1.1 Basic information

Full title	Safer and more efficient vital signs monitoring to identify the deteriorating patient: An observational study towards deriving evidence-based protocols for patient surveillance on the general hospital ward
Short title	Frequency of observations (FOBS)
Protocol version	1.2
Protocol issue date	20th March 2019

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

1.2 Research reference numbers

IRAS Number:	253229
UoP internal reference number:	15188
UOx internal reference number:	HMR02850
UoS internal reference number:	301558
PHT internal reference number:	PHT/2019/70
NIHR Number:	17/05/03
REC Reference	19/SC/0190
CAG Reference	19/CAG/0132 (originally 19/CAG/0070)
CRN CPMS ID	41913
ISCRTN number:	10863045

1.3 Signatures

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 Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

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 investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publically 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 from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date:

Name (please print):

Position:

Chief Investigator:

Signature: Date:

Name: (please print): Prof Jim Briggs

1.4 Version control

Version	Released	Changes since previous version
1.2	16th December 2019	Added CRN, REC and CAG references (section 1.1). Add maternity cover details (section 1.6). Amend dates for data collection in order to facilitate before/after analysis (section 2.4.1.3). Clarification of stakeholder engagement activities (section 2.4.2.2).
1.1	20th March 2019	Add ISCRTN number Amend protocol for selecting hospitals for WP3 (section 2.4.3). Add section 2.4.3.8 on observing malpractice
1.0	19th October 2018	Initial protocol

1.5 Table of contents

1.6 Key study contacts

Chief Investigator	Prof Jim Briggs Centre for Healthcare Modelling and Informatics, University of Portsmouth Tel: 023 9284 6438 Email: jim.briggs@port.ac.uk
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Committees	See section 1.8.2

1.7 Funding

Funder(s) (Names of ALL organisations providing funding and/or support in kind for this study)	**Financial and non-financial support given**
National Institute for Health Research, Health Services & Delivery Research Programme	£867,319.37

Funder(s) (Names of ALL organisations providing funding and/or support in kind for this study)	**Financial and non-financial support given**
University of Portsmouth	In kind contribution of difference between full economic cost and grant
University of Southampton	In kind contribution of difference between full economic cost and grant
University of Oxford	In kind contribution of difference between full economic cost and grant

1.8 Role of study sponsor

The sponsor for this project is the University of Portsmouth.

It assumes overall responsibility for the initiation and management of the study.

1.9 Roles and responsibilities

1.9.1 Oversight Group

1.9.1.1 Role

The role of the Project Oversight Group (POG) is to provide overall supervision for a project on behalf of the Project Sponsor and Project Funder and to ensure that the project is conducted to the rigorous standards set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice.

The main features of the POG are as follows:

- To provide advice, through its Chair, to the Trial/Project Funder, the Trial/Project Sponsor, the Chief Investigator, the Host Institution and the Contractor on all appropriate aspects of the project.
- To concentrate on progress of the trial/project, adherence to the protocol, patient safety (where appropriate) and the consideration of new information of relevance to the research question.
- The rights, safety and well-being of the participants are the most important considerations and should prevail over the interests of science and society.
- To ensure appropriate ethical and other approvals are obtained in line with the project plan.
- To agree proposals for substantial protocol amendments and provide advice to the sponsor and funder regarding approvals of such amendments.
- To provide advice to the investigators on all aspects of the trial/project.

The Oversight Group will meet at approximately six-month intervals to conduct its business. Meetings will be minuted. Email correspondence may be used between meetings to address urgent matters.

1.9.1.2 Membership

Name	Role	Affiliations
Rachel Binks	Nurse Consultant	Airedale NHS Foundation Trust (employed)
Prof Jim Briggs	Professor of Informatics	University of Portsmouth (employed);
Miss Candice Downey	Higher Specialty Trainee in General Surgery	University of Leeds (employed); Leeds Teaching Hospitals NHS Trust (honorary)
Lesley Durham	Director and Lead Nurse	North of England Critical Care Network (employed)
Prof Ruth Endacott	Professor	University of Plymouth (employed)
Prof Peter Griffiths	Chair of Health Services Research	University of Southampton (employed)
Prof Mohammed Mohammed	Professor of Healthcare Quality and Effectiveness	University of Bradford (employed); Calderdale and Huddersfield Hospitals NHS Trust (employed); Bradford Hospitals (honorary)
Mrs Faith Ponsonby	PPI rep	nil
Dr Chris Subbe (chair)	Consultant in Acute, Respiratory and Critical Care Medicine	Ysbyty Gwynedd (employed); Bangor University (honorary)
Prof Peter Thomas	Professor	Bournemouth University (employed)

1.9.2 Management group

1.9.2.1 Role

The day-to-day management of the project is the responsibility of the Chief Investigator. The Project Management Group (PMG) has been set up to assist with this function.

The PMG will meet monthly, normally by teleconference but occasionally by face-to-face meeting. Meetings will be minuted as a formal record of progress.

1.9.2.2 Membership

Membership comprises key individuals from the collaborating organisations, a PPI rep, plus the work package leaders.

The membership is:

- Prof Jim Briggs (UoP, Chief Investigator and WP0, WP5 lead)
- Prof Peter Griffiths (UoS, Deputy Chief Investigator and WP3 lead)
- Dr Peter Watkinson (UOx)

