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Evaluation of the physiological variables and scoring systems at intensive care discharge as predictors of clinical deterioration and readmission

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ABSTRACT

Rationale: Scoring systems are commonly used throughout the NHS to monitor patient deterioration. After intensive care (ICU) discharge, patients are at high risk of subsequent deterioration with associated morbidity and mortality risk.

Aims: To determine, using routinely collected data and common scoring systems, whether parameters seen at ICU discharge can be predictive of subsequent clinical deterioration.

Design/setting: A single-centre retrospective study located in a tertiary hospital in the south of England.

Participants: 1868 patients who were admitted and discharged from ICU between 1st April 2023 to 30th March 2024 were screened for eligibility. A total of 1393 patients were included in the final analysis, including 122 patients who classified in the 'deteriorated' subgroup.

Interventions: Assessment of vital signs, blood markers of infection and inflammation and 3 scoring systems (NEWS2, APACHE II and SOFA score) taken within 24hrs prior ICU discharge.

Primary outcomes: Assessment of predictors of deterioration after ICU discharge.

Secondary outcomes: Reasons for readmission to ICU, acute hospital mortality, ICU length of stay and time before readmission to ICU.

Results: Heart rate, conscious level (AVPU scale) and SOFA score were independent predictors of deterioration after ICU discharge (AUC 0.85, CI 0.79-0.90, specificity 82.3%, sensitivity 79.7%) in multivariable models. Of these, a reduced level of consciousness was the most significant predictor of clinical deterioration (OR 19.6, CI 11.4-35.0). NEWS2 was an independent predictor for deterioration on univariable analysis. Mortality was significantly increased in patients who experienced deterioration after ICU discharge, as was ICU length of stay.

Conclusions: Predictive models may be useful in assisting clinicians with ICU discharge decisions. Further research is required to develop patient tailored scoring systems that incorporate other factors that are needed for decisions around ICU discharge.

Article Summary

Strengths and limitations:

Strength:

- Large dataset of over 1300 patients
- Adjusted for collinearity between vital sign values and scoring systems
- Assessed individual parameters and vital signs before forming overall predictive models

Limitation:

- Single centre
- Comorbidities not assessed

INTRODUCTION

The decision to discharge patients from intensive care is complex and often based on multiple factors such as patient's clinical and nursing needs, resolution of initial illness, recovery trajectory, planned interventions, ICU and ward bed status and unit staffing levels. For most, an ideal combination of these factors leads to a timely discharge to the most appropriate ward facility. However, some patients experience unanticipated clinical deterioration after discharge leading to unplanned readmission with associated adverse outcomes [1-3]. It is important to identify and risk-stratify patients who are at-risk of clinical deterioration prior to ICU discharge. Currently, there is no ideal clinical variable or scoring system available to guide suitability of patient discharge from ICU. While there are several methods utilised to identify potential patients who could deteriorate, there is no clear consensus [4, 5]. Some studies suggest scoring systems, such as the National Early Warning Score 2 (NEWS2), a system with widespread usage already in the UK and worldwide, could be an easy and effective method of screening for patients at risk of deterioration prior to ICU discharge [6-8]. This may enable closer monitoring of patients after discharge or, alternatively, delay discharge until further stabilisation, minimising readmission rates, thereby improving patient outcomes.

Developed by the Royal College of Physicians, the National Early Warning Score (NEWS2) is a system used to quantitatively score routine physiological parameters to identify those acutely ill or with deteriorating clinical status [9, 10]. Combining routine vital sign measurements (respiratory rate (RR) (per minute), systolic blood pressure (SBP), heart rate (HR) (per minute), temperature (^{0}C), oxygen saturations ($SpO_{2,}$) along with a measurement of consciousness (Alert, confused, voice, pain, unresponsive scale) and supplemental oxygen requirement, it allows for a current evaluation of physiological function. Although its use is almost universal in UK hospital wards to predict patients at-risk of deterioration [9], the use of NEWS2 to assess suitability of ICU discharge has not been validated in ICU patients and as such is not routinely used in ICU.

In comparison, the Sequential Organ Failure Assessment score (SOFA) is validated in ICU cohorts [11, 12]. Based on organ systems, SOFA score uses a multisystem based approach to assess acute morbidity and mortality of critical illness. In recent years, this has been applied to the identification and monitoring of sepsis through the work of Sepsis-3 [13]. Calculated on admission to ICU and recalculated daily using the most abnormal value from the preceding 24hrs, SOFA is mostly commonly used as a mortality prediction tool [12]. A further score often used in ICU is the Acute physiology and Chronic Health Evaluation II Score (APACHE II). APACHE II estimates disease severity based on physiological measurements, including blood markers, along with considerations for age and chronic health conditions [14, 15]. It is used at the time of admission and recalculated daily in ICU for prognostic scoring, having been shown to be an accurate measurement of illness severity with correlations to clinical outcomes [15]. A scoring matrix for NEWS2, SOFA and APACHE II can be seen in Appendix 1. Given their potential use, we aim to evaluate these scoring systems, along with routinely collected variables such as vital signs and blood markers, to determine if measurements taken before ICU discharge can predict those who will unexpectedly deteriorate after leaving intensive care.

MATERIALS AND METHODS

Study Design and setting

This is a retrospective analysis of a 31-bed general intensive care (ICU) admissions and discharges between 1st April 2023 to 30th March 2024 based at a large tertiary hospital in the south of England. Patients were identified using databases that are routinely used by the ICU auditing team performed as part of the Intensive Care National Audit and Research Centre (ICNARC) data collection [16]. This study is part of a wider study investigating outcomes of critical illness in intensive care (CRIT-CO). CRIT-CO is sponsored by University Hospital Southampton NHS Foundation Trust (RHM CRI 0370) and has approval from the NHS Health Research Authority (HRA, UK: IRAS 232922, 26/11/2018). This study was also registered as a quality improvement project by the University Hospital Southampton Service Evaluation Team (Ref: QI/0272). This study follows local ethical standards, and no identifiable data is presented here. Given its retrospective nature and no additional information required, consent was waivered.

Patient and Public involvement

Patients and the public were not directly involved in this research study. However, the foundations of this research were developed after discussions with patients who had experienced unexpected deterioration after discharge from intensive care.

Data collection

Patients were identified using the Intensive Care database (MetaVision-iMDsoft, Israel). The inclusion criteria were patients 18 years and older, admitted and discharged from the ICU during a single hospital admission and had vital sign monitoring undertaken before ICU discharge. The exclusion criteria were patients who died in ICU during the first admission, discharged on an end-of-life care pathway (palliation), discharged to another ICU department (same hospital), transferred to another hospital, transferred to another care provider on ICU discharge (e.g. rehabilitation unit, care home), discharged directly home or self-discharged. Patients who deteriorated were separated from the main dataset through review of the ICU records. As part of routine audit data, a patients discharge location, hospital outcome and ≤48hr/>48hr ICU readmission are recorded. Deterioration was defined as anyone who was either readmitted back to the ICU during the same hospital admission or who died on the ward after being discharged with active treatment ongoing. Any patient who had more than one admission to the ICU over the year period, but which occurred in separate hospital admissions, were included individual entries.

We collected standard variables such as age, gender and body mass index (BMI). Individual vital sign (heart rate, respiratory rate, systolic blood pressure, etc) data was collected using the last recorded set of vital signs before ICU discharge. For all, these measurements were within the preceding 4 hours before discharge. For assessment of SOFA and APACHE II scores, these were calculated using the most abnormal values in the preceding 24hrs prior to discharge[12, 15]. NEWS2 was calculated using the vital sign data as described previously. Biochemical data (total white cell count (WCC), lymphocyte count, neutrophil count and C-reactive protein (CRP) was taken using the last recorded value, which for all was within 24hrs prior to ICU discharge. Other data, such as length of ICU stay, hospital mortality, timing and reason for readmission were determined via review of ICU records.

Outcomes

The main outcome of this study was to identify patients discharged from ICU who had unexpected clinical deterioration to determine if there were any predictors of subsequent deterioration at ICU discharge. Secondary outcomes included determining reasons for

readmission to ICU, timing of ICU readmission, acute hospital mortality and ICU length of stay.

Statistical and data analysis

Differences in baseline characteristics between groups were described with median and interquartile ranges (IQR) and median for continuous variables and counts with percentages for categorical groups. Each vital sign parameter was analysed individually and GICU discharge data (This included: length of stay (LOS), APACHE II score on admission, SOFA Score on discharge, laboratory markers of infection/inflammation). Comparisons of between groups were made using Kruskal-Wallis and Fischer's exact test for continuous and binary variables, respectively.

Logistic regression models were constructed for the prediction of re-escalation. Variables with a significance threshold of $P<0.25$ within univariable models were included in multivariable analysis. Subsequently, backwards selection was performed using the Akiake information criterion (AIC) to produce the final models. Overall models were further described with Receiver-operating characteristic curves (ROC) and McFaddens pseudo-R^2. On significance testing, *P* values <0.05 were deemed significant throughout the analysis. All analyses were performed using R (Version 4.2.2). All figures were formed using Biorender.com.

RESULTS

We screened 1868 discharges for this 12-month period. After exclusion of patients who died on ICU, required other ICU/hospital/rehabilitation transfer, self-discharged or directly discharged home, discharged to a ward on a palliative pathway and those with incomplete data, we included 1393 patients with 122 patients who clinically deteriorated (8.76%), of those 74 patients were readmitted (Figure 1).

Figure 1: Flowchart showing the formulation to the final dataset[17].

