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RESEARCH ARTICLE

Community-onset pediatric status epilepticus: Barriers to care and outcomes in a real-world setting

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Abstract

Objective: Status epilepticus (SE) is a neurological emergency in childhood, often leading to neuronal damage and long-term outcomes. The study aims to identify barriers in the pre-hospital and in-hospital management of community-onset pediatric SE and to evaluate the effectiveness of pediatric scores on outcomes prediction.

Methods: This monocentric observational retrospective cohort study included patients treated for community-onset pediatric SE in a tertiary care hospital between 2010 and 2021. Data were extracted following Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Inclusion criteria were community-onset SE (according to the International League Against Epilepsy [ILAE] Task Force on SE Classification), admission to the pediatric emergency department (PED), age: 1 month to 18 years. Pre-hospital, in-hospital management and outcomes were analyzed. Pediatric scores for prediction of clinical worsening (Pediatric Early Warning Score - PEWS) and SE outcome (Status Epilepticus in Pediatric patients Severity Score - STEPSS; Pre-status Epilepticus PCPCS, background Electroencephalographic abnormalities, Drug refractoriness, Semiology and critical Sickness Score - PEDSS) were retrospectively assessed for their accuracy in predicting short-term and long-term outcomes.

Results: A total of 103 consecutive episodes of SE were included. Out-of-hospital rescue medications administration occurred in 54.4% of cases and was associated with higher SE resolution rate before PED admission (48.2% vs 27.6%, $p = .033$). Longer in-PED time to treatment was observed in case of delay to PED referral ($r = 0.268$, $p = .048$) or non-red triage labels (12 vs 5 min, $p = 0.032$), and was associated with longer in-PED duration of SE ($r = 0.645$, $p < .001$). Longer SE duration was observed in episodes leading to hospitalization compared to those discharged

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(50 vs 16 min, $p < .001$). In-PED electroencephalography (EEG) recordings were available in 39.8% of events. Predictive scores varied in accuracy, with PEWS ≥5 showing high sensitivity for intensive care unit (ICU) admission but low specificity. No patients died, 6.3% of SE was refractory.

Significance: Effective pre-hospital administration of rescue medications and prompt PED management are crucial to reduce SE duration and improve outcomes. Predictive scores can aid in assessment of the severity and prognosis of SE; their utility is still not defined. Identifying and addressing actionable care barriers in SE management pathways is essential to enhance patient outcomes in pediatric SE.

KEYWORDS

childhood, management, outcomes, seizures, treatment

1 | INTRODUCTION

Status epilepticus (SE) is the most common neurological emergency in childhood, resulting either from the failure of the mechanisms of seizure termination or from the initiation of mechanisms leading to abnormally prolonged seizures.[1] The estimated incidence is up to 49.1 per 100 000 children per year in northern Italy, and epidemiological data worldwide report 10–73 cases per 100 000 children per year depending on different study settings. A peak of 135–156 per 100 000 is observed among infants and children younger than 2 years, especially within the first year of life.[2–7]

As a result of the prolonged epileptic activity, SE can lead to neuronal death, neuronal injury, and alteration of neuronal networks. Consequently, patients can experience a spectrum of brief and long-term outcomes, such as neurological, cognitive, and behavioral impairment. Death occurs in 5%–9% of patients of pediatric age.[1,8,9] Several factors can determine the outcome of SE, such as its etiology, age at onset, and duration.[9–12] Acknowledging the influence of duration on the outcome of SE points out the pivotal role of its early detection and management. Several gaps are possible in terms of acute seizure treatment in the pre-hospital or in-hospital chain of care, such as seizure-onset recognition, availability of rescue medication and proper administration, and staff delays in the emergency room.[13,14] Therefore, assessing the barriers to care in the SE care pathway is paramount to bridge these care gaps and eventually improve outcomes.[15] The aim of the study was first to describe pre-hospital and in-hospital management of community-onset childhood SE to identify any possible barriers to care; and second, to assess the real-world accuracy of different proposed pediatric scores in predicting brief and long-term outcomes of SE.

Key points

- Barriers to care limit or prevent people from receiving adequate care for specific conditions, including community-onset pediatric status epilepticus (SE).
- Barriers to care for community-onset SE include underuse of rescue medications, delayed assistance, and missed diagnosis of nonconvulsive SE.
- Longer SE duration and higher hospitalization rate occur in the aftermath of barriers to care in the care pathway for pediatric SE.
- The use of predictive scores may be helpful to assess the risk of poor outcomes.

2 | METHODS

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed.[16]

2.1 | Study design and participants

This monocentric observational retrospective cohort study enrolled all patients consecutively referred to our center's pediatric emergency department (PED) for community-onset SE between 2010 and 2021. More specifically, the inclusion criteria were: (1) the occurrence of SE, defined as a continuous seizure activity according to the operational dimension t1 from the International League Against Epilepsy (ILAE) Task Force on Classification of Status Epilepticus[1]; (2)

SE onset outside the hospital setting; (3) admission to the PED for SE; (4) SE occurring from January 1, 2010, to December 31, 2021; (5) age at onset: 1 month to 18 years; and (6) enduring (E-SE) or solved (S-SE) events on arrival at the PED. The exclusion criteria were (1) inconsistency with the definition of SE; (2) seizure clusters; and (3) incomplete or unavailable information about SE management from medical records. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

2.2 | Assessment methods

Clinical data were extracted from medical reports, and Figure S1 shows the events selection process. First, all electronic medical records with a final diagnosis of "status epilepticus" were checked for compliance with the inclusion criteria by two independent investigators (L.B. and A.F.). Medical records with a diagnosis of "epilepsy" or "seizure" were also checked to look for possible missed SE diagnoses. Second, ineligible records ($n = 39$) were excluded from an initial pool due to lack of information. Demographic data, patients' history, and SE features (semiology, etiology, age at onset) were anonymized and collected. SE semiology and etiology were classified according to the ILAE Task Force criteria for SE.[1] In the case of E-SE on arrival at the PED, the semiology was classified according to description of the event supplied by witnesses and pre-hospital emergency care staff. The etiology of SE was classified by analyzing medical records and diagnostic procedure results (i.e., neuroimaging, genetics, and laboratory tests).

2.2.1 | Pre-hospital and in-hospital management

Pre-hospital data, including SE onset time, availability of rescue medications, and timing of their administration were obtained from PED medical records, relying on information gathered from caregivers and/or emergency medical services (EMS).

Data about the timing for PED referral, time to treatment in the PED, and details about diagnostic procedures (e.g., electroencephalography [EEG]) were collected. Accessibility to EEG recordings in the PED was assessed by considering the time at PED admission and machine availability according to scheduled shifts (full availability: Monday–Friday 7.30 am–5 pm; Saturday 7.30 am–1 pm; limited availability: on-call EEG during the remaining hours in case of suspected non-convulsive SE [NCSE]). The categorization into triage color tags on arrival in the PED was also assessed by analyzing a four-tier color chromatic gradation system that classifies the condition's acuity according to the Manchester Protocol and global triage guidelines.[17,18] Depending on anamnestic information, vital signs, and physical findings, red codes were applied to emergencies and critical conditions requiring immediate evaluation and care; yellow was used for urgent conditions requiring quick evaluation; green symbolized less urgent conditions; and white was given to non-urgent conditions (Figure S2).

2.2.2 | Outcomes

The brief-term outcomes of SE were described considering refractoriness, admission to the pediatric intensive care unit (PICU), and death. Refractory SE was defined as SE persisting despite the administration of at least two appropriately selected and dosed parenteral medications including a benzodiazepine (BZD), with no specific seizure duration required.[19] In-hospital death was defined as death during hospitalization, regardless of the cause.[20]

The long-term outcomes of SE were evaluated considering the occurrence of neurological sequelae during the follow-up. To identify changes in patients' neurological status, the modified Rankin Scale for Children (mRSC)[21] and the Pediatric Cerebral Performance Category Scale (PCPCS),[22] were retrospectively calculated from medical records before SE; at discharge; and over a 1, 3, and 12 month period follow-up. A worsening of the scores was identified as a "poor outcome."