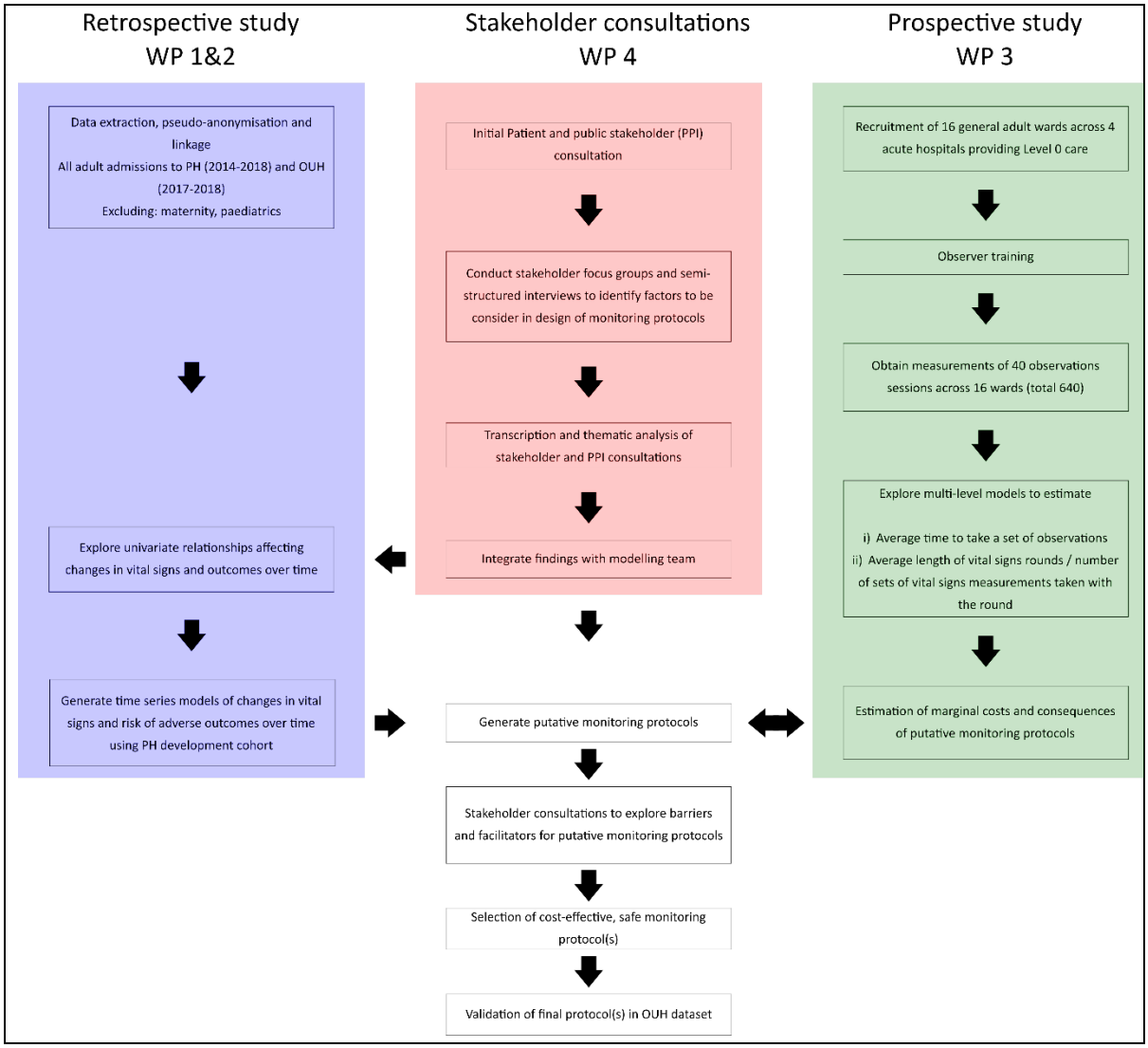
- Prof David Prytherch (UoP)
- Julie Darbyshire (UOx, project manager and WP4 lead)
- Rachel Henning / Verity Westgate (UOx and project administrator)
- Dr Oliver Redfern (UOx, WP2 lead)
- Dr Paul Meredith (PHT, WP1 lead)
- Robert Lawrence (PPI)

Membership may be reviewed by the Chief Investigator as needs demand.

1.10 Protocol contributors

This protocol has been drawn up by Jim Briggs, with contributions from Julie Darbyshire, Peter Griffiths, David Prytherch and Oliver Redfern.

1.11 Study flow chart



1.12 Acknowledgements

This study/project is funded by the National Institute for Health Research (NIHR) Health Services & Delivery Research Programme (project reference 17/05/03). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

2 Protocol

2.1 Background

The frequency at which patients should have their vital signs (e.g. blood pressure, pulse, oxygen saturations) measured on general medical and surgical wards is currently unknown. Monitoring protocols in use at present are based on expert opinion [1]–[3], but supported by little empirical evidence[4]. NICE recommends that all patients in acute hospitals are observed at least every 12 hours and more frequently if abnormal physiology is detected[2]. Early warning score systems, such as the National Early Warning Score (NEWS)[1], provide the means to quantify that abnormality by combining observations into a single score. However, while there is some evidence to support the use of early warning scores to identify patients most at risk of adverse outcomes (e.g. death, cardiac arrest, unanticipated ICU admission)[5]–[7], the associated monitoring protocols are currently based solely on expert consensus[1], [4]. The absence of data to inform clinical practice is a major patient safety issue, as treatment will be delayed if deterioration is missed due to under-observation[8]–[10]. Likewise, over-observation redirects nursing time away from other essential aspects of patient care. Indeed, several studies have shown that adherence to current monitoring protocols is often poor[11]–[14], with many observations missed, particularly at night. This is in part due to available nursing resources[15].

One solution would be to continuously monitor all patients, as is the case on high-dependency wards. However, at present this is costly[4] and a recent systematic review of clinical trials concluded that current evidence is “insufficient to recommend continuous vital signs monitoring in general wards as routine practice” [16].

2.2 Rationale

2.2.1 What is the problem being addressed?

Measuring patients’ vital signs (e.g. blood pressure, pulse, oxygen saturations) is key to safe care on general medical and surgical wards. However, monitoring protocols in use are based on expert opinion [1]–[3], but supported by little empirical evidence[4]. The absence of such evidence to inform clinical practice is a major patient safety issue[3], [8], [13]. Under-observation risks failure to identify deteriorating patients and subsequent delay in treatment[8]–[10]. Likewise, over-observation redirects valuable nursing time away from other essential aspects of patient care[15], [17], [18].

In 2007, NICE recommended that all patients in acute hospitals should have their vital signs measured and recorded at least every 12 hours and more frequently if abnormal vital signs are observed[2]. In addition, they advised the use of a “system” to identify patients at risk of deterioration. In response to this, UK hospitals have tended to use early warning scores (EWS) as the “system”.

In 2012, the Royal College of Physicians London (RCP) introduced the National Early Warning Score (NEWS[1]) to encourage a consistent approach across the NHS. EWS systems, NEWS included, permit a set of vital signs observations to be converted into a single integer score, quantifying a patient’s overall level of physiological disturbance. As part of the NEWS system, the NEWS score is also used to guide how frequently the patient should be monitored[1]. While there is an evidence base to support the use of the NEWS to predict which patients are more

likely to experience adverse outcomes (in-hospital mortality, cardiac arrest, unanticipated ICU admission)[5]–[7], [19], the associated monitoring schedules were based on recommendations from the committee[1]. A recent revision of the protocol (NEWS2) made no significant changes to these monitoring schedules [20]. With no data to support clinical practice, monitoring protocols still vary widely across NHS trusts and may well waste limited staff resources.

This study aims to recommend subsequent observation frequency based on the risk of missing significant deterioration in the intervening period. Prospective observations of nursing staff will allow us to quantify the cost of different monitoring protocols, based on varying thresholds of risk.