Patient characteristics and readmission profile

The average age was similar between the two groups (stable: 63.0 (50.0-74.0), deterioration: 68 (54.0-77.5)). The proportion of male patients was also similar (57.9% male in stable group, 60.6% in deterioration group). Both groups had a mean BMI within 'overweight' group according to NHS guidance [18] (stable: 26.3 (22.7-30.5), deterioration: 26.6 (22.6-29.7)). Of those readmitted, 41.9% required treatment for acute hypoxia and 18.9% for unplanned post-operative care. Other reasons for readmission included hypotension (5/74 (6.8%)), bleeding

(4/74 (5.4%)), renal support (5/74 (6.8%)), reduced GCS (6/74 (8.1%)) and seizure activity (5/74 (6.8%)). 15 patients had more than one reason (e.g. hypoxia and hypotension) and so were included in both categories. 10 patients (13.5%) developed sepsis on the ward requiring organ support and 3 patients had a cardiac arrest on the ward leading to ICU readmission. 4 patients (5.4%) became more unwell without one defining factor and so were classified as 'increasing acuity needs' (Table 1).

Table 1: Patient characteristics, scores and outcomes

Patient Characteristics			
	Stable N= 1271	Deterioration N= 122	Significance (*p*)
Age	63.0 (50.0-74.0)	68.0 (54.0-77.5)	n/a
BMI	26.3 (22.7-30.5)	26.6 (22.6-29.7)	n/a
Sex, Male (%)	737 (57.9%)	74 (60.6%)	n/a
Patient scores			
NEWS2 at discharge	2.0 (1.0-4.0)	4.0 (2.0-6.0)	**<0.0**
NEWS2 on readmission		7.0 (5.00-10.0)	**<0.0***
APACHE II	16.0 (12.0-19.0)	16.0 (14.0-19.3)	**0.0**
SOFA	4.0 (3.0-5.0)	4.0 (3.0-6.0)	0.4
Patient outcomes			
First admission LOS ICU	3.0 (1.8-5.0)	4.0 (2.0-8.0)	**<0.0**
Hospital mortality		54.1% (66/122)	n/a
Time (hours) before readmission		94.5(50.0-250.3)	n/a
Number of patients readmitted		74/1393 (5.3%)	n/a
Reason for readmission	Hypoxia: 31/74 (41.9%) Hypotension:5/74 (6.8%) Post-operative: 14/74 (18.9%) Renal:5/74 (6.8%) Bleeding: 4/74 (5.4%) Low GCS: 6/74 (8.1%)		

	Seizure activity: 5/74 (6.8%) Sepsis: 10/74 (13.5%) Airway issue: 3/74 (4.1%) Cardiac arrest: 3/74 (4.1%) Increasing acuity needs: 4/74 (5.4%)
*Comparing NEWS2 at discharge to NEWS2 at readmission Statistics reported as Median (IQR) unless specified as percentage (n) LOS: Length of stay, APACHE II: Acute Physiology and Chronic Health Evaluation Score, SOFA: Sequential Organ Failure Assessment, BMI: Body Mass Index	

Comparison of vital signs at the point of discharge

Median RR was 18 pm for both groups with differences in IQR distinguishing the two (stable: 16.0-20.0, deterioration 17.0-20.0). HR was higher in those that deteriorated (86.0 (IQR 77.0-95.3)) than those that remained stable (82.0 (IQR 72.0-93.0)). Oxygen saturations and SBP were lower in those that deteriorated (SpO_2 95.0 (IQR 93.8-96.0), SBP 123.5 (IQR 110.0-139.3)) compared with those that remained stable (SpO_2 96.0 (IQR 94.0-97.0), SBP 127.0 (IQR 113.0-141.0)). A higher proportion of patients were discharged with supplemental oxygen in the deterioration group, 54.9% vs 39.8%, p=0.0. AVPU for both groups had a majority rated 'Alert' (stable: 88.7%, deterioration 82.8%) and temperature did not differ (36.7^{0}C (IQR 36.5-37.0) for both groups.

Analysis of individual vital signs prior ICU discharge showed statistically significant differences in RR, HR, oxygen saturations, AVPU and oxygen requirement between the two groups (Table 2). Although differences in RR is statistically significant, it is not clinically significant given that the median value is 18.0 for both groups. Moreover, despite the statistical difference, the heart rate and the oxygen saturation in the deteriorated group remained within normal range.

Table 2: Statistical analysis of vital signs included in the NEWS2 score taken before discharge

Parameter	Stable N= 1271		Deterioration N=122		
	Median	IQR	Median	IQR	Significance (p)
RR	18.0	16.0-20.0	18.0	17.0-20.0	**0.0**

HR	82.0	72.0-93.0	86.0	77.0-95.3	**0.0**
SpO_2	96.0	94.0-97.0	95.0	93.8-96.0	**0.0**
SBP	127.0	113.0-141.0	123.5	110.0-139.3	0.2
Temperature	36.7	36.5-37.0	36.7	36.5-37.0	0.3
AVPU	Alert (88.7%)		Alert (82.8%)		0.1
Supplemental oxygen requirement	39.8%		54.9%		**0.0**

IQR: Interquartile range, RR: Respiratory rate, HR: Heart rate, SpO_2: Oxygen saturation, SBP: Systolic blood pressure, AVPU: Alert/voice/pain/unresponsive
Significance tested using Kruskal-Wallis and Fischer's exact test for continuous and binary variables, respectively.

Comparison of blood markers for infection and inflammation

For those that remained stable, WCC (10.8 (IQR 7.0-14.8)), neutrophils (8.2 (IQR 5.7-12.1)), lymphocytes (1.2 (IQR 0.8-1.7)) and CRP (90.0 (IQR 27.0-156.3)) were similar to those who deteriorated (WCC (10.8 (IQR 8.0-15.1), neutrophils (8.2 (IQR 5.7-11.4), lymphocytes (1.1 (IQR 0.6-1.7), CRP (82.5 (IQR 26.3-149.3)).

There was no significant difference in WCC, neutrophils, lymphocytes, or CRP (Table 3). No blood marker was predictive of ICU readmission upon univariable regression analysis (Table 3).

Table 3: Statistical analysis of blood markers taken before discharge

Parameter	Normal range	Stable	Deterioration	Significance (*p*)
White cell count (10*9/L)	4.0-10.0	10.8 (7.0-14.8)	10.8 (8.0-15.1)	0.8
Neutrophils (10*9/L)	2.0-7.0	8.2 (5.7-12.1)	8.2 (5.7-11.4)	0.8
Lymphocytes (10*9/L)	1.5-4.0	1.2 (0.8-1.7)	1.1 (0.6-1.7)	0.1

C-Reactive protein (mg/L)	0-5.0	90.0 (27.0-156.3)	82.5 (26.3-149.3)	0.7
Parameters reported as median (IQR) Significance tested using Kruskal-Wallis testing				

Comparison of common scoring systems at discharge

NEWS2

NEWS2 taken before discharge from ICU had significant difference between the two groups. For those in the stable group, the average NEWS2 was 2.0 (1.0-4.0) compared to 4.0 (2.0-6.0), in those who clinically deteriorated. NEWS2 on readmission was significantly increased to 7.6 (IQR 5.0-9.8) as expected when patients returned to the unit critically unwell. Upon univariable logistic regression (Table 4), higher NEWS2 values were associated with deterioration after discharge (OR 1.1, CI 1.0-1.2). However, NEWS2 alone was a poor predictor of readmission with area under the curve (AUC): 0.6 (0.5-0.6). As NEWS2 is formed from the individual vital signs, we did not include it in the multivariable models to limit collinearity.

APACHE II

The APACHE II on first admission was similar between the two groups (stable 16.0 (12.0-19.0), deterioration 16.0 (14.0-19.3)). When APACHE II was considered in regression analysis, it did not show correlations to clinical deterioration after ICU discharge (OR: 1.1, CI: 1.0-1.1).

SOFA

SOFA score at first discharge was similar between the groups (stable: 4.0 (3.0-5.0), Deterioration: 4.0 (3.0-6.0)). SOFA score showed no correlation with readmission in univariable logistic regression (OR:1.1, CI: 1.0-1.2). However, using AIC to form multivariable models, SOFA score improved the overall model when included with HR and AVPU (Figure 2, B).

Table 4: Analysis using Univariable and Multivariable Regression						
	Univariable			Multivariable		
	OR	95% CI	*p*	OR	95% CI	*p*
Scoring systems						
APACHE II Score on admission	1.1	1.0-1.1	0.1			
SOFA Score on discharge	1.1	1.0-1.2	0.1	1.1	1.0-1.3	0.1
NEWS2 on discharge	1.1	1.0-1.2	0.0			
Individual parameters						
HR	1.0	1.0-1.1	0.0	1.0	1.0-1.1	0.0
Oxygen requirement	1.3	1.1-1.6	0.0			
SBP	1.0	1.0-1.1	0.5			
RR	1.0	1.0-1.1	0.1			
SpO_2	1.0	0.9-1.0	0.3			
Conscious level to voice, pain or unresponsive (VPU)	19.3	11.3-34.1	0.0	19.6	11.4-35.0	0.0
Temperature	0.9	0.5-1.8	0.8			
White Cell count	1.0	1.0-1.1	0.6			
Neutrophils	1.0	1.0-1.1	0.4			
Lymphocytes	0.9	0.7-1.1	0.6			
C-Reactive protein	1.0	1.0-1.1	>0.9			
OR- Odds Ratio CI- Confidence Interval						

Multivariable modelling and receiver operator characteristic curves

ROC curves produced from backwards step elimination using AIC produced two multivariable models. The first model (Figure 2, A) considered all vital sign parameters (HR, RR, etc) included within the NEWS2 score. After backwards step elimination HR and AVPU were predictive of clinical deterioration (AUC: 0.84, CI 0.8-0.9, specificity 86.2%, sensitivity 75.4%, Pseudo R^2 0.2). The second model (Figure 2, B) additionally considered SOFA and APACHE II with HR and AVPU included as predictors of deterioration after ICU discharge. After backwards step elimination, SOFA, HR and AVPU were included in the model (AUC 0.84, CI 0.8-0.9, specificity 89.9%, sensitivity 71.0%, Pseudo R^2 0.2). Of the final predictors, reduced conscious level at discharge (VPU on AVPU scale) held the strongest predictive power of post ICU deterioration.