2.2.3 | Predictive scores

Three scores were retrospectively calculated by two independent researchers (A.B. and R.R.), blinded to the outcome, using the information available during the PED stay: (1) the Pediatric Early Warning Score (PEWS), usually used to assess the risk of clinical deterioration or intensive care unit (ICU) admission using physiological parameters such as heart rate, respiratory rate, temperature, blood pressure, and level of consciousness[23]; (2) the SE in Pediatric patients Severity Score (STEPSS), a recent pediatric suggested version of the SE Severity Score (STESS) for predicting unfavorable outcome including four clinical variables (age of the patient, level of consciousness, past history of seizures, and type of SE)[24]; (3) the Pre-status Epilepticus PCPCS, background Electroencephalographic abnormalities, Drug refractoriness, Semiology, and critical Sickness (PEDSS) score, a 6-point score recently proposed as a predictor of mortality and poor outcome.[25]

Second, we calculated the scores' accuracy in predicting brief-term outcomes (PEWS, PEDSS) and long-term outcomes (PEWS, PEDSS, STEPSS).

The following scores were considered as cutoff: ≥5 for PEWS, >3 for STEPSS, and ≥3 for PEDSS, as suggested previously by the authors.[24–26]

2.3 | Statistical analysis

Descriptive statistics were provided for the study population through mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and absolute (*n*) and relative (%) frequency for categorical ones. The normality of continuous variables distribution was checked using the Skewness-Kurtosis test. Continuous variables were compared by the Mann–Whitney *U* test or Student's *t* test, whereas categorical variables by the chi-square test or Fisher's exact test, as appropriate. Linear association between continuous variables was expressed by correlation coefficients (Pearson's or Spearman's, depending on data distribution). *P*-values were corrected for multiple testing using the Simes method to control the false discovery rate (FDR).

Univariate and multivariate logistic regressions were performed to identify the factors most associated with the decision about triage color tagging, quantifying the strength of the association through odds ratios (ORs) with confidence intervals (95% CIs). To assess changes in therapeutic approaches over time, we established 3-year intervals: 2010–2013, 2014–2017, and 2018–2021. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the curve (AUC) were used to assess the diagnostic ability of the tests (PEWS, PEDSS score, and STEPSS), using as reference standard each of the following outcomes: ICU admission, refractory status epilepticus, PCPCS worsening at 1 year, and mRSC worsening at 1 year.

3 | RESULTS

We screened 674 eligible records and eventually included 103 consecutive SE episodes. These occurred in 75 patients,the median age at SE was 4 years (IQR 1.7–7.4, range 0–16 years); 58.7% patients were assigned female at birth. The relevant clinical features are listed in Table 1.

Overall, 38.8% of SE (*n* = 40) were solved before admission to the PED (S-SE): 26.2% were efficaciously treated with pre-PED rescue medications (*n* = 27) and 12.6% resolved spontaneously (*n* = 13). Conversely, enduring SE (E-SE) was observed in 61.2% of cases (*n* = 63) at the time of PED admission: in 28.2% of cases (*n* = 29) pre-PED rescue medications were ineffective, and in 33% of cases (*n* = 34) pre-PED rescue medications were not administered.

TABLE 1 Status epilepticus features and patients' history.

Characteristics	*N* (%)
SE semiology	
CSE	74/103 (71.8%)
NCSE	29/103 (28.2%)
SE etiology	
Acute	14/103 (13.6%)
Remote	36/103 (35%)
Progressive	2/103 (1.9%)
SE in defined electroclinical syndromes	19/103 (18.4%)
Febrile SE	22/103 (21.4%)
Unknown	10/103 (9.7%)
SE history	
SE in PWE	57/103 (55%)
New-onset SE	46/103 (45%)
Previous SE	47/103 (45.6%)
Previous FSE	7/103 (6.8%)
Repeated SE	
Two SE episodes	11/75 (14.7%)
Three SE episodes	5/75 (6.7%)
Four SE episodes	1/75 (1.3%
Five SE episodes	1/75 (1.3%)
Epilepsy history	
Epilepsy classification in PWE	
Focal epilepsy	50/57 (87.7%)
Generalized epilepsy	2/57 (3.5%)
Combined	5/57 (8.8%)
Epilepsy etiology in PWE	
Structural	29/57 (51%)
Genetic	28/57 (49%)
Concurring treatment with ASMs	49/57 (47.6%)

Abbreviations: ASMs, anti-seizure medications; CSE, convulsive status epilepticus; NCSE, non-convulsive status epilepticus; PWE, people with epilepsy; SE, status epilepticus.

3.1 | Management before arrival in the PED

Caregivers or EMS administered pre-PED rescue medications in 54.4% of events (*n* = 56). Factors associated with less frequent administration of rescue medications were no history of epilepsy (new-onset SE: 39.1%, SE in people with epilepsy [PWE] 66.6%, *p* = .005), no history of SE (first SE: 44.6%, previous SE: 65.9%, *p* = .031), and non-prominent motor features (NCSE: 27.6%, CSE:

64.9%, $p < .001$). Over the 12-year study period, the percentage of patients receiving pre-PED BZD increased from 48.0% (2010–2013) to 52.8% (2014–2017) and 59.5% (2018–2021), but this trend was not statistically significant (OR = 1.061, 95% CI 0.940–1.199, $p = .333$). The use of rescue medications led to more-frequent pre-PED SE resolution (treated: 48.2%, untreated: 27.6%, $p = 0.033$). Of note, rescue medications were prescribed to 87.7% of PWE ($n = 50/57$), and the frequency of administration in this group did not differ significantly in history of SE or not (71.4% vs 53.3%, $p = .202$).

The median latency for PED admission from SE onset was 49 min (IQR 31–88). This was significantly long in PWE (63 vs 39 min, $p < .001$), administration of pre-PED rescue medications (52 vs 44 min, $p = .037$), and solved SE (63 vs 39 min, $p < .001$). Moreover, we observed a tendency toward longer time for PED admission in higher age at onset (time for admission–age correlation: $r = .339$, $p < .001$). No significant difference was observed in terms of median time to admission depending on the time of onset of SE (48 min for admission in case of onset during the day vs 50 min during the night, respectively; $p = 0.722$).

3.2 | Triage in the PED

E-SE was more frequently tagged as red code than S-SE (65.1%, $n = 41/63$, vs 10%, $n = 4/40$, $p < 0.001$). However, yellow and green codes accounted for 31.7% ($n = 20/63$) and 3.1% ($n = 2/63$; one NCSE and one myoclonic SE) of E-SE, respectively. Among S-SE, yellow and green codes were 62.5% ($n = 25/40$) and 27.5%, ($n = 11/40$), respectively. No white codes were recorded either for E-SE or S-SE. Table 2 shows the influence of demographic and clinical variables on triage tags.

Taking into account E-SE episodes, the following conditions were significantly associated with a higher risk of non-red codes on admission: non-febrile SE (OR 7.1, 95% CI 1.4–34.4, $p = .015$), PEWS <5 (OR 4.6, 95% CI 1.5–14.3, $p = .008$), age ≥4 years (OR 4.5, 95% CI 1.5–13.6, $p = .008$), concurrent treatment with ASMs (OR 3.7, 95% CI 1.2–11.2, $p = .019$), and time from onset to admission on PED ≥90 min (OR 2.6, 95% CI 1.1–6.2, $p = .024$). Multivariable analysis identified the following independent factors: non-febrile SE (OR 8.4, 95% CI 1.6–44.4, $p = 0.012$) and PEWS <5 (OR 4.8, 95% CI 1.4–16.4, $p = .011$).

