Study Title:

Post-Intensive Care Risk-adjusted Alerting and Monitoring (PICRAM) study. Phase 2

Ethics reference – Phase 1: 11\SC\0440

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All investigators confirm no conflict of interests

Signatures/dates:

1. Amendment history

Amendment No.	Protocol Version	Date issued	Author(s) of changes	Changes made
1	1.1	12th October 2012	Julie Darbyshire	Informed consent process updated and clarified
2	1.2	25th January 2013	Julie Darbyshire	Informed consent process updated to include consultee opinion in the event that eligible patients lack capacity to consent for themselves to enter the study.
3	1.3	22nd March 2013	Julie Darbyshire	Inclusion criteria altered to allow any patient discharged from the Intensive Care Unit to be eligible, regardless of length of stay.
4	1.4	1st January 2014	Nicola Blakey	Withdrawal process altered to allow patients to remove the equipment but remain on trial for full fourteen days (or seventeen if readmitted to ICU) in which only observational data will be collected.
5	2.0	16th May 2014	Nicola Blakey	Exclusion criteria updated to include age restriction; previous enrolment with PICRAM; ICU readmissions; post ICU discharge time limit and location (if outside trial remit). Consent to collection of observations data, regardless of wearing the device or not.
6	2.1	20th August 2014	Nicola Blakey	Clarification to exclusion criteria.

2. Synopsis

Study Title	Post-Intensive Care Risk-adjusted Alerting and Monitoring (PICRAM) study. Phase 2.
Study Design	Observational
Study Participants	Patients discharged from adult general intensive care units; Oxford University NHS Trust and Royal Berkshire NHS Foundation Trust
Number of Participants	250 - 500
Planned Study Period	30 months
Primary Objective	To collect a large dataset containing physiological data on patients after ICU discharge and develop algorithms for data collection, cleaning and data fusion.
Secondary Objectives	To demonstrate the feasibility of using commercially available wireless data acquisition systems as the basis for continuous patient monitoring in a manner easily tolerable to ambulatory patients.
Intervention (s)	There are no interventions under study. The study requires attachment of continuous monitoring equipment to patients after discharge from the intensive care units.

3. Background and rationale

3.1 Unmet healthcare need.

The 240 UK ICUs admit about 110,000 patients annually. Data on admissions to 185 ICUs in 2006-8 (ICNARC, Intensive Care Audit and Research Centre database) revealed that 77% of patients were discharged to the ward recovering from their acute illness, but 11% then died before leaving hospital. Most deaths occurred without readmission to the ICU, suggesting that physiological changes preceding agonal events went unrecognised and so treatment to prevent the patient's demise could not be delivered. Failure to recognise and act on physiological indicators of worsening acute illness in acute hospital wards is a generic problem that was recognised over a decade ago and which prompted the NICE clinical guidelines number 50 (2007). These guidelines recommend "Track and Trigger" physiological scoring systems, coupled with a graded response including critical care outreach services (CCOSs). In spite of NICE endorsement and widespread adoption, limited evaluation shows these systems have low sensitivity and positive predictive values, albeit with high specificity. Research commissioned by the National Institute for Health Research Service Delivery and Organisation (NIHR SDO) showed that neither the implementation of "Track and Trigger" systems nor the commissioning of CCOSs per se influenced post-ICU mortality. Post-ICU patients who were regularly reviewed by any member of the ICU team did however derive a survival benefit, but ICUs were very rarely resourced for this, especially outside office hours. Thus there is an unmet need for a far more effective recognition/response system for acutely unwell patients generally, and a specific need for patients discharged from ICU, who after an expensive and traumatic period of treatment still experience a high in-hospital mortality, amounting to over 9000 deaths annually in the UK, some of which are demonstrably avoidable.

The PICRAM project overall will use risk-prediction models applied to data collected during a patient's ICU stay to adjust the alarm thresholds generated by a "wearable", telemetry-based physiological monitoring system attached to the patients after ICU discharge.

This protocol covers phase 2, which involves collecting a large dataset containing physiological data on patients after ICU discharge and developing

algorithms for data collection, cleaning and data fusion. In addition a practical wireless monitoring/data collection system will be developed.

3.2 Importance of the proposed work.

Deaths in patients discharged alive from ICUs represent about four times the annual road traffic fatalities in the UK. These patients are part of a larger group of acutely unwell and deteriorating patients in hospital heavily targeted by policy makers over the last decade. In the current economic climate relatively expensive services above and beyond core healthcare provision, such as CCOSs and follow up of post-ICU patients on the ward, are at risk and more economical solutions are needed.

