Airwave Health Monitoring Study Follow-up Phase

Project Protocol

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Contents

Summary

The Airwave Health Monitoring Study (AHMS) is an epidemiological occupational cohort study open to all police forces in UK. It was established to investigate possible long-term health effects associated with use of the TETRA radio system among the police forces. It is recognised that the cohort also provides a valuable opportunity for broader research into common diseases affecting a well-defined occupational group, including substantial numbers of both men and women who are being followed up for many years. Participants who took part in health screen gave broad consent for collection and storage of blood and urine samples for future research, and linkage to health and other records. Up to 95% of the volunteers who have been screened have given consent for this option. Those who have opted out of this clause have had their samples destroyed after testing in laboratory.

Since the launch of the study in 2003, 28 (of 54) police forces agreed to participate. As of March 2015, we have recruited c. 50,000 participants into the study of whom c. 45,000 have undergone a health screening that includes extensive lifestyle and questionnaire data, cognitive tests, clinical measurements and collection of biological samples at base line. Follow-up of the cohort is progressing through access to past and future medical and other health related records.

In 2013 AHMS was given Tissue Bank status by NRES under the HTA licence held by Imperial College Healthcare Trust.

The Airwave Health Monitoring Study (AHMS) has benefited from being a tissue bank as it has a rich resource of DNA, plasma, sera and urine samples. It has facilitated programmes of research without need for individual project-based ethical approval. The study has been set up to collect and store samples and data to establish a sampling framework (stage 1 activity) from which people, with and without health problems, can be selected on the basis of their genotype and / or phenotype to be invited for observational studies or clinical trials (stage 2 activity).

The value of the study will be greatly enhanced if we do a follow-up health screening of the participants in the cohort as researchers will be able to detect developments or changes in the characteristics of the target population at both the group and the individual level. As longitudinal studies extend beyond a single moment in time, they can establish sequences of events.

The average age of the cohort at baseline was 40 years. Ten years have now elapsed since the study commenced, and it is therefore an appropriate time to perform follow up screen, to help identify the evolution and aetiology of chronic diseases (e.g. diabetes and incidence of metabolic syndrome) and diseases that may be related to Airwave exposure (mainly cancer). Cognitive function tests will help researchers in following and understanding cognitive decline in a younger population (including neuropsychiatric and neurodegenerative effects which may be linked to sickness absence and early retirements).

Only previously recruited and screened officers and staff will be invited to come back for a re-screen, which will be at a conveniently located screening centre within commuting distance of their home. To help Imperial College deliver the study nationally we have contracted the screening services organisation Tohealth Ltd (http://www.tohealth.com/), a well-established health screening company. The

assessment will be performed by health care professionals who will be trained and monitored by Imperial College London.
The participants will be offered a comprehensive health screen (clinical measurements, collection of biological samples, and a questionnaire).

Informed consent will be obtained by trained staff at the clinics. The consent is broad and requests permission to carry out future research using the samples and data collected and to follow up their health in future via medical records and also to contact them in the future.

The clinical measurements performed will include height, weight, waist-hip, blood pressure, bio-impedance, electrocardiogram (ECG), pulse-wave velocity (PWV), grip strength, spirometry, step test and heel ultrasound.

Some of blood samples taken are used for carrying out haematology and a range of clinical chemistry tests. The remaining samples will be stored for future use in research and to recall participant's for *stage 2 activity*..

A feedback of baseline clinical measurements including ECG and blood test results (haematology and clinical chemistry) is given to the participants. If any of the results are of clinical significance, they will be referred to their GP for follow up/treatment, subject to the participant giving consent. ECG is interpreted by a cardiologist who advises on any referral to the participant's GP.As part of *stage 2 activity* (recall for more sample or new data), participants would be contacted by the AHMS study team. They would be approached because of their genotype/phenotype collected from *stage1 activity* (recruitment and health screening*).* Information regarding further studies would be provided and the risks and benefits explained. If they express interest in taking part, they will be sent an invitation for joining in further research or providing more samples according to that study's protocol. Each stage 2 study will need to obtain consent for its specific objectives..