3.3 | In-PED management

Only the management of E-SE will be described from now on. The median time to treatment from triage was 6 min (IQR 4–13.5); later treatment was provided in case of non-red codes (median time to treatment: 12 min vs 5 min, $p = .032$) and NCSE (12 min vs 5 min, $p = .0401$).

A tendency for a longer time to treatment was observed in older age at onset (time to treatment–age correlation: $r = .330$, $p = .013$), and longer latency to admission (time to admission–time to treatment correlation: $r = .268$, $p = .048$). Treatment delays longer than 15 min occurred more frequently in PWE than in new-onset SE (40.9% vs 11.7%, $p = .012$).

In the PED, SE was treated with BZDs alone (89%, $n = 49$), BZDs and anti-seizure medications (ASMs; 9%, $n = 5$), or ASMs alone (1%, $n = 1$). Overall, second-line treatment with ASMs was required in 10.9% of E-SE ($n = 6$). Over the 12-year study period, there was no significant difference in the type of therapy administered (BZDs, BZDs and ASM, or ASMs alone, $p = 0.279$) or in the number of BDZ doses given ($p = .289$).

Oral or rectal BZDs instead of intravenous (IV) BZDs were more frequently administered as the first treatment to patients with a lower median time to referral (33 vs. 57 min, $p < .001$), who did not receive pre-PED rescue medications (51.1% vs 14.8%, $p < .001$), to those with no previous epilepsy diagnosis (46% vs 20%, $p = .006$), and no concomitant chronic treatment with ASMs (40.7% vs 21.2%, $p = .036$). At the time of PED admission, in-PED EEG recording was accessible in 39.8% of total events ($n = 41/103$): 30% of S-SE ($n = 12/40$) and 46% of E-SE ($n = 29/63$), depending on the machine and technician availability at the time of the event.

The median time to EEG was 23 min (IQR 11–46.5) in the case of E-SE occurring during full EEG availability daytime, and it increased to 11 h (IQR 5–16) in the case of E-SE during limited EEG availability (e.g., night) ($p < .001$). Seventeen children with NCSE arrived in the PED at a time with limited EEG availability. The PED did not seek for on-call neurophysiology during times with on-site EEG unavailability (i.e. during the night): 13 patients underwent EEG at the earliest time of full availability (e.g., the morning after); 4 PWE were diagnosed with possible NCSE considering their history of recurrent non-motor seizure and NCSE, and they underwent EEG in the pediatrics or neurology ward. Of interest, at the time of EEG recording, 22% of S-SE ($n = 9/40$) showed electroclinical uncoupling and required treatment.

3.4 | Post-PED management

The median length of stay in the PED was 1 h and 30 min (IQR 1–3.3 h). Overall, SE led to hospitalization in 77.7% of cases ($n = 80$), of which 12.5% ($n = 10$) were admitted to the PICU, and the remaining entered the neuropediatric ward (NPW). Episodes leading to hospitalization had a

TABLE 2 Influence of demographic and clinical variables on triage color code.

	Enduring status epilepticus ($n=63$)			
Variables *n* (%)	**Red ($n=41$)**	**Yellow ($n=19$)**	**Green ($n=3$)**	***p*-value***
Sex				.898
Female	25 (61)	13 (68.4)	2 (66.7)	
Male	16 (39)	6 (31.6)	1 (33.3)	
Age (median; IQR)	2.3 (1.1–3.9)	4.6 (1.1–9.7)	6.6 (5.7–9.1)	**.038**
Semiology				.801
CSE	28 (68.3)	11 (57.9)	2 (66.7)	
NCSE	13 (31.7)	8 (42.1)	1 (33.3)	
SE Etiology				**.001**
Acute	5 (12.2)	3 (15.8)	0 (0)	
Remote	4 (9.8)	12 (63.2)	1 (33.3)	
Progressive	2 (4.9)	0 (0)	0 (0)	
SE in defined electroclinical syndromes	9 (21.9)	1 (5.3)	1 (33.3)	
Febrile SE	17 (41.5)	1 (5.3)	1 (33.3)	
Unknown	4 (9.8)	2 (10.5)	0 (0)	
Previous epilepsy diagnosis	12 (29.3)	11 (57.9)	2 (66.7)	.056
Concurring treatment with ASMs	10 (24.4)	10 (52.6)	2 (66.7)	**.044**
Previous SE	14 (34.1)	9 (47.4)	1 (33.3)	.730
Previous FS	3 (7.3)	0 (0)	1 (33.3)	.109
RM before the PED	20 (48.8)	9 (47.4)	0 (0)	.402
Time from onset to admission on PED (median; IQR)	38 (17.1–51.1)	39.2 (29.9–63.9)	136.6 (104.3–224.8)	**.039**
PEWS (median; IQR)	6 (3–8)	3 (2–6)	0 (0–1)	**.001**

Note: The table describes the demographic and clinical variables associated with different color codes on triage in the subgroup of patients with enduring status epilepticus (E-SE). *statistically significant P-values (<.05)are reported in bold.

Abbreviations: ASMs, anti-seizure medications; CSE, convulsive epilepticus status; FS, febrile status epilepticus; RM: rescue medications; NCSE, non-convulsive status epilepticus; PEWS, Pediatric Early Warning Score.

significantly longer total duration compared to those discharged from the PED (50 min vs 16 min, $p<.001$). CSE was more frequent than NCSE among cases requiring hospitalization (66.3% vs 33.7%, $p=.019$), and new-onset SE was less frequently discharged than SE in PWE (21.7% vs 78.3%, $p=.012$). No significant difference was observed in hospitalization rates depending on SE etiology.

3.5 | Outcomes

Resolution of E-SE was observed in the PED (88.9%, $n=56/63$), in the (4.8%, $n=3/63$) or the PICU (6.3%, $n=4/63$), the latter accounting for the rate of refractory SE; no deaths were observed. The median duration of E-SE from onset and from PED admission was 40 min (IQR 20–80) and 23 min (IQR 10–50), respectively. A strong positive correlation was found between the latency to PED admission and the total duration of SE ($r=.811$, $p<.001$), and between the duration of SE from triage and the time to treatment ($r=.645$, $p<.001$). NCSE lasted longer than CSE considering both the median duration from onset (72 vs 30 min, $p<.001$), and the median duration from PED admission (37 vs 18 min, $p=.044$). Table 3 shows the association of SE duration with demographic, clinical, and management variables.

Figure 1 shows the mean scores in the mRSC and PCPCS scale before SE, at discharge, and during the follow-up. No significant association was found between functional scales changes and the clinical, demographic, or management variables examined. A diagnosis of epilepsy was provided to 36.9% of new-onset SE ($n=17/46$) during follow-up.

3.6 | Accuracy of predicting scores

Retrospective calculation revealed PEWS ≥5 in 37% of SE, PEDSS score ≥3 in 21% of SE, and STEPSS ≥3 in 21.4% of SE when arrived in PED.

TABLE 3 Influence of demographic and clinical variables on SE duration and in-hospital admission.

