Thrombosis Journal

RESEARCH

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Association of initial national early warning score with clinical deterioration in pulmonary embolism

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Abstract

Background The National Early Warning Score (NEWS2) predicts clinical deterioration in hospitalized patients. Its role in pulmonary embolism (PE) risk stratification remains underexplored. This study assessed the association of initial NEWS2 with clinical deterioration and advanced interventions during hospitalization.

Methods We retrospectively analyzed a PE response team (PERT) registry of adults with submassive and massive PE from 11 emergency departments (2016–2024). Initial NEWS2 was calculated for each registry patient. The primary outcome was in-hospital PE-related clinical deterioration (death, cardiac arrest, vasoactive medications for hypotension, or emergent respiratory interventions). The secondary outcome was advanced intervention use. We calculated odds ratios (OR) for different NEWS2 cut-offs. We used multivariable analysis to assess the association of NEWS2 and study outcomes, and decision curve analysis to determine net benefit of clinical deterioration.

Results Among 2119 patients (mean age 62.2 [16.8], 51.2% female, 168 [7.9%] with massive PE, and 1951 [92.1%] with submassive PE), 309 patients (14.6%) experienced clinical deterioration and 488 (23.0%) required advanced interventions. Mean NEWS2 was higher in patients with vs. without clinical deterioration (6.0 ± 3.3 vs. 3.0 ± 2.4; $p < 0.001$) and in those with vs. without advanced interventions (4.8 ± 3.1 vs. 3.0 ± 2.5; $p < 0.001$). NEWS2 cut-off of ≥ 3 identified patients at risk of clinical deterioration: sensitivity 87% (82–90%), OR 6.1 (95% CI: 4.3–8.5), and negative predictive value (NPV) 96% (94–97%). NEWS2 cut-off ≥ 4 had specificity of 62% (60–65%), OR of 5.1 (95% CI: 3.9–6.7), and NPV of 94% (92–95%). As a continuous variable, NEWS2 had an OR of 1.2 (95% CI: 1.1–1.3). NEWS2 cut-offs from 3 to 5 showed an improved net benefit (0.08, 0.16, and 0.34) compared with treating all patients as high risk for clinical deterioration.

Conclusion Patients with PE and initial NEWS2 scores ≥ 3 had a four-fold to eight-fold higher odds of clinical deterioration than those with NEWS2 < 3. NEWS2 is useful for predicting clinical deterioration and guiding intervention strategies in PE.

Keywords Pulmonary embolism, Clinical deterioration, Risk stratification, Intervention, Mortality, National early warning score, Outcomes, Adverse events, Early warning scores

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Background

The National Early Warning Score (NEWS) was developed by the Royal College of Physicians in the United Kingdom (UK) to improve early notification of acutely ill patients in the hospital at risk of clinical deterioration and facilitate timely and effective interventions aimed at reducing mortality among this patient population [1]. NEWS has been widely used in the National Health Service (NHS) of the UK since its launch in 2012, and has been adopted internationally as well [1]. An updated version of NEWS called NEWS2 has been validated for use in sepsis, where a cut-off score ≥ 5 is used to trigger urgent assessment and intervention, demonstrating superior predictive accuracy compared to the quick sepsis-related organ failure assessment (qSOFA) [1–4]. NEWS2 has also been widely applied in acute respiratory infectious illnesses (e.g., pneumonia, COVID-19), where rising scores have been associated with increased intensive care unit (ICU) admissions and mortality [5–9]; however, few studies report use of NEWS or NEWS2 in patients with pulmonary embolism (PE) [10].

The scoring approach of NEWS2 acknowledges the complex nature of physiologic abnormalities (Table 1). The multi-tiered ordinal structure of NEWS2 differs from binary categorical scoring found in other clinical risk stratification tools. For example, bradycardia and tachycardia, which represent different conditions and may portend clinical deterioration, are assigned greater weight in NEWS2 scoring than heart rates within the normal range. The weight of the score for each parameter correlates with the magnitude of the deviation from normal. Conversely, PE risk stratification tools (e.g., Pulmonary Embolism Severity Index [PESI], simplified PESI [sPESI], Hestia, Bova score) use binary assessments of vital signs and other clinical markers, which may fail to capture subtle, progressive, physiological deterioration [11–14].

The prognostic performance of NEWS2 across the spectrum of PE severity, including those with right ventricular dysfunction (RVD), is unclear. Patients with PE and RVD are more challenging to manage than those without RVD due to their higher risk of clinical deterioration. Some PE-risk stratification tools currently in use factor in RVD status [14–16], but some do not [11–13]. Those that do not factor in RVD categorize patients as low-risk or not low-risk for an outcome of 30-day all-cause death. But, providers at the point-of-care care more about shorter term outcomes, such as clinical deterioration and need for advanced interventions within days of PE diagnosis. NEWS2 also does not incorporate specific markers of RVD or myocardial strain; however, some have studied use of NEWS2 in PE risk stratification and found potential utility in predicting mortality or intensive care admission [17–20].

Those who have studied NEWS/NEWS2 in PE used different clinical endpoints and time frames and recommended cut-offs of 3, 4, 5, and 7, with varying predictive performance. Some of these studies only included lower acuity PE patients and mortality was rare [17–20]. In its 2017 evaluation report, however, the Royal College of Physicians (RCP) stated a NEWS score ≥ 5 created the fewest alerts or triggers for patients at risk of significant clinical deterioration (defined as combination of death, cardiac arrest or unexpected ICU admission within 24 h). They reported NEWS was the most efficient among 33 early warning tools in terms of sensitivity (how often a response is triggered) and specificity (how often the trigger is associated with clinical deterioration) [1, 21]. Thus, the RCP recommended NEWS2 ≥ 5 should be the urgent response threshold, with a monitoring standard set at a minimum of once per hour with available skilled healthcare providers [1].

We aimed to determine the association of initial NEWS2 with PE-related adverse outcomes in a regional healthcare system's PE response team (PERT) registry of emergency department (ED) patients. Our primary outcome was PE-related clinical deterioration; our secondary outcome was use of advanced PE interventions. This study sought to bridge the gap in PE risk stratification by evaluating whether NEWS2 provides prognostic value in identifying early clinical deterioration before overt hemodynamic instability. By integrating NEWS2 into PE risk assessment, we may enhance early recognition of patients requiring closer monitoring or escalation of care.

Methods

Study design and patient population

This study is a retrospective analysis of an ongoing observational database of the Clinical Outcomes in Pulmonary Embolism Research Registry (COPERR). COPERR includes ED patients with acute PE for whom a multidisciplinary PERT activation, known as "CODE PE," was initiated. The EDs are part of a regional healthcare system in North Carolina, USA, with an integrated electronic medical record (EMR). Patients were treated according to our CODE PE guidelines, with allowances for provider preferences and discretion. We extracted data for patients entered into the COPERR database between August 2016 and August 2024.

COPERR and observational reports from its database were approved by the local institutional review board. Our reporting of results adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies [22].

We included patients with ED diagnosis of PE with right ventricle to left ventricle diameter ratio (RV:LV) ≥ 1.0 by computed tomography (CT) pulmonary

Table 1 National early warning score (NEWS2) in patients with pulmonary embolism*

Predictors	**Points**						
	3	**2**	**1**	**0**	**1**	**2**	**3**
Systolic blood pressure, mmHg	≤ 90	91–100	101–110	111–219			≥ 220
Heart rate, beats per minute	≤ 40		41–50	51–90	91–110	111–130	≥ 131
Respiratory rate, breaths per minute	≤ 8		9–11	12–20		21–24	≥ 25
Temperature, °Fahrenheit	≤ 95		95.1–96.8	96.9–100.4	100.5–102.2	≥ 102.3	
Supplemental oxygen use?		Yes		No (room air)			
Level of Consciousness **				Alert (GCS = 15)			Altered: New-onset confusion (or disorientation/agitation), **or** responds to verbal voice commands, **or** responds to pain (localizes, withdraws, or opens eyes), **or** unresponsive (GCS = 3)
Hypercapnic Respiratory Failure: If No, use*Scale 1*; if Yes, use*Scale 2*							
Scale 1: Oxygen saturation by pulse oximetry,	≤ 91%	92–93%	94–95%	≥ 96%			
Scale 2: Oxygen saturation by pulse oximetry	≤ 83%	84–85%	86–87%	88–92%, ≥ 93% on room air	93–94% on supplemental oxygen	95–96% on supplemental oxygen	≥ 97% on supplemental oxygen

Abbreviations: GCS = Glasgow Coma Scale

* A report by the Royal College of Physicians recommends using NEWS to influence the following four features of subsequent clinical care: urgency of the response, skills and experience of the responders, clinical monitoring frequency, and hospital setting selected for ongoing care [1].