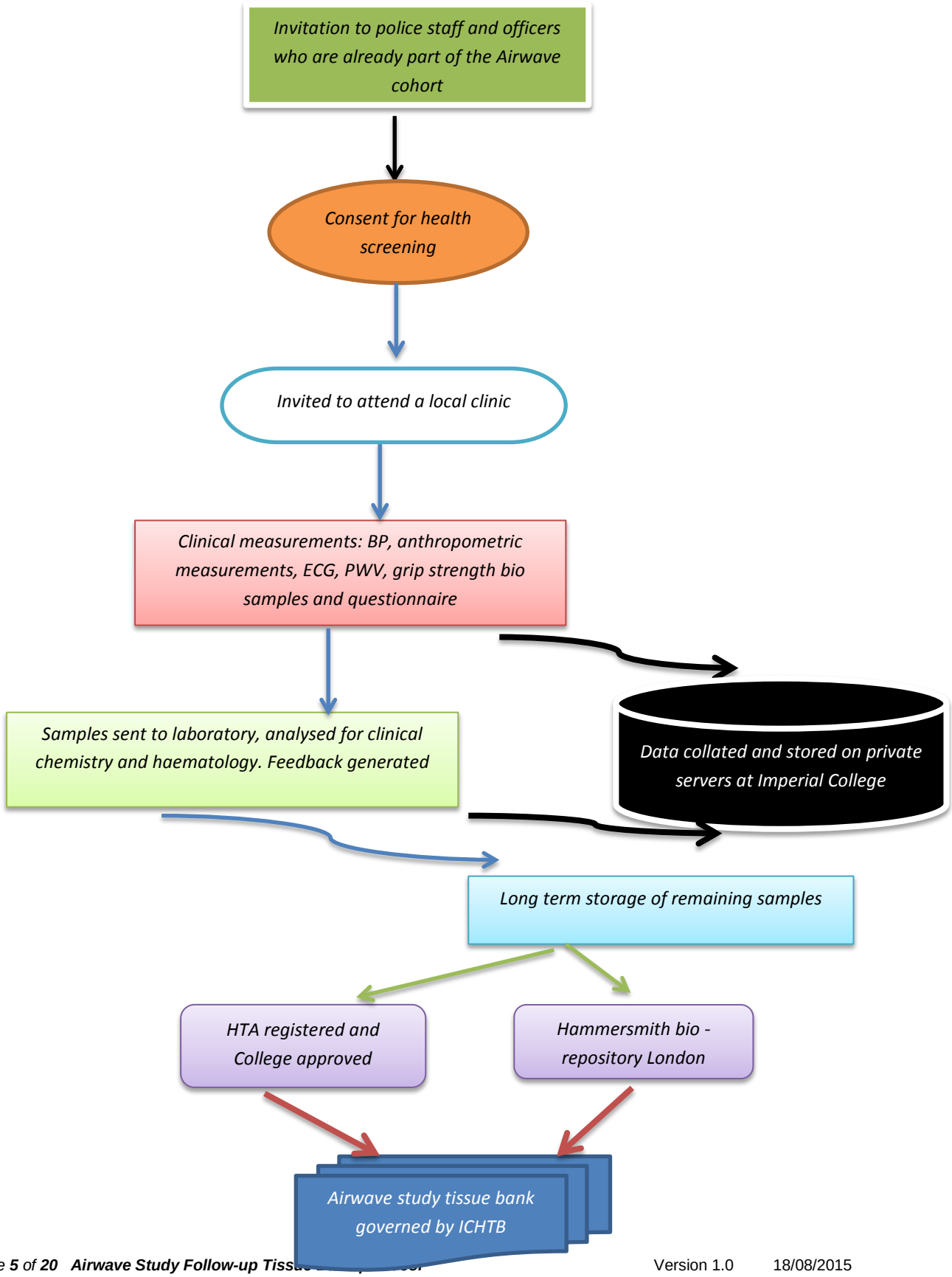
There will be no obligation to take part in these additional studies, participants are free to withdraw from the Airwave Study at any time, and have their biological samples destroyed.

Each subsequent individual study will submit an application for access to samples and/or data. On the basis of this application it will be decided if any of the participants need to be recalled. Participants can only be contacted by the tissue bank staff. Each study will have a different protocol that will be submitted to ICHTB tissue management committee who will decide on the scientific merit of the study. They will then give approval to release samples/data as appropriate.

All samples taken at the clinic will be labelled with a unique barcode linked to a patient identifier recorded on the health care professionals' workstation. After collection in the field, all information will be stored on a secure network at Imperial College.

Biological samples will be processed and analysed at Charing Cross Hospital, London. A proportion of each sample will be transferred to Imperial College's Biorepository facility at Hammersmith campus and a backup set sent to external providers (HTA registered), approved by the College, for long term storage.

Figure 1: Flow chart showing collection of samples and data



Objectives of the tissue bank

The primary aim of this tissue bank (TB) is to promote collaboration with other research groups both within and outside the college to avoid wasteful competition in the use of limited and precious resources.

The AHMS study is a rich resource with comprehensive phenotyping (the observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences) of its participants. State-of-the art methods can be used on the many participants within AHMS to investigate genetic and environmental causes of disease, as well as the pathways to those diseases.

The tissue bank will provide a national cohort of volunteers who wish to participate in clinical research, and are willing to provide clinical information and samples that enable identification of suitable volunteers for future studies by genotype and phenotype.

By collecting and storing tissue and data the TB is providing the foundation for:

- Research related to specific disease or group of diseases, or could range more widely across biomedicine generally for yet unspecified research questions.
- Research into the molecular mechanisms involved in disease development and its response to possible resistance to treatment.
- The discovery and validation of new targets and biomarkers for detection, diagnosis, treatment stratification, and development.

The TB will endeavour to make bio samples available to researchers provided that:

1. the stated research objectives have been approved by the TB Management Board
2. the proposed research is covered by the scope of the donor consent covering the uses of bio-samples
3. the research is sufficiently funded and resourced
4. the necessary bio-samples can be sourced and supplied
5. the research project is supported by the institution or organisation in which it will take place
6. the researcher's organisation enters into a contract that governs the transfer and use of bio-samples and data supplied

These samples are banked to provide an invaluable resource for collaborative research projects that encompass a wide variety of techniques including biochemistry, molecular biology, and biomarker studies with research groups involved in a range of medical conditions with the aim of devising new treatments and therapies. It may also be possible to help prevent them from happening in the future.