3.3 Overview of existing technologies.

There are no scoring systems available that estimate the risk of post-ICU death or deterioration at the point of discharge from the ICU. The systems available at present all rely solely on detecting impending problems using changes in vital signs after ICU discharge. The simplest technology to detect deterioration in patients after discharge from an ICU is a paper “Track and Trigger” form onto which vital signs are recorded. Each vital sign (for example heart rate, blood pressure, breathing rate, temperature, oxygen saturation, etc) is turned into a numeric score, and the sum of the scores determines whether further action is needed. This system is very vulnerable to human error, especially in busy, understaffed wards. The scoring systems (Early Warning Scores) used on both paper and paperless systems to convert vital signs to a single linear scale for simple alerting were until very recently all empirical with unknown measurement properties.

3.4 Work/analyses undertaken on existing data

We have already produced an equation to estimate the probability of a patient dying in hospital after ICU discharge using data held by ICNARC on 198,000 admissions to 185 UK ICUs. This model is limited by the dataset we used to derive it, which only contains information about the patient during the first 24 hours of admission to an ICU, as it is primarily used for case-mix adjustment and comparative audit. To overcome this limitation we are constructing two mathematical models to estimate the probability of post-ICU death from detailed datasets covering the whole ICU stay which are available for about 8000 admissions over the last 13 years in Oxford and 3000 admissions over 6 years in Reading, recorded on the Clinical Information Systems (CIS). Techniques

have been developed during other studies to extract, clean and validate data of interest from these databases. The databases held on the CIS's contain a large number of variables, so some selection has been undertaken prior to modelling. We have done this using a systematic review of the literature on variables associated with post ICU mortality and an expert panel.

These risk predictions will be used in phase 2 of the study to develop a technique to combine these estimates with parameters extracted from physiological monitoring to provide patient-specific alerts, so high-risk patients have lower alerting thresholds.

4. Objectives

4.1 Primary Objective

To collect a large dataset containing physiological data on patients after ICU discharge and develop algorithms for data collection, cleaning and data fusion.

4.2 Secondary Objectives

To demonstrate the feasibility of using commercially available wireless data acquisition systems as the basis for continuous patient monitoring in a manner easily tolerable to ambulatory patients.

5. Study design

5.1 Summary of Study Design

Observational design looking at in-hospital vital signs following discharge from the Intensive Care Unit. Patient observational data will be collected by one of two means; either the placing of wearable physiological monitoring equipment and/or the collection of the patients' routine observational data ('Track and Trigger' chart) for up to a maximum of 17 days following ICU discharge.

5.2 Study Participants

5.2.1 Overall Description of Study Participants

All patients discharged from the Intensive Care Unit to ward care from Adult Intensive Care Units in two trusts (Oxford University Hospitals NHS Trust and Royal Berkshire NHS Foundation Trust) will be eligible assuming they meet the inclusion/exclusion criteria listed below.

5.2.2 Inclusion Criteria

- Participant is willing and able to give informed consent for participation in the study; or favourable consultee opinion has been given (see section *Patients who lack capacity to consent to enter the study)*
- Aged ≥16 years (for patients between 16-18 years of age, parents or guardians to be informed and included in the decision to take part where this is possible).
- Discharged from adult intensive care unit.

5.2.3 Exclusion Criteria

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

- Patients discharged for palliative care.
- Patients whose anatomy, condition or prior surgery precludes the use of the wearable monitoring equipment (this does not apply to patients who consent to 'Track and Trigger' data collection only).
- Patients who cannot understand written English and for whom no translator can be found.
- If the patient or consultee is unable to provide written informed consent.
- Patients who have been discharged from the intensive care unit and admitted to an acute hospital within the OUH Trust or Royal Berkshire Hospital and subsequently been admitted back into ICU prior to hospital discharge.
- Patients under the age of 16 years.
- Patients previously enrolled in PICRAM and outside of the data collection timeframe. This timeframe is 14 days for patients who have not been readmitted to ICU; and up to 17 days for patients who have been readmitted.
- Patients discharged to a ward outside of the trial remit.
- If more than 24 hours have passed since ICU discharge (this does not apply to patients who are being approached for consent to the obs chart collection only option).

