Health Research Authority

FULL/LONG TITLE OF THE TRIAL

Feasibility of Virtual Safe Drug Consumption Technology, Using Respiratory Monitoring to Reduce Drug Harm

SHORT STUDY TITLE/ACRONYM

RESCU-2

PROTOCOL VERSION NUMBER AND DATE:

RESCU-2 Protocol V2 03122024

- **This protocol has regard for the HRA guidance and order of content**

RESEARCH REFERENCE NUMBERS

STUDY REGISTRY NUMBER AND DATE: TBC – STUDY WILL BE REGISTERED ON ISRCTN

SPONSOR: University of Dundee

SPONSOR REFERENCE NUMBER: 2-056-24

REC NUMBER: 24/107

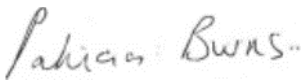
SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

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

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

For and on behalf of the Study Sponsor:

Signature: 

Date: .20 Dec 2024

.....

Name (please print):

Patricia Burns

Position: Senior Research Governance Manager

Chief Investigator:

Signature: 

Date: 19/12/2024

.....

Name: (please print): Prof John Dillon

.....

KEY STUDY CONTACTS

Insert full details of the key trial contacts including the following

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Collaborator	Prof Sir John Strang Head of National Addiction Centre Kings College London john.strang@kcl.ac.uk
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Sponsor	Patricia Burns Research Governance Manager University of Dundee Tayside Medical Science Centre tascgovernance@dundee.ac.uk 01382 383297
Funder(s)	Scottish Health and Industry Partnership Group (SHIP) Scottish Government Office of Life Sciences
Clinical Trials Unit	Tayside Clinical Trials Unit tctu@dundee.ac.uk

Key Protocol Contributors	Full contact details including phone, email and fax numbers (If applicable) For example: imaging lead, pathology lead. Catriona Cowan Clinical Research Manager, PneumoWave Catriona.cowan@pneumowave.com Dr Andrew Radley Directorate of Public Health, NHS Tayside Andrew.Radley@nhs.scot Dr Osian Meredith Chief Scientific Officer, PneumoWave osian@pneumowave.com Dr Basak Tas Research Fellow, King's College London Basak.tas@kcl.ac.uk Dr Elizabeth Appiah-Kusi Clinical Research Fellow, King's College London Elizabeth.appiah-kusi@kcl.ac.uk Dr Will Lawn Lecturer, King's College London Will.lawn@kcl.ac.uk
Committees	Trial Management Group

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ii. LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the study. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.

AE	Adverse Event
AR	Adverse Reaction
AIR	Assessment of Injecting Risk
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CTA	Clinical Trial Authorisation
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
DSUR	Development Safety Update Report
ECG	Electrocardiogram
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.
IMP	Investigational Medicinal Product
IP	Intellectual Property
ISF	Investigator Site File (This forms part of the TMF)
ISRCTN	International Standard Randomised Controlled Trials Number
KCL	King's College London
MA	Marketing Authorisation
MHRA	Medicines and Healthcare products Regulatory Agency
NHS R&D	National Health Service Research & Development
NIMP	Non-Investigational Medicinal Product
PI	Principal Investigator
PIS	Participant Information Sheet
PW	PneumoWave
PM	Project Manager
QA	Quality Assurance

QC	Quality Control
QP	Qualified Person
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SHIP	Scottish Health and Industry Partnership Group
SIRD	Substance Induced Respiratory Depression
SOP	Standard Operating Procedure
SmPC	Summary of Product Characteristics
SSI	Site Specific Information
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee
UKCA	United Kingdom Conformity Assessed

iii. STUDY SUMMARY

Study Title	Feasibility of Virtual Safe Drug Consumption Technology, Using Respiratory Monitoring to Reduce Drug Harm	
Internal ref. no. (or short title)	RESCU-2	
Clinical Phase	Phase II	
Study Design	Observational	
Study Participants	People who use drugs living in supported accommodation	
Planned Sample Size	Around 50 participants to use the Pneumowave DC Mobile System Up to 20 participants to take part in semi-structured interviews Up to 20 participants to take part in focus group(s) Up to 20 site staff to take part in focus group(s)	
Observation duration	Minimum of one night, up to 4 weeks, with a continuous option to extend for a further 4 weeks.	
Follow up duration	N/A	
Planned Study Period	1 Year 6-8 months recruitment 4-6 months data analysis	
	Objectives	Outcome Measures
Primary	To capture chest motion data using the PneumoWave DC Mobile system.	Evidence of reduced chest movement collected by PW DC Mobile system.
Secondary	Potential causes for Substance Induced Respiratory Depression	Participant reported drug use; drug diary, Assessment of Injecting Risk (AIR) Tool. Participant reported existing respiratory condition; CRF
Secondary	User and staff experience and acceptability.	Participant reported outcomes; participant and staff questionnaires, satisfaction survey, interviews, focus groups;
Investigational Product(s)	PneumoWave DC Mobile System	
Route of Administration	Biosensor worn on the chest, attached by ECG electrode adhesive patch. Biosensor connected via Bluetooth to a	

	Mobile Device running an App. Mobile Device is required to be connected to the internet via wi-fi or mobile data.

iv. FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this trial)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
SHIP	**Financial Support**
Scottish Government Office of Life Sciences	**Financial Support**
PneumoWave	**Supply of devices and software support**

v. ROLE OF STUDY SPONSOR AND FUNDER

The roles and responsibilities of the Sponsor and Funder will be detailed in the Clinical Research Agreement.

