Changes in the Management of Children With Brief Resolved Unexplained Events (BRUEs)

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abstract

BACKGROUND: In May 2016, the American Academy of Pediatrics published a clinical practice guideline for brief resolved unexplained events (BRUEs). We evaluated for changes in the management of BRUE after guideline publication.

METHODS: Using a pediatric multicenter administrative database, we compared rates of admission, testing, revisits, and diagnoses in patients diagnosed with a BRUE or apparent life-threatening event (ALTE) during 2017 with rates of admission, testing, revisits, and diagnoses in patients diagnosed with ALTE during 2015. We used interrupted time series analysis to test if the guideline was associated with changes in admission rate for all patients with ALTE or BRUE between 2015 and 2017. We stratified analyses by age (0–60 and 61–365 days).

RESULTS: A total of 9501 patients were included (5608 in 2015 and 3893 in 2017). The admission rate decreased by 5.7% (95% confidence interval, 3.8% to 7.5%) for infants 0 to 60 days and by 18.0% (95% confidence interval, 15.3% to 20.7%) for infants 61 to 365 days from 2015 to 2017. Patients in 2017 had lower rates of EEG, brain MRI, chest radiography, laboratory testing, and urinalyses compared with patients in 2015. In the interrupted time series analysis model ($n = 13\,977$), guideline publication was associated with decreasing admission rates (0.2% per week) for infants 61 to 365 days ($P < .001$).

CONCLUSIONS: Compared with patients evaluated in 2015, patients with BRUE or ALTE in 2017 have lower rate of admissions and testing. Findings may be due to changes in the definition of BRUE and guideline recommendations.

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Drs Ramgopal and Noorbakhsh conceptualized and designed the study, drafted the initial manuscript, collected data, and conducted the initial analyses; Drs Wilson, Callaway, and Pitetti designed the study and critically revised the manuscript for intellectually important content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: In 2016, the American Academy of Pediatrics published a clinical practice guideline in which the name of apparent life-threatening events was changed to brief resolved unexplained events (BRUEs). This guideline allowed for risk stratification and provided guidance for low-risk BRUE.

WHAT THIS STUDY ADDS: In this review of a pediatric multicenter administrative database, BRUE admissions decreased after guideline implementation without an increase in revisits or high-acuity diagnoses. These findings reveal that changes in practice have not resulted in worse outcomes.

ARTICLE

In 2016, the subcommittee on apparent life-threatening events (ALTEs) in the American Academy of Pediatrics published a practice guideline renaming ALTEs to brief resolved unexplained events (BRUEs).[1] ALTE was defined in 1986 as "a frightening episode to the caregiver with apnea, choking, gagging, or changes in color, or muscle tone."[2] BRUE refers to a diagnosis of exclusion in which a normal-appearing infant at presentation has an event characterized by a combination of changes in color (cyanosis or pallor), breathing, tone, or responsiveness and for whom no other identifiable cause for the event can be detected on the basis of history and physical examination.[1] The guideline not only redefined concerning episodes for pediatricians but also provided recommendations regarding risk stratification and management for patients with low-risk BRUE.

It is unknown whether the guideline has resulted in hospital-based management changes for infants with BRUE, including rates of admission and diagnostic testing. Furthermore, it is unknown if practice changes have resulted in alterations in rates of serious outcomes. The majority of research addressing ALTE and BRUE are single-center studies.[3–12] In no previous analyses, within the United States[13] or internationally,[14] have authors, using administrative data sets, evaluated if changes in management of BRUE after guideline implementation resulted in poor outcomes or emergency department (ED) revisits. Given the rarity of poor outcomes associated with ALTE and BRUE,[15,16] the use of large data sets is necessary to evaluate outcomes and to measure trends across multiple institutions.

Our primary objective for this study was to compare rates of admission for patients with ALTE or BRUE since the publication of the guideline. Our secondary objectives were to measure changes in the frequency of specific diagnostic tests and in the frequency of revisits to the ED. We hypothesized that, after publication of the guideline, the frequency of testing would decline and the rate of ED revisits would increase.

METHODS

Data Source

We used the Pediatric Health Information System, an administrative database that contains ED, inpatient, ambulatory surgery, and observation data from children's hospitals in the United States affiliated with the Children's Hospital Association (Overland Park, KS). Contributing hospitals are located in 26 states and the District of Columbia. Data are de-identified but are given unique patient identifiers to facilitate tracking across multiple encounters. The Children's Hospital Association and participating hospitals jointly ensure the data quality and integrity. The University of Pittsburgh Institutional Review Board deemed this study exempt from requirements for informed consent. We excluded data from 5 sites because of insufficient or incomplete data.

Patient Inclusion and Exclusion

We included patients ≤365 days of age with *International Classification of Diseases, Ninth Revision* (ICD-9) and *International Classification of Diseases, 10th Revision* (ICD-10) primary or secondary diagnosis codes for ALTE and BRUE between 2015 and 2017. During this period, ALTE and BRUE shared a single ICD-9 or ICD-10 code (ICD-9 code 788.2 before October 1, 2015, and ICD-10 code R68.13 after this date). Patients >1 year of age and encounters for ambulatory surgery were excluded. Because data from referring hospitals were not available, we excluded patients transferred from a referring hospital. We analyzed patients in subgroups of 0 to 60 and 61 to 365 days of age.

