

# Outcome Prediction of Higher-Risk Brief Resolved Unexplained Events

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## ABSTRACT

**OBJECTIVES:** Brief resolved unexplained events (BRUEs) are classified as higher risk on the basis of patient and event characteristics, but there is limited evidence to guide management decisions. The authors of this study aim to describe patients with a higher-risk BRUE, determine the yield of diagnostic evaluation, and explore predictors of clinical outcomes.

**METHODS:** A retrospective medical record review was conducted for patients  $\leq 365$  days of age who were evaluated in a tertiary-care pediatric emergency department with a discharge diagnostic code indicative of a BRUE. Demographic and clinical characteristics, including diagnostic evaluation, are reported. Univariate and multivariate analyses were used to test the association of risk factors with clinical outcomes (serious underlying diagnosis, recurrent events, and return hospitalization).

**RESULTS:** Of 3325 patients, 98 (3%) met BRUE criteria and 88 were classified as higher risk; 0.6% of laboratory and 1.5% of ancillary tests were diagnostic, with 4 patients having a serious underlying diagnosis. Nine patients had recurrent events during hospitalization, and 2 were readmitted for a recurrent BRUE after their index visit. Prematurity was the only characteristic significantly associated with an outcome, increasing the odds of a recurrent event (odds ratio = 9.4;  $P = .02$ ).

**CONCLUSIONS:** The majority of patients with a BRUE are higher risk, but the yield of diagnostic evaluation is low. Published risk criteria do not appear to be associated with adverse clinical outcomes except for prematurity and recurrent events. Future multicentered prospective studies are needed to validate risk stratification and develop management guidance for the higher-risk BRUE population.



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It is common for caregivers of children <1 year of age to become concerned about transient changes in their children's breathing, tone, or skin color. Oftentimes, clinicians can attribute these events to normal manifestations of infant physiologic immaturity (eg, periodic breathing). Occasionally, the cause is not clear, raising concern for serious underlying pathology. Once termed apparent life-threatening events (ALTEs), the American Academy of Pediatrics (AAP) more precisely defined these events in a clinical practice guideline (CPG) as brief resolved unexplained events (BRUEs).<sup>1</sup> The term BRUE denotes a sudden, brief, unexplained, and resolved episode in an infant <1 year of age that is characterized by 1 or more of the following: cyanosis or pallor; absent, decreased, or irregular breathing; marked change in tone; or altered level of responsiveness. A diagnosis of a BRUE is made after a comprehensive history and physical examination does not yield a cause of the event. By using evidence-based criteria, infants with a BRUE should be classified as being at lower or higher risk of having a recurrent event or a serious underlying cause. The CPG provides evidence-based recommendations for the evaluation and management of patients with a lower-risk BRUE but does not provide recommendations for higher-risk infants because of insufficient evidence.<sup>1</sup>

The criteria for higher-risk BRUEs are based on patient characteristics (age <2 months and prematurity) and event characteristics (recurrence, duration, and cardiopulmonary resuscitation [CPR] required). Patients with a higher-risk BRUE continue to challenge clinicians because they represent a heterogeneous group of patients whose risk factors have not been studied enough to determine if a subset may be included in the lower-risk group. The relative contribution of each risk factor and how to effectively use that information to diagnose a vast array of serious underlying problems (eg, child abuse) or to reassure caregivers remains unclear.<sup>2-4</sup> A tiered approach to the evaluation of these patients was recently published, but an improved understanding of the patients with higher risk and their

risk criteria could help to inform the current framework for the evaluation of this population.<sup>2</sup> Thus, our aim in this study is to describe patients with higher-risk BRUEs, including event characteristics, the yield of diagnostic evaluation, and hospital course, and to explore whether the higher-risk factors predict key clinical outcomes.

## METHODS

This retrospective study was approved by the institutional review board and conducted at a midwestern, inner-city, freestanding children's hospital with a level 1 trauma center and ~80 000 pediatric emergency department (ED) visits and 12 000 inpatient admissions annually.