2.2.2 Why is it important?

2.2.2.1 Implications for patient safety

There is now substantial evidence that inadequate monitoring is a major patient safety issue, contributing to avoidable deaths and other significant adverse outcomes[3], [8], [13]. The Keogh review into 14 hospital trusts with high mortality rates noted that “a consistent theme throughout almost all of the organisations reviewed was the management of complex deteriorating patients and the monitoring of Early Warning Scores”[9]. The Keogh report is not unique. Numerous reports into patient safety and avoidable deaths have identified the failure to observe or respond to patient deterioration as a significant contributory factor[1], [8], [9], [20]. This is often referred to as “failure to rescue” and is thought to be sensitive to levels of nurse staffing[15], [17], [18]. While progress in statistical modelling techniques and development of electronic medical records will likely lead to more sophisticated and accurate risk prediction algorithms to detect deterioration from vital signs and other clinical data[21], [22], they will not directly provide evidence on how frequently these measurements should be obtained.

2.2.2.2 Implications for staff resources

Whereas under-observation can delay the opportunity to detect patient deterioration and initiate remedial treatment[8], [9], over-observation uses valuable nursing resources that could be better deployed to other essential aspects of patient care. Indeed, compliance with current monitoring protocols is often poor, with many observations missed or delayed[11]–[14]. This is particularly evident at night[12], [23], [24], when staffing is at its lowest. Preliminary results from our current HS&DR “Missed Care” study (ISRCTN: 17930973) show that compliance with vital signs observations is significantly ($p<0.05$) associated with the level of available nursing staff. Estimates of the time required to take observations are scarce, but a survey of 2917 registered nurses across 46 acute hospitals in England showed that one-third had felt unable to undertake all necessary patient surveillance due to lack of time on their last shift[15]. However, even when staffing is sufficient, there are valid clinical reasons why nursing staff will deviate from protocols. Therefore, it is essential to have a monitoring protocol that is achievable on the ward and does not compromise other aspects of care.

With this in mind, and by adapting techniques from our previous work[15], [25], [26], part of this study will be a prospective observation of recording vital signs across a range of wards. This will allow us to understand better the impact on staff workload and factors that might affect compliance with patient surveillance.

2.2.3 Evidence explaining why this research is needed now

Current UK professional guidance[1], [2], [13], [27], [28] suggests that the frequency of monitoring should be determined by some measure of physiological disturbance. One such measure is the National Early Warning Score (NEWS)[5], which provides a simple integer score based on the degree to which a patient's vital signs are outside the normal range. There is now some evidence to support its ability to predict a patient's risk of adverse outcomes[5], [7], [29]–[31], albeit with high false positive rates. However, we were unable to identify any large studies to support the vital sign monitoring intervals suggested by the original guidelines from the Royal College of Physicians[1]. For example, the NEWSDIG recommended at least hourly observations for any patient with acuity of NEWS 5 or more. To put this recommendation into context, the surveillance protocol for patients with NEWS 5 at Portsmouth Hospitals is 4 hourly, and there is only 50-70% compliance with protocol at this frequency, for a number of potentially legitimate reasons. Without an evidence base, compliance is seen mainly as a superficial mechanistic proxy for quality of care.

As discussed above, under-observing patients runs the risk of missing early signs of deterioration, but taking repeated measurements in patients is also a drain on valuable staff resources. Obtaining vital sign measurements is one part of the "chain of prevention"[32], necessary to effectively recognise and manage the deteriorating patient. For example, a national enquiry into patients who underwent cardiopulmonary resuscitation in hospital[8] showed 20-40% did not have a clear monitoring plan in the 48 hours prior to the event, despite over 70% having significant physiological abnormalities. It is therefore crucial for safety that patients' observations are correctly targeted and escalated appropriately. However, this must be balanced with other negative consequences. For example, obtaining observations can be disturbing for patients[33] and might be associated with negative health outcomes if they contribute to sleep disruption[24], [34]. Monitoring protocols that demand observations when staff deem it futile in particular situations, in particular if these may have adverse effects, risks delegitimising the EWS protocol.

One solution would be to implement continuous monitoring for all patients. However, systems for continuous monitoring are at present costly[4] and there is scarce evidence that they improve patient outcomes [16], [35], [36]. There are also legitimate concerns that continuous monitoring might introduce other risks, such as loss of nurse interaction with patients to pick up soft signs, alarm fatigue, and technology failures (e.g. detached monitoring devices). A recent systematic review and meta-analysis[16] of randomised trials of continuous and intermittent observation concluded there was "insufficient evidence to recommend continuous vital signs monitoring in general wards as routine practice". Despite a number of trials of wearable devices to measure vital signs outside intensive care[37], [38], no device is capable of measuring all vital signs required to generate the NEWS (e.g. blood pressure is rarely possible). In the UK, we found one current randomised controlled trial (ISRCTN: 60999823) of a continuous monitoring device, but this is restricted to surgical inpatients and will only measure heart rate, respiratory rate and temperature. A prospective cohort study (SNAP40-ED) aims to trial the use of a wearable device to detect deterioration in patients in the emergency department [40].

We will use our combined database to investigate the variation in the rate of critical changes in vital signs over the course of a patient's hospital stay and how this

relates to the risk of adverse outcomes. This study will be the first to provide evidence to clinicians on how frequently to observe patients, given their current degree of physiological instability, in order to spot deterioration early and mitigate its effects.

We will design monitoring protocols to most efficiently detect significant patient deterioration, whilst minimising unnecessary monitoring. We will also be able to calculate the total number of observations required for each ward on a typical day, when testing the performance of these protocols in each validation cohort (Oxford). Combining these totals with our estimates of staff workload generated by prospective observation of recording and responding to vital signs will enable us to model the costs and consequences of implementing a protocol on a ward, given its average acuity.

2.3 Research question/aim(s)

This study aims to recommend subsequent observation frequencies based on the risk of missing significant deterioration in the intervening period. Prospective observations of nursing staff will allow us to quantify the cost of different monitoring protocols, based on varying thresholds of risk. We will exploit a large database of vital sign observations, laboratory data and diagnostic codes from 2 acute hospitals (Oxford and Portsmouth), supplemented by prospective observation in 4 hospitals to estimate nursing workload associated with these observations.