Recent advances in biochemical techniques using NMR spectroscopy (metabonomics) have suggested that biochemical patterns found in blood or urine can be highly predictive of disease process *(Brindle et al 2002).*

Experimental medicine studies involving a relatively small number of individuals recruited according to clinical, genetic and molecular phenotype can rapidly advance understanding of disease mechanisms, identify potential drug targets, and improve insight into the therapeutic potential and limitations of existing and emerging therapies. A number of population based resources that allow selective recall of subjects have been established across the country

as an initiative within NIHR Biomedical Research Centres (BRCs), and are already answering questions related to genotype-phenotype interactions and therapeutic responses. Airwave TB hopes to add onto this rich resource.

The TB is licensed by the Human Tissue Authority (HTA) and the collection and storage of bio samples has been ethically approved by NRES. The Airwave Study has Research Tissue Bank status with generic approval status for projects receiving material or data within the college. All external researchers will need to have project specific ethics approval before they can apply for data or samples from Airwave TB.

Information for patient and public

Donation of samples to the tissue bank (TB) is a gift and we are very grateful to everyone who consents to donate. Consenting to donate, or refusing to donate samples to the TB does not affect routine care in any way and all donor personal details remain confidential. Samples and their associated data will only be used for ethically and scientifically approved research. Everybody who has given consent for long term storage of samples since the start of the study is a part of the tissue bank.

When researchers are issued with samples for projects, the samples are assigned a unique TB number so no-one can be identified by their samples. Only relevant clinical information is released to researchers with all participant identifiers removed. The aim of this tissue bank is to maximise patient benefit by research. This TB will be based within one of the most outstanding NHS and University partnerships in the country, who are leaders in scientific translation – taking research at the bench to the bedside. We rely on patients and healthy volunteers to donate samples and wish to involve them in the research process. We will seek opinions from patient groups and public representatives and are developing a public area of our website where members of the public can become actively involved by contributing to research questions and helping to improve information for patients.

There will also be updates on the website that will in future list links to scientific publications and project websites that involve the use of Airwave Study samples and data. Airwave study website (www.police-health.org.uk) will keep the volunteers updated on the progress of the TB. Periodically a newsletter will also be sent by email to the participants.

Sample information for researchers

Bio-samples are collected, documented, stored, and processed according to standard operating procedures. For each case, the TB aims to collect blood, urine, and saliva samples. A subset of the blood samples are analysed to give haematology and clinical chemistry results.

Data Information

Samples supplied to the researcher are pseudo-anonymised and the researcher can request clinical information, which includes gender, age at diagnosis, any medical conditions, and clinical measurements such as BP (Blood pressure), BMI (body mass index), Hb (haemoglobin), HDL (high density lipid). Clinical follow up and outcome data can be made available subject to separate approval by the HSCIC.

The TB has a detailed security policy designed to minimise the risk that individual participants can be identified from the data received by researchers. In the event that

it were possible to identify an individual through analysis, all researchers are bound by written undertaking that they will maintain the privacy of that individual.

As part of the process of issuing bio samples and clinical information, researchers are asked to supply raw data obtained by using TB samples back to the TB following publication or completion of the research project. This is so that the TB can help in the direction of future research projects and promote collaboration between groups.

TB Design: collection of sample and data

Sample size

We have interest from the existing cohort for a re-screen. We hope to re-screen at least 50% of the current cohort – or 20,000 people, funding permitting.

Identification and invitation:

All police forces in UK will be invited to take part in the follow up re-screen. Support of the Police Federation has also been garnered to increase uptake and improve participation across the country.

Invitation letters will be sent out on a region-by-region basis to the current cohort. This letter will be sent out to participants within reasonable commuting distance to the clinic location identified.

The interested participants in the cohort can then book an appointment either by text, phone or through an online booking system. Contact details will be provided on the invitation letter.

Inclusion Criteria: Anyone who is already a part of the Airwave cohort and has previously had a health screening will be eligible to participate.

Exclusion criteria: People who have only filled in the questionnaire and not had a health screen will not be allowed to take part.

Follow up Assessment

Participants who attend a follow up clinic will be screened and a feedback will be provided to them on their blood and ECG results.

All clinical measurements and venepuncture is carried out by trained health care professionals with appropriate duty of confidentiality.

The physical measurements included in the Airwave Study protocol were selected based on their relevance, reliability, and resources (time and money) available. With respect to relevance, the inclusion of a measure at baseline was dependent on other epidemiological studies having indicated that it was significantly associated with health outcomes. For reliability, methods were chosen within a quality assurance framework that involved calibration, maintenance, ease of use, training, monitoring and data transfer to IT systems.

The follow up screenings will build on the existing data that has been collected with a few more additions.

Physical Measurements:

Blood Pressure: Blood pressure (and pulse rate) will be measured using the Omron 705-IT blood pressure monitor. After correctly applying the blood pressure cuff, staff need only press a button on the monitor before waiting for the cuff to automatically inflate then deflate. Following this, the health care professional will need to enter the values; systolic and diastolic blood pressure (and pulse rate) readings to an electronic form specifically designed for their computer. 3 consecutive BP readings will be recorded at an interval of 30 sec. The blood pressure measurement process is quick (taking two to three minutes in total) and simple.