5.2.4 Removal of the PICRAM equipment

If the patient is wearing the equipment, it will be removed from the patient in the following circumstances:

- If the patient is readmitted to the ICU.
- If the patient has completed the trial:
    - Fourteen days have passed since ICU discharge and they have had no readmissions to ICU during this time.
    - The patient has had a readmission to ICU within fourteen days since starting the trial and a maximum of three days of observational data has been collected following their second ICU discharge (a maximum of 17 days of observational data).
- If the patient requests that the equipment is removed, or withdraws from the study.

5.2.5 Withdrawal

Patients wearing the monitoring equipment can request that this is removed without withdrawing from the study. The research team will continue to collect observational data from the patient's 'Track and Trigger' charts for up to a maximum of seventeen days unless the patient specifically requests otherwise.

All patients will continue to have their data collected until any of the following occur:

- Discharge from the acute hospital containing the ICU (John Radcliffe, Churchill or Royal Berkshire Hospital)
- Death or change of treatment goals to palliative care.
- If the patient requests all data collection to stop.

Patients may withdraw from the study at any time without giving a reason. If they do give a reason, this will be recorded in the study data collection. Data collected up until the point at which they withdraw will be included in the final analysis unless the patient specifically requests otherwise.

5.3 Study Procedures

The study procedures are listed in Appendix A.

5.3.1 Informed Consent

The PICRAM research nurses and other GCP-trained research team members at Oxford and Reading will take consent from patients once they have been identified as ready for discharge by the medical staff. Patients will be given an information sheet to read and will have an opportunity to ask questions or consult their relatives about the study before signing their consent to take part.

5.3.2 Patients who lack capacity to consent to enter the study:

It is common for patients treated on the ICU to be in a state of mental confusion when they are discharged from the unit. Where the researcher feels that the patient does not sufficiently understand what is happening to them, their personal consultee (usually the next of kin but see also section *Loss of capacity during the study* below for more information) will be asked to offer their opinion on whether they think the patient would be interested in taking part in the study. They will be given an information sheet to read and will have an opportunity to ask questions before signing the declaration form.

In the event that a personal consultee cannot be identified, a nominated consultee will be sought. Instances where this may be required include:

- where no family member or friend is willing and able to act as consultee
- where the family or friends live a long distance away and/or are not in frequent contact with the person who lacks capacity
- where the regular carers of the person who lacks capacity are doing so for payment or in a professional capacity (e.g. care home staff or nurses)
- where someone is acting in a professional role (e.g. their GP or solicitor).

Following DH guidance, if the hospital trust does not currently have a panel of suitable consultees which we could access, it is believed that a consultant physician would be best placed to act as a nominated consultee in the absence of anyone available or willing to act as personal consultee. The ward consultants are not in any way connected with the study, and are well placed to have established a relationship with the patient over several weeks of treatment. The nominated consultee will, wherever possible, consult with any available person who has knowledge of the patient, e.g. via telephone with a relative who is unable to visit the patient.

5.3.3 Regaining capacity:

When participants regain capacity they will be asked by research staff for consent to use data already obtained and to continue in the study. Written information will be provided.

5.3.4 Loss of capacity during the study:

We expect that some patients who deteriorate are likely to lose capacity to consent, at least temporarily, because of this deterioration. Since a full evaluation of the value of the monitoring equipment cannot be made without studying these patients, we feel it is justified to continue using the equipment during this phase of their illness.

Under the Mental Capacity Act (2005) a person lacking capacity is defined as someone unable:

- To understand information relevant to the decision
- To retain that information
- To use or weigh that information
- To communicate a decision

The research team will decide on the mental capacity of the patients at each interaction with the patient. The assessment regarding their capacity will be made in line with the Mental Capacity Act 2005. The quality of consent will be ascertained from the responses given during each interaction. Questions will be encouraged and an opportunity to clarify information provided. The research team will be trained in the consent process. They will also complete a good clinical practice course which contains capacity training (provided by the University of Oxford) and the Oxford Radcliffe NHS Trust's Mental Capacity Act (2005) on-line course. The named researcher for the patient will also be consulted, as being best placed to inform the research team of any reservations voiced or exhibited by the patient.

For those patients deemed to lack capacity to confirm their consent to continue in the study, the Department of Health 'Guidance on Nominating a Consultee for Research Involving Adults Who Lack Capacity To Consent' document will be used to guide the identification of a consultee, which preferably will be a 'personal' consultee (a family member or friend). Where this is not possible we will seek a 'nominated' consultee.