Figure 2: Receiver operator characteristic curves: A: Curve for model 1 which included heart rate and AVPU scoring. **B:** Curve for model 2 which included heart rate, AVPU and SOFA scoring. Area under the curve (AUC) is reported on each graph with their respective confidence intervals. Point 0.0 represents the point of optimum specificity (%), sensitivity (%) [19].

Outcomes: Duration of ICU stay

Patients who deteriorated stayed an average of 1 day longer in ICU (4.0 (IQR 2.0-8.0)), before discharge compared to those who remained stable (3.0 (1.8-5.0)). Readmissions occurred at a median of 94.5 hours (50.0-250.3) after discharge from ICU.

Outcomes: Hospital mortality

The overall hospital mortality was 287/1614 (17.7%), which includes 193 patients who died in ICU, 28 palliative patients who died expectedly on the ward and 66 patients who unexpectedly deteriorated. Mortality data was not available for those who were excluded due to other discharge destinations. The hospital mortality was 54.1% (66/122) in those that deteriorated after ICU discharge. Of those, the subgroup that required readmission had an overall hospital mortality of 28.4% (21/74).

DISCUSSION

In this study, we identified 1393 patients discharged from general intensive care unit with 122 patients needing unanticipated readmission during this 1-year study period. All these patients were discharged from ICU with active treatment plans and subsequently deteriorated requiring ICU readmission. Whilst the evaluation of clinical variables and scoring systems at discharge suggest HR, oxygen requirement, and NEWS2 are predictive on univariate analysis, multivariate modelling suggest HR, AVPU and SOFA score to be predictive of clinical deterioration after intensive care discharge (Table 4). ICU length of stay was longer during the 1st admission for those who subsequently deteriorated, with associated higher mortality (Table 1). Although our readmission rate is slightly higher (5.3%) than the UK-wide audit data from the ICNARC (1.2%), which only includes unplanned readmission rate within the first 48 hours of discharge, our data is inclusive of all readmissions at any time point post discharge [16]. However, our patient demographics and readmission rates were similar to previously published work [20-22]. To our knowledge, this is the largest study in the UK assessing the predictive capabilities of routinely collected individual vital signs and NEWS2 scoring at discharge from a general ICU.

Previous studies [7, 23-25] have suggested that NEWS scoring at discharge can be predictive of clinical deterioration after ICU discharge. Of these studies, two report similar NEWS values to our results, with average NEWS for stable patients of 2.5 and 2.3 compared to 3.7 and 5.5 for those that showed clinical deterioration [7, 25]. The other two studies report much higher average NEWS values of 3.0 and 4.0 for stable patients and 9.1 and 10.0 in those that deteriorated after

ICU discharge [23, 24]. These differences may have been due to other factors such as population, resources and clinical pressures. We found NEWS2 scoring to be predictive of clinical deterioration after ICU discharge on univariable analysis. On breakdown of NEWS2 components, only HR and AVPU were predictive in our final models. The predictivity of heart rate has been assessed in only a few studies with all including it within multivariable models[26-28]. In comparison, acute changes to level of consciousness have been shown to be a sign of clinical deterioration in isolation [29-31]. In this study, patients with a conscious level to voice, pain or unresponsive were 19x more likely to deteriorate after leaving ICU compared to those who were classified as alert at ICU discharge. Compared to the other factors in our final model, AVPU was the most sensitive marker of subsequent unexpected deterioration. Oh et al also reported a predictive ability of altered conscious level, yet in their study only 10% of patients discharged from ICU had a GCS below 13 and an average GCS of 14.4 at discharge [29]. This supports our data with an over 80% majority in both groups reported as 'Alert' on an AVPU scale. It is possible that reducing conscious level is a marker of patient deterioration that may be limited by the broad categories of AVPU within the NEWS2 score.

In our study, the median NEWS2 score was 4 for those subsequently deteriorated and 2 for those that remained stable. Although statistically significant, according to NEWS2 protocol both scores would classify in the 'Low clinical risk' category (if no more than 3 in any one category). Although HR, RR and oxygen saturations were different between the two groups, these were only marginal differences, and so clinical relevance of this should be considered. The low NEWS2 score at discharge suggests that these patients were physiologically stable for de-escalation to a ward environment. Moreover, the availability of other level-2 areas such as respiratory high dependency and surgical high dependency units allows us to safely discharge stable patients requiring ongoing level 2 support. In comparison to other UK hospitals, studies reporting average NEWS values are limited. Chiu et al assessed discharge NEWS after cardiac ICU discharge [32]. Although no value is reported, only 33% of patients reached a threshold of NEWS >3 after 24hrs post discharge, suggesting a low average NEWS value. Scott et al used NEWS2 to assess all-cause deterioration and found 50% to have low values of 1-2 on admission [20]. This therefore highlights that subtle changes in NEWS2/vital sign values are likely to be the early clues for acute deterioration. We therefore suggest that an awareness of trends is likely to be a better clinical representation of overall physiology.

The median time from discharge to readmission was 94 hours, which is similar to previous work by Johnson et al who found an average 4 day stay before readmission [33]. Studies assessing

EWS often use time cut offs, most commonly 48hrs, before readmission to determine their cohorts [34, 35]. Although they highlight patients who quickly deteriorated, our findings of an average ward stay of over 3 days before ICU readmission suggests that limits of under two days are likely to exclude a large proportion of patients in subsequent analysis and models. It also emphasizes the need for careful patient monitoring within the first 4 days after ICU discharge. At our centre, patients discharged from critical care have daily surveillance by critical care outreach teams (CCOT) up until clinically stable or placed on palliative care pathways. The ability to provide outreach CCOT service aims to identify deteriorating patients early enabling faster escalation to appropriate specialist and critical care teams. The use of CCOT is recommended by NICE for patients at risk of acute deterioration, but not standardised within the UK with CCOT provision varying greatly between centres [36].

There are several notable limitations to our study. This was a single centre, retrospective, observational study and the NEWS2 and vital sign parameters were taken as a single snapshot of physiology at discharge. As the electronic systems used within our hospital change at ICU discharge, we were unable to track NEWS2 changes over time which may have provided valuable trend analysis. The data presented here are related to general ICU admissions and are not specific to specialists ICU patients such as cardiac. Our hospital has separate neuro ICU and cardiac ICU and as a result our patient cohort primarily consisted of general intensive care patients. Consequently, the results may not be transferable to other specialist centres. We have not included comorbidities or the initial diagnosis in our analysis and as such we are unable to identify patient specific factors that may increase the risk of readmission. Despite these limitations, this is one of the largest studies to explore the predictive variables of readmission risk captured at ICU discharge. Moreover, there were no exclusions, and we included all ICU admissions and discharges with the intention for subsequent escalation if there is clinical deterioration.

At present, there is no consensus for a risk stratification tool prior to ICU discharge. The Society for Critical Care medicine suggests that "discharge parameters should be based on ICU admission criteria, the admitting criteria for the next lower level of care, institutional availability of these resources, patient prognosis, physiologic stability, and ongoing active interventions" and that 'severity of illness scores should not be used as a sole reason for discharge'[37]. This is supported by the work into predictive modelling whereby single models are outperformed by those trained with targeted approaches or machine learning [38, 39]. Together, these suggests that although physiological factors on discharge may be useful in

determining the predictability of post-ICU deterioration, further work is required to develop decision aids that combine multiple predictors tailored to each patients' individual risks, of which scoring systems may play a role. At present, there is no single model or score that should be used in isolation and discharge remains a clinician dependent decision. While this study highlights that there are some helpful predictive markers of deterioration at discharge, the variables are may be still regarded as within the range of physiological normality. Moreover, there are several other factors such as patient specific variables, disease specific variables, availability of CCOT and the frequency of monitoring will all require consideration and as such, no single scoring system is comparable to clinical judgement.

CONCLUSION

Our study found predictive ability of HR, AVPU and SOFA score at discharge between those that were subsequently deteriorated after ICU discharge and those who remained physiologically stable. Together, these show that acute physiological changes prior to discharge, alongside severity of organ dysfunction secondary to ICU illness, are important factors to consider when discharging patients. Scoring systems, including NEWS2, may have a role as supportive tools but should not be used as a sole indicator for ICU discharge. Further work using predictive modelling and scoring systems is required.

