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BMJ Open

Testing a digital system that ranks the risk of unplanned Intensive Care Unit admission in all ward patients: protocol for a prospective observational cohort study

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Keywords:	Clinical deterioration, INTENSIVE & CRITICAL CARE, Predictive score, Electronic Patient Record

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TITLE PAGE**Testing a digital system that ranks the risk of unplanned Intensive Care Unit admission in all ward patients: protocol for a prospective observational cohort study****AUTHORS**

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26 **Word count**

27 1690 words
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30 **ABSTRACT**

31 **Introduction**

32 Traditional early warning scores (EWS) use vital sign derangements to detect clinical
33 deterioration in patients treated on hospital wards. Combining vital signs with demographics
34 and laboratory results improves EWS performance. We have developed the Hospital Alerting
35 Via Electronic Noticeboard (HAVEN) system. HAVEN uses vital signs, as well as
36 demographic, comorbidity and laboratory data from the electronic patient record (EPR), to
37 quantify and rank the risk of unplanned admission to an Intensive Care Unit (ICU) within 24
38 hours for all ward patients.
39
40

41
42 The primary aim of this study is to find additional variables, potentially missed during
43 development, which may improve HAVEN performance. These variables will be sought in the
44 medical record of patients misclassified by the HAVEN algorithm during testing.
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46

47 **Methods**

48 This will be a prospective, observational, cohort study conducted at the John Radcliffe Hospital,
49 part of the Oxford University Hospitals National Health Service Foundation Trust in the United
50 Kingdom.
51

52 Each day during the study periods, we will document all highly ranked patients (i.e. those with
53 the highest risk for unplanned ICU admission) identified by the HAVEN system. After 48 hours
54 we will review the progress of the identified patients. Patients who were subsequently *admitted*
55 to the ICU will be removed from the study (as they will have been correctly classified by
56 HAVEN). Highly ranked patients *not admitted* to ICU will undergo a structured medical notes
57 review. Additionally, at the end of the study periods, all patients who had an unplanned ICU
58 admission but whom HAVEN *failed to rank highly* will have a structured medical notes review.
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5 The review will identify candidate variables, likely associated with unplanned ICU admission,
6 not included in the HAVEN algorithm
7

8 **Ethics and dissemination**

9 Approval has been granted for gathering the data used in this study (South Central – Oxford C,
10 Research Ethics Committee) REC reference: 16/SC/0264, 13th June 2016) and Confidentiality
11 Advisory Group (16/CAG/0066).
12
13

14 **Discussion**

15 Our study will use a clinical expert conducting a structured medical notes review to identify
16 variables, associated with unplanned ICU admission, not included in the development of the
17 HAVEN algorithm. These variables will then be added to the algorithm and evaluated for
18 potential performance gain. To our knowledge, this is the first study of this type. We anticipate
19 that documenting the HAVEN development methods will assist other research groups
20 developing similar technology.
21
22

23 **Study registration**

24 This is a sub-study of the primary project ‘HAVEN’ which was registered in the ISRCTN
25 registry (ISRCTN12518261) on 27th July 2016.
26
27

28 **KEYWORDS**

29 Clinical deterioration, intensive care unit, critical care unit, predictive score, electronic patient
30 record, qualitative medical note review
31
32

33 **Strengths and limitations of the study**

- 34 • The study methodology is in accordance with the STROBE guidelines
- 35 • We describe a method that combines algorithm testing with a structured medical notes
36 review conducted by a clinical expert for the iterative improvement of a digital system
37 that quantifies risk for unplanned Intensive Care Unit admission in all ward patients
- 38 • To our knowledge, this is the first study of this type
39
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41

42 **BACKGROUND**

43 **Introduction**

44 Early Warning Score (EWS) systems, such as the National Early Warning Score (NEWS),
45 combine abnormalities in patient vital signs into an aggregate score. [1] This score triggers a
46 clinical response when a threshold is exceeded. Despite wide-scale adoption of EWS systems,
47 significant clinical patient deterioration on hospital wards still occurs. [1,2] Additionally, high
48 numbers of false alerts lead to alert ‘fatigue’ and inefficient use of response teams. [3] Adding
49 additional clinical information to such systems, such as laboratory results and co-morbidities,
50 improves specificity. [4–12] However, identifying and adding new variables requires a
51 systematic approach to avoid needless complexity. [13]
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54

55 We have developed a system to predict (within 24 hours) the need for unplanned Intensive Care
56 Unit (ICU) admission in ward patients. It is called Hospital Alerting Via Electronic Noticeboard
57 (HAVEN). [14] To identify potential variables for inclusion in HAVEN, we used a modified
58 Delphi process and a systematic literature review. [15] Those identified variables that were
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5 available within the EPR were extracted from datasets comprising all patients admitted to two
6 National Health Service (NHS) Trusts. [12] We then used a machine learning method [16] to
7 select the optimal combination of variables for the HAVEN algorithm. In contrast to EWS
8 systems, HAVEN was not designed to produce alerts. Instead, HAVEN provides a list of
9 patients in the hospital, ranked from most to least at risk of requiring an ICU admission. The
10 intent is that HAVEN will improve patient safety by informing the use of clinical response
11 teams.
12