** We classified Level of Consciousness using Alert (0 points) or Altered (3 points [verbal, pain, and unresponsive]) based on components of the Glasgow Coma Scale (GCS). To distinguish 'Alert' versus 'Altered' for level of consciousness: Select 'Alert' if GCS was 15; select 'Altered' if GCS was not 15 but the patient was altered in some way with the following responses to verbal or pain stimuli:

1) Verbal: Select if the patient responded to verbal commands

2) Pain: Select if the patient localized pain, withdrew from pain, or if eye opening was in response to pain (GCS not 15)

3) Unresponsive: Select if GCS was 3

angiography or echocardiography or abnormal troponin measurements. We used troponin I or high-sensitivity troponin assays (Abbott, Abbott Park, IL) measured in ng/mL. Normal values for troponin I were less than 0.07 ng/mL. Normal values for high-sensitivity troponin were less than 12 for females and less than 20 for males. Abnormal troponin levels were higher than above-mentioned cut-offs. We excluded those with cardiac arrest at presentation without measurable vital signs to calculate NEWS2.

Patients were stratified into massive, severe submassive, and non-severe submassive PE categories based on established criteria. Massive PE was defined as acute PE presenting with hypotension, characterized by a systolic blood pressure (BP) less than 90 mmHg for more than 15 min, the use of vasoactive medications, or cardiopulmonary arrest attributed to PE. Submassive PE was defined as acute PE with evidence of RVD, identified either by imaging (CT or echocardiography) or biomarker elevation (troponin or brain natriuretic peptide). Submassive PE was further divided into severe and non-severe categories. Severe submassive PE included patients with one or more of the following: episodic hypotension (transient systolic BP less than 90 mmHg), a sustained shock index greater than 1.0 (heart rate divided by systolic BP), presyncope or syncope as presenting symptoms, the presence of a clot-in-transit, or hypoxia with respiratory distress. Non-severe submassive PE encompassed cases of acute PE with RVD that did not meet the criteria for severe submassive PE.

Data collection

We used data available in COPERR for demographics, clinical presentation features, comorbidities, PE risk factors, PE risk stratification criteria, and PE-related outcomes and interventions. Sex, race, and ethnicity were based on EMR data. Trained data extractors retrieved information from the EMR and entered data into COPERR. Data for NEWS2 calculation were collected and points assigned as per Table 1. We used the first recorded vital signs and oxygen saturation at or after ED triage. The level of consciousness component of NEWS2 was determined with the assistance of surrogate Glasgow Coma Scale (GCS) used in clinical assessments in the EMR [23]. Overall NEWS2 ranged from 0 points for lowest to 20 points for highest clinical severity.

Outcomes

The primary outcome was **in-hospital PE-related clinical deterioration**, defined as one or more of the following events during index PE hospitalization: death, cardiac arrest, emergent mechanical ventilation or positive pressure ventilation, use of inotropic or vasopressor medications for symptomatic hypotension (e.g., dobutamine, norepinephrine, dopamine, vasopressin, epinephrine). We also reported a subset of the primary outcome, which only included the most severe ends of the clinical deterioration spectrum (cardiac arrest and death). The secondary outcome was **use of advanced interventions** (systemic thrombolysis, catheter-directed intervention [thrombolysis, aspiration thrombectomy, or mechanical thrombectomy], surgical embolectomy, or mechanical circulatory support with veno-arterial extracorporeal membrane oxygenation [ECMO]).

Statistical analysis

Sample size was determined by the number of patients in the COPERR database with components to calculate the NEWS2 and outcomes. We calculated counts, percentages, means, and standard deviations for descriptive statistics. We used chi-square, t test, or Mann-Whitney to determine statistical differences in groups with and without the primary outcome (clinical deterioration) and with and without the secondary outcome (use of advanced interventions). We examined overall NEWS2 as an independent variable (with a value range of 0–20 points). Based on the NHS NEWS guidelines [1], we then examined three sets of binary categorizations of NEWS2: (1) above and below 3 points, (2) above and below 5 points, and (3) above and below the optimal NEWS2 cut-off identified by Youden's index for the primary outcome (clinical deterioration). We reported sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operating curve (AUC), all with 95% confidence intervals (CIs). We used random forest imputation for missing values using the R package `missForest`.

To determine net clinical benefit of NEWS2 for primary outcome (clinical deterioration), we fit a standardized decision curve analysis using the 'rmda' package in R [24]. The decision curve was based on a simple logistic model to estimate probabilities at different NEWS2 thresholds. We reported discrimination with C statistic and calibration with both intercept (for calibration-at-large) and slope for under and overestimation of risk prediction. We used the following interpretation guideline: A slope < 1.0 suggests estimated risks are exaggerated, whereas slope > 1 suggests risks are underestimated. For intercept, an optimal value is 0; negative values suggest overestimation and positive values suggest underestimation. Based on this fitted model we plotted a decision curve with x-axis mapped to NEWS2 thresholds (as opposed to probabilities), and also plotted sensitivity versus odds comparison of positive prediction between true positives and false positives [25, 26]. Net benefit was interpreted according to guidelines by Van Calster et al. [27]

For multivariable analyses, we used least absolute shrinkage and selection operator (LASSO) to determine associations of candidate variables with the primary outcome (clinical deterioration). Candidate variables were selected a priori by the team of investigators based on plausibility, previous evidence, and our study objectives. Pre-selected candidate variables used to form our initial "full" model were: PE risk factors, initial vital signs, initial NEWS2, demographic data, PE severity classification criteria and the resulting PE severity classification. From this full model consisting of 62 candidate predictor variables, we used LASSO regression with 10-fold cross-validation to perform variable selection and identify key predictors to include in a reduced model. The LASSO model started with NEWS2 expressed as a continuous variable, as well as the three binary cut-offs (3, 5, and Youden's optimal cut-off). We fit multivariable models to assess the association between NEWS2 and clinical deterioration. By LASSO, associations were expressed as odds ratios with 95% CIs. Clinical deterioration, a composite of clinical events, was expressed as a binary variable -i.e., YES (presence of one or more clinical deterioration events) or NO (none of the events occurred). The secondary outcome was also expressed as a binary variable -i.e., YES (one or more advanced interventions used) or NO (anticoagulation monotherapy).

Results

Patient characteristics

All 2119 patients included in the analysis met the criteria for NEWS2 calculation (Fig. 1). As shown in Table 2, mean age was 62.2 (± 16.8 years), with 51.2% identifying as female. Racial demographics revealed 1298 patients (61.3%) were White, 730 (34.5%) were Black, and the remaining 4.2% identified as other racial groups. At the time of PE diagnosis in the ED, 168 patients (7.9%) were classified as having massive PE, 945 (44.6%) as severe submassive PE, and 1006 (47.5%) as non-severe submassive PE based on institutional PERT activation criteria. Mean aggregate NEWS2 at ED presentation was 3.4 (± 2.8). A total of 1133 patients (53.5%) required admission to the ICU. Mean hospital length of stay was 5.8 days.

Missingness was very low (data not shown). The NEWS2 component with the highest missingness (12.5%) was initial temperature for patients with cardiac arrest or death, but its overall missingness was 2.8%. Other NEWS2 components had missingness between 0.1% and 0%. Imputation thus had a negligible impact on our findings.

Primary outcome

As shown in Tables 2 and 309 patients (14.6%) experienced at least one clinical deterioration event during their hospital stay. Patients who experienced clinical deterioration had a significantly higher mean NEWS2 score of 6.0 (± 3.3) compared to 3.0 (± 2.4) in those without clinical deterioration ($p < 0.001$). All components of the NEWS2 score shown in Table 2 were significantly different between groups, except temperature differences were not clinically significant (98.0℉ [± 1.4] vs. 98.2℉ [± 0.7]). Hypercapnic respiratory failure was rare, occurring in less than 1% of patients. New confusion or altered mental status was present in 120 patients (5.7%). Among those with clinical deterioration, 71 (23.0%) had altered mental status or new confusion compared to 49 patients (2.7%) without clinical deterioration.

