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Study Protocol

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Abstract

Background

Despite the exponential growth of wearable technology, previous research indicates a lack of statistically significant evidence to support the hypothesis that implementation of wearable ambulatory vital sign monitoring systems impact early patient deterioration detection and clinical outcomes. This highlights the need for large, rigorous studies to address this gap. The objective of this feasibility trial is to assess the impact of an ambulatory monitoring system (AMS) on deterioration detection and clinical outcomes in hospitalised patients, compared to standard care. As a secondary objective we will assess the feasibility of conducting a full randomised controlled trial (RCT).

Methods

Between 120 and 240 patients will be recruited and randomised equally to either an AMS or standard care group. Wearable devices will include a pulse oximeter (monitoring pulse rate and oxygen saturation), a chest patch (monitoring heart rate, respiratory rate and temperature) and a wireless blood pressure cuff (monitoring systolic and diastolic blood pressure). Both groups will wear the devices during their ward length of stay, however only data and alerts from the AMS group will be visible to clinical staff.

Discussion

Recruitment of participants is expected to start in January 2022, with an anticipated completion date of December 2022. This feasibility RCT will test the early impact of our AMS implementation in a non-intensive care ward and provide data to support the design and deployment of a full RCT which will provide much-needed evidence of the impact of AMS on early deterioration detection and clinical outcomes.

Background

Failure to identify and act on physiological indicators of worsening illness in acute hospital wards is a generic problem that was recognised over a decade ago [1, 2]. General surgical emergency admissions are the largest group of all surgical admissions to UK hospitals [3]. Patients who undergo emergency major bowel surgery have a high mortality, with people aged over 80 years old having a mortality risk of up to 50% [4].

Current practice uses physiological early warning scoring (EWS) systems to monitor “standard” vital signs, including pulse rate, respiratory rate, blood pressure, oxygen saturations and temperature, coupled with a graded response such as referral for a senior review or increasing monitoring frequency [5]. Despite the National Institute for Health and Care Excellence (NICE) endorsement in the UK and widespread international adoption, the value of EWS systems is still open to debate, with conflicting evidence as to their overall reliability and sensitivity [6].
Contextual factors identified as influencing the usefulness of EWS include timely escalation, poor understanding of illness severity, lack of situational awareness and halted escalation [7]. In addition, EWS systems are limited by dependence on correct frequency of physiological observations tailored to specific patient needs [8]. Studies have identified current ward-based monitoring of patients as time consuming [9] and limited by the prescribed frequency and completeness of observations not being achieved [10]. Vital signs monitoring technology within healthcare is limited in its efficiency, but these potentially more sustainable, accurate and less time-consuming monitoring methods require validation within the healthcare context.

Wearable monitors may provide an alternative continuous monitoring system, affording patients more mobility, less discomfort, reduce nursing time and improve the early detection of abnormal physiological parameters [11]. As a result of current healthcare monitoring limitations wearable technological innovations are extending the capabilities of commercially available wearable ambulatory vital sign monitoring equipment [12]. Barriers to the successful implementation of these wearable devices have been reliability, efficiency and data processing systems [12].

In response to current limitations in healthcare monitoring, companies are extending the capabilities of commercially available wearable vital sign monitoring systems [12]. These non-wired monitors may provide an alternative continuous monitoring system, affording patients more mobility, less discomfort, reduce nursing time and improve the early detection of abnormal physiological parameters [11].

A recent meta-analysis suggested that patients continuously monitored using non-invasive devices had a 39% decreased mortality risk when compared to those receiving intermittent monitoring; as well as a trend of reduced intensive care unit (ICU) transfer, rapid response team activation and hospital length of stay [13]. Another recent review analysed the validation, feasibility, clinical outcomes and costs of 13 different wearable devices and concluded that these were predominantly in the validation and feasibility testing phases [14], highlighting the lack of studies exploring clinical outcomes. While there are many devices claiming the ability to safely monitor patients at risk of deterioration [15], evidence assessing the impact of ambulatory monitoring systems in clinical outcomes remains inconclusive, limiting implementation and clinical use [15].

**Previous work**

This study is the final phase of the virtual High Dependency Unit (vHDU) project, comprising several studies that have led to this study.

