin to hospital wards such as care homes.[16,] This benefit does not appear to extend to kindergartens, where close contact between children and staff is likely to be ubiquitous.[17] In situations of close contact, face masks are far more likely to reduce disease transmission.

One promising avenue towards filling the gaps in our knowledge on how to maximise the benefits of using mitigation devices is the use of computational modelling that offers the capability of predicting air flow efficiency in a variety of scenarios. AI technologies have been recently developed by our group and others to expedite analysis.[18,19] Our work is now showing that this modelling can provide optimal mitigation strategies which are tailored to each individual clinical environment, and with further development it will be possible to generate this information almost real-time.[20] We have published a series of papers which demonstrate that we already have a basic AI driven tool for identifying the best ways to deploy the relevant solutions[21-23].

Air quality affects all, but there are particularly vulnerable populations, and these groups are over-represented in hospitals. People with underlying respiratory conditions are notably at increased risk as are those with immunosuppression from blood dyscrasias or undergoing chemotherapy for cancer.[24,25] The elderly are all at higher risk due to the physiological senescence of the immune system, particularly in those with multiple comorbidities.[26] A very important group which came to

the fore during the recent pandemic is medical and other hospital staff. They were particularly badly affected during the early stages of the pandemic with infection rates not only many times higher than the general population, but also with prolonged side effects ('long Covid').[27,28] This was particularly severe amongst frontline staff from ethnic minorities.[29] This is not new. Tuberculosis and norovirus have been noted to spread to frontline staff for many years.[30]

It is worth emphasising one group again: hospital in-patients. During the COVID-19 pandemic, nosocomial transmission became a major source of morbidity and mortality. Safe air in hospitals is therefore likely to bring benefits to the most vulnerable patients and staff alike.

3. OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary Objective

Primary Objective: To determine in hospital outpatient consulting rooms, aerosol generating procedure rooms and wards, when using mitigations for airborne disease transmission according to recommendations of the AISaT software tool, the reduction in the relative number of airborne aerosol droplets per standard time period which will be breathed by clinicians compared to when no mitigations are used or when mitigations are used as decided by the clinician using the relevant space.

3.2 Secondary Objective(S)

Mixed methods evaluation of staff experiences of using the tool and the mitigation approaches that are recommended (based on analysis of acceptability by staff and feasibility of implementation).

3.3 Outcome measures/endpoints

Primary measures/endpoint:

- Average number of aerosol droplets per minute per clinical encounter as measured by an air particle counter (APC) installed next to the clinician and at up to 4 other fixed locations in the room or ward bay. (A clinical encounter is defined as *one* outpatient consultation, AGP procedure or ward session.)

Secondary measures/endpoint:

- Normalisation Measure Development Questionnaire (NoMAD)
- Ethnographic observations using formal and informal interviews to explore practitioners' views on the importance of AISaT, usability, management of the AISaT software and challenges to fidelity in implementation, and how team members can work together effectively to support implementation
- An estimation of the cost efficiency of AISaT

4. TRIAL DESIGN

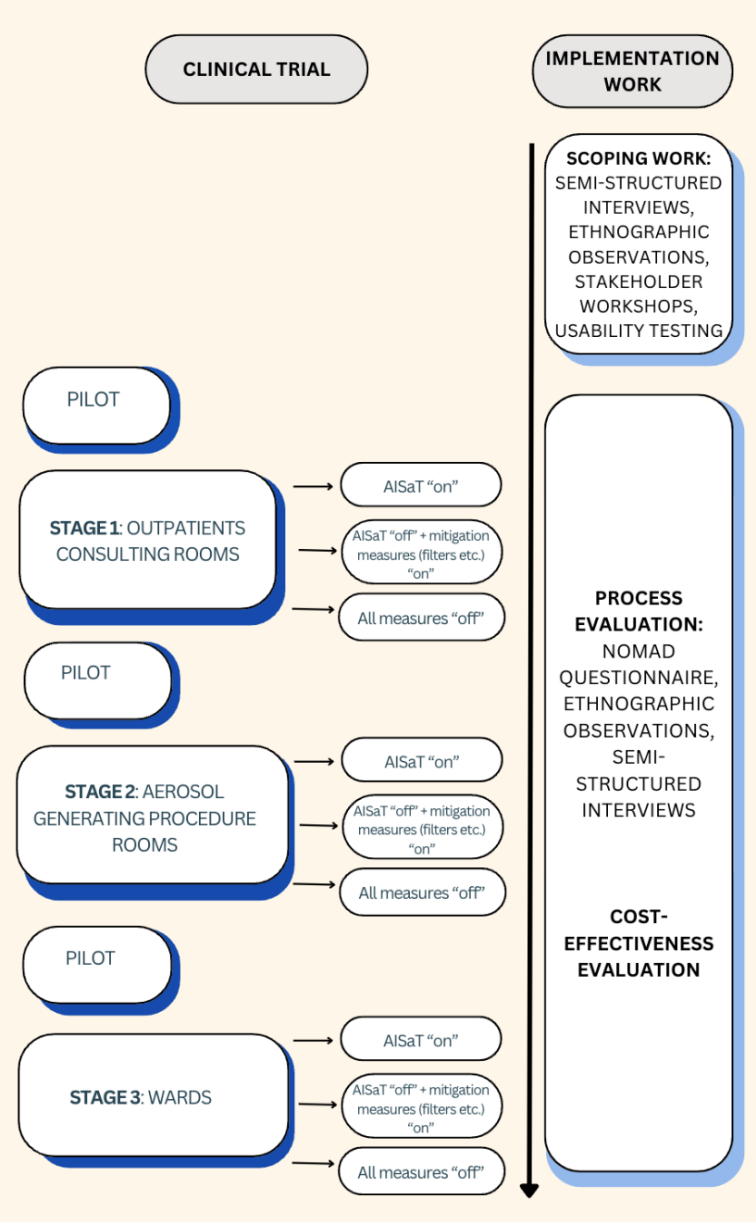


Figure 1. Schematic diagram of overall trial design

The trial will be run in a staged way as a series of crossover randomised control trials (RCTs) in 2 hospitals, each trial stage being in a different clinical location, preceded by a pilot phase. The locations are in increasingly complex areas. The first location will be an outpatient consulting room. The second will be in a room where aerosol generating procedures (AGP) are performed, e.g. in endoscopy or in Ear Nose and Throat (ENT), and the third will be inpatient ward bays. **Randomisation will be by clinician, not patient**. The order in which the clinicians receive each intervention is determined at random.

Pilot Phase

Before each RCTs commence, a **pilot phase** will identify the optimal settings to use in each setting. The pilots will happen first in consulting rooms during clinics with doctors and patients present. Aerosol droplet generation will be determined using 2 different approaches, to confirm work that has been previously done in a laboratory setting: (a) simply relying on aerosol droplets generated by the doctor-patient clinical interaction in the room; (b) using a 'breathing' robot that we have already developed which generates pre-defined levels of aerosolised saline (salt water).[31] Up to 4 different sets of conditions will be tested (saline solution at 3 rates of aerosolisation, 1 with only aerosol droplets generated by humans) during routine clinical interactions to determine the optimum approach to achieve the trial endpoints. Air particle counters (APCs) will be installed next to the clinician. We will measure the number of aerosol droplets on average per minute per clinical encounter as measured by an air particle counter (APC) installed next to the clinician and other fixed locations in the room or ward bay. We will perform each set of conditions three times to confirm reproducibility. In total, a maximum of 12 clinic sessions will be included in consulting rooms in the pilot phase. Prior to the second and third clinical trial phases, optimum conditions will again be tested in aerosol generating procedure (AGP) rooms and ward bays where further changes may be needed. It is envisaged that no more than 9 AGP sessions, which are usually half days, and 3 full ward days (up to 24 hour periods, although it is likely that studies can be concluded within a few hours) will be needed to achieve this.

The pilot phases will be informed by initial work on <u>understanding the perspectives of staff and patients</u> in relation to the intervention. This will consist of the following work:

To explore the perspectives of national expert building engineering and infection control leads, management leads, clinical and estates staff, patients and the public we will conduct
i. *Ethnographic observations*, and informal interviews with, infection control leads, clinical and estates staff to consider use of ventilation devices, how they are deployed, how are they used, challenges and solutions to their use.
ii. Up to 15 *semi-structured interviews* designed according to key tenets of NPT with management leads, clinical and estates staff. We will develop an understanding of views on critical issues, such as:
a. the importance of a focus on reducing transmission of viral illnesses
b. challenges hospitals might face reducing transmission
c. strategies already implemented to reduce transmission (including aerosol-based transmission)
d. likely acceptability and use of an AI solution to this issue. In what circumstances would they use such technology and what would we need to do to encourage use.
e. A key part of this work will be to identify affordable retrofit approaches that our Air Safety Tool (AISaT) software should be able to assess to bring both maximum utility and uptake in clinical settings.

The study will also involve <u>usability testing</u> of the AISaT: We will carry out a rapid qualitative study with staff to capture their views on the new tool and how it can be integrated into normal clinical

workflows and pathways. Staff will have the opportunity to test the tool and reflect on their experiences through a series of "Think Aloud" interviews (a common approach used in the usability testing of technological innovations). The researchers will observe the members of staff as they use the tool and will use questions in a pre-established interview topic guide to engage staff members in verbalising their thoughts as they are using the tool. The researcher will also carry out observations as the member of staff uses the tool and will record these in the form of fieldnotes. The research team will rely on regular feedback loops to share emerging findings from the usability testing with the clinical trial implementation team, and with the engineering team to refine the tool. Successive iterations of the AISaT software will be presented to an existing patient advisory group and professional stakeholder panel, to explore perceptions of members, ensure that development in the next period aligns with patient needs and to optimise the user interface.