13 **Aims and Objectives**

14
15 The primary aim of this study is to discover additional candidate variables, not recognised
16 during the data driven derivation process, that would improve the performance of the HAVEN
17 algorithm. We will review the medical records of *misclassified* patients, i.e. patients ranked
18 highly by HAVEN but who were not admitted to the ICU; or patients who were never ranked
19 highly by HAVEN but had an unplanned ICU admission.
20

21 **The HAVEN risk score**

22
23 The HAVEN risk score is calculated using both *static* and *dynamic* variables extracted in real-
24 time from the EPR.
25

26
27 Static variables refer to patient-level data available at admission: age, gender, co-morbidities
28 (classified according to the Elixhauser Co-morbidity index [17]), and Hospital Frailty Risk
29 Score. [18] As diagnostic coding in the UK occurs after a patient has been discharged, the co-
30 morbidity index and frailty scores are calculated using a patient's admissions over the previous
31 two years.
32

33
34 Dynamic variables refer to measurements taken repeatedly during hospital admission, i.e.
35 laboratory results and vital signs. The HAVEN risk score is currently updated according to the
36 most recent measurements of: albumin, bilirubin, C-reactive protein (CRP), haemoglobin,
37 platelets, white cell count, potassium, sodium, urea, creatinine, heart rate, systolic blood
38 pressure, respiratory rate, body temperature, a neurological status assessment using either the
39 Alert-Verbal-Painful-Unresponsive (AVPU) scale or the Glasgow Coma Scale (GCS),
40 peripheral oxygen saturation from pulse oximetry (SpO₂) and the estimated fraction of inspired
41 oxygen. [19] A patient's HAVEN score is re-calculated each time a new dynamic variable is
42 received by the system and the score is further adjusted for the time since hospital admission.
43

44 **METHODS**

45
46 The study will be reported according to the Strengthening Reporting of Observational Studies
47 in Epidemiology (STROBE) guidelines. [20]
48

49 **Design and setting**

50
51 This is a prospective, observational, cohort study conducted in the John Radcliffe Hospital, part
52 of Oxford University Hospitals National Health Service Foundation Trust in the UK. The John
53 Radcliffe Hospital is a tertiary hospital with over 800 beds and serves a population over 650,000
54 people, who are generally more affluent and with higher life expectancy than the national
55 average. [21]
56

57 **Data Collection**

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5 Data collection will occur during four, full, non-consecutive weeks in 2019. The notes review
6 will be undertaken by a senior critical care physician. Patients who are discharged or die during
7 the study period will have these details recorded. They will remain in the analysis dataset.
8

9 **Participants**

10 *Eligibility criteria*

11 All adult patients (16 years or over) admitted to any medical or surgical ward will be eligible
12 for inclusion. We will exclude patients for whom a score cannot be generated (i.e. those with
13 no recorded vital sign or laboratory measurements) and patients in groups not included in the
14 datasets used for score development (i.e. obstetric and emergency department patients).
15
16

17 *Sample size*

18 We will sample two sub-groups of patients:
19

- 20 1. False High Rank (FHR)
- 21 2. False Low Rank (FLR)

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23
24 The False High Rank (FHR) group will consist of patients ranked highly by HAVEN but who
25 were not admitted to the ICU. To identify this group, we will record the five highest ranked
26 patients on the HAVEN system at 9am each morning of the study. After 48 hours, we will
27 remove any patients who were subsequently admitted to the ICU. The remaining patients'
28 records will be reviewed.
29

30
31 The False Low Rank (FLR) group will be identified at the end of the study and consist of all
32 patients who had an unplanned ICU admission during the study period and were not present in
33 any of the daily high-ranking groups. These patients' records will also undergo a medical notes
34 review.
35

36 The study will run for four non-consecutive weeks with an expected recruitment of between
37 130 and 150 patients.
38

39 **Structured medical notes review**

40
41 We will carry out a structured review of patient medical notes (electronic and paper-based) for
42 the two sample groups described above. From these, we will construct a medical summary,
43 looking specifically at patient-centred and system-based variables associated with decisions
44 around ICU admission. We will use a modified version of the Hogan et al. qualitative note
45 review techniques. [22] We will then conduct a thematic analysis of the extracted data. [23] It
46 is expected that from within the themes the additional variables will be identified. Along with
47 the *as yet unknown* variables, the following data will be extracted:
48
49

- 50 1. Primary diagnosis
 - 51 2. Comorbidities and past medical history (where not available from previous admissions)
 - 52 3. Any treatment limitations put in place and the reasons for these including "Do not attempt
53 resuscitation" (DNAR) documents
 - 54 4. Current medication
 - 55 5. Radiological imaging
 - 56 6. Point-of-care blood gas analysis
 - 57 7. Clinical Frailty Score. [24]
- 58
59
60

Qualitative methods

Qualitative data (e.g. information in free text) will be analysed thematically, using methods of constant comparison. [25] A coding framework will be constructed to assist understanding of the data. We will use Nvivo Software (QSR International Pty Ltd, www.qsrinternational.com) to support the qualitative analysis process.