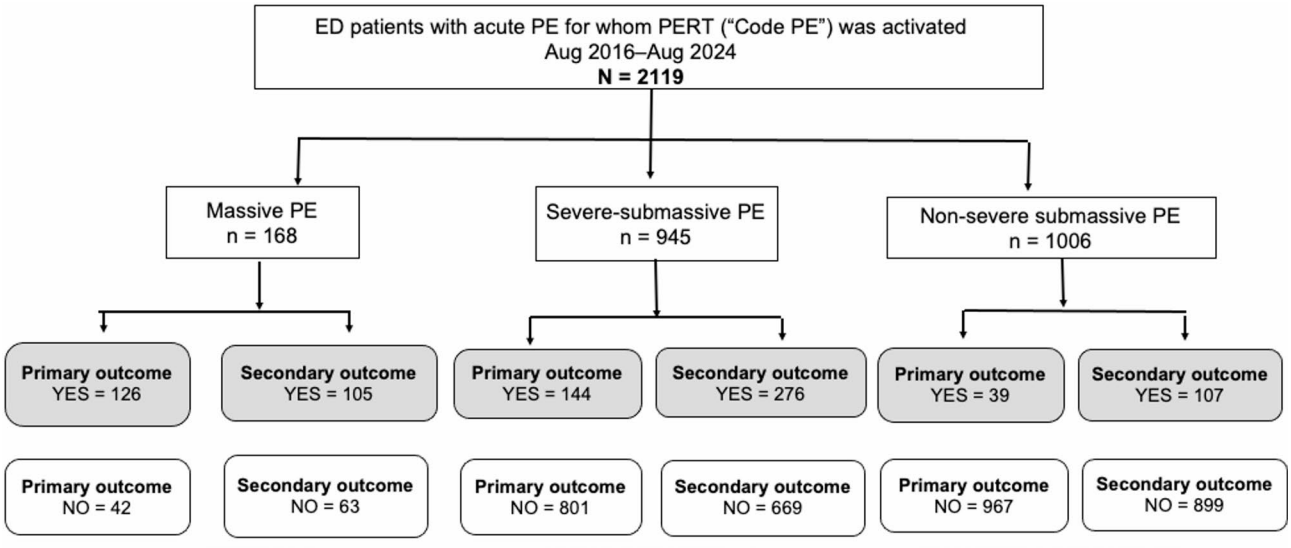

Fig. 1 Study flow diagram
Primary outcome: Subsequent in-hospital clinical deterioration Secondary outcome: Advanced PE intervention
Abbreviations: PE = pulmonary embolism, PERT = pulmonary embolism response team

Table 2 Patient characteristics by PE-related clinical deterioration (primary outcome)*

Characteristics	Positive (*N* = 309)	Negative (*N* = 1810)	Overall (*N* = 2119)	*P*-Value
Age, mean (SD)	62.3 (16.2)	62.2 (16.9)	62.2 (16.8)	0.93
Gender				
Male	134 (43.4%)	900 (49.7%)	1034 (48.8%)	0.154
Female	175 (56.6%)	910 (50.3%)	1085 (51.2%)	
Race				
American Indian/Alaskan Native	4 (1.3%)	19 (1.0%)	23 (1.1%)	0.02
Black	129 (41.7%)	601 (33.2%)	730 (34.5%)	
Unknown	10 (3.2%)	37 (2.0%)	47 (2.2%)	
White	164 (53.1%)	1134 (62.7%)	1298 (61.3%)	
Asian	0 (0%)	6 (0.3%)	6 (0.3%)	
Other	1 (0.3%)	12 (0.7%)	13 (0.6%)	
Pacific Islander/Native Hawaiian	1 (0.3%)	1 (0.1%)	2 (0.1%)	
Ethnicity				
Non-Hispanic/Latino	289 (93.5%)	1681 (92.9%)	1970 (93.0%)	
Hispanic/Latino	9 (2.9%)	45 (2.5%)	54 (2.5%)	0.69
Unknown	11 (3.6%)	84 (4.6%)	95 (4.5%)	
PE severity at PERT activation				
Non-severe submassive	39 (12.8%)	967 (53.4%)	1006 (47.5%)	< 0.001
Severe submassive	144 (46.7%)	801 (44.3%)	945 (44.6%)	
Massive	126 (40.5%)	42(2.3%)	168 (7.9%)	
PE severity classification criteria available during ED phase of care				
RV dilation by CT (RV: LV ≥ 1.0)	232 (75.1%)	1464 (80.9%)	1696 (80.0%)	0.02
RV dilatation by echocardiography	107 (34.6%)	450 (24.9%)	557 (26.3%)	< 0.001
Initial cardiac arrest	74 (23.9%)	0 (0%)	74 (3.5%)	< 0.001
Initial vasopressor use	114 (36.9%)	0 (0%)	114 (5.4%)	< 0.001
Sustained hypotension (15 min or more)	98 (31.7%)	31 (1.7%)	129 (6.1%)	< 0.001
Episodic hypotension (less than 15 min)	43 (13.9%)	83 (4.6%)	126 (5.9%)	< 0.001
Sustained elevated shock index (> 1.0 for 15 min or more)	145 (46.9%)	252 (13.9%)	397 (18.7%)	< 0.001
Hypoxia with respiratory distress (< 92% on room air or supplemental oxygen)	206 (66.7%)	602 (33.3%)	808 (38.1%)	< 0.001
Abnormal troponin	261 (84.5%)	1247 (68.9%)	1508 (71.2%)	< 0.001
Abnormal brain natriuretic peptide	203 (65.7%)	1044 (57.7%)	1247 (58.8%)	0.003
PE risk factors				
Previous venous thromboembolism	63 (20.4%)	443 (24.5%)	506 (23.9%)	0.13
Missing	1 (0.4%)	0 (0%)	1 (0.0%)	
Hospitalization within previous 4 weeks	74 (23.9%)	240 (13.3%)	314 (14.8%)	< 0.001
Missing	1 (0.3%)	3 (0.2%)	4 (0.2%)	
Total Charlson index, mean (SD)	1.89 (2.37)	1.50 (2.20)	1.55 (2.23)	0.004
Recent limb immobilization	26 (8.4%)	81 (4.5%)	107 (5.0%)	0.004
Missing	1 (0.4%)	6 (0.3%)	7 (0.3%)	
Recent trauma within 6 weeks	17 (5.5%)	40 (2.2%)	57 (2.7%)	0.002
Family history of veno-thromboembolism	17 (5.5%)	164 (9.1%)	181 (8.5%)	0.04
Missing	1 (0.3%)	12 (0.7%)	13 (0.6%)	
Clotting disorder	10 (3.2%)	64 (3.5%)	74 (3.5%)	1.0
Missing	1 (0.4%)	13 (0.7%)	14 (0.7%)	
Tobacco user	177 (57.3%)	1055 (58.3%)	1232 (58.1%)	1.0
Missing	129 (42.4%)	771 (41.8%)	887 (41.9%)	
Known pulmonary hypertension	20 (6.5%)	82 (4.5%)	102 (4.8%)	0.15
Chronic obstructive pulmonary disease	67 (21.7%)	309 (17.1%)	376 (17.7%)	0.107
Renal disease	42 (13.6%)	193 (10.7%)	235 (11.1%)	0.14
Missing	0 (0%)	1 (0.1%)	1 (0.0%)	
Congestive heart failure	37 (12.0%)	142 (7.8%)	179 (8.4%)	0.02
Dementia	26 (8.4%)	126 (7.0%)	152 (7.2%)	0.34

Table 2 (continued)

