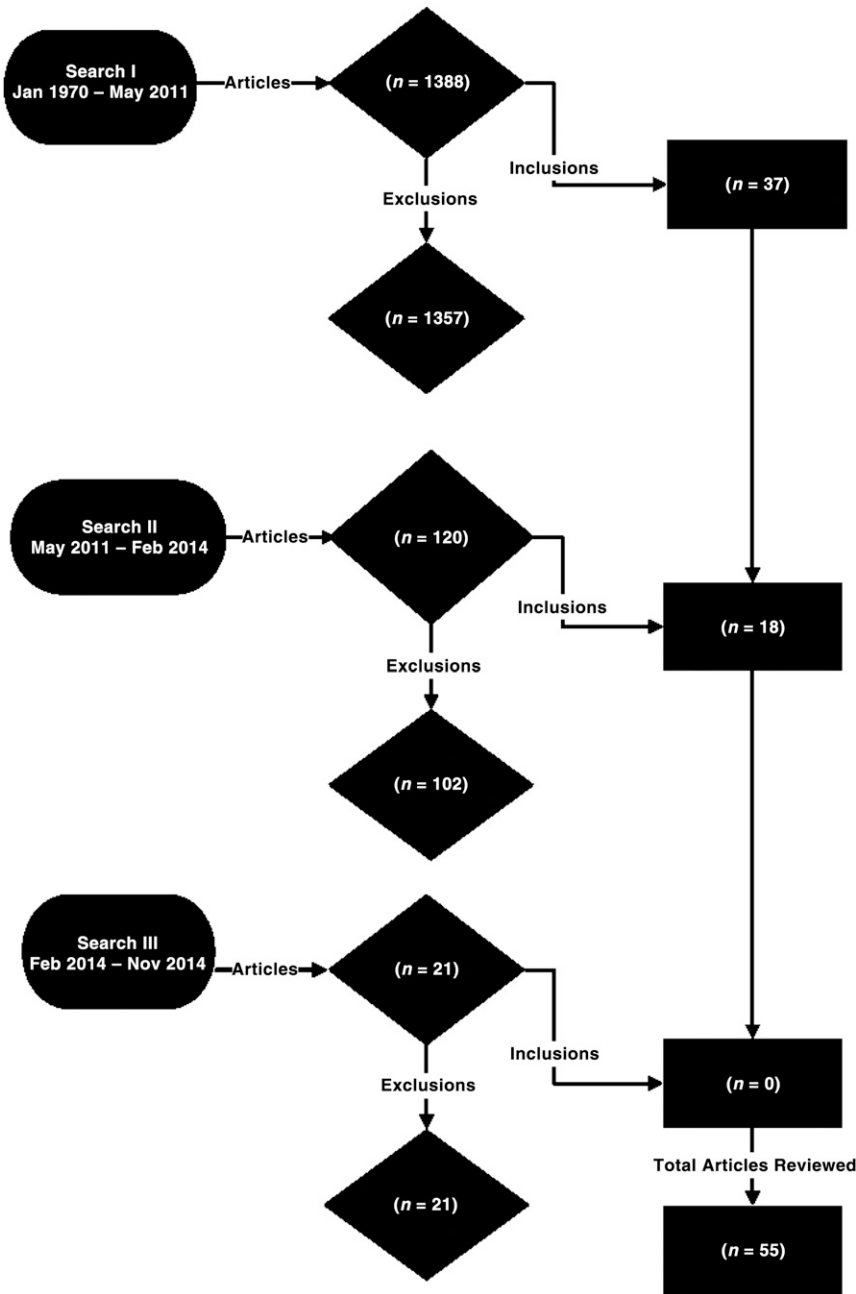


Supplemental Information



SUPPLEMENTAL FIGURE 3
BRUE literature search and identification of relevant articles.