Patient safety and public involvement

As an observational study of patient records with no intervention, adverse events related to research interventions are not possible. In the event that inadequate care is identified during the structured medical note review, local NHS Trust protocols will be followed. Reviewers will act in accordance with the General Medical Councils Good Medical Practice Guidelines (2013). This action includes acting immediately if a patient is not receiving basic care to meet their needs. If patients are at risk because of inadequate premises, equipment or other resources, policies or systems, we will correct the matter if possible and raise our concerns in line with workplace policy. All measures will be documented as per local policies.

The HAVEN project has had two lay members on the management committee throughout. They have been involved in regular discussions regarding the aims and remit of the HAVEN project.

DISCUSSION

Main findings

This study will use structured medical notes review on ward patients misclassified by HAVEN to identify variables that, if added to the algorithm, may enhance performance.

Strengths and limitations of the study

This study is part of a project wide process to document HAVEN's development methodology such that it is thorough, transparent, repeatable, reportable and useful for other groups developing similar technology.

Unplanned ICU admission is an outcome measure subject to bias, such as the decision-making of individual physicians, local practice guidelines and bed availability. [26,27] This study is limited to one hospital and results may not be generalisable to other hospitals without external validation. Identified variables may not be available in the EPR and therefore not available for evaluation in the HAVEN algorithm.

Implications

To our knowledge, this is the first protocol to describe a study of this type. We hope this protocol it will assist future development of similar systems.

DECLARATIONS

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Ethics approval and consent

Health Research Authority (South Central – Oxford C, Research Ethics Committee [REC]) approval was obtained for gathering the data used in this study from the (REC reference: 16/SC/0264, 13th June 2016) and Confidentiality Advisory Group (16/CAG/0066). Informed consent will not be obtained from the patients, however patients who have requested that their data are not used for research purposes will be identified and removed from the study database. Patients will be allocated a study ID and all data transferred to the research database will have direct identifiable information removed. All documents will be stored securely and only accessible by study staff and authorised personnel. The study will comply with the UK Data Protection Act 2018.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analysed during the study will not be publicly available but anonymised extracts may be available from the corresponding author on reasonable request.

Competing Interests

PW is Chief Medical Officer for Sensyne Health (<https://www.sensynehealth.com/>). The remaining authors declare that they have no competing interests.

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 Wellcome Trust/Department of Health. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

Author contributions

JM and OR designed the study, undertook the methodological planning and wrote the protocol. DY and PW assisted in study design and GL commented on successive drafts of the manuscript. All authors read and approved the final manuscript.

REFERENCES

- 1 Royal College of Physicians (London). National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS. 2017.
- 2 Care Quality Commission. Opening the door to change NHS safety culture and the need for transformation. 2018.
- 3 Curry J, Jungquist CR. A critical assessment of monitoring practices, patient deterioration, and alarm fatigue on inpatient wards: a review. *Patient Saf Surg*

2014;**8**:29. doi:10.1186/1754-9493-8-29

- 4 Churpek MM, Yuen TC, Park SY, *et al.* Using Electronic Health Record Data to Develop and Validate a Prediction Model for Adverse Outcomes in the Wards. *Crit Care Med* 2014;**42**:841–8. doi:10.1097/CCM.0000000000000038
- 5 Kang MA, Churpek MM, Zdravetz FJ, *et al.* Real-time risk prediction on the wards: A feasibility study. *Crit Care Med* 2016;**44**:1468–73. doi:10.1097/CCM.0000000000001716
- 6 Alvarez CA, Clark CA, Zhang S, *et al.* Predicting out of intensive care unit cardiopulmonary arrest or death using electronic medical record data. *BMC Med Inform Decis Mak* 2013;**13**:28.
- 7 Bailey TCC, Chen Y, Mao Y, *et al.* A trial of a real-time Alert for clinical deterioration in Patients hospitalized on general medical wards. *J Hosp Med* 2013;**8**:236–42. doi:10.1002/jhm.2009
- 8 Escobar GJ, LaGuardia JC, Turk BJ, *et al.* Early detection of impending physiologic deterioration among patients who are not in intensive care: Development of predictive models using data from an automated electronic medical record. *J Hosp Med* 2012;**7**:388–95. doi:10.1002/jhm.1929
- 9 Hackmann G, Chen M, Chipara O, *et al.* Toward a two-tier clinical warning system for hospitalized patients. *AMIA . Annu Symp proceedings AMIA Symp* 2011;**2011**:511–9. doi:10.7936/K70V8B1G
- 10 Tam V, Frost SA, Hillman KM, *et al.* Using administrative data to develop a nomogram for individualising risk of unplanned admission to intensive care. *Resuscitation* 2008;**79**:241–8. doi:10.1016/j.resuscitation.2008.06.023
- 11 Kipnis P, Turk BJ, Wulf DA, *et al.* Development and validation of an electronic medical record-based alert score for detection of inpatient deterioration outside the ICU. *J Biomed Inform* 2016;**64**:10–9. doi:10.1016/j.jbi.2016.09.013
- 12 Redfern OC, Pimentel MAF, Prytherch D, *et al.* Predicting in-hospital mortality and unanticipated admissions to the intensive care unit using routinely collected blood tests and vital signs: Development and validation of a multivariable model. *Resuscitation* 2018;**133**:75–81. doi:10.1016/j.resuscitation.2018.09.021
- 13 Collins GS, Reitsma JB, Altman DG, *et al.* Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD Statement. *Eur Urol* 2015;**67**:1142–51. doi:10.1016/j.eururo.2014.11.025
- 14 Watkinson, P., Young, J. D., Prytherch, D., Tarassenko, L., Clifton, D., & Briggs J. Hospital Alerting Via Electronic Noticeboard (HAVEN) Study Protocol. 2016. <https://ora.ox.ac.uk/objects/uuid:322561c7-866e-4c>
- 15 Malycha J, Bonnici T, Clifton DA, *et al.* Patient centred variables with univariate associations with unplanned ICU admission: a systematic review. *BMC Med Inform*