Characteristics	Positive (*N* = 309)	Negative (*N* = 1810)	Overall (*N* = 2119)	*P*-Value
Hemiplegia or paraplegia	17 (5.5%)	25 (1.4%)	42 (2.0%)	< 0.001
Malignant leukemia or localized tumor	33 (10.7%)	213 (11.8%)	246 (11.6%)	0.63
AIDS	3 (1.0%)	9 (0.5%)	12 (0.6%)	0.40
Metastatic solid tumor	29 (9.4%)	154 (8.5%)	183 (8.6%)	0.59
Breakdown of clinical deterioration events during hospitalization (primary outcome)				
Cardiac arrest	125 (40.5%)	0 (0%)	125 (5.9%)	< 0.001
Need for mechanical or positive pressure ventilation	198 (64.1%)	0 (0%)	198 (9.3%)	< 0.001
Use of vasoactive medication	207 (67.0%)	0 (0%)	207 (9.8%)	< 0.001
PE-related death	125 (45.1%)	0 (0%)	125 (5.9%)	< 0.001
Total NEWS2, mean (SD), points (Range: 0 to 20 points)	6.0 (3.3)	3.0 (2.4)	3.4 (2.8)	< 0.001
NEWS2 components				
Initial systolic blood pressure, mean (SD), mmHg	118 (29.5)	133 (23.4)	130 (24.9)	< 0.001
Missing	1 (0.4%)	0 (0%)	1 (0.0%)	
Initial heart rate, mean (SD), beats per minute	109 (23.4)	103 (21.0)	104 (21.4)	< 0.001
Missing	1 (0.4%)	0 (0%)	1 (0.0%)	
Initial respiratory rate, mean (SD), breaths/minute	23.7 (8.09)	20.7 (5.27)	21.1 (5.86)	< 0.001
Missing	1 (0.4%)	0 (0%)	1 (0.0%)	
Temperature, mean (SD), degrees Fahrenheit	98.0 (1.35)	98.2 (0.71)	98.2 (0.828)	< 0.001
Missing	26 (9.5%)	34 (1.8%)	60 (2.8%)	
Initial oxygen pulse oximetry, mean (SD), %	91.5 (11.2)	94.8 (5.29)	94.3 (6.59)	< 0.001
Missing	2 (0.7%)	1 (0.1%)	3 (0.1%)	
Hypercapnic respiratory failure	0 (0%)	2 (0.1%)	2 (0.1%)	1.0
Supplemental oxygen use	172 (56.6%)	472 (26.0%)	644 (30.4%)	< 0.001
Altered mental status				
Alert	238 (77.0%)	1761 (97.3%)	1999 (94.3%)	< 0.001
New confusion/altered mental status	71 (23.0%)	49 (2.7%)	120 (5.7%)	
NEWS2 cut-off of 3				
< 3	41 (13.5%)	870 (47.9%)	911 (43.0%)	< 0.001
≥ 3	263 (86.5%)	945 (52.1%)	1208 (57.0%)	
NEWS2 cut-off of 4				
< 4	74 (24.3%)	1130 (62.3%)	1204 (56.8%)	< 0.001
≥ 4	230 (75.7%)	685 (37.7%)	915 (43.2%)	
NEWS2 cut-off of 5				
< 5	109 (35.9%	1346 (74.2%)	1455 (68.7%)	< 0.001
≥ 5	195 (64.1%)	469 (25.8%)	664 (31.3%)	
Advanced PE intervention (secondary outcome)	163 (52.8%)	325 (18.0%)	488 (23.0%)	< 0.001
Systemic thrombolysis	95 (30.7%)	101 (5.6%)	196 (9.2%)	< 0.001
Catheter-directed intervention	41 (13.3%)	169 (9.3%)	210 (9.9%)	0.05
Surgical embolectomy	9 (2.9%)	1 (0.1%)	10 (0.5%)	< 0.001
Right ventricular assist device	0 (0%)	0 (0%)	0 (0%)	1.0
Extracorporeal membrane oxygenation	13 (4.2%)	0 (0%)	13 (0.6%)	< 0.001
Other	1 (0.3%)	4 (0.2%)	5 (0.2%)	0.499
Intensive care unit admission	267 (86.4%)	866 (47.8%)	1133 (53.5%)	< 0.001
Hospital length of stay, mean (SD), days	9.9 (16.6)	5.1 (9.6)	5.8 (11.0)	< 0.001

* Abbreviations: PE = pulmonary embolism, SD = standard deviation, RV = right ventricle, LV= left ventricle, AIDS = acquired immunodeficiency syndrome, NEWS2 = National Early Warning Score

Supplemental Table 1 shows 160 (7.6%) patients experienced either death or cardiac arrest, whereas 1959 (92.4%) did not. Ninety (4.3%) patients had cardiac arrest and died during index PE hospitalization. The mean NEWS2 score for patients who died or had cardiac arrest was 6.6 (± 3.4) compared with 3.2 (± 2.5) for those without ($p < 0.001$). Those with death or cardiac arrest had significantly higher points for all NEWS2 components compared to those without death or cardiac arrest.

Table 2 also shows frequencies and proportions of those with and without clinical deterioration using initial NEWS2 cut-offs. Using the NEWS2 cut-off of 3 points,

1208 (57.0%) had NEWS2 ≥ 3 points. Of 309 patients with clinical deterioration, 268 (86.4%) had NEWS2 ≥ 3 points. Of 1810 without clinical deterioration, 940 (51.9%) had NEWS2 ≥ 3 points ($p < 0.001$). Using a NEWS2 cut-off of 5 points, 664 patients (31.3%) had NEWS2 ≥ 5 points. Of those with clinical deterioration, 196 (63.4%) had NEWS2 ≥ 5 points, whereas 468 (25.9%) without clinical deterioration had NEWS2 ≥ 5 points ($p < 0.001$). Using a cut-off of 4 points, which was the optimal NEWS2 cut-off for clinical deterioration by Youden's index (Table 3), 915 patients (43.2%) had NEW2 ≥ 4 points. Of those with clinical deterioration, 233 (75.4%) had NEWS2 ≥ 4 points, whereas 682 (37.7%) without clinical deterioration had NEWS2 ≥ 4 points ($p < 0.001$).

Supplemental Table 1 shows proportions with death or cardiac arrest with NEWS2 at or above cut-offs of 3, 4, and 5 points were 144 (90.0%), 127 (79.4%), and 110 (68.8%), respectively. Of the 1959 patients with no deaths or cardiac arrests, proportions with NEWS2 at or above cut-offs of 3, 4, and 5 were 1064 (54.3%), 788 (40.2%), and 554 (28.3%), respectively.

Net benefit of NEWS2 for primary outcome

Figure 2 shows the calibration plot of the fitted logistic model to estimate probabilities by NEWS cut-offs yielded an adequately calibrated model: C statistic 0.77 (0.74 to 0.80), intercept 0.00 (-0.13 to 0.13), and slope 1.00 (0.87 to 1.13). As shown in Fig. 3, NEWS2 cut-offs from 3 to 5 showed an improved net benefit over the strategy of treating all patients as high risk for clinical deterioration. The difference in net benefit values between our model and the "treat-all" approach for NEWS2 cut-offs of 3, 4, and 5 were 0.08, 0.16, and 0.34, respectively. Figure 4 shows the ratio of predicted high-risk patients (true positives + false positives) by high-risk patients who actually had clinical deterioration (true positives) at each NEWS2 cut-off. Figure 5 shows the sensitivity and ratio of true positives to false positives (TP: FP) at each NEWS2 cut-off. With a cut-off of 3, we estimated a sensitivity of 0.87 and TP: FP of approximately 1:3.5, meaning we expect 1 true positive for every 3.5 false positives. A cut-off of 4 yielded lower sensitivity of 0.75 but an improved TP: FP of approximately 1:3, meaning we expect 1 true positive for every 3 false positives. A NEWS2 cut-off of 5 improved TP: FP to approximately 1:2.4, but decreased sensitivity below 70%.

Secondary outcome

Table 4 shows 488 (23.0%) of 2119 patients had advanced PE interventions. Of the 488, 196 (40.2%), 210 (43.0%), 10 (2.0%), and 13 (2.7%) received systemic thrombolysis, catheter-directed intervention, surgical embolectomy, and ECMO, respectively. Mean NEWS2 were 4.8 (3.1) and 3.0 (2.5) points for those with and without advanced interventions, respectively ($p < 0.001$). All components of the NEWS2 score were significantly different between outcome groups, except temperature differences were not clinically significant (98.0℉ [± 1.4] vs. 98.2℉ [± 0.8]). New confusion or altered mental status were present in 120 patients (5.7%). Of those with advanced interventions, 52 (10.7%) had altered mental status or new confusion compared to 68 patients (4.2%) without advanced intervention.

Using the NEWS2 cut-off of 3 points, 1208 patients (57.0%) had NEWS2 ≥ 3 points. Of 488 patients with advanced intervention, 378 (77.5%) had NEWS2 ≥ 3 points. Of 1631 without advanced interventions, 830 (50.9%) had NEWS2 ≥ 3 points ($p < 0.001$). Using a NEWS2 cut-off of 5 points, 664 (31.3%) had NEWS2 ≥ 5 points. Of those with advanced interventions, 247 (50.6%) had NEWS2 ≥ 5 points, whereas 417 patients (25.6%) without advanced intervention had NEWS2 ≥ 5 points ($p < 0.001$). The optimal NEWS2 cut-off for advanced intervention use by Youden's index was 4 (Table 5). Of 2119 patients, 915 (43.2%) had NEWS2 ≥ 4 points. Of 488 patients with advanced intervention use, 310 patients (63.5%) had NEWS2 ≥ 4 points, whereas 605 patients (37.1%) without advanced intervention had NEWS2 ≥ 4 points ($p < 0.001$).