### Study Population

The study included patients ≤365 days of age evaluated in the pediatric ED between January 1, 2010, and April 30, 2016, with an International Classification of Diseases, 9th Revision or 10th Revision discharge diagnostic code indicative of a BRUE (Supplemental Table 5).<sup>5-7</sup> Using brief medical record review, 1 of the authors (R.H.) excluded patients with a preexisting medical condition, such as congenital heart disease, chronic lung disease, and metabolic or genetic syndromes. Patients with insufficient or missing ED documentation were also excluded. The remaining records were then reviewed by 1 of the authors (R.H.) to identify patients who met BRUE criteria. Patients not meeting BRUE criteria were excluded. Patients categorized as having a BRUE (or not) were reviewed by another author (A.D.), and any discrepancies were discussed until consensus was achieved. The final study population underwent detailed chart abstraction for the index visit and return visits to our institution within 90 days. The study data were collected and managed by using Research Electronic Data Capture tools.<sup>8</sup>

### Definitions

#### BRUE

A BRUE was defined in accordance with the AAP definition as a sudden, brief, and resolved episode that included 1 or more of the following: (1) cyanosis or pallor; (2) absent, decreased, or irregular breathing; (3) marked change in tone; or (4) altered

responsiveness. To meet the AAP definition, documentation needed to demonstrate that a patient appeared to be well at the time of their initial ED evaluation. It also needed to demonstrate that there was an absence of additional symptoms, abnormal vital signs for age, or an explanation for the event based on the history and/or physical examination.<sup>1</sup>

#### Risk Stratification

A BRUE was further classified as higher risk per the AAP CPG if there was documentation of the following: (1) age <60 days, (2) gestational age <32 weeks or gestational age of 32 to <37 weeks with a postconceptual age of <45 weeks, (3) CPR performed by a medical provider, (4) event lasted >1 minute, or (5) >1 event before ED evaluation.<sup>1,9</sup> The results reported below focus on patients with a higher-risk BRUE.

#### Diagnostic Interpretation

Laboratory studies were interpreted as normal or abnormal on the basis of published age reference ranges.<sup>10</sup> Imaging and ancillary studies (EEG and pH probe) were interpreted as normal or abnormal on the basis of the report provided in the electronic medical record. Electrocardiograms (ECGs) were reviewed by a pediatric cardiologist and classified as normal or abnormal. All studies were considered diagnostic and/or clinically significant if they resulted in a definitive diagnosis or contributed to a change in patient management.

#### Serious Underlying Diagnosis

For the purposes of this study, a serious underlying diagnosis was defined as one that (1) is historically associated with brief events,<sup>11</sup> (2) is identified through diagnostic testing, (3) is potentially life-threatening or may be associated with negative clinical sequelae (eg, apnea with respiratory syncytial virus), and (4) may benefit from immediate therapy. Examples of serious underlying diagnoses include seizures, meningitis, bacteremia, urinary tract infection, metabolic disorders, and nonaccidental trauma.<sup>11</sup>

The primary outcome of interest was a serious underlying diagnosis identified during the index visit and after laboratory,

imaging, and/or ancillary studies. Secondary outcomes included (1) recurrent events either in the ED or during inpatient hospitalization and (2) a readmission for a BRUE within 90 days of the index visit.

### Statistical Analysis

We summarized categorical variables using descriptive statistics. Continuous variables are reported by mean and SD, whereas nonnormally distributed continuous variables are reported by median and interquartile range (IQR). Pearson's  $\chi^2$  test was used to analyze the distribution of categorical variables by groups, provided no expected frequency was  $<1$ , and no more than 20% of the cells had an expected frequency  $<5$ ; otherwise, Fisher's exact test was used for the analysis. We calculated an odds ratio (OR) with a 95% confidence interval (CI) to compare the categorical variables by groups. We used SAS version 9.4 (SAS Institute, Inc, Cary, NC). The significance level was set at 0.05.