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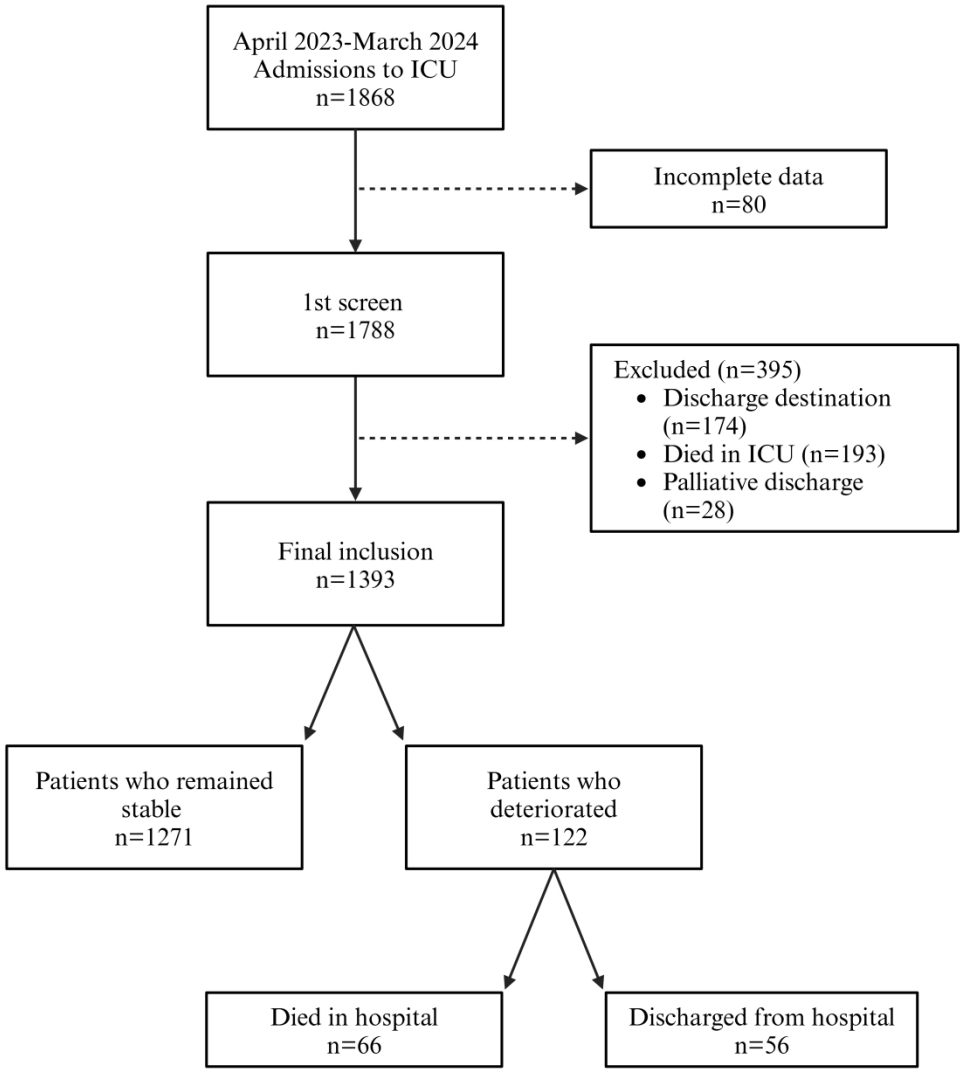

Figure 1: Flowchart showing the formulation to the final dataset17.

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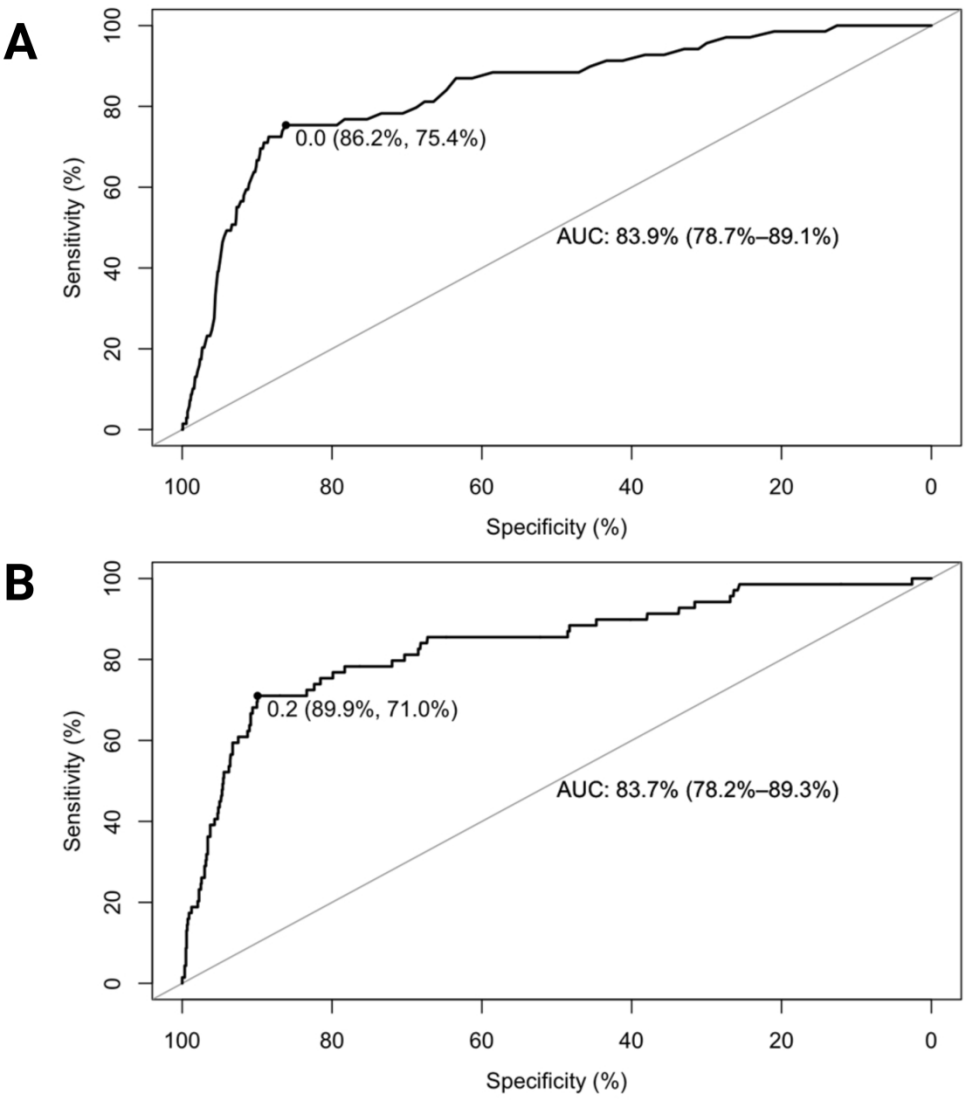

Figure 2: A: Curve for model 1 which included heart rate and AVPU scoring. B: Curve for model 2 which included heart rate, AVPU and SOFA scoring. Area under the curve (AUC) is reported on each graph with their respective confidence intervals. Point 0.0 represents the point of optimum specificity (%), sensitivity (%)19.

458x510mm (236 x 236 DPI)

Appendix 1: Scoring system tables

Each table represents the system used to calculate the respective physiological score.

1.1 NEWS2

Table 1: Components of the National Early Warning Score 2 (NEWS2) and its scoring system

Physiological variable	Score						
	3	2	1	0	1	2	3
Respiratory rate (per minute)	≤8		9-11	12-20		21-24	≥25
SpO2 Scale 1 (%)	≤91	92-93	94-95	≥96			
SpO2 Scale 2 (%)	≤83	84-85	86-87	≥93 on air 88-92	93-94 on oxygen	95-96% on oxygen	≥97 on oxygen
Air or Oxygen		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Pulse (per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Consciousness				Alert			CVPU
Temperature (^{0}C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

1.2 Sequential Organ Failure Assessment (SOFA)

Table 2: Components of the Sequential Organ Failure Assessment Score					
	SOFA Score				
Variable	0	1	2	3	4
Respiratory	PaO_2/FiO_2: >400 SpO_2/FiO_2: >302	PaO_2/FiO_2: <400 SpO_2/FiO_2: <302	PaO_2/FiO_2: <300 SpO_2/FiO_2: <221	PaO_2/FiO_2: <200 SpO_2/FiO_2: <142	PaO_2/FiO_2: <100 SpO_2/FiO_2: <67
Cardiovascular (Doses in mcg/kg/min)	MAP ≥ 70 mmHg	MAP ≥ 70 mmHg	Dopamine ≤ 5 or any dobutamine	Dopamine > 5, Noradrenaline ≤ 0.1, Phenylephrine ≤ 0.8	Dopamine > 15, Noradrenaline > 0.1, Phenylephrine > 0.8
Liver (Bilirubin, mg/dL)	< 1.2	1.2-1.9	2.0-5.9	6.0-11.9	> 12
Renal (Creatinine, mg/dL)	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9	> 5.0
Coagulation (Platelets x $10^3/mm^3$)	≥ 150	< 150	< 100	< 50	< 20
Neurology (Glasgow Coma score)	15	13-14	10-12	6-9	< 6

1.3 Acute physiology and Chronic Health Evaluation II Score

Table 3: Components of the Acute physiology and Chronic Health Evaluation II Score

	Acute physiological variable		High abnormal range					Low abnormal range			
			+4	+3	+2	+1	0	+1	+2	+3	+4
1	Temperature (^{0}C)		≥ 41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤ 29.9
2	Mean Arterial Pressure (mmHg)		≥ 160	130-159	110-129		70-109		50-69		≤ 49
3	Heart rate		≥ 180	140-179	110-139		70-109		50-69	40-54	≤ 39
4	Respiratory rate		≥ 50	35-49		25-34	12-24	10-11	6-9		≤ 5
5a	Oxygenation (A-a gradient if $FiO_2 \geq 0.5$ or PaO_2 if $FiO_2 \leq 0.5$)	A-a gradient	≥ 500	350-499	200-349		< 200				
5b		PaO_2					>70	61-70		55-60	<54
6a	Arterial pH		≥ 7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
6b	HCO_3 (mEq/l) (to use instead of pH if only venous sample available)		≥ 52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
7	K (mEq/l)		≥ 7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
8	Na (mEq/l)		≥ 180	160-179	155-159	150-154	130-149		120-129	111-119	≤ 110
9	Serum Creatinine (mqm/dl)		≥ 3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
10	Haematocrit (%)		≥ 60		50-59.9	46-49.9	30-45.9		20-29.9		<20
11	White cell count(10^3/cc)		≥ 40		20-39.9	15-19.9	3.0-14.9		1.0-2.9		≤ 1.0
12	Glasgow Coma Score		Points= 15 – calculated Glasgow coma score								

