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RESEARCH ARTICLE

Validation of a modified bedside Pediatric Early Warning System score for detection of clinical deterioration in hospitalized pediatric oncology patients: A prospective cohort study

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Abstract

Background: Hospitalized pediatric oncology patients are at risk of severe clinical deterioration. Yet Pediatric Early Warning System (PEWS) scores have not been prospectively validated in these patients. We aimed to determine the predictive performance of the modified BedsidePEWS score for unplanned pediatric intensive care unit (PICU) admission and cardiopulmonary resuscitation (CPR) in this patient population.

Methods: We performed a prospective cohort study in an 80-bed pediatric oncology hospital in the Netherlands, where care has been nationally centralized. All hospitalized pediatric oncology patients aged 0–18 years were eligible for inclusion. A Cox proportional hazard model was estimated to study the association between BedsidePEWS score and unplanned PICU admissions or CPR. The predictive performance of the model was internally validated by bootstrapping.

Results: A total of 1137 patients were included. During the study, 103 patients experienced 127 unplanned PICU admissions and three CPRs. The hazard ratio for unplanned PICU admission or CPR was 1.65 (95% confidence interval [CI]: 1.59–1.72) for each point increase in the modified BedsidePEWS score. The discriminative ability was

Abbreviations: CI, confidence interval; CPR, cardiopulmonary resuscitation; EHR, electronic health records; HR, hazard ratio; IQR, interquartile range; PEWS, Pediatric Early Warning System; PICU, pediatric intensive care unit.

moderate (D-index close to 0 and a C-index of 0.83 [95% CI: 0.79–0.90]). Positive and negative predictive values of modified BedsidePEWS score at the widely used cutoff of 8, at which escalation of care is required, were 1.4% and 99.9%, respectively.

Conclusion: The modified BedsidePEWS score is significantly associated with requirement of PICU transfer or CPR. In pediatric oncology patients, this PEWS score may aid in clinical decision-making for timing of PICU transfer.

KEYWORDS
intensive care, mortality, oncology, pediatric, pediatric early warning score

1 | INTRODUCTION

Unrecognized clinical deterioration in hospitalized pediatric patients may lead to adverse outcomes, such as cardiac arrest or death. Pediatric oncology patients are especially at risk for rapid deterioration, given their severity of illness, toxicity of treatment, and associated immunosuppression. Up to 38% of patients require admission to the pediatric intensive care unit (PICU) during their disease course, with sepsis and respiratory failure as main reasons for unplanned PICU admission.[1,2] Mortality rates of pediatric oncology patients requiring PICU admission exceed that of the general PICU population, ranging from 7% to 15% versus 2%–5%.[3–5] Unplanned PICU admissions, often preceded by clinical deterioration, have the highest PICU mortality.[6] In addition, pediatric oncology patients are approximately three times less likely to survive cardiopulmonary arrest than general pediatric patients.[7] Early detection of clinical deterioration resulting in timely escalation of care may therefore ultimately improve patients' outcomes.

A broad range of Pediatric Early Warning System (PEWS) scores are currently used for detection of clinical deterioration in hospitalized children. One of the most used scores, the BedsidePEWS, has been developed for routine use in clinical care for general pediatric patients, showing an excellent performance to identify children at risk for cardiopulmonary arrest.[8,9] In addition, it was one of the best-performing PEWS scores in predicting clinical deterioration.[8,9] A multicenter cluster randomized trial showed a significant reduction in late PICU admission after implementation of the BedsidePEWS score.[10,11] This score has also been implemented in our pediatric oncology center, yet has not been validated in this patient population. It has been shown that early warning scores may need different interpretation in specific patient populations. For instance, the early warning score was found to have poor discriminatory value in identifying deteriorating adult cancer patients requiring critical care.[12] Despite the widespread implementation of PEWSs, few studies have assessed the performance of a PEWS in pediatric oncology patients.[4,13–16] However, the majority of these studies were retrospective studies.[4,13–15] In addition, some of these studies were conducted in oncological subgroups, for example, stem cell transplant patients, or patients in resource-limited settings, thereby limiting generalizability.[13,14,16] Moreover, most studies used matched case–control designs or the maximum PEWS score in the 24 hours prior to unplanned PICU admission,[4,13–15] which may have resulted in overestimating the predictive performance of these scores.

