CLINICAL PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics

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Brief Resolved Unexplained Events (Formerly Apparent Life-Threatening Events) and Evaluation of Lower-Risk Infants

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abstract

This is the first clinical practice guideline from the American Academy of Pediatrics that specifically applies to patients who have experienced an apparent life-threatening event (ALTE). This clinical practice guideline has 3 objectives. First, it recommends the replacement of the term ALTE with a new term, brief resolved unexplained event (BRUE). Second, it provides an approach to patient evaluation that is based on the risk that the infant will have a repeat event or has a serious underlying disorder. Finally, it provides management recommendations, or key action statements, for lower-risk infants. The term BRUE is defined as an event occurring in an infant younger than 1 year when the observer reports a sudden, brief, and now resolved episode of ≥1 of the following: (1) cyanosis or pallor; (2) absent, decreased, or irregular breathing; (3) marked change in tone (hyper- or hypotonia); and (4) altered level of responsiveness. A BRUE is diagnosed only when there is no explanation for a qualifying event after conducting an appropriate history and physical examination. By using this definition and framework, infants younger than 1 year who present with a BRUE are categorized either as (1) a lower-risk patient on the basis of history and physical examination for whom evidence-based recommendations for evaluation and management are offered or (2) a higher-risk patient whose history and physical examination suggest the need for further investigation and treatment but for whom recommendations are not offered. This clinical practice guideline is intended to foster a patient- and family-centered approach to care, reduce unnecessary and costly medical interventions, improve patient outcomes, support implementation, and provide direction for future research. Each key action statement indicates a level of evidence, the benefit-harm relationship, and the strength of recommendation.

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INTRODUCTION

This clinical practice guideline applies to infants younger than 1 year and is intended for pediatric clinicians. This guideline has 3 primary objectives. First, it recommends the replacement of the term apparent life-threatening event (ALTE) with a new term, brief resolved unexplained event (BRUE). Second, it provides an approach to patient evaluation that is based on the risk that the infant will have a recurring event or has a serious underlying disorder. Third, it provides evidence-based management recommendations, or key action statements, for lower-risk patients whose history and physical examination are normal. It does not offer recommendations for higher-risk patients whose history and physical examination suggest the need for further investigation and treatment (because of insufficient evidence or the availability of clinical practice guidelines specific to their presentation). This clinical practice guideline also provides implementation support and suggests directions for future research.

The term ALTE originated from a 1986 National Institutes of Health Consensus Conference on Infantile Apnea and was intended to replace the term "near-miss sudden infant death syndrome" (SIDS).[1] An ALTE was defined as "an episode that is frightening to the observer and that is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging. In some cases, the observer fears that the infant has died."[2] Although the definition of ALTE eventually enabled researchers to establish that these events are separate entities from SIDS, the clinical application of this classification, which describes a constellation of observed, subjective, and nonspecific symptoms, has raised significant challenges for clinicians and parents in the evaluation and care of these infants.[3] Although a broad range of disorders can present as an ALTE (eg, child abuse, congenital abnormalities, epilepsy, inborn errors of metabolism, and infections), for a majority of infants who appear well after the event, the risk of a serious underlying disorder or a recurrent event is extremely low.[2]

CHANGE IN TERMINOLOGY AND DIAGNOSIS

The imprecise nature of the original ALTE definition is difficult to apply to clinical care and research.[3] As a result, the clinician is often faced with several dilemmas. First, under the ALTE definition, the infant is often, but not necessarily, asymptomatic on presentation. The evaluation and management of symptomatic infants (eg, those with fever or respiratory distress) need to be distinguished from that of asymptomatic infants. Second, the reported symptoms under the ALTE definition, although often concerning to the caregiver, are not intrinsically life-threatening and frequently are a benign manifestation of normal infant physiology or a self-limited condition. A definition needs enough precision to allow the clinician to base clinical decisions on events that are characterized as abnormal after conducting a thorough history and physical examination. For example, a constellation of symptoms suggesting hemodynamic instability or central apnea needs to be distinguished from more common and less concerning events readily characterized as periodic breathing of the newborn, breath-holding spells, dysphagia, or gastroesophageal reflux (GER). Furthermore, events defined as ALTEs are rarely a manifestation of a more serious illness that, if left undiagnosed, could lead to morbidity or death. Yet, the perceived potential for recurring events or a serious underlying disorder often provokes concern in caregivers and clinicians.[2,4,5] This concern can compel testing or admission to the hospital for observation, which can increase parental anxiety and subject the patient to further risk and does not necessarily lead to a treatable diagnosis or prevention of future events. A more precise definition could prevent the overuse of medical interventions by helping clinicians distinguish infants with lower risk. Finally, the use of ALTE as a diagnosis may reinforce the caregivers' perceptions that the event was indeed "life-threatening," even when it most often was not. For these reasons, a replacement of the term ALTE with a more specific term could improve clinical care and management.