<table>
<tr>
<td></td>
<td>
Age points (years):
<table>
<tr><td>≤ 44y</td><td>0</td></tr>
<tr><td>45-54y</td><td>+2</td></tr>
<tr><td>55-64y</td><td>+3</td></tr>
<tr><td>65-74y</td><td>+5</td></tr>
<tr><td>≥ 75y</td><td>+6</td></tr>
</table>
</td>
<td>
Chronic health points:
<table>
<tr><td>Non-operative, or emergency post-op with any of the below conditions*</td><td>+5</td></tr>
<tr><td>Elective operation with any of the conditions below *</td><td>+2</td></tr>
<tr><td colspan="2">*Cirrhosis with portal hypertension or encephalopathy; class IV heart failure; chronic hypoxia; chronically increased CO_2 or polycythaemia; long term dialysis; immunocompromised; chronic restrictive or vascular disease resulting in severe exercise restriction (i.e. unable to climb stairs)</td></tr>
</table>
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<tr>
<td></td>
<td colspan="2">Total APACHE II Score: Age points + Chronic health points + Acute physiology points</td>
</tr>
</table>

BMJ Open

Evaluation of the physiological variables and scoring systems at intensive care discharge as predictors of clinical deterioration and readmission: A single-centre retrospective study

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Evaluation of the physiological variables and scoring systems at intensive care discharge as predictors of clinical deterioration and readmission: A single-centre retrospective study

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ABSTRACT

Objectives: We aim to determine, using routinely collected data and common scoring systems, whether parameters seen at intensive care unit (ICU) discharge can be predictive of subsequent clinical deterioration.

Design/setting: A single-centre retrospective study located in a tertiary hospital in the south of England.

Participants: 1868 patients who were admitted and discharged from ICU between 1st April 2023 to 31st March 2024 were screened for eligibility. A total of 1393 patients were included in the final analysis, including 122 patients who classified in the 'deteriorated' subgroup.

Interventions: Assessment of vital signs, blood markers of infection and inflammation and 3 scoring systems (NEWS2, APACHE II and SOFA score) taken within 24hrs prior ICU discharge.

Primary outcomes: Assessment of predictors of deterioration after ICU discharge.

Secondary outcomes: Reasons for readmission to ICU, hospital mortality, ICU length of stay and time before readmission to ICU.

Results: Heart rate, conscious level (AVPU scale) and SOFA score were independent predictors of deterioration after ICU discharge (AUC 0.85, CI 0.79-0.90, specificity 82.3%, sensitivity 79.7%) in multivariable models. Of these, a reduced level of consciousness was the most significant predictor of clinical deterioration (OR 19.6, CI 11.4-35.0). NEWS2 was an independent predictor for deterioration on univariable analysis. Mortality was significantly increased in patients who experienced deterioration after ICU discharge, as was ICU length of stay.

Conclusions: Predictive models may be useful in assisting clinicians with ICU discharge decisions. Further research is required to develop patient tailored scoring systems that incorporate other factors that are needed for decisions around ICU discharge.

Article Summary

Strengths and limitations:

Strength:

- Large dataset of over 1300 patients
- Adjusted for collinearity between vital sign values and scoring systems
- Assessed individual parameters and vital signs before forming overall predictive models

Limitation:

- Single centre
- Comorbidities not assessed

INTRODUCTION

The decision to discharge patients from intensive care is complex and often based on multiple factors. For most, an ideal combination of clinical, nursing and management factors lead to a timely discharge to the most appropriate ward facility. However, some patients experience unanticipated clinical deterioration after discharge leading to unplanned readmission and adverse outcomes [1-3]. Currently, there is no ideal clinical variable or scoring system available to guide suitability of patient discharge from the intensive care unit (ICU). While there are several methods utilised to identify potential patients who could deteriorate, there is no clear consensus [4, 5]. Some studies suggest scoring systems, such as the National Early Warning Score 2 (NEWS2), a system with widespread usage already in the UK and worldwide, could be an easy and effective method of screening for patients at risk of deterioration prior to ICU discharge [6-8].

Developed by the Royal College of Physicians, NEWS2 is a system used to quantitatively score routine physiological parameters to identify those acutely ill or with deteriorating clinical status [9, 10]. Although its use is almost universal in UK hospital wards to predict patients at-risk of deterioration [9], the use of NEWS2 to assess suitability of ICU discharge has not been validated in ICU patients and as such is not routinely used in ICU. In comparison, the Sequential Organ Failure Assessment score (SOFA) is validated in ICU cohorts [11, 12]. Based on organ systems, SOFA score uses a multisystem based approach to assess acute morbidity and mortality of critical illness. In recent years, this has been applied to the identification and monitoring of sepsis through the work of Sepsis-3 [13]. A further score often used in ICU is the Acute physiology and Chronic Health Evaluation II Score (APACHE II). APACHE II estimates disease severity based on physiological measurements, including blood markers, along with considerations for age and chronic health conditions [14, 15]. It is used at the time of admission and recalculated daily in ICU for prognostic scoring, having been shown to be an accurate measurement of illness severity with correlations to clinical outcomes [15].

Given their potential use, we aim to evaluate these scoring systems, along with routinely collected variables such as vital signs and blood markers, to determine if measurements taken

before ICU discharge can predict those who will unexpectedly deteriorate after leaving intensive care.

MATERIALS AND METHODS

Study Design and setting

This is a retrospective analysis of a 31-bed general intensive care (ICU) admissions and discharges between 1st April 2023 to 31st March 2024 based at a large tertiary hospital in the south of England. Patients were identified using databases that are routinely used by the ICU auditing team performed as part of the Intensive Care National Audit and Research Centre (ICNARC) data collection [16]. This study is part of a wider study investigating outcomes of critical illness in intensive care (CRIT-CO). CRIT-CO is sponsored by University Hospital Southampton NHS Foundation Trust (RHM CRI 0370) and has approval from the NHS Health Research Authority (HRA, UK: IRAS 232922, 26/11/2018). This study was also registered as a quality improvement project by the University Hospital Southampton Service Evaluation Team (Ref: QI/0272)**.** This study follows local ethical standards, and no identifiable data is presented here. Given its retrospective nature and no additional information required, consent was waivered.

Patient and Public involvement

Patients and the public were not directly involved in this research study. However, the foundations of this research were developed after discussions with patients who had experienced unexpected deterioration after discharge from intensive care.

Data collection

Patients were identified using the Intensive Care database (MetaVision-iMDsoft, Israel). The inclusion criteria were patients 18 years and older, admitted and discharged from the ICU during a single hospital admission and had vital sign monitoring undertaken before ICU discharge. The exclusion criteria were patients who died in ICU during the first admission, discharged on an end-of-life care pathway (palliation), discharged to another ICU department (same hospital), transferred to another hospital, transferred to another care provider on ICU discharge (e.g. rehabilitation unit, care home), discharged directly home or self-discharged. Patients who deteriorated were separated from the main dataset through review of the ICU records. As part of routine audit data, a patients discharge location, hospital outcome and ≤48hr/>48hr ICU readmission are recorded. Deterioration was defined as anyone who was either readmitted back to the ICU during the same hospital admission or who died on the ward

after being discharged with active treatment ongoing. Any patient who had more than one admission to the ICU over the year period, but which occurred in separate hospital admissions, were included individual entries.

We collected standard variables such as age, gender and body mass index (BMI). Individual vital sign (heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), temperature (^{0}C), oxygen saturation (SpO_2) and conscious level (Alert, voice, pain, unresponsive scale (AVPU))) data was collected using the last recorded set of vital signs before ICU discharge. For all, these measurements were within the preceding 4 hours before discharge. For assessment of SOFA and APACHE II scores, these were calculated using the most abnormal values in the preceding 24hrs prior to discharge[12, 15]. NEWS2 was calculated using the vital sign data as described previously. Biochemical data (total white cell count (WCC), lymphocyte count, neutrophil count and C-reactive protein (CRP) was taken using the last recorded value, which for all was within 24hrs prior to ICU discharge. A scoring matrix for NEWS2, SOFA and APACHE II can be seen in Appendix 1. Other data, such as length of ICU stay, hospital mortality, timing and reason for readmission were determined via review of ICU records.

Outcomes

The main outcome of this study was to identify patients discharged from ICU who had unexpected clinical deterioration to determine if there were any predictors of subsequent deterioration at ICU discharge. Secondary outcomes included determining reasons for readmission to ICU, timing of ICU readmission, hospital mortality and ICU length of stay.

Statistical and data analysis

Differences in baseline characteristics between groups were described with median and 25th-75th percentile (25. percentile-75. percentile) for continuous variables and counts with percentages for categorical groups. Each vital sign parameter was analysed individually and ICU discharge data (This included: length of stay (LOS), APACHE II score on admission, SOFA Score on discharge, laboratory markers of infection/inflammation). Comparisons of between groups were made using Mann-Whitney U and Fischer's exact test for continuous and binary variables, respectively.

Logistic regression models were constructed for the prediction of re-escalation. Variables with a significance threshold of P<0.25 within univariable models were included in multivariable analysis. Subsequently, backwards selection was performed using the Akiake information

criterion (AIC) to produce the final models. Overall models were further described with Receiver-operating characteristic curves (ROC) and McFaddens pseudo-R^2. On significance testing, *P* values <0.05 were deemed significant throughout the analysis. All analyses were performed using R (Version 4.2.2). All figures were formed using Biorender.com.