Control Cohort

To evaluate if outcomes were confounded by secular trends, we identified a separate control cohort of all ED encounters from infants ≤365 days of age in the studied hospitals during the inclusion period without an ICD-9 or ICD-10 code of ALTE or BRUE using the same exclusions as the primary cohort.

Data Abstraction

For all patients, we abstracted age, sex, race, ethnicity, hospital region using US Census categories (Northeast, South, Midwest, West), and payment (classified into public, private, self-pay, and other or unknown) data. Admission was defined as hospital admission or observation status. We included observation status as a type of hospitalization because observations refer to a billing designation for hospitalization lengths of stay lasting ≤48 hours and constitute up to 40% of pediatric admissions for visits <1 day in duration.[17] Additionally, resource use between observation and inpatient stays overlap substantially, suggesting that observation visits do not account for a lower-acuity cohort of patients.[18] Using billing codes, we identified whether the following tests were performed during hospitalization: (1) clinical studies of electrocardiogram (ECG) and EEG; (2) testing of cerebrospinal fluid (CSF); (3) imaging for computed tomography (CT) of the head, MRI of the brain, echocardiography, chest radiography, abdominal ultrasound, and gastrointestinal fluoroscopy; and (4) testing for blood gas, blood glucose measurement, electrolyte measurement, hepatic function panel testing, hematologic testing, *Bordetella pertussis* testing, urine studies, and testing for inborn errors of metabolism. Tests for inborn errors of metabolism included tests

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for aldolase, alkaline phosphatase isoenzyme, amino acids and peptides, ammonia, angiotensin-converting enzyme, biotinidase, carbohydrate metabolites, carnitine, ceruloplasmin, copper, creatine kinase, cystatin, galactose, glucagon, glucose-6-phosphate dehydrogenase, glutathione reductase, hexosaminidase, homocysteine, ketone bodies, lactic acid, methylmalonic acid, mucopolysaccharides, pyruvate kinase, pyric acid, tyrosine, uric acid, and very long–chain fatty acid as well as tests for other specified amino acids and peptides, other specified carbohydrates and metabolites, other specified enzyme and isoenzymes, and phenylketonuria.

Because ALTE or BRUE may represent sentinel events of diseases with delayed presentations, we evaluated diagnoses on patient revisits. We used the *International Classification of Diseases* (ICD)–based diagnosis grouping system (DGS) developed by the Pediatric Emergency Care Applied Research Network (PECARN) Core Data Project, in which ICD-9 codes were reclassified to form 21 major groups with 5 levels of acuity.[19,20] We converted ICD-10 codes to ICD-9 codes using the general equivalence mappings developed and maintained by the Centers for Medicare and Medicaid services.[21] Because our interest lied in identifying potential missed pathologies, only diagnoses of high acuity, (severity scores of 4 and 5) were retained.[20]

Analysis 1: ALTE or BRUE Management Before and After Guideline

Our primary outcome was rate of admission. Our secondary outcomes were rates of revisits and studies performed on index visit. We compared patients admitted in 2015 (2015 cohort; before guideline publication) with those seen in 2017 (2017 cohort; after guideline

publication) by reporting the difference in proportions with 95% confidence intervals (CIs). To assess for the interaction of secular trends on the rates of ALTE or BRUE management, we developed separate models for each variable of interest using multivariable logistic regression. Each variable of interest (ie, rate of admission, performance of chest radiography, etc) was used as an outcome. Covariates included time period (2015 or 2017), ALTE or BRUE diagnosis, and an interaction effect between an ALTE or BRUE diagnosis and the time period. A positive interaction effect for an outcome of interest would reveal an increasing rate of that outcome over time, irrespective of overall trends in patients (with inclusion of all patients in the control cohort), and a negative interaction effect would signify the opposite.

Analysis 2: Interrupted Time Series Analysis

We conducted an interrupted time series analysis (ITSA) with segmented linear regression models to evaluate trends of admission over time. An ITSA is a quasi-experimental methodology to evaluate the effect of sudden events (such as a dissemination of a guideline) on time series data.[22] The ITSA allows for identification of both a discrete change of rate and changes in trends (ie, slope) related to the event. Our outcome was admission rate (admissions over total encounters), parceled into 1-week bins. We included eligible encounters for the week starting on January 4, 2015 (the first full week in the inclusion period), to December 24, 2017 (the last full week in the inclusion period). Because our aim was to assess for a change in rates of admission before and after guideline dissemination, patients from the year 2016 were included for this analysis. The intervention period was after the week ending April 30, 2016 (week 69), because the guideline was

electronically published April 25, 2016. We determined the baseline admission rate ($\beta 0$), baseline trend over time in admission rate ($\beta 1$), and whether the introduction of the guideline was associated with a change in the outcome level ($\beta 2$) or a change in trend over time ($\beta 3$) using ordinary least squares regression. Autocorrelation was tested by using the generalized Durbin-Watson test. The study and control cohorts were analyzed separately. In a separate analysis for patients diagnosed with ALTE or BRUE presenting after guideline implementation (weeks 70–156), we performed linear regression to assess if the week of presentation (independent variable) was associated with a change in the number of patients diagnosed with this condition (dependent variable). We considered tests with $P < .05$ statistically significant.