Multivariable analyses

Table 3 compares prediction metrics of NEWS2 cut-offs of 3, 4 (optimal cut-off by Youden's index), and 5 for PE-related **clinical deterioration (primary outcome)**. The NEWS2 cut-off of 3 had best sensitivity 0.87 (0.82, 0.90) compared to 0.76 (0.71, 0.80) and 0.64 (0.59, 0.69) for NEWS2 cut-offs of 4 and 5, respectively. NEWS2 cut-off of 3 also had the highest NPV 0.96 (0.94, 0.97). NEWS2

Table 3 Prediction metrics of NEWS2 cut-offs for clinical deterioration (primary outcome)*

Variable	Sensitivity	Specificity	PPV	NPV	AUC	OR
NEWS2 ≥ 3	0.87 (0.82, 0.90)	0.48 (0.46, 0.50)	0.22 (0.20, 0.24)	0.96 (0.94, 0.97)	0.67 (0.27, 0.73)	6.1 (4.3, 8.5)
NEWS2 ≥ 4 (Youden's optimal cut-off)	0.76 (0.71, 0.80)	0.62 (0.60, 0.65)	0.25 (0.22, 0.28)	0.94 (0.92, 0.95)	0.69 (0.24, 0.73)	5.1 (3.9, 6.7)
NEWS2 ≥ 5	0.64 (0.59, 0.69)	0.74 (0.72, 0.76)	0.29 (0.26, 0.33)	0.93 (0.91, 0.94)	0.69 (0.17, 0.81)	5.0 (3.9, 6.4)

* Abbreviations: PE = pulmonary embolism PPV = positive predictive value, NPV = negative predictive value, AUC = area under the curve, OR = odds ratio

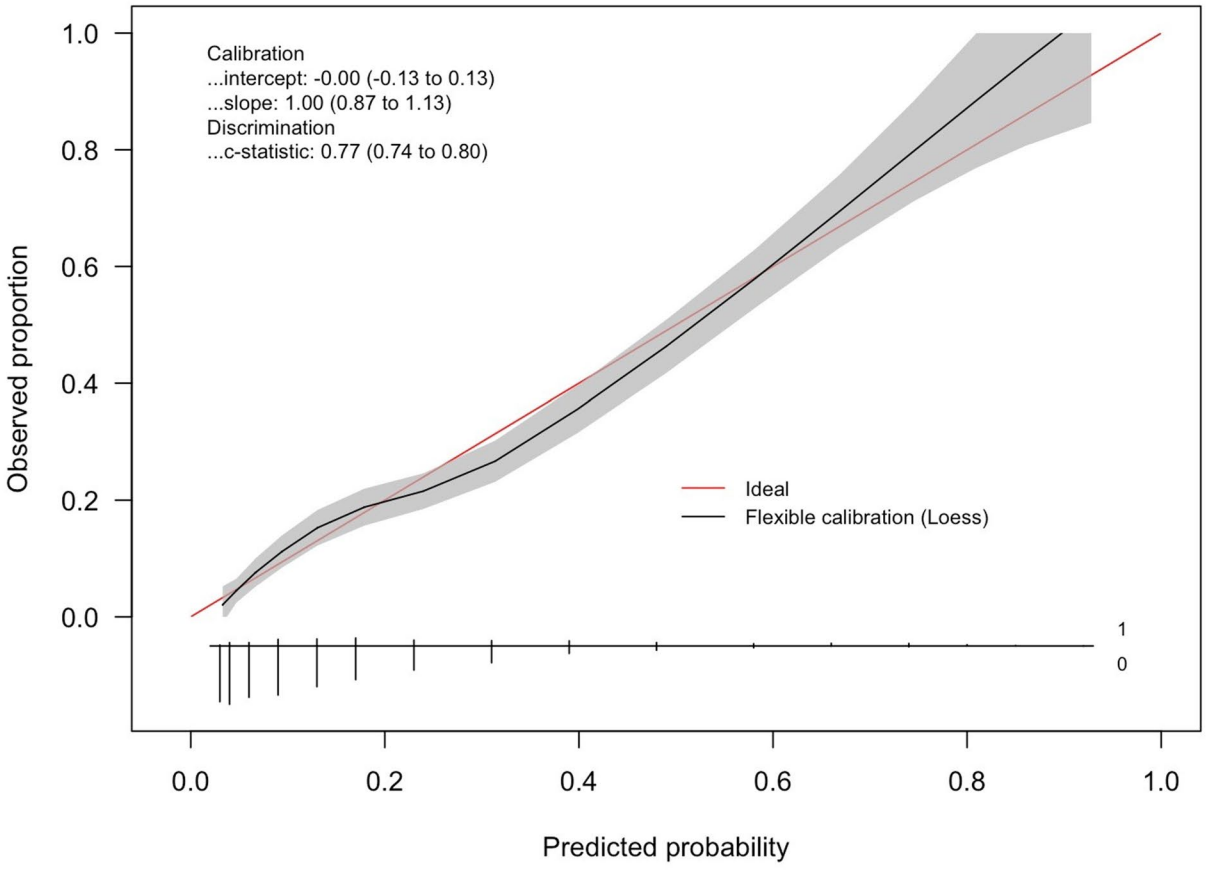

Fig. 2 Predicted versus actual clinical deterioration at NEWS2 cut-offs

cut-off of 3 had the lowest specificity and PPV. NEWS2 at 5 had the lowest sensitivity and highest specificity 0.74 (0.72, 0.76) and PPV 0.29 (0.26, 0.33). The predictive performance of a NEWS2 cut-off of 4 was between those for cut-offs of 3 and 5: sensitivity 0.76 (0.71, 0.80), specificity 0.62 (0.60, 0.65), and PPV 0.25 (0.22, 0.28). Unlike other performance metrics, AUC for NEWS2 cut-offs had wide confidence intervals. For clinical deterioration, odds ratios (OR) of NEWS2 at cut-offs of 3, 4, and 5 were: 6.1 (4.3, 8.5), 5.1 (3.9, 6.7), and 5.0 (3.9, 6.4), respectively. All ORs were statistically significant (unity not included within the confidence range). Performance metrics for NEWS2 at cut-offs of 3, 4, and 5 were similar for the subset of the primary outcome (death or cardiac arrest) and the primary outcome (Supplemental Table 2).

Table 5 compares prediction metrics of NEWS2 cut-offs of 3, 4 (optimal cut-off by Youden's index), and 5 for **advanced intervention (secondary outcome)**. The NEWS2 cut-off of 3 had best sensitivity (0.78 [0.74, 0.81]) compared to 0.64 (0.59, 0.68) and 0.51 (0.46, 0.55) for NEWS2 cut-offs of 4 and 5, respectively. NEWS2 cut-off of 3 also had the highest NPV 0.88 (0.86, 0.90). NEWS2 cut-off of 3 had the lowest specificity (0.49 [0.47, 0.52]) and PPV (0.31 [0.29, 0.34]). A NEWS2 cut-off of 5 had the lowest sensitivity (0.51 [0.46, 0.55]) and highest specificity (0.74 [0.72, 0.77]) and PPV (0.37 [0.34, 0.41]). The predictive performance of a NEWS2 cut-off of 4 was between those for cut-offs of 3 and 5: sensitivity 0.64 (0.59, 0.68), specificity 0.63 (0.61, 0.65), and PPV 0.34 (0.31, 0.37). AUCs for all cut-offs had wide confidence intervals. Odds ratios were highest for cut-off of 3 (3.3 [2.6, 4.2]) and similar for cut-offs of 4 and 5.

Table 6 shows the LASSO model retained NEWS2 as a continuous predictor and discarded the binary NEWS2 versions, yielding an OR of 1.2 (1.1, 1.3) with $p < 0.001$, suggesting that for each additional unit increase in NEWS2, there was a 20% increased odds of clinical deterioration. Variables with higher and significant predictive ORs were sustained hypotension and ICU admission disposition.