A personal consultee will be contacted with the assistance of the ward nurse caring for the patient at the time of deterioration, and will be, wherever possible, the next of kin or a close family member/friend. In most cases where a patient deteriorates, their family will be present or contacted by the ward staff to discuss the change in the patient. A member of the research team will then discuss continuation in the PICRAM study in person wherever possible.

Where a personal consultee is not available, a nominated consultee will be sought. Instances where this may be required include:

- where no family member or friend is willing and able to act as consultee
- where the family or friends live a long distance away and/or are not in frequent contact with the person who lacks capacity
- where the regular carers of the person who lacks capacity are doing so for payment or in a professional capacity (e.g. care home staff or nurses)
- where someone is acting in a professional role (e.g. their GP or solicitor).

Following the DH guidance, if the hospital trust does not currently have a panel of suitable consultees which we could access it is believed that a consultant

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The DH document outlines the role of the consultee in respect to a participant's loss of capacity in the course of a study he/she has already consented to. They advise that the consultee should understand that the participant has already consented to the study, but should be encouraged to consider any factors which they believe may be relevant to this initial consent, in light of their deterioration. The document also advises that it should be made clear that they are not consenting to any further data collection or interventions than those initially consented to by the patient.

When participants regain capacity they will be asked by a member of the research team for consent to use data already obtained and to continue in the study. Written information will be provided.

5.4 Study Assessments

Screening: Local clinical and nursing staff will share a list of patients who are ready for discharge and who they consider suitable for the study based on the inclusion/exclusion criteria. The research team will only approach eligible patients to discuss their participation in the study. Screening logs will be maintained to capture the number considered/discounted/approached.

Baseline Assessments: Following consent, a member of the research team will fit the patient with the monitoring device if they have consented to wear the equipment. At this point they will manually enter some clinical information from the last few days of their stay in ICU. These data are to be determined during Phase 1 of the project.

If the patient has consented to observational chart collection only (not wearing the device):

The research staff will record some clinical information onto the CRF from the last few days of their stay in ICU. The patient will be followed on the Electronic Patient Record system (EPR) and their 'Track and Trigger' charts collected up to a maximum of 17 days post ICU discharge.

Subsequent Assessments: If a study patient is wearing the device they will be reviewed at least once daily (excluding weekends) by a member of the research team who will check that the monitoring device has power (this may require a regular change of batteries), is transmitting correctly and is still acceptable to the patient.

Patients who have agreed to their 'Track & Trigger' chart (observational data) collection only will not be visited on a regular basis by the research team.

6. Definition of end of study

The end of the clinical portion of the study is the date the last patient is either discharged from hospital, dies, completes the study, or withdraws consent. The trial will only be stopped prematurely if required by the ethics committee. There is no provision or need for interim reviews.

7. Interventions

There are no interventions, this is an observational study. Study procedures are listed in Appendix A.

8. Safety

8.1 Electrical safety

Electrical safety. The devices used in the wearable monitor are battery operated and CE marked and present no risk. There are no risks to staff.

8.2 Definition of Serious Adverse Events

The standard definition of a serious adverse event (SAE) is:

"A serious adverse event is any untoward medical occurrence that:

- Results in death,
- Is life-threatening,

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.

- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity, or
- Is a congenital anomaly/birth defect.
- Other important medical events.*

*Other events that may not result in death, are not life threatening, or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above."

It is highly unlikely that this study, which has no intervention, would result in an SAE. Should an event related to the study, of any type, cause patient harm it will be reported to the Chief Investigator who in turn will report to the sponsors and the ethics committee in writing within 15 working days.

9. Interim reports:

The Chief Investigator will submit a progress report to the REC and R&D on request.

10. Statistics and analysis

10.1 Number of Participants

PICRAM will aim to recruit a minimum of 250 patients. It is anticipated that approximately two thirds will be recruited from the Adult ICUs in Oxford and approximately one third will be recruited from Reading.

Population available: Approximately 1500 patients annually are discharged alive from the Intensive Care Units based in Oxford and Reading. 24% of those admitted as surgical cases, and only admitted overnight and of the remainder we would expect between 10-30% (estimate based on other similar studies) of them to refuse consent. Due to the practicalities of the research team cover, we will not be able to recruit patients discharged at weekends or on public holidays thus limiting the possible numbers further.