Randomised Controlled Trial (RCT) Stages

Each **RCT stage** will be run in a cross-over format with aerosol droplet generation determined by the outcomes of the pilot phase.

The first two RCT stages will involve hospital clinicians at each hospital running a weekly session in the same clinic or AGP rooms. Each clinician will be involved for 3 weeks. There will be different configurations each week to allow direct comparison. The AISaT will be turned on and air quality safety measures will be implemented (including the use of air filters, screens, fans etc.), turned off completely with no extra air quality safety measures or air quality safety measures given to the clinician to use and place as they choose. The weekly order of these 3 different configurations will be randomised. These 3 segments of the trial will each be conducted over 3 consecutive weeks.

Fifty four clinicians and their patients will be invited to join, equating to roughly 27 clinicians per hospital. All patients attending either their outpatient clinic appointment or their AGP will be invited to join. Educational material will be made available in multiple languages to encourage broad participation from patients.

As these are cross-over trials, each clinician will be their own control.

Air particle counters (APCs) will be installed next to participating clinicians and at up to 4 other fixed locations in the room or ward bay, to measure the average number of aerosol droplets per minute per clinical encounter. A clinical encounter is defined as *one* outpatient consultation, AGP procedure or ward session. A small aerosol-producing device(s) may also be installed within the room, if needed, as determined in the pilot phase.

To assess numbers of people in the rooms and amount of movement (each of which will impact airflows and infective respiratory particle numbers) an infrared camera will be used throughout to generate video heatmaps (figure 2). The camera will detect heat emanating from people in the room but will not be able to identify any individual person.

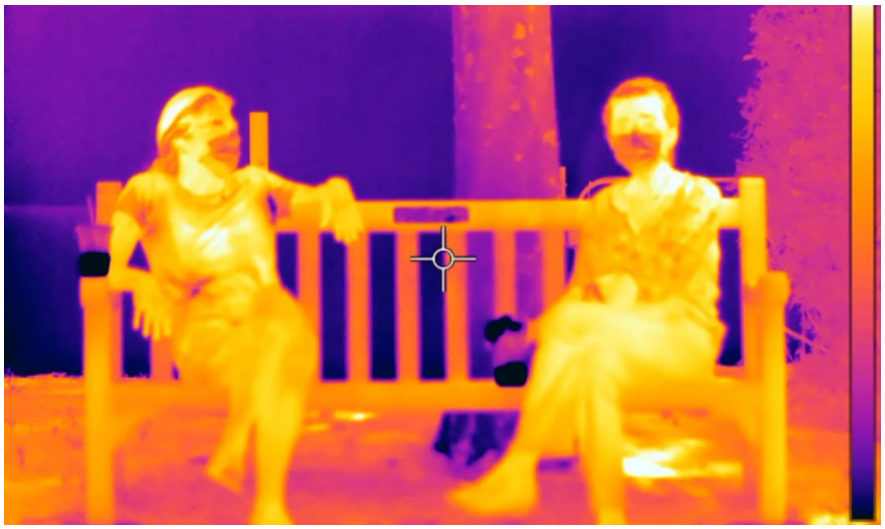


Figure 2. A heatmap of 2 people sitting on a park bench. Whilst it is possible to locate them precisely, it is not possible to identify them.

For the trial in the 3rd environment (in the ward bays with approximately 6 beds), the trial will be run on 3 consecutive days. As with the other 2 stages, the configurations will be different on each day, to allow direct comparisons. The AISaT will be turned on and air quality safety measures will be implemented, turned off completely with no extra air quality safety measures or air quality safety devices (such as filters, fans and screens etc.) given to the senior nurse on the ward to use and place as they see fit. The daily order of these 3 different configurations will be randomised.

This trial will be conducted across 12 ward bays (6 in each hospital). APCs will be installed next to each bed in the ward.

Running alongside the trial will be mixed methods implementation studies. These will include exploratory research interviews and usability testing in the pilot phase and process evaluation during the main RCT stages.

STOP-GO Criteria

Each trial is due to complete within 6 months, with a 3-month buffer to deal with unforeseen problems.

STOP CRITERIA:

1. The pilot phase for the first trial in consulting rooms will recruit 20% of the patients in 5 weeks.

The trial will STOP if we don't recruit 60% of expected number (i.e. 12% of the total recruitment).

a. Management:

The trial team will report to the trial management group (TMG) at the end of week 5. If recruitment is inadequate, TMG will discuss with the trial team why recruitment failed and explore ideas to improve recruitment before deciding on whether to restart. Discussions may also be had with our programme PPIE panel. The trial will restart if TMG confident it can complete recruitment within 9 months.

2. AISaT tool may not be able to compute a solution to reduce aerosol transmission in the rooms we wish to use for trial.

a. Management: The TMG will allow an extra 3 months to find rooms that the tool can be used in. If we cannot find suitable clinic rooms, TMG will stop the trial.

3. A report will be produced by engineering team at end of pilot on numbers of aerosol droplets measured. Trial statisticians will ensure it will be possible to determine statistically whether the trial could reach predefined end points. If not, TMG will discuss with engineering team how to seed the room with more droplets and then implement. Although unlikely that doctors or patients will notice changes, we will perform a further pilot. TMG will stop second trial if we cannot recruit adequately during pilot as above.

4. Statistical report at the end of the pilot will identify variance in aerosol droplet concentrations between consulting rooms. Even apparently identical rooms may have different airflows. If current sample size inadequate to achieve statistical power needed, statisticians will advise the TMG of a new sample size. TMG to discuss with trial team extra patient recruitment. If unachievable within 9 months, TMG will stop trial.

5. At the end of pilot, trial team will also ask hospital staff whether AI generated mitigations interfere with clinic, procedure room or ward e.g. due to noise or trip hazards. TMG will discuss with engineering team adjusting AISaT system. If not achievable, trial will be stopped.

6. Ensuring adequate research support staff to run trials. This is costed in SoeCAT. We know that NHS Trusts are under pressures and may not have research staff available to enable recruitment If recruitment in pilot phase is too low, TMG will decide whether to stop the trial at that point.

7. For trial stage 2, based in procedure rooms, issues 1-6 remain relevant. Ventilation rates are higher than in standard consulting rooms, and there is more movement of people as well as intermittent aerosolising equipment use and use of personal protective equipment (PPE) by staff. All these factors may increase standard deviation in aerosol droplet levels. Study sample size may therefore need to be larger, but we will apply the same stop/go criteria as for trial stage 1.

8. All issues above remain relevant in the ward trial stage 3. Here operational risks are key. Ward changes happen for many reasons and are impossible to predict. If a change to wards is needed, the statisticians will advise whether this will impact on trial delivery. If not possible to complete within the time frame, TMG will decide whether to stop the trial.

Duration of Participation in the Trial

For most participants who are only taking part in the clinical trials in pilot phases, stage 1 and 2, participation will be limited to one day for patients (the day they attend clinic), whereas for clinicians it will be 3 weeks. In the ward trial in stage 3, both patient and clinician participation will be for 3 days.

For the small number of participants who are invited to take part in the process evaluation work, participation will be until all interviews are completed. This may take up to 4 months.

5. SAMPLING METHODS

5.1 Inclusion Criteria

Inclusion Criteria:

1. Clinicians working at relevant clinical testing environments (1st trial outpatient consulting room, 2nd trial AGP room, 3rd trial ward bay). Adult clinical areas will be targeted.

2. All patients (and accompanying persons) that attend the clinics and wards where the clinical trials take place at the 2 trial hospitals (UCL Hospital and Lister Hospital) will be eligible and invited to join the research, as long as they are able and willing to provide informed consent.

3. Usability testing may also include people working in estates teams, hospital managers and other healthcare staff.

5.2 Exclusion criteria

1. Obstetric, psychiatric and paediatric clinical areas will be excluded, to minimise the risks of ethical complications involving children, pregnant women or patients with psychiatric illnesses that may have difficulty consenting. As the risks of the study are very low, pregnant women attending the trial clinical areas who wish to take part will be allowed to do so with no special precautions needed.
2. People under the age of 18 years old will be excluded.

5.3 Recruitment

Participant recruitment at a site will only commence when:

1. the trial has been initiated by the Sponsor (or its delegated representative) and
2. has been issued with Confirmation of Capacity and Capability from each participating site

Clinicians: The clinicians will be recruited from UCLH and Lister Hospital by contacting clinicians who will be working in the relevant clinical spaces at the time that the study is planned to take place. This will be determined in consultation with hospital management and review of clinic lists.

Patients: For the study stages 1 and 2 in the clinics and procedure rooms, information leaflets will be sent to all patients attending relevant clinics by post or email at least 24 hours before they attend for their appointments. Potential participants will then be approached by a member of the research team on the day that they attend to sign a consent form.

Materials will be made available in relevant languages to ensure that participation is as broad as possible.

The local PIs will recommend colleagues to take part in the process evaluation studies that the research team will then invite via email.

Sampling for initial exploration and usability testing prior to pilot trial will take place in conjunction with the two pilot hospitals, with access for observations negotiated via local contacts, we anticipate shadowing staff for up to two weeks in each hospital. We will then recruit up to approximately 15 staff for formal interviews based on what we find from observations.