In this clinical practice guideline, a more precise definition is introduced for this group of clinical events: brief resolved unexplained event (BRUE). The term BRUE is intended to better reflect the transient nature and lack of clear cause and removes the "life-threatening" label. The authors of this guideline recommend that the term ALTE no longer be used by clinicians to describe an event or as a diagnosis. Rather, the term BRUE should be used to describe events occurring in infants younger than 1 year of age that are characterized by the observer as "brief" (lasting <1 minute but typically <20–30 seconds) and "resolved" (meaning the patient returned to baseline state of health after the event) and with a reassuring history, physical examination, and vital signs at the time of clinical evaluation by trained medical providers (Table 1). For example, the presence of respiratory symptoms or fever would preclude classification of an event as a BRUE. BRUEs are also "unexplained," meaning that a clinician is unable to explain the cause of the event after

an appropriate history and physical examination. Similarly, an event characterized as choking or gagging associated with spitting up is not included in the BRUE definition, because clinicians will want to pursue the cause of vomiting, which may be related to GER, infection, or central nervous system (CNS) disease. However, until BRUE-specific codes are available, for billing and coding purposes, it is reasonable to apply the ALTE International Classification of Diseases, 9th Revision, and International Classification of Diseases, 10th revision, codes to patients determined to have experienced a BRUE (see section entitled "Dissemination and Implementation").

TABLE 1 BRUE Definition and Factors for Inclusion and Exclusion

	Includes	Excludes
Brief	Duration <1 min; typically 20–30 s	Duration ≥1 min
Resolved	Patient returned to his or her baseline state of health after the event	At the time of medical evaluation:
	Normal vital signs	Fever or recent fever
	Normal appearance	Tachypnea, bradypnea, apnea
		Tachycardia or bradycardia
		Hypotension, hypertension, or hemodynamic instability
		Mental status changes, somnolence, lethargy
		Hypotonia or hypertonia
		Vomiting
		Bruising, petechiae, or other signs of injury/trauma
		Abnormal weight, growth, or head circumference
		Noisy breathing (stridor, sturgor, wheezing)
		Repeat event(s)
Unexplained	Not explained by an identifiable medical condition	Event consistent with GER, swallow dysfunction, nasal congestion, etc
		History or physical examination concerning for child abuse, congenital airway abnormality, etc
Event Characterization		
Cyanosis or pallor	Central cyanosis: blue or purple coloration of face, gums, trunk	Acrocyanosis or perioral cyanosis
	Central pallor: pale coloration of face or trunk	Rubor
Absent, decreased, or irregular breathing	Central apnea	Periodic breathing of the newborn
	Obstructive apnea	Breath-holding spell
	Mixed obstructive apnea	
Marked change in tone (hyper- or hypotonia)	Hypertonia	Hypertonia associated with crying, choking, or gagging due to GER or feeding problems
	Hypotonia	Tone changes associated with breath-holding spell
		Tonic eye deviation or nystagmus
		Tonic-clonic seizure activity
		Infantile spasms
Altered responsiveness	Loss of consciousness	Loss of consciousness associated with breath-holding spell
	Mental status change	
	Lethargy	
	Somnolence	
	Postictal phase	

BRUE DEFINITION

Clinicians should use the term BRUE to describe an event occurring in an infant <1 year of age when the observer reports a sudden, brief, and now resolved episode of ≥1 of the following:

- **cyanosis or pallor**
- **absent, decreased, or irregular breathing**
- **marked change in tone (hyper- or hypotonia)**
- **altered level of responsiveness**

Moreover, clinicians should diagnose a BRUE only when there is no explanation for a qualifying event after conducting an appropriate history and physical examination (Tables 2 and 3).