Weight and Bio-impedance: Marsden digital weighing scales are used to measure the weight. This is done twice.

Bio-impedance is measured using the Tanita BC-418 MA body composition analyser. Staff will ask participants to remove shoes and heavy outer clothing and then step onto the footpads of the body composition analyser. The staff member then presses a button to start the analysis, during which weight (and several other variables) is measured. The health care professional again enters the values on the electronic form. This whole process takes around 3 minutes. People contraindicated for using Tanita includes people with metal implants, pacemakers, joint replacements, and pregnant females.

Standing and sitting height: is measured using a SECA Leicester Stadiometer.

Both measurements are shoeless. A stool of fixed height is used for measuring the sitting height. The values are entered by the health care professional onto the form on the computer. The process takes about 3 minutes.

Waist and Hip circumference: is measured using a Wessex tape.

Waist circumference at the level of the umbilicus will be measured using a Wessex non-stretchable sprung tape measure. Hip circumference is point yielding maximum circumference below the waist. Staff will manually enter the readings into the computer, which will automatically warn staff of impossible or implausible values.

Electrocardiogram (ECG): Atria 6100 is used to take ECG recordings. A 12-lead ECG would allow the detection of asymptomatic ECG abnormalities, such as silent myocardial infarction, left ventricular hypertrophy, left axis deviation and ventricular ectopic beats.

The ECG Core Lab in Glasgow (University of Glasgow) will manage, review and Minnesota Code 12 lead/25 mm/s ECGs for all participants. Staff members are responsible for sending to the ECG Core Lab, by telephone transmission, good quality ECG recordings with correct patient demographic data. Each ECG received at the ECG core lab will be reviewed and assessed by Professor Peter Macfarlane (ECG Core Lab Director), or in his absence, when an immediate report is required, a Consultant Cardiologist, and the 'Confirmed' copies sent to the main study centre at Imperial College London on a monthly basis. Professor

Macfarlane also reviews the Minnesota Codes assigned to each ECG by the Glasgow computer system and edits them if required.

Pulse Wave Analysis (PWA) This is measured using Vicorder. The Vicorder provides non-invasive measurement of peripheral and central blood pressures in combination with haemodynamic parameters and arterial stiffness. The cuffs will be applied over the brachial and femoral artery. Arterial pulse waveforms are recorded using PVR (pulse volume recording) measurements from a standard vascular cuff. The waveforms can be acquired in up to two sites simultaneously to provide pulse transit time (TT) and pulse wave velocity (PWV) measurements for the assessment of arterial stiffness.

Spirometry: **Vitalograph alpha touch 6000 will be used to measure lung function. Staff will be trained to demonstrate use of the equipment to participants, in order to increase the likelihood that two technically acceptable measurements are obtained. We will take 3 measurements of lung functions within a maximum of 6 minutes. Electronic data capture of the flow curves will provide feedback to staff about the quality of measurement.**

Grip Strength **will be measured using Jamar J 00105 hydraulic hand dynamometer. Total muscle strength declines with increasing age and it has been hypothesized to be a predictor of morbidity, loss of function and mortality in later life. Grip strength is the simplest method of assessment of muscle function in clinical practice.**

Follow up questionnaire

Collection of lifestyle and other potentially health-related information through self-completed questionnaires and interview complements the physical measurements and biological samples collected at the baseline assessment visit for Airwave Study. Baseline medical history can also be used to select populations of interest within the cohort to follow with respect to molecular and genetic predictors of disease progression and prognosis. Following completion of the consent procedures, the touch-screen self-administered questionnaire is used to collect the majority of information. This questionnaire typically takes participants 30-40 minutes to complete. Because it is self-administered, it ensures confidentiality and privacy to participants' response to potentially sensitive questions.

The questionnaire can be categorised into the following broad areas of interest: socio-demographics and occupation; lifestyle exposures (including smoking, alcohol, physical activity and diet); psychological state; cognitive function; family history of illness; and medical history and general health.

All the questions selected are from validated questionnaires and have been previously used in large population studies.

Sample collection and processing:

Blood Samples:

The aim is to collect samples that would allow the widest possible range of assays that could plausibly be envisaged for future studies. **About 40 ml (8 teaspoons) of blood is collected during the follow-upassessment visit.** The "vacutainer" system is used to collect these blood and urine samples. During venepuncture, the hypodermic needle is connected to these vacutainer tubes. These tubes contain the required additives. They are held under a slight vacuum, which draws sufficient blood to fill them. Each tube has a unique barcode, which is the participant's identifier number. The blood has to be collected in a defined order to avoid cross contamination b/w anticoagulants. The blood samples are non-fasting.

Fractions and aliquots of blood and urine samples

Blood sample	***Quantity***	***Purpose***	***Aliquots***
SST	*3 X5ml*	*Biochemistry*	*5 serums*
EDTA	*1X 9ml*	*Haematology and HbA1C*	*2 plasma + 2RBC+1buffy coat*
PST (Li Hep)	*1X 4ml*	*Plasma*	*1 Plasma*
ACD	*1X6ml*	*DMSO blood*	*2 vials of whole blood*
Tempus RNA tube	*4ml*	*RNA*	*2 vials*
Urine	*1x12ml*	*Storage for future*	*5 vials*

Blood samples are collected in the order as shown above to avoid contamination.