For usability testing, purposive sampling will be conducted to reach a total sample of 20 members (10 staff at UCLH and 10 at the Lister Hospital). The participants will be sampled to ensure experiences of use of the AISaT software can be captured across the hospital settings of interest to the study. The research team will ask the local PIs at each site to recommend colleagues who could be responsible for using the software in practice, to share feedback on its usability.

No payments will be made to any study participant.

If a patient chooses not to be included in the trial, the data from the time that they are in the consulting room with the clinician will not be used. Saline aerosolisation and mitigation measures or other machinery needed for the trial that are already in the room will be removed or turned off.

5.4 Informed Consent

For the clinical trials, all clinical trial participants will be given sufficient time to read the participant information sheet (PIS) and prepare any questions they may have. Patients of recruited clinician's clinic lists will receive the PIS at least 24 hours in advance and given an opportunity to read all relevant information and ask questions. Nevertheless, due to the last-minute nature of some patient bookings in clinics within the NHS, it is possible that patients may be approached on the day of their visit in clinic waiting rooms ahead of their appointment. Given the low impact of this study, it is proposed that where the information leaflet has not been sent in advance, the PI may offer the participant entry to the study at the time of their visit to the clinic. If a patient has an accompanying person with them (e.g. family member etc.) to their appointment who will also be in the clinic room, they will be invited to consent to the study also. There will be no accompanying persons in AGP rooms, and it is not practical to consent accompanying persons in ward setting.

For patients in ward bays, consent will be obtained from all patients in the relevant bay before the trial starts. For patients who move into the trial bay whilst the trial is ongoing, consent will be obtained before they enter the bay. If they deny consent, they will not be moved into the bay so that the trial can continue uninterrupted. This will be coordinated with the lead nurse for the ward.

All participants will be provided a PIS and given the opportunity to read the information and ask the study team any questions they may have. Patients will be encouraged to ask questions and the person taking informed consent will check their understanding of the study before enrolling them. Participants do not have to give a reason for not wanting to participate in the study, but sites should capture this information if it is available. No screening requirements are necessary, as the exclusion criteria refer to medical specialities and not patients. Materials will be made available in relevant languages to ensure that participation is as broad as possible. Regarding the process evaluation: the Participant Information Sheet (PIS) and a consent form will be sent via email or directly provided to all potential participants at least 24 hours in advance of any planned interviews or observations. Potential participants will then be given the opportunity to discuss the PIS with the researchers and ask questions to ensure understanding before requesting written informed consent from them. If the participant would like to have the interviews conducted by telephone or over teleconferencing software, the researcher will request contact information. The consent form may be given directly to the researcher before the planned interview or observation, or emailed back to the research team in advance. Participants will be able to withdraw consent at any time before or during interviews and observations. In the event of consent being withdrawn after the completion of data collection, the data provided prior to withdrawal will be retained (anonymised fully) for analysis and publication. Interviews and observations may occur at the hospital, or via teleconferencing.

For the pre-trial fieldwork, observations with will be captured using fieldnotes, while interviews will be audio recorded and transcribed for analysis. Written consent will be taken for observations of infection control leads, clinical and estates staff and recording of interviews. The Participant Information Sheet (PIS) and a consent form will be sent via email or directly provided to all potential participants at least 24 hours in advance and all participants will have the opportunity to withdraw their data prior to analysis (two weeks). For observations, posters informing people that observations of estates staff is happening will be provided, and staff will be informed via their Trust's normal method of communication. Any staff member who is observed to be interacting with infection control leads, clinical and estates staff being shadowed will initially be asked for verbal consent when they interact with the person being shadowed, and written consent if we want to use anything they say. The person subject to shadowing will provide written consent. Due to the busy nature of hospitals, it is not possible to collect written consent for all the people who may interact with the person being shadowed but notes will only be taken with verbal consent and written consent taken where information is collected that is directly relevant to understanding the use of ventilation devices in hospitals. No observations will be made of individual patients or conversations about their care.

Regarding the usability testing: the Participant Information Sheet (PIS) and a consent form will be sent via email or directly provided to all potential participants at least 24 hours in advance of any planned usability testing session. Potential participants will then be given the opportunity to discuss the PIS with the researchers and ask questions to ensure understanding before requesting written informed consent from them. If the participant would like to have the usability session conducted by telephone or over teleconferencing software, the researcher will request contact information. The consent form may be given directly to the researcher before the planned usability testing session or emailed back to the research team prior to the usability testing session. Participants will be able to withdraw

consent at any time before or during usability testing sessions. In the event of consent being withdrawn after the completion of a session, the data provided prior to withdrawal will be retained (anonymised fully) for analysis and publication. Usability testing may occur at the hospital, or via telephone/teleconferencing.

For any person who might be eligible to take part in both the main clinical trial, process evaluation and pre-trial fieldwork, they may withhold consent from taking part in any section of the work without impacting on their inclusion in other parts of the work.

The investigator or a delegated member of the research team will explain that participants are under no obligation to enter the trial and that they can withdraw at any time during the trial, without having to give a reason and without prejudicing his/her further treatment. Data and samples collected up to the point of withdrawal can only be used after withdrawal if the participant has consented for this. Any intention to utilise such data should be outlined in the consent form. Where a participant is required to re-consent or new information is required to be provided to a participant, it is the responsibility of the Investigator to ensure that this is done in a timely manner.

No trial procedures, including the collection of identifiable participant data (unless the study has prior approval from the Confidentiality Advisory Group (CAG) and the Research Ethics Committee (REC), will be conducted prior to the participant giving consent by signing the Consent form. Consent will not denote enrolment into trial.

A copy of the signed Informed Consent form will be given to the participant. The original signed form will be retained in the Investigator Site File and a copy placed in the medical notes.

The PIS and consent form will be reviewed and updated if necessary, throughout the trial (e.g. where new safety information becomes available) and participants will be re-consented as appropriate.

Electronic consenting

Following consultation with our programme's PPIE patient advisory group, we may use REDCAP, UCL's Research Data Collection Service. This may be used for eConsent and data collection, either for collection of all source data, or as an alternative to paper methods. Refer here for further information: https://www.ucl.ac.uk/isd/it-for-slms/redcap-research-data-collection-service. Data will be stored in the UCL Safe Haven.

6. PRODUCT/INTERVENTIONS

6.1 Name and description of intervention under investigation

The AI engine, Artificial Intelligence air Safety Tool (AISaT) is computer software that learns the optimal ways to minimise the risks of airborne disease transmission for a given combination of room, ventilation, and other conditions such as available mitigation devices such as screens, fans and air filters. It recommends the best mitigations to use and the best placement that is tailored to the given conditions.

7. TRIAL PROCEDURES

7.1 Pre-intervention assessments

The only assessments will be of specialities to approach for inclusion of clinicians in the study. No screening of individual patients will be needed.

7.2 Registration/Randomisation Procedures

Participant registration will be undertaken by the local site team. Following participant consent, appropriately trained and qualified research personnel will register participants and each participant will be added to a Trial Participant Enrolment Log.

Clinician participants will be randomised into one of the three settings per clinic and this will be undertaken centrally by the coordinating trial team using a random number generator. The team includes a statistician who works at the UCL CCTU and all procedures will be done in line with CCTU best practice.

Patient (and accompanying person) participants will not be randomised.

All patients and clinicians will be unblinded, however the trial statistician, who is a member of the UCL CCTU team, will be blinded so that statistical analysis will be performed in a blinded way. Unblinding will be done at the end of analysis for each trial stage.

7.3Baseline data

There will be a confounding factor list form completed. Confounding factors include but are not limited to: number of people in the room, baseline ventilation, room size, room shape, connection to corridors (open or closed), breathing assist devices, curtains, use of masks, temperature, humidity, factors related to surface based transmission, frequency of people entering and leaving the room, outside visitors, activity level of participants, sex, age to nearest decade, approximate height and weight, ethnicity, history of respiratory difficulties.

7.4Intervention Procedures

Each participant will take part on the day(s) that they attend the clinical environment, e.g. the clinic, AGP room or ward. Following consenting, the initial demographics/baseline data questionnaire will be completed with the research team member. This should take only several minutes. The patient (and accompanying person where applicable) will enter the clinical consulting room, AGP room or ward (depending on stage of trial).

The consented clinician will already have been randomised to one of the three settings:

Configuration 1: The AISaT will be turned on and air quality safety measures will be implemented. These may include the use of air filters, fans, screens etc.

Configuration 2: AISaT will be turned off completely with no extra air quality safety measures

Configuration 3: Air quality safety measures will be offered to the clinician to use and place as they see fit. The daily order of these 3 different configurations will be randomised.

The room will be set up accordingly by the research team. There will be no additional requirements from the patient or clinician throughout the duration of the clinic appointment, as the researchers set up the room themselves.

Some participants will also consent to take part in the implementation work which will involve follow-up questionnaires, such as the NoMAD questionnaire which will be conducted online. A schedule of all trial assessments and procedures is set out in Appendix 1.

The implementation research team will conduct their scoping work (semi-structured interviews, ethnographic observations, stakeholder workshops, usability testing) in a pilot phase, followed by Process Evaluation work during the clinical trials phase (NoMAD questionnaire, ethnographic observations, semi-structured interviews) and cost-effectiveness evaluation.

For an overview, please see Figure 1 in section *4. Trial Design.*

7.5 Subsequent assessments and procedures

Each participant will take part on the day that they attend the clinical environment. Some participants will also consent to take part in the implementation work. A schedule of all trial assessments and procedures is set out in Appendix 1.