SUPPLEMENTAL TABLE 6 Differential Diagnosis of an Infant Presenting With a Lower- or Higher-Risk BRUE

Otolaryngologic	Pulmonary
Maxillary hypoplasia	Aspiration
Micrognathia	Asthma
Macroglossia	Foreign body
Choanal atresia	Congenital airway anomalies/malacia
Pyramidal aperture stenosis	Infection
Laryngomalacia/anomalies	Hemorrhage
Subglottic stenosis	Upper and lower respiratory tract infection
Tracheomalacia/anomalies	Infectious
Adenotonsillar hypertrophy	Bronchiolitis
OSA	Pneumonia
Vaso-vagal response	Croup
Unintentional suffocation	Upper respiratory infection
Gastrointestinal	UTI
GER	Sepsis
Dysphagia/choking	Meningitis
Esophageal dysmotility	Gastroenteritis
Laryngeal chemoreflex	Viral syndrome
Bowel obstruction	Specific organisms (pertussis, RSV, and other respiratory viruses)
Gastroenteritis	Genetic/metabolic
Tracheoesophageal fistulas	IEMs (fatty acid oxidations disorders, urea cycle disorders)
Esophageal foreign body	Mitochondrial disorders
Intussusception	Electrolyte disturbance
Cardiovascular	Hypocalcemia
Channelopathies (prolonged QT syndromes, Brugada syndrome, short QT syndrome)	Hypoglycemia
Congenital heart disease	Child maltreatment
Cardiomyopathy/myocarditis	Abusive head trauma
Vascular ring/sling/compression	Caregiver-fabricated illness (also known as Münchausen by proxy and medical child abuse)
Ventricular pre-excitation (Wolff-Parkinson-White syndrome)	Intentional suffocation
Arrhythmia	Poisoning
Sepsis	Medical neglect
Syncope	Toxin exposure
Neurologic	Medication adverse effect
Seizures	Substance exposure via human milk
Stroke	Environmental exposure
Intracranial mass lesion	Vaccine reaction
Brain/intracranial structural or vascular abnormality	Miscellaneous
Intracranial hemorrhage	Acrocyanosis
Hydrocephalus	Hypothermia
Neuromuscular disorder	Breath-holding spell
Congenital central hypoventilation syndrome	Idiopathic
Apnea of prematurity	
Infant botulism	
Demyelinating disorder (transverse myelitis, multiple sclerosis, acute disseminated encephalomyelitis)	

SUPPLEMENTAL TABLE 7 Studies (N = 18) Included in the Updated Systematic Review: 2011–2014

First Author, Year	Ref	Study Design	Sample Size	Control Group	Primary Setting	Age	Inclusion Criteria	Exclusion Criteria	Follow-up Period	Outcome or Endpoint	Risk Factors Assessed	Major Findings Reported	Major Limitations or Sources of Bias
Anjos, 2009	13	Prospective cross-sectional	30	—	ED	0–24 mo	NIH definition Single ALTE		6 mo	Underlying disorder Morbidity/mortality	Discharge diagnosis, epilepsy, additional ALTE, PE finding, laboratories	Epilepsy should be included in differential diagnosis of ALTE, particularly a recurrent ALTE. 50% of cases were idiopathic. 13.4% of cases were caused by epilepsy/seizure disorder.	Methodologic flaws that affect conclusion No subjects considered low risk Small number
Doshi, 2012	14	Retrospective case series	313	—	IP	0–12 mo	NIH definition Single ALTE within 24 h of presenting	Prematurity PICU admission Known past medical history that may explain ALTE	6 mo	Need for hospitalization Details of PMH, HPI, PE	Medical history, discharge diagnosis	Identifies GERD as risk factor for readmission GERD patients are more likely to have rescue breaths and to call 911. History of choking events associated with GERD	Clinical diagnosis of GERD Common ED testing would have already been done
Franco, 2011	15	Retrospective case control	35	19						Underlying disorders Testing		Sleep arousal patterns of ALTE infants are different than those of historical comparison of SIDS infants.	Narrow case series Underpowered Methodologic flaws that affect conclusion