Differences between the terms ALTE and BRUE should be noted. First, the BRUE definition has a strict age limit. Second, an event is only a BRUE if there is no other likely explanation. Clinical symptoms such as fever, nasal congestion, and increased work of breathing may indicate temporary airway obstruction from viral infection. Events characterized as choking after vomiting may indicate a gastrointestinal cause, such as GER. Third, a BRUE diagnosis is based on the clinician's characterization of features of the event and not on a caregiver's perception that the event was life-threatening. Although such perceptions are understandable and important to address, such risk can only be assessed after the event has been objectively characterized by a clinician. Fourth, the clinician should determine whether the infant had episodic cyanosis or pallor, rather than just determining whether "color change" occurred. Episodes of rubor or redness are not consistent with BRUE, because they are common in healthy infants. Fifth, BRUE expands the respiratory criteria beyond "apnea" to include absent breathing, diminished breathing, and other breathing irregularities. Sixth, instead of the less specific criterion of "change in muscle tone," the clinician should determine whether there was marked change in tone, including

hypertonia or hypotonia. Seventh, because choking and gagging usually indicate common diagnoses such as GER or respiratory infection, their presence suggests an event was not a BRUE. Finally, the use of "altered level of responsiveness" is a new criterion, because it can be an important component of an episodic but serious cardiac, respiratory, metabolic, or neurologic event.

For infants who have experienced a BRUE, a careful history and physical examination are necessary to characterize the event, assess the risk of recurrence, and determine the presence of an underlying disorder (Tables 2 and 3). The recommendations provided in this guideline focus on infants with a lower risk of a subsequent event or serious underlying disorder (see section entitled "Risk Assessment: Lower- Versus Higher-Risk BRUE"). In the absence of identifiable risk factors, infants are at lower risk and laboratory studies, imaging studies, and other diagnostic procedures are unlikely to be useful or necessary. However, if the clinical history or physical examination reveals abnormalities, the patient may be at higher risk and further evaluation should focus on the specific areas of concern. For example,

- possible child abuse may be considered when the event history is reported inconsistently or is incompatible with the child's developmental age, or when, on physical examination, there is unexplained bruising or a torn labial or lingual frenulum;
- a cardiac arrhythmia may be considered if there is a family history of sudden, unexplained death in first-degree relatives; and
- infection may be considered if there is fever or persistent respiratory symptoms.

TABLE 2 Historical Features To Be Considered in the Evaluation of a Potential BRUE

Features To Be Considered
Considerations for possible child abuse:
Multiple or changing versions of the history/circumstances
History/circumstances inconsistent with child's developmental stage
History of unexplained bruising
Incongruence between caregiver expectations and child's developmental stage, including assigning negative attributes to the child
History of the event
General description
Who reported the event?
Witness of the event? Parent(s), other children, other adults? Reliability of historian(s)?
State immediately before the event
Where did it occur (home/elsewhere, room, crib/floor, etc)?
Awake or asleep?
Position: supine, prone, upright, sitting, moving?
Feeding? Anything in the mouth? Availability of item to choke on? Vomiting or spitting up?
Objects nearby that could smother or choke?
State during the event
Choking or gagging noise?
Active/moving or quiet/flaccid?
Conscious? Able to see you or respond to voice?
Muscle tone increased or decreased?
Repetitive movements?
Appeared distressed or alarmed?
Breathing: yes/no, struggling to breathe?
Skin color: normal, pale, red, or blue?
Bleeding from nose or mouth?
Color of lips: normal, pale, or blue?
End of event
Approximate duration of the event?
How did it stop: with no intervention, picking up, positioning, rubbing or clapping back, mouth-to-mouth, chest compressions, etc?
End abruptly or gradually?
Treatment provided by parent/caregiver (eg, glucose-containing drink or food)?
911 called by caregiver?
State after event
Back to normal immediately/gradually/still not there?
Before back to normal, was quiet, dazed, fussy, irritable, crying?
Recent history
Illness in preceding day(s)?
If yes, detail signs/symptoms (fussiness, decreased activity, fever, congestion, rhinorrhea, cough, vomiting, diarrhea, decreased intake, poor sleep)
Injuries, falls, previous unexplained bruising?
Past medical history
Pre-/perinatal history
Gestational age
Newborn screen normal (for IEMs, congenital heart disease)?
Previous episodes/BRUE?
Reflux? If yes, obtain details, including management
Breathing problems? Noisy ever? Snoring?
Growth patterns normal?
Development normal? Assess a few major milestones across categories, any concerns about development or behavior?
Illnesses, injuries, emergencies?
Previous hospitalization, surgery?
Recent immunization?
Use of over-the-counter medications?
Family history
Sudden unexplained death (including unexplained car accident or drowning) in first- or second-degree family members before age 35, and particularly as an infant?
Apparent life-threatening event in sibling?
Long QT syndrome?
Arrhythmia?