RESULTS

We screened 1868 discharges for this 12-month period. After exclusions, the final dataset included a total of 1393 patients, with 122 patients who clinically deteriorated (8.76%). Of these 122, 74 patients were readmitted to ICU (5.3% readmission rate) (Figure 1).

Patient characteristics and readmission profile

The average age was similar between the two groups and the proportion of male patients was also similar Both groups had a mean BMI within 'overweight' group according to NHS guidance [18] (Table 1). Of those readmitted, 41.9% required treatment for acute hypoxia and 18.9% for unplanned post-operative care. Other reasons for readmission included hypotension (5/74 (6.8%)), bleeding (leading to haemodynamic compromise) (4/74 (5.4%)), renal support (5/74 (6.8%)), reduced level of consciousness (6/74 (8.1%)) and seizure activity (5/74 (6.8%)). 15 patients had more than one reason (e.g. hypoxia and hypotension) and so were included in both categories. 10 patients (13.5%) developed sepsis on the ward requiring organ support and 3 patients had a cardiac arrest on the ward leading to ICU readmission. 4 patients (5.4%) became more unwell from medical and nursing perspectives without one defining factor and so were classified as 'increasing acuity needs'. Similar proportions of each group were discharged out of hours including over the weekend.

Table 1: Patient characteristics, scores and outcomes

Patient Characteristics			
	Stable n= 1271	Deterioration n= 122	Significance (*p*)
Age	63.0 (50.0-74.0)	68.0 (54.0-77.5)	n/a
BMI	26.3 (22.7-30.5)	26.6 (22.6-29.7)	n/a
Sex, Male (%)	737 (57.9%)	74 (60.6%)	n/a
Patient scores			
NEWS2 at discharge	2.0 (1.0-4.0)	4.0 (2.0-6.0)	**<0.01**
NEWS2 on readmission		7.0 (5.00-10.0)	**<0.01***

APACHE II	16.0 (12.0-19.0)	16.0 (14.0-19.3)	**<0.01**
SOFA	4.0 (3.0-5.0)	4.0 (3.0-6.0)	0.45
Patient outcomes			
First admission LOS ICU	3.0 (1.8-5.0)	4.0 (2.0-8.0)	**<0.01**
Discharged out of hours**	43.8% (557/1271)	50.8% (62/122)	0.54
Discharged on a weekend	25.6% (326/1271)	35.2% (43/122)	0.16
Hospital mortality		54.1% (66/122)	n/a
Time (hours) before readmission		94.5(50.0-250.3)	n/a
Number of patients readmitted		74/1393 (5.3%)	n/a

*Comparing NEWS2 at discharge to NEWS2 at readmission

** Out of hours defined as 20:00-08:00 Monday to Friday and all day Saturday and Sunday

Statistics reported as Median (25th percentile-75th percentile) unless specified as percentage (n)

LOS: Length of stay, APACHE II: Acute Physiology and Chronic Health Evaluation Score, SOFA: Sequential Organ Failure Assessment, BMI: Body Mass Index

Comparison of vital signs at the point of discharge

Median RR was 18 pm for both groups with differences in 25th-75th percentile distinguishing the two (stable: 16.0-20.0, deterioration 17.0-20.0). HR, SpO_2 and SBP were different in those that deteriorated compared to those that remained stable. A higher proportion of patients were discharged with supplemental oxygen in the deterioration group, 54.9% vs 39.8%, p=0.01. AVPU for both groups had a majority rated 'Alert' (stable: 88.7%, deterioration 82.8%) and temperature did not differ for both groups (Table 2).

Analysis of individual vital signs prior ICU discharge showed statistically significant differences in RR, HR, oxygen saturations, AVPU and oxygen requirement between the two groups (Table 2). Although differences in RR is statistically significant, it is not clinically significant given that the median value is 18.0 for both groups. Moreover, despite the statistical difference, the heart rate and the oxygen saturation in the deteriorated group remained within normal range.

Table 2: Statistical analysis of vital signs included in the NEWS2 score taken before discharge					
Parameter	Stable N= 1271		Deterioration N=122		
	Median	25^{th}-75^{th} percentile	Median	25^{th}-75^{th} percentile	Significance (*p*)
RR	18.0	16.0-20.0	18.0	17.0-20.0	**<0.01**
HR	82.0	72.0-93.0	86.0	77.0-95.3	**<0.01**
SpO_2	96.0	94.0-97.0	95.0	93.8-96.0	**0.02**
SBP	127.0	113.0-141.0	123.5	110.0-139.3	0.24
Temperature	36.7	36.5-37.0	36.7	36.5-37.0	0.32
AVPU	Alert (88.7%)		Alert (82.8%)		0.05
Supplemental oxygen requirement	39.8%		54.9%		**0.01**

RR: Respiratory rate, HR: Heart rate, SpO_2: Oxygen saturation, SBP: Systolic blood pressure, AVPU: Alert/voice/pain/unresponsive

Significance tested using Mann-Whitney U and Fischer's exact test for continuous and binary variables, respectively.

Comparison of blood markers for infection and inflammation

For those that remained stable, WCC neutrophils, lymphocytes and CRP were similar to those who deteriorated.

There was no significant difference in WCC, neutrophils, lymphocytes, or CRP (Table 3). No blood marker was predictive of ICU readmission upon univariable regression analysis (Table 4).

Table 3: Statistical analysis of blood markers taken before discharge				
Parameter	Normal range	Stable	Deterioration	Significance (*p*)

White cell count (10*9/L)	4.0-10.0	10.8 (7.0-14.8)	10.8 (8.0-15.1)	0.85
Neutrophils (10*9/L)	2.0-7.0	8.2 (5.7-12.1)	8.2 (5.7-11.4)	0.75
Lymphocytes (10*9/L)	1.5-4.0	1.2 (0.8-1.7)	1.1 (0.6-1.7)	0.12
C-Reactive protein (mg/L)	0-5.0	90.0 (27.0-156.3)	82.5 (26.3-149.3)	0.72
Parameters reported as median (25^{th}-75^{th} percentile) Significance tested using Mann-Whitney U				

Comparison of common scoring systems at discharge

NEWS2

NEWS2 taken before discharge from ICU was significantly different between the two groups. For those in the stable group, the average NEWS2 was 2.0 (1.0-4.0) compared to 4.0 (2.0-6.0), in those who clinically deteriorated. NEWS2 on readmission was significantly increased to 7.0 (5.0-10.0) as expected when patients returned to the unit critically unwell. Upon univariable logistic regression (Table 4), higher NEWS2 values were associated with deterioration after discharge (OR 1.1, CI 1.0-1.2). However, NEWS2 alone was a poor predictor of readmission with area under the curve (AUC): 0.6 (0.5-0.6). As NEWS2 is formed from the individual vital signs, we did not include it in the multivariable models to limit collinearity.

APACHE II

The APACHE II on first admission was similar between the two groups (stable 16.0 (12.0-19.0), deterioration 16.0 (14.0-19.3)). When APACHE II was considered in regression analysis, it did not show correlations to clinical deterioration after ICU discharge (OR: 1.1, CI: 1.0-1.1).

SOFA

SOFA score at first discharge was similar between the groups (stable: 4.0 (3.0-5.0), Deterioration: 4.0 (3.0-6.0)). SOFA score showed no correlation with readmission in univariable logistic regression (OR:1.1, CI: 1.0-1.2). However, using AIC to form multivariable models, SOFA score improved the overall model when included with HR and AVPU (Figure 2, B).

Table 4: Analysis using Univariable and Multivariable Regression						
	Univariable			Multivariable		
	OR	95% CI	*p*	OR	95% CI	*p*
Scoring systems						
APACHE II Score on admission	1.1	1.0-1.1	0.05			
SOFA Score on discharge	1.1	1.0-1.2	0.12	1.1	1.0-1.3	0.10
NEWS2 on discharge	1.1	1.0-1.2	0.03			
Individual parameters						
HR	1.0	1.0-1.1	0.03	1.0	1.0-1.1	<0.01
Oxygen requirement	1.3	1.1-1.6	<0.01			
SBP	1.0	1.0-1.1	0.50			
RR	1.0	1.0-1.1	0.05			
SpO_2	1.0	0.9-1.0	0.30			
Conscious level to voice, pain or unresponsive (VPU)	19.3	11.3-34.1	<0.01	19.6	11.4-35.0	<0.01
Temperature	0.9	0.5-1.8	0.80			
White Cell count	1.0	1.0-1.1	0.60			
Neutrophils	1.0	1.0-1.1	0.40			
Lymphocytes	0.9	0.7-1.1	0.60			
C-Reactive protein	1.0	1.0-1.1	>0.90			
OR- Odds Ratio CI- Confidence Interval						

Multivariable modelling and receiver operator characteristic curves

ROC curves produced from backwards step elimination using AIC produced two multivariable models. The first model (Figure 2, A) considered all vital sign parameters (HR, RR, etc) included within the NEWS2 score. After backwards step elimination, HR and AVPU were predictive of clinical deterioration (AUC: 0.84, CI 0.8-0.9, specificity 86.2%, sensitivity 75.4%, Pseudo R^2 0.2). The second model (Figure 2, B) additionally considered SOFA and APACHE II with HR and AVPU included as predictors of deterioration after ICU discharge. After backwards step elimination, SOFA, HR and AVPU were included in the model (AUC 0.84, CI 0.8-0.9, specificity 89.9%, sensitivity 71.0%, Pseudo R^2 0.2). Of the final predictors, reduced conscious level at discharge (VPU on AVPU scale) held the strongest predictive power of post ICU deterioration.