Sample size: This is not an interventional study so conventional study size calculations are not appropriate. The phase 2 clinical portion of the study will produce an estimated 60,000 data points for each physiological variable, after data cleaning and sampling the time series, more than adequate for model development. We have previously successfully developed or validated novelty detection algorithms on samples of 150-200 patients.

10.2 Analysis of Endpoints

A static data fusion algorithm using the physiological variables recorded by the ambulatory monitors will be developed using machine learning techniques based on probabilistic models of data in multi-dimensional spaces. This builds in part on our previous work with conventional physiological monitoring variables from bedside monitors by applying the techniques to the different set of sensor data we plan to use in this study. This will produce a static data fusion model based on the distribution of the sensor data for our target population.

The development of the static data fusion algorithm has three components. The first is feature extraction. The heart rate is determined from the R-R interval of the ECG waveform or the interval between consecutive salient points on the pulse oximeter photoplethysmogram (PPG) signal. The respiratory rate is derived from the modulation of the PPG amplitude or the sinus arrhythmia on the ECG or the chest wall movement from the integration of the accelerometer signal. The second component is a modified Kalman filter used to fuse estimates of the same physiological variable (heart rate and respiratory rate) acquired from different sensors, to ensure that the best estimate of each variable is used, essentially increasing the signal to noise ratio. The final step is to produce a probabilistic model of “normality” in five dimensions, using the five variables (heart rate, respiratory rate, skin temperature, movement resolved to a single vector from the 3 axis accelerometer, arterial oxygen saturation) from the data acquired from the training data set. The static data fusion algorithm will combine the five variables in order to produce a single estimate of the probability that the variables acquired from the patient being monitored can be considered to be “normal”. This gives the patient’s position on the frequency distribution of the fused variables derived from the training set. Validation will be undertaken using bootstrapping procedures (there is insufficient time and funding available to generate a separate validation dataset). Bootstrapping involves repeatedly randomly selecting a subset of patients and time points in the development set and determining how well the model describes this subset. The distribution of probabilities in this subset should match that of the full dataset.

We are already undertaking analysis of a large retrospective database of patients stay whilst in Intensive Care. We will develop models of patients risk of death on the wards following discharge from ICU from this database. We will also develop probability of normality models from the physiological variables seen in the last three days of a patient's ICU stay.

Using data from the ward ambulatory modelling phase (including data from the ICU stay of the patients we recruit) we will determine how best to combine the estimate of the patient's risk of post ICU death, the probability of normality generated from the last three days of the patient's ICU admission, and the constantly-updated probability generated from the physiological data monitoring after ICU discharge. Various methods for combining the three probability estimates into a single estimate are available, but in practice most aggregation techniques rely on a linear or logarithmic weighted combination of the individual probability estimates, often referred to as a linear or logarithmic opinion pool. These are extensively used in meteorology, economics and other fields where multiple models exist to estimate the probability of the same event or point estimate. We will apply these techniques, determining the optimal weights using the data set derived in this study. At the time of writing we have not decided exactly how these weights should be determined, but this will form part of the research programme.

This combined value (expressed as a probability) will be the value that is compared with a threshold value to determine whether an alert is generated. Using this probabilistic, data driven, approach to alerting has several advantages. It is generic, so an alert simply indicates that the patient's physiology at the point of the alert is outside the expected range for patients who have a similar risk of post-ICU death and ICU discharge physiological status. This means the alerts are not designed to detect specific problems, merely abnormal patterns. In addition, the alert threshold can be set at any probability. In previous work this has been 0.05, so the alerts will be generated 5% of the time. The sensitivity and specificity of the alerts can be predictably modified simply by changing the probability threshold.

11. Ethics

11.1 Declaration of Helsinki:

The Chief Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

11.2 ICH Guidelines for Good Clinical Practice:

The Chief Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.

11.3 Approvals:

The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), and host institution(s) for written approval. The Chief Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

11.4 Data monitoring

The study may be monitored or audited by representatives of the Oxford University Clinical Trials and Research Governance Group for compliance with the Department of Health Research Governance Framework for Health and Social Care 2005.

11.5 Direct access to data/source documents

Direct access will be granted to authorised representatives from the sponsor (Oxford University), host institution(s) and the regulatory authorities to permit trial-related monitoring, audits and inspections.

12. Data handling and record keeping

Detailed data handling and security measures to ensure confidentiality and security are given in the NIGB application document and supporting papers (NIGB Ref: ECC 7-05(f)/2011). These documents are available from the Chief Investigator or NIGB.