### RESULTS

Among 3325 patients identified after the electronic query, 98 (3%) met the definition for a BRUE: 10 (10%) were classified as lower risk, and 88 (90%) were classified as higher risk (Fig 1). Overall, BRUE accounted for 98 of 565 677 (0.017%) total pediatric ED visits during the study period.

### Demographics

Patients were predominantly African American (60%) and boys (53%), with a median age of 18.5 days (IQR: 8–61). More than half of the patients (63%) were transferred to our institution from another ED. The majority of patients (89%) were admitted for a median of 27.5 hours (IQR: 19–50). Additional demographics are reported in Table 1.

### Event Characteristics and Risk Criteria

The most commonly reported event characteristic was abnormal breathing (80%). Additional event characteristics are reported in Table 2. The most common higher-risk factor was age  $<60$  days (75%). Thirty-six patients (41%) had a single higher-risk factor, whereas 40 (45%) had 2 risk factors, and 12 (14%) had 3 risk

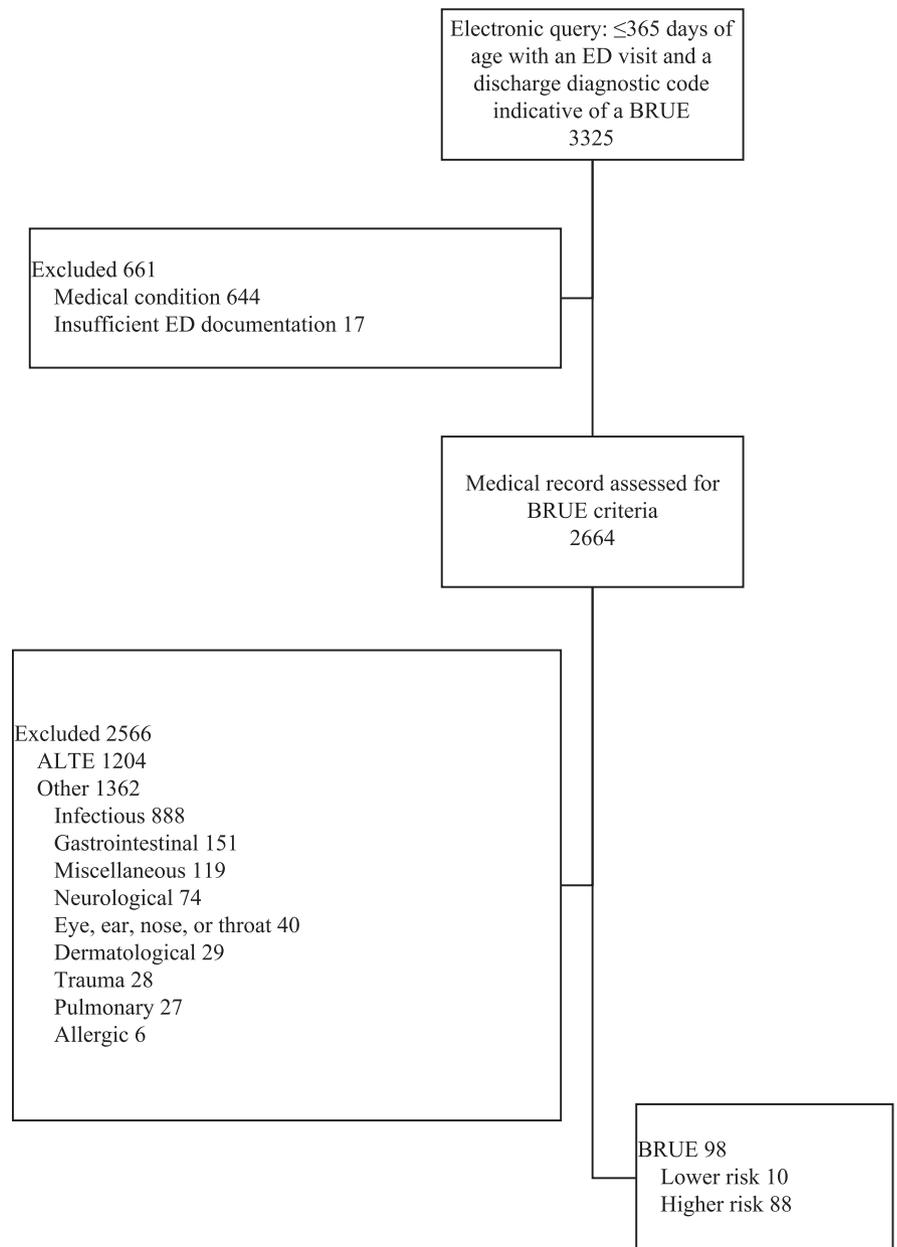


FIGURE 1 Study population.

factors. Higher-risk factors are summarized in Table 2.

### Laboratory, Imaging, and Ancillary Studies

Overall, patients had varied and inconsistent laboratory, imaging, and ancillary studies performed (Table 3). Most patients (88%) underwent laboratory testing. Four of 720 laboratory tests (0.6%) were considered diagnostic for a serious underlying

diagnosis: 1 positive blood culture result for *Staphylococcus hominis*, 2 positive respiratory polymerase chain reaction (PCR) panel results (enterovirus and influenza B), and 1 positive cerebrospinal fluid (CSF) PCR result for enterovirus. The patient with enterovirus detected by respiratory and CSF PCR also had a positive PCR result for enterovirus in the blood. Most patients (82%) also had imaging or ancillary studies performed, but none of the