- 1
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4
5 *Decis Mak* 2019;**19**:98. doi:10.1186/s12911-019-0820-1
6
7 16 Chen T, He T, Benesty M, *et al.* Extreme Gradient Boosting Package ‘xgboost’.
8 2018;:54.
9
10 17 Quan H, Sundararajan V, Halfon P, *et al.* Coding algorithms for defining comorbidities
11 in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;**43**:1130–9.
12 doi:10.1097/01.mlr.0000182534.19832.83
13
14 18 Gilbert T, Neuburger J, Kraindler J, *et al.* Development and validation of a Hospital
15 Frailty Risk Score focusing on older people in acute care settings using electronic
16 hospital records: an observational study. *Lancet* 2018;**391**:1775–82. doi:10.1016/S0140-
17 6736(18)30668-8
18
19 19 Malycha J, Farajidavar N, Pimentel MAF, *et al.* The effect of fractional inspired oxygen
20 concentration on early warning score performance: A database analysis. *Resuscitation*
21 2019;**139**:192–9. doi:10.1016/j.resuscitation.2019.04.002
22
23 20 von Elm E, Altman DG, Egger M, *et al.* The Strengthening the Reporting of
24 Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting
25 observational studies. *J Clin Epidemiol* 2008;**61**:344–9.
26 doi:10.1016/j.jclinepi.2007.11.008
27
28 21 Public Health England. Oxford Health Profile. 2017.
29
30 22 Hogan H, Healey F, Neale G, *et al.* Preventable deaths due to problems in care in English
31 acute hospitals: A retrospective case record review study. *BMJ Qual Saf* 2012;**21**:737–
32 45. doi:10.1136/bmjqs-2011-001159
33
34 23 Braun, Virginia; Clarke V. Using thematic analysis in Psychology. *Qual Res Psychol*
35 2006;**3**:77–101. doi:10.1017/CBO9781107415324.004
36
37 24 Ke LS. Frailty in the elderly: A concept analysis. *J Nurs* 2013;**60**:105–10.
38 doi:10.1503/cmaj.050051
39
40 25 Huo X, Liu C, Bai X, *et al.* RSC Advances Aqueous extract of Cordyceps sinensis
41 potentiates the antitumor effect of DDP and attenuates. *RSC Adv* 2017;**7**:37743–54.
42 doi:10.1136/bmj.320.7227.114
43
44 26 Robert R, Coudroy R, Ragot S, *et al.* Influence of ICU-bed availability on ICU admission
45 decisions. *Ann Intensive Care* 2015;**5**:1–7. doi:10.1186/s13613-015-0099-z
46
47 27 Robert R, Reignier J, Tournoux-Facon C, *et al.* Refusal of intensive care unit admission
48 due to a full unit: Impact on mortality. *Am J Respir Crit Care Med* 2012;**185**:1081–7.
49 doi:10.1164/rccm.201104-0729OC
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5 TITLE PAGE

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11 ABSTRACT

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42 DISCUSSION

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49 DECLARATIONS

50 Acknowledgements

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Author contributions

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5 1 **TITLE PAGE**6
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23 **ABSTRACT**

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25 Traditional early warning scores (EWS) use vital sign derangements to detect clinical
26 deterioration in patients treated on hospital wards. Combining vital signs with demographics
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28 Via Electronic Noticeboard (HAVEN) system. HAVEN uses vital signs, as well as
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33 The primary aim of this study is to find additional variables, potentially missed during
34 development, which may improve HAVEN performance. These variables will be sought in the
35 medical record of patients misclassified by the HAVEN risk score during testing.

37 **Methods**

38 This will be a prospective, observational, cohort study conducted at the John Radcliffe Hospital,
39 part of the Oxford University Hospitals National Health Service Foundation Trust in the United
40 Kingdom.