	SE duration from onset		Admission either to NPW or ICU	
Categorical variables	**Median (IQR)**	***p*-value***	***n*° (%)**	***p*-value***
Sex		.072		.287
Male	28.5 (19–70)		30 (71.4)	
Female	45 (27.5–92.5)		50 (82)	
Semiology		**.002**		**.038**
CSE	30 (20–65)		53 (71.6)	
NCSE	72 (43–184)		27 (93.1)	
SE Etiology		.552		.642
Acute	28.5 (20–70)		11 (78.6)	
Remote	30 (11–80.5)		26 (72.2)	
Progressive	54 (39–69)		2 (100)	
SE in defined electroclinical syndromes	42.5 (30–107.5)		16 (84.2)	
Febrile SE	49 (36–75)		19 (86.4)	
Unknown	36.5 (15–70)		6 (60)	
Previous epilepsy diagnosis		.077		**.031**
Yes	30 (15–85)		39 (68.4)	
No	50 (36–75)		41 (89.1)	
Concurring treatment with ASM		.089		**.038**
Yes	27 (15–81)		33 (67.3)	
No	50 (30–80)		47 (87)	
Previous SE		.532		.858
Yes	32.5 (18–90)		36 (76.6)	
No	47.5 (25–75)		44 (78.6)	
Rescue therapy before PED		.375		.615
BZDs	39 (18–80)		42 (75)	
No	45 (23–80)		38 (80.8)	
Triage		**.044**		**<.001**
Red	47.5 (33–77.5)		43 (95.6)	
Yellow	40 (20–98)		33 (73.3)	
Green	15 (10–30)		4 (30.8)	
Type of therapy in PED		.103		.999
BZD	58.5 (40–80)		48 (96)	
BZD + ASM	162.5 (115–210)		5 (100)	
ASM	180 (180–180)		1 (100)	
RSE				.642
Yes			4 (100)	
No			74 (76.3)	

Continuous/ordinal variables	**Correlation coefficient**	***p*-value***	**Admission either to NPW or ICU—*median (IQR)***	**No admission Median (IQR)**	***p*-value***
Age	−0.0369	.727	3.1 (1.6–6)	6.3 (4.7–9.5)	**.005**
Latency from onset to admission in PED	0.1963	.089	45 (29–86)	52.5 (46–107)	.128
TTT from admission in PED	**0.6075**	**<.001**	6 (4–14)	130.9 (7.8–254)	.228
TTT from the beginning of SE	**0.8685**	**<.001**	47 (26.2–78.6)	177 (59–295)	.228
SE duration			50 (30–90)	16 (10–25)	**.001**

Note: The table describes the association of demographic and clinical variables on SE duration and pre-hospital admission; the upper table describes the categorical variables, and the lower table describes continuous or ordinal variables. Only patients with enduring SE on PED admission are considered. **P*-value adjusted for false discovery rate (FDR); statistically significant P-values (<.05) are reported in bold.

Abbreviations: BZD, benzodiazepine; ICU: intensive care unit; NPW, neuropediatric ward; PED, pediatric emergency department; RSE, refractory status epilepticus; TTT, time to treatment.

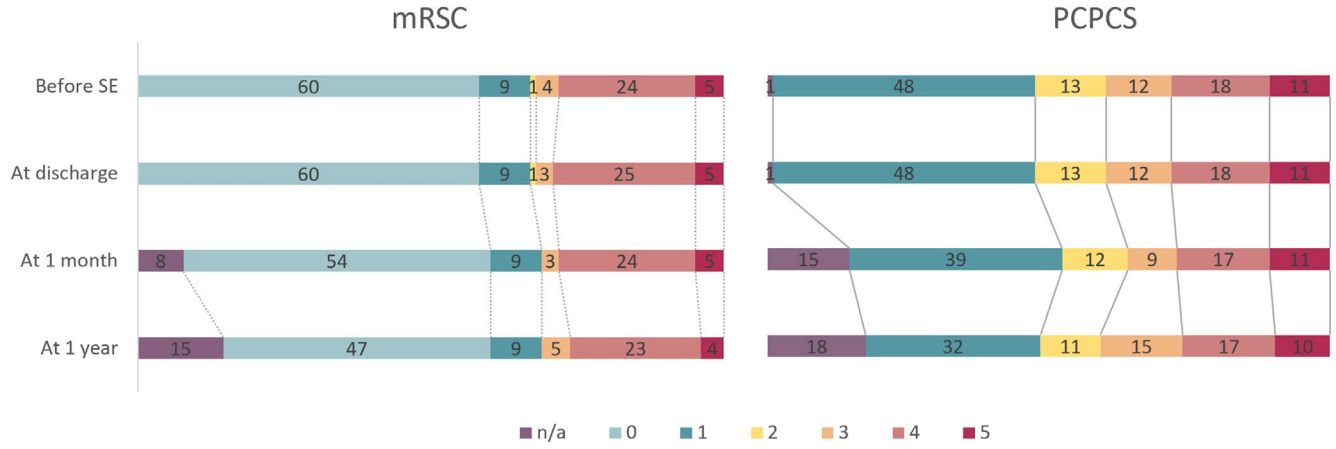

FIGURE 1 Pediatric performance scale variation before and after status epilepticus. At discharge, no cognitive outcome deterioration was observed via the PCPCS, with one data point missing. One child briefly experienced a 1-point decrease in the mRSC score (from 3 to 4), which normalized within a month. After 1 year, 7 of 77 available cases showed declines in PCPCS, whereas 1 of 88 had a drop in mRSC scores. mRSC, modified Rankin Scale for Children; PCPCS, Pediatric Cerebral Performance Category Scale; SE, status epilepticus; n/a, not available.

The accuracy in predicting short-term and long-term outcomes is reported in Figure 2.

4 | DISCUSSION

Although several authors previously explored barriers in the SE care pathway,[12,14,27] this is, to the best of our knowledge, the first research addressing these challenges in a real-world setting by describing the community-onset childhood SE care pathway and the related outcomes in a Western European tertiary care pediatric hospital.

Timely and proper management of SE is critical in contemporary health care to prevent sequelae such as neurological, cognitive, and behavioral impairment, and, ultimately, death. In this study, the administration of out-of-hospital rescue medications was associated with more frequent SE resolution before PED admission; moreover, longer latency to the PED and non-red codes on triage were associated with longer time to treatment, leading to longer duration of SE and more frequent hospitalization.

4.1 | Demographic and clinical features

Overall, this cohort's demographic and clinical features are consistent with literature reports for community-onset SE in the pediatric age group.

The median age at admission was 4 years, consistent with other studies with a higher occurrence of community-onset pediatric SE in the 1–5 year age range.[4,10,20,28–30] In our study, nearly half of the episodes were classified as new-onset SE. There is substantial variability in the rate of new-onset SE in the published cohorts of pediatric SE (17.2%–50.5%), probably depending on different study settings.[31–33]

Published data about SE cohorts mainly regard CSE, given that the majority of SE in children is convulsive.[20,28,34] As a matter of fact, most events were classified as CSE in this cohort as well, but NCSE was included.

Remote etiology due to underlying genetic or structural conditions was the most frequent cause of SE. Febrile SE accounted for the second most frequent cause, and acute SE occurred in the minority compared to other reports about pediatric SE.[20] This may be due to a variety of factors. First, this cohort gathered more childhood-onset SE than neonatal and infantile episodes, in which acute symptomatic etiology prevails, probably reflecting differences in the maturation of the developing brain.[11] Indeed, half of the acute SE occurred in infants (i.e., younger than 2 years of age) in this study. Another possible explanation could be the different spread of pathogens targeting the central nervous system (CNS) in different geographical areas. Ultimately, different SE etiologies among pediatric cohorts may depend on the different age groups and different geographical areas involved in the studies.[11] Missing data due to the retrospective nature of this study cannot be excluded, as well.