1. **vHDU Phase 1**: Wearability testing of ambulatory vital sign monitoring devices. A prospective observational cohort study [16].
2. **vHDU Phase 2**: A qualitative study of patient and nursing staff experiences of monitoring practices in a surgical ward and early opinions of wearable continuous monitoring [17].
3. vHDU Hypoxia: diagnostic accuracy study to evaluate the specificity and sensitivity of ambulatory monitoring systems in the prompt detection of hypoxia and during movement.
   
   a. Protocol [18]
   b. Pulse oximeters diagnostic accuracy [19]
   c. Chest patch validation [20]

4. vHDU Phase 3: Locational testing of ambulatory monitoring systems on a surgical ward (non-published).


6. vHDU Phase 4: Ambulatory monitoring system user interface integration and alerting algorithm development (ongoing).

7. Systematic review: The impact of wearable continuous vital sign monitoring on deterioration detection and clinical outcomes in hospitalised patients: a systematic review and meta-analysis [22,23].

**Objective**

The primary objective of this study is to assess the impact of AMS integration (with active clinical alerts) versus standard care in deterioration detection.

Secondary objectives include other deterioration detection and clinical outcomes, trial progression outcomes, staff impact and alerting system performance, overall system reliability and patient experience (described below).

**Methods/design**

**Study Design**

This study is a superiority feasibility randomised controlled trial with two-arm parallel groups and 1:1 allocation ratio to compare the use of an ambulatory monitoring system with standard care in hospitalised patients. We will also use it to explore recruitment rate, calculate required sample size, number of sites and recruitment period for a full definitive RCT.

Participants will be recruited in one or more surgical wards inside a UK based local trust. Patients will be screened, recruited and participate in this study throughout their hospital stay, and no follow-up visits will be required.

Participants will be asked to wear one pulse oximeter (Nonin WristOx2 3150 OEM BLE, shorted to “Nonin”, hereafter) measuring pulse rate (PR) and oxygen saturation (SpO2), one chest patch (VitalPatch) that will continuously measure their heart rate (HR), respiratory rate (RR), temperature; and one A&D UA-1200 BLE Blood Pressure device, intermittently measuring systolic and diastolic blood pressure. Clinical staff will be
able to access and interact with real-time vital signs through a dashboard. This system also provides clinical alerts, according to the patient’s EWS score.

The control group will also be fitted with these devices. However, clinical staff will not be able to access the bedside tablet, the dashboard display or receive alerts.

The trial will include a calibration period inside the Surgical Emergency Unit (SEU) where we will refine out alerting system. During this period, we will optimise our alerts through continuous analysis and feedback from the relevant clinical teams. Randomisation will still happen during this period.

This feasibility trial will run in surgical units at the local trust. This will:

- Assess the feasibility of a definitive RCT
- Support sample size calculation for full study
- Assess recruitment rate and the need for inclusion of more wards inside the local Trust.
- Staff focus groups or interviews will be held to gather feedback on the system which may inform further refinements, including usability, perceived effect on workload and appropriateness of alerts.
- Multi-professionals staff interviews will be held to assess the acceptability of the vHDU system in clinical practice. Interviews will be held with some patients who have worn the monitoring, to gain their perceptions of the system, including wearability, sense of safety and potential improvements.

### Alert calibration period

Considering previous evidence [23], we have added an alert calibration period in this trial where an initial proportion of the randomised patients will be used for calibration of our alerting system and threshold adjustment. We require a certain number of episodes of physiological instability to occur to be able to refine the alerts. We estimate to require between 20 and 50 monitored patients to achieve enough deteriorations for the alerts to be calibrated.

Physiological instability will be defined as all periods where the synchronised vital-sign values (collected from the AMS, namely, HR, RR, SpO2, Temperature, and Blood Pressure), are abnormal for more than 4 minutes in a 5-minute window (the period ending if there are less than 2 minutes of abnormality in a 3-minute window). The thresholds to determine an abnormal set of vital signs (including both single highly abnormal vital sign or combinations of moderately abnormal vital signs) will be defined according to the local early warning score.

We will take a pragmatic approach and simultaneously collect feedback from staff during this period to optimise the alerting system (aiming to avoid false alerts and optimise staff responses to the alerts). We will do this through individual qualitative feedback collection and focus groups in the Surgical Emergency Unit ward at strategic time-points throughout the calibration period.