**TABLE 1** Demographic Characteristics

Demographic Characteristic	Higher Risk ( <i>N</i> = 88)
Age, d, median (IQR)	18.5 (8–61)
Male sex, <i>n</i> (%)	47 (53)
Race, <i>n</i> (%)	
African American	53 (60)
White	22 (25)
Other	13 (15)
Insurance, <i>n</i> (%)	
Government	78 (89)
Private	7 (8)
Other	3 (3)
PED length of stay, h, median (IQR)	4:03 (2:58–5:11)
PED transfer, <i>n</i> (%)	55 (63)
PED disposition, <i>n</i> (%)	
Admitted	78 (89)
Discharged	10 (11)
Admission unit, <i>n</i> (%)	
Inpatient floor	63 (81)
Critical care (NICU or PICU)	15 (19)
Admission length of stay, h, median (IQR)	27.5 (19–50)
PED discharge diagnosis ( <i>n</i> = 10), <i>n</i> (%)	
Normal examination	3 (30)
Periodic breathing	3 (30)
ALTE	0 (0)
Apnea	2 (20)
Gastroesophageal disease or choking	2 (20)
Other	3 (30)
Hospital discharge diagnosis ( <i>n</i> = 78), <i>n</i> (%)	
ALTE	49 (63)
Gastroesophageal reflux disease or choking	18 (23)
Benign conditions of infancy	10 (13)
Apnea	8 (10)
Periodic breathing	6 (6)
Infection	4 (5)
Seizure	4 (5)
Altered mental status	1 (1)
Failure to thrive	1 (1)

PEDS, XXX

primary purpose of continuous cardiorespiratory monitoring, none required critical interventions,<sup>12</sup> including intubation, CPR, or inotropic support, and there were no deaths. One patient (1%) required respiratory support (high-flow nasal cannula) for sustained hypoxia in the context of enteroviral meningitis with sepsis. Other inpatient therapies included intravenous fluids (37%), gastric acid suppression therapy (19%), antibiotics (18%), and antiviral (12%) and antiepileptic (1%) medications.