vi. ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

The study will be coordinated by a Trial Management Group (TMG), consisting of the grant holders, including the CI, collaborators, statistician, trial manager and 3rd sector workers where appropriate. Details of membership of the TMG will be held in the Trial Master File (TMF). The TMG will meet regularly to ensure all practical details of the study are progressing well and working well and everyone within the study understands them. Minutes of the TMG meetings will be maintained in the TMF.
The functions of the Trial Steering Committee (TSC) will be undertaken by the TMG. No independent TSC or Data Monitoring Committee (DMC) will be convened for this study.
The CI will be responsible for the conduct of the study. Site delegate(s) will oversee the study and will be accountable to the CI. A study-specific Delegation Log will be prepared for the study sites, detailing the duties of each member of staff working on the study.

vii. Protocol contributors

TCTU Portfolio Trial Manager: Lewis Beer, initial draft

Chief Investigator, Prof John Dillon, review

Principal Investigator, Dr Andrew Radley, review

TCTU Senior trial manager: Dr Sarah Inglis, review

PneumoWave Clinical Research manager: Catriona Cowan, review

PneumoWave CSO: Dr Osian Meredith, review

King's College London Research Associate: Dr Alexandra Hayes, review

King's College London Research Fellow: Dr Basak Tas, review

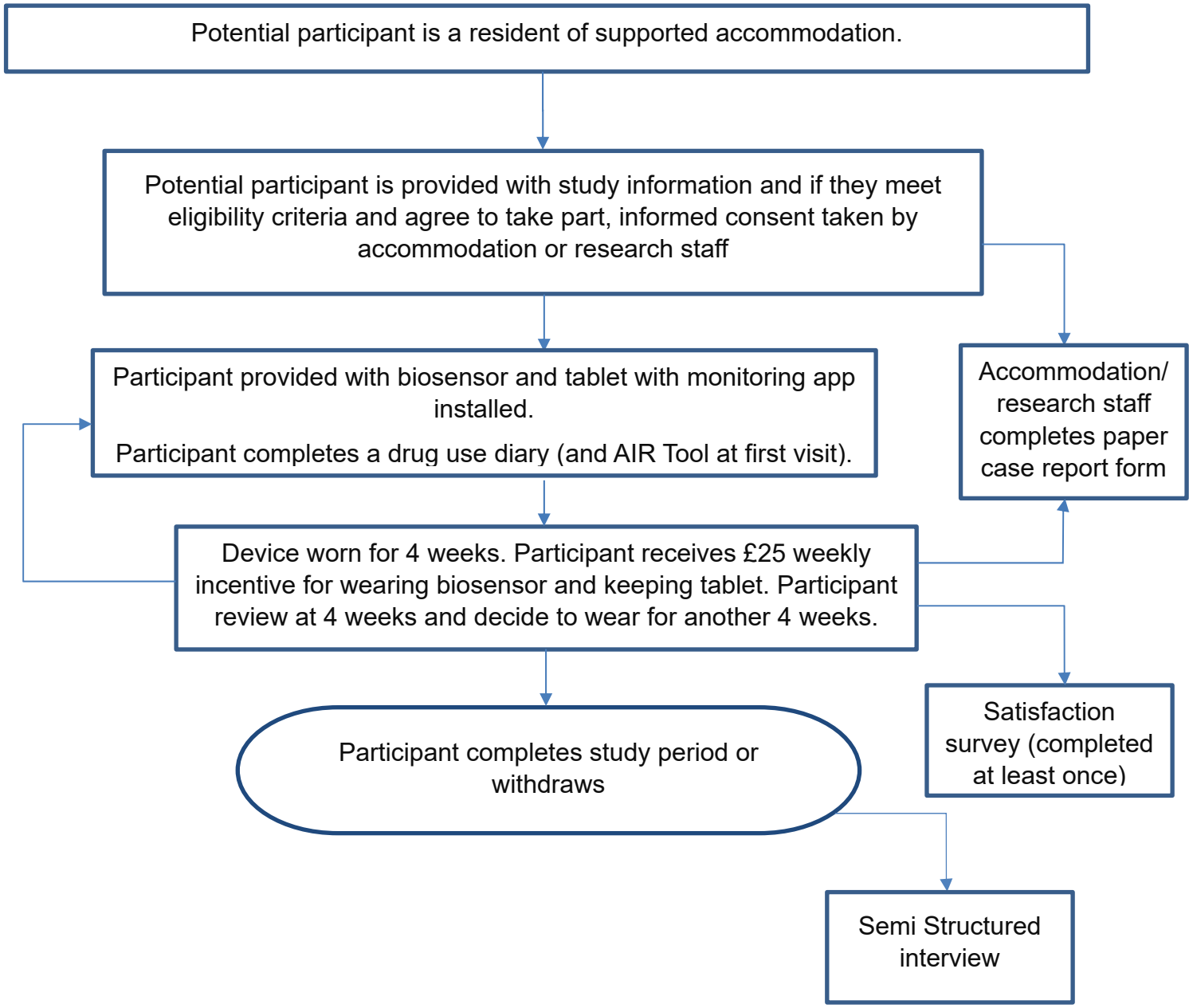
King's College London Clinical Research Fellow: Dr Elizabeth Appiah-Kusi, review