41 Each day during the study periods, we will document all highly ranked patients (i.e. those with
42 the highest risk for unplanned ICU admission) identified by the HAVEN system. After 48 hours
43 we will review the progress of the identified patients. Patients who were subsequently *admitted*
44 to the ICU will be removed from the study (as they will have been correctly classified by
45 HAVEN). Highly ranked patients *not admitted* to ICU will undergo a structured medical notes
46 review. Additionally, at the end of the study periods, all patients who had an unplanned ICU
47 admission but whom HAVEN *failed to rank highly* will have a structured medical notes review.

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5 1 The review will identify candidate variables, likely associated with unplanned ICU admission,
6 2 not included in the HAVEN risk score

8 3 **Ethics and dissemination**

9 4 Approval has been granted for gathering the data used in this study (South Central – Oxford C,
10 5 Research Ethics Committee) REC reference: 16/SC/0264, 13th June 2016) and Confidentiality
11 6 Advisory Group (16/CAG/0066).
12 7

14 8 **Discussion**

15 9 Our study will use a clinical expert conducting a structured medical notes review to identify
16 10 variables, associated with unplanned ICU admission, not included in the development of the
17 11 HAVEN risk score. These variables will then be added to the risk score and evaluated for
18 12 potential performance gain. To our knowledge, this is the first study of this type. We anticipate
19 13 that documenting the HAVEN development methods will assist other research groups
20 14 developing similar technology.
21 15

23 16 **Study registration**

24 17 This is a sub-study of the primary project ‘HAVEN’ which was registered in the ISRCTN
25 18 registry (ISRCTN12518261) on 27th July 2016.
26 19

28 20 **KEYWORDS**

29 21 Clinical deterioration, intensive care unit, critical care unit, predictive score, electronic patient
30 22 record, qualitative medical note review
31 23

33 24 **Strengths and limitations of the study**

- 35 25 • The study methodology is in accordance with the STROBE guidelines
- 36 26 • We describe a method that combines risk score testing with a structured medical notes
37 27 review conducted by a clinical expert for the iterative improvement of a digital system
38 28 that quantifies risk for unplanned Intensive Care Unit admission in all ward patients
- 39 29 • To our knowledge, this is the first study of this type
40 30

42 31 **BACKGROUND**

44 32 **Introduction**

45 33 Early Warning Score (EWS) systems, such as the National Early Warning Score (NEWS),
46 34 combine abnormalities in patient vital signs into an aggregate score. [1] This score triggers a
47 35 clinical response when a threshold is exceeded. Despite wide-scale adoption of EWS systems,
48 36 significant clinical patient deterioration on hospital wards still occurs. [1,2] Additionally, high
49 37 numbers of false alerts lead to alert ‘fatigue’ and inefficient use of response teams. [3] Adding
50 38 additional clinical information to such systems, such as laboratory results and co-morbidities,
51 39 improves specificity. [4–12] However, identifying and adding new variables requires a
52 40 systematic approach to avoid needless complexity. [13]

53 41 We have developed a system to predict the risk of unplanned ICU admission (within 24 hours)
54 42 for patients on general medical and surgical wards. It is called Hospital Alerting Via Electronic
55 43 Noticeboard (HAVEN). [14] To identify potential variables for inclusion in HAVEN, we used
56 44 a modified Delphi process and a systematic literature review. [15] Those identified variables

1 that were available within the Electronic Patient Record (EPR) were extracted from datasets
2 comprising all patients admitted to two National Health Service (NHS) Trusts (a Trust is a legal
3 entity that provides goods and services for the purposes of the provision of hospital, community
4 and/or other aspects of patient care). [12] We then used a machine learning method [16] to
5 select the optimal combination of variables for the HAVEN risk score. In contrast to EWS
6 systems, HAVEN was not designed to produce alerts. Instead, HAVEN provides a list of
7 patients in the hospital, ranked from most to least at risk of requiring an ICU admission. The
8 intent is that HAVEN will improve patient safety by informing the use of clinical response
9 teams.

10 **Aims and Objectives**

11 The primary aim of this study is to discover additional candidate variables, not recognised
12 during the data driven derivation process that would improve the performance of the HAVEN
13 risk score. We will review the medical records of *misclassified* patients, i.e. patients ranked
14 highly by HAVEN but who were not admitted to the ICU; or patients who were never ranked
15 highly by HAVEN but had an unplanned ICU admission.

16 **The HAVEN risk score**

17 The HAVEN risk score is calculated using both *static* and *dynamic* variables extracted in real-
18 time from the EPR.

19 Static variables refer to patient-level data available at admission: age, gender, co-morbidities
20 (classified according to the Elixhauser Co-morbidity index [17]), and Hospital Frailty Risk
21 Score. [18] As diagnostic coding in the United Kingdom (UK) occurs after a patient has been
22 discharged, the co-morbidity index and frailty scores are calculated using a patient's admissions
23 over the previous two years. Score performance in patients with no previous admissions (and
24 potentially undocumented comorbidities) will be evaluated separately.