13. Financing and insurance

13.1 Funding

This study is wholly funded through the Health Innovation Challenge Fund (HICH) which is managed jointly by the Department of Health and the Wellcome Trust.

13.2 Negligent Harm

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment which is provided.

13.3 Non-Negligent Harm

The University has arrangements in place to provide for non-negligent harm arising from participation in the study for which the University is the Research Sponsor

14. Publication 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 the Health Innovation Challenge Fund: Department of Health and Wellcome Trust. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged. The authors have no vested interest in the results, which will be published regardless of outcome, in peer-reviewed journals. The final version will be agreed by the project management committee before submission.

Appendix A: details of procedures

Consent:
Patients will be offered the chance to participate in the study by a GCP-trained member of the study team. This will occur after firm plans for ICU discharge have been made or within 24 hours of ICU discharge if the patients are discharged out of hours. The opinion of a responsible consultee will be sought for patients who are unable to consent for themselves.

Types of participation:
The patients will be offered the chance to participate in the study by either:
a) wearing the monitoring system and the collection of their 'Track and Trigger' charts for up to 17 days post ICU discharge, or;
b) not wearing the monitoring system and only having their 'Track and Trigger' charts collected for up to 17 days post ICU discharge.

Fitting of equipment:
If the patient has consented to the wearing the monitoring system, the device will be fitted by a member of the research team employed on the study. The equipment will come in three variants: an arm-band mounted recording unit with two ECG leads and a pulse oximeter probe, a recording unit mounted on a chest band that also contains ECG electrodes with a pulse oximeter probe, and a recording unit contained in a bag with a neck/shoulder strap with two ECG leads and a pulse oximeter probe. Functionally these are very similar, the choice will be made during a discussion between the patient and research staff. The patients will be taught how to remove/reattach the devices for washing/care etc.

Daily visits to patients' wearing the monitoring device:
Each patient wearing a monitoring device will receive a daily follow-up visit (excluding weekends and bank holidays) from a member of the research team. The batteries in the recording device will be replaced, and the device's function checked. The research staff will also record details of any practical/comfort problems with the device. A clinical dataset will be recorded by the research staff containing:

- Daily clinical events – defined by a pick list
- Returns to ICU, including treatments – defined by a pick list
- All charted vital signs observation sets, including 'Track-and-Trigger' scores
- Escalation in the frequency of observations
- The date and time of hospital discharge

Final visit to patients' wearing the monitoring device:
The equipment will be removed once firm discharge plans have been made or on the morning of the 14th day after ICU discharge, whichever happens first. The patients will be thanked for their participation in the study and provided with a study completion letter which includes contact details for the research team.
If the patient has had an ICU readmission during the fourteen day trial period, observational data may be collected up to a period of 17 days (ie up to three days' after their second ICU discharge).

Data extraction from the CIS record:
This will occur after a patient is discharged from ICU and the CIS has created an archive of the patient's data (1-2 days after discharge). Accessing the "live" database which is used for clinical care is not required for this phase of the project as all data will be analysed retrospectively. The patient's permission to do this forms part of the consent process.

Data analysis:
In brief, data will be cleaned and checked and then loaded into a study database present on the NHS network servers. After cleaning, the data are anonymised by removing identifiers and converting dates to time periods, and then moved to University of Oxford servers. Three derivatives are then created, a probability of post-ICU death generated from CIS data, a time series of novelty indices created from physiological variables recorded in the last three days of ICU care, and a time series of novelty indices created from physiological variables recorded after ICU discharge. These will be fused to form a composite indicator combining risk of post ICU death with the degree of novelty of the physiological data. This is the required outcome for this phase of the study. All the required confidentiality/data protection permissions are in place (NIGB Ref: ECC 7-05(f)/2011).

As the final recording device specification has not yet been determined it is not possible to define the exact physiological monitoring that will occur however it is likely to include some/all of the following, either recorded directly from the device or manually entered:

- Oxygen saturation
- Heart rate
- Respiratory rate
- Temperature
- Blood Pressure

The device will not be ‘active’ for this project, in that it will record and process data but will not feedback to the ward staff, or patients.

The monitoring equipment will be stored in the secure research facility and cleaned using standard antibacterial cleaning materials used in the Trusts. Maintenance of the devices will be provided by the manufacturers.