TABLE 2 Continued

Features To Be Considered
Inborn error of metabolism or genetic disease?
Developmental delay?
Environmental history
Housing: general, water damage, or mold problems?
Exposure to tobacco smoke, toxic substances, drugs?
Social history
Family structure, individuals living in home?
Housing: general, mold?
Recent changes, stressors, or strife?
Exposure to smoke, toxic substances, drugs?
Recent exposure to infectious illness, particularly upper respiratory illness, paroxysmal cough, pertussis?
Support system(s)/access to needed resources?
Current level of concern/anxiety; how family manages adverse situations?
Potential impact of event/admission on work/family?
Previous child protective services or law enforcement involvement (eg, domestic violence, animal abuse), alerts/reports for this child or others in the family (when available)?
Exposure of child to adults with history of mental illness or substance abuse?

The key action statements in this clinical practice guideline do not apply to higher-risk patients but rather apply only to infants who meet the lower-risk criteria by having an otherwise normal history and physical examination.

RISK ASSESSMENT: LOWER- VERSUS HIGHER-RISK BRUE

Patients who have experienced a BRUE may have a recurrent event or an undiagnosed serious condition (eg, child abuse, pertussis, etc) that confers a risk of adverse outcomes. Although this risk has been difficult to quantify historically and no studies have fully evaluated patient-centered outcomes (eg, family experience survey), the systematic review of the ALTE literature identified a subset of BRUE patients who are unlikely to have a recurrent event or undiagnosed serious conditions, are at lower risk of adverse outcomes, and can likely be managed safely without extensive diagnostic evaluation or hospitalization.[3] In the systematic review of ALTE studies in which it was possible to identify BRUE patients, the following characteristics most consistently conferred higher risk: infants <2 months of age, those with a history of prematurity, and those with more than 1 event. There was generally an increased risk from prematurity in infants born at <32 weeks' gestation, and the risk attenuated once infants born at <32 weeks' gestation reached 45 weeks' postconceptional age. Two ALTE studies evaluated the duration of the event.[6,7] Although duration did not appear to be predictive of hospital admission, it was difficult to discern a BRUE population from the heterogeneous ALTE populations. Nonetheless, most events were less than one minute. By consensus, the subcommittee established <1 minute as the upper limit of a "brief event," understanding that objective, verifiable measurements were rarely, if ever, available. Cariopulmonary resuscitation (CPR) was identified as a risk factor in the older ALTE studies and confirmed in a recent study,[6] but it was unclear how the need for CPR was determined. Therefore, the committee agreed by consensus that the need for CPR should be determined by trained medical providers.

PATIENT FACTORS THAT DETERMINE A LOWER RISK

To be designated lower risk, the following criteria should be met (see Fig 1):

- Age >60 days
- Prematurity: gestational age ≥32 weeks and postconceptional age ≥45 weeks
- First BRUE (no previous BRUE ever and not occurring in clusters)
- Duration of event <1 minute
- No CPR required by trained medical provider
- No concerning historical features (see Table 2)
- No concerning physical examination findings (see Table 3)

Infants who have experienced a BRUE who do not qualify as lower-risk patients are, by definition, at higher risk. Unfortunately, the outcomes data from ALTE studies in the heterogeneous higher-risk population are unclear and preclude the derivation of evidence-based recommendations regarding management. Thus, pending further research, this guideline does not provide recommendations for the management of the higher-risk infant. Nonetheless, it is important for clinicians and researchers to recognize that some studies suggest that higher-risk BRUE patients may be more likely to have a serious underlying cause, recurrent event, or an adverse outcome. For example, infants younger than 2 months who experience a BRUE may be more likely to have a congenital or infectious cause and be at higher risk of an adverse outcome. Infants who have experienced multiple events or a concerning social assessment for child abuse may warrant increased observation to better document the events or contextual factors. A list of differential diagnoses for BRUE patients is provided in Supplemental Table 6.