In this prospective cohort study, we aimed to determine the predictive performance of a modified BedsidePEWS score for unplanned PICU admission or cardiopulmonary resuscitation (CPR) in hospitalized pediatric oncology patients.

2 | METHODS

2.1 | Study design and setting

A detailed description of the study rationale and design was previously described.[17] We performed a prospective cohort study between February 1, 2019 and February 1, 2021 at the Princess Máxima Center, an 80-bed national referral center for pediatric oncology in the Netherlands. The study was approved by the ethical review board of our hospital (IRB protocol number 16-572/C). All hospitalized patients with International Classification of Diseases in Oncology (ICD-O) diagnosis of pediatric malignancy (morphology code 1, 2, or 3) aged 0–18 years were eligible for inclusion. Patients admitted as outpatients for routine diagnostic and therapeutic procedures were excluded. In addition, patients with restrictions in care (palliative care only, do-not-resuscitate orders, no PICU admission) were excluded from the moment restriction in care was registered.

We evaluated the BedsidePEWS as used in our hospital. At implementation in our hospital in 2014, the score had been slightly modified by adding temperature and categorization of oxygen therapy (Table S1 and Figure S1). Modified BedsidePEWS scores were assessed and documented in patients' electronic health record (EHR) by nursing staff as part of routine care on all inpatient wards. Nurses could manually enter either the subitems of the score, followed by automated calculation of the score, or the sum score directly into the EHR. In both cases, the required corresponding clinical action was shown. To optimize the adherence to the scoring algorithm, several efforts were made with focus on education, communication, and workflow. These included multiple refresher courses, procedures to train newly hired staff, identifying barriers and facilitators, and encouragement to review BedsidePEWS scores at rounds and change of shifts. In addition, quality monitoring on BedsidePEWS scoring was aided by a weekly dashboard

showing the nurses' performance of scoring in the different shifts at the wards.

2.2 | Data collection

Data on patient characteristics, hospital admissions, outcome measures, vital signs, and BedsidePEWS scores were extracted from the EHRs (HiX, Chipsoft, Amsterdam, the Netherlands). Detailed information about data collection and preparation is provided in Supporting Information.

2.3 | Primary and secondary outcomes

The primary outcome was the composite of an unplanned PICU admission or CPR. A single patient could experience the primary outcome event multiple times during a hospital stay. Therefore, the unit of study was an uninterrupted inpatient ward admission. This admission was ended when (a) the outcome event occurred, (b) the patient was discharged from the ward, (c) a restriction in care was registered, or (d) the patient turned 18 years. A new uninterrupted ward admission was started when the patient was discharged from PICU to the ward or was re-admitted to the hospital.

Secondary outcomes included minor clinical deterioration events requiring escalation of care (i.e., the initiation of high-flow oxygen therapy or non-rebreathing mask, fluid bolus, epinephrine intramuscular, or an urgent PICU consultation) not resulting in a PICU transfer or CPR, and any clinical deteriorations (i.e., the combination of significant clinical deterioration requiring PICU transfer or CPR and minor clinical deterioration events, see Supporting Information).

2.4 | Statistical analysis

The modified BedsidePEWS score is a severity of illness score reflecting the clinical condition of the patient. This clinical condition may vary per patient and during a hospital stay. Therefore, we analyzed the modified BedsidePEWS as a time-varying covariate by estimating a Cox proportional hazard model[18] (see detailed description in Supporting Information). Time to event was the time between a current PEWS and the subsequent PEWS or a clinical deterioration event, whichever comes first. In this way, we incorporated all documented modified BedsidePEWS scores of all patients, accounting for the time-varying nature of the PEWS score and reoccurrence of the event within one single patient. Cancer diagnosis groups (solid tumors, hemato-oncology, and neuro-oncology) were also included as prognostic factors in the model. Finally, the same model was used to estimate the association between modified BedsidePEWS and secondary outcomes (see detailed description in Supporting Information). Internal validation of the model was performed by using Efron's bootstrap.[19]

Several threshold-based prediction measures were estimated for the score cutoff of 8—the threshold at which escalation of care is required—and additionally for cutoffs 5 through 11, using the last modified BedsidePEWS score prior to event. These measures included sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and number needed to evaluate (calculated as 1/PPV)[20] (see Supporting Information).