7.6Laboratory assessments

Local laboratories:

None. Particle counters will collect data in the clinical area. No analysis will be undertaken anywhere else.

7.7 Discontinuation/withdrawal of participants

The only reason a participant will withdraw from the trial, is due to withdrawing consent.

If they withdraw, any data collected that has not yet been anonymised will be deleted. This information will be in the PIS.

The decision to withdraw a participant from the trial will be recorded in the CRF and medical notes/electronic health record system. The participant will be invited to share the reason for withdrawal and to allow that to be recorded. If a participant explicitly states they do not wish to contribute this data to the trial their decision will be respected and recorded in the CRF.

7.8 Definition of End of Trial

The expected duration of the trial is **27 months** (1 July 2025 to 30th September 2027) from recruitment of the first participant.

The end of trial is the date of completion of the last follow-up questionnaire issued as part of the implementation science section of Stage 3 (wards study).

8. FINANCE AND SUPPLY OF EQUIPMENT

This study/project is funded by the National Institute for Health and Care Research (NIHR) under its Programme Grants for Applied Research Programme (Ref: NIHR 205439). None of the trial management members, CI or PI have any conflicts of interest or anything else to disclose. The SoeCAT will be paid by NIHR.

Funding award start date: 01 July 2024 (5 years)

Funding amount: £2,958,272.69

9. DATA MANAGEMENT

9.1 Confidentiality

The study will be collecting the following personal data which will be collected directly from participants and from medical records of patient participants: activity level of participants, sex, age, height, weight, ethnicity, history of respiratory difficulties. The Case Report Forms (CRFs) will also include the participant's initials and trial identification number. This will be clearly explained in the participant information sheet (PIS). Participant consent for this will be sought. For all subsequent analyses, pseudo-anonymised data will be used. The data and the linking code will be maintained securely in separate locations using encrypted digital files within password protected folders and storage media.

Where participants are patients, the source data will be the hospital medical record. For non-patient participants, the CRF will also be the source data.

Data will be recorded either on paper-based case report forms which will be stored in a locked cupboard in the trial coordinating office at UCL controlled by the CI, or in an electronic data capture system such as RedCAP stored in the UCL Data Safe Haven which will be maintained by the Chief Investigator. The UCL Data Safe Haven has been certified to the ISO27001 information security

standard and conforms to NHS Digital's Information Governance Toolkit. Built using a walled garden approach, where the data is stored, processed and managed within the security of the system, the DSH avoids the complexity of assured end point encryption. A file transfer mechanism enables information to be transferred into the walled garden simply and securely. Alternatively, the identifiable data may be in a secure encrypted network and website. The data will be encrypted at rest and in transit conforming to all of the NHS information governance toolkit as well as the NHS Digital NIST recommendations, NHS Digital / Improvement Health and Social Care Cloud Security – Good Practice Guide 2018. Specifically, SSL transfer of digital information. Password creation and security confirm to the recommendations in the NHS Digital advised NIST guidelines. Identical security will be applied for information stored at rest conforming to the same guidelines.

The study will be compliant with the requirements of the General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018). All Investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing and disclosure of personal information, and will uphold the Act's core principles.

UCL is the data controller; the UCL Data Protection Officer is data-protection@ucl.ac.uk. The data processor is University College London and East and North Hertfordshire NHS Trust (for Lister Hospital).

The data custodian is Professor Ramani Moonesinghe, Professor of Perioperative Medicine at UCL and Chief Investigator of the Central London Patient Safety Research Collaborative.

Data access will be limited to the minimum number of individuals necessary for quality control, audit and analysis.

Data collected in the participating hospitals will be transferred to UCL using an encrypted method, such as direct entry into the UCL Data Safe Haven or uploading scans of paper CRFs to a UCL SharePoint server. Paper CRFs will only be used if the EDC system for entering eCRF data is not working. In this case, the completed original CRFs will be sent via post to Sharon Cheung (Senior Clinical Trials Coordinator, UCL, 3rd Floor, 43-45 Foley St, London W1W 7TY) and a copy kept at site.

Identifiable data will not be transferred outside the study team or outside UCL. In the unlikely event that any data needs to be transferred to another institution, the data will be fully anonymised by removing the patient link and changing the participant's age to the nearest decade.

There will not be a formal data monitoring committee, although there will be both a trial management group (TMG) and independent programme steering committee which will act as the trial steering committee (TSC). See section 13.

Data will be stored for the time recommended by UCL for non-interventional clinical trials used in regulatory submissions, as it is conceivable that a regulatory submission could develop following this work. This is set at 10 years.

9.2 Data collection tools and source document identification

Data will be collected from sites on trial specific case report forms (CRFs) or data collection tools such as electronic CRFs.

Source data are contained in source documents and must be accurately transcribed on to the CRF.

A source document list will be implemented prior to the start of the trial to identify:

- which data is to be recorded directly onto the CRF;
- which data is recorded firstly into source documents, such as medical notes, and then transcribed into the CRF; and
- which data is not to be recorded in the CRF but only recorded in source documents, e.g. participant questionnaires.

The methods used to maximise completeness of data will include collecting the data on the day the participant attends the study site and emailing or telephoning participants who have not completed this data before leaving the study site.

It is the responsibility of the investigator to ensure the accuracy of all data entered in the CRFs and eCRFs. The delegation log will identify all those personnel with responsibilities for data collection and handling, including those who have access to the trial database.

9.3 Completing Case Report Forms

All CRFs must be completed and signed by staff that are listed on the site staff delegation log and authorised by the CI/ PI to perform this duty. The CI/PI is responsible for the accuracy of all data reported in the CRF.

Paper CRFs will only be used if the EDC system for entering eCRF data is not working. In this case, the completed original CRFs will be sent via post to Sharon Cheung (Senior Clinical Trials Coordinator, UCL, 3rd Floor, 43-45 Foley St, London W1W 7TY) and a copy kept at site, or they may be uploaded to a UCL Sharepoint server. The CRFs must be returned within 14 days of the participant visit.

9.4 Data Handling

In the study, data will be collected from patients in accordance with the patient consent form, patient information sheet and section 7.3.1 of this protocol.

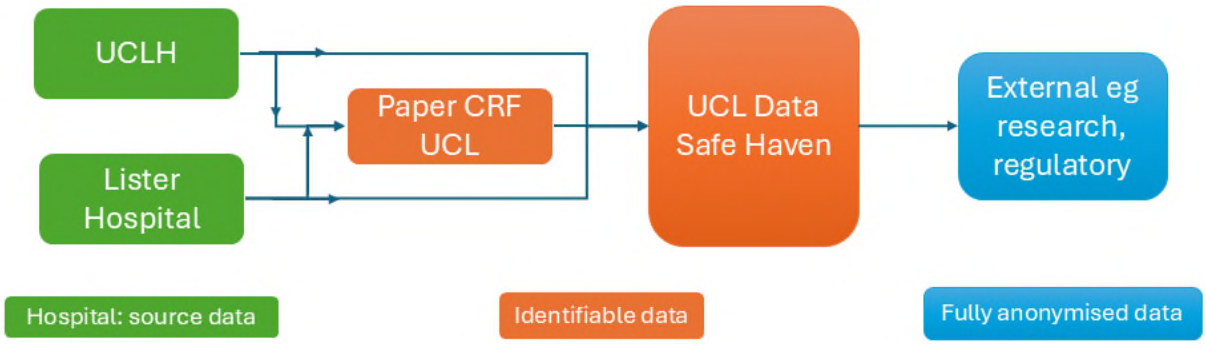
The data controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

All study data will be analysed by internal study personnel. The trial lead statistician is Hakim-Moulay Dehbi [h.dehbi@ucl.ac.uk] and UCL, as the study sponsor, is the data controller.

UCL will process, store and dispose of all study data in accordance with all applicable legal and regulatory requirements, including the Data Protection Act 2018 and any amendments thereto. Any

paper CRFs will be stored centrally at UCL at in a locked filing cabinet controlled by the Chief Investigator.

Direct access to the data will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections, in line with participant consent.



The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality. The Chief Investigator will inform the sponsor should he/she have concerns, which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

9.5 Personal Data breaches

Personal data breaches will be immediately reported to the UCL Information Security Group (ISG) and the UCL Data Protection Officer [data-protection@ucl.ac.uk], and to the Sponsor via the UCL JRO research incident reporting form (as per form and guidance: https://www.ucl.ac.uk/legal-services/guidance/reporting-loss-personal-data). The following information will be provided: full details as to the nature of the breach, an indication as to the volume of material involved, and the sensitivity of the breach (and any timeframes that apply). Sites will additionally follow their Trust incident reporting mechanisms, and will document this within their TMF/ISFs.

10.STATISTICAL CONSIDERATIONS

10.1 Primary outcome

Outcome Measure: Average number of aerosol droplets per minute per clinical encounter as measured by an air particle counter (APC) installed next to the clinician and at up to 4 other fixed locations in the room or ward bay.

10.2 Secondary outcome(s)

Secondary Objective: Mixed methods evaluation of staff experiences of using the tool and the mitigation approaches that are recommended (based on analysis of acceptability by staff and

feasibility of implementation), as well as questionnaires for patients and the cost-efficiency evaluation.