The objectives are to:

- Develop a data warehouse of linked admission records with information on patient demographics, vital signs observations and adverse events (cardiac arrests, unanticipated ICU admissions, in-hospital mortality).
- Estimate the rate of clinically significant changes in vital signs over the course of patients' admission.
- Explore the relationship between vital signs and adverse outcomes over time.
- Determine the extent to which relationships between the time to deterioration and risk of adverse outcomes vary across different patient groups (e.g. medical and surgical; elective and non-elective surgical patients; age; co-morbidities).
- Organise stakeholder (nurse, doctor, patient) events to identify additional factors relevant for selecting an optimal monitoring protocol.
- Undertake prospective observations of nursing care to estimate the time taken to obtain and respond to vital signs observations, using techniques adapted from previous work[26] and our HS&DR funded "CLECC" study[25].
- Derive a set of simple monitoring protocols by identifying any threshold effects between the risks over time predicted by our models.
- Use estimates from our observational work to model the marginal costs and consequences for all protocols with better or equal performance to the current protocols at Portsmouth and Oxford for detecting deterioration.
- Use results to inform design of a prospective clinical trial.

2.4 Study design/methods

This study comprises two observational studies, one retrospective and the other prospective. Additionally we will undertake focus groups with key informants. These

will be conducted at large acute NHS hospitals, with the overall aim of deriving a safe, achievable, evidenced-based protocol for monitoring patients' vital signs on the general hospital ward.

2.4.1 Retrospective analysis

2.4.1.1 Setting and context

The retrospective study will take place across all general adult wards (excluding maternity, intensive care and other wards where continuous monitoring is in regular use) in Portsmouth (PHT) (approx. 32 wards and 1200 beds) and Oxford University (OUHT) (approx. 58 wards and 1000 beds) NHS trusts. PHT and OUHT both provide acute services to populations in excess of 650,000 people. Portsmouth is in the top 20% of areas in England for deprivation (deprivation index 27.1, average for England 21.8)[39] with lower than average life expectancy for men and women. In contrast, Oxfordshire is in the top 20% most affluent areas (deprivation index 11.5) [39]. In 2015-2016, PHT was placed 120 out of 135 acute trusts in England, according to the standardised hospital mortality index (SHMI)[40], with OUHT placed at 29. However, both were determined to have a 30 day mortality "as expected".

2.4.1.2 Sample and recruitment

The retrospective analysis will be based on routinely collected data at each site, encompassing all hospital in-patients, excluding those:

- under the age of 16
- in maternity, paediatric and high-dependency wards
- who do not have any clinical signs such as vital signs or blood tests recorded

2.4.1.3 Data collection and sampling

Data for the retrospective study will be derived from repositories of vital signs obtained using the Vitalpac™ (PHT) and SEND (OUHT) systems, both of which enable nursing staff to record physiological measurements at the bedside using electronic devices[41], [42]. At both sites, we will obtain all measurements of heart rate, respiratory rate, systolic and diastolic blood pressure, temperature, oxygen saturations, current oxygen therapy (device and flow rate) and level of consciousness (on the AVPU scale). At Portsmouth, Vitalpac™ implements the National Early Warning Score (NEWS)[1], which is used to recommend the time to the next observation, based on a minor modification of guidelines from the Royal College of Physicians[1]. At Oxford, SEND uses the Centile Early Warning Score (CEWS)[43] to recommend the time to the next observation. The recommended time to next observation used in each system will also be collected, as it could impact our modelled risk estimates.

Vital signs data will be linked to the local patient administration, laboratory, theatre management, intensive care and cardiac arrest databases. This will provide information on patient demographics (age, co-morbidities), in-hospital mortality, unanticipated ICU admissions (i.e. those resulting from deterioration on the wards) and cardiac arrests. In this project, we expect to extract vital signs data (approximately 6 million observations from 200,000 patient admissions) from

completed admissions from both sites over a 10-year period (2010-2020) from PHT[1]. A compatible data set from OUHT will be extracted from a 4-year period (2017-2020) in which the SEND system had maximal coverage of OUHT[2].

We will also extract blood test results from laboratory systems to allow us to better model the risk of adverse outcomes and permit sub-group identification (e.g. patients with chronic renal failure).

2.4.1.4 Data analysis

Intermittent observations of vital signs show some specific features that should be properly accounted for in any modelling framework. They are longitudinal in nature, i.e. multiple observations are taken over the same sample unit (patients) over time, and are multivariate as multiple variables (e.g. pulse, blood pressure) are jointly measured at each observation time. These data also show serial dependence and high correlation between measurements within patients. A natural way to account for these features is to use State Space Models (SSMs), as they provide a framework of flexible time-dependent models. SSMs cast multivariate distributions (see [44] for a review), accounting for the serial dependence, heterogeneity between patients, and transitions between states that depend on other covariates. We will use this modelling approach to estimate changes in vital signs over time and the probability of adverse events (e.g. in-hospital mortality, unanticipated ICU admission, cardiac arrest).

Our reference modelling setting will be the multivariate Hidden Markov Model (HMM)[45], a well-known type of SSM. Its use is justified by its versatility and mathematical tractability:

- the availability of all moments
- the likelihood computation is linear with respect to the number of observations; the marginal distributions are easy to determine and missing observations can be handled with minor effort
- the conditional distributions are available, outlier identification is possible, and forecast distributions can be calculated

For vital signs data collected during routine monitoring on the ward, there are additional clinical processes that have the potential to introduce bias our analysis. Firstly, these data have been collected in the context of existing monitoring protocols, where the time to the next observation is determined by an early warning score (NEWS[1], [5], Portsmouth; CEWS[43], Oxford). Secondly, previous work[12] by our group and others shows that in practice, nursing staff often undertake “observation rounds”, in the early mornings and evenings. These observations result in deviations from the patient-specific schedule dictated by the early warning score. Thirdly, there will be observation sets taken when patients report additional symptoms or are deemed to “look unwell”; information that will not captured in available variables in our data set.

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[1] The period has been extended back before 2014 in order to carry out a before/after analysis of the introduction of new procedures at PHT.

[2] Both the PHT and OUHT periods have been extended to include data that will be available for analysis before the end of the project.

Within the HMM framework, it is relatively straightforward to address these issues. We will build a structured conditional model in which variation in clinical practice affects the distribution of the observed data and/or the evolution of vital signs observations over time, starting from a multivariate model in which the distribution of the observed data is approximated by a (time-varying) mixture of multivariate continuous distributions (whose components reflect the vital signs observations), This conditioning effect can be modelled using regression models. For example, we will incorporate time-to-next-observation and time of day to model changes between mixture components over time[46]. These mixture components provide a flexible mathematical tool to account for heterogeneity, but may also have a physical meaning reflecting health conditions. As adverse events can arise during the observation period, we can include a further absorbing mixture component which reflects adverse events and has a binary distribution[47]. Finally, we can account for different lengths of longitudinal observations by defining a pattern mixture model as shown by Maruotti[48].