METHODS

In July 2013, the American Academy of Pediatrics (AAP) convened a multidisciplinary subcommittee composed of primary care clinicians

TABLE 3 Physical Examination Features To Be Considered in the Evaluation of a Potential BRUE

Physical Examination
General appearance
Craniofacial abnormalities (mandible, maxilla, nasal)
Age-appropriate responsiveness to environment
Growth variables
Length, weight, occipitofrontal circumference
Vital signs
Temperature, pulse, respiratory rate, blood pressure, oxygen saturation
Skin
Color, perfusion, evidence of injury (eg, bruising or erythema)
Head
Shape, fontanelles, bruising or other injury
Eyes
General, extraocular movement, pupillary response
Conjunctival hemorrhage
Retinal examination, if indicated by other findings
Ears
Tympanic membranes
Nose and mouth
Congestion/coryza
Blood in nares or oropharynx
Evidence of trauma or obstruction
Torn frenulum
Neck
Mobility
Chest
Auscultation, palpation for rib tenderness, crepitus, irregularities
Heart
Rhythm, rate, auscultation
Abdomen
Organomegaly, masses, distention
Tenderness
Genitalia
Any abnormalities
Extremities
Muscle tone, injuries, limb deformities consistent with fracture
Neurologic
Alertness, responsiveness
Response to sound and visual stimuli
General tone
Pupillary constriction in response to light
Presence of symmetrical reflexes
Symmetry of movement/tone/strength

and experts in the fields of general pediatrics, hospital medicine, emergency medicine, infectious diseases, child abuse, sleep medicine, pulmonary medicine, cardiology, neurology, biochemical genetics, gastroenterology, environmental health, and quality improvement. The subcommittee also included a parent representative, a guideline methodologist/informatician, and an epidemiologist skilled in systematic reviews. All panel members declared potential conflicts on the basis of the AAP policy on Conflict of Interest and Voluntary Disclosure. Subcommittee members repeated this process annually and upon publication of the guideline. All potential conflicts of interest are listed at the end of this document. The project was funded by the AAP.

The subcommittee performed a comprehensive review of the literature related to ALTEs from 1970 through 2014. Articles from 1970 through 2011 were identified and evaluated by using "Management of Apparent Life Threatening Events in Infants: A Systematic Review," authored by the Society of Hospital Medicine's ALTE Expert Panel (which included 4 members of the subcommittee).[3] The subcommittee partnered with the Society of Hospital Medicine Expert Panel and a librarian to update the original systematic review with articles published through December 31, 2014, with the use of the same methodology as the original systematic review. PubMed, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Library databases were searched for studies involving children younger than 24 months by using the stepwise approach specified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[8] Search terms included "ALTE(s)," "apparent life threatening event(s)," "life threatening event(s)," "near miss SIDS" or "near miss sudden infant death syndrome," "aborted crib death" or "aborted sudden infant death syndrome," and "aborted SIDS" or "aborted cot death" or "infant death, sudden." The Medical Subject Heading "infantile apparent life-threatening event," introduced in 2011, was also searched but did not identify additional articles.

In updating the systematic review published in 2012, pairs of 2 subcommittee members used validated methodology to independently score the newly identified abstracts from English-language articles (n = 120) for relevance to the clinical questions (Supplemental Fig 3).[9,10] Two independent reviewers then critically appraised the full text of the identified articles (n = 23) using a structured data collection form based on published guidelines for evaluating medical literature.[11,12] They recorded each study's relevance to the clinical question, research design, setting, time period covered, sample size, patient eligibility criteria, data source, variables collected, key results, study