TABLE 7 Continued

First Author, Year	Ref	Study Design	Sample Size	Control Group	Primary Setting	Age	Inclusion Criteria	Exclusion Criteria	Follow-up Period	Outcome or Endpoint	Risk Factors Assessed	Major Findings Reported	Major Limitations or Sources of Bias
Hoki, 2012	16	Retrospective cohort	485	—	ED	<12 mo	NIH definition	Known past medical history that could explain ALTE Apparent diagnosis on presentation that could explain ALTE Respiratory findings Known child abuse	7.7 ± 1 y	Underlying disorders Testing	Family history of SIDS Prematurity Previous ALTEs Death	Majority of ALTEs are not of cardiac origin. If cardiac screening is undertaken, ECG is sensitive for significant arrhythmic and structural heart disease after ALTE.	No cardiac testing done in 55% of patients Family history not assessed uniformly
Kaji, 2013	17	Observational analysis	513	—	—	<12 mo	NIH definition EMS transported ALTEs	>12 mo; not transported by EMS	30 d	Need for hospitalization Critical care workup	Multiple ALTEs, suspicion for abuse	Approximately 10% of infants with ALTE brought in by EMS required pediatric critical care interventions Predictors of those warranting intensive care monitoring include a history of: resuscitation attempt, having ≥1 ALTE in 24 h, history of facial/body cyanosis	Generalizability Narrow case series
Kaji, 2013	6	Prospective cohort	832	—	ED	<12 mo	NIH definition	>1 y Repeat visit with ALTE within previous 72 h Another ALTE in ED Known child abuse, respiratory findings	1 wk	Need for hospitalization	Family history of SIDS Prematurity PE findings Laboratories Interventions Occurrence of additional ALTE Discharge diagnosis	Three criteria identified 89% of patients admitted with ALTE: obvious need for admission, significant medical history, and >1 ALTE in 24 h	Required 2 of 4 NIH definition criteria High percentage of study population had significant medical history (tertiary care bias)

TABLE 7 Continued

First Author, Year	Ref	Study Design	Sample Size	Control Group	Primary Setting	Age	Inclusion Criteria	Exclusion Criteria	Follow-up Period	Outcome or Endpoint	Risk Factors Assessed	Major Findings Reported	Major Limitations or Sources of Bias
Kant, 2013	18	Retrospective case series	174	—	ED	0–6 mo	NIH definition Single ALTE	Unstable vital signs, respiratory findings, PICU admission, history of seizure disorder (hypocalcemia)	34 mo	Morbidity/mortality Testing Need for hospitalization Details of PMH, HPI, PE Underlying disorders Testing	Previous ALTE Prematurity Death	Low but actual risk of mortality post-ALTE Two patients (1.1%) had died at time of follow-up; deaths occurred within 2 wk of ED visit. ALTE patients had increased arousal and increased NREM discontinuity as expressed by CAP analysis compared with controls. Increased arousal in ALTE subjects with no family history of SIDS may be a protective mechanism in contrast to previous report of decreased arousal in SIDS victims.	Underpowered Methodologic flaws that affect conclusion, including index case
Miano, 2012	19	Case/control	26	36	Single	0.5–9 mo	Single ALTE Within 24 h of presenting American Academy of Sleep Medicine definition			Testing	Medical records Family history of SIDS Prematurity PE findings Laboratories Interventions	ALTE patients had increased arousal and increased NREM discontinuity as expressed by CAP analysis compared with controls.	Small number
Mittal, 2012	20	Prospective cohort		—	ED	<12 mo	NIH definition Single ALTE	Apparent diagnosis on presentation that could explain the ALTE		Need for hospitalization Testing Critical care workup Morbidity/mortality	Medical history Prematurity Laboratories Death Interventions Features of ALTE event	Use of the clinical decision rule would have decreased hospital admissions by 40%.	One institution