King's College London Lecturer: Dr Will Lawn, revie

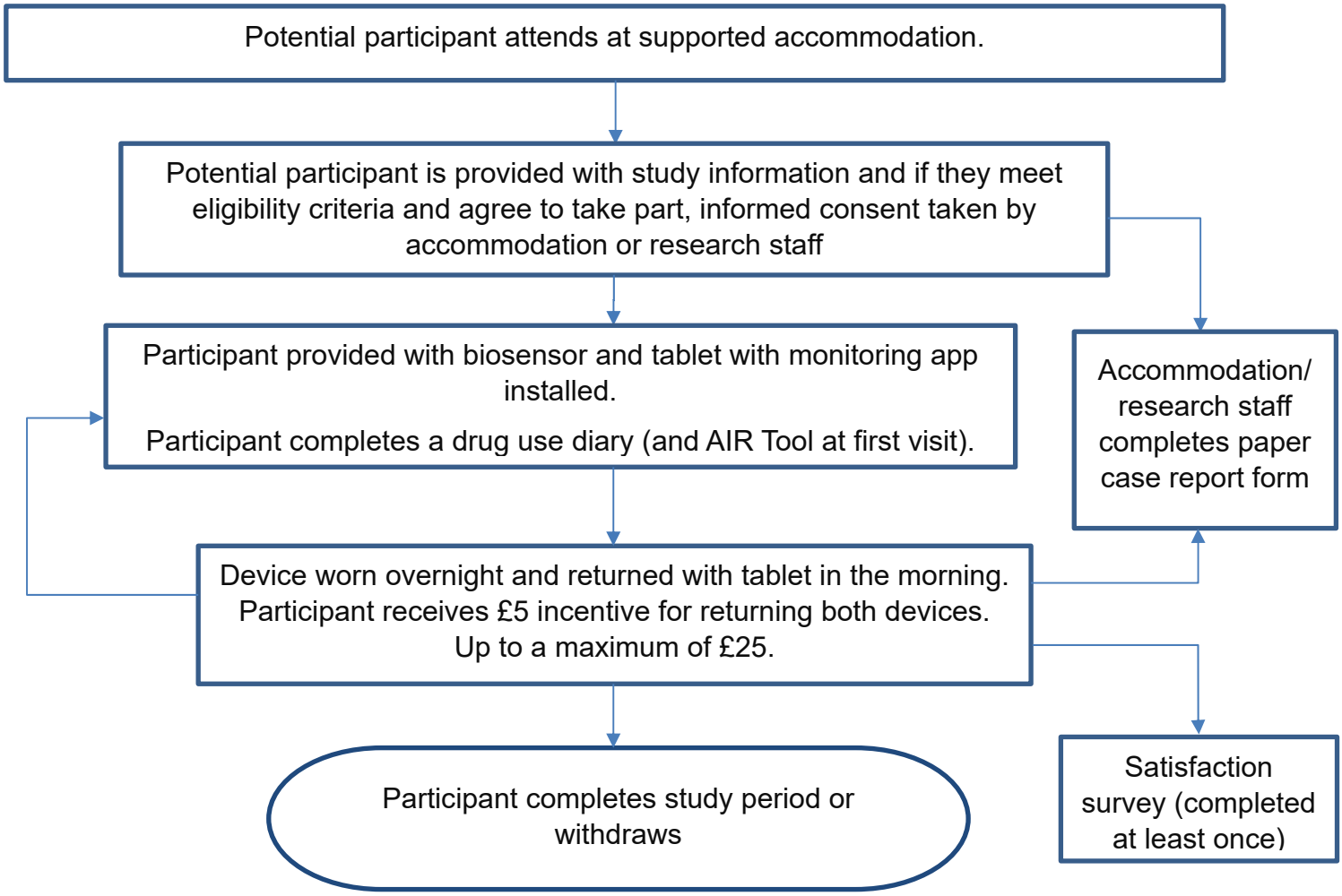
viii. Key Words

SIRD, overdose, biosensor, respiratory rhythm, reduced chest movement, monitoring session, algorithm,

ix. STUDY FLOW CHART – LONG TERM RESIDENTS – 4 WEEKS+



x. STUDY FLOW CHART – SHORT TERM RESIDENTS



1 BACKGROUND

Opioid overdose is now the largest cause of accidental death in most developed countries. In the UK and US last year there were more than 80,000 deaths (CDC.gov, 2021). The Opioid Crisis is a public health emergency with a catastrophic socioeconomic impact (Ciccarone, 2019). All existing measures have failed to stop deaths increasing year-on-year and technology that can successfully prevent deaths by linking accurate diagnosis with rapid naloxone administration presents a very large commercial opportunity, creating multiple highly-skilled jobs, and placing the UK at the forefront of addressing the Opioid Crisis. Death from overdose is caused by opioids blocking respiratory rhythm generating centres in the brain leading to slow, irregular breathing progressing to complete cessation of respiratory effort (Palkovic, 2020). While the effect is dose related, other factors make susceptibility to overdose unpredictable. In 2019, PneumoWave conducted an Innovate UK funded project evaluating multiple sensor technologies. Accelerometers were identified as the most appropriate sensor for the purpose of overdose detection due to the robust and accurate provision of continuous longitudinal data from which conscious level and a number of features of respiration can be derived. Added benefits of accelerometers include reliability, availability, low power usage, cost, and small size. A commercially ready version of the PneumoWave biosensor is currently being used in multiple clinical studies (*RESCU,* UK and *OD-SEEN,* Australia), with positive clinician and lived-experience patient feedback, giving a high degree of confidence in suitability of the chosen sensor and device methodology.

2 RATIONALE

Recently, technological developments in wireless ‘wearable’ devices have enabled real-world, real-time measurement of physiological functioning. Remote measurement of respiratory, cardiovascular, and motor function has the potential to detect opioid overdose automatically and reliably (Goldfine, 2020). However, currently available wearable devices have no ability to detect respiratory depression and have limited utility for use as regulated medical devices. Existing chest-worn vital sign sensors are not practical or economically viable for individual use in the community. In addition, little research into the efficacy of remote overdose detection has been conducted. A chest sensor that reliably detects the overdose breathing signature could alert the emergency services and save lives, when fully developed and used in the community. Qualitative study results indicate that this technology would be positively accepted by people who use drugs (PWUD) (Tas, 2023).

The PneumoWave DC Mobile chest biosensor is a small cylindrical device (40mm diameter 14mm height) that sticks onto the chest using a small plastic patch (an ECG sticker) and measures chest motion. PneumoWave are developing an Alert algorithm (that will be incorporated in the DC Mobile system) that will detect reduced chest movement linked to Substance Induced Respiratory Depression (SIRD). To gather device utility and wearability feedback, and refine the Alert analysis algorithm a study is required on patients at high risk of SIRD to capture chest motion during times when possible consumption events might be occurring, where absence or presence of overdose can be externally verified.