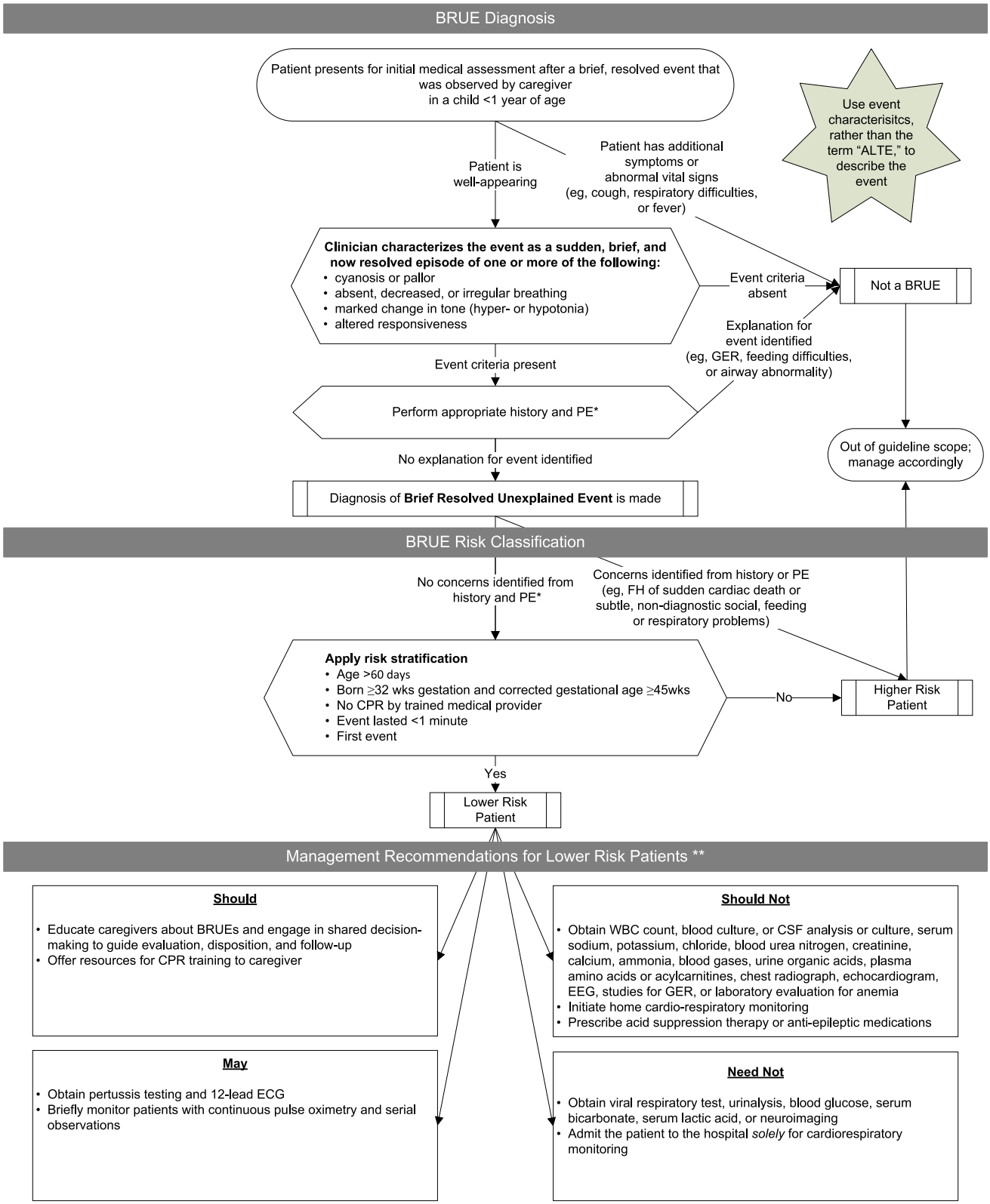

FIGURE 1

Diagnosis, risk classification, and recommended management of a BRUE. *See Tables 3 and 4 for the determination of an appropriate and negative FH and PE. **See Fig 2 for the AAP method for rating of evidence and recommendations. CSF, cerebrospinal fluid; FH, family history; PE, physical examination; WBC, white blood cell.