### Outcome measures
Primary outcome

1. Time from first period of unexpected physiological instability to set of observations

Physiological instability periods definition:

We define physiological instability as per the calibrated alerting algorithm. We will report and explore these according to the following:

- **Unexpected**: Physiological abnormality periods related to deterioration. We will retrospectively log this in the relevant spreadsheet and complete the relevant Case Report Form (CRF) with more details on the event.
- **Expected**: related to patient condition or reported by clinical staff, for which, if appropriate, vital signs or algorithm thresholds might be adjusted after discussion with responsible clinicians (during the calibration period). We will log these in the relevant spreadsheet for further analysis (as required).

Unexpected physiological instability timings:

For both control and intervention groups, a period of unexpected deterioration:

- Starts: first detected physiological instability after period of normality (alert in the intervention arm).
- Ends: when a set of observations is recorded by the clinical team.

Secondary outcomes

2. Other deterioration detection related outcomes

2.1. Frequency and duration of physiological instability periods and nursing visits

We will compare deterioration time and frequency as defined by the alerting algorithm.

2.2. Time and frequency of unscheduled interventions

We will collect time to/of, and frequency of, unscheduled interventions (as defined in the above intervention examples) in both groups. This will be collected through completion of the relevant CRF/spreadsheet, from the following information:

- Unscheduled interventions examples (not limited to these):
  - Antibiotics
  - Acute changes to therapy/medication (e.g. drugs to treat cardiac arrhythmia)
  - Supplementary oxygen
  - Fluids
  - Radiological intervention (x-ray, CT, etc.)
- Chest physiotherapy
- Escalation to specialist (e.g. surgeon, renal consultant) outside of treatment plan

Timings:

For both control and intervention groups, the time to unscheduled intervention is the following:

- Starts: as soon as period of physiological instability is detected
- Ends: recorded time of unscheduled intervention

2.3. ICU Admission

We will collect intensive care unit transfers and (where possible) establish which of these were unscheduled. This will be collected through completion of the relevant CRF.

2.4. Cardiac Arrest team call

We will collect cardiac arrest team calls and compare in both groups. This will be collected through completion of the relevant CRF:

2.5. Complications and adverse events

We will collect all complications and adverse events in both groups. This will be collected through completion of the relevant CRF, collecting the following information:

**Complication category.** Using the Clavien-Dindo system [24] to grade the level of surgical complications [25,26].

This system is divided in 5 grades:

**Grade I:** Any deviation from the normal post-operative course not requiring surgical, endoscopic or radiological intervention. This includes the need for certain drugs (e.g. antiemetics, antipyretics, analgesics, diuretics and electrolytes), treatment with physiotherapy and wound infections that are opened at the bedside

**Grade II:** Complications requiring drug treatments other than those allowed for Grade I complications; this includes blood transfusion and total parenteral nutrition (TPN)

**Grade III:** Complications requiring surgical, endoscopic or radiological intervention

**Grade IV:** Life-threatening complications; this includes CNS complications (e.g. brain haemorrhage, ischaemic stroke, subarachnoid haemorrhage) which require intensive care, but excludes transient ischaemic attacks (TIAs)

**Grade V:** Death of the patient
2.6. Control group only: Time difference between deterioration detection by nurse and AMS

As participants in the control group will also be wearing these devices we aim to assess the time difference between when the first unexpected deterioration occurred (as defined above) and when the clinical staff detected it. We will also explore time differences to intervention and related clinical outcomes.

3. Other clinical outcomes

3.1. Mortality

We will collect the following information regarding mortality:

- ICU mortality
- Hospital mortality
- 30-day mortality

3.2. Length of stay

We will collect the following information regarding patient length of stay:

- Ward length of stay
- ICU length of stay
- Hospital total length of stay

4. Trial progression outcomes

4.1. Recruitment rate

Including the proportion of ineligible patients (with reasons for non-eligibility) and non-consented (with reason for non-consent).

4.2. Patient and staff adherence

We will collect reasons for non-adherence in both groups. For example, this can include the number of patients who do not wear one or more of the devices for a long period during the feasibility study.

4.3. Outcome selection

To explore collected outcomes (as outlined throughout this section) to finalise the primary and secondary outcomes for the definitive trial. This will also contribute to the sample size calculation for the definitive trial.