- ***SST:*** **The 3 tubes stand for 40 minutes before spinning at 4300 RPM for 10 minutes on a centrifuge at the clinic.**
- ***PST:*** **to be spun for 12 minutes at 3000 RPM at the clinic.**
- ***RNA Tempus:*** **the health care professional will be required to shake the tube vigorously for 15 seconds so that the whole blood mixes well with RNA stabilising agent and stabilizes the RNA and transcript profile for future use.**
- **The blood will be sent in an overnight courier at 4 - 8 ^{0}C temperature to Charing Cross Hospital laboratory where it is aliquoted, analysed, and stored temporarily in -80^{0}C freezers before onward transport to long-term storage.**

Urine sample: **A mid-stream urine sample is collected in a sterile urine pot and stored for future use as described above.**

Analysis:

***SST*: sample is used for measuring serum blood chemistry. Biochemistry profile includes cholesterol, HS C-reactive protein, HDL, GGT, HbA1c, Apo-lipoprotein A1, Apo-lipoprotein b, Creatinine, triglycerides.**

***EDTA*: is to be used for haematology analysis and HbA1c. Haematology profile includes RBC, WBC, Haemoglobin, Haematocrit (HCT), Mean cell volume (MCV), Mean cell haemoglobin (MCH), Mean cell haemoglobin concentration (MCHC), platelets and DLC.**

***ACD:* These aliquots can be used subsequently for immortalization of peripheral lymphocytes with Epstein Barr virus in order to produce replenishable supplies of high molecular weight genomic DNA representative of all genomic regions, as well as mRNA transcripts**

***Tempus RNA:* These aliquots can be used to measure gene expression profile of important gene targets. Gene expression measurement is becoming an increasingly important tool in research.**

***Urine:* These aliquots can be used subsequently for assay of the urine proteome and metabolome and potentially, for characterization of the gut microbiome.**

Long-Term Follow Up

Permission is obtained at screening from all participants to access their past and future medical and other health-related records. These health records are used to supplement information recorded at enrolment about previous medical history, family history, investigations (e.g. radiology reports, blood tests) and exposures (e.g. medication, occupational health). Most importantly, access to such records is needed to provide follow-up information related to cancers, cause-specific mortality and other health events.

The most reliable single identifier is the NHS number. The NHS tracing service can use the NHS number, or name, address, sex and date of birth, to obtain updated GP details and address when people move. Identifiers (such as name, date of birth, address, and general practice) will also be obtained during enrolment, to allow linkage to other types of health-related information. Further information will also be sought during enrolment (including mobile telephone numbers and e-mail addresses) which will help us to re-contact the person for future research. These different identifiers help to ensure that participants are not lost during follow-up.

Any re-contact with donors for future research activity will be by the AHMS TB staff only. No personal or contact information will be released to the future researchers.

If they do not consent to long-term follow up from medical records they cannot be part of the study or the tissue bank as it would be difficult to contact them in the long term.

Death and Cancer registries

We will "flag" participants through Medical Research Information Service (MRIS) in order to be notified regularly of cancers and the certified causes of all deaths, as well as the loss of follow-up due to emigration.

Hospital Records

The Airwave Study data repository needs to include information about health events and activities that are experienced by participants when they attend hospitals. HES are the national statistical data warehouse for England of the care provided by NHS hospitals and for NHS hospital patients treated elsewhere. For each episode of care, HES includes information about:

- Patient identifiers (including NHS number);
- In-patient, day case and out-patient episodes, maternity records and psychiatric census;
- Administrative details (e.g. admission and discharge date) and the organisation providing the treatment;
- Clinical information relating to diagnoses (ICD10 codes) and procedures
- OPCS4 codes: Classification of Interventions and Procedures (OPCS-4) is a procedural classification for the coding of operations, procedures and interventions performed during in-patient stays, day case surgery and some out-patient attendances in the National Health Service (NHS).

In all cases, the provision of these data to Airwave Study should be acceptable since all participants have given signed consent at enrolment for extraction of their individual hospital records and other health-related information.

Data handling and security

The Airwave Study is committed to protecting the confidentiality of data and samples. Systems are established for the secure data flow and storage of data in order to protect confidentiality. Data and samples are anonymised. The purpose and intent of these security measures are explained to participants during the consent process.

A robust data security model has been designed to protect sensitive personal and medical data from the potential risk of unauthorised access. The information held in the database will be sensitive in nature and therefore requires protection from unauthorised access or distribution. All information input, viewed or extracted will be protected so that only users with the correct authority and access can create, view, amend or delete information. Access to the system will be governed by authentication and authorisation privileges that check:

- Access is by an authorised person.

- The user accessing the system is who they say they are. This is controlled by a username and complex password;

- The user accessing the system is authorised to do what they are attempting to do. That includes searching, updating, deleting and uploading information at the appropriate authorised level for the database(s) or table(s).

In summary, the security architecture provides the maximum protection available through implementing best practice network, hardware, software and data security measures.

All information will be stored within Imperial College's secure environment. This is a fully managed infrastructure and secure environment providing high availability, resilience and business continuity through multiple servers, back-ups and disaster recovery measures.