Over a six to eight month period, we aim to capture approximately 50 participants known to use opiate drugs, including opioid injection, wearing the device for multiple nights in supported accommodation centres in the UK. Participants will consent to wear the chest-worn device during their residence at the supported accommodation. Chest motion data will be collected on the device securely and pseudo-anonymously (i.e. study ID will be used; no personally identifiable information will be stored alongside chest motion data) and streamed to a secure cloud.

The data collected here will be used to test and further develop respiratory ‘signatures’ to accurately detect SIRD and differentiate from patterns that occur following substance use but do not result in an overdose. Wearing the device will not alter the services participants receive at the supported accommodation.

2.1 Assessment and management of risk

There is zero to minimal risk to participants from the biosensor itself. It may be mildly uncomfortable to wear initially but participants should soon become used to it. Several Clinical Research projects have been conducted with the technology (eg. *RESCU: RESpiratory monitoring reduCing drUg harm,* IRAS 301153*)* with over 150 participants and 15,000 hours of wear. No adverse events related to the biosensor have been reported.

There is no risk of personal data being revealed via the DC Mobile software. All chest movement data is anonymous.

Participants are people who actively use drugs and may be at risk of accidental overdose. Supported accommodation sites involved in the study have trained staff to administer naloxone, to reverse the effects of an opioid overdose or to administer first aid. Participants will be informed that the device will not issue an alert in the event of a potential overdose. Supported accommodation staff perform regular wellness checks on residents who show signs of drug use throughout the evening. Staff will continue to perform these checks on study participants, so there is no change to the risk of accidental overdose.

Sites provide advice and additional services to help residents stop using opiates and other drugs. Participants will not be disincentivised from using these services.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

To establish that the DC Mobile can be used in a supported accommodation environment to record and retrospectively detect changes in chest movement consistent with respiratory patterns of an accidental drug overdose.

3.1 Table of endpoints/outcomes

Objectives	**Outcome Measures**	**Timepoint(s) of evaluation of this outcome measure (if applicable)**
Primary Objective To capture chest motion data using the PneumoWave DC Mobile system	Evidence reduced chest movement using PW DC Mobile system.	End of study
Secondary Objectives Usability and functionality of the DC Mobile biosensor	Participant reported satisfaction survey, feasibility questionnaire, semi-structured interviews, focus group	Day 0 to end of study
Secondary Objectives Potential SIRD events linked to participant drug use behaviour or existing respiratory condition. Substance use and staff-measured outcomes (including overdose) by attendees of supported accommodation	AIR tool questionnaire, drug use diary, CRF	Day 0 to end of study

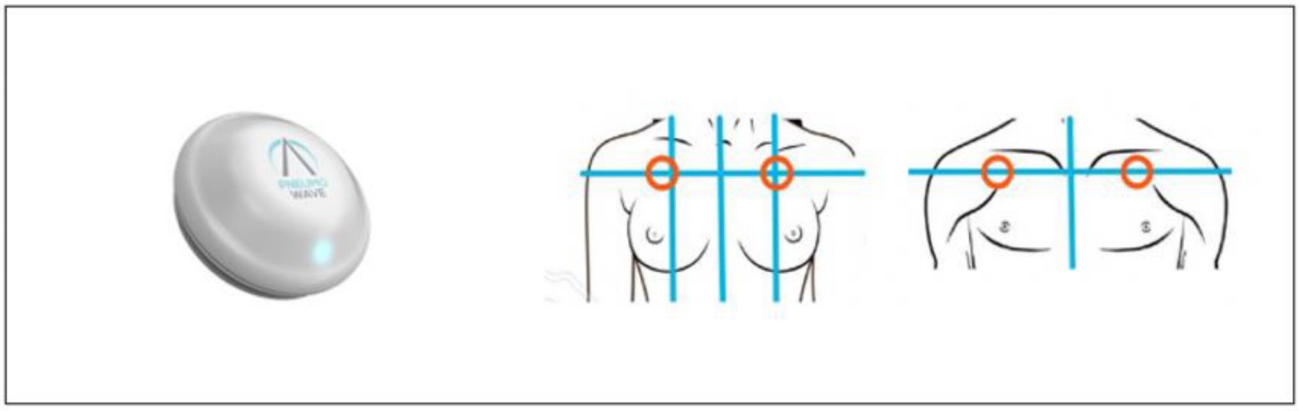
4 STUDY DESIGN

This is an observational study. It will not incorporate any randomisation or intervention. Participants' health care and the management of any potential SIRD event will not be altered by the procedures of the protocol.

People who use drugs often live in supported accommodation, either for short periods or over a period of years. Many may continue to use drugs while on these premises. To stay at these premises people must be registered as a resident. Short term residents must register before they take up accommodation. Potential participants will be opportunistically recruited by staff working in these premises who are trained to fully explain the study and take informed consent. Drug use is discussed with residents for their own safety. Accommodation staff engage regularly with this population and will be able to identify those who may be eligible. This lowers the risk of them approaching people who do not use drugs and potentially causing unintentional offence or stereotyping. Some supported accommodations will provide injecting equipment on request. This would identify a potentially eligible participant. Consented participants will be recorded on an enrolment log at each participating site. The enrolment log is for administration purposes only and will only be available to site personnel.

The study will utilise the PneumoWave DC Mobile biosensor and data collection platform which includes a wearable biosensor that attaches to the press-stud on a supplied and approved ECG electrode. The biosensor can be placed in a number of locations on the chest and diaphragm area, and automatically connects to a Data Hub via Bluetooth (Fig. 1). The position of the biosensor should be changed weekly. In this study the Hub will be a mobile computing platform (Application running on a tablet). The tablet will be held in a secure location, remaining in range of connection for the PneumoWave DC Mobile biosensor. The tablet has no functionality beyond running the monitoring app. Participants will be informed of this and the tablet's location in their residence. Please see further details in the Study Assessments section (section 7.4).