We will also examine the effect of patient-level factors on the estimates generated from our models, including acute diagnoses and co-morbidities. We will use our stakeholder consultations to identify a number of key subgroups (for example, patients with Chronic Obstructive Pulmonary Disease, COPD) where the relationship between deterioration and vital signs could differ substantially from other patient groups[49][49]. We will then introduce these sub-group categories (i.e. point in clinical pathway or diagnosis) into our models to see whether this results in significantly different estimates of risk. Should this be the case, we will examine how these factors could be incorporated into our suggested observation schedules, without introducing a complexity that would be impractical to implement in most trusts, particularly those without electronic vital signs systems. We will explore the potential to obtain additional data to consider the point in the patient's clinical pathway (e.g. transfer from ITU/HDU to a general ward, or in the immediate post-operative period) in a similar fashion.

2.4.1.5 Data management

Study data on vital signs, patient admissions and adverse outcomes will be extracted on site by Portsmouth and Oxford University Hospitals Trusts and all patient-identifiable information will undergo local pseudo-anonymization. These de-identified data will be held in secure clinical data repositories, which will be subject to additional security checks and only be accessible to relevant members of the research team for the purposes of the study. Data sets for analysis will be generated from the repository, using algorithms developed as part of the HAVEN (ISRCTN12518261) and Missed Care (ISRCTN17930973) projects to link them. All transfers of individual patient data will use secure data transfer protocols.

2.4.2 Consultation stages

2.4.2.1 PPI

We will run focus groups for patients to identify the factors that they believe should be taken into account in designing monitoring protocols.

We will ask them to consider the following questions:

1. What factors influence their thinking on how frequently a patient should be monitored?

2. How can clinical staff best communicate to a patient the factors affecting their monitoring frequency and differences they might notice from that of other patients?
3. How should monitoring protocols strike a balance between the patient's safety and their inconvenience (e.g. waking from sleep)?
4. What can be done in the future to improve the way in which observations are made?
5. Is there a difference to be made between how frequently vital signs should be taken and how frequently escalations in care should happen?

Each group will be run by a trained facilitator. The patient groups will alsoin addition be attended by at least one of our PPI representatives. After obtaining appropriate consent from participants, the discussions in each focus group will be audio recorded. The recordings will subsequently be analysed by two further independent assessors. Combining these notes with those from the facilitator, we will undertake a thematic analysis to identify key factors in response to the questions above.

The results of these focus groups will be used to inform the design and refinement of our monitoring protocols. Participants' feedback will also be incorporated into the final report and other publications.

2.4.2.2 Stakeholder engagement (focus groups and interviews)

Early in the project, we will engage with key clinical stakeholder groups (nurses, doctors, healthcare assistants) to identify additional factors to be considered in designing monitoring protocols. We will collect views from these key professional groups though focus groups, interviews, ad-hoc discussion, and facilitated/mediated Twitter Chat sessions. Focus groups will contain a mix of senior and junior staff from each discipline. Nursing staff will form a substantial proportion, as this group is most directly involved in obtaining and responding to vital signs observations. We will ask them to consider the following questions:

1. What factors are most important in determining observation frequency?
2. What factors are most likely to affect adherence to current monitoring protocols?
3. How are "observation rounds" incorporated into current monitoring protocols?

Semi-structured discussions (for example, interviews and Twitter Chat sessions) with staff will be structured around topic guides that will be developed/evolved from focus group and observation results.

Towards the end of the project, further focus groups will be held to report our results and proposed observation protocols to key stakeholders. We will address the following questions:

1. What are the potential technical barriers to implementing these protocols, given the range of systems for recording vital signs observations (both electronic and paper-based)?
2. What are the potential barriers to integrating these protocols into current nursing workflows and workloads?
3. What modifications to the protocols could facilitate implementation?

In addition, we will revisit areas previously observed to confirm themes identified through these later focus groups.

This mixed methods approach will enable triangulation of the qualitative data collection, developing a richer understanding of the process of patient monitoring. This in turn will enhance the interpretation of the quantitative results from other phases of the project.

Therefore the results of these focus groups will be used to inform the design and refinement of our monitoring protocols. Participants' feedback will also be incorporated into the final report and other publications.

2.4.3 Prospective Observational Study

2.4.3.1 Study setting

The observational study to provide reliable estimates of the nursing work involved in measuring vital signs[3] will be undertaken in 16 adult general wards at 4 acute general NHS hospital Trusts. ~~Our 2 core study sites (see above) both use electronic recording for vital signs. We will therefore seek to recruit 2 additional Trusts that retain paper and pen recording.~~

2.4.3.2 -Sample and recruitment

We will undertake observations on wards of the two study sites and two additional sites recruited from volunteer Trusts within the Wessex region, selected with a view to sampling a variety of approaches to the recording of vital signs and activation of the EWS alerts.

Eligible wards are those classified as adult general (medical / surgical) wards. As there is no generally accepted precise definition of this, we will ask participating Trusts to identify wards against the following criteria:

i) Adult (18+) patients. Wards that occasionally admit adolescents of younger age would remain eligible provided this was not a common occurrence.
ii) Open at weekends with most patients experiencing overnight stays of one day or more
iii) Ward provides Levels of Care 0, or 0 and 1

Exclusions

i) Wards which routinely cater for large number of younger people (<18)
ii) Wards in which a significant proportion of patients require protective isolation
iii) Wards that are intended to exclusively provide Level 1+ care
iv) Wards where the risk of acute deterioration is low or where the primary reason for continued hospital stay is not medical / surgical treatment / recovery (e.g. rehabilitation units, other post-acute wards)
v) Wards where full vital signs measurements are not routinely taken
vi) Small wards

[3] Because of the potential confusion that arises in this observational study where we observe nurses taking observations, we will use the term 'vital signs measurement' and 'vital signs rounds' etc. to refer to nurses making vital signs observations of patients. The term 'observation' will be used for researchers' observation of nursing care.

At each Trust, we will ask the local PI to identify all eligible wards to take part in the study. We will also ask them to collate basic profile information to describe Trust and ward level policies / practices relating to vital signs measurement and to determine willingness to take part.

We will randomly select 4 wards from each Trust which to undertake the research and initially we will consent ward managers to take part. If a selected ward manager does not consent we will randomly select another ward.

We will organise a meeting with the ward manager for each ward and provide detail about the study. We will also use this meeting to gain more information and to characterise in detail the approach to taking vital signs measurement in each participating ward (e.g. use of EWS and local protocols, scheduled or customary observation rounds, staff who undertake vital signs measurements). Where we have access to electronic vital signs observation data we will use this to identify patterns of vital signs measurement in the participating wards.