Finally, we performed a post-hoc qualitative analysis of the modified BedsidePEWS in the 24-hour period prior to the primary outcome events. All statistical analyses were performed using R-statistical software, version 3.6.2 (2019-12-12), and associated packages (see Supporting Information).[21] Reporting of this validation study was performed using the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines (Table S2).[22]

3 | RESULTS

A total of 5628 ward admissions of 1137 unique patients, and 119.813 modified BedsidePEWS scores were included. Table 1 reports the clinical characteristics of the included patients. The median (interquartile range [IQR]) age of the included patients was 8 [4–14] years and 43.3% were female. There were 127 unplanned PICU admissions and three CPRs among 103 patients. Following CPR and during the PICU admissions, 14 patients died (10.8%).

3.1 | Compliance to the scoring algorithm

Compliance to the scoring algorithm is shown in Table S3. For modified BedsidePEWS score categories 0–3 and 4–5, the median time intervals were below the intended time limit of the scoring algorithm, whereas for BedsidePEWS score category 6–7, the median time interval was higher than the intended time limit. In 85% of all modified BedsidePEWS score ≥8, a physician was called to evaluate the patient.

3.2 | Performance of the modified BedsidePEWS: Unplanned PICU admission or CPR

The modified BedsidePEWS was significantly associated with time to unplanned PICU admission or CPR, with a hazard ratio (HR) of 1.65 (95% confidence interval [CI]: 1.59–1.72) for each point increase in the modified BedsidePEWS score (Table 2). The HRs [95% CI] per diagnosis group were 1.16 [0.78–1.75] for hemato-oncology diagnosis and 1.09 [0.49–2.43] for neuro-oncology diagnosis, with solid tumors as reference category.

Internal validation of the model has been performed by using bootstrap. For the discriminative ability of the modified BedsidePEWS score, the C-index [95% CI] was 0.83 [0.79–0.90] and the discrimination index D [95% CI] was 0.20 [0.16–0.26]. The model was well calibrated with an index-corrected slope of 0.99 (Table 2).

Table 3 shows the distribution of the modified BedsidePEWS score related to occurrence of the primary outcome event. A cutoff of 8, at

TABLE 1 Demographic and clinical characteristics of included patients

Characteristic	Total patients ($n = 1137$)	Patients without primary outcome event ($n = 1034$)	Patients with primary outcome event ($n = 103$)
Age (years), median [IQR]	8.4 [3.7–13.6]	8.4 [3.8–13.7]	7.6 [2.9–13.2]
Female sex, *n* (%)	495 (43.5)	446 (43.1)	49 (47.6)
Oncological diagnosis, *n* (%)			
Hemato-oncological	482 (42.4)	422 (40.8)	60 (58.3)
Solid tumor	412 (36.2)	375 (36.53)	37 (35.9)
Brain/central nervous system tumor	243 (21.4)	237 (22.9)	6 (5.8)
HSCT recipient, *n* (%)	125 (11.0)	100 (9.7)	25 (24.3)
Allogeneic	58 (5.1)	45 (4.4)	13 (12.6)
Autologous	67 (5.9)	55 (5.3)	12 (11.7)
CAR-T cell therapy recipient, *n* (%)	20 (1.8)	16 (1.5)	4 (3.9)
Number of primary outcome events per patient, *n* (%)			
0	1037 (91.2)	1034 (100)	0 (0)
1	82 (7.2)	0	82 (79.6)
2	16 (1.4)	0	16 (15.5)
3	4 (0.4)	0	4 (3.9)
4	1 (0.2)	0	1 (1.0)

Abbreviations: CAR-T, chimeric antigen receptor T cell; CPR, cardiopulmonary resuscitation; HSCT, hematopoietic stem cell transplantation; IQR, interquartile range.