Twelve patients (14%) had a total of 18 return visits to our institution within 90 days of their index visit for related reasons. All clinic visits (100%) were scheduled: 9 (50%) with a pediatric subspecialist and 2 (11%) with a general pediatrician. The remaining 7 visits (39%) were to the pediatric ED, and 2 patients (29%) were subsequently hospitalized. Final diagnoses for these 12 patients included gastroesophageal reflux disease (*n* = 5; 42%), ALTE (*n* = 4, 33%), anemia of prematurity (*n* = 1; 8%), patent foramen ovale (*n* = 1; 8%), oral candidiasis (*n* = 1; 8%), staring spell (*n* = 1; 8%), and nonspecific movements (*n* = 1; 8%). Two patients (*n* = 2; 17%) were diagnosed with seizure; 1 was initially diagnosed during the index visit, and a second (EEG-negative) was started on antiepileptic therapy during a return visit hospitalization.

### Higher-Risk Criteria and Outcomes of Interest

As mentioned, in our sample, 4 patients had serious underlying diagnoses identified during their index visit (primary outcome), 9 patients had recurrent events either in the ED or during hospitalization (secondary outcome), and 2 patients were readmitted for a BRUE within 90 days of the index visit (secondary outcome). In the univariate analysis examining the higher-risk criteria and these outcomes, prematurity was the only risk factor that significantly increased the odds of a recurrent event (OR = 9.38; 95% CI 1.69–51.96; *P* = .022). The other risk criteria did not increase the odds of a recurrent event, and none of the risk criteria were associated with a serious underlying diagnosis or a return visit

101 imaging tests were diagnostic. Among the 70 ancillary studies performed, 1 EEG result (1.5%) was abnormal and considered to aid in the identification of a serious underlying diagnosis. In sum, the 4 serious underlying diagnoses identified in this sample included *S hominis* bacteremia (*n* = 1), influenza B (*n* = 1), enteroviral meningitis with sepsis (*n* = 1), and seizure (*n* = 1).

### ED and Hospital Course and Return Visits

Nine patients (10%) had a total of 11 recurrent events: 4 had events in the ED, 3 had events during hospital admission, and 2 had events in both settings. Nearly all patients (97%) received cardiorespiratory monitoring. Although 15 patients (19%) were admitted to a critical-care unit for the

**TABLE 2** Event Characteristics and Risk Criteria

	Higher Risk (N = 88), n (%)
Event characteristic	
Color change	50 (57)
Abnormal breathing	70 (80)
Abnormal tone	39 (44)
Altered mental status	36 (41)
Higher-risk criteria	
Age <60 d	66 (75)
Past history of BRUE	6 (7)
Duration, min	
<1	48 (55)
≥1	36 (41)
Not specified	4 (5)
Recurrent events in 24 h	41 (47)
No. events	
2	24 (51)
3–5	13 (28)
≥6	2 (4)
Not specified	2 (4)
History of prematurity	7 (8)
Category of prematurity	
Moderate to late prematurity (32 to <37 wk)	5 (71)
Very premature (<32 wk)	2 (29)
Gestational age <45 wk	7 (100)
CPR by a trained medical provider	0 (0)

resulting in hospitalization (Table 4). Similarly, the number of risk criteria present and multivariable analyses did not demonstrate an association between the risk criteria and our outcomes of interest (Table 4). However, all 4 patients with a serious underlying diagnosis reported 2 risk factors, one of which was younger age (4, 4, 12, and 27 days).

## DISCUSSION

By introducing the term BRUE in a CPG,<sup>1</sup> the AAP aimed to more precisely define a population of patients who historically presented clinicians with a diagnostic and management challenge. Although the CPG focuses on patients with a lower-risk BRUE, our results highlight that the majority of patients presenting to a tertiary ED are higher risk. Diagnostic testing for these patients is common and varied yet rarely helpful. Furthermore, although the majority of patients were hospitalized, few required

significant interventions. Prematurity is associated with a recurrent event, but otherwise, the higher-risk criteria are not predictive of a serious underlying diagnosis, a recurrent event, or a return hospitalization.