Analyses were conducted with R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/) and Stata version 15.1 (StataCorp LLC, College Station, TX).

RESULTS

Study Inclusion

Of 16 556 infants identified from the initial search query, 9501 patients were retained in the cohort analysis and 13 977 were retained for the ITSA (Fig 1). The control cohort included 1 386 190 patients.

Analysis 1: Admissions, Interventions, and Revisits in Cohorts

Demographics

A total of 5508 patients were 0 to 60 days of age (3238 in the 2015 cohort and 2270 in the 2017 cohort), and 3993 patients were 61 to 365 days of age (2370 in the 2015 cohort and 1623 in the 2017 cohort) (Table 1). There were 26.8% less 0- to 60-day-old patients and 31.5% less
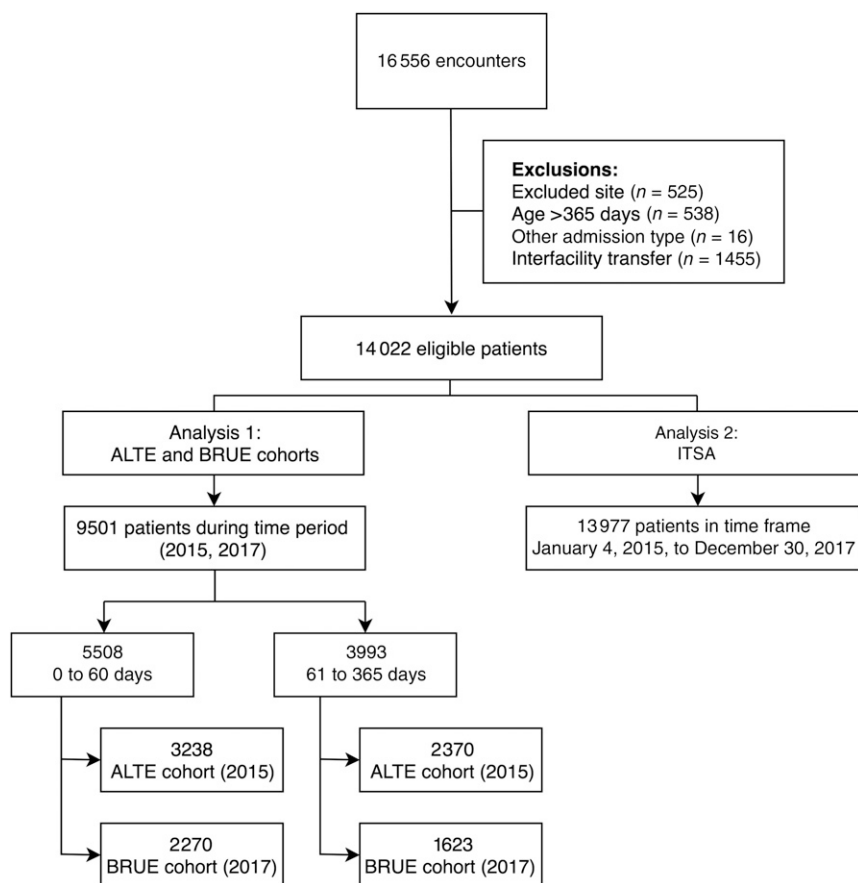
FIGURE 1
Study patient inclusion.

61- to 365-day-old patients in the 2017 cohort compared with the 2015 cohort. Overall rates of high-acuity diagnoses were lower in the 2017 cohort (Table 2).

Admissions and Interventions on Initial Visit

The proportions of admissions in the 2017 cohort were lower than in the 2015 cohort in both age groups, particularly for infants 61 to 365 days of age (from 86.2% in 2015 to 68.2% in 2017; percent difference: 18.0% [95% CI, 15.3% to 20.7%]) (Table 3). Across both age groups, patients in 2017 had lower rates of EEGs, brain MRIs, chest radiographs, complete blood counts, electrolyte studies, hepatic function panels, and urinalyses performed. Infants 0 to 60 days of age had lower rates of blood gas measurement, capillary

blood sugar testing, head CT, metabolic studies, and CSF testing performed in the 2017 cohort.

Revisits

In patients 0 to 60 days of age, the proportion with 3-day revisits were slightly lower in the 2017 cohort compared with the 2015 cohort (from 5.2% in 2015 to 3.7% in 2017; percent difference: 1.5% [95% CI, 0.4% to 2.6%]). In all other tested return periods, revisit rates were similar (Table 4). Rates of clinical testing (Supplemental Table 6) and significant diagnoses during revisits were similar (Supplemental Table 7).

Comparison With Control Cohort

The control cohort included 458 476 patients in 2015 and 464 616 in 2017. Diagnoses on initial visits are presented in Supplemental Table 8.

The difference in proportions for all outcomes was <1% (Supplemental Table 9). For outcomes of admission (EEG, head CT, brain MRI, chest radiography, upper gastrointestinal series, blood gas measurement, capillary blood sugar measurement, complete blood count, electrolyte studies, hepatic function studies, CSF testing, urinalyses, metabolic studies, and 3-day revisits), there was a negative interaction between time and ALTE or BRUE diagnosis (Supplemental Table 10), suggesting that the decreased rates of these outcomes in patients with ALTE or BRUE are independent of secular trends over time.