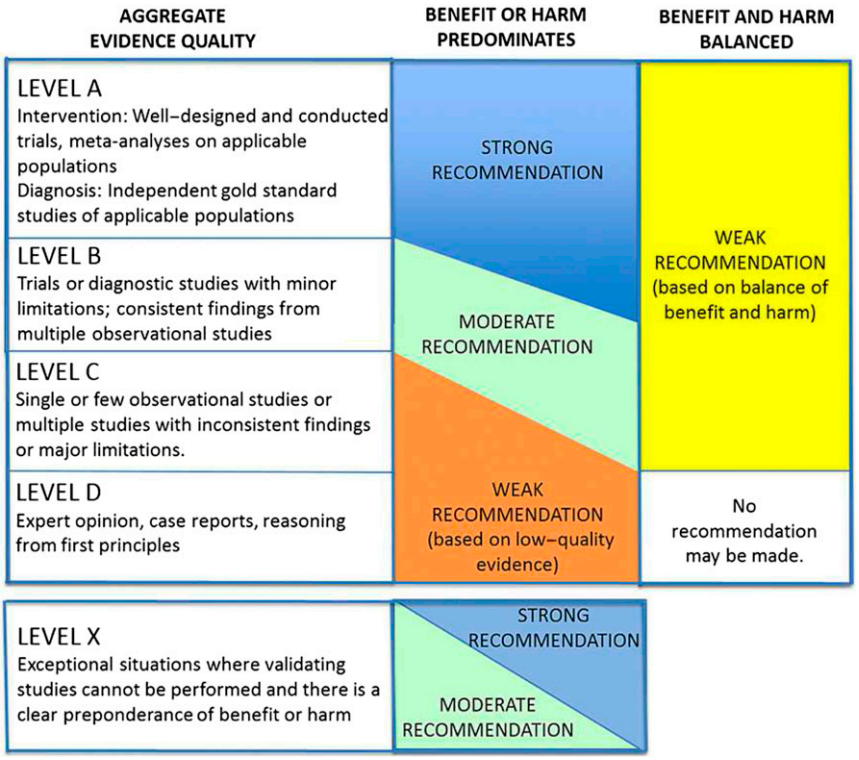

FIGURE 2
AAP rating of evidence and recommendations.

limitations, potential sources of bias, and stated conclusions. If at least 1 reviewer judged an article to be relevant on the basis of the full text, subsequently at least 2 reviewers critically appraised the article and determined by consensus what evidence, if any, should be cited in the systematic review. Selected articles used in the earlier review were also reevaluated for their quality. The final recommendations were based on articles identified in the updated (n = 18) and original (n = 37) systematic review (Supplemental Table 7).[6,7,13–28] The resulting systematic review was used to develop the guideline recommendations by following the policy statement from the AAP Steering Committee on Quality Improvement and Management, "Classifying Recommendations for Clinical Practice Guidelines."[29] Decisions and the strength of recommendations were based on a systematic grading of the quality of evidence from the updated literature review by 2 independent reviewers and incorporation of the previous systematic review. Expert consensus was used when definitive data were not available. If committee members disagreed with the rest of the consensus, they were encouraged to voice their concern until full agreement was reached. If full agreement could not be reached, each committee member reserved the right to state concern or disagreement in the publication (which did not occur). Because the recommendations of this guideline were based on the ALTE literature, we relied on the studies and outcomes that could be attributable to the new definition of lower- or higher-risk BRUE patients.

Key action statements (summarized in Table 5) were generated by using BRIDGE-Wiz (Building Recommendations in a Developers Guideline Editor), an interactive software tool that leads guideline development teams through a series of questions that are intended to create clear, transparent, and actionable key action statements.[30] BRIDGE-Wiz integrates the quality of available evidence and a benefit-harm assessment into the final determination of the strength of each recommendation. Evidence-based guideline recommendations from the AAP may be graded as strong,

TABLE 4 Guideline Definitions for Key Action Statements

Statement	Definition	Implication
Strong recommendation	A particular action is favored because anticipated benefits clearly exceed harms (or vice versa) and quality of evidence is excellent or unobtainable.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate recommendation	A particular action is favored because anticipated benefits clearly exceed harms (or vice versa) and the quality of evidence is good but not excellent (or is unobtainable).	Clinicians would be prudent to follow a moderate recommendation but should remain alert to new information and sensitive to patient preferences.
Weak recommendation (based on low-quality evidence)	A particular action is favored because anticipated benefits clearly exceed harms (or vice versa), but the quality of evidence is weak.	Clinicians would be prudent follow a weak recommendation but should remain alert to new information and very sensitive to patient preferences.
Weak recommendation (based on balance of benefits and harms)	Weak recommendation is provided when the aggregate database shows evidence of both benefit and harm that appear to be similar in magnitude for any available courses of action.	Clinicians should consider the options in their decision-making, but patient preference may have a substantial role.

TABLE 5 Summary of Key Action Statements for Lower-Risk BRUEs

When managing an infant aged >60 d and <1 y and who, on the basis of a thorough history and physical examination, meets criteria for having experienced a lower-risk BRUE, clinicians:	Evidence Quality; Strength of Recommendation
1. Cardiopulmonary evaluation	
1A. Need not admit infants to the hospital solely for cardiorespiratory monitoring.	B; Weak
1B. May briefly monitor patients with continuous pulse oximetry and serial observations.	D; Weak
1C. Should not obtain a chest radiograph.	B; Moderate
1D. Should not obtain a measurement of venous or arterial blood gas.	B; Moderate
1E. Should not obtain an overnight polysomnograph.	B; Moderate
1F. May obtain a 12-lead electrocardiogram.	C; Weak
1G. Should not obtain an