Figure 1:



Participants receive the device to wear and a tablet with the DC Mobile app downloaded to record data while they are in their accommodation. The wearable device battery will be changed 1-2 times per week.

Long term residents: monitored for 4 weeks or longer up to 8 months

Supported accommodation staff will check in weekly with participants to ensure the device is being worn, is working and the associated tablet is also present and in a working condition. Participants will receive £25 per week if these conditions are met (further detailed in Payment section). This will encourage participants to look after the device and tablet as only a limited number of each will be available at each site. Site staff will check in on participants overnight to check the device is being

worn and the app is running and note any potential drug use. Participants will be asked to wear the device for 4 weeks initially, with an option to extend the period, if agreed. This continues until the participant declines to be part of the study any longer or the study end point is reached, whichever is first.

Short term residents: monitored overnight

Participants will receive the biosensor and tablet to use overnight and return in the morning. They will receive £5 for returning both the biosensor and device in the morning. Up to a maximum of £25. If they remain a resident, they will recollect the biosensor and tablet for all nights that they are resident. This continues until the participant declines to be part of the study any longer or the study end point is reached, whichever is first. Site staff will be trained to ask for ongoing consent if there are three or more nights where the participant has not been resident at the supported accommodation, following initial informed consent. Site staff will check in on participants to check the device is being worn and the app is running and note any potential drug use.

Applicable to all residents/participants:

It is not expected that participants will always be at a participating site. When leaving the site, the biosensor should be left behind along with the tablet. The biosensor can continue to collect chest movement data while out of range of the tablet for 10-12 hours, once back in range, data will automatically be sent to the tablet. A light on the biosensor will flash red for the duration of time it is out of range.

During their stay at the supported accommodation, participants will be asked to complete a questionnaire on device feasibility and a satisfaction survey at least once on how they felt about wearing the device. Participants who remain at the site longer may complete the survey more than once to record fluctuating levels of acceptance. During study registration, participants will be asked to complete an AIR tool, which captures the participants' injecting habits over the previous 6 months. They will also be asked to complete a drug use diary. A sub-section of participants will be asked to take part in semi-structured interviews and/or focus groups to discuss wearing the device, ease of use and to help determine any other potential issues with the device or software.

Staff participants:

Staff participants will be asked to complete a study questionnaire at least once during the study to indicate their satisfaction with the PneumoWave DC Mobile biosensor. This may be completed more than once to capture changing opinion.

Some staff will be invited to take part in a semi-structured interview and/or focus group to discuss their experience with the PneumoWave DC Mobile biosensor.

5 STUDY SETTING

Supported accommodation managed by HumanKind, Thames Reach, St Mungo's and Hillcrest Futures in locations in the UK.

Supported accommodation consists of a small flat with sleeping area, bathroom, a kitchen and living space. These are designed to allow an individual privacy and to minimise disturbance at nights. There is limited communal space in these facilities, this will maintain the privacy of participants as it will not be immediately obvious to other residents of their participation.

6 PARTICIPANT ELIGIBILITY CRITERIA

6.1 Inclusion criteria

- Over 18 years of age
- Living in supported accommodation
- Participant reported current opiate drug use
- Willing to wear biosensor device while living in supported accommodation
- Able to provide informed consent (not intoxicated at time of consent)
- Able to converse in and understand English

6.2 Exclusion criteria

- Does not meet one or more of the inclusion criteria
- Skin sensitivity to ECG electrode patch
- Broken skin over chest area
- Implanted pacemaker device in-situ
- Not suitable for enrolment in opinion of site staff or investigators

7 STUDY PROCEDURES

7.1 Recruitment

Potential participants are provided with study information during their registration at the participating supported accommodation or approached by the site staff if they are already residents. If they meet the inclusion and exclusion criteria, then informed consent is taken and the participant provided with the DC Mobile system.

Potential participants' residency within the supported accommodation is not conditional of taking part in the study.

7.1.1 Participant identification

Potential participants will be identified by site staff based on their existing knowledge of the population and by those who make themselves known by requesting injecting equipment (where sites provide this).

7.1.2 Screening

No formal screening processes.

7.1.3 Payment

Long term resident participants will receive £25 per week dependent on evidence of wearing the biosensor and the tablet remaining in situ in their residence.

Short term participants will receive £5 for returning the biosensor and tablet the morning after use. Up to a maximum of £25.

Participants will receive £20 for taking part in semi-structured interview and £10 for participation in a focus group.

To avoid supported accommodation keeping physical money on-site, where possible participant payments will be made using the Cash Out system (https://tinyurl.com/mr9c75kn). This involves the supported accommodation staff sending a text message to the participant, stating the cash value to be received. This text message can be presented at any PayPoint location and the participant will receive the cash value. If a participant does not have a mobile telephone, arrangements will be made to provide the participant with the cash sum or a shopping voucher of the corresponding value.

7.2 Consent

Due to the transient nature of the target population and the likelihood that some potential participants will only reside in the supported accommodation for one evening, it is important that study information can be provided and informed consent taken at the same time. This will limit missing out on potential participants. Although any potential participants who would like more time to consider participation will be granted it. Potential participants will be given a participant information sheet by site staff at an appropriate time. Either during registration, a welfare check or if a participant requests injecting equipment. Where potential participants may have literacy difficulties, a member of site staff will support in these instances. All accommodation staff who will take consent will be trained on the process by TCTU trial management staff.

Consent is ongoing, should a participant return after being away from their accommodation for a period of at least three days, provided they have followed study procedures, they will be asked if they would like to continue in the study and receive the biosensor and tablet as normal.