Analysis 2: ITSA

Of 13 977 patients included for ITSA, 8120 (58.1%) were 0 to 60 days of age and 5857 (41.9%) were 61 to 365 days of age. The starting level of admission proportion ($\beta 0$) was 0.897 and 0.865 in infants 0 to 60 days of age and 61 to 365 days of age, respectively, without a detectable trend over time in either group ($\beta 1$). Guideline publication was associated with an immediate change in the rate of admission ($\beta 2$) for infants 0 to 60 days of age (−0.047; 95% CI, −0.077 to −0.017; $P = .002$) and for infants 61 to 365 days of age (−0.046; 95% CI, −0.086 to −0.007; $P = .022$). Guideline publication was not associated with any change in trend in admission rates ($\beta 3$) for infants 0 to 60 days of age, but rates of admission decreased weekly after guideline publication for infants 61 to 365 days of age (−0.002; 95% CI, −0.003 to −0.001; $P < .001$) (Table 5, Fig 2). A control ITSA of 1 378 332 ED encounters (258 882 infants 0–60 days of age and 1 119 450 infants 61–365 days of age) during the same period did not reveal changes in the level or slope of admissions (Supplemental Table 11). After guideline implementation, there was no weekly trend in rates of diagnosis of BRUE for patients overall (slope: 0.00; $P = .96$) or for patients in

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TABLE 1 Demographics of Included Infants in the 2015 and 2017 Cohorts

	Total	2015 Cohort	2017 Cohort
Patients 0–60 d of age			
No. ED encounters	5508	3238	2270
Age, median (IQR), d	25 (12–41)	25 (12–41)	24 (11–41)
No. boys (%)	2594 (47.1)	1520 (46.9)	1074 (47.3)
Race, *n* (%)			
White	3002 (54.5)	1784 (55.1)	1218 (53.7)
African American	1316 (23.9)	777 (24.0)	539 (23.7)
Asian American	79 (1.4)	48 (1.5)	31 (1.4)
Other or unknown	1111 (20.2)	629 (19.4)	482 (21.2)
Ethnicity, *n* (%)			
Hispanic	1181 (21.4)	683 (21.1)	498 (21.9)
Not Hispanic	3925 (71.3)	2333 (72.1)	1592 (70.1)
Not known	402 (7.3)	222 (6.9)	180 (7.9)
Geographic region, *n* (%)			
Midwest	1184 (21.5)	711 (22.)	473 (20.8)
South	2497 (45.3)	1475 (45.6)	1022 (45.0)
Northeast	803 (14.6)	455 (14.1)	348 (15.3)
West	1024 (18.6)	597 (18.4)	427 (18.8)
Payment, *n* (%)			
Public insurance	3796 (68.9)	2274 (70.2)	1522 (67.0)
Private insurance	1434 (26.0)	839 (25.9)	595 (26.2)
Self-pay	159 (2.9)	85 (2.6)	74 (3.3)
Other or unknown	119 (2.2)	40 (1.2)	79 (3.5)
Patients 61–365 d of age			
No. ED encounters	3993	2370	1623
Age, median (IQR), d	113 (80–182)	113 (81–178)	112 (80–186)
No. boys (%)	2080 (52.1)	1243 (52.4)	837 (51.6)
Race, *n* (%)			
White	2294 (57.5)	1370 (57.8)	924 (56.9)
African American	823 (20.6)	491 (20.7)	332 (20.5)
Asian American	52 (1.3)	33 (1.4)	19 (1.2)
Other or unknown	824 (20.6)	476 (20.1)	348 (21.4)
Ethnicity, *n* (%)			
Hispanic	865 (21.7)	501 (21.1)	364 (22.4)
Not Hispanic	2846 (71.3)	1723 (72.7)	1123 (69.2)
Not known	282 (7.1)	146 (6.2)	136 (8.4)
Geographic region, *n* (%)			
Midwest	845 (21.2)	529 (22.3)	316 (19.5)
South	1784 (44.7)	1049 (44.3)	735 (45.3)
Northeast	538 (13.5)	305 (12.9)	233 (14.4)
West	826 (20.7)	487 (20.5)	339 (20.9)
Payment, *n* (%)			
Public insurance	2837 (71.0)	1719 (72.5)	1118 (68.9)
Private insurance	999 (25.0)	582 (24.6)	417 (25.7)
Self-pay	77 (1.9)	44 (1.9)	33 (2.0)
Other or unknown	80 (2.0)	25 (1.1)	55 (3.4)

IQR, interquartile range.

the 0- to 60-day (slope: 0.01; *P* = .84) or 61- to 365-day (slope: −0.01; *P* = .62) age groups assessed by linear regression.

DISCUSSION

Through an evaluation of a large nationally representative registry of pediatric hospitals, we identified significant reductions in rates of admission and diagnostic testing for patients with ALTE or BRUE in 2017 compared with those with ALTE or BRUE in 2015. Additionally, the proportion of infants diagnosed with BRUE or ALTE in 2017 was ~25% lower than that of infants diagnosed with BRUE or ALTE in 2015. After publication of the guideline, the admission rate for infants aged 61 to 365 days with BRUE or ALTE decreased steadily over the next 20 months.