Outcome Measures:

1. Normalisation Measure Development Questionnaire (NoMAD)
2. Ethnographic observations using formal and informal interviews to explore hospital staffs' views on the importance of AISaT, usability and management of the AISaT software and challenges to fidelity in implementation, and how team members can work together effectively to support implementation
3. An estimation of the cost efficiency of AISaT

10.3 Sample size calculation

Participants: 3 consulting rooms or 3 AGP rooms in each hub hospital. 54 clinicians who regularly use these rooms (27 per hospital approximately) will be invited to take part, each for 3 consecutive weeks.

A 3-period, 3-treatment cross-over design will be used to test whether there is a difference in the 3 means. The comparison will be made using a Geisser-Greenhouse corrected F-test with a Type I error rate (α) of 0.05. The group means under the null hypothesis are assumed to be equal. The standard deviation across subjects at the same period is assumed to be 1 (and the means are expressed, see below, as a fraction of the standard deviation, which allows us to calculate a sample size using the Cohen's D approach). The assumed pattern of the covariance matrix is 'all correlations equal' (compound symmetry) with a correlation of 0.5 between adjacent time point measurements. To detect group means of '0 0.25 0.5' with 90% power, the needed number of clinicians is 53 (each measured 3 times). Given that there are six possible sequence combinations of the 3 treatments, the sample size is increased to the closest multiplicator of 6, which is 54. The sample size was computed using PASS 2024, version 24.0.2.

10.4 Planned recruitment rate

Two hospitals are recruiting to this study. The crucial participants to recruit for the first pilot and trial stage 1 is 27 clinicians in each hospital who perform outpatient consultations or aerosol generating procedures (AGPs). Of these, 12 will take part in both the pilot and the stage 1 trial. UCLH has a clinical staff of many thousands and sees 1,800,000 out-patients each year. This equates to around 200,000 separate clinic sessions in multiple clinical areas and there are many dozens of clinical consulting and AGP rooms throughout the estate. The Lister Hospital also has over 2,000 clinical staff and sees 800,000 outpatients each year (around 90,000 separate clinic sessions) and also has multiple clinical areas available. The PI at each site will engage local clinical colleagues, managers and clinical directors to support the work and clinicians who are expected to be in clinic for 3 weeks consecutively will be targeted for recruitment. We expect a dropout rate of around 5% as clinicians must give a minimum of 6 weeks' notice to cancel a clinic, so it is expected that the vast majority of clinicians who agree to take part will attend the relevant clinic sessions.

Recruitment is anticipated to be 10 clinicians per month for stage 1 and its pilot. For stage 2 (and its pilot), 54 clinicians will again be needed. Some of these may be the same ones who participated in stage 1. Recruitment is again anticipated to be 10 clinicians per month. The PI at the Lister Hospital and the CI, who works at UCLH, are both active clinicians who work in outpatients and AGP rooms. This should make recruitment of their clinical colleagues relatively straightforward. The dropout rate is again around 5% as described above.

Of patients attending these clinics and AGP sessions, almost 100% will be eligible and all of these will be invited to take part in the studies (we will not recruit in paediatric, obstetric or psychiatric clinics). Recruitment of patients is therefore likely to be around 300 with approximately 150 accompanying persons per month in both trial stages 1 and 2. Patients will either accept and enrol in the trial, or will not. If they accept and enrol, we do not expect drop-outs. If there were to be, this should have no major impact on the trial endpoints as we will be able to control for this in the data analysis phase. For a 4-hour clinical session, we expect to have 3 hours of analysable data approximately.

For trial stage 3 and its pilot, a total of 12 patient bays is required, 6 at each hospital and each will participate for 3 days. There is no formal sample size calculation for stage 3, as it requires inputs that we do not possess at the moment, including the correlation between the measurements within a bay, as well as the correlation over time. The design is a cluster randomised cross-over control trial. Given that there are 6 possible sequences of the 3 configurations, we chose 12 bays so that there are 2 bays per sequence.

Decisions about wards will be driven by senior clinical management. In wards, if patients accept the study, they will be in the bay until they are discharged, so no drop out is expected. Recruitment of other hospital staff to join the implementation science elements of the study is expected to be around 8-10 per month across the two sites for the duration of the study.

Loss to follow up is not considered to be relevant as participation is only for a very short period of time.

10.5 Randomisation methods

In study stages 1 and 2, clinicians will be randomised using simple randomisation to the order of the three different interventions. In study stage 3, ward bays will be randomised using simple randomisation. Each clinician or ward bay acts as its own control. Randomisation will be implemented using random permuted blocks. Hakim-Moulay Dehbi, Head of Statistics at the Comprehensive Clinical Trials Unit at UCL, will be in charge of randomisation using standard CCTU approaches.

10.6 Statistical analysis

10.7 Summary of baseline data and flow of participants

Baseline variables: Room used (categorical), clinician in the room (categorical), mean number of patients seen in time period and standard deviation, mean age and proportion of patients of each sex, mean number of accompanying persons per time period. A consort flow diagram will be generated for each trial stage.

10.8 Primary outcome analysis

Data analysis will be linear mixed modelling of the paired data (3 conditions for each clinician) controlling for confounding factors which may include: number of people in the room, baseline ventilation, room size, room shape, temperature, humidity and various other factors (see full list of suggested confounding factors in study design section). The power of the trial based on the UK sites alone is 90%.

Data analysis relies on properly functioning aerosol generators and particle counters. In stages 1 and 2, we will check each piece of machinery is working properly before the beginning of the clinical session. Where we do not manage to collect data for at least 2 hours in a clinical session, that session will be withdrawn from the study and repeated in its entirety. We expect this to happen in less than 5% of clinic sessions. For stage 3, a minimum of 6 hours data per day is required otherwise that day's randomisation will need to be rerun.

There are no plans for predefined subgroup analyses in stages 1 and 2. For stage 3, subgroup analyses will include daytime (8 am to 8pm) versus nighttime (8 pm to 8 am).

We will employ the intention-to-treat (ITT) analysis method to ensure the integrity and validity of our RCTs.

10.9 Secondary outcome analysis

Overall Secondary Objective: Mixed methods evaluation of staff experiences of using the tool and the mitigation approaches that are recommended (based on analysis of acceptability by staff and feasibility of implementation).

Pilot phase:

Semi-structured interviews will use framework analysis, guided by the core constructs of the NPT.

Qualitative data analysis in the evaluation phase will be carried out using the RREAL Sheet for real-time analysis and framework analysis for in-depth analysis.

- **Outcome 1:** Normalisation Measure Development Questionnaire (NoMAD)

Outcome 1 Analysis: Descriptive statistics will be used to present the findings from the NoMAD questionnaire.

- **Outcome 2:** Ethnographic observations using formal and informal interviews to explore hospital staffs' views on the importance of AISaT, usability and management of the AISaT software and challenges to fidelity in implementation, and how team members can work together effectively to support implementation

Outcome 2 Analysis: Process evaluation: Details of the precision or power calculation used to estimate the required sample size (for analysis of the primary outcome), should contain all information required to reproduce the sample size calculation including:

Observations will be analysed using framework analysis, organised according to the core constructs of Normalisation Process Theory (NPT) using the format of context, mechanism and action according to each observation.

Based on these data a convergence coding matrix will be generated using normalisation process theory (NPT).

- **Outcome 3: Estimation of Cost effectiveness**

Outcome 3 Analysis: Data envelope analysis (DEA) to rank the efficiency of AISaT in removing air droplets in different settings. Cost-utility analysis to calculate the mean incremental cost of AISaT compared to current practice. This will be calculated using information from the DEA combined with data from the literature on the relationship between air droplets and common air born infections such as influenza.

Using Data Envelope Analysis (DEA) we will examine the technical efficiency of AISaT plus HEPA filters and other available items (screens and fans) in the hospital to improve air quality. This will include inputs including size of the room, number of beds/patients seen, training, clinical, engineering and other staff and costs of the AI system; and outputs with regards to droplets removed.

Whereas a standard cost-effectiveness ratio reports the mean incremental cost per change in outcome, averaging across units, we have chosen DEA analysis to better reflect the heterogeneity in efficiency across rooms and hospitals. Similar to cost-effectiveness analysis it is used in situations where the unit of output, in this case reduction in droplets, has no natural market value[31]. DEA is particularly useful in ranking and hence will help us identify the maximum efficiency of the AISaT in hospital consultation rooms and wards; information that could then potentially be contrasted with the efficiency of full installations of air filters.

The decision making units (DMU) will be defined as the room or ward where AISaT mitigations are being put in place. The definition of a DMU is important in DEA as it determines the units to be compared to each other and ranked. As different rooms/wards may have different efficiency based on a wide range of factors, from the room itself to clinician and patient behaviour, it makes sense to make them the DMU. Given that consultation rooms and wards will have very different input costs and potentially output the two will be analysed separately. They will also have different units of

analysis for costs, with the unit of analysis for wards being bed days and the unit of analysis for consultations number of patients seen. The output will be the ratio of droplets removed with and without AISaT mitigations. This is likely to result in data points across multiple 60 minute time windows for the different units with and without AISaT, which is likely to be a sufficient sample size top conduct the analysis, although consideration will be made as to the impact of sample size changes by partitioning the data on the results[33.] Inputs will include the number of HEPA filters, screens and fans in the room and the cost per hour to run the system based on the cost of electricity to run the HEPA filters. Costs for clinical or engineering staff time in training and installation and any fixed costs for the AISaT system will also be included in the inputs. DEA then is concerned with identifying the maximum output (ratio of droplets removed) for minimal cost. In this case we will look at cost per consultation and cost per bed day.