25 Dynamic variables refer to measurements taken repeatedly during hospital admission, i.e.
26 laboratory results and vital signs. The HAVEN risk score is currently updated according to the
27 most recent measurements of: albumin, bilirubin, C-reactive protein (CRP), haemoglobin,
28 platelets, white cell count, potassium, sodium, urea, creatinine, heart rate, systolic blood
29 pressure, respiratory rate, body temperature, a neurological status assessment using either the
30 Alert-Verbal-Painful-Unresponsive (AVPU) scale or the Glasgow Coma Scale (GCS),
31 peripheral oxygen saturation from pulse oximetry (SpO₂) and the estimated fraction of inspired
32 oxygen. [19] A patient's HAVEN score is re-calculated each time a new dynamic variable is
33 received by the system and the score is further adjusted for the time since hospital admission.

34 **METHODS**

35 The study will be reported according to the Strengthening Reporting of Observational Studies
36 in Epidemiology (STROBE) guidelines. [20]

37 **Design and setting**

38 This is a prospective, observational, cohort study conducted in the John Radcliffe Hospital, part
39 of Oxford University Hospitals National Health Service Foundation Trust in the UK. The John
40 Radcliffe Hospital is a tertiary hospital with over 800 beds and serves a population over 650,000
41 people, who are generally more affluent and with higher life expectancy than the national
42 average. [21]

1 Data Collection

2 Data collection will occur during four, full, non-consecutive weeks in 2019. The notes review
3 will be undertaken by a senior critical care physician. Patients who are discharged or die during
4 the study period will have these details recorded. They will remain in the analysis dataset.

5 Participants

6 *Eligibility criteria*

7 Emergency and elective adult patients (16 years or over) admitted to medical, surgical,
8 observational or short stay wards will be eligible for inclusion. We will exclude patients for
9 whom a score cannot be generated (i.e. those with no recorded vital sign or laboratory
10 measurements).

11 *Sample size*

12 We will sample two sub-groups of patients:

- 13 1. False High Rank (FHR)
- 14 2. False Low Rank (FLR)

15 The False High Rank (FHR) group will consist of patients ranked highly by HAVEN but who
16 were not admitted to the ICU. To identify this group, we will record the five highest ranked
17 patients on the HAVEN system at 9am each morning of the study. After 48 hours, we will
18 remove any patients who were subsequently admitted to the ICU. The remaining patients'
19 records will be reviewed.

20 The False Low Rank (FLR) group will be identified at the end of the study and consist of all
21 patients who had an unplanned ICU admission during the study period and were not present in
22 any of the daily high-ranking groups. These patients' records will also undergo a medical notes
23 review.

24 The study will run for four non-consecutive weeks with an expected recruitment of between
25 130 and 150 patients.

26 Structured medical notes review

27 We will carry out a structured review of patient medical notes (electronic and paper-based) for
28 the two sample groups described above. From these, we will construct a medical summary,
29 looking specifically at patient-centred and system-based variables associated with decisions
30 around ICU admission. We will use a modified version of the Hogan et al. qualitative note
31 review techniques. [22] We will then conduct a thematic analysis of the extracted data. [23] It
32 is expected that from within the themes the additional variables will be identified. Along with
33 the *as yet unknown* variables, the following data will be extracted:

- 34 1. Primary diagnosis
- 35 2. Comorbidities and past medical history (where not available from previous admissions)
- 36 3. Any treatment limitations put in place and the reasons for these including "Do not attempt
37 resuscitation" (DNAR) documents
- 38 4. Current medication
- 39 5. Radiological imaging
- 40 6. Point-of-care blood gas analysis
- 41 7. Clinical Frailty Score. [24]

1 **Qualitative methods**

2 Qualitative data (e.g. information in free text) will be analysed thematically, using methods of
3 constant comparison. [25] A coding framework will be constructed to assist understanding of
4 the data. We will use Nvivo Software (QSR International Pty Ltd, www.qsrinternational.com)
5 to support the qualitative analysis process.

6 **Patient safety and public involvement**

7 As an observational study of patient records with no intervention, adverse events related to
8 research interventions are not possible. In the event that inadequate care is identified during the
9 structured medical note review, local NHS Trust protocols will be followed. Reviewers will act
10 in accordance with the General Medical Councils Good Medical Practice Guidelines (2013).
11 This action includes acting immediately if a patient is not receiving basic care to meet their
12 needs. If patients are at risk because of inadequate premises, equipment or other resources,
13 policies or systems, we will correct the matter if possible and raise our concerns in line with
14 workplace policy. All measures will be documented as per local policies. The HAVEN project
15 has had two lay members on the management committee throughout. They have been involved
16 in regular discussions regarding the aims and remit of the HAVEN project.

17 **DISCUSSION**

18 **Main findings**

19 This study will use structured medical notes review on ward patients misclassified by HAVEN
20 to identify variables that may enhance performance. Any identified variables will be
21 systematically introduced into our score development pipeline to evaluate whether they
22 improve score performance.