Outcomes: Duration of ICU stay

Patients who deteriorated stayed an average of 1 day longer in ICU (4.0 (2.0-8.0)), before discharge compared to those who remained stable (3.0 (1.8-5.0)). Readmissions occurred at a median of 94.5 hours (50.0-250.3) after discharge from ICU.

Outcomes: Hospital mortality

The hospital mortality was 287/1614 (17.7%), which includes 193 patients who died in ICU, 28 palliative patients who died expectantly on the ward and 66 patients who unexpectedly deteriorated and died. This total patient number includes all those included in the final data set plus those that died during their first ICU admission or were discharged palliatively. Mortality data was not available for those who were excluded due to other discharge destinations or those with incomplete data. The hospital mortality was 54.1% (66/122) in those that deteriorated after ICU discharge. Of those, the subgroup that required readmission had an overall hospital mortality of 24.3% (18/74). All three patients who required readmission after cardiac arrest died within 72 hours of the event. They all experienced asystolic cardiac arrests with evidence of hypoxic-ischaemic encephalopathy on subsequent testing.

DISCUSSION

In this study, we identified 122 patients from 1393 ICU discharges that experienced unexpected deterioration during the 1-year study period. Secondary deterioration after ICU discharge was associated with a higher hospital mortality and a longer 1st admission ICU length of stay. Whilst the evaluation of clinical variables and scoring systems at discharge suggest HR, oxygen requirement, and NEWS2 are predictive on univariable analysis, multivariable modelling suggests HR, AVPU and SOFA score to be predictive of clinical deterioration after ICU discharge (Table 4). Although our readmission rate is higher (5.3%) than the UK-wide audit data from the ICNARC (1.2%), which only includes unplanned readmission rate within the first 48 hours of discharge, our data is inclusive of all readmissions at any time point post discharge [16]. However, our patient demographics and readmission rates were similar to previously published work [20-22]. To our knowledge, this is the largest study in the UK assessing the predictive capabilities of routinely collected individual vital signs and NEWS2 scoring at discharge from a general ICU.

Previous studies [7, 23-25] have suggested that NEWS scoring at discharge can be predictive of clinical deterioration after ICU discharge. Of these studies, two report similar NEWS values to our results, with average NEWS for stable patients of 2.5 and 2.3 compared to 3.7 and 5.5 for

those that showed clinical deterioration [7, 25]. The other two studies report much higher average NEWS values of 3.0 and 4.0 for stable patients and 9.1 and 10.0 in those that deteriorated after ICU discharge [23, 24]. These differences may have been due to other factors such as population, resources and clinical pressures. We found NEWS2 scoring to be predictive of clinical deterioration after ICU discharge on univariable analysis. On breakdown of NEWS2 components, only HR and AVPU were predictive in our final models. The predictivity of heart rate has been assessed in only a few studies, with all including it within multivariable models[26-28]. In comparison, acute changes to level of consciousness have been shown to be a sign of clinical deterioration in isolation [29-31]. In this study, patients with a conscious level to voice, pain or unresponsive were 19x more likely to deteriorate after leaving ICU compared to those who were classified as alert at ICU discharge. Compared to the other factors in our final model, AVPU was the most sensitive marker of subsequent unexpected deterioration. Oh et al also reported a predictive ability of altered conscious level, yet in their study only 10% of patients discharged from ICU had a GCS below 13 and an average GCS of 14.4 at discharge [29]. This supports our data with an over 80% majority in both groups reported as 'Alert' on an AVPU scale. It is possible that reducing conscious level as a marker of patient deterioration may be limited by the broad categories of AVPU within the NEWS2 score.

In our study, the median NEWS2 score was 4 for those subsequently deteriorated and 2 for those that remained stable. Although statistically significant, according to NEWS2 protocol both scores would classify in the 'Low clinical risk' category (if no more than 3 in any one category). Although HR, RR and oxygen saturations were different between the two groups, these were only marginal differences, and so clinical relevance of this should be considered. In comparison to other UK hospitals, studies reporting average NEWS values are limited. Chiu et al assessed discharge NEWS after cardiac ICU discharge [32]. Although no value is reported, only 33% of patients reached a threshold of NEWS >3 after 24hrs post discharge, suggesting a low average NEWS value. Scott et al used NEWS2 to assess all-cause deterioration and found 50% to have low values of 1-2 on admission [20]. This therefore highlights that subtle changes in NEWS2/vital sign values are likely to be the early clues for acute deterioration. We therefore suggest that an awareness of trends is likely to be a better clinical representation of overall physiology.

The median time from discharge to readmission was 94 hours, which is similar to previous work by Johnson et al who found an average 4 day stay before readmission [33]. Studies assessing EWS often use time cut offs, most commonly 48hrs, before readmission to determine their

cohorts [34, 35]. Although they highlight patients who quickly deteriorated, our findings of an average ward stay of over 3 days before ICU readmission suggests that limits of under two days are likely to exclude a large proportion of patients in subsequent analysis and models. It also emphasizes the need for careful patient monitoring within the first 4 days after ICU discharge. At our centre, patients discharged from critical care have daily surveillance by critical care outreach teams (CCOT) up until clinically stable or placed on palliative care pathways. The use of CCOT is recommended by NICE for patients at risk of acute deterioration, but not standardised within the UK with CCOT provision varying greatly between centres [36].

There are several notable limitations to our study. This was a single centre, retrospective, observational study and the NEWS2 and vital sign parameters were taken as a single snapshot of physiology at discharge. As the electronic systems used within our hospital change at ICU discharge, we were unable to track NEWS2 changes over time which may have provided valuable trend analysis. The data presented here are related to general ICU admissions and are not specific to specialists ICU patients such as cardiac. Consequently, the results may not be transferable to other specialist centres. We have not included comorbidities or the initial diagnosis in our analysis due to limitations with data collection and as such we are unable to identify patient specific factors that may increase the risk of readmission. Despite these limitations, this is one of the largest studies to explore the predictive variables of readmission risk captured at ICU discharge. Moreover, there were no exclusions, and we included all ICU admissions and discharges with the intention for subsequent escalation if there is clinical deterioration.

At present, there is no consensus for a risk stratification tool prior to ICU discharge. The Society for Critical Care medicine suggests that "discharge parameters should be based on ICU admission criteria, the admitting criteria for the next lower level of care, institutional availability of these resources, patient prognosis, physiologic stability, and ongoing active interventions" and that 'severity of illness scores should not be used as a sole reason for discharge'[37]. This is supported by the work into predictive modelling whereby single models are outperformed by those trained with targeted approaches or machine learning [38, 39]. Together, these suggests that although physiological factors on discharge may be useful in determining the predictability of post-ICU deterioration, further work is required to develop decision aids that combine multiple predictors tailored to each patients' individual risks, of which scoring systems may play a role. While this study highlights that there are some helpful

predictive markers of deterioration at discharge, the variables are may be still regarded as within the range of physiological normality. Moreover, there are several other factors such as patient specific variables, disease specific variables, availability of CCOT and the frequency of monitoring will all require consideration and as such, no single scoring system is comparable to clinical judgement.

CONCLUSION

Our study found predictive ability of HR, AVPU and SOFA score at discharge between those that were subsequently deteriorated after ICU discharge and those who remained physiologically stable. Together, these show that acute physiological changes prior to discharge, alongside severity of organ dysfunction secondary to ICU illness, are important factors to consider when discharging patients. Scoring systems, including NEWS2, may have a role as supportive tools but should not be used as a sole indicator for ICU discharge. Further work using predictive modelling and scoring systems is required.

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Conflicts of interest: The authors declare no conflict of interest

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Figure 1: Flowchart showing the formulation to the final dataset[17].

Figure 2: Receiver operator characteristic curves: A: Curve for model 1 which included heart rate and AVPU scoring. **B:** Curve for model 2 which included heart rate, AVPU and SOFA scoring. Area under the curve (AUC) is reported on each graph with their respective confidence intervals. Point 0.0 represents the point of optimum specificity (%), sensitivity (%) [19].