The rate of admissions for patients with ALTE or BRUE in 2017 was lower than the rate of admissions for patients diagnosed with ALTE or BRUE in 2015, particularly for older infants. Although the guideline does not clearly recommend dispositions for patients, it does aim to reduce

TABLE 2 Associated Diagnoses of High Acuity (PECARN DGS Severity Scores 4 and 5) From Initial Visits for Infants in the 2015 and 2017 Study Cohorts

	0–60 d of Age			61–365 d of Age		
	2015 Cohort (n = 3238), n (%)	2017 Cohort (n = 2270), n (%)	Percentage Difference (95% CI)	2015 Cohort (n = 2370), n (%)	2017 Cohort (n = 1623), n (%)	Percentage Difference (95% CI)
Patients with additional diagnosis	954 (29.5)	582 (25.6)	3.8 (1.4 to 6.2)[a]	679 (28.6)	377 (23.2)	5.4 (2.6 to 8.2)[a]
Allergic, immunologic, and rheumatologic	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.1)	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.2)
Child abuse	0 (0.0)	0 (0.0)	—	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.2)
Circulatory and cardiovascular disease	96 (3.0)	27 (1.2)	1.8 (1.0 to 2.5)[a]	114 (4.8)	69 (4.3)	0.6 (−0.8 to 1.9)
Eye disease	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.1)	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.2)
Endocrine, metabolic, and nutritional disease	47 (1.5)	35 (1.5)	−0.1 (−0.8 to 0.6)	52 (2.2)	25 (1.5)	0.7 (−0.2 to 1.5)
ENT, dental, and mouth disease	78 (2.4)	34 (1.5)	0.9 (0.1 to 1.7)[a]	50 (2.1)	5 (0.3)	1.8 (1.1 to 2.5)[a]
Fluid and electrolyte disorders	22 (0.7)	15 (0.7)	0.0 (−0.4 to 0.5)	31 (1.3)	19 (1.2)	0.1 (−0.6 to 0.9)
Gastrointestinal disease	12 (0.4)	2 (0.1)	0.3 (0.0 to 0.6)	6 (0.3)	2 (0.1)	0.1 (−0.2 to 0.4)
Genital and reproductive disease	0 (0.0)	1 (0.0)	0.0 (−0.2 to 0.1)	0 (0.0)	0 (0.0)	—
Hematologic disease	13 (0.4)	7 (0.3)	0.1 (−0.3 to 0.4)	3 (0.1)	1 (0.1)	0.1 (−0.2 to 0.3)
Musculoskeletal and connective-tissue disease	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.1)	1 (0.0)	2 (0.1)	−0.1 (−0.3 to 0.2)
Neoplastic disease (cancer, not benign neoplasms)	0 (0.0)	0 (0.0)	—	0 (0.0)	1 (0.1)	−0.1 (−0.2 to 0.1)
Neurologic disease	100 (3.1)	55 (2.4)	0.7 (−0.2 to 1.6)	132 (5.6)	55 (3.4)	2.2 (0.9 to 3.5)[a]
Psychiatric, behavioral, and substance abuse	1 (0.0)	0 (0.0)	0.0 (−0.1 to 0.1)	0 (0.0)	1 (0.1)	0.0 (−0.2 to 0.1)
Respiratory disease	433 (13.4)	224 (9.9)	3.5 (1.8 to 5.2)[a]	397 (16.8)	259 (16.0)	0.8 (−1.6 to 3.2)
Skin, dermatologic, and soft-tissue disease	0 (0.0)	0 (0.0)	—	0 (0.0)	0 (0.0)	—
Systemic states	53 (1.6)	46 (2.0)	−0.4 (−1.2 to 0.4)	49 (2.1)	46 (2.8)	−0.8 (−1.8 to 0.3)
Toxicological emergencies	0 (0.0)	0 (0.0)	—	2 (0.1)	0 (0.0)	0.1 (−0.1 to 0.3)
Trauma	2 (0.1)	0 (0.0)	0.1 (−0.1 to 0.2)	7 (0.3)	0 (0.0)	0.3 (0.0 to 0.6)[a]
Urinary tract disease	16 (0.5)	9 (0.4)	0.1 (−0.3 to 0.5)	10 (0.4)	1 (0.1)	0.4 (0.0 to 0.7)[a]
Other	365 (11.3)	241 (10.6)	0.7 (−1.1 to 2.4)	35 (1.5)	14 (0.9)	0.6 (−0.1 to 1.3)

Because patients may have >1 high-acuity diagnosis, summed numbers of individual diagnoses do not equal total patients with high-acuity diagnoses. ENT, ear, nose, and throat; —, not applicable.