23 **Strengths and limitations of the study**

24 This study is part of a project-wide process to document the development of the HAVEN
25 system such that it is thorough, transparent, repeatable, reportable and the methodology could
26 be useful for other groups developing similar technology.

27
28 Unplanned ICU admission is an outcome measure subject to bias, such as the decision-making
29 of individual physicians, local practice guidelines and bed availability. [26,27] This study is
30 limited to one hospital and the results may not be generalisable to other hospitals. Variables
31 identified from the thematic analysis may not be available in the EPR and therefore cannot risk
32 score be used to improve the performance of the HAVEN risk score. Likewise, patients with
33 no previous admissions to the John Radcliffe Hospital will have no available comorbidity data,
34 potentially limiting performance of the risk score in these patients. To assess the impact of these
35 missing data, we will undertake sub-groups analyses in those patients with/without prior
36 admissions.

37
38 While a significant proportion of ICU admissions are referred directly from the Emergency
39 Department (ED), the HAVEN system was designed specifically for ward patients needing the
40 attention of the critical care team. By excluding these ED referrals we are reducing the number
41 of eligible patients for this study.

42 **Implications**

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5 1 To our knowledge, this is the first protocol to describe a study of this type. We hope this
6 2 protocol it will assist future development of similar systems.
7 3
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9 4 **DECLARATIONS**

10 5 **Acknowledgements**

11 6 JM would like to acknowledge the University of Adelaide, Department of Acute Medicine,
12 7 who are administering his PhD.
13 8

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17 12 Department of Health and Wellcome Trust. The views expressed in this publication are those
18 13 of the author(s) and not necessarily those of the Department of Health or Wellcome Trust.
19 14

20 15 **Ethics approval and consent**

21 16 Health Research Authority (South Central – Oxford C, Research Ethics Committee [REC])
22 17 approval was obtained for gathering the data used in this study from the (REC reference:
23 18 16/SC/0264, 13th June 2016) and Confidentiality Advisory Group (16/CAG/0066). Informed
24 19 consent will not be obtained from the patients, however patients who have requested that their
25 20 data are not used for research purposes will be identified and removed from the study database.
26 21 Patients will be allocated a study ID and all data transferred to the research database will have
27 22 direct identifiable information removed. All documents will be stored securely and only
28 23 accessible by study staff and authorised personnel. The study will comply with the UK Data
29 24 Protection Act 2018.
30 25

31 26 **Consent for publication**

32 27 Not applicable.
33 28

34 29 **Availability of data and materials**

35 30 The datasets generated and analysed during the study will not be publicly available but
36 31 anonymised extracts may be available from the corresponding author on reasonable request.
37 32

38 33 **Competing Interests**

39 34 PW is Chief Medical Officer for Sensyne Health (<https://www.sensynehealth.com/>). The
40 35 remaining authors declare that they have no competing interests.
41 36

42 37 **Publication policy**

43 38 The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press
44 39 releases and any other publications arising from the study. Authors will acknowledge that the
45 40 study was funded by the Wellcome Trust/Department of Health. Authorship will be determined
46 41 in accordance with the ICMJE guidelines and other contributors will be acknowledged.
47 42

48 43 **Author contributions**

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1 JM and OR designed the study, undertook the methodological planning and wrote the protocol.
 2 DY and PW assisted in study design and GL commented on successive drafts of the manuscript.
 3 All authors read and approved the final manuscript.

4 REFERENCES

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- 1 Royal College of Physicians (London). National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS. 2017.
 - 2 Care Quality Commission. Opening the door to change NHS safety culture and the need for transformation. 2018.
 - 3 Curry J, Jungquist CR. A critical assessment of monitoring practices, patient deterioration, and alarm fatigue on inpatient wards: a review. *Patient Saf Surg* 2014;**8**:29. doi:10.1186/1754-9493-8-29
 - 4 Churpek MM, Yuen TC, Park SY, *et al*. Using Electronic Health Record Data to Develop and Validate a Prediction Model for Adverse Outcomes in the Wards. *Crit Care Med* 2014;**42**:841–8. doi:10.1097/CCM.0000000000000038
 - 5 Kang MA, Churpek MM, Zdravec FJ, *et al*. Real-time risk prediction on the wards: A feasibility study. *Crit Care Med* 2016;**44**:1468–73. doi:10.1097/CCM.0000000000001716
 - 6 Alvarez CA, Clark CA, Zhang S, *et al*. Predicting out of intensive care unit cardiopulmonary arrest or death using electronic medical record data. *BMC Med Inform Decis Mak* 2013;**13**:28.
 - 7 Bailey TCC, Chen Y, Mao Y, *et al*. A trial of a real-time Alert for clinical deterioration in Patients hospitalized on general medical wards. *J Hosp Med* 2013;**8**:236–42. doi:10.1002/jhm.2009
 - 8 Escobar GJ, LaGuardia JC, Turk BJ, *et al*. Early detection of impending physiologic deterioration among patients who are not in intensive care: Development of predictive models using data from an automated electronic medical record. *J Hosp Med* 2012;**7**:388–95. doi:10.1002/jhm.1929
 - 9 Hackmann G, Chen M, Chipara O, *et al*. Toward a two-tier clinical warning system for hospitalized patients. *AMIA . Annu Symp proceedings AMIA Symp* 2011;**2011**:511–9. doi:10.7936/K70V8B1G
 - 10 Tam V, Frost SA, Hillman KM, *et al*. Using administrative data to develop a nomogram for individualising risk of unplanned admission to intensive care. *Resuscitation* 2008;**79**:241–8. doi:10.1016/j.resuscitation.2008.06.023
 - 11 Kipnis P, Turk BJ, Wulf DA, *et al*. Development and validation of an electronic medical record-based alert score for detection of inpatient deterioration outside the ICU. *J Biomed Inform* 2016;**64**:10–9. doi:10.1016/j.jbi.2016.09.013
 - 12 Redfern OC, Pimentel MAF, Prytherch D, *et al*. Predicting in-hospital mortality and