Since publication of the AAP CPG in 2016, 3 studies have retrospectively characterized patients with BRUE. Using billing codes and chart review, Meyer et al<sup>13</sup> examined 321 patients presenting to the ED or to the inpatient unit of a community hospital, of whom 20 met criteria for BRUE. Of these, 19 (95%) were classified as higher risk. Similarly, Colombo et al<sup>14</sup> retrospectively applied the BRUE criteria to admitted infants who were identified using International Classification of Diseases (ICD) codes and categorized 33 of 84 infants (39%) as higher risk. Finally, Ramgopal et al<sup>15</sup> performed a secondary analysis of a prospective ALTE registry and classified 256 of 326 patients (78.5%) who met BRUE

criteria as higher risk. Our study aligns with the literature published to date because we have also found that in a tertiary-care ED setting, patients with a higher-risk BRUE outnumber their lower-risk counterparts. Thus, evidence-based recommendations are needed to help clinicians with the evaluation and management of higher-risk BRUEs.

In the absence of recommendations, a framework for the evaluation of patients with a higher-risk BRUE was recently published.<sup>2</sup> However, with limited available evidence, it is still unclear how clinicians should balance the potential yield of testing against the potential harms to the patient and family. On the basis of the aforementioned studies, the current approach varies.<sup>13–15</sup> For instance, an ECG was obtained in 100% of patients with a higher-risk BRUE in the inpatient setting, whereas only 10% of patients had an ECG when evaluated through the ED.<sup>13,14</sup> We specifically examined the testing outlined in the AAP CPG and have also found that diagnostic evaluation is not standardized. More importantly, we note that the yield is also very low because few patients had a serious underlying diagnosis despite often extensive evaluations. Although diagnostic testing for patients with a BRUE has declined since publication of the CPG,<sup>16</sup> a key question still remains: which testing should be performed in the evaluation of patients with a higher-risk BRUE?

One patient in our study was diagnosed with *S hominis* bacteremia and included as a serious underlying diagnosis because the patient was treated with a 10-day course of antibiotics. *S hominis* is often considered a contaminant, and neonatal sepsis secondary to coagulase-negative *Staphylococcus* is more common among premature infants.<sup>17</sup> Although this particular patient was born term, because of age (27 days) and the association between coagulase-negative *Staphylococcus* and neonatal sepsis, the patient received antibiotics and appeared to remain clinically well during the hospitalization. Overall, routine testing for bacteremia is thought to be low yield, and consequently, a blood culture is not included in the current