We will also consider allocative efficiency, in regards to cost-effectiveness. Using similar input and outputs as in the technical efficiency analysis, we will calculate marginal costs per patient seen, per session or per bed day as appropriate when AISaT is used compared to current practice. We will look at the literature to determine the evidence for the relationship between droplet reduction and the reduction in infections for both ward bed days and consultations. This is likely to be based on the D50, or the mean dose of an infective agent required to cause an infection in 50% of susceptible individuals, with the D50 of Influenza-A for example estimated at 790 viral copies[34]. The relative reduction of air droplets is then used to estimate the reduction in viral copies in the air and hence the reduced risk of infection[35]. There is ongoing evidence generation occurring in this field, so we will revisit the literature at the point of analysis to determine the best evidence base for the relationship between droplet removal and reduced risk of infection. The predominant infectious diseases and their incidence also change over time, and hence the values modelled will need to reflect the state of play at the time of analysis. The marginal cost of AISaT will then be contrasted with the cost of reduced infections, calculated based on the average cost per infection treated as obtained from the literature. We will also search the literature for any evidence of impact on quality adjusted life years (QALYs) as a result of reduced infections.

10.10 Sensitivity and other planned analyses

At the end of the clinic, a member of the research staff will ensure that there was compliance to the randomised setting and a log will be kept in order to track this data. The measurements will be reviewed for reliability.

At the end of each pilot phase, an interim statistical analysis will be performed to assess whether the main study is likely to meet the study goals.

Data analysis will be linear mixed modelling of the data controlling for confounding factors. Sensitivity analyses will remove measurements that are considered potentially, or definitely, unreliable. These analyses will be compared to the analyses that keep all collected data points. Interpretation of the main findings

Full data analysis will be undertaken by our co-I at CCTU and his team at the end of each stage of the clinical trials and will again perform data analysis using linear mixed modelling of the data (3 conditions for each clinician) controlling for confounding factors.

Decision criteria used to judge the interim results as part of a guideline for early stopping

Each trial is due to complete within 6 months, with a 3 month buffer to deal with unforeseen problems. The pilot phase for the first trial in consulting rooms will recruit 20% of the patients in 5 weeks. The trial will STOP if we don't recruit 60% of expected number (i.e. 12% of the total recruitment).

The AISaT tool may not be able to compute a solution to reduce aerosol transmission in the rooms we wish to use for trial. If this occurs, the TMG will allow an extra 3 months to find rooms that the tool can be used in. If we cannot find suitable clinic rooms, TMG will stop the trial.

A report will be produced by engineering team at end of each pilot on numbers of aerosol droplets measured. Trial statisticians will ensure it will be possible to determine statistically whether the trial could reach predefined end points. If not, TMG will discuss with engineering team how to seed the room with more droplets and then implement. Although unlikely that doctors or patients will notice changes, we will perform a further pilot. TMG will stop second trial if we cannot recruit adequately during pilot as above. The statistical report at the end of each pilot will identify variance in aerosol droplet concentrations between the clinical areas. Even apparently identical rooms may have different airflows. If current sample size inadequate to achieve statistical power needed, statisticians will advise the TMG of a new sample size. TMG to discuss with trial team extra patient recruitment. If unachievable within 9 months, TMG will stop trial. At the end of each pilot, trial team will also ask hospital staff whether AI generated mitigations interfere with clinic, procedure room or ward e.g. due to noise or trip hazards. TMG will discuss with engineering team adjusting AISaT system. If not achievable, trial will be stopped. Ensuring adequate research support staff to run trials. This is costed in SoeCAT. We know that NHS Trusts are under pressures and may not have research staff available to enable recruitment If recruitment in pilot phase is too low, TMG will decide whether to stop the trial at that point. For trial stage 2, based in procedure rooms, the issues above remain relevant. Ventilation rates are higher than in standard consulting rooms, and there is more movement of people as well as intermittent aerosolising equipment use and use of personal protective equipment (PPE) by staff. All these factors may increase standard deviation in aerosol droplet levels. Study sample size may therefore need to be larger, but we will apply the same stop/go criteria as for trial stage 1. All issues above remain relevant in the ward bay trial stage 3. Here operational risks are key. Ward changes happen for many reasons and are impossible to predict. If a change to wards is needed, the statisticians will advise whether this will impact on trial delivery. If not possible to complete within the time frame, TMG will decide whether to stop the trial.

Management

The trial team will report to the trial management group (TMG) at the end of week 5. If recruitment is inadequate, TMG will discuss with the trial team why recruitment failed and explore ideas to improve recruitment before deciding on whether to restart. Discussions may also be had with our programme PPIE panel. The trial will restart if TMG confident it can complete recruitment within 9 months.

Who will see the outcome data while the study is ongoing?

The operational trial staff will collect and collate the data while the study is ongoing. The trial statisticians will also see the data and will share it with the TMG if necessary, according to the stop criteria listed above.

Whether these individuals will remain blinded to the trial groups

This is an unblinded trial. The statistician will be responsible for producing the randomisation lists, and so will not be blinded.

How the integrity of the trial implementation will be protected (e.g. maintaining blinding) when any adaptions to the trial are made

We will involve key stakeholders, including the trial statisticians, early in the design planning process for any trial adaptations. This will help us anticipate potential challenges and develop robust blinding procedures. We have pre-specified in the protocol pilot phases for each trial stage. These allow for interim analyses and implementation of decision rules for adaptations such as stopping the trial early for efficacy or futility, adjusting sample sizes, or modifying treatment arms. By pre-specifying these adaptations, we will ensure that changes are made systematically and transparently, whilst maintaining the integrity of trial implementation.

Who has the ultimate authority to stop or modify the study e.g. the CI, Trial Steering Committee, or the Sponsor?

The ultimate authority to stop or modify the trials lies with the trial steering committee, to whom the CI is answerable.

Stopping criteria for futility are described earlier in this section.

Stopping criteria for harm include if participants experience significant adverse health effects that are directly attributable to the study. These might be due to unexpected problems such as trip hazards, patients throwing filters etc (particularly in the stage 3 study) or if device malfunctions cause risks to participants. In all of these cases, an adverse event report will be completed and the CI, in consultation with the TMG and/or the TSC will decide whether to terminate the study early.

The strategies to maximise follow-up and prevent missing data

No follow-up is required. We will collect only essential information to reduce participant burden. Strategies to minimise the risk of missing data include ensuring that are CRFs are user-friendly, and electronic CRFs will have mandatory data fields and data validation checks. We will also provide

thorough training to the clinical trials staff to ensure that they check CRF data at the time they are completed. The pilot study phases will also identify potential issues before the main studies begin.

How recording of reasons for missing data will be undertaken

Recording reasons for missing data will be undertaken using standardised forms to capture these reasons. The forms will be developed and iterated throughout the pilot phases and as the trials progress. Study personnel will also be trained regularly and encouraged throughout the trials to document reasons for missing data in a detailed way. This includes noting the specific circumstances and any relevant participant feedback when data is missed.

Where participant interviews are undertaken, follow-up interviews will be offered to those who miss appointments or data collection points. This will help the study team gather insights into the reasons for missing data and address any issues that may prevent future participation.

Finally, regular monitoring and audits will be undertaken to review the completeness and accuracy of the recorded reasons for missing data.

How missing data will be handled in the analysis and whether there are any planned methods to impute missing outcome data, including which variables will be used in the imputation process

Initially, we will perform a complete-case analysis, where only participants (clinicians or ward bays) with complete data from all entire study periods are included. This approach helps to understand the extent and pattern of missing data. We will then conduct sensitivity analyses to assess the impact of missing data on our results. This includes comparing the results of complete-case analysis with those obtained using imputation methods.

We will use multiple imputation (MI) to handle missing data. MI involves creating multiple datasets by imputing missing values based on observed data, analysing each dataset separately, and then combining the results to produce final estimate. Full information maximum likelihood (FIML) will be used as an alternative method, which estimates model parameters directly using all available data without imputing missing values.

The imputation process will include the following variables to ensure accurate and unbiased estimates: **Baseline Characteristics**: Age range, sex, body size, **Outcome Measures**: Primary outcome measure of respiratory particle counts. **Auxiliary Variables**: Additional variables that are correlated with the missing data and the outcomes, such as environmental factors and room conditions will be analysed.

The procedure for reporting any deviation(s) from the original statistical plan

We will document deviations, including details of the nature, reason and potential impact of the deviation on the study outcomes.

Significant deviations that may affect the study validity, reliability, or participant safety will be reported immediately to the TMG and the study sponsor and will also be reported to the TSC. The PI and local study team will conduct an assessment and root cause analysis of the deviation. This involves identifying who deviated from the protocol, what the deviation was, when and how it occurred, and its impact on the study. Based on the assessment, an action plan will be developed to address the deviation. This plan will include steps to mitigate any negative impact and prevent similar deviations in the future.

Minor deviations (which are not considered to be adverse events for participants) will be documented and reported to the TMG during regular progress reports. All deviations and the corresponding action plans will be transparently reported in the final study report and any publications resulting from the study to make the scientific community aware of changes to the original statistical plan.

11.ASSESSMENT AND MANAGEMENT OF RISK

The known and potential risks and benefits to human participants

The known and potential risks include trip hazards in all study stages when air safety mitigation devices are placed in unsuitable places when following the AISaT guidance, for example in the middle of the floor, with leading wires left uncovered. There is a risk, most keenly in the stage 3 ward trial of portable filters and similar devices falling over, delirious inpatients throwing them, of not having enough plug sockets to plug devices into and getting in the way of emergency procedures such as cardiac arrest calls. There is a risk that mitigation devices may make too much noise which could interfere with patients hearing doctors or with sleep. Aerosolised saline is not known to cause any risks to humans.