We will decide on the outcomes and describe how these will be optimised using this feasibility trial data.
4.4. Randomisation method and confounders

Assess how we can optimise randomisation process. Identify and plan how to minimise any potential confounders.

5. Staff impact and alerts

5.1. Proportion of false alerts and alert optimisation process during calibration period

We will also explore the rate of false alarms throughout the feasibility trial and steps taken during its calibration.

5.2. Staff perception of the system

We aim to assess the perceived impact of AMS integration on staff workload, including the perception of appropriateness of alerts, and usability of the system, through individual feedback and/or focus groups.

We aim to assess the perceived acceptability of use of the system in clinical practice through individual interviews with multi-professional staff members.

6. System reliability

6.1. Level of agreement between AMS and manual EWS and individual vital signs

Assess individual device and whole system EWS accuracy against standard care inside each group.

6.2. Frequency and duration of data drop-out for each vital sign parameter

Report non-patient related data loss for each vital sign parameter.

6.3. Causes of system down-time

Report non-patient related causes for system-downtime, e.g. devices or server connectivity, battery, malfunction, etc.

6.4. Waveform quality

Evaluate:

- VitalPatch Electrocardiogram waveform signal quality (used in HR and RR);
- VitalPatch Accelerometer waveform signal quality (used in RR, Posture, Steps);
- VitalPatch temperature waveform signal quality;
- Nonin Infrared Photoplethysmography waveform signal quality (used in SpO2 and PR);
Compare waveform signal quality and respective numerical parameters (HR, RR, SpO2, temperature) distributions.

7. Patient reported outcomes and experience

7.1. PROMs

Participants will be asked to complete a questionnaire collecting wearability information

7.2. Patient compliance with wearable devices

Report proportion of time window each vital sign is recorded versus time device is worn.

7.3. Patient experience

Patient perception of the system will be explored through qualitative interviews with a purposive sub-group of patients who have worn the system.

Recruitment

Patient identification

Recruitment will start with a Surgical Emergency Unit (SEU) inside the local hospital. If appropriate, we will expand recruitment to other surgical wards upon discussion with the ward manager/matron and relevant ward clinicians.

The research team will contact the Ward Coordinator for patient identification and discussion of the admission/surgery timings.

Clinical staff will discuss the study with patients and request verbal consent for the research staff to approach. Patients will then be given verbal information about the study and a participant information sheet (PIS, Appendix 1). Informed consent procedures are outlined below.

Population

Surgical patients.

Qualitative patient interviews

Trial participants consenting to be approached for qualitative interviews during or/and after the trial.

Clinical staff (focus groups and interviews)

During the initial months of the trial, a proportion of clinical staff will be invited to focus groups or individual interviews to provide feedback on the usability of the system. In the later stages, interviews
with patients, family members and multi-professional staff will also be held to explore the perceptions of staff using the system, including acceptability of use in clinical practice. Participants will be purposively selected to provide a range of views and experiences [27].

For user focus groups, purposive groups of clinical staff using the AMS throughout the trial (including the calibration period). Staff may be asked to periodically review the system and alerts as the trial progresses.

For interviews of staff perception of the system, multi-professional staff members (e.g. nurses, clinical support workers, doctors, physiotherapists, etc.) will be purposively sampled to offer maximal variation of the sample in terms of profession, staff grade and experience with the system.

**Eligibility**

Patient eligibility will be confirmed with the responsible clinical team. Once eligibility has been confirmed and verbal consent given to the clinical team, one of the research team members will approach patients and talk through the procedures of the study.

Patients will be given sufficient time to consider and discuss information. Due to the monitoring window for this study, we will only consider participants that decide to participate up to 24 hours after being approached.

**Inclusion Criteria**

**Patients**

- Any patient admitted to the participating surgical unit (including post-ICU patients) who is not currently monitored with standard continuous monitoring
- Patient stable for at least 6 hours with at least one of the following:
  - NEWS2 $\leq 2$ and in some exceptional cases NEWS $>2$ (confirmed with clinical staff, e.g. patients with comorbidities).
  - Frequency of observations of $>4$ hours at the time of randomisation.
- Participant is willing and able to give informed consent for participation in the trial.
- Male or Female, aged 18 years or above.