TABLE 2 Overview of the performance of modified BedsidePEWS score

		Internal validation after bootstrapping ($n = 500$)			
	Cox proportional hazard model		Discrimination	Calibration slope	
Outcome measure	HR [95% CI]	*p*-Value	C-index [95% CI]	D [95% CI]	
Unplanned PICU admission or CPR	1.65 [1.59–1.72]	<.01	0.83 [0.79–0.90]	0.20 [0.16–0.26]	0.99
Minor clinical deterioration events[a]	1.77 [1.71–1.83]	<.01	0.86 [0.83–0.88]	0.17 [0.15–0.19]	0.99
All clinical deterioration events[b]	1.75 [1.70–1.81]	<.01	0.84 [0.82–0.87]	0.16 [0.15–0.18]	0.99

Abbreviations: CI, confidence interval; C-index, concordance-index; D, discrimination index; HR, hazard ratio; PICU, pediatric intensive care unit.
[a]Clinical deterioration events: the initiation of high-flow oxygen therapy or non-rebreathing mask, fluid bolus, epinephrine intramuscular, or an urgent PICU consultation not resulting in a PICU transfer or CPR.
[b]Total of unplanned PICU admissions, CPR and minimal clinical deterioration events.

which escalation of care is required, yielded a negative predictive value of 99.9%, a positive predictive value of 1.5%, a sensitivity of 33.8%, specificity of 97.7%, and a number needed to evaluate was 67. Results corresponding to different thresholds of the modified BedsidePEWS are shown in Table S4. Lowering the cutoff threshold resulted in an increased sensitivity, a decreased specificity, a decreased positive predictive value, and a higher number needed to evaluate. On the contrary, raising the cutoff threshold results in a decreased sensitivity, accompanied by an increased specificity, and a higher positive predictive value with lower number needed to evaluate.

3.3 | Performance of the modified BedsidePEWS: Minor and any clinical deterioration events

Of the 1137 included patients, 234 patients experienced a total of 463 minor clinical deteriorations, and 276 patients experienced 583 clinical deterioration events (i.e., combined unplanned PICU admission, CPR and minor clinical deterioration events). The modified BedsidePEWS was significantly associated with time to minor clinical deterioration as well as any clinical deterioration event; HR [95% CI]: 1.77 [1.71–1.83] and 1.75 [1.70–1.81], respectively (Table 2). The discrimination index D,

TABLE 3 Distribution of modified BedsidePEWS score and occurrence of unplanned PICU admission or CPR

Modified BedsidePEWS score	No event occurred (frequency)	Event occurred (frequency)	No event occurred (%)	Event occurred (%)
0	34,653	6	100	0
1	34,526	14	100	0.1
2	21,763	13	99.9	0.1
3	11,197	10	99.9	0.1
4	6290	8	99.9	0.1
5	3658	7	99.8	0.2
6	2878	13	99.6	0.5
7	1893	15	99.2	1.3
8	1035	11	98.9	1.2
9	721	8	98.9	1.1
10	461	6	98.7	2.2
11	281	7	97.6	3.6
12	148	3	98.0	3.2
13	70	2	97.2	9.1
14	42	4	91.3	12.5
15	32	1	97.0	3.0
16	14	2	87.5	12.5
17	1	0	100	0

Note: The modified BedsidePEWS scores were arranged within a single clinical episode from one PEWS score to the next one (time interval between scores), with at the end of each time interval the patients' status whether or not an event occurred.
Abbreviations: CPR, cardiopulmonary resuscitation; PEWS, Pediatric Early Warning System; PICU, pediatric intensive care unit.

C-index, and calibration were similar to those of the primary outcome event, as shown in Table 2.

The distribution of the modified BedsidePEWS scores and occurrence of a minor clinical deterioration event is shown in Table S5 and for all clinical deterioration events in Table S6. Like the primary outcome, the negative predictive value for minor deterioration events as well as all clinical deterioration events was high (99.6% for both outcomes). The positive predictive value at the cutoff of 8 was 8.3% for minor clinical deterioration and 9.6% for any clinical deterioration.