For each ward we will undertake 8 hours of observations in 4 sessions, aiming to capture at least 10 sets of vital signs measurements per 2 hour session. This will result in a *minimum* sample of 640 (4 sessions x 4 wards x 4 hospitals X 10) sets of observations. Based on these preliminary investigations, we will define observation schedules for each ward *a priori* designed in order to estimate the nursing time involved in taking a representative sample of observations and aiming to observe a range of staff and both 'responsive' (scheduled according to individual patient need) and routine (rounds) vital signs measurement. Where vital signs rounds mean that activities are clustered at specific times of day we will split observation sessions in order to capture more than one round on the same day where feasible.

During the observation sessions, we will seek to recruit all nurses working on the ward. Explicit consent will be gained on behalf of staff from the ward manager who agrees to take part. All staff on shifts chosen for observation sessions will be given clear opportunity to opt out and so individual consent will be implied & recorded, based on ward rosters.

Patients and relatives will be informed about the study through posters displayed on the ward, information leaflets distributed during sessions and personal explanations by the researcher and / or nurse being observed where relevant. No personal information will be collected from or about patients although basic contextual information that can be readily observed will be recorded, for example the patient's position and presence of relatives while the vital signs measurements are being taken.

2.4.3.3 Observation session

Observations will be undertaken by one or more trained researchers, who will act as non-participant observers. They will position themselves to be able to discreetly observe a group of patients whose vital signs observations will fall due, or else discreetly shadow a nurse who is about to undertake a vital signs observation round.

We will adapt tools and techniques from the HS&DR funded 'CLECC' study [25] and Wong et al.[26] Data will be recorded on a tablet device using software designed for recording nurse patient interactions on wards (QITool) with records taken at both the session level and the 'interaction' level (in this case a set or group of vital signs measurements). For each observation session we will record the number of patients and the number and grades (RN band 5 and above, HCA and other assistant staff

band 1-4) of all nursing care staff on the ward. For each patient whose vital signs are recorded we will assign a session-specific identifier and record basic details that can be discerned from distant observation, such that would be available to any visitor to the ward (for example position and the presence of visitors). The type of staff taking vital signs measurements will be recorded and categorised (e.g. registered nurse, care assistants).

We will record start and finish times for both vital signs rounds and individual vital signs measurements. For a vital signs 'round' an interaction record will be opened with a start time recorded when the nurse begins to assemble the necessary equipment and ended when the nurse moves away from the patient bed space and engages on another task (i.e. other than taking vital signs measurements from the next patient) unrelated to vital signs measurements. Therefore, each set vital signs measurements will be clustered with a vital signs 'round' which will include one of more sets of vital signs measurements. Observation sessions will continue for 2 hours with observer discretion to extend the session if the required number of vital signs measurements have not been recorded.

Observers will not intervene in care but should they observe practice that risks causing the patient harm they will alert the nurse in charge.

2.4.3.4 Sample size

Based on the standard errors of mean times observed in the study by Wong et al.[26] (a study with a similar clustering structure), the minimum sample size that would be acquired (640 sets of observations) would allow us to estimate a mean observation time with a precision of approximately +/- 10%. This precision will be increased by including more vital signs observations if this proves feasible within the scheduled observation 'budget' and, as we have more clusters and fewer observations per cluster than the Wong study, this is likely to be a conservative estimate of precision.

2.4.3.5 Observer training

The observer will be trained prior to undertaking observations using protocols and training material from Wong et al[26] and the QITool. We will also undertake intermittent reliability tests to ensure there is no deterioration in observer performance over time. Although we cannot easily discount the effects of observers on nurses' performance of vital signs measurements, we will seek to undertake observations in as unobtrusive fashion as possible and emphasise to participating staff that we are not evaluating their practice.

It seems most likely that observer effects will increase diligence, which may lead to increased estimates of the time taken to obtain vital signs measurements. For those hospitals using electronic vital signs recording, we will analyse the routine data obtained from the retrospective analysis, by looking for evidence that incomplete observations were less frequent during observation periods. We will consider the potential implications of any observer effects through sensitivity analysis in our economic modelling

2.4.3.6 Data analysis

We aim to estimate the time taken to undertake vital signs observations and to understand systematic sources of variation that may influence the 'burden' of vital signs observations. We will determine the extent to which estimates of time taken

are sensitive to predictable factors and use this as the basis of a sensitivity analysis when estimating associated costs.

Our data will consist of a series of interactions that represent a complete set of vital signs measurements. Measurements will be grouped into rounds, where one or more sets of vital signs observations and associated actions are recorded. Additionally, there may be other actions associated with vital signs measurement that we are not able to record because they do not occur within vital signs rounds.

We will estimate the time taken for vital signs measurement in 2 ways.

i) Average time to take a set of observations (based on individual sets of measures)
ii) Average length of vital signs rounds / number of sets of vital signs measurements taken with the round

We will use multilevel mixed-effects models to determine the influence of patient, nurse, ward and hospital factors on the length of observation. Factors considered will include the average number of measurements taken in a round in order to identify efficiencies that may be associated with undertaking formal observation rounds. The coefficients from these models will be used to estimate adjusted (conditional) mean work (time) associated with taking observations based upon these factors. We will use our stakeholder consultations (see main protocol) in order to identify whether any further allowances should be added to estimated times based on unobserved work associated with vital signs measurements. These factors and the differences between estimated values will be used in sensitivity analyses in the economic analysis (below)

2.4.3.7 Data management

The QITool provides a platform for data recording with automated secure upload to a central server. This server and the associated databases are located at and managed by the IT team of the University of Southampton. Both the tablet, the data transfer and the centrally stored files are encrypted with password protected access available to members of the project team and database managers only. No personal data is stored or transferred. All data will be retained as part of a central database with extracts made for analysis for this study. These extracts will be processed on individual staff computers and may be shared more widely across the project team but will always be stored on password protected and encrypted machines. Again, no personal data will be contained within these files and codes identifying wards and trusts will be stored separately and are only accessible by the project team. These codes, which link back to wards, will be erased at the earliest possible opportunity, depending upon the requirements of other regulatory approvals and (for example) requirements to report accruals to the CRN Portfolio.

2.4.3.8 Malpractice

While undertaking observations of nursing staff measuring patients' vital signs, the delivery of an unacceptable standard of clinical practice may become apparent or be strongly suspected by one or more members of the research team. Such incidents will be classified as either sub-optimal or unsafe practice.

2.4.3.8.1 Sub-optimal practice

Observers may witness events which they do not consider represent 'best practice', but which do not pose a direct and immediate risk to patients or others. In such

circumstances researchers will use a ‘manager test’ in order to determine how to proceed.