Febrile SE was the second most frequent etiology in this study, and it occurred mainly with concurrent respiratory infections. Febrile SE was classified and analyzed separately in this study according to previous approaches in large pediatric populations with SE,[35] given the probable lack of direct CNS involvement in febrile seizures.[11]

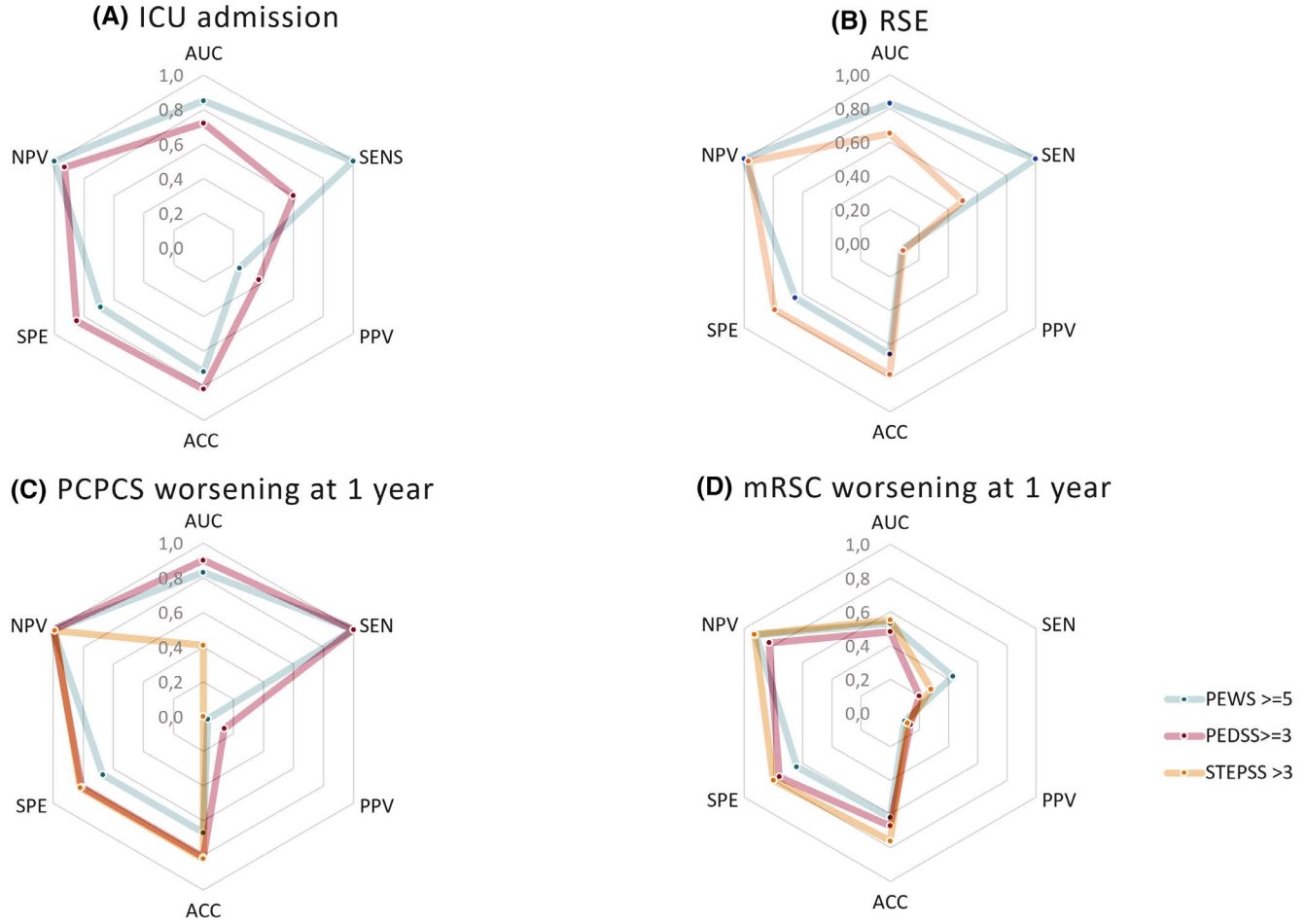

FIGURE 2 Accuracy of scores in predicting status epilepticus outcomes. (A) Intensive Care Unit (ICU) admission: The Pediatric Early Warning Score (PEWS) ≥5 had 100% sensitivity (SEN) and 69% specificity (SPE) in predicting ICU admission. Positive predictive value (PPV) was 24% and negative predictive value (NPV) was 100% Accuracy (ACC) = 72%; area under the curve (AUC) = 0.85. Pre-status Epilepticus PCPCS, background Electroencephalographic abnormalities, Drug refractoriness, Semiology, and critical Sickness (PEDSS) score ≥3 had 60% SEN and 85% SPE in predicting ICU admission. PPV was 37% and NPV was 93%; ACC = 82%; AUC = 0.72. (B) Refractory status epilepticus: PEWSS ≥5 had 100% SEN and 65% SPE in predicting RSE. PPV was 8% and NPV was 100%. ACC = 66%; AUC = 0.83. SE in Pediatric patients Severity Score (STEPSS) >3 had 50% SEN and 79% SPE in predicting RSE. PPV was 9% and NPV was 97%; ACC = 78%; AUC = 0.65. (C) Pediatric Cerebral Performance Category Scale (PCPCS worsening at 1 year): PEWS ≥5 had 43% SEN and 64% SPE in predicting PCPCS worsening at 1 year. PPV was 10% and NPV was 92%; ACC = 62%; AUC = 0.53. PEDSS ≥3 had 20% SEN and 76% SPE in predicting PCPS worsening (≥1) at 1 year. PPV was 14% and NPV was 83%; ACC = 67%; AUC = 0.48. STEPSS >3 had 28% SEN and 80% SPE in predicting PCPS worsening (≥1) at 1 year with a 12% PPV and 93% NPV. ACC = 76%; AUC = 0.55. (D) modified Rankin Scale for Children (mRSC) worsening (≥1) at 1 year: PEDSS ≥3 had 100% SEN and 81% SPE in predicting mRSC worsening (≥1) at 1 year. PPV 14%; NPV 100%; ACC = 81%; AUC = 0.90. STEPSS >3 had 0% SENS and 82% SPE in predicting mRSC worsening (≥1) at 1 year. PPV 0%, NPV 99%. ACC = 82%; AUC = 0.41.

4.2 | Barriers to care

The focus of acute treatment in community-onset SE is rescue therapy and safety; therefore bridging the gap between seizure onset and first treatment in the outpatient setting is crucial.[36] Nearly half of the patients with community-onset SE did not receive rescue medications from caregivers or EMS before arriving at the PED, albeit spending a median time of 49 min in the pre-hospital setting. Missing this first-line treatment represents a relevant barrier to care for SE; indeed timely administration of rescue medications was associated with higher chances of SE resolution before the admission to the PED in this study. This is consistent with other literature reports, underscoring that a prompt administration of rescue medications is associated with a higher chance of SE resolution and reduction of access to the PED.[37,38] Moreover, earlier administration of rescue medications is likely associated with a shorter time for seizure termination and overall seizure duration.[39] Despite their crucial role, rescue medications are often underutilized in community-onset SE,[14,40,41] particularly in the case of new-onset SE, but also in a minority of PWE. Indeed, one third of PWE in this cohort did not receive out-of-hospital treatment despite rescue

medication prescriptions. This may be due to a variety of causes including insufficient training or discomfort about rescue medication administration, which is often a multistep, error-prone process.[41–45]

Guidelines recommend the use of BZDs as first-line treatment for SE, however the choice of which BZD to use and its route of administration in the real-world setting is often based on the accessibility and approval of these drugs in different countries. For instance, buccal midazolam was approved for the treatment of prolonged seizures in children and adolescents in 2011 by the European Medicines Agency, and in 2017 in the United Kingdom; intranasal midazolam was approved in 2019 by the United States Food and Drug Administration (FDA).[46–48] Before these, rectal diazepam was often the only formulation approved for treatment in community-onset SE.[48]

Of interest, studies found that most caregivers make at least one error when handling rescue medications, with rectal administration being more prone to mistakes.[49] To prevent the underuse of rescue medications, their management should be discussed and encouraged during health care visits. Considering the best treatment options depending on caregivers' confidence in its administration, as well as providing targeted training, could be helpful to overcome such barriers.[41,45,50] It is relevant to note that there was no significant difference in terms of rescue medication administration depending on history of SE within the group of PWE. This might reflect a higher confidence in identifying seizures requiring treatment by caregivers or EMS in PWE. The lack of treatment in this group may be related to parental discomfort in managing the acute condition, or drug administration.