**Qualitative patient interviews**

- Participant taking part in the trial
- Able and willing to consent to participate in an interview
- Able to speak and understand English

**Clinical staff (focus groups and interviews)**
• Any clinical staff member with experience of caring for patients included in the trial, and actively using the system.

Exclusion Criteria

Patients (including interviews)

The participant may not enter the trial if ANY of the following apply:

• Intra-cardiac device
• Used vHDU system for less than 24 hours

Clinical staff (focus groups and interviews)

• Any staff member not consenting to participate

**Informed consent**

Once patient is deemed eligible, consent will be obtained by a trained member of the research team. The participant must personally sign and date the latest approved version of the Informed Consent form (Appendix 2).

Written and verbal versions of the Participant Information and Informed Consent will be presented to the participants detailing no less than:

• the exact nature of the trial
• what it will involve for the participant,
• the implications and constraints of the protocol,
• the known side effects
• any risks involved in taking part

It is clearly stated that the participant is free to withdraw from the trial at any time for any reason without prejudice to future care, without affecting their legal rights and with no obligation to give the reason for withdrawal.

The participant will be allowed sufficient time (up to 24 hours) to consider the information, and the opportunity to question the Investigator or other independent parties to decide whether they will participate in the trial.

**Patient qualitative interviews**

Semi-structured interviews will be conducted with up to 30 patients, following removal of the AMS. Interviews will be conducted either face to face during their hospital stay, in a quiet room or at the bedside if deemed appropriate, or by telephone after they have been discharged from hospital. If it is not possible
to hold the interview during the patients’ hospital stay, a telephone interview may be arranged with the patient for after their discharge. Interviews will use a topic guide with questions focused on acceptability of the monitoring system.

**Clinical staff interviews**

Semi-structured interviews will be conducted with up to 30 members of clinical staff. These will be held in a room away from the clinical area, or by video call (using MS Teams) or telephone, and will be audio recorded. Participants will be asked to review the relevant Interview Participant Information Sheet and sign the consent form. If interviews are held by telephone or video call, the participant will meet with research staff prior to this to discuss the study and sign an Informed Consent Form.

The interviewer will explain that the session will be audio recorded and that they may stop the focus group at any time. Participants will have the aims of the interview explained to them. The participant must personally sign and date the latest approved version of the Informed Consent form before any study specific procedures are performed.

**Clinical staff focus groups**

Focus groups will be conducted with up to 50 members of clinical staff.

Staff focus groups will be held in a room away from the clinical area, or by video call (using MS Teams) or telephone, and will be audio recorded. Participants will be asked to review the relevant Focus Group Participant Information Sheet and sign the consent form. If focus groups are held by telephone or video call, the participant will meet with research staff prior to this to discuss the study and sign an Informed Consent Form.

The focus group lead will explain that the session will be audio recorded and that they may stop the focus group at any time. Participants will have the aims of the focus group explained to them. The participant must personally sign and date the latest approved version of the Informed Consent form before any study specific procedures are performed.

Interviews/focus group participants will be free to withdraw from the study at any time until their point at which their interview data are anonymised, and this will be made explicit.

**Randomisation**

Participants will be randomised with a 1:1 allocation ratio between the two groups. A stratified permuted block approach will ensure the two groups are well balanced on important prognostic factors:

1. Sex (male, female)
2. Age (<45, 45-65, >65)
The randomisation will be implemented using an online system such as https://www.sealedenvelope.com to ensure allocation concealment.

**Baseline Assessments**

Participants will be assigned a study number at the time of consent and before being randomised. All data collected will be pseudonymised with this study number. A link between identifiable data (e.g. participant name and hospital number) and study number will be held in a password protected document stored on a secure server held by the University of Oxford. This will be destroyed at the end of the study when all data have been verified.

Participants randomised to the intervention group will have the AMS attached and will be instructed in its use by a member of the research team. They will be free to remove the device(s) at any time but will be encouraged to use them throughout their ward length of stay and log reasons for removal. There will be instructions on how to apply the monitor made available for participants and clinical staff. However, we expect device application is likely to be done by a research team member (at least initially). To minimise disruption to data collection, there may be instances where clinical staff or patients reapply the devices, which will be clearly explained by the research team.