Data Processing

Once the data collection process is complete, data for groups of participants is transferred securely to the Imperial's secure network, where the disparate datasets collected on each individual will be linked. This will also be the long-term store for the data, and will serve as the resource for future researchers. External researchers will have access only to pseudo-anonymised information on participants. Only a restricted number of people employed by Imperial College will have access to the personally identifiable data.

Information on bio samples will be held on the College's internal network and is maintained by the laboratory technicians. This will also be logged onto the ICHTB online database *https://cisbic.bioinformatics.ic.ac.uk/tissue_bank/* for purposes of audits and HTA licence regulations. This TB is registered as a sub collection under the HTA licence held by Imperial College Healthcare Tissue Bank (ICHTB).

Maintaining Confidentiality

The Airwave Study TB is committed to maintaining confidentiality of personal data and samples collected from the population. This research project is registered for data protection and the requirements of the Act apply in full. All personal information collected will be used solely for medical research purposes and will be stored and disposed of in a secure manner.

Anonymisation

During enrolment, the clinic will need to hold identifying information (such as name, address, birth date, sex) together with information collected from the participant during the visit. This information will be encrypted for security. All identifying information will be separated from participants' data and samples where possible. It will be linked using a code that has no external meaning (not the NHS number, for example). All identifying information will be held centrally by Imperial College in a restricted access database. Only a few named people within Imperial College will have access to the "key" to the code for relinking the participants' identifying information with their data and samples (i.e. "reversible anonymisation"). It is necessary to retain this link with identifying information to: allow follow-up of participants' health; to verify correctness and completeness of data against original records; to establish correct linkages among databases; recall participants for stage two; and, to find specific data or samples if participants withdraw.

Re-identification

All Airwave Study staff will be required to sign confidentiality agreements as part of their contracts. Researchers will not be able to identify individual participants from the anonymised data or samples that are provided to them.

Ethical issues

Consent

Consent is obtained from all participants to take part in the Airwave Study. Participation is offered as an opportunity to get an inclusive health screening along with getting a feedback. Because it is not possible to anticipate all future research uses from the samples and data collected, generic consent is being sought for future research in general, subject to approval by relevant ethics board.

By consenting, an individual becomes a participant. An informed consent is obtained by the research health care professional at the clinic. They are then given a copy of the consent form to sign which is countersigned by the health care professional obtaining consent. This allows the clinic visit to proceed in compliance with the approved Airwave protocol.

The participant will already have been provided with an information leaflet prior to his/her visit, explaining about the follow-up study and what to expect in the clinic. They will be encouraged to ask any questions and get satisfactory answers before signing the consent

Studies within the organisation (Imperial College) and Airwave study group have generic ethical approval as part of this tissue bank. Any studies submitted outside of this will have to apply for NRES approval before submission to the tissue bank for access to sample or data.

The consent to participate in Airwave Study will apply throughout the lifetime of TB unless the participant withdraws. Further consent will be sought for any proposed activities that do not fall within the existing consent.

Reporting of results

A feedback letter is generated after a person attends a health screen and results are sent to the participant only.. The feedback includes the measurements carried out in the initial visit and blood test report. By reporting standard ranges, the participant is provided with sufficient information to give meaning to the measurements taken, so that they may act on the results if necessary and arrange to see their general practitioner or other relevant health professional.

The legal duty of care for staff conducting enrolment is determined by the research context, and will apply mainly to safe and competent collection of questionnaire data, baseline measurements, and blood or other samples. They will not have the same duty of care that they would have in a clinical setting. However, even in this research context, there may be occasions when staff consider there to be a professional or ethical obligation to draw attention to abnormal measurements (such as elevated blood pressure) or incidental findings

(such as possible melanoma). In such circumstances, participants will be encouraged to contact a relevant health professional.

The ECG Core Lab in Glasgow (University of Glasgow) manages and reviews Minnesota Code 12 lead/25 mm/s ECGs for all participants enrolled into the study. Each ECG received at the ECG core lab is reviewed and assessed by Professor Peter Macfarlane (ECG Core Lab Director) or in his absence, when an immediate report is required, a Consultant Cardiologist, and the 'Confirmed' copies sent to the main study centre at Imperial College London on a monthly basis. If the cardiologist while assessing the ECG feels that a person needs to see a specialist urgently, he informs the Imperial team about it; who will than liaise with the participant and give him a copy of his ECG to take to his GP.

The feedback generally takes up to 8 weeks to be sent back to the participant.

Stage 2 Activity

If any findings are made of clinical significance to the individual during future research, (as yet undefined), the patient would not be notified directly, but his/her GP or clinical care team may be made aware of the finding. It would be their judgement whether the finding is relevant to the patient's care and if necessary they may invite the patient for a further sample that will be tested in an accredited NHS laboratory and/or refer to a specialist.

If a donor does not have a GP, we would explain why it is necessary to register with a GP in the light of information that has become available to us. Ethically the tissue bank team will not be qualified to provide any treatment, counselling or support and so we will explain to patient about the importance of seeking professional help. Research staff will be trained on how to communicate with patients on sensitive information.

The clinical team/GP in charge of the donor's day-to-day care would than undertake any necessary support related to this information.