**TABLE 3** Laboratory, Imaging, and Ancillary Studies

Investigation	Higher-Risk BRUE, n (%)		
	Performed	Abnormal	Diagnostic
<b>Chemistry</b>			
Sodium	52 (59)	5 (10)	0 (0)
Potassium	54 (61)	20 (37)	0 (0)
Chloride	52 (59)	0 (0)	0 (0)
Carbon dioxide	52 (59)	22 (42)	0 (0)
Glucose	52 (59)	10 (19)	0 (0)
Blood urea nitrogen	46 (52)	13 (28)	0 (0)
Creatinine	46 (52)	9 (20)	0 (0)
Calcium	48 (55)	2 (4)	0 (0)
Ammonia	3 (3)	2 (67)	0 (0)
Lactic acid	2 (2)	0 (0)	0 (0)
Blood gas	57 (65)	7 (12)	0 (0)
Urinalysis	26 (30)	6 (23)	0 (0)
<b>Metabolic screen</b>			
Plasma amino acids quantitation	4 (5)	0 (0)	0 (0)
Urine organic acid screen	3 (3)	1 (33)	0 (0)
Quantitative plasma acylcarnitines	1 (1)	0 (0)	0 (0)
<b>Hematology</b>			
White blood cell count	58 (66)	0 (0)	0 (0)
Hemoglobin	58 (66)	7 (12)	0 (0)
<b>Microbiology</b>			
Blood culture	24 (27)	1 (4)	1 (100)
Urine culture	20 (23)	0 (0)	0 (0)
CSF culture	15 (17)	0 (0)	0 (0)
CSF herpes simplex virus 1 and 2 PCR	12 (14)	0 (0)	0 (0)
CSF enterovirus PCR	4 (5)	1 (25)	1 (100)
<i>Bordetella pertussis</i> PCR	2 (2)	0 (0)	0 (0)
Respiratory PCR panel	29 (33)	2 (7)	2 (100)
<b>Imaging</b>			
Abdominal radiograph	2 (2)	0 (0)	0 (0)
Abdominal ultrasound	1 (1)	0 (0)	0 (0)
Chest radiograph	58 (66)	4 (7)	0 (0)
Head ultrasound	34 (39)	5 (15)	0 (0)
Computed tomography brain	2 (2)	0 (0)	0 (0)
MRI brain	4 (5)	0 (0)	0 (0)
<b>Ancillary studies</b>			
EEG	41 (47)	1 (2)	1 (100)
ECG	17 (19)	0 (0)	0 (0)
Echocardiogram	11 (13)	0 (0)	0 (0)
pH probe	1 (1)	0 (0)	0 (0)

diagnosis of a BRUE.<sup>1</sup> Younger children with viral upper respiratory tract infections are, however, more likely to be asymptomatic,<sup>18</sup> and age was the most common higher-risk criterion in our sample. Yet, not all patients had nucleic acid amplification testing for respiratory viruses. A positive result in an asymptomatic patient should be cautiously interpreted because it may reflect residual shedding or viral persistence.<sup>19</sup> The exact role of respiratory viruses in higher-risk BRUE therefore remains unclear. As we continue to develop our understanding of patients with a higher-risk BRUE, our findings align with the tiered pathway for the evaluation of a higher-risk BRUE, in which a rapid viral respiratory panel is included in the initial evaluation.<sup>2</sup>

Imaging and ancillary tests were also found to be of limited value in our study for the evaluation of patients with a higher-risk BRUE. Only 1 EEG result was positive, with seizures diagnosed in 1 admitted patient during the index visit. A second patient (EEG-negative) was diagnosed with seizures during our follow-up period. Colombo et al<sup>14</sup> also reported that seizures were diagnosed in 3 patients with a higher-risk BRUE. On the basis of the ALTE literature, inpatient neurologic evaluation is low yield because half of the patients with chronic epilepsy are diagnosed within 1 week of their event.<sup>20</sup> Inpatient EEG and neuroimaging are therefore not recommended in the evaluation of patients with a lower-risk BRUE.<sup>1</sup> Their role in the evaluation of patients with a higher-risk BRUE is less clear, but in the event of recurrent or paroxysmal events, a prolonged EEG should be considered during the secondary evaluation of patients hospitalized after a higher-risk BRUE.<sup>2</sup>

While the optimal approach to the diagnostic evaluation for patients with a higher risk BRUE remains unclear, it is also not known which patients need to undergo evaluation. The absence of higher-risk factors was intended by the AAP to identify patients unlikely to benefit from testing and hospitalization. However, there was not enough evidence for the AAP to determine risk and make clinical recommendations when 1 or more of the risk factors were

framework for the evaluation of patients after a higher-risk BRUE.<sup>2</sup>

In contrast, half of the patients with a serious underlying diagnosis in our study had a self-limiting viral illness. The CPG

recommends against testing patients with a lower-risk BRUE for respiratory viruses because patients with an acute viral infection should be symptomatic (eg, fever, cough, and coryza), thereby precluding the