The PI retains overall responsibility for the conduct of research. This includes the taking of informed consent of participants at the sites. They will ensure that any person delegated responsibility to

participate in the informed consent process is duly authorised, trained and competent to participate according to the ethically approved protocol, principles of GCP and Declaration of Helsinki.

Consent will be taken by supported accommodation staff who will be trained in this process to GCP standards by a member of the trial management team who is authorised to do.

Where a participant requests to speak with a physician from the trial team the consent process will not be completed until the participant has spoken to the physician and had all their questions answered to their satisfaction.

For adults who lose capacity their previous wishes will remain legally binding and this will remain valid unless the protocol changes significantly. If the protocol changes significantly, a participant who has lost capacity will be withdrawn.

In all cases the PI or delegate will consult with carers and take note of any signs of objection or distress from the participant – the participant will be withdrawn if they raise objection.

Staff participants – site staff who take part in semi-structured interviews or focus groups will be provided with a participant information sheet in advance and consent taken by the researcher before the interview or focus group begins or a questionnaire is completed.

7.3 Baseline data

Baseline data will be collected at registration per schedule of procedures, Appendix 1 and as described below.

7.4 Study assessments

Participants will answer questions to determine their demographics such as age, BMI and gender at birth. If required, participant will be weighed and measured to calculate their BMI. Participants will be asked if they have any existing respiratory medical conditions. After wearing the biosensor, participants will complete a short satisfaction survey on their experience of PneumoWave DC. Participants should complete this at least once. Participants who stay at the site for a longer period may complete more than one to show fluctuating levels of acceptance. Participants will be asked to complete a drug use diary and an AIR tool to describe their drug use. Drug use and care is discussed with participants so these can be completed in the presence of and with support of, site staff.

During welfare checks, site staff will record any evidence of drug use in the pCRF. If a participant requires intervention due to a potential overdose event, site staff will record this in the pCRF, along with the level of intervention required, if the participant is unresponsive. Where possible the biosensor will be left on the participant during the intervention, and removed once the participant has sufficiently recovered or prior to leaving the facility (i.e. transfer to a medical facility).

A subsection of participants will be asked to partake in semi-structured interviews, lasting no longer than 60 minutes, to describe their experience wearing the device.

A further subsection of participants, including those who may have had an interview, will be asked to take part in focus groups to discuss the PneumoWave DC Mobile and the prototype for the Alert system and the perceived benefits or downsides it may have.

Staff from across all participating supported accommodation will be invited to take part in a semi-structured interview and/or a focus group to discuss their views on, perceived benefits of or barrier to use of the biosensor and DC Mobile system.

7.5 Qualitative assessments

To understand the attitudes, feelings and perceptions of participants and staff about the acceptability of wearing the device through semi structured interviews, focus groups, satisfaction surveys and questionnaires.

7.6 Withdrawal criteria

Participants are free to withdraw at any time and are not obliged to give reason(s). The CI, PI or delegate will make a reasonable effort to ascertain the reason(s), both for those who express their right to withdraw and for those lost to follow up, while fully respecting the individual's rights.
The investigator may withdraw a participant at any time if it is in the best interest of the participant and continuation in the study would be detrimental to the participant's wellbeing. A full explanation will be provided in these instances.

7.7 End of trial

The end of trial at all Sites is defined as last participant last visit. The Sponsor and /or CI have the right at any time to terminate the trial for clinical or administrative reasons.

The end of the trial will be reported to the Sponsor and Research Ethics Committee (REC) within 90 days, or 15 days if the trial is terminated prematurely. The CI will ensure that any appropriate follow up is arranged for all participants.

A final clinical trial report will be submitted to the CA within 1 year of the end of the trial and will also be provided to the Sponsor and REC.

8 STUDY DEVICE AND SOFTWARE

8.1 Name and description of investigational medicinal product(s)

The PneumoWave DC Mobile device comprises:

Hardware:

- Small, discreet, chest-worn Bluetooth biosensor (40mm diameter x 14 mm thick) mounting on an adhesive patch (single, off-the-shelf ECG electrode)

Software:

- Participant/Administrator mobile device app including user interface, storing and transmitting biosensor data
- Researcher dashboard to review anonymous historic biosensor data
- Backend cloud data management infrastructure for data storage.

Outwith of PneumoWave DC Mobile, proprietary Alert algorithms for retrospectively analysing data for signs of SIRD.

8.2 Regulatory status of the device

PneumoWave DC Mobile (PW-DCM) is a UKCA Class 1 medical device registered with MHRA, and a Declaration of Conformity with the UK Medical Devices Regulations 2002 is provided by PneumoWave.

8.3 Study restrictions

This study is purely observational.

8.4 Assessment of compliance with treatment

Compliance will be assessed by the downloading of anonymous respiratory patterns from devices that are returned by participants after use.

9 DEVICE SAFETY

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, PWUD or other persons whether or not related to the investigational medical device.
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device. NOTE 1- This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device. NOTE 2- This includes any event that is a result of a use error or intentional abnormal use of the investigational medical device.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • 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. NOTE: The term "life-threatening" in the definition of "serious" 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.

Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Serious Adverse Device Effect (USADE	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report. • NOTE: Anticipated SADE (ASADE): an effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report

9.2 Operational definitions for (S)AEs

Only (S)AEs deemed directly related to the wearing of the device while on study site premises will be reported by site staff to the research team.

As this population is expected to be actively using opioids and other illicit drugs, any events attributed to illicit drug use will not be reported as an (S)AE.

9.3 Recording and reporting of SAEs, SARs AND SUSARs

An AE related to the wearing of the device will be reported as a study outcome.

Only SAEs deemed to be directly related to participation in this study will be recorded and reported to Sponsor as necessary.

9.4 Responsibilities

Site staff:

• Confirmation of eligibility criteria

Research Team:

- Identifying AEs based on participant responses recorded in the CRF or interviews.