The administration of rescue medications was also associated with longer latency to PED admission in the case of E-SE. This latency was mostly related to the unsuccessful attempt to provide out-of-hospital management for SE in PWE. However, a timely referral is crucial in case of rescue medication failure or when non-prominent motor symptoms occur (e.g., electroclinical uncoupling), given the risk of subsequent clinical deterioration.[41,42] Therefore, delayed PED referral could be overcome by providing patients and caregivers with easily accessible, individualized (acute) seizure action plans (SAPs) including a guide to identify escalation strategies in cases requiring further assistance after rescue medication administration.[36,51–54]

Eventually, the organization of EMS on a "scoop and run" or "stay and play" basis is relevant in terms of timing for rescue medication administration and escalation to the PED.[40,55]

Rapid administration of rescue medications and ASMs is associated with shorter seizure duration and more favorable outcomes both in out-of-hospital and in-hospital settings.[9,27] In this study, we found a good positive correlation between time to treatment in the PED and SE duration, and events leading to hospitalization had a significantly longer median duration compared to those discharged. This confirms that in-hospital treatment delays are actionable barriers to care. Longer time to treatment was observed in the case of longer latency to PED admission, older age, SE in PWE, and triage yellow/green codes. This evidence may be confounded by factors such as the need to stabilize more critically ill patients before admission, or the fact that red triage flags may be a proxy for the recognition of SE rather than an independent predictor of outcomes. In-hospital treatment delays in PWE could be explained by early pitfalls in the chain of care. Relevant details about treatments (e.g., dose, timing and proper absorption) can be blurred in the out-of-hospital first-line administration of rescue medications. This can hamper the handover between out- and in-hospital care and, ultimately, cause delay in the ideal treatment workflow. Indeed, untimely out-of-hospital first-line therapy was found to correlate with the timing of in-hospital second- and third-line treatments in a multicenter prospective cohort study, possibly causing further delay in the chain of care.[9]

The use of seizure-oriented tools, such as seizure codes,[27] could help to prioritize the goal of timely treatment administration, even in case of conditions not labeled as red codes according to standard triage. This could positively influence outcomes associated with longer SE duration. Moreover, investigating the efficacy of new ASMs or other treatment options (e.g., ketamine) after BZD failure in large populations could ultimately streamline time-saving treatment approaches for community-onset SE in the PED.[56]

The study confirms the importance of performing EEG recordings in the PED. One-third of S-SE plus nearly half of E-SE underwent EEG in the PED. The EEG recording was paramount to diagnose NCSE in acute consciousness, behavioral, and autonomic changes from baseline, with or without subtle motor signs. Moreover, one-fifth of CSE that were labeled as S-SE due to the resolution of motor symptoms showed electroclinical uncoupling and required treatment. Although EEG is not mandatory to diagnose and treat CSE, its use should be considered for several reasons.[57] First, persistent or recurrent seizures are common in the first 24 h after CSE, and up to 75% of patients can show evidence of seizures on EEG with no associated clinical findings.[58,59] Second, specific EEG patterns after CSE can correlate significantly with prognosis.[60] However, the optimal duration of EEG recordings in such circumstances is still debated.[57,61] Although continuous EEG is a cheap, non-invasive, accurate diagnostic technique, it is often not routinely used in the emergency setting, where short, "emergency" EEG is usually preferred.[57] A variety of algorithms and scores exist

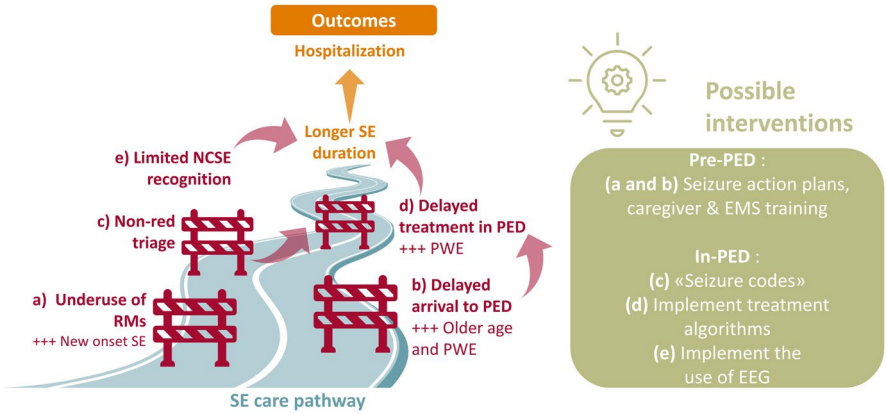

FIGURE 3 Barriers to care in pediatric status epilepticus management. The figure shows the main barriers to care that emerged in the study and the main influencing factors; arrows link those that showed direct correlation with each other and with short-term outcomes (in orange). Possible interventions to overcome each of these are suggested in the green box.

to guide the decision about the optimal EEG duration in critically ill patients (e.g., 2HELPS2B score).[59,62,63] In any case, the limited availability of EEG recordings accounts for another barrier to care for SE in the PED.

4.3 | Outcomes of status epilepticus and accuracy of predicting scores

The duration of SE was mainly influenced by longer latency to PED admission and time to treatment in the PED, and longer duration was associated with more frequent hospitalization after SE. By influencing SE duration, these barriers to care showed an impact on outcomes related to hospitalization. Moreover, hospitalization rates were higher in cases of longer SE duration, CSE, and new-onset SE. Figure 3 shows the main barriers to care, outcomes, and possible interventions.

SE etiology and low rates of refractory SE may account for the low mortality and the overall good long-term outcomes in this cohort. Indeed, mortality rates for unprovoked and febrile SE are lower (down to 0.2%) than acute symptomatic CSE (up to 12.5%–16%) in a variety of different populations around the world.[28,31,38,64,65] Moreover, super-refractory SE was shown to be a risk factor for in-hospital mortality and short-term neurological dysfunction in a large population-based study.[20]

The differing long-term variation rates between mRSC and PCPCS may reflect their distinct focuses: PCPCS on neurological function and mRSC on overall function and independence.[21,22]

The examined predicting scoring systems showed different utilities and limitations. PEWS confirmed its role as a useful tool for predicting ICU admission in the PED setting,[23] when rapid assessment is needed, and high sensitivity is prioritized over specificity for the early identification of patients at risk of deterioration. Surprisingly, it also had good sensitivity in predicting RSE. Otherwise, as expected, it showed low specificity and poor strength in predicting long-term consequences.

Both PEDSS and STEPSS are intended to predict poor outcomes and mortality for pediatric SE. They demonstrated low sensitivity in predicting PCPCS worsening, with significantly lower AUC values compared to the existing literature data.[25]

PEDSS calculation is based on a variety of information (e.g., drug refractoriness, critical illness, and EEG abnormalities) and it had excellent sensitivity and NPV in predicting mRSC worsening in this study. Its use may be particularly helpful in clinical settings where neurological and neurophysiological monitoring are available. STEPSS is a quicker bedside tool; nonetheless it showed lower accuracy and sensitivity than reported in the literature in our analysis.[24,66] Therefore, it may play a role as an adjunctive tool for risk stratification in such settings when more comprehensive information is not quickly available.

4.4 | Limits and perspectives

This study has several limitations. First, its retrospective design sometimes hampered data collection (for instance, with regard to the time of SE onset and predictive score calculation). Second, data were gathered from a single university hospital located in a high-income setting; therefore SE management and outcomes may not be representative of middle or low-income countries. Further larger, prospective, multicenter studies are needed to explore community-onset pediatric SE barriers to care and the related long-term outcomes, as well as the impact on patients' and families' quality of life. Future studies should prioritize the development of interventions to overcome these barriers, especially with regard to the areas where access to first-line rescue medications is challenging.