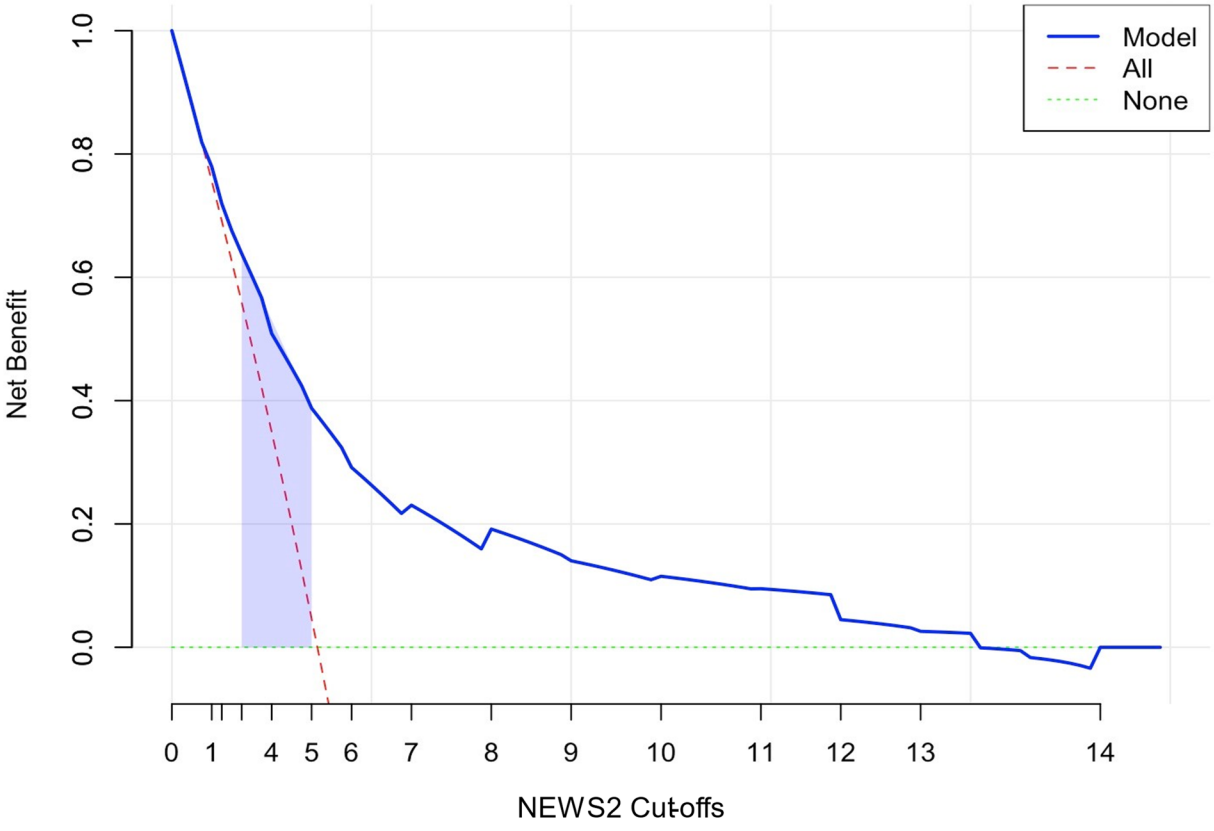

Fig. 3 Net benefit decision curve for clinical deterioration

Discussion

Using data from a large, multi-center PERT database, we identified a strong association between initial NEWS2 scores and both primary and secondary outcomes during the index hospitalization. We found patients with higher initial NEWS2 scores were at significantly increased risk of PE-related clinical deterioration and use of advanced interventions. At a NEWS2 cut-off of 3, patients with PE had an OR of 6.1 (95% CI: 4.3, 8.5) for clinical deterioration compared to those with NEWS2 scores below 3. Based on the lower and upper confidence limits, patients with NEWS2 ≥ 3 had a fourfold to eightfold higher odds of clinical deterioration than those with NEWS2 < 3 points. A cut-off of 4 also demonstrated significant predictive value, with an OR of 5.1 (95% CI: 3.9, 6.7), while a cut-off of 5 yielded a similar OR of 5.0 (95% CI: 3.9, 6.4). These findings highlight that even modest elevations in NEWS2 scores are associated with a significant increase in adverse outcomes.

While higher NEWS2 cut-offs (≥ 4 and ≥ 5) improved specificity and PPV, they compromised sensitivity, potentially missing patients who could benefit from closer monitoring or earlier intervention. NEWS2 cut-off of 3, on the other hand, had high sensitivity (87%). In severe forms of PE, where timely recognition of clinical deterioration is critical, sensitivity must be prioritized to minimize the risk of adverse outcomes. Although NEWS2 cut-off of 3 resulted in lower specificity, over-triaging is an acceptable tradeoff when the consequences of under-triaging include missed opportunities for intervention or preventable deterioration. This pattern of prediction metrics for NEWS2 cut-offs was similar for the subset of the primary outcome (in-hospital death or cardiac arrest). Of note, NEWS2 expressed as a continuous variable was a better predictor than NEWS2 with a cut-off.

Results of our multivariable analyses and decision curve analysis were in agreement with the above findings. Multivariable analyses showed NEWS2 was an independent predictor of clinical deterioration, with every additional

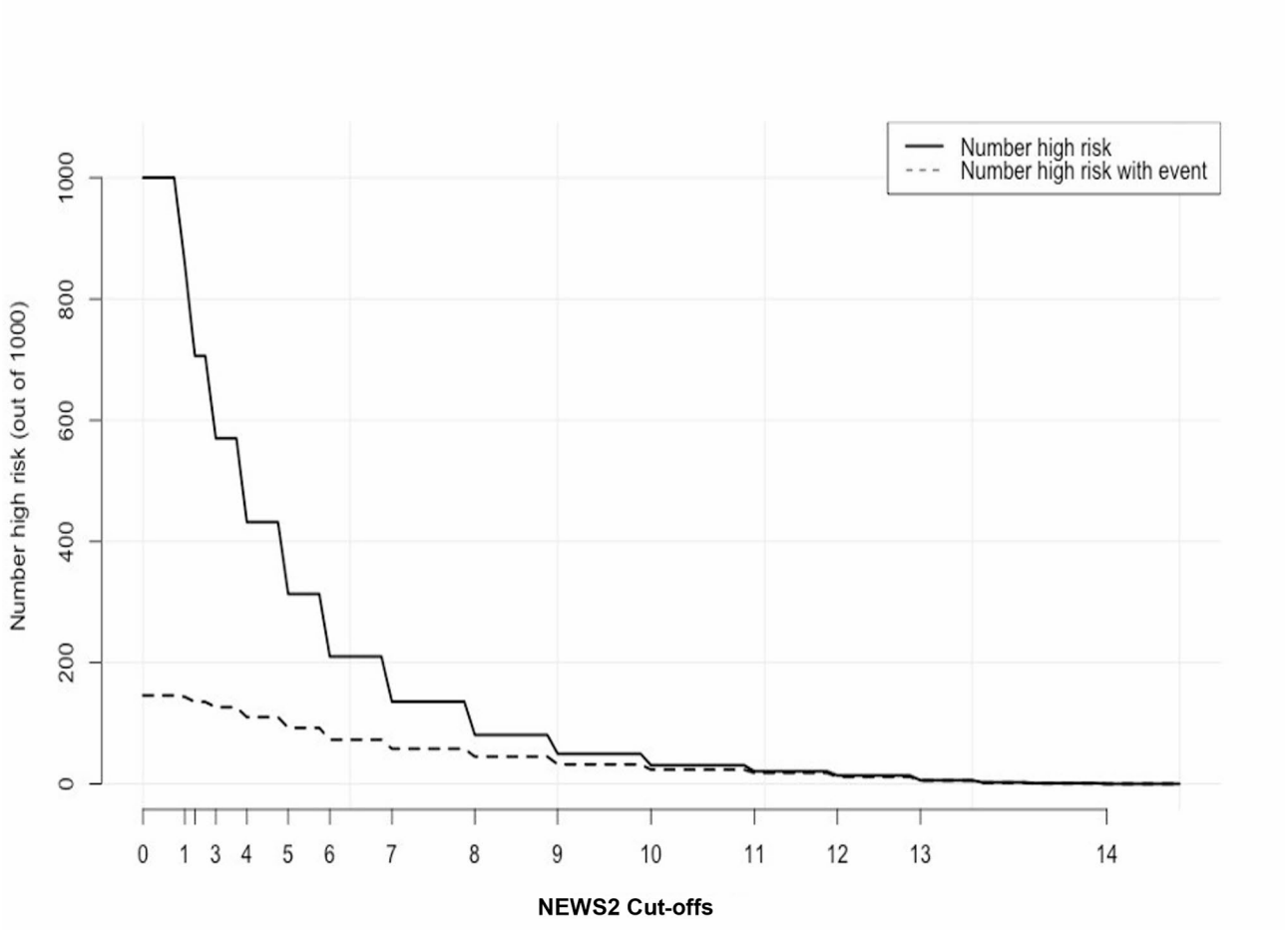

Fig. 4 Predicted high-risk by true positive for each NEWS2 cut-off

increase in NEWS2 points increasing odds of clinical deterioration by 20%. The decision curve analysis showed NEWS2 cut-offs of 3–5 provided a net benefit over the strategy of treating all patients, while yielding adequate to good sensitivity. In this range, the model effectively reduced false positives and/or increased correct treatments. NEWS2 cut-offs > 5 reduced false positives but at the cost of a substantial decrease in sensitivity, which would result in an unacceptable rate of missed cases (missed true positives).

Previous studies evaluating NEWS2 in PE have generally studied cohorts with lower disease severity, limiting their applicability to higher acuity settings. Rodriguez et al. evaluated NEWS2 in a population of patients with hemodynamically stable PE that had a prevalence of 7.4% for 30-day mortality or hemodynamic collapse. They recommended cut-offs of 5 and 7 to optimize specificity and PPV [17]. In contrast, the study by Bumroongkit et al. demonstrated a higher NEWS cut-off (≥ 9) was associated with significantly elevated 30-day mortality risk (adjusted relative risk 2.96, 95% CI: 2.13–4.12), particularly in patients with a higher prevalence of active malignancy and comorbidities [28]. While their study highlighted the utility of NEWS for mortality prediction, it included incidental PEs, which are known to have minimal complications. Our study focused on a higher-acuity population with RVD, assessing not only mortality risk but also the association between NEWS2 scores and advanced PE interventions. Notably, we demonstrated even modest elevations in NEWS2 scores (e.g., from 3 to 4 or 5) corresponded to significant increases in clinical deterioration.