3.4 | Modified BedsidePEWS scores in the 24 hours prior to non-elective PICU admission or CPR

The characteristics of the 127 unplanned PICU admissions and three CPRs are shown in Table 4. The three most common reasons for PICU admission were respiratory failure (35%), sepsis (16%), and cardiovascular failure (15%). The median [IQR] PICU length of stay was 2 [1–6] days, with a range of 0–79 days. Visual inspection of the modified BedsidePEWS scores clustered into 1-hour periods prior to unplanned PICU admissions or CPR showed an increasing modified BedsidePEWS score in the 24 hours prior to the event; however, there is still large variation from low to high values (Figure 1).

In the 24 hours prior to the event, 67 of the 130 primary outcome events (52%) had a maximum modified BedsidePEWS <8, whereas 63/130 events (48%) had a maximum BedsidePEWS of ≥8 (Table 4). A majority of the unplanned PICU admissions with a maximum BedsidePEWS <8 included patients requiring a PICU transfer because of an upper airway problem (e.g., acute vocal cord paralysis or mediastinal mass, $n = 14$), malignant hypertension ($n = 5$), neurologic deterioration ($n = 7$), or unplanned postoperative care ($n = 16$).

4 | DISCUSSION

We prospectively investigated the performance of a modified BedsidePEWS score to predict clinical deterioration in hospitalized pediatric oncology patients. This score is significantly associated with unplanned PICU admission or CPR, as well as with minor clinical deterioration and any clinical deterioration. We found a high negative predictive value (99.9%) for the widely used cutoff score of 8, indicating that the BedsidePEWS is highly accurate in hospitalized pediatric oncology patients.

However, the results of the predictive performance reveal several nuances to the use of the modified BedsidePEWS score as a prediction tool to timely detect clinical deterioration. First, we found a moderate discriminative ability of the modified BedsidePEWS, as reflected by a C-index of 0.8 and a D-index close to 0. This could be explained by the low incidence rate of the primary outcome. A second nuance is

TABLE 4 The maximum modified BedsidePEWS score in the 24 hours prior to primary outcome events (unplanned PICU admission or CPR) related to the PICU admission reason

	Number of events $n = 130$	Maximum PEWS score <8 $n = 67$	Maximum PEWS score ≥8 $n = 63$
Unplanned PICU admission, *n* (%)	127 (98)	66 (99)	61 (97)
PICU admission reason:			
Respiratory failure, *n* (%)	45 (35)	15 (22)	30 (48)
Upper airway problems	14	10	4
Pulmonary problems	31	5	26
Sepsis, *n* (%)	21 (16)	8 (12)	13 (21)
Cardiovascular failure, *n* (%)	20 (15)	11 (16)	9 (14)
Hypotension/shock	15	8	7
Malignant hypertension	5	3	2
Unplanned postoperative, *n* (%)	17 (13)	16 (24)	1 (2)
Neurological deterioration, *n* (%)	9 (7)	7 (10)	2 (3)
Renal failure, *n* (%)	3 (2)	1 (1)	2 (3)
Hepatic failure, *n* (%)	1 (1)	0 (0)	1 (2)
After cardiopulmonary resuscitation, *n* (%)	2 (2)	1 (1)	1 (2)
Other, *n* (%)	9 (7)	7 (10)	2 (3)
CPR (not followed by PICU admission), *n* (%)	3 (2)	1 (1)	2 (3)

Abbreviations: CPR, cardiopulmonary resuscitation; PEWS, Pediatric Early Warning System; PICU, pediatric intensive care unit.