The manager test: If the researcher were working clinically as a registered practitioner in the clinical setting and observed the incident in question (incompetence, misconduct or other unsafe practice), is it of such severity that they would they feel obliged to report the incident to the manager of the individual involved? If yes, this is defined as unsafe practice, and the guidelines below would be followed. If no, no further action would be taken.

2.4.3.8.2 Unsafe practice

This is defined for the purposes of this study as incompetence, misconduct or other unsafe practice that a registered practitioner would feel obliged to report to the manager of the individual involved if working in a practice capacity. (Note this is a higher test than whether a professional would simply discuss the incident with that person directly). This will include any behaviour that is clearly illegal or dangerous, placing individuals at direct risk of harm.

Unsafe practice is likely to be a very rare occurrence. If it does occur, the research team member will take the following actions:

If unsafe practice is observed/suspected during an observation:

1. Halt the observation.
2. Explain to the staff member that the practice must be reported due to its potentially serious nature and it may not be possible to maintain anonymity.
3. Outline the process for doing this (use local Trust reporting system).
4. Terminate the observation session and follow the guidelines below.

2.4.3.8.3 Guidelines for taking further action:

- The patient/visitor/staff member is given the required time and support and empathic approach to the issue.
- The patient/visitor/staff member is given a thorough explanation of the course of action required to ensure the event is fully investigated and acted upon.
- The patient/visitor/staff member is treated with respect and dignity at all times.
- The researcher maintains responsibility for keeping the patient/visitor/staff member informed and involved where appropriate, until the incident is reported to senior trust personnel.
- The patient/visitor/staff member is offered support and guidance in line with research governance.
- The researcher collates the necessary information from the patient/visitor/staff member to report to the most appropriate senior personnel in order to take further action.

Although this response would breach the assumption of confidentiality, it is considered that the potential benefit to others should outweigh the desirability of maintaining anonymity

2.4.4 Generating putative monitoring protocols

In the later stages of the project, the findings from the observational studies and stakeholder consultations will be brought together to create and validate protocols. The primary outcome of WP2 will be a data-driven schedule for monitoring patients’

vital signs, based on their current acuity. Using estimates from our state-space models we will explore the following:

1. Given a level of physiological abnormality what is the average chance that this value will be higher at any given point of time in the future?
2. Given a level of physiological abnormality, what is the average chance that an adverse event will occur at any given point of time in the future?

We will explore grouping patients using early warning scores (e.g. NEWS, CEWS). We aim to identify points in time where there is a significant risk that patients' vital signs have changed adversely. We will manually inspect these to look for threshold effects across time. For example, for low-acuity patients who deteriorate (i.e. increase in acuity), what is the earliest point in the future that this could be detected? A limitation of the study is that we can only explore average rates of deterioration, as we do not have access to data on interventions or individual diagnoses. However, we will explore how our estimates change in subsets of patients (e.g. elective surgery, emergency surgery and medicine). Exploring the data in this way will permit us to propose different monitoring schedules, designed to increase the likelihood that a new vital signs observation picks up deterioration if and when it happens.

We will also undertake a variety of computer simulation studies, where estimates from our models are used to simulate the performance of current monitoring protocols (e.g. those proposed by the RCP[1]) and our new ones. This will allow us to quantify: (a) the number of observations required; and (b) the risk that deterioration will be missed.

The estimates obtained from WP3 will then be used to model the marginal costs and consequences for all protocols whose performance is equivalent to or exceeds that of the current NEWS protocol for detecting deterioration. In addition, we will model potential reductions in mortality and changes in ICU use (e.g. admission/acuity at admission/length of stay) associated with improved detection. Finally, stakeholders will be consulted to review the protocols and comment on their likely effectiveness.

2.4.5 Economic analysis

Data from the observational studies will be used to determine the additional staffing costs associated with any proposed observation schedules. Incremental costs associated with proposed new protocols will be compared with both current protocols and current practice (estimated using observation frequency and compliance with current protocols from wards in sites using electronic recording).We will estimate daily and annual staffing costs associated with taking observations for

i. Current observed observation frequency
ii. Current planned observation frequency (current protocol)
iii. Alternative observation schedules (alternative protocol)
iv. Alternative observation schedules allowing for non-compliance.

Current observed observation frequency and planned observation frequency will be determined by records of complete and omitted vital signs observations. The alternative observation frequencies will be estimated by using current vital signs observations to simulate observations schedules according to the new protocols.

The cost of each observation regimen will be estimated by multiplying the cost of staff time (hours) associated with the regimen (length X number of observation estimated from the profile of NEWS scores on similar wards) by the appropriate unit

costs derived from current (at time of study) Agenda for Change pay bands, adjusted for on-costs and overheads (see table below for examples; reference years will be the latest available updates) following established methods [50].

Costs				Source
RN hours	Employed / Bank staff	Band 5 Band 6	£35 £44	CURTIS, L. & BURNS, A. 2016. Unit Costs of Health and Social Care 2016, Canterbury, PSSRU, University of Kent. [50]
HCA hours	Employed / Bank staff	Band 2 Band 3	£22 £28	

We will initially assume that the grade of staff taking observations is unchanged, so if 50% of observations are currently undertaken by Band 2 HCAs we will assume 50% of observations under the new regime are also undertaken by Band 2 HCAs. The estimate of staff costs will be weighted accordingly.

We will estimate costs for regimens assuming full compliance and partial compliance based on currently observed rates. As we know that compliance with vital signs observations is highly correlated with the scheduled frequency we will use adjusted and unadjusted rates such that (for example) we assume that 80% of all observations are taken under both old and new regimes (unadjusted) or we stratify estimated compliance by observation frequency so that (for example) 100% of 12 hourly observations are taken whereas 50% of 4 hourly observations are taken. As a secondary analysis we will also consider changes in staff skill mix, for example if a new regime increases the number of observations then we might assume that all additional observations are undertaken by Band 2 HCA.

Cost differences will be calculated by determining the difference in cost between two regimes. Marginal consequences will be estimated differences in resource use (time and grade/type of staff conducting observations and follow-up). We will derive estimates of possible benefits (e.g. reduced mortality, length of stay in ICU) by relating the time of detection of deterioration associated with a given monitoring protocol, to coefficients derived from published studies that report the benefits of early detection and/or increased frequency of observations[51]–[54]. The incremental benefits of each proposed protocol will be compared to the incremental staffing costs and a cost per life saved estimated. We will also estimate QALYS on the assumption that life expectancy and quality of the ‘lives saved’ will be similar to that of the group of patients who died using standard estimates of QALE adjusted for patient demographic factors[55]. If reductions in ICU admissions, hospital stay or other resource use are identified as outcomes these will also be considered in the estimated cost differences. These will be costed using Department of Health Reference Costs 2015-2016 (or latest available update).