In another study by Rodriguez et al., NEWS2 was evaluated specifically in patients with intermediate to high-risk PE [20]. This study demonstrated that NEWS2 had greater predictive power than traditional risk stratification tools like PESI and sPESI for identifying patients at risk of clinical deterioration. This aligns closely with our results. Yolcu et al. evaluated NEWS2, NEWS, and the qSOFA score in a cohort of 245 patients with PE and found NEWS2 to have the highest prognostic value for predicting one-week mortality [19]. They did not test for association with advanced intervention use. Our study

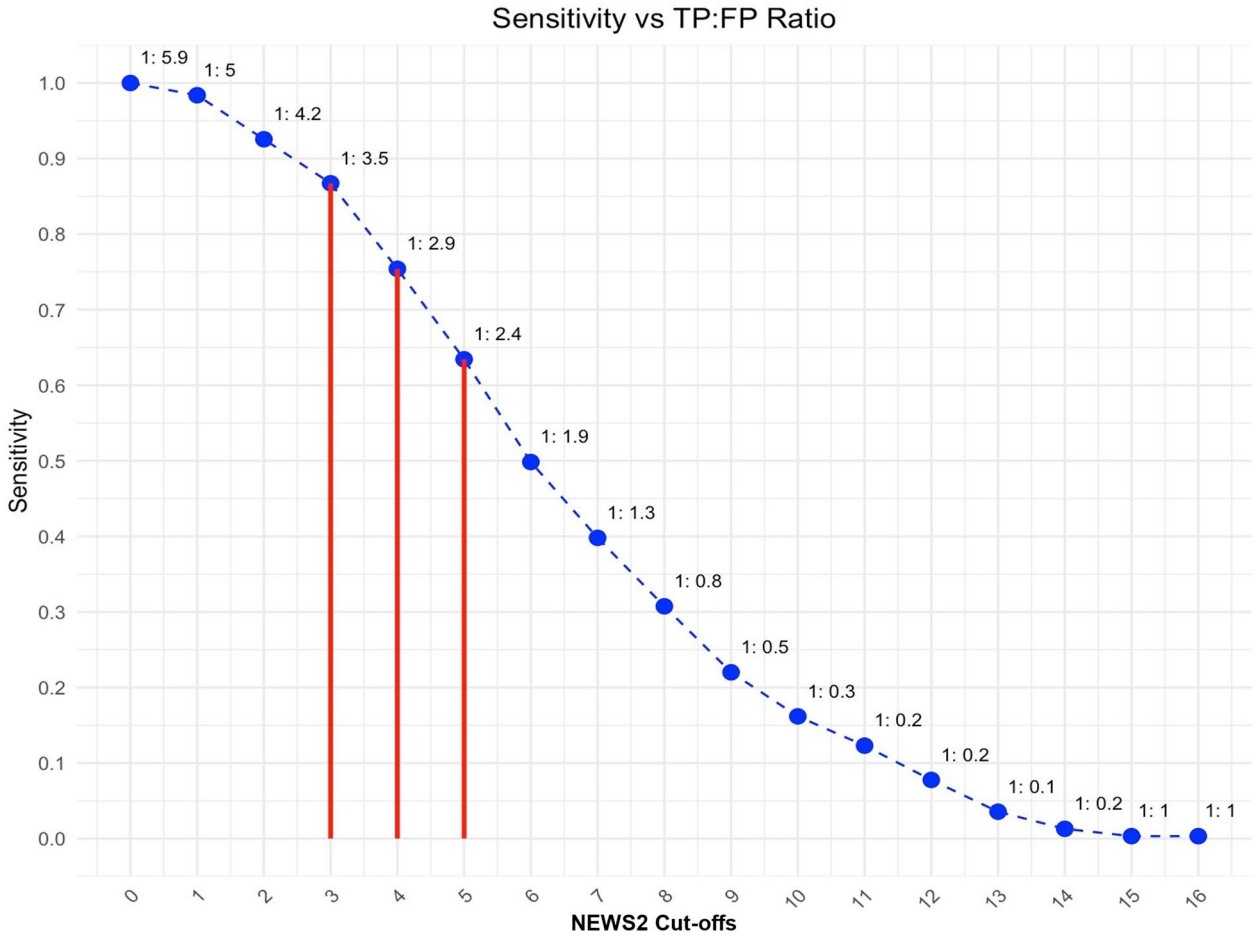

Fig. 5 Sensitivity versus true positive: false positive ratio plot of NEWS2 cut-offs for clinical deterioration

identified clinically meaningful NEWS2 cut-offs that predict not only mortality but also clinical deterioration and the need for advanced interventions. While Yolcu et al. included patients with varying levels of disease severity, our study concentrated on a high acuity population with RVD, offering additional perspective on the prognostic value of NEWS2 in acute care settings.

A strength of our study is the decision curve analysis to assess net clinical benefit. Given the importance of adequately capturing patients truly at high risk for clinical deterioration, we prioritized NEWS2 models with high sensitivity. In determining the trade-off of under and over triaging NEWS2 alert triggers, we considered the cost of false negatives to be significantly higher than the cost of false positives, and therefore erred on the side of patient safety, allowing for a high rate of false positives relative to true positives. Healthcare organizations can then determine the net benefit of the NEWS2 cut-off they adopt [27]. Determining the best NEWS2 cut-off overall depends on clinical impact for the specific pulmonary embolism cohort (assuming net benefit translates to better patient outcomes), specificity versus sensitivity, alternative models available, and implementation feasibility in the hospital or institutions under their purview.

Our research study addresses the Zuin et al. report on clinical needs and research gaps for determining predictors of clinical deterioration in patients with PE and RVD [29]. By incorporating NEWS2 into existing risk stratification models, clinicians can enhance their ability to predict short-term outcomes and assign resources more effectively. However, prospective validation of NEWS2 in larger cohorts is warranted. Research should focus on integrating NEWS2 into clinical workflows to complement existing risk stratification tools. This research should assess its impact on outcomes, such as length of stay, ICU admission rates, and overall survival. Additionally, exploring serial NEWS2 trends may offer deeper insights into the optimal timing of clinical interventions.

Limitations

Our study had several limitations. The retrospective design introduced the potential for selection and

Table 4 Patient characteristics by use of advanced intervention (secondary outcome)