Re-contact with participant

It will be explained to participants that they may be re-contacted by Airwave Study for various reasons, including:

- To collect new information (such as questionnaire data, measures or samples) for the resource.
- To seek consent to propose new uses for the samples and data that have passed scientific and ethics review but does not fall within the existing consent.
- To ask participants whether they would be willing for researchers to contact them to discuss possible involvement in a study that requires new information or samples.

It will be emphasised that agreeing to re-contact is voluntary and they will still be part of Airwave Study even if they decline to be re-contacted in future.

No personal contact details will be shared with any third party researchers and so any re-contact will always be by Airwave Study TB staff.

Right to Withdraw

Participants have been advised at enrolment that they have the right to withdraw from Airwave Study at any time without giving any reasons. This is essential to preserve and demonstrate the voluntary nature of participation. During enrolment, we provide information to participants about the options for withdrawal:

- *"No further contact":* Airwave Study would no longer contact the participant directly, but would still have their permission to use information and samples provided previously and to obtain further information from their health records.

- *"No further access":* Airwave Study would no longer contact the participant or obtain further information from their health records in the future, but would still have their permission to use the information and samples provided previously.

- *"No further use":* In addition to no longer contacting the participant or obtaining further information about them, any information or samples collected previously would no longer be available to researchers. Airwave Study would destroy their samples (although it may not be possible to trace and destroy all distributed anonymised sample remnants) and would only hold their information for archival audit purposes. The participant's signed consent and withdrawal would be kept as a record of their wishes. Such a withdrawal would prevent information about them from contributing to further analyses, but it would not be possible to remove their data from analyses that had already been done.

If, having discussed their concerns and options, a participant decides to withdraw then Airwave Study would seek written confirmation of the level of withdrawal from the participant. We will need to retain some minimal personal data for a number of reasons, which include ensuring that participants who have withdrawn are not re-contacted.

Expectation of financial gain

Participants will not be offered any material financial or other inducement to contribute to Airwave Study, irrespective of whether the use of data or samples might ultimately lead to profit. Imperial College may work in partnership with the private sector (e.g. the pharmaceutical or biotech industry) to develop any invention for the benefit of patients. Part of the profits earned from inventions may come back to Imperial College.

Access and stewardship of samples and data

This tissue bank will provide a national cohort of healthy volunteers who wish to participate in clinical research, and are willing to provide clinical information and samples that enable recall to future studies by genotype (internally coded, inheritable information carried by living organisms) and phenotype (outward, physical manifestation of an organism).

This tissue bank is registered as a sub collection under the HTA (Human Tissue Act) licence held by Imperial College Healthcare Tissue Bank (ICHTB). The Airwave Study access policy applies equally to academics, private or public sector researchers whether they work in, or with, a profit or not for profit organisation subject to them having relevant ethics approval. Studies within the organisation and study group have generic consent as part of the tissue

bank. Any studies submitted outside of this will have to apply for NRES approval before submission to the tissue bank for sample or data.

Access to human biomaterials is by formal application to the Airwave Study access committee. They will than pass on the application after initial approval to ICHTB Tissue Management Committee (TMC), a sub-committee of the Trust's Research Governance Committee. The researcher must satisfy the TMC that their research is ethically and scientifically valid and that it makes a contribution to scientific knowledge. The standard template of ICHTB application form for access to samples will be used. Once the TMC is convinced about the scientific validity of the research it will instruct the Airwave Study TB to identify the samples/data for release.

Once approved by NRES, this TB will be open to access by researchers. Any researcher wishing to utilise the Airwave Study resource will complete an application form and summarise the nature of the experiment they propose. This tissue bank will work in accordance with all relevant legislation and comply with the highest standards of ethics and quality control. It has national ethical approval for its research projects and deals with all ethical and legal requirements including full informed consent of every patient donating bio samples, to allow research project to commence swiftly, secure in the knowledge that all appropriate consents and approvals are in place. It complies with the Human Tissue Act and has ethical approval for its research via NRES.

Informed consent will be always be taken prior to collecting blood or data using the approved stage 2 research study consent form and information sheet. The consent will be kept with volunteers' records by the Airwave team with an anonymised proof of consent form being passed on to the researcher for their records to show evidence that consent has been obtained for each sample they receive.

Airwave Study Tissue Bank research governance structure

Airwave Study is registered as sub collection under the HTA licence held by Imperial College Healthcare Tissue Bank (ICHTB). The Designated Individual for the HTA Licence is Professor Gerry Thomas. The clinical teams that collect material for sub-collections are responsible for obtaining consent from their donors, and this is also subject to regular rolling audit by the tissue bank manager. Annual reports are provided to the Quality and Safety Committee of Imperial College Healthcare NHS Trust and include information on consent issues.

A two-tiered approach will be in place to protect the interests of the participants when giving out the samples and data to other researchers:

- Airwave study has an 'Access Committee' consisting of PI, study coordinator, an epidemiologist and a representative of the Police Federation (layman), who will initially review applications from research groups to provide samples and data; A Memorandum of Understanding (MoU) to this effect has been signed by the study PI prof Paul Elliott and ICHTB (Imperial College Healthcare Tissue Bank) designated individual Prof Gerry Thomas.

- A full research proposal will be requested, in which the researcher may be asked to provide proof of peer review and confirmation that the research is scientifically and ethically sound.