We will have a "Study pack" per patient that consists of:

- 1 tablet
- 2 VitalPatches
- 1 pulse oximeter + 8 AAA batteries + 1 replacement strap
- 1 BP monitor
- 1 user guide
- 1 wearability questionnaire
- 1 device removal log

**Clinical Events recording**

Wherever relevant, non-device related clinical deteriorations or events will be recorded in the “Clinical Event” CRF. This will allow us to clarify and gather information on any clinical event relevant to the study. This will include extracted information from hospital records and/or discussion with patient and clinical staff on the following:

- Type of event
- Date and time noticed by clinical staff
- Action taken (e.g. unscheduled visits, medication, etc...)


Trial interventions

All randomised patients will use our ambulatory monitoring system (AMS) consisting of one pulse oximeter, one chest patch, one blood pressure monitor and one computer tablet.

A. Pulse Oximeter - Nonin WristOx2 3150 OEM BLE

The selected pulse oximeter is the Nonin WristOx2 3150 OEM BLE (Figure 1). This is a wrist worn device with a finger probe using Photoplethysmography (PPG) signals of red and infrared light through tissue to calculate SpO2 and pulse rate.

Data is directly downloaded from the device via BLE (Bluetooth-low-energy). The device Uses AAA batteries with approximately 48 hour battery life with continuous use. The device is not waterproof.

B. Chest Patch – VitalPatch

The VitalPatch (Figure 2) is a single-lead ECG chest patch that measures heart rate, respiratory rate, steps, body position and skin temperature. Precautions while using this device are the following:

- Not to be used with intra-cardiac devices or any type of defibrillator
- Not to be used during an MRI
- Wounds which preclude the VitalPatch use
- Sensitivity or allergy to adhesives.

Data is transmitted via Bluetooth in real-time (live data) or stored inside the device (stored data) when connectivity to the tablet is not available. The stored data is retrieved via Bluetooth upon the next connectivity to the tablet. This patch is of single use only and battery life usually lasts around 5 days.

C. Blood Pressure device – A&D UA-1200BLE

An upper-arm blood pressure device (Figure 3) that measures pulse rate and systolic and diastolic blood pressure intermittently.

Data is directly transmitted via BLE. The battery life is 100 measurements.

D. Tablet

The Tablet used in the study is a Samsung Galaxy Tab A and is kept by the participant bedside. A bespoke app has been developed (Figure 4), which displays the data obtained from the wearable devices. The data is streamed to the Tablet using encrypted BLE. Each device has a unique ID to enable correct
identification and security. Participants must be registered using their hospital number (MRN), which will be cross-checked with the Hospital system to confirm correct identity. The tablet then streams the data through Wi-Fi to a secure server, for viewing on the dashboard (web-interface).

E. AMS Client

The AMS client is a secure web-interface accessible for enabled users from the NHS network. The application shows data from the list of patients allocated to the users’ specific wards. This application works in two configurations: “Dashboard”- or “PDA” (Personal Digital Assistant). The users’ wards are set up at the first login. The users’ client configuration is defined when their accounts are created.

E.1. Dashboard configuration:

The Dashboard configuration has three different pages:

- Main screen (Figure 5) – Displays a “card” for each participant with their vital signs from the remote monitors as well as their last vital signs from hospital’s electronic system for recording nurse observations of vital signs (e-obs), SEND [28], and respective EWS. The card also displays any technical or clinical alerts that may arise. Information on the connectivity and battery status of the monitors is also available.

- Observations chart – Displays an expanded chart of all the observations over time, including those from SEND. Vital-sign values from the wearable devices can be filtered to time intervals of 5, 15, 30 and 60 minutes.

- Patient viewer – This page displays both the live numerical data (HR, RR, SpO2, Temp) and waveforms (ECG and PPG), the last set of nurse observations (from the SEND system), and the respective EWS, for a selected participant from the VitalPatch and Nonin wearable devices. It also contains “mini cards” for each participant with numerical values of their latest vital signs automatically required by the AMS from the wearable devices. Clicking on one of these mini-cards will switch the display to that participant.

In this configuration, the alerts are shown for all the patients in the users’ wards.

**Intervention Group**

Patients randomised to the intervention group will receive the AMS in addition to standard care; this will be connected to the dashboard and the alerting system.