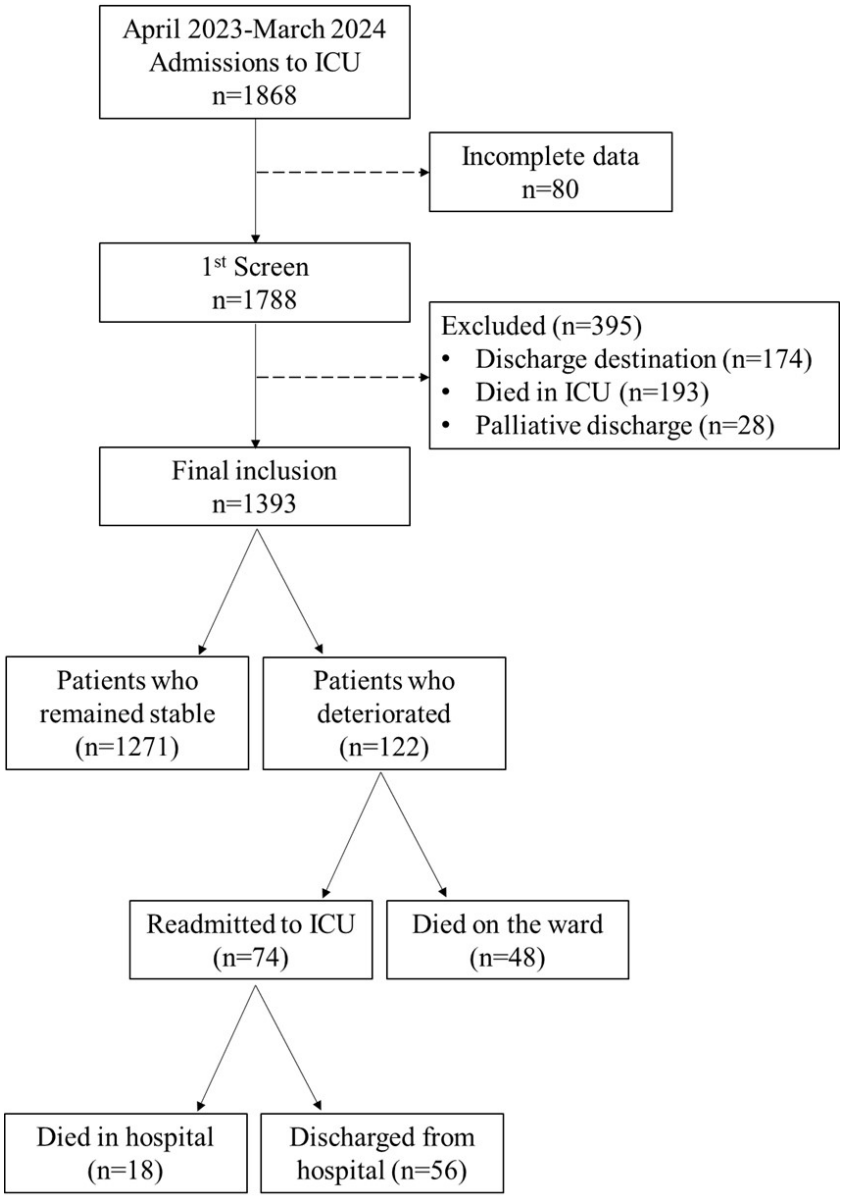

Figure 1: Flowchart showing the formulation to the final dataset17.

144x207mm (150 x 150 DPI)

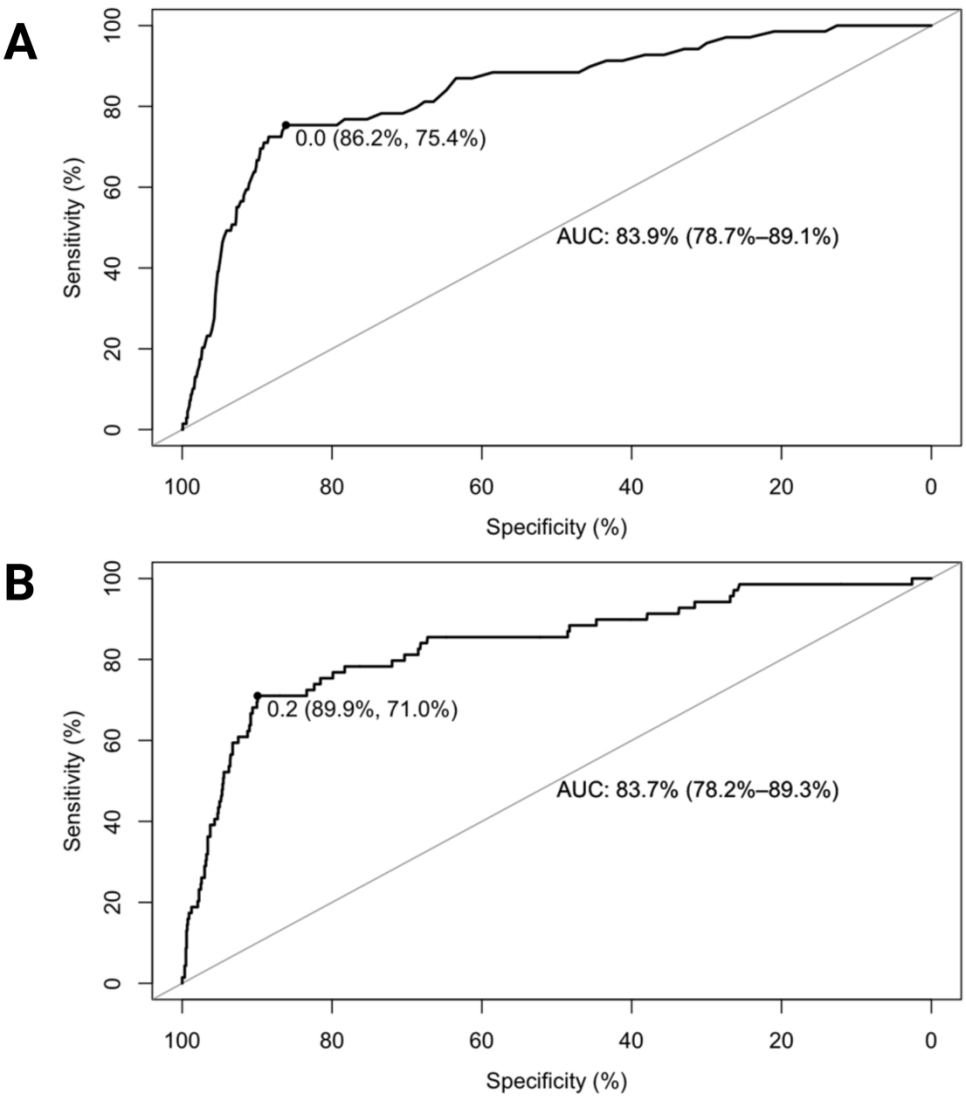

Figure 2: A: Curve for model 1 which included heart rate and AVPU scoring. B: Curve for model 2 which included heart rate, AVPU and SOFA scoring. Area under the curve (AUC) is reported on each graph with their respective confidence intervals. Point 0.0 represents the point of optimum specificity (%), sensitivity (%)19.

458x510mm (236 x 236 DPI)

Appendix 1: Scoring system tables

Each table represents the system used to calculate the respective physiological score.

1.1 NEWS2

Table 1: Components of the National Early Warning Score 2 (NEWS2) and its scoring system

Physiological variable	Score						
	3	2	1	0	1	2	3
Respiratory rate (per minute)	≤8		9-11	12-20		21-24	≥25
SpO2 Scale 1 (%)	≤91	92-93	94-95	≥96			
SpO2 Scale 2 (%)	≤83	84-85	86-87	≥93 on air 88-92	93-94 on oxygen	95-96% on oxygen	≥97 on oxygen
Air or Oxygen		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Pulse (per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Consciousness				Alert			CVPU
Temperature (^{0}C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

1.2 Sequential Organ Failure Assessment (SOFA)

Table 2: Components of the Sequential Organ Failure Assessment Score					
	SOFA Score				
Variable	0	1	2	3	4
Respiratory	PaO_2/FiO_2: >400 SpO_2/FiO_2: >302	PaO_2/FiO_2: <400 SpO_2/FiO_2: <302	PaO_2/FiO_2: <300 SpO_2/FiO_2: <221	PaO_2/FiO_2: <200 SpO_2/FiO_2: <142	PaO_2/FiO_2: <100 SpO_2/FiO_2: <67
Cardiovascular (Doses in mcg/kg/min)	MAP ≥ 70 mmHg	MAP ≥ 70 mmHg	Dopamine ≤ 5 or any dobutamine	Dopamine > 5, Noradrenaline ≤ 0.1, Phenylephrine ≤ 0.8	Dopamine > 15, Noradrenaline > 0.1, Phenylephrine > 0.8
Liver (Bilirubin, mg/dL)	< 1.2	1.2-1.9	2.0-5.9	6.0-11.9	> 12
Renal (Creatinine, mg/dL)	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9	> 5.0
Coagulation (Platelets x $10^3/mm^3$)	≥ 150	< 150	< 100	< 50	< 20
Neurology (Glasgow Coma score)	15	13-14	10-12	6-9	< 6

1.3 Acute physiology and Chronic Health Evaluation II Score

Table 3: Components of the Acute physiology and Chronic Health Evaluation II Score

	Acute physiological variable		High abnormal range					Low abnormal range			
			+4	+3	+2	+1	0	+1	+2	+3	+4
1	Temperature (^{0}C)		≥ 41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤ 29.9
2	Mean Arterial Pressure (mmHg)		≥ 160	130-159	110-129		70-109		50-69		≤ 49
3	Heart rate		≥ 180	140-179	110-139		70-109		50-69	40-54	≤ 39
4	Respiratory rate		≥ 50	35-49		25-34	12-24	10-11	6-9		≤ 5
5a	Oxygenation (A-a gradient if $FiO_2 \geq 0.5$ or PaO_2 if $FiO_2 \leq 0.5$)	A-a gradient	≥ 500	350-499	200-349		< 200				
5b		PaO_2					>70	61-70		55-60	<54
6a	Arterial pH		≥ 7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
6b	HCO_3 (mEq/l) (to use instead of pH if only venous sample available)		≥ 52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
7	K (mEq/l)		≥ 7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
8	Na (mEq/l)		≥ 180	160-179	155-159	150-154	130-149		120-129	111-119	≤ 110
9	Serum Creatinine (mqm/dl)		≥ 3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
10	Haematocrit (%)		≥ 60		50-59.9	46-49.9	30-45.9		20-29.9		<20
11	White cell count(10^3/cc)		≥ 40		20-39.9	15-19.9	3.0-14.9		1.0-2.9		≤ 1.0
12	Glasgow Coma Score		Points= 15 – calculated Glasgow coma score								

Age points (years):

≤ 44y	0
45-54y	+2
55-64y	+3
65-74y	+5
≥ 75y	+6

Chronic health points:

Non-operative, or emergency post-op with any of the below conditions*	+5
Elective operation with any of the conditions below *	+2

*Cirrhosis with portal hypertension or encephalopathy; class IV heart failure; chronic hypoxia; chronically increased CO_2 or polycythaemia; long term dialysis; immunocompromised; chronic restrictive or vascular disease resulting in severe exercise restriction (i.e. unable to climb stairs)

Total APACHE II Score: Age points + Chronic health points + Acute physiology points