Once satisfied that the application meets the terms of consent of donor and scientific critique, it will be passed on to the ICHTB management committee for approval.

The ICHTB Tissue management Committee (TMC) will then further assess the scientific merit of the project and make suitable recommendations for release of sample and data. All material will be provided to the researcher in an anonymised form.

Researchers are asked to provide their results back to the tissue bank using the unique participant identifier, which then permits linkage to results from other projects using samples from the same donor.

All researchers will also sign a Material and Data Transfer Agreement. This stipulates that, following completion of their project, any material that has not been used should be returned to the bank.

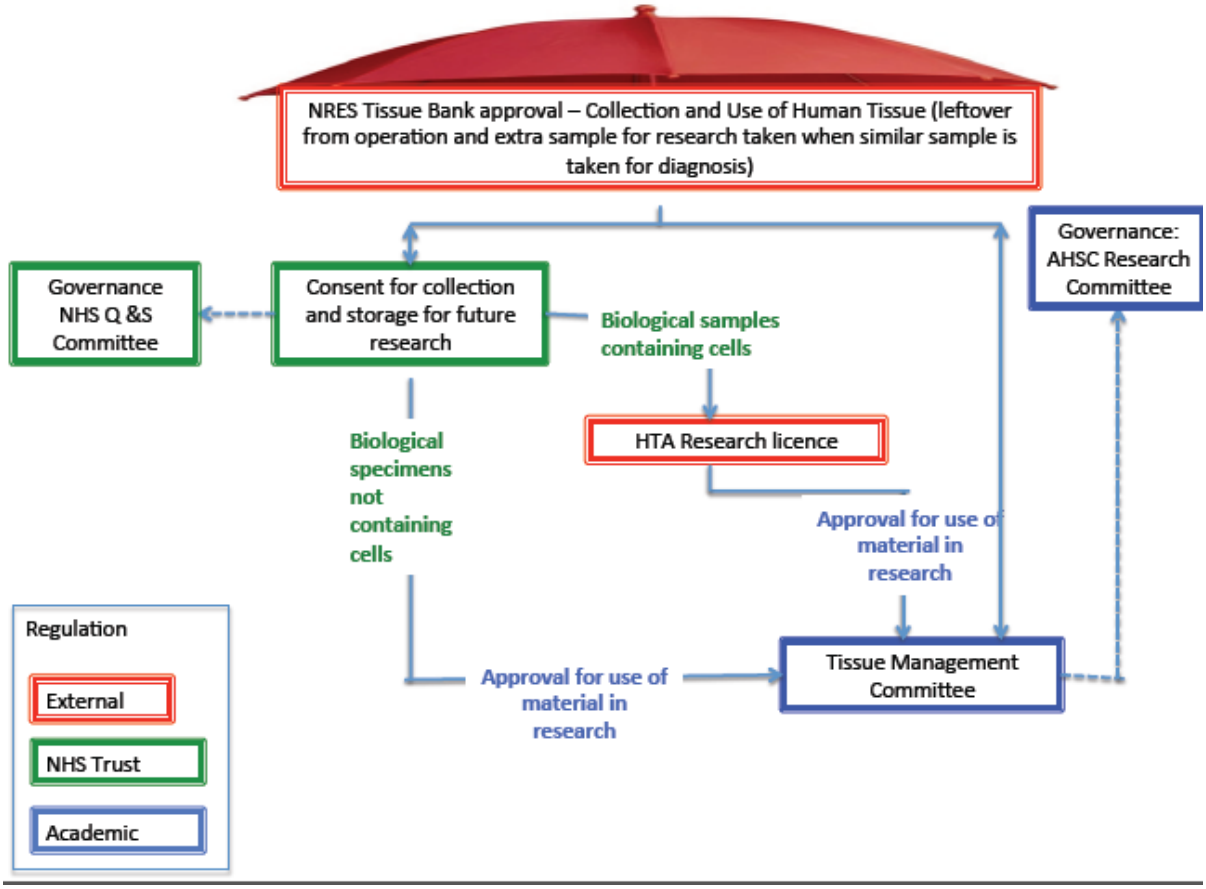
Returned tissue is not reissued to researchers as the tissue bank cannot guarantee the condition of this material.

The Tissue Management Committee (TMC) will oversee issues concerning the use of material/data released from it. The TMC meets quarterly. Terms of Reference for, and membership of, the Committee are set out in Annex separately. Annual reports on accrual and release of samples, and publications using ICHTB material, are provided to the Academic Health Science Centre (AHSC) Research Committee. This Committee is a joint committee that oversees all research carried out in the Academic Health Science Centre which is a fusion of the clinical research section of the NHS Trust and the clinical research section of Imperial College London. A representative of the Joint Research Office of the AHSC sits on the Tissue Management Committee.

The Airwave Study is managed day to day by the clinical Co-ordinator, who report to PI, Professor Paul Elliott. He in turn reports to Research Committee of the Directorate of Public Health and Primary Care and this report into the College's Joint Research Office (JRO).

The samples collected will be temporarily stored at Charing Cross hospital, which is part of Imperial College Healthcare Trust. In the long term, samples will be removed to the College's biorepository at Hammersmith, or an HTA-approved outsourced provider. A tender for the outsourced provider is ongoing.

Figure 4 : Governance structure for ICHTB



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