**Control Group**

Patients in the control group will also receive the AMS, however monitoring outputs will not be displayed on the ward dashboard and clinical staff will not be able to access these patient’s continuous vital signs.
**Statistical Analysis**

The primary outcomes will be analysed using a linear regression model. The output of the model will be the mean difference between arms, along with the 95% confidence interval and associated p-value.

A sensitivity analysis of the primary outcome will additionally adjust for stratification variables in the regression model.

Continuous secondary outcomes will be analysed in the same manner as the primary outcome. Dichotomous secondary outcomes will be analysed using a logistic regression model.

**Sample size**

The study will aim to recruit at least 120 participants, and up to 240. Since the primary outcome is continuous, the sample size calculation is carried out on the basis of a t-test being used to analyse it. 120 participants (i.e. 60 per group) will give 80% power to detect a standardised effect size of 0.52 (i.e. a medium effect), whilst 240 participants will give 80% power to detect a difference of 0.37. If 10% of participants were to withdraw, 120 and 240 participants recruited would still enable detection of differences 0.55 and 0.39 respectively.

We will take a pragmatic approach when a participant withdraws from the study. If there is either less than 24 hours continuous data collected or the participant requested that their data not be used in the final study analysis, we will add an extra participant to our sample size.

For the patient interviews, up to 30 participants will be recruited, with recruitment ceasing when data saturation has been achieved (i.e. no new themes are identified).

**Blinding**

Due to the nature of this study neither patients, clinicians nor researchers will be blinded.

**Data Management and Monitoring**

**Data access and protection**

Source documents are where data are first recorded, and from which participants’ CRF data are obtained. These include, but are not limited to, hospital records (from which medical history and previous and concurrent medication may be summarised into the CRF), clinical and office charts, laboratory and pharmacy records, diaries, microfiches, radiographs, and correspondence.

Direct access will only be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations. All documents will be stored safely in confidential conditions. On all study specific documents the participant will be referred to by the
study participant number/code, not by name. The ID log will be kept on a password protected computer only accessible by clinical members of the research team behind two locked doors.

Data Monitoring Committee

Not applicable. Committees to be established after feasibility trial.

Discussion

Study Team

The study team include clinical research nurses and critical care researchers part of the Critical Care Research Group, and engineers based in the Institute of Biomedical Engineering. This team will conduct all activities related to this trial, from study management to patient recruitment.

Study flow and procedures

The feasibility trial recruitment and randomisation process are outlined in the below flowchart (Figure 6). The SPIRIT figure outlining procedures throughout study is available in Figure 7.

Timelines and deliverables

We aim to complete this feasibility study within 18 months of recruitment start (estimated start in January 2022). The calibration period is estimated to last up to 3 months, where we will implement and test the alerting algorithm whilst training clinical staff and optimise recruitment and randomisation processes. The total recruitment period will last up to 12 months. Data analysis and report writing will last a further 6 months.

Progression criteria for a full randomised controlled trial

This feasibility trial will be conducted in surgical units at the local Trust. This will:

- Assess the feasibility of a definitive RCT
- Support sample size calculation for full study
- Assess recruitment rate and the need for inclusion of more wards inside the local Trust. Staff focus groups or interviews will be held to gather feedback on the system which may inform further refinements, including usability, perceived effect on workload and appropriateness of alerts.

In order to progress to a definitive RCT this feasibility trial has the following progression criteria:
1. Recruitment of at least 120 patients within 12 months.
   a. Assess feasibility of expanding to other surgical wards inside the local Trust.
   b. Assess feasibility of expanding to other trusts.

2. Missing data
   a. <30% withdrawal rate/data loss

This feasibility study will allow us to gather preliminary data for the planning and application of the full, potentially multicenter, randomised controlled trial.

**Pipeline to trial design**

This protocol aimed to describe the background work of our feasibility randomised controlled trial. Our previous phases included: device wearability testing [16], qualitative exploration of current vital sign monitoring practices [17], accuracy device testing [29,30], reliability testing (unpublished), [21] a systematic review of previous comparative studies [23], and an emergency optimisation and deployment, without the alerting, on the Infectious Disease Ward of the John Radcliffe Hospital prompted by the COVID-19 pandemic [21]. All of which is now converging in this trial for a final assessment of the feasibility of implementing AMS ion general wards for early deterioration detection and impact on clinical outcomes.