How high the risk is compared to normal standard practice

All the risks described above are already present in clinical areas and in the study are only minimally higher than normal.

Frequency of risk

In an evaluation of HEPA filters which has been undertaken for a year at the National Hospital for Neurology and Neurosurgery, filters have been left next to patient beds in 12 patient bays and side-rooms, comprising almost 60 patient beds. The risks described above were all identified by ward staff at the beginning of the work, but none of these have yet happened except for not having

enough plug sockets, which was sorted by bringing in extension cables. No patient has complained of not being able to hear or sleep. The frequency of these risks is therefore considered to be very low.

How the risk will be minimised/managed

The table below summarise the risks and mitigations of all test above standard care that are being performed in a table:

Intervention	Potential Risk	Risk Management
Trip hazard	Participant falling and injuring themselves	The AISaT will be trained not to recommend that a mitigation device be placed in the centre of a space where people might walk
Portable mitigation devices falling or being thrown	Other staff or patients being injured	It will not be possible to secure devices to the wall but holders may be used to minimise the risk of devices falling or being picked up
Inadequate plug sockets	Other important medical devices or the mitigation device may be unplugged	Staff will be trained not to unplug any other medical devices. Where there is a lack of plug sockets, this will be identified before the trial starts and extension leads will be used. A note will be fixed to the mitigation device plug telling people not to turn it off
Excess noise	Patients unable to hear doctor or unable to sleep	All machines must meet NHS noise standards. Noisy machines will be removed and fixed.

12.RECORDING AND REPORTING OF ADVERSE EVENTS

12.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or trial participant, which does not necessarily have a causal relationship with the intervention involved.
Serious Adverse Event (SAE).	Any adverse event that: • results in death, • is life-threatening*,

	• requires hospitalisation or prolongation of existing hospitalisation**, • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect. • Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences
* A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. ** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.	

12.2 Assessments of Adverse Events

Each adverse event (AEs) will be assessed for severity, causality, seriousness and expectedness as described below. AEs will be reported within 14 days. The point where recording/reporting starts will be from the time of consent.

12.3 Severity

The generic categories below are given for use as a guide. You may have a more specific scale that you want to use related to the disease (e.g. CTCAE criteria), amend as required.

Category	**Definition**
Mild	The adverse event does not interfere with the participant's daily routine, and does not require further intervention; it causes slight discomfort
Moderate	The adverse event interferes with some aspects of the participant's routine, or requires further intervention, but is not damaging to health; it causes moderate discomfort

Severe	The adverse event results in alteration, discomfort or disability which is clearly damaging to health

12.4 Causality

It is of particular importance in this trial to capture events related to the use of mitigation devices recommended by AISaT. The assessment of relationship of an adverse event to this/these additional safety issue(s) will also be carried out as part of the trial.

The differentiated causality assessments will be captured in the trial specific AE Log and SAE Log.

The following categories will be used to define the causality of the adverse event:

Category	**Definition**
Related	A causal relationship between the intervention and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.
Not related	There is no reasonable possibility of a causal relationship between the intervention and an adverse event.
Not Assessable	Unable to assess on information available.

12.5 Expectedness

All SAEs assigned by the Investigator or delegate as suspected to be related to the intervention will be assessed for expectedness as defined in this protocol.

Category	Definition
Expected	An adverse event which is consistent with the information about the intervention **clearly defined in this protocol.**

Unexpected	An adverse event which is not consistent with the information about the intervention **clearly defined in this protocol.**

** This includes listed events that are more frequently reported or more severe than previously reported.*

The reference document to be used to assess expectedness against the Intervention is Health Technical Memorandum 03-01 Specialised ventilation for healthcare premises.

The following events listed below describe expected procedural/disease related AEs:

- Participants tripping over without sustaining serious injury
- Excess noise affecting participants ability to hear or sleep

12.6 Recording of Adverse Events

All adverse events will be recorded in the CRF until the participant completes the trial. All adverse events will also be recorded on the non-CTIMP Adverse Event (AE) log, and stored in the site files (provided by the JRO).

12.7 Procedures for recording and reporting Serious Adverse Events (SAEs)

All serious adverse events will be recorded in the medical records and the CRF, and the sponsor's SAE log which will be collated on the electronic RedCAP database stored in the UCL Data Safe Haven throughout the trial, from which a line listing of the SAEs can be extracted for review. The AE and SAE logs will also be stored in the Investigator Site File and may be subject to Sponsor monitoring and auditing.

All SAEs (except those specified in the protocol as not requiring reporting to the Sponsor) will be reported to the Sponsor within 24 hours of becoming aware. The CI/PI or designated individual will complete the Sponsor's online Research Incident Reporting Form (https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo) within 24 hours of becoming aware of the event. The Chief or Principal Investigator will respond to any SAE queries raised by the Sponsor as soon as possible.

Where the SAE is unexpected and thought to be related to the intervention, this must be reported by the Investigator to the main REC that approved the study within 15 days of the Investigator becoming aware of the event, using the non-CTIMP safety report to REC form. This form can be found on the HRA website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/. The Sponsor should be copied into this, so they are aware.

Although the trial statistician works at the CCTU, there is no CTU involved in the management of this trial.

12.8 Managing serious adverse events across research sites

The timeframe for reporting SAEs will be 72 hours. The PI will send the report to a central coordinating team (based with the CI or a CTU). The CI will review the report first before it is notified to the sponsor and will inform site PIs by email or phone if safety information needs to be disseminated. This is not anticipated to be complex as there are only two sites participating in the trials.

SAEs will be reported to the Sponsor until the end of the trial.

Participants must be followed up until the event has stabilised. Follow-up should continue after completion of protocol treatment and/or trial follow-up if necessary. Follow-up SAE reports (clearly marked as follow-up) will be completed via https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo and submitted to the JRO as further information becomes available.

12.9 Incidental Findings in Research

Incidental findings are highly unlikely to occur in this study. All research staff must follow participating sites' incidental findings policies, and training will be provided as part of initiation to the research study (where applicable).

12.10 Unblinding

The only people blinded in this study are the study statisticians. No emergency unblinding of participants is therefore needed.

12.11 Reporting Urgent Safety Measures

If any urgent safety measures are taken the CI/ PI shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice in the form of a substantial amendment to the relevant REC and Sponsor of the measures taken and the circumstances giving rise to those measures.

12.12 Protocol Deviations and Violations

Protocol violations during the trial conduct phase will be recorded by completion of the online JRO Research Incident Reporting Form: https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo. All protocol violations will be recorded on the Protocol Violation Log and filed in the site file.

Protocol deviation examples include where one of the mitigation devices such as an air filter is not deployed correctly.

12.13 NHS Serious Incidents and Near Misses

Serious Incidents and near misses will be reported to the Sponsor and Trust Quality & Safety department as soon as the study team becomes aware of them.

12.14 Complaints from research participants

In the first instance, research participant complaints (patients or health volunteers) will be reported to the CI/PI to investigate, as documented in the patient information sheet(s), and to the Sponsor via research-incidents@ucl.ac.uk, following the *UCL Complaints from Research Subjects about UCL Sponsored Studies and Trials* policy. For participants who are NHS patients, complaints will be reported to the NHS Complaints Manager at the Trust where the recruitment and study procedures were undertaken. Complaints from NHS patients are handled under NHS complaints policies and procedures, with involvement from PALS and the Sponsor where necessary.

13.OVERSIGHT COMMITTEES

13.1 Trial Management Group (TMG)

The TMG will include the Chief Investigator and trial staff. The TMG will be responsible for overseeing the trial. The group will meet at least quarterly and will send updates to PIs.

The TMG will review recruitment figures, SAEs and substantial amendments to the protocol prior to submission to the REC. All PIs will be kept informed of substantial amendments through their nominated responsible individuals.

13.2 Other committees

The NIHR-funded Air Safety programme has an independent programme steering committee (PSC). The PSC will also act as the Trial Steering Committee (TSC). The TSC will oversee the safety of participants, ensure trial integrity to ensure compliance with regulatory and ethical standards, review interim data, protect scientific validity, recommend trial continuation or termination, assess benefit-risk balance and guide on unanticipated ethical or practical issues that arise, as well as offer support for trial adaptations. TSC members are listed in the 'Key Contacts' table in this document.

The role of the TSC is to provide overall supervision of the trial. The TSC will review the reports of the TMG and, on consideration of this information, recommend any appropriate amendments/actions for the trial as necessary. The TSC acts on behalf of the funder(s) and Sponsor.

There will be no separate data monitoring committee for this study.

13.3 REGULATORY REVIEW AND PATIENT AND PUBLIC INVOLVEMENT

13.4 Regulatory Review

The Sponsor will ensure that the trial protocol, participant information sheet, consent form, and submitted supporting documents have been approved by the appropriate research ethics committee, prior to any participant recruitment. The protocol, all other supporting documents including and

agreed amendments, will be documented and submitted for ethical and regulatory approval as required. Amendments will not be implemented prior to receipt of the required approval(s).

The study was deemed to require regulatory approval from the following bodies: REC Favourable Opinion and HRA Approval. Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that the appropriate regulatory approvals have been issued, and NHS Confirmations of Capacity and Capability and Sponsor green lights are in place.