5 | CONCLUSION

The study identified a variety of barriers in the care pathway for community-onset pediatric SE in a high-income,

real-world setting. The main barriers were missed administration of pre-hospital rescue medications, longer time to PED referral, non-red triage, longer time to treatment, and EEG unavailability. Possible actions to overcome these barriers, to promote timely treatment, to reduce SE duration and the risk of hospitalization are the use of seizure action plans, triage seizure codes, cEEG monitoring in the PED, training of caregivers and emergency services, and adherence to treatment algorithms for SE. The combined use of PEWS, PEDSS, and STEPSS systems can be helpful to stratify the risk of clinical deterioration and poor outcome during SE.

AUTHOR CONTRIBUTIONS

A.F., L.B., A.D., M.L., and D.M.C. designed the study and supervised every step of the work. A.F., L.B., A.B., R.R., C.G., and F.S. took part in the data-retrieval process. A.F., L.B., L.M.B.B., and L.V. analyzed the data. A.F., L.B., F.S., C.G., and L.M.B.B. wrote the first draft of the work. A.D., M.L., A.R., L.V., M.C.M., and D.M.C. revised the work.

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CONFLICT OF INTEREST AND ETHICAL PUBLICATION STATEMENT

The authors declare they have no conflicts of interest to disclose for this work. The local ethics committee was advised of the study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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BIBLIOGRAPHY

1. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus—report of the ILAE task force on classification of status epilepticus. Epilepsia. 2015;56(10):1515–23.
2. Govoni V, Fallica E, Monetti VC, Guerzoni F, Faggioli R, Casetta I, et al. Incidence of status epilepticus in southern Europe: a population study in the Health District of Ferrara. Italy European Neurology. 2007;59(3–4):120–6.
3. Abend NS, Loddenkemper T. Pediatric status epilepticus management. Curr Opin Pediatr. 2014;26(6):668–74.
4. Chin RFM, Neville BGR, Peckham C, Bedford H, Wade A, Scott RC. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study. Lancet. 2006;368:1328.
5. Nishiyama I, Ohtsuka Y, Tsuda T, Inoue H, Kunitomi T, Shiraga H, et al. An epidemiological study of children with status epilepticus in Okayama. Japan Epilepsia. 2007;48(6):1133–7.
6. Wu YW, Shek DW, Garcia PA, Zhao S, Johnston SC. Incidence and mortality of generalized convulsive status epilepticus in California. Neurology. 2002;58(7):1070–6.
7. Singh RK, Stephens S, Berl MM, Chang T, Brown K, Vezina LG, et al. Prospective study of new-onset seizures presenting as status epilepticus in childhood. Neurology. 2010;74(8):636–42.
8. Sculier C, Gaínza-Lein M, Sánchez Fernández I, Loddenkemper T. Long-term outcomes of status epilepticus: a critical assessment. Epilepsia. 2018;59(S2):155–69.
9. Gaínza-Lein M, Sánchez Fernández I, Jackson M, Abend NS, Arya R, Brenton JN, et al. Association of Time to treatment with short-term outcomes for pediatric patients with refractory convulsive status epilepticus. JAMA Neurol. 2018;75(4):410–8.
10. Raspall-Chaure M, Chin RF, Neville BG, Scott RC. Outcome of paediatric convulsive status epilepticus: a systematic review. The Lancet Neurology. 2006;5(9):769–79.
11. Raspall-Chaure M, Chin RFM, Neville BG, Bedford H, Scott RC. The epidemiology of convulsive status epilepticus in children: a critical review. Epilepsia. 2007;48(9):1652–63.
12. Sánchez Fernández I, Gaínza-Lein M, Barcia Aguilar C, Amengual-Gual M, Loddenkemper T. The burden of decisional uncertainty in the treatment of status epilepticus. Epilepsia. 2020;61(10):2150–62.
13. Seinfeld S, Shinnar S, Sun S, Hesdorffer DC, Deng X, Shinnar RC, et al. Emergency management of febrile status epilepticus: results of the FEBSTAT study. Epilepsia. 2014;55(3):388–95.
14. Jackson MC, Vasquez A, Ojo O, Fialkow A, Hammond S, Stredny CM, et al. Identifying barriers to Care in the Pediatric Acute Seizure Care Pathway. Int J Integr Care. 2022;22(1):28.
15. Loddenkemper T. Detect, predict, and prevent acute seizures and status epilepticus. Epilepsy Behav. 2023;141:109141.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335(7624):806–8.
17. Mackway-Jones K, Marsden J, Windle J. Emergency triage: Manchester Triage Group. 3rd ed. Wiley; 2013. Emergency Triage | Wiley Online Books Available from: https://onlinelibrary.wiley.com/doi/book/10.1002/9781118299029
18. Zachariasse JM, Seiger N, Rood PPM, Alves CF, Freitas P, Smit FJ, et al. Validity of the Manchester triage system in emergency care: a prospective observational study. PLoS One. 2017;12(2):e0170811.
19. Hirsch LJ, Gaspard N, Van Baalen A, Nabbout R, Demeret S, Loddenkemper T, et al. Proposed consensus definitions for new-onset refractory status epilepticus (NORSE), febrile infection-related epilepsy syndrome (FIRES), and related conditions. Epilepsia. 2018;59(4):739–44.