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- 1 unanticipated admissions to the intensive care unit using routinely collected blood tests
2 and vital signs: Development and validation of a multivariable model. *Resuscitation*
3 2018;**133**:75–81. doi:10.1016/j.resuscitation.2018.09.021
- 4 13 Collins GS, Reitsma JB, Altman DG, *et al.* Transparent reporting of a multivariable
5 prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD
6 Statement. *Eur Urol* 2015;**67**:1142–51. doi:10.1016/j.eururo.2014.11.025
- 7 14 Watkinson, P., Young, J. D., Prytherch, D., Tarassenko, L., Clifton, D., & Briggs J.
8 Hospital Alerting Via Electronic Noticeboard (HAVEN) Study Protocol.
9 2016.<https://ora.ox.ac.uk/objects/uuid:322561c7-866e-4c>
- 10 15 Malycha J, Bonnici T, Clifton DA, *et al.* Patient centred variables with univariate
11 associations with unplanned ICU admission: a systematic review. *BMC Med Inform*
12 *Decis Mak* 2019;**19**:98. doi:10.1186/s12911-019-0820-1
- 13 16 Chen T, He T, Benesty M, *et al.* Extreme Gradient Boosting Package ‘xgboost’.
14 2018;:54.
- 15 17 Quan H, Sundararajan V, Halfon P, *et al.* Coding algorithms for defining comorbidities
16 in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;**43**:1130–9.
17 doi:10.1097/01.mlr.0000182534.19832.83
- 18 18 Gilbert T, Neuburger J, Kraindler J, *et al.* Development and validation of a Hospital
19 Frailty Risk Score focusing on older people in acute care settings using electronic
20 hospital records: an observational study. *Lancet* 2018;**391**:1775–82. doi:10.1016/S0140-
21 6736(18)30668-8
- 22 19 Malycha J, Farajidavar N, Pimentel MAF, *et al.* The effect of fractional inspired oxygen
23 concentration on early warning score performance: A database analysis. *Resuscitation*
24 2019;**139**:192–9. doi:10.1016/j.resuscitation.2019.04.002
- 25 20 von Elm E, Altman DG, Egger M, *et al.* The Strengthening the Reporting of
26 Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting
27 observational studies. *J Clin Epidemiol* 2008;**61**:344–9.
28 doi:10.1016/j.jclinepi.2007.11.008
- 29 21 Public Health England. Oxford Health Profile. 2017.
- 30 22 Hogan H, Healey F, Neale G, *et al.* Preventable deaths due to problems in care in English
31 acute hospitals: A retrospective case record review study. *BMJ Qual Saf* 2012;**21**:737–
32 45. doi:10.1136/bmjqs-2011-001159
- 33 23 Braun, Virginia; Clarke V. Using thematic analysis in Psychology. *Qual Res Psychol*
34 2006;**3**:77–101. doi:10.1017/CBO9781107415324.004
- 35 24 Ke LS. Frailty in the elderly: A concept analysis. *J Nurs* 2013;**60**:105–10.
36 doi:10.1503/cmaj.050051
- 37 25 Huo X, Liu C, Bai X, *et al.* RSC Advances Aqueous extract of *Cordyceps sinensis*

- 1
2
3
4
5 1 potentiates the antitumor effect of DDP and attenuates. *RSC Adv* 2017;**7**:37743–54.
6 2 doi:10.1136/bmj.320.7227.114
7
8 3 26 Robert R, Coudroy R, Ragot S, *et al*. Influence of ICU-bed availability on ICU admission
9 4 decisions. *Ann Intensive Care* 2015;**5**:1–7. doi:10.1186/s13613-015-0099-z
10
11 5 27 Robert R, Reignier J, Tournoux-Facon C, *et al*. Refusal of intensive care unit admission
12 6 due to a full unit: Impact on mortality. *Am J Respir Crit Care Med* 2012;**185**:1081–7.
13 7 doi:10.1164/rccm.201104-0729OC
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Author contributions

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