For any amendments to the study, the Chief Investigator or designee, in agreement with the Sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments as well as the study delivery team) to confirm ongoing Capacity and Capability for the study.

All correspondence with the Sponsor, REC and HRA will be retained. The Chief Investigator will notify the Sponsor and REC of the end of the study.

It is the Chief Investigator's responsibility to produce the annual progress reports when required; an annual progress report (APR) will be submitted to the Sponsor and REC within 30 days of the anniversary date on which the favourable opinion was issued, and annually until the study is declared ended.

Within 90 days after the end of the trial, the CI will ensure that the main REC is notified that the trial has finished. If the trial is terminated prematurely, those reports will be made within 15 days after the end of the trial.

Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the Sponsor and to the REC and HRA.

13.5 Peer Review

The study has been peer reviewed in accordance with the requirements outlined by UCL.

The Sponsor considers the procedure for obtaining funding from the National Institute for Health Research (NIHR) to be of sufficient rigour and independence to be considered an adequate peer review.

13.6 Patient and public involvement (PPI)

This research is based on extensive patient engagement. We have a dedicated patient advisory group (PAG), which meets approximately twice annually as part of our Air Safety programme grant.

Our research team has a funded dedicated Patient and Public involvement lead, Simon Watt (UCL).

The implementation work in this proposal was designed to gain vital insights from relevant patient groups to understand potential barriers of the AISaT tool, and develop a better understanding of perceptions, feasibility and usability following direct consultation with PAG, following which, the design of the research was shaped. The PAG will remain involved in assessing the acceptability of the

research to patients. The PAG will not be involved in management, undertaking of analysis of the research findings.

14.MONITORING AND AUDITING

A trial specific oversight and monitoring plan will be established for studies. The trial will be monitored in accordance with the agreed plan. The degree of monitoring will be proportionate to the risks associated with the trial. Risk will be assessed on an ongoing basis by the Chief Investigator, and adjustments made accordingly (in conjunction with the Sponsor).

The Chief Investigator will be responsible for the day-to-day monitoring and management of the study. The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the Sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

The UCLH/UCL Joint Research Office, on behalf of UCL as Sponsor, will conduct random audits on a selection of studies in its clinical research portfolio. Monitoring and auditing will be conducted in accordance with the UK Policy Framework for Health and Social Care Research, and in accordance with the Sponsor's monitoring and audit policies and procedures.

15.TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files. Training may require renewal when new clinical trials staff are appointed. This will be assessed regularly by the TMG.

16.INSURANCE AND INDEMNITY

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

Participants may also be able to claim compensation for injury caused by participation in this clinical study without the need to prove negligence on the part of University College London or another party. Participants who sustain injury and wish to make a claim for compensation should be advised to do so in writing in the first instance to the Chief Investigator, who will pass the claim to the Sponsor's Insurers, via the Sponsor's office.

Hospitals selected to participate in this clinical study shall provide clinical negligence insurance cover for harm caused by their employees and a copy of the relevant insurance policy or summary shall be provided to University College London upon request.

Additionally, UCL does not accept liability for sites such as GP surgeries in primary care; investigators/collaborators based in these types of sites must ensure that their activity on the study is covered under their own professional indemnity.

17.RECORD KEEPING AND ARCHIVING

UCL and each participating site recognise that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that he/she will archive the Trial Master File at UCL for the period stipulated in the protocol and in line with all relevant legal and statutory requirements. The Principal Investigator at each participating site agrees to archive his/her respective site's study documents in line with all relevant legal and statutory requirements. Study documents will be archived for a minimum of 5 years from the study end, and no longer than 20 years from the study end.

The Trial Master File will be archived at UCL, in accordance with the UCL Retentions Schedule. It will be archived for a minimum of 5 years from the study end, and no longer than 20 years from study end.

NB: UCL do not archive student projects and therefore, the length of storage is not subject to the standard Sponsor requirements.

18.INTELLECTUAL PROPERTY

No IP is expected for this study. As per the NIHR Air Safety Programme contractual agreement, UCL owns IP for programme.

All background intellectual property rights (including licences) and know-how used in connection with the study shall remain the property of the party introducing the same and the exercise of such rights for purposes of the study shall not infringe any third party's rights.

All intellectual property rights and know-how in the protocol, the study data and in the results arising directly from the study, but excluding all improvements thereto or clinical procedures developed or used independently of the study by each participating site, shall belong to UCL. All intellectual property rights deriving or arising from the material or any derivations of the material provided to UCL by the participating site shall belong to UCL. Each participating site agrees that by giving approval to conduct the study at its respective site, it agrees hereby to effectively assign all such intellectual property rights ("IPR") to UCL and to disclose all such know-how to UCL.

Each participating site agrees to, at the request and expense of UCL execute all such documents and do all acts necessary to fully vest the IPR in UCL.

Nothing in this section shall be construed so as to prevent or hinder the participating site from using know-how gained during the performance of the study in the furtherance of its normal activities of providing or commissioning clinical services, teaching and research to the extent that such use does not result in the disclosure or misuse of confidential information or the infringement of an intellectual

property right of UCL or its funder. This does not permit the disclosure of any of the results of the study, all of which remain confidential.

19.PUBLICATION AND DISSEMINATION

All proposed publications will be discussed with and reviewed by the Sponsor prior to publishing other than those presented at scientific forums/meetings. Please refer to UCL Publication Policy.

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21. APPENDICES

Please find Schedule of Assessments below. Please find all Participant Information Sheets, Informed Consent Forms, delegation log and questionnaires in separate documents.

21.1 APPENDICE 1: Schedule of Assessments for RCT: Outpatients consulting room and AGP room setting (stage 1&2)

	Screening (Pre-treatment assessment)	**Clinical Trial**		**Implementation Questionnaire(s)**
	Day X minus 4 weeks	Day X minus 1 day	Day X (clinic visit)	Approx 1-2 weeks later (online)
Identifying suitable clinicians	X			
Phone Patient & send PIS (where possible)		X	X (if not possible to send ahead of day of appointment)	
Clinician Randomisation		X		
Informed Consent			X	
Questionnaire to obtain confounding factors info			X	
Aerosol Particle Counter (APC) measurement			X	
NoMaD Questionnaire				X

21.2 APPENDICE 2: Schedule of Assessments for RCT: Ward setting (stage 3)

	Screening (Pre-treatment assessment)	**Clinical Trial**		**Implementation Questionnaire(s)**
	Day X minus 4 weeks	Day X minus 1 day	Days 1-3 (ward setting)	Approx 1-2 weeks later (online)
Identifying suitable clinicians	X			
Phone Patient & send PIS (where possible)		X	X (if not possible to send ahead of day of appointment)	
Clinician Randomisation		X		
Informed Consent			X	
Questionnaire to obtain confounding factors info			X	
Aerosol Particle Counter (APC) measurement			X	
NoMaD Questionnaire				X

21.3 APPENDICE 3: Schedule of Assessments for Semi-Structured interviews

Activity	Semi-structured interviews - pilot phase	Semi-structured interviews - main trial phase
Identification of participants (15 participants)	1 hour (local PI or researcher time)	1 hour (local PI or researcher time)
Informed consent (15 participants)	1 hour in total (researcher time) 30 minutes per participant (participant time)	1 hour in total (researcher time) 30 minutes per participant (participant time)
Semi-structured interview (15 participants)	15 hours in total (researcher time) 1 hour per participant (participant time)	15 hours in total (researcher time) 1 hour per participant (participant time)

21.4 APPENDICE 3: Schedule of Assessments for Usability Testing

Activity	Usability testing round 1	Usability testing round 2
Identification of participants (10 participants)	1 hour (local PI or researcher time)	1 hour (local PI or researcher time)
Informed consent (10 participants)	1 hour in total (researcher time) 30 minutes per participant (participant time)	1 hour in total (researcher time) 30 minutes per participant (participant time)
Usability testing session (10 participants)	10 hours in total (researcher time) 1 hour per participant (participant time)	10 hours in total (researcher time) 1 hour per participant (participant time)

21.5 APPENDICE 3: Schedule of Assessments for Ethnographic Observations

Activity	Ethnographic observations including informal interviews- pilot phase	Ethnographic observations including informal interviews - main trial phase
Identification of participants (maximum 10 participants)	1 hour (researcher time)	1 hour (researcher time)
Informed Consent	30 minutes per participant (participant and researcher time)	30 minutes per participant (participant and researcher time)
Ethnographic observations including informal interviews	Up to 40 hours over a period of two weeks	Up to 40 hours over a period of two weeks

21.6 APPENDICE 4: Associated Documents

Document Name	Document Version	Document Date
Delegation Log	1	21FEB2025
Draft interviews topic guide development AISaT platform - patients	1	21FEB2025
Draft interviews topic guide development AISaT platform - staff	1	21FEB2025
Usability testing draft topic guide	1.1	19JUN2025
NoMAD Questionnaire (template)	1	21FEB2025
Clinical Trial_Clinician_Participant Information Sheet	3	17JUL2025
Clinical Trial_Consent form	2	17JUL2025
Clinical Trial_Patient_Participant Information Sheet	3	17JUL2025
Staff ethnography + interviews_Consent form	2	17JUL2025
Staff ethnography + interviews_Participant Information Sheet	2	17JUL2025
Usability testing_Consent form	2	17JUL2025
Usability testing_Participant Information Sheet	2	17JUL2025
WP3_patient interviews_Consent form	2	17JUL2025
WP3_patient_interviews_Participant Information Sheet	2	17JUL2025