[a] 95% CIs do not cross 0.

rates of clinical, radiologic, and laboratory testing for patients with low-risk BRUE. This reduction did not appear to increase the rate of revisits. A decreased rate of testing additionally carries the benefit of decreased requirement for venipuncture, radiation exposure, hospital length of stay, and cost. Previous concerns for missed sudden infant death syndrome led experts to initially recommend routine admission for all patients with ALTE.[7,23,24] Subsequent research has revealed that the majority of patients with ALTE do not require hospitalization.[11,12,14,25,26] Because BRUE is a diagnosis of exclusion, this group may have an even lower requirement for admission and

cardiorespiratory monitoring, although this will require further prospective evaluation. Additionally, associated high-acuity diagnoses for patients in 2017 were lower in both initial visits and revisits, which may relate to the changing case definition of BRUE, resulting in a cohort of patients with lower acuity who require less testing. Notably, we found a reduction in rates of admission and diagnostic testing in infants 0 to 60 days of age, a group that is at higher risk on the basis of age, despite the fact that the guideline does not provide recommendations to this subset of infants. We were unable to classify infants 61 to 365 days of age within this administrative data set into low- and higher-risk groups

using billing data. However, in our evaluation of the number of infants diagnosed with BRUE after guideline implementation, we did not identify a statistically significant declining rate of patients with BRUE from week to week, suggesting that the lower rate of admissions was not only because the diagnosis of BRUE was being applied toward a smaller but progressively lower-risk group of infants over time, although the possibility of a type II error remains.

Fewer patients were diagnosed with ALTE or BRUE in 2017 than those diagnosed with ALTE in 2015. This difference is likely because BRUE is a diagnosis of exclusion. ALTE has previously been associated with

TABLE 3 Rates of Admission and Evaluations Performed for Infants in the 2015 and 2017 Study Cohorts

	0–60 d of Age			61–365 d of Age		
	2015 Cohort (n = 3238), n (%)	2017 Cohort (n = 2270), n (%)	Percent Difference (95% CI)	2015 Cohort (n = 2370), n (%)	2017 Cohort (n = 1623), n (%)	Percent Difference (95% CI)
Admitted from ED	2908 (89.8)	1910 (84.1)	5.7 (3.8 to 7.5)[a]	2043 (86.2)	1107 (68.2)	18.0 (15.3 to 20.7)[a]
Clinical investigations						
ECG	1230 (38.0)	905 (39.9)	−1.9 (−4.5 to 0.8)	924 (39.0)	630 (38.8)	0.2 (−0.3 to 3.3)
EEG	390 (12.0)	200 (8.8)	3.2 (1.6 to 4.9)[a]	452 (19.1)	257 (15.8)	3.2 (0.8 to 5.7)[a]
Radiology studies						
Head CT	253 (7.8)	133 (5.9)	2.0 (0.6 to 3.3)[a]	240 (10.1)	151 (9.3)	0.8 (−1.1 to 2.7)
Brain MRI	124 (3.8)	58 (2.6)	1.3 (0.3 to 2.2)[a]	146 (6.2)	76 (4.7)	1.5 (0.0 to 2.9)[a]
Echocardiogram	406 (12.5)	273 (12.0)	0.5 (−1.3 to 2.3)	254 (10.7)	147 (9.1)	1.7 (−0.3 to 3.6)
Chest radiograph	1515 (46.8)	839 (37.0)	9.8 (7.2 to 12.5)[a]	1144 (48.3)	597 (36.8)	11.5 (8.3 to 14.6)[a]
Abdominal sonogram	109 (3.4)	76 (3.3)	0.0 (−1.0 to 1.0)	78 (3.3)	44 (2.7)	0.6 (−0.5 to 1.7)
Upper gastrointestinal series	128 (4.0)	45 (2.0)	2.0 (1.1 to 2.9)[a]	84 (3.5)	41 (2.5)	1.0 (−0.1 to 2.1)
Laboratory studies						
Blood gas	389 (12.0)	216 (9.5)	2.5 (0.8 to 4.2)[a]	274 (11.6)	160 (9.9)	1.7 (−0.3 to 3.7)
Capillary blood sugar	749 (23.1)	435 (19.2)	4.0 (1.8 to 6.2)[a]	440 (18.6)	274 (16.9)	1.7 (−0.8 to 4.1)
Complete blood count	1580 (48.8)	860 (37.9)	10.9 (8.2 to 13.6)[a]	1049 (44.3)	555 (34.2)	10.1 (7.0 to 13.2)[a]
Electrolyte studies	1508 (46.6)	872 (38.4)	8.2 (5.5 to 10.8)[a]	1065 (44.9)	593 (36.5)	8.4 (5.3 to 11.5)[a]
Hepatic function studies	1059 (32.7)	646 (28.5)	4.2 (1.7 to 6.7)[a]	583 (24.6)	339 (20.9)	3.7 (1.0 to 6.4)[a]
CSF studies	545 (16.8)	265 (11.7)	5.2 (3.3 to 7.0)[a]	127 (5.4)	67 (4.1)	1.2 (−0.1 to 2.6)
Urinalysis	940 (29.0)	501 (22.1)	7.0 (4.6 to 9.3)[a]	525 (22.2)	264 (16.3)	5.9 (3.4 to 8.4)[a]
Metabolic studies	281 (8.7)	144 (6.3)	2.3 (0.9 to 3.8)[a]	205 (8.6)	116 (7.1)	1.5 (−0.2 to 3.2)
B pertussis testing	21 (0.6)	14 (0.6)	0.0 (−0.4 to 0.5)	36 (1.5)	15 (0.9)	0.6 (−0.1 to 1.3)