Characteristics	Yes (*N* = 488)	No (*N* = 1633)	Overall (*N* = 2119)	*P*-Value
Age, mean (SD), years	57.6 (15.6)	63.6 (16.8)	62.2 (16.8)	< 0.001
Gender				
Male	242 (49.6%)	792 (48.6%)	1034 (48.8%)	0.718
Female	246 (50.4%)	839 (51.4%)	1085 (51.2%)	
Race				
American Indian/Alaskan Native	2 (0.4%)	21 (1.3%)	23 (1.1%)	0.021
Asian	1 (0.2%)	5 (0.3%)	6 (0.3%)	
Black	189 (38.7%)	541 (33.2%)	730 (34.5%)	
Other	0 (0%)	13 (0.8%)	13 (0.6%)	
Pacific Islander/Native Hawaiian	1 (0.2%)	1 (0.1%)	2 (0.1%)	
Unknown	10 (2.1%)	37 (2.3%)	47 (2.2%)	
White	285 (58.4%)	1013 (62.1%)	1298 (61.3%)	
Ethnicity				
Non-Hispanic/Latino	458 (93.9%)	1512 (92.7%)	1970 (93.0%)	0.731
Hispanic/Latino	10 (2.0%)	44 (2.7%)	54 (2.5%)	
Unknown	20 (4.1%)	75 (4.6%)	95 (4.5%)	
PE severity at PERT activation				
Non-severe submassive	107 (22.0%)	899 (55.1%)	1006 (47.5%)	< 0.001
Severe submassive	276 (56.6%)	669 (41.0%)	945 (44.6%)	
Massive	105 (21.6%)	63 (3.9%)	168 (7.9%)	
Advanced PE interventions (secondary outcome)				
Systemic thrombolysis	196 (40.2%)	0 (0%)	196 (9.2%)	< 0.001
Catheter-directed intervention	210 (43.0%)	0 (0%)	210 (9.9%)	< 0.001
Surgical embolectomy	10 (2.0%)	0 (0%)	10 (0.5%)	< 0.001
Right ventricular assist device	0 (0%)	0 (0%)	0 (0%)	1
Extracorporeal membrane oxygenation	13 (2.7%)	0 (0%)	13 (0.6%)	< 0.001
Other	5 (1.0%)	0 (0%)	5 (0.2%)	< 0.001
Total NEWS, mean (SD), points (Range: 0 to 20 points)	4.8 (3.1)	3.0 (2.5)	3.4 (2.8)	< 0.001
NEWS2 components				
Initial systolic blood pressure, mean (SD), mmHg	122 (26.4)	133 (23.9)	130 (24.9)	< 0.001
Missing	0 (0%)	1 (0.1%)	1 (0.0%)	
Initial heart rate, mean (SD), beats per minute	112 (22.2)	102 (20.7)	104 (21.4)	< 0.001
Missing	0 (0%)	1 (0.1%)	1 (0.0%)	
Initial respiratory rate, mean (SD), breaths/minute	22.4 (5.92)	20.7 (5.79)	21.1 (5.86)	< 0.001
Missing	0 (0%)	1 (0.1%)	1 (0.0%)	
Temperature, mean (SD), degrees Fahrenheit	98.0 (0.95)	98.2 (0.78)	98.2 (0.83)	< 0.001
Missing	22 (4.5%)	38 (2.3%)	60 (2.8%)	
Initial oxygen pulse oximetry, mean (SD), %	93.2 (8.02)	94.6 (6.06)	94.3 (6.59)	< 0.001
Missing	1 (0.2%)	2 (0.1%)	3 (0.1%)	
Hypercapnic respiratory failure	0 (0%)	2 (0.1%)	2 (0.1%)	1
Supplemental oxygen use	197 (40.5%)	447 (27.4%)	644 (30.4%)	< 0.001
Altered mental status				
Alert	436 (89.3%)	1563 (95.8%)	1999 (94.3%)	< 0.001
New confusion/altered mental status	52 (10.7%)	68 (4.2%)	120 (5.7%)	
NEWS2 cut-off of 3				
< 3	110 (22.5%)	801 (49.1%)	911 (43.0%)	< 0.001
≥ 3	378 (77.5%)	830 (50.9%)	1208 (57.0%)	
NEWS2 cut-off of 4				
< 4	178 (36.5%)	1026 (62.9%)	1204 (56.8%)	< 0.001
≥ 4	310 (63.5%)	605 (37.1%)	915 (43.2%)	
NEWS2 cut-off of 5				
< 5	241 (49.4%)	1214 (74.4%)	1455 (68.7%)	< 0.001

Table 4 (continued)

Characteristics	Yes (*N* = 488)	No (*N* = 1633)	Overall (*N* = 2119)	*P*-Value
≥ 5	247 (50.6%)	417 (25.6%)	664 (31.3%)	
Clinical deterioration during hospitalization (primary outcome)	163 (33.4%)	146 (9.0%)	309 (14.6%)	< 0.001
Breakdown of clinical deterioration events during hospitalization				
Cardiac arrest	83 (17.0%)	42 (2.6%)	125 (5.9%)	< 0.001
Need for mechanical or positive pressure ventilation	112 (23.0%)	86 (5.3%)	198 (9.3%)	< 0.001
Use of vasoactive medication	135 (27.7%)	72 (4.4%)	207 (9.8%)	< 0.001
PE-related death	61 (12.5%)	64 (3.9%)	125 (5.9%)	< 0.001

Table 5 Prediction metrics of NEWS2 cut-offs for advanced intervention (secondary outcome)*

Variable	Sensitivity	Specificity	PPV	NPV	AUC	OR
NEWS2 ≥ 3	0.78 (0.74, 0.81)	0.49 (0.47, 0.52)	0.31 (0.29, 0.34)	0.88 (0.86, 0.90)	0.63 (0.30, 0.70	3.3 (2.6, 4.2)
NEWS2 ≥ 4 (Youden's optimal cut-off)	0.64 (0.59, 0.68)	0.63 (0.61, 0.65)	0.34 (0.31, 0.37)	0.85 (0.83, 0.87)	0.63 (0.24, 0.76)	3.0 (2.4, 3.6)
NEWS2 ≥ 5	0.51 (0.46, 0.55)	0.74 (0.72, 0.77)	0.37 (0.34, 0.41)	0.84 (0.82, 0.85)	0.63 (0.21, 0.79)	3.0 (2.4, 3.7)

* Abbreviations: PE = pulmonary embolism PPV = positive predictive value, NPV = negative predictive value, AUC = area under the curve OR = odds ratio

Table 6 LASSO regression model for PE-related clinical deterioration (primary outcome)*

	PE-related clinical deterioration (primary outcome)		
Predictors	*Unadjusted Odds Ratios*	*Confidence Interval*	*P-value*
NEWS2	1.2	1.1–1.3	< 0.001
Sustained hypotension	2.6	1.4–4.7	0.002
Severe submassive PE classification	2.1	1.4–3.2	0.001
Massive PE classification	15.8	8.7–29.0	< 0.001
ICU admission	3.8	2.6–5.6	< 0.001
Observations	2119		
R^2 Tjur	0.34		

* Abbreviations: ICU = intensive care unit, PE = pulmonary embolism, NEWS2 = National Early Warning Score

information biases. As a multi-center study within a single healthcare system in North Carolina, the findings may not be generalizable to other populations or clinical settings. Additionally, while NEWS2 demonstrated strong associations with clinical deterioration and advanced interventions, it is primarily a physiologic score and does not account for PE-specific factors, such as imaging findings, clot burden, or changes in biomarker levels, which are critical components of risk stratification. In addition, sex, race, and ethnicity were based on EMR data and not based on the patient's self-report as recommended by Sex and Gender Equity in Research guidelines [30, 31]. Accuracy of data and interpretation of sex and race may improve in prospective studies that rely on patients' self-reporting of demographic data [32]. We used initial NEWS2, which is taken upon arrival when the patient is standing, seated, or supine. Patients with PE often report dyspnea with exertion. Of the six physiologic parameters measured in NEWS2, heart rate, respiratory rate, and oxygen saturation derangements can be unmasked or accentuated with ambulatory assessments when feasible or safe, not just taken at rest. Finally, we did not include serial NEWS2 data collected during hospitalization, which might provide additional insights into the dynamic progression of disease and response to interventions.

Readers should note the results of our decision curve analysis did not point to the ideal NEWS2 cut-off to use. Rather, net benefit depends on the NEWS2 cut-off chosen by the healthcare team or institution for specific diseases or conditions based on a cost-benefit analysis [27]. Cut-offs identified for NEWS2 performance may require external validation in diverse healthcare systems and patient populations.

Conclusions

This study supports the use of NEWS2 as an effective tool for early risk stratification in patients with acute PE. A cut-off ≥ 3 provided strong sensitivity and NPV, enabling timely identification of patients at risk for clinical deterioration or advanced interventions. NEWS2 score cut-offs of 3–5 provided a "net benefit" over a "treat all" approach. These findings advocate for the integration of NEWS2 as part of comprehensive risk stratification strategies in emergency and inpatient settings.

Abbreviations

AIDS	Acquired immunodeficiency syndrome
AUC	Area under the receiver operating curve
BP	Blood pressure
COPERR	Clinical outcomes in pulmonary embolism research registry

CI	Confidence interval
CT	Computed tomography
ECMO	Extracorporeal membrane oxygenation
ED	Emergency department
EMR	Electronic medical record
GCS	Glasgow coma scale
ICU	Intensive care unit
LASSO	Least absolute shrinkage and selection operator
LV	Left ventricle
NEWS/NEWS2	National Early Warning Score (original and updated versions)
NHS	National Health Service
NPV	Negative predictive value
OR	Odds ratio
PE	Pulmonary embolism
PERT	Pulmonary embolism response team
PESI	Pulmonary embolism severity index
PPV	Positive predictive value
qSOFA	Quick sepsis-related organ failure assessment
RV	Right ventricle
RVD	Right ventricular dysfunction
SD	Standard deviation
sPESI	Simplified pulmonary embolism severity index
TP:FP	Ratio of true positives to false positives

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12959-025-00735-7.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
Nicole Wellinsky Johnson: for database construction and initial supervision of database and data extraction.

Author contributions
Study conception and design by AJW. AJW, ALP, and MMH supervised the conduct of the trial and data collection. AJW, FC, EC, HAO, ALP, SF, and DC performed data extraction. NSO performed statistical analysis and interpretation of the data. AJW, FC, DRT, and KLG drafted the manuscript. All authors contributed substantially to article revision for important intellectual content. AJW takes responsibility for the paper as a whole.

Funding
None.

Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
We extracted data for patients entered into the Clinical Outcomes in Pulmonary Embolism Research Registry. The registry and observational studies using its data (including this study) were approved by the Advocate Health–Wake Forest University School of Medicine Institutional Review Board with a waiver of informed consent (IRB Study #IRB00082657).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 24 January 2025 / Accepted: 7 May 2025
Published online: 16 May 2025

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