TABLE 7 Continued

First Author, Year	Ref	Study Design	Sample Size	Control Group	Primary Setting	Age	Inclusion Criteria	Exclusion Criteria	Follow-up Period	Outcome or Endpoint	Risk Factors Assessed	Major Findings Reported	Major Limitations or Sources of Bias
Mittal, 2013	7	Prospective cohort	300		ED	<12 mo	NIH definition	Apparent diagnosis on presentation that could explain the ALTE	1 mo	Underlying disorders Testing Recurrence risk	Medical history PE findings Laboratories Interventions Discharge diagnosis Occurrence of additional ALTEs	An abnormal pneumogram is not predictive of an increased risk of recurrent ALTE. Infants with GERD diagnosis have an increased incidence of recurrent ALTE. Treatment of GERD with antireflux medications may reduce the incidence of recurrent ALTE.	
Mosalli, 2011	21	Retrospective cohort	25		IP	<12 mo	NIH definition Single ALTE Need for resuscitation in hospital	Known past medical history that could explain the ALTE		Underlying disorder	Maternal historical info, medical history, PE findings, laboratories	25(OH)D should be considered part of secondary biochemical assessment in infants with ALTE found to have hypocalcemia.	Narrow case series
Parker, 2011	22	Prospective cohort	563		IP	0–24 mo	NIH definition	Obvious diagnosis at time of presentation	1 y	ALTE definition, need for hospitalization, testing	Prematurity Family history of SIDS Previous ALTE(s), death, laboratories, intervention	Those with a diagnosis of child abuse are more likely to have abnormal PE and lower hemoglobin compared with those not abused.	Workup in ED did not adhere to existing guidelines

TABLE 7 Continued

First Author, Year	Ref	Study Design	Sample Size	Control Group	Primary Setting	Age	Inclusion Criteria	Exclusion Criteria	Follow-up Period	Outcome or Endpoint	Risk Factors Assessed	Major Findings Reported	Major Limitations or Sources of Bias
Poets, 2012	23	Case/control	34	93	Multi	<24 h	Severe ALTE definition	Prematurity		Details of PMH, HPI, PE	Medical records Historical information	The significant risk factors for severe ALTE or sudden infant death within 24 h of birth include primipara and being found in a potentially asphyxiating position.	
Semmekrot, 2010	24		115				Single ALTE 0–2 y			Underlying disorders Details of PMH, HPI, PE Testing Morbidity/mortality	Family history of SIDS Medical history Death Length of stay Laboratories Interventions Prematurity	10% recurrence rate ALTE patients were more likely to be pre- or post-term rather than full-term.	Findings do not support author's conclusion
Tieder, 2013	25	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Wasilewska, 2011	26	Prospective case/control	17	30	Single	Not stated	Single ALTE Definition from ESPID				Primary hospital records Laboratories (bBCM-7 and DPPIV activity)	Highest concentration of bBCM-7 in ALTE patients fed formula with casein All ALTE cases had lower DPPIV activity.	Controls were not appropriate Small number
Weiss, 2010	27	Retrospective case series	69	IP	IP	<12 mo	NIH definition Single ALTE			ALTE definition Testing Details of PMH, HPI, PE Discharge diagnosis	Hospital data (medical records) Prematurity Previous ALTEs	The yield of testing is very low.	Small number

TABLE 7 Continued

First Author, Year	Ref	Study Design	Sample Size	Control Group	Primary Setting	Age	Inclusion Criteria	Exclusion Criteria	Follow-up Period	Outcome or Endpoint	Risk Factors Assessed	Major Findings Reported	Major Limitations or Sources of Bias
Zimbric, 2012	28	Retrospective case series	469		IP	<12 mo	NIH definition Single ALTE	Known past medical history that could explain ALTE, prematurity, known child abuse, unstable vital signs	7.8 y (average)	Long-term outcomes of ALTE Mortality/morbidity Relevance of GI/GER Details of PMH, HPI, PE	Medical history Prematurity Previous ALTE(s) Interventions Discharge diagnosis Occurrence of additional ALTE(s)	Long-term outcomes of ALTE and recurrence are not affected by treatment with acid suppression therapy for GERD. Adverse outcomes associated with GERD are rare after an ALTE. Diagnosis of GER/GERD is not predictive of GI outcomes.	Clinical diagnosis of GERD Limited diagnostic testing

bBGM-7, bovine β -casomorphin-7; CAP, cycling alternating pattern; DPPIV, dipeptidyl peptidase-IV; ED, emergency department; EMS, emergency medical services; ESPID, European Society for Paediatric Infectious Diseases; GERD, gastroesophageal reflux disease; GI, gastrointestinal; HPI, history of present illness; IP, inpatient; N/A, not applicable; NIH, National Institutes of Health; NREM, non-rapid eye movement; PE, physical examination; PMH, past medical history; 25(OH)D, 25-hydroxyvitamin D.