[a] 95% CIs do not cross 0.

nonaccidental trauma,[3–5] seizures,[6,7] infections,[27] metabolic disease,[28] and cardiac disease.[8] The association of these and other diagnoses with BRUE remains unexplored. Patients with corresponding historical or physical examination characteristics for a secondary condition would not fit under the diagnostic criteria for BRUE. Two retrospective single-center studies have revealed widely varying proportions of patients with ALTE who meet criteria for BRUE.[9,10] In our review of a single-center prospective registry, approximately half of patients diagnosed with ALTE met criteria for BRUE, although patients with higher-risk BRUE and ALTE had similar rates of deleterious health outcomes, including repeat ALTE events, trauma, airway abnormalities, and infection.[29] Our finding that patients with BRUE had lower rates of serious diagnoses on their initial visit supports appropriate guideline use and the classification of BRUE toward a subset of patients with lower rates of significant comorbid disease. However, it is notable that significant outcomes in patients with BRUE were not eliminated entirely, suggesting that a high degree of vigilance is required in the evaluation of these patients.[1]

These findings have implications for research efforts. The test characteristics of the guideline require prospective validation. Because a goal of the guideline is to promote the development of distinct ICD codes for low- and high-risk BRUE, future research may be able to identify the rates of serious pathology, including traumatic, cardiac, neurologic, and infectious diagnoses in patients categorized as having low-risk BRUE.

Our study is subject to the limitations of using administrative databases, including limitations with detail availability and coding accuracy.[30]

TABLE 4 Rates of Repeat Visits for Patients in the 2015 and 2017 Study Cohorts

	0–60 d of Age			61–365 d of Age		
	2015 Cohort (n = 3238), n (%)	2017 Cohort (n = 2270), n (%)	Percent Difference (95% CI)	2015 Cohort (n = 2370), n (%)	2017 Cohort (n = 1623), n (%)	Percent Difference (95% CI)
3-d revisits	168 (5.2)	84 (3.7)	1.5 (0.4 to 2.6)[a]	138 (5.8)	111 (6.8)	−1.0 (−2.6 to 0.6)
7-d revisits	256 (7.9)	150 (6.6)	1.3 (−0.1 to 2.7)	208 (8.8)	164 (10.1)	−1.3 (−3.2 to 0.6)
30-d revisits	561 (17.3)	370 (16.3)	1.0 (−1.0 to 3.1)	409 (17.3)	318 (19.6)	−2.3 (−4.8 to 0.2)
No revisit	2677 (82.7)	1900 (83.7)	−1.0 (−3.1 to 1.0)	1961 (82.7)	1305 (80.4)	2.3 (−0.2 to 4.8)

[a] 95% CIs do not cross 0.

TABLE 5 ITSA of Weekly Admission Rates for Patients in the Study Cohort Before and After Guideline Publication

	Estimate (95% CI)	P
Infants 0–60 d of age		
Intercept (β0)	0.897 (0.882 to 0.913)	<.001
Baseline trend (β1)	0.000 (0.000 to 0.001)	.517
Level change after guideline (β2)	−0.047 (−0.077 to −0.017)	.002
Trend change after guideline (β3)	0.000 (−0.001 to 0.000)	.214
Postintervention linear trend	0.000 (−0.001 to 0.000)	.273
Infants 61–365 d of age		
Intercept (β0)	0.865 (0.840 to 0.891)	<.001
Baseline trend (β1)	0.000 (−0.001 to 0.000)	.605
Level change after guideline (β2)	−0.046 (−0.086 to −0.007)	.022
Trend change after guideline (β3)	−0.002 (−0.003 to −0.001)	<.001
Postintervention linear trend	−0.002 (−0.003 to −0.001)	<.001