All variables included in the economic analysis are estimated subject to (parameter) uncertainty, while model type, the models and assumptions made in building them are subject to methodological and structural uncertainties. We will address methodological and structural uncertainty through scenario analyses testing the robustness of the results to model type, scope and other key structural assumptions. Parameter uncertainty will be addressed through deterministic sensitivity analyses

(using statistically-derived limits for input variables, where possible), scenario analyses (using alternative data sources, if available) and (data and model permit) probabilistic sensitivity analysis. The estimates of cost effectiveness derived in this way will further inform the assessment of feasibility of the observation protocol. While such estimates would need validating in a trial, this preliminary modelling will inform judgements as to whether a given monitoring protocol has the potential to be judged cost-effective

2.5 Ethical and regulatory compliance

The research is not an interventional study and therefore poses negligible risk to patients or other participants. It nevertheless requires ethical review.

2.5.1 Declaration of Helsinki

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

2.5.2 Guidelines for Good Clinical Practice

The Investigators will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

2.5.3 Research Ethics Committee (REC) and other Regulatory review & reports

Before the start of the study, a favourable opinion will be sought from a REC for the study protocol, informed consent forms and other relevant documents e.g. advertisements.

Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site.

All correspondence with the REC will be retained.

It is the Chief Investigator's responsibility to produce the annual reports as required.

The Chief Investigator will notify the REC of the end of the study.

If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination.

The Chief Investigator shall submit on request, a progress report to the REC Committee, host organisation and Sponsor. In addition, an End of Study notification and final report will be submitted to the same parties.

2.5.4 Regulatory Review & Compliance

Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that appropriate approvals from participating organisations are in place.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment.

2.5.5 Peer review

The research has been peer reviewed as part of the NIHR funding process.

This protocol has also been viewed by two experts drawn from the membership of the Project Oversight Group.

2.5.6 Patient & Public Involvement

Two PPI representatives have been recruited to the project team. One is a co-applicant and will be a member of the Management Committee.

The frequency with which patients are monitored while in hospital is a major area of public concern following the Francis Inquiry and other reports. This proposal has been developed with this concern in mind. During the preparation of this application, we have involved two experienced expert patients. They were asked to provide insight into a patient's perspective on the issues.

Issues raised included:

- A patient might deteriorate quite significantly in the gap between observations, but to keep patients under too frequent observation would create a high workload for nursing staff as well as inconvenience to patients (especially if they have to be woken up during the night). What are the trade-offs between frequency and sleep?
- There are issues surrounding a patient's understanding of why they are getting more observations (or not as many as the person in the next bed). How is this best communicated?
- Future work should look at ways in which observations can be made without disturbing the patient at all but, for the moment, we will focus on minimising this.
- Seeking patients' and clinicians' views should be an important part of the study. We have budgeted for a third PPI representative to be involved in the project and expect to recruit someone whose experience complements that of the current members.

During the project, the PPI representatives will be invited to attend all the Advisory Group meetings, and the PPI co-investigator will attend Management Group meetings.

In addition, at least one of the PPI representatives will attend each of the patient stakeholder focus group meetings both to help explain the purpose and context of the project to attendees and to help interpret the responses received.

In previous projects, we have been very open to expanding the role of the PPI reps and finding other ways in which they can contribute to the project, depending on their interests, availability and other commitments. We expect to do the same here.

2.5.7 Protocol compliance

All members of the project team will be given copies of this protocol and briefed on its contents.

Where a deviation from the protocol occurs, this must be documented and reported to the Chief Investigator as soon as practicable. Serious deviations, or those that have put at risk confidentiality or safety shall also be reported to the Sponsor.

2.5.8 Data protection and patient confidentiality

The study will comply with the Data Protection Act, which requires personal/identifiable data to be anonymised as soon as it is practical to do so. All documents will be stored securely and only accessible by study staff and authorised personnel. Data stored will be subject to all standard NHS security and confidentiality policies.

2.5.9 Access to the final study dataset

Three datasets will be constructed with access restricted as follows:

Dataset	Access
1. Clinical dataset	Members of the WP2 and WP3 teams
2. Prospective observation of practice	All members of the team
3. Stakeholder consultations	Members of the WP4 team

The Management Group will have access to all data in order to be able to verify the conclusions of the study.

Members of the WP5 (dissemination) team will have access to data relevant to the publications they are working on.

The Chief Investigator can approve exceptional access by other members of the project team to facilitate analysis or to cover for absences.

2.6 Dissemination plan

The research outputs from this project will be of interest to a wide audience. We expect a number of papers for academic peer-reviewed journals that will contribute to the emerging literature on deteriorating patients and their care. Anticipated papers include:

- What are the factors that need to be taken into account in determining the frequency of observation?
- Are there specific factors that need to be taken into account for particular groups of patients?
- What will be the costs/consequences of different policies?

We will prioritise journals read by a broad audience of health researchers and professionals and which have options for gold / green open access. The key medical journals that cover this area of work are *Resuscitation* (in Europe) and *Critical Care Medicine* (in the USA), in which we have published previous papers. These will be important in engaging the medical community in the conclusions from our work.

In addition to the peer review papers, we are committed to dissemination to a wider audience of health service managers. We will disseminate summaries of findings and implications via journals such as the Health Service Journal and Nursing Times, and networks such as the Health Services Research Network, NHS Employers and professional bodies working in the field of the deteriorating patient. We will work closely with each participating organisation's media team to ensure that members of the project team are given full support and training in dealing with media enquiries.

We will work during the project to identify key stakeholders (e.g. the Royal College of Physicians' NEWS group, NICE re relevant guidelines, NHS Improvement re nurse staffing implications), and with each to identify a key contact with a view to giving them a personal briefing and identifying dissemination opportunities towards the end of the study.

We anticipate that some of the key stakeholder organisations will be represented on our Project Advisory Group, and therefore will be involved in all stages of the project.

Additionally, where resources permit, we will present findings at key national and international conferences with likely candidates being the annual meeting of the

International Society for Rapid Response Systems, the US Academy Health annual research meeting, International Forum on Quality and Safety in Healthcare, RCN International Research Conference, as well as conferences targeted at NHS managers.

We also intend to draft materials for incorporation into patient information leaflets. These will be useful in informing patients about why and when they are having their vital signs observed. We will use existing networks to disseminate these.

Each output will be produced by a specific "author team", normally led by the corresponding author. The inclusion of authors, and their order, will be determined by a protocol that is agreed at the start of the project and that is compatible with ICMJE recommendations.

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2.8 Appendices

Nil