**Amendments**

No protocol amendments have been submitted yet. We will update all relevant parties if any substantial amendments are submitted, and this will be reported in the final manuscript.

**Limitations**

We foresee some limitations that might needed to be considered/addressed throughout this feasibility study and in the full RCT. One is the recruitment bias, as the patient population more likely to consent to take part are the stable patients. If this is the case, we have some strategies in place to address this, such as approaching patients as soon as they are admitted to the ward (e.g. after surgery or intensive care).

Another predicted challenge is that this feasibility study does not include patients without capacity, that might restrict our population. If we find, during recruitment, that there is a high percentage of patients under the Mental Capacity Act (MCA), we might apply for an amendment and Confidentiality Advisory Group (CAG) permission to include these patients in the trial.

**Comparison with Prior Work**
According to our recent systematic review [23], there is no current statistically significant evidence that implementation of AMS impacts early deterioration detection and associated clinical outcomes. The review highlighted the need for more rigorous research to support AMS implementation and deployment, to be achieved subsequently with a full RCT.

**Conclusions**

Our study aims to test the feasibility of deploying our ambulatory monitoring system inside non intensive care wards in a local NHS trust. We will assess if this implementation has any impact on early deterioration detection and clinical outcomes. We will also use this data to determine whether to assess the feasibility and plans for a full randomised controlled trial.

**Abbreviations**

AMS: Ambulatory Monitoring System

BLE: Bluetooth Low Energy

BP: Blood pressure

CAG: Confidentiality Advisory Group

CRF: Case Report Form

CNS: Central Nervous System

ECG: Electrocardiogram

EWS: Early warning score

HCD: Human-Centred Design

HR: Heart rate

ICJME: International committee of medical journal editors

ICU: Intensive care unit

JMIR: Journal of Medical Internet Research

LoS: Length of stay

MCA: Mental Capacity Act

MRN: Medical Records Number
Declarations

Status update


Ethical approval and consent to participate.

This study was reviewed and approved by the Wales Research Ethics Committee 5 on the 24th August 2021 (reference 21/WA/0250). Informed consent procedures are described in the manuscript “Informed Consent” section.

Consent for publication

Not applicable.
Availability of data and materials

Not applicable for protocol. The final study dataset sharing permission and procedure will be outlined in the final report, in accordance to the Sponsor and local NHS Trust requirements in place at the time.

Competing Interests

PW and LT report significant grants from the National Institute of Health Research (NIHR), UK and the NIHR Biomedical Research Centre, Oxford, during the conduct of the study. PW and LT report modest grants and personal fees from Sensyne Health, outside the submitted work. LT works part-time for Sensyne Health and has share options in the company. PW holds shares in the company.

The study Sponsor (University of Oxford) and Funding Body (NIHR Oxford BRC) were not involved in the study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.

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Authors contributions

CA, SV and MS conceptualised and made the initial design for this trial. SG designed the statistical analysis plan. PW and LT approved the final version of the study protocol. CA wrote the initial draft of this manuscript. All authors contributed to and reviewed both the study protocol and this manuscript.

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Not applicable.

Publication and dissemination policy

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by NIHR Oxford Biomedical Research Centre. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.
Sponsorship

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Reporting guidelines

This protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guideline [31], Appendix 3.

References


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**Figures**

**Figure 1**
Nonin Pulse Oximeter

**Figure 2**
VitalPatch

**Figure 3**
A&D UA-1200BLE blood pressure monitor
Figure 4

vHDU tablet dashboard

Figure 5

vHDU client dashboard main screen
**Figure 6**

Trial Flowchart.

a NEWS: National Early Warning Score 2

b AMS: Ambulatory Monitoring System

**Figure 7**

Schedule of enrolment, interventions, and assessments.

*etc. is up until patient stops wearing the devices or is discharged from the ward

**Supplementary Files**
This is a list of supplementary files associated with this preprint. Click to download.

- vHDUPhase5PatientInformationSheetV1.101Sep2021.pdf
- vHDUPhase5Consentv1.001Jun2021.pdf
- SPIRITChecklistdownload8Jan13.doc