**TABLE 4** Higher-Risk Criteria and Outcomes

	Serious Underlying Diagnosis, OR (95% CI)	Repeat Events, OR (95% CI)	Return Visit Hospitalization, OR (95% CI)
Higher-risk criteria (univariate)			
Age <60 d	—	0.63 (0.14–2.78)	0.32 (0.02–5.39)
Prematurity	4.33 (0.39–48.28)	9.38 (1.69–51.96)*	13.33 (0.74–240.70)
Previous event and/or clustered events	1.15 (0.16–8.58)	4.63 (0.91–23.72)	—
Event >1 min duration	1.47 (0.20–10.95)	0.70 (0.16–2.99)	—
CPR by a trained medical provider	—	—	—
No. higher-risk criteria			
1	—	0.38 (0.07–1.94)	1.46 (0.09–24.08)
2	3.81 (0.38–38.15)	0.96 (0.24–3.83)	—
3	2.21 (0.21–23.20)	3.89 (0.83–18.32)	6.82 (0.40–117.06)
Higher-risk criteria (multivariable)			
Age <60 d and prematurity	6.67 (0.56–79.29)	7.24 (1.03–50.85)	20.5 (1.08–390.85)
Age <60 d, prematurity, and previous event and/or clustered events	—	4.81 (0.39–59.13)	42.0 (1.88–938.25)
Age <60 d, prematurity, previous event and/or clustered events, and event >1 min duration	—	—	—

Fisher's exact test was used to estimate the OR (95% CI). —, not applicable.

\* $P < .022$ .

present. In our study, among the higher-risk factors, only prematurity emerged as significantly associated with recurrent events. This is in keeping with the ALTE literature, in which prematurity was identified as a risk factor for hospitalization, extreme events, and medical intervention.<sup>21–23</sup> Although age was not significant in our results, as would be expected on the basis of the ALTE literature,<sup>21</sup> our findings are likely undermined by our small sample size because all 4 patients with a serious underlying diagnosis were <30 days of age. Furthermore, all patients with a serious underlying diagnosis in our study had 2 higher-risk factors, but our small sample size limits meaningful conclusions regarding which risk factors confer the greatest risk. Nevertheless, our study is the first to attempt to examine the role of the higher-risk criteria in predicting key clinical outcomes, and these preliminary results suggest that age, prematurity, and the interplay of the higher-risk factors need to be further examined in a larger sample so that a prediction tool providing meaningful guidance for clinicians can be developed.

The results of this study need to be considered in light of several important limitations. First, this is a retrospective

study using ICD codes and record review. We only included ICD codes associated with BRUE. Consequently, our results are limited by selection bias because we may have missed patients with a serious underlying diagnosis (eg, sepsis or nonaccidental trauma) who could have presented with a BRUE. Determining if a patient met BRUE criteria was then based solely on the subjective interpretation of variably complete medical records. Although we used a systematic approach to medical record review and 2 physicians confirmed patient inclusions, we may have underestimated the number of patients with a BRUE. Second, this is a single-center study from a tertiary-care setting serving an urban population. Our sample is further biased by the large number of patients transferred for evaluation; this may have altered clinical practice because of the perceived need for a higher level of care. Thus, our results cannot be generalized to other practice settings. Third, our sample size may be too small to detect an association with rare outcomes. Finally, we do not include longitudinal follow-up, and our short-term follow-up was only for visits within our own institution. As a result, we may not have identified all important adverse events for our patient sample.

## CONCLUSIONS

The majority of patients seen in a tertiary pediatric ED who meet BRUE criteria are higher risk. For these patients, diagnostic evaluation is low yield. In our small sample, only prematurity was associated with recurrent events, and the higher-risk criteria do not predict a serious underlying diagnosis or a return admission. Larger, multicenter studies are needed to better quantify both the relative contribution of individual risk factors and their combination to guide the evaluation and management of patients with a higher-risk BRUE.

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