that despite the high negative predictive value of 99.9%, 67 of the 130 unplanned PICU admissions and CPRs were preceded by a maximum modified BedsidePEWS of <8 in the 24 hours prior to these events. There may be several explanations for this observation. Some types of critical decline are not captured by the modified BedsidePEWS (e.g., upper airway problems or neurological deterioration). In addition, unplanned postoperative patients often require PICU transfer as a result of an acute perioperative complication. Low modified BedsidePEWS scores preceding the operating room may represent a good clinical preoperative condition. As we used the scores as documented by nurses in daily practice, there may be missing items in the score possibly resulting in a lower score. This is a common problem described in previous PEWS validation studies.[10,23] A third nuance to the use of the modified BedsidePEWS as a prediction tool involves the low positive predictive value of 1.5% when using a modified BedsidePEWS cutoff score of 8. The number needed to evaluate of 67 at this cutoff indicates that of the 67 times any patient is evaluated for a modified BedsidePEWS score ≥8, one time the patient truly requires to be transferred to the PICU. This may lead to alarm fatigue.[24] On the other hand, given the trade-off between positive and negative predictive values, one may accept this false alarm rate in order to not miss any patient. We showed that lowering the modified BedsidePEWS threshold resulted in higher sensitivity. However, this was accompanied with lower positive predictive values and higher numbers needed to evaluate. This risks even more alarm fatigue or suboptimal adherence to the scoring algorithm.[25] Therefore, lowering the threshold at which patient evaluation is required may not necessarily have the desired effect of improving detection of clinical deterioration. Raising the threshold further decreases the sensitivity, which may risk missing patients. Taking these considerations into account, we feel that the threshold of 8 is the optimal score cutoff.

Our study shows that the modified BedsidePEWS score is a strong prognostic factor for the time to PICU transfer or detecting clinical deterioration. This supports its use in clinical decision-making for timing of PICU transfer or escalation of care. Our results are in line with other studies validating a PEWS score in pediatric oncology patients. These studies reported a good predictive performance of PEWS scores for unplanned PICU transfer,[4,13–16] or the early detection of critically ill patients.[26] They all found a high area under the receiver operating characteristic (AUROC) for a PEWS score for the outcome of unplanned PICU transfer, ranging from 0.83 to 0.96.[4,13–16] In addition, it was demonstrated that PEWS may aid in triage of transfer to the PICU.[27]

In contrast to these previous studies, we employed a prospective cohort design including all subgroups of pediatric oncology patients, such as HSCT patients. In addition, we included all modified BedsidePEWS scores as documented in the EHR. This is the first study validating a PEWS in pediatric oncology patients using the time-to-event data. The use of an uninterrupted inpatient ward admission as a study unit as opposed to a single patient allowed us to account for re-occurrence of the outcome event within the same hospitalization period. Taking these points into consideration, we believe that this study yields a valid estimation of the predictive performance of the modified BedsidePEWS in pediatric oncology patients.

Our study has several limitations. First, we used clinical data as documented in the EHRs in a real-life setting. Inherently, this means that