CI/medically qualified PI or delegate:

• Ensuring that AEs and ARs are recorded and reported to the sponsor in line with the requirements of the protocol.

9.5 Notification of deaths

Only in the unlikely event of death being related to the device will they be reported to Sponsor as SAEs as per Section 9.3.

9.6 Pregnancy reporting

Pregnancy is not a risk factor. A pregnant person may use this device.

If a pregnancy is reported by a participant, participant will be advised they can continue in the study if they wish or they can choose to withdraw. Pregnancies will not be followed up.

9.7 Reporting urgent safety measures

Not applicable

10 STATISTICS AND DATA ANALYSIS

10.1 Sample size calculation

This is a feasibility study and therefore recruitment target is not based on a sample size calculation, rather it is based on practical constraints and the length of the study.

10.2 Planned recruitment rate

We aim to recruit around 50 participants over a period of 6-8 months.

10.3 Statistical analysis plan

A statistical analysis plan will be finalised prior to data lock.

10.3.2 Primary outcome analysis

- Biosensor data analysed to determine whether or not an alarm would have been raised (and possibly the timing of the alarm)
- Staff measured outcomes reviewed to categorise whether there was cause for concern about the participant
- Above measures compared to determine either True Positive / False Positive / True Negative / True Positive events
- Sensitivity and Specificity are calculated for the complete data set (ideally with error bars calculated by an appropriate statistical method)

10.3.3 Secondary outcome analysis

Qualitative methods will be used to analyse staff and participant interviews. These will include a phenomenological approach to the lived experience of the participants and stakeholders, through systematic thematic analysis of transcripts and interpretation of themes in the light of underpinning theory

10.4 Procedure(s) to account for missing or spurious data

Biosensor data will be reconciled with staff and patient reported data. Those that do not reconcile will be excluded.

10.5 Other statistical considerations.

N/A

10.6 Economic evaluation

No economic evaluation will be performed.

11 DATA MANAGEMENT

11.1 Data collection tools and source document identification

Data will be collected via:

Case report form to collect participant demographics, any existing respiratory conditions, record potential SIRD events and outcomes and record issue/return of biosensor and tablet.

AIR Tool Questionnaire to assess participants' drug use behaviours. Completed once during the study.

Drug use diary to establish drug use, immediately prior to and during site stay. Completed at participants' discretion.

Satisfaction survey, completed at least once during the study.

Cloud data management for app respiratory data. The variability of normal respiratory patterns will be analysed using proprietary algorithms, facilitated by PneumoWave. This is fully anonymous.

Semi-structured interviews and focus group. Detailed in section 7.5 (Qualitative assessments)

11.2 Data handling and record keeping

The data management system will be an Excel spreadsheet. Password protected and stored on the University of Dundee server. No personal data will be held on the spreadsheet. This will be a pseudonymised data set, linked back to participants by unique study identifier and the enrolment log held at site. Data will be entered by a TCTU trial coordinator, transcribed from the CRFs, AIR tools and drug diaries collected from the participating sites. Data analysis will be carried out by King's College London (KCL). KCL will receive the entered pCRF data as a pseudonymised excel spreadsheet. Shared via encrypted email.

Interview and focus groups will be digitally recorded. All audio transfers will be conducted via audio recorder to a University (UoD or KCL) secured laptop. The interviews/focus group recordings will then be sent to KCL, who will complete a data sharing agreement with UoD. KCL will remove the audio file and related transcripts from their server within 30 days post transcription. Transcription will be completed by a research fellow at KCL. The transcriber will generate an anonymised transcript of the interview/ focus group recordings. Please note is not possible to safeguard against respondents compromising their anonymity or that of others during an interview/focus group, thus the need to anonymise during transcribing. No identifiable data such as interviewee names or interview locations and times will be attached to the audio file, i.e. all audio files will be labelled with an identifier number (which is only known and can only be linked to potentially identifiable information by the delegated researcher). These participant details including the identification number will be stored in a password protected digital file in University of Dundee/KCL, and only the delegated researcher will have access to this file. Participants will be assigned a unique study ID in order to protect their identity. The interview data will not be explicitly linked to specific clinical data for any participants.

Interview/focus group recordings will be deleted once the transcriptions have been received.

Interview/focus group transcripts will be stored on a secure University of Dundee/KCL device. They will be analysed and coded using thematic analysis. This process will be carried out by the research team. Thematic analysis will aid the identification of semantic meanings emerging from the interviews/focus groups, as well as allowing for interpretation of latent meanings. The analysis will help

understand the attitudes, feelings and perceptions of participants about the acceptability of wearing the device in the context of their daily lives and will allow identification of appropriate intervention strategies for the development of a clinical intervention pathway.

KCL will analyse the anonymised transcripts of the interviews and focus groups.

11.3 Access to Data

The CI, PIs and all institutions involved in the trial will permit trial related-monitoring, audits, REC review, and regulatory inspection. In the event of an audit, the CI and/or PI will allow the Sponsor, representatives of the Sponsor or regulatory authorities direct access to all trial records and source documentation.

11.4 Archiving

Archiving of study documents will be for ten years after the end of study.

12 MONITORING, AUDIT & INSPECTION

No formal monitoring is planned. The trial coordinator will be in regular contact with sites to ensure trial procedures are being followed correctly and participant safety and data integrity safeguards are in place.

13 ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee (REC) review& reports

The study will be conducted in accordance with the principles of good clinical practice (GCP).
In addition to Sponsorship approval, a favourable ethical opinion will be obtained from the appropriate REC(s) will be obtained prior to commencement of the study.

13.2 Public and Patient Involvement

People with lived experience of injecting drug use have been consulted about this study and have been involved in focus groups discussing the PneumoWave technology platform.

13.4 Regulatory Compliance

Before any site can enrol participants into the trial, the CI, PI or delegate will ensure that appropriate approvals from participating organisations are in place.