20. Wang T, Wang J, Dou Y, Yan W, Ding D, Lu G, et al. Clinical characteristics and prognosis in a large paediatric cohort with status epilepticus. Seizure. 2020;80:5–11.
21. Bigi S, Fischer U, Wehrli E, Mattle HP, Boltshauser E, Bürki S, et al. Acute ischemic stroke in children versus young adults. Ann Neurol. 2011;70(2):245–54.
22. Fiser DH. Assessing the outcome of pediatric intensive care. J Pediatr. 1992;121(1):68–74.
23. Gold DL, Mihalov LK, Cohen DM. Evaluating the pediatric early warning score (PEWS) system for admitted patients in the pediatric emergency department. Acad Emerg Med. 2014;21(11):1249–56.
24. Soydan E, Gonullu A, Aksoy Y, Guzin Y, Ceylan G, Topal S, et al. Pediatric status epilepticus severity score (STEPSS): predictive performance of functional outcomes: a prospective single-center study. J Child Neurol. 2022;37(12–14):956–62.
25. Tiwari R, Chakrabarty B, Gulati S, Jauhari P, Lodha R, Sankar J, et al. Development of a novel outcome prediction score (PEDSS) for pediatric convulsive status epilepticus: a longitudinal observational study. Epilepsia. 2020;61(12):2763–73.
26. Monaghan A. Detecting and managing deterioration in children. Paediatr Nurs. 2005;17(1):32–5.
27. Stredny CM, Abend NS, Loddenkemper T. Towards acute pediatric status epilepticus intervention teams: do we need "seizure codes"? Seizure. 2018;58:133–40.
28. Gurcharran K, Grinspan ZM. The burden of pediatric status epilepticus: epidemiology, morbidity, mortality, and costs. Seizure. 2019;68:3–8.
29. Shinnar S, Pellock JM, Moshé SL, Maytal J, O'Dell C, Driscoll SM, et al. In whom does status epilepticus occur: age-related differences in children. Epilepsia. 1997;38(8):907–14.
30. Sánchez Fernández I, Amengual-Gual M, Barcia Aguilar C, Gaínza-Lein M. Descriptive epidemiology and health resource utilization for status epilepticus in the emergency department in The United States of America. Seizure. 2021;87:7–16.
31. Chetan C, Sharma S, Mathur SB, Jain P, Aneja S. Clinical profile and short-term outcome of pediatric status epilepticus at a tertiary-care Center in Northern India. Indian Pediatr. 2020;57(3):213–7.
32. Meyer S, Langer J, Poryo M, Bay JG, Wagenpfeil S, Heinrich B, et al. Epileptic status in a PEDiatric cohort (ESPED) requiring intensive care treatment: a multicenter, national, two-year prospective surveillance study. Epilepsia Open. 2023;8(2):411–24.
33. Jafarpour S, Hodgeman RM, De Marchi CC, De Lima MTA, Kapur K, Tasker RC, et al. New-onset status epilepticus in pediatric patients: causes, characteristics, and outcomes. Pediatr Neurol. 2018;80:61–9.
34. DeLorenzo RJ, Hauser WA, Towne AR, Boggs JG, Pellock JM, Penberthy L, et al. A prospective, population-based epidemiologic study of status epilepticus in Richmond. Virginia Neurology. 1996;46(4):1029–35.
35. Hesdorffer DC, Logroscino G, Cascino G, Annegers JF, Hauser WA. Incidence of status epilepticus in Rochester, Minnesota, 1965-1984. Neurology. 1998;50(3):735–41.
36. Patel AD, Becker DA. Introduction to use of an acute seizure action plan for seizure clusters and guidance for implementation. Epilepsia. 2022;63(S1):S25–S33.
37. Mitchell WG, Conry JA, Crumrine PK, Kriel RL, Cereghino JJ, Groves L, et al. An open-label study of repeated use of diazepam rectal gel (Diastat) for episodes of acute breakthrough seizures and clusters: safety, efficacy, and tolerance. Epilepsia. 1999;40(11):1610–7.
38. Shatirishvili T, Kipiani T, Lomidze G, Gabunia M, Tatishvili N. Short-term outcomes and major barriers in the management of convulsive status epilepticus in children: a study in Georgia. Epileptic Disord. 2015;17(3):292–8.
39. Misra SN, Jarrar R, Stern JM, Becker DA, Carrazana E, Rabinowicz AL. Rapid rescue treatment with diazepam nasal spray leads to faster seizure cluster termination in epilepsy: an exploratory post hoc cohort analysis. Neurol Ther. 2024;13(1):221–31.
40. Amengual-Gual M, Sánchez Fernández I, Vasquez A, Abend NS, Anderson A, Arya R, et al. Pediatric status epilepticus management by emergency medical services (the pSERG cohort). Seizure: European. J Epilepsy. 2023;111:51–5.
41. Leviton A, Patel AD, Loddenkemper T. Self-management education for children with epilepsy and their caregivers. A Scoping Review Epilepsy & Behavior. 2023;144:109232.
42. Genna C, Thekkan KR, Geremia C, Di Furia M, Campana A, DallOglio I, et al. Parents' process of recognition and response to clinical deterioration of their children with medical complexity at home: a grounded theory. J Clin Nurs. 2023;32(15–16):4677–93.
43. Shafer PO, Santilli N, Buchhalter J, Gilchrist B, Kukla A, French JA, et al. The rescue therapy in epilepsy project part 2: insights from people with epilepsy and families on expert-derived preferred practices. Epilepsy Behav. 2021;125:108444.
44. Arzimanoglou A, Lagae L, Cross JH, Beghi E, Mifsud J, Bennett C, et al. The administration of rescue medication to children with prolonged acute convulsive seizures in a non-hospital setting: an exploratory survey of healthcare professionals' perspectives. Eur J Pediatr. 2014;173(6):773–9.
45. Shankar R, Jory C, McLean B, Tittensor P, Walker M. Epilepsy awareness and emergency rescue training: ignorance is bliss! Epilepsy Behav. 2017;70:212–6.
46. European Medicines Agency. BUCCOLAM, Midazolam. 2011 Available from: https://www.ema.europa.eu/en/documents/overview/buccolam-epar-summary-public_en.pdf
47. Epistatus 10 mg Oromucosal Solution - Summary of Product Characteristics (SmPC)—(emc). 2024 Available from: https://www.medicines.org.uk/emc/product/2679/smpc#gref
48. Wheless JW. A critical evaluation of midazolam nasal spray for the treatment of patients with seizure clusters. Expert Rev Neurother. 2021;21(11):1195–205.
49. Kaune A, Schumacher PM, Hoppe SC, Syrbe S, Bernhard MK, Frontini R, et al. Administration of anticonvulsive rescue medication in children—discrepancies between parents' self-reports and limited practical performance. Eur J Pediatr. 2016;175(9):1139–46.
50. Nunley S, Glynn P, Rust S, Vidaurre J, Albert DVF, Patel AD. A hospital-based study on caregiver preferences on acute seizure rescue medications in pediatric patients with epilepsy: intranasal midazolam versus rectal diazepam. Epilepsy Behav. 2019;92:53–6.
51. Penovich P, Glauser T, Becker D, Patel AD, Sirven J, Long L, et al. Recommendations for development of acute seizure action plans (ASAPs) from an expert panel. Epilepsy Behav. 2021;123:108264.

52. Herman ST, Detyniecki K, O'Hara K, Penovich P, Rao VR, Tatum W, et al. Written seizure action plans for adult patients with epilepsy: distilling insights from emergency action plans for other chronic conditions. Epilepsy Behav. 2023;140: 109002.
53. Neville KL, McCaffery H, Baxter Z, Shellhaas RA, Fedak Romanowski EM. Implementation of a standardized seizure action plan to improve communication and parental education. Pediatr Neurol. 2020;112:56–63.
54. Chiu M, Peinhof S, De Guzman C, Borhani M, Siu C, Kuzeljevic B, et al. Seizure action plans in the pediatric population with epilepsy: uptake, determinants, and parental interest in a mobile application. Epilepsy Behav. 2021;117:107860.
55. Al-Shaqsi S. Models of international emergency medical service (EMS) systems. OMJ. 2010;25(4):320-3. doi: 10.5001/omj.2010.92.
56. Buratti S, Giacheri E, Palmieri A, Tibaldi J, Brisca G, Riva A, et al. Ketamine as advanced second-line treatment in benzodiazepine-refractory convulsive status epilepticus in children. Epilepsia. 2023;64(4):797–810.
57. Raucci U, Pro S, Di Capua M, Di Nardo G, Villa MP, Striano P, et al. A reappraisal of the value of video-EEG recording in the emergency department. Expert Rev Neurother. 2020;20(5): 459–75.
58. Zehtabchi S, Silbergleit R, Chamberlain JM, Shinnar S, Elm JJ, Underwood E, et al. Electroencephalographic seizures in emergency department patients after treatment for convulsive status epilepticus. J Clin Neurophysiol. 2022;39(6):441–5.
59. Fung FW, Abend NS. EEG monitoring after convulsive status epilepticus. J Clin Neurophysiol. 2020;37(5):406–10.
60. Jaitly R, Sgro JA, Towne AR, Ko D, DeLorenzo RJ. Prognostic value of EEG monitoring after status epilepticus: a prospective adult study. J Clin Neurophysiol. 1997;14(4):326–34.
61. Rosenthal ES. Seizures, status epilepticus, and continuous EEG in the intensive care unit. CONTINUUM: lifelong learning. Neurology. 2021;27(5):1321–43.
62. Struck AF, Ustun B, Ruiz AR, Lee JW, LaRoche SM, Hirsch LJ, et al. Association of an Electroencephalography-Based Risk Score with Seizure Probability in hospitalized patients. JAMA Neurol. 2017;74(12):1419–24.
63. Struck AF, Tabaeizadeh M, Schmitt SE, Ruiz AR, Swisher CB, Subramaniam T, et al. Assessment of the validity of the 2HELPS2B score for inpatient seizure risk prediction. JAMA Neurol. 2020;77(4):500–7.
64. Ostrowsky K, Arzimanoglou A. Outcome and prognosis of status epilepticus in children. Semin Pediatr Neurol. 2010;17(3):195–200.
65. Halawa EF, Draz I, Ahmed D, Shaheen HA. Predictors of outcome of convulsive status epilepticus among an Egyptian pediatric tertiary hospital. J Child Neurol. 2015;30(13):1736–42.
66. Null S, Sharma S, Jain P, Mathur SB, Malhotra RK, Kumar V. Status epilepticus in pediatric patients severity score (STEPSS): a clinical score to predict the outcome of status epilepticus in children- a prospective cohort study. Seizure. 2019;71:328–32.

SUPPORTING INFORMATION

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

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