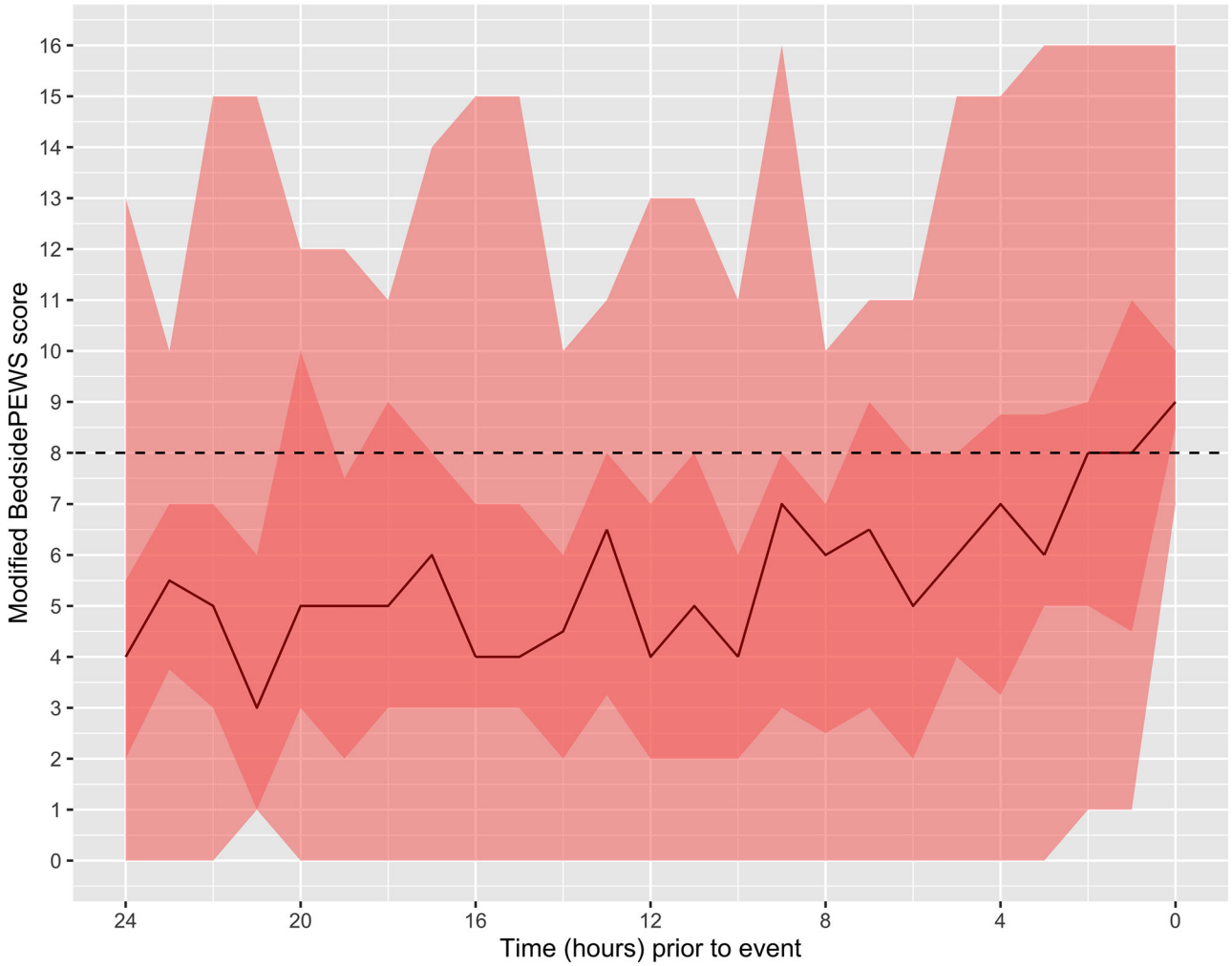

FIGURE 1 The median modified BedsidePEWS score, clustered per hour, with the interquartile range (minimum and maximum), in the 24 hours prior to unplanned pediatric intensive care unit (PICU) admission. A score cutoff of 8, at which escalation of care is required, is marked by a dashed line. The primary outcome events occur at $t = 0$, which is at the right of the plot.

modified BedsidePEWS scores may not have been completely scored or adherence to the scoring algorithm was not perfect. Considering the outcome events, there could be documentation errors, mainly of the secondary outcome events as these events were extracted from the physicians' and nurses' daily reports. Missing items in the PEWS score often lead to a lower score and may lead to an undervaluation of the severity of illness.[23] Completing all items of a PEWS score or a sustainable adherence to the scoring algorithm remains challenging in daily practice, as was demonstrated by other studies validating a PEWS score.[23,28] To address these problems, multiple refresher courses and feedback on the scoring were provided throughout the study period. Yet, there were also barriers impeding PEWS implementation; for example, the manual entry of the vital signs in the computer, which we were unable to fully resolve during the study period. Currently, we are working toward an automatized process of registration of the vital signs and simultaneous calculation of a PEWS score in the EHR. Second, prevention of clinical deterioration is also dependent on the initiation of timely and appropriate interventions. Two before-and-after studies showed a reduction in the rate and the severity of clinical deterioration events following PEWS implementation, implicating improved recognition and timely treatment of clinically deteriorating patients.[29,30] This timely identification, followed by the appropriate intervention may influence the need for PICU transfer. Due to the observational design of the study, we are unable to identify the underlying cause of the clinical deterioration (e.g., failure of PEWS, inappropriate interventions, delay in treatment). This is a fundamental limitation that is inherently part of all studies validating a PEWS in a real-life setting. We addressed this problem by analyzing the minor clinical deterioration events in our study, as these reflect the care interventions for a clinically deteriorating patient. The HR for these outcome measures, as well as the discriminative ability, are comparable to the primary outcome measure. Last, the validation of one modified BedsidePEWS score in a setting of a single pediatric oncology hospital may limit the generalizability of our findings to other settings.