For any amendment to the trial, the CI, PI or delegate, in agreement with the sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The CI, PI or delegate will work with sites so they can put the necessary approvals and arrangements in place to implement the amendment to confirm their support for the trial as amended.

13.5 Protocol compliance

Prospective, planned deviations or waivers to the protocol are not allowed, e.g. it is not acceptable to enrol a participant if they do not meet the eligibility criteria or restrictions specified in the trial protocol. Trial staff will not implement deviations to the protocol except where necessary to eliminate an immediate hazard to trial participants.

Accidental protocol breaches can happen at any time. They will be adequately documented on the relevant forms and reported to the CI and Sponsor using the TASC Breach Reporting and Corrective Actions/Preventative Actions Form. If there is a breach of the protocol, the nature of and reasons for the breach will be recorded in the TMF and documented in the trial Breach Report Log. Breaches from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

13.6 Notification of Serious Breaches to GCP and/or the protocol

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

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

The sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase. The sponsor of a clinical trial will notify the licensing authority in writing of any serious breach of

a) the conditions and principles of GCP in connection with that trial; or
b) the protocol relating to that trial, as amended from time to time.

If a serious breach of the protocol or GCP is suspected, this will be reported to the Sponsor immediately using the Breach Reporting & Corrective Actions/Preventative Actions Form and will be recorded in the CRF and documented in the study Breach Report Log.

If a breach necessitates a subsequent protocol amendment, this will be submitted as per section 13.10.

13.7 Data protection and patient confidentiality

The CI and trial staff will comply with the requirements of the General Data Protection Regulation (EU) 2016/679 (GDPR) and the UK Data Protection Act 2018 or any subsequent amendment or replacement thereof with regard to the collection, storage, processing and disclosure of personal data and will uphold the principles of GDPR in Article 5.

While there is no NHS involvement in the study, the CI and trial staff will adhere to the NHS Scotland Code of Practice on Protecting Participant Confidentiality or local equivalent.

All trial records and data will be managed in a manner designed to maintain participant confidentiality. All records, electronic or paper, will be kept in a secure storage area with access limited to appropriate trial staff only. Computers used to collate data will have limited access measures via usernames and passwords. Age and gender will be the only personal identifiable details held on the Excel data management system.

Personal data or data concerning health will not be released without the existence of a legal basis for processing under Articles 6 and 9 of GDPR, such as official authority 6(1)e or substantial public interest 9(2)g. The CI and trial staff will not disclose or use for any purpose other than performance of the trial, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the trial. Prior written agreement from the Sponsor will be required for the disclosure of any said confidential information to other parties.

Access to collated participant data will be restricted to the CI and appropriate delegated trial staff. PneumoWave will not have access to personal identifiable details.

Published results will not contain any personal data that could allow identification of individual participants.

13.8 Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall trial management

Not applicable.

13.9 Indemnity

The University of Dundee are Sponsoring the trial.

Insurance. – The University of Dundee holds Clinical Trials indemnity cover which covers the University's legal liability for harm caused to participant

Indemnity. The Sponsor does not provide trial participants with indemnity in relation to participation in the Trial but have insurance for legal liability as described above.

13.10 Amendments

Amendments to the protocol will be conducted in compliance with Sponsor Standard Operating Procedures. The decision to amend the protocol will lie with the CI after consultation with the TMG and trial statistician. The CI will seek Sponsor approval for any amendments to the Protocol or other approved trial documents. The Sponsor will decide whether an amendment is substantial or non-substantial. The CI will be responsible for submitting the amendment to the appropriate regulatory authorities and communicating amendments to sites. Amendments to the protocol or other trial documents will not be implemented without approval from the Sponsor and subsequent approval from the appropriate REC and/or CA, as appropriate, and appropriate site approvals The amendment history will be detailed in an Amendment Log.

13.11 Access to the final trial dataset

The CI and Trial Statistician will have access to the final trial dataset. Access to the final trial dataset to others will be approved by the CI.

14 DISSEMINATION POLICY

14.1 Dissemination policy

Ownership of the data arising from this study resides with the study team and the University of Dundee. On completion of the study, the study data will be analysed and tabulated, and a clinical study report will be prepared.

The clinical study report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the study.

Summaries of results will also be made available to Investigators for dissemination within their clinical areas (where appropriate and according to their discretion).

The results of the study will be disseminated to participants' who remain living in the supported accommodation at the time of publication. Results will be disseminated in the form of a newsletter, provided by the study team to the supported accommodation.

15 REFERENCES

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3. Palkovic B, Marchenko V, Zuperku EJ, Stuth EAE, Stucke AG. Multi-Level Regulation of Opioid-Induced Respiratory Depression. Physiology (Bethesda). 2020 Nov 1;**35**(6):391-404.
4. Jolley, C. J., et al. (2015). "Understanding Heroin Overdose: A Study of the Acute Respiratory Depressant Effects of Injected Pharmaceutical Heroin." PLOS ONE **10**(10): e0140995.
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6. Tas B, Walker H, Lawn W, Matcham F, Traykova EV, Evans RAS, Strang J. What impacts the acceptability of wearable devices that detect opioid overdose in people who use opioids? A qualitative study. Drug Alcohol Rev. 2023 Aug 19.
7. doi: 10.1111/dar.13737. Epub ahead of print. PMID: 37596977.

16. APPENDICES

16.1 Appendix 1 – Schedule of Procedures

Procedures	Baseline	Ongoing until end of study	End of study
Informed consent	X		
Demographics	X		
Respiratory medical history	X		
Eligibility assessment	X		
AIR Tool[a]	*	*	*
Fit device and issue tablet	X	X	
Satisfaction Survey[b]		X	
Adverse Events		X	
Drug Use Diary		X	
Interview[c]			X
Focus Group[c]			X

[a] = completed once during the study

[b] = completed at least once, but can be completed multiple times

[c] = sub-section of participants