Our intention a priori was to identify changes in management of BRUE after the implementation of a guideline. However, changes in rates of diagnoses of BRUE compared with ALTE require historical and physical examination data, which are not present in the Pediatric Health Information System. As such, we were unable to review cases for diagnostic suitability for ALTE or BRUE or to classify patients with BRUE into low- and higher-risk groups. Although this study was performed in the time period during which ICD codes
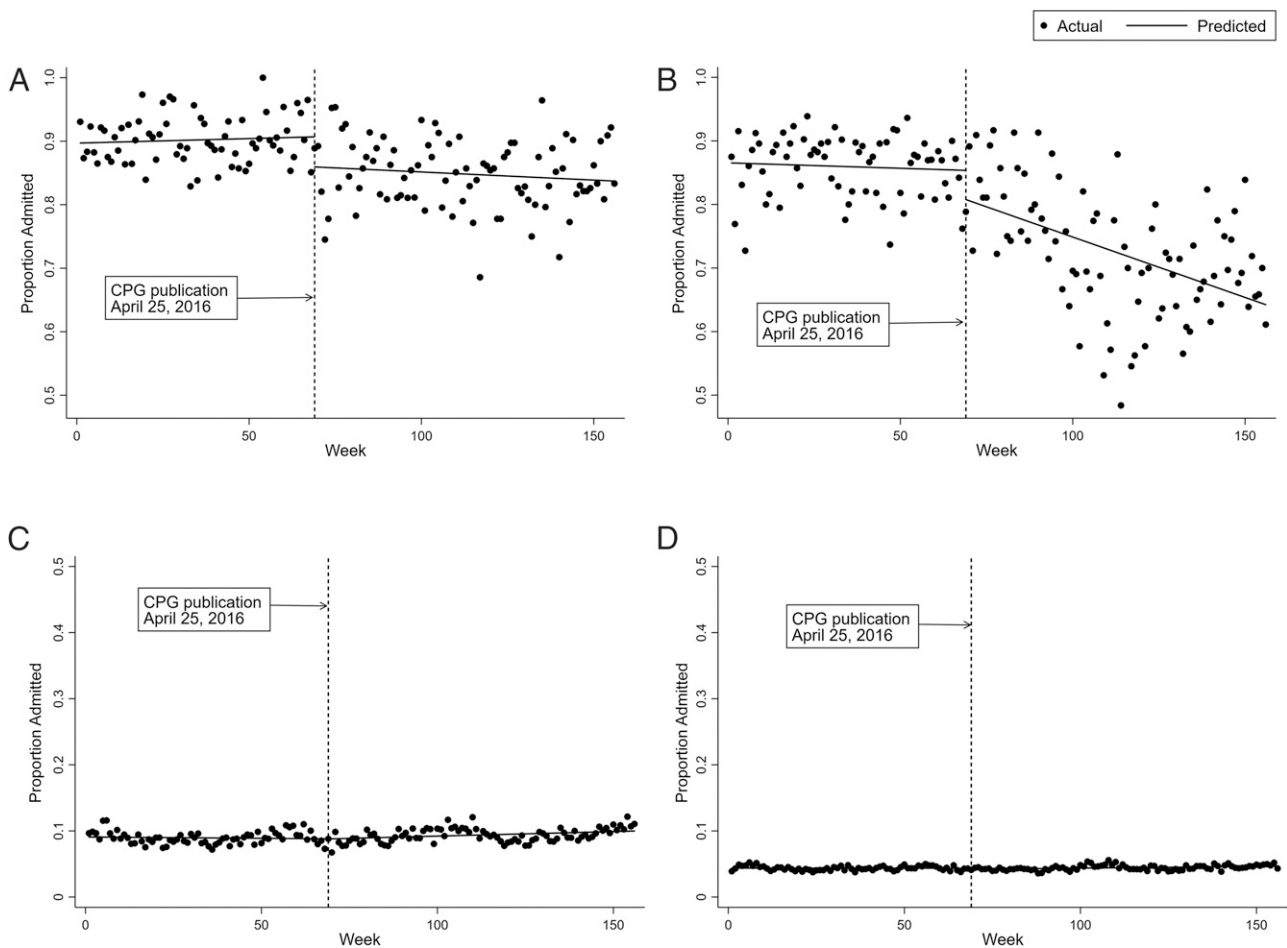

FIGURE 2
ITSA revealing predicted (solid line) and actual (discrete points) proportions of admissions for infants in weekly bins over the tested period. The dashed line represents date corresponding to electronic publication of the CPG. A, Infants 0 to 60 days of age with a diagnosis code for ALTE or BRUE. B, Infants 61 to 365 days of age with a diagnosis code for ALTE or BRUE. C, All infants 0 to 60 days of age evaluated in the ED with all other diagnoses. D, All infants 61 to 365 days of age evaluated in the ED with all other diagnoses. CPG, clinical practice guideline.

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transitioned from ICD-9 to ICD-10, a repeated analysis to coincide with changes after initiation of *ICD-10* in the United States between the periods of October 1, 2015, to April 30, 2016, and October 1, 2016, to April 30, 2017, revealed similar trends with respect to admission rates, investigations, revisits, and diagnoses, suggesting that this was likely not a confounder of our results (not shown). We were required to convert ICD-10 diagnoses to ICD-9 diagnoses using general equivalence mappings to classify diagnoses by using the DGS. Although this methodology has been previously validated in other populations, it has not been performed in the United States.[31] Despite these limitations, these findings reveal that the recent changes in management of BRUE have not resulted in missed diagnoses of significance.

CONCLUSIONS

Through an analysis of a multicenter, retrospective administrative database, we found that after institution of a practice guideline, fewer patients are diagnosed with ALTE or BRUE. These patients have a lower rate of diagnostic testing and a progressively lower rate of admission over time. Despite these changes in management, rates of revisits were slightly lower. These findings can serve as a basis for quality improvement efforts and future research in risk stratification of these infants.

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ABBREVIATIONS

ALTE: apparent life-threatening event
BRUE: brief resolved unexplained event
CI: confidence interval
CSF: cerebrospinal fluid
CT: computed tomography
DGS: diagnosis grouping system
ECG: electrocardiogram
ED: emergency department
ICD: *International Classification of Diseases*
ICD-9: *International Classification of Diseases, Ninth Revision*
ICD-10: *International Classification of Diseases, 10th Revision*
ITSA: interrupted time series analysis
PECARN: Pediatric Emergency Care Applied Research Network

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