The results of our study contribute to the evidence-based use of a PEWS to support clinical decision-making of timing of escalation of care or PICU transfer in pediatric oncology patients. For future research, we see several opportunities to improve the timely

recognition of clinical deterioration in pediatric oncology patients. Currently, the modified BedsidePEWS score leverages only a small fraction of the EHR content, as this score was originally designed to be tabulated manually by nurses.[8] The widespread implementation of EHRs facilitates the development of more sophisticated systems incorporating additional routinely collected patient data, oncology-specific factors, or contextual factors such as parents' or clinicians' "gut feeling," which may improve the predictive performance of a model to detect clinical deterioration in pediatric oncology patients.[31] The combination with the possibility for continuous monitoring and big data analytics may further improve prediction, situation awareness, and personalized risk assessment.[32–34] Embedding this score in the digital workflow is important to improve adherence to the scoring algorithm and reduce administrative burden.[35]

After this study was performed, we have implemented the DutchPEWS in our center, a national PEWS score. As this score incorporates caregivers' gut feeling and neurological deterioration, this might at least partially address the missing of patients with specific types of critical deterioration, for example, neurological deterioration, though the predictive performance of this DutchPEWS is yet to be assessed. Additionally, we have improved the digital workflow, with automated calculation of all PEWS scores, and are working toward automated registration of vital signs in the EHR.

Of note, to prevent delay in escalation of care and to ultimately improve patient outcome, a monitoring tool that timely detects deterioration is not enough. A robust implementation of PEWS is essential for its validity and impact on patients' outcome. A PEWS is a complex socio-technological intervention that requires consideration at the levels of the individual healthcare provider, multidisciplinary team, hospital, and policy. Several barriers and enablers for successful implementation have been identified.[36] Agulnik et al. demonstrated how barriers could be turned into enablers using targeted strategies, such as early engagement of all stakeholders, and a time-limited pilot followed by adaptation.[37] It is necessary to embed a PEWS within a system that stimulates situational awareness, with available resources and continuous quality monitoring and improvement.[38] Besides the optimization of recognition of clinical deterioration, research should focus on evaluation of decision-making and response, quality improvement of implementation, and the effect of implementation with robust, valid, and clinically meaningful outcome parameters.[39]

This prospective study shows that increasing modified BedsidePEWS scores are significantly associated with requirement of PICU transfer or CPR in hospitalized pediatric oncology patients. Although it does not capture some specific clinical deterioration conditions, the modified BedsidePEWS is a valuable adjunct to clinical decision-making in the timing of escalation of care in this high-risk patient population.

AUTHOR CONTRIBUTIONS

Marijn Soeteman, Roelie Wösten-van Asperen, Marry van den Heuvel-Eibrink, and Teus Kappen conceptualized the study. Marijn Soeteman wrote the initial version of the paper. All authors contributed to subsequent drafts and agreed for the final version to be submitted. Marijn Soeteman, Martine van Engelen, Maartje Marcelis, and Ellen Kilsdonk carried out data curation. Marijn Soeteman, Teus Kappen, and Marta Fiocco undertook data analyses. Roelie Wösten-van Asperen, Edward Nieuwenhuis, Teus Kappen, and Wim Tissing contributed to clinical interpretation of the findings. Roelie Wösten-van Asperen and Teus Kappen had access to and verified all of underlying data in this study. All authors had full access to all study data and take responsibility for the integrity of the data, the accuracy of the analysis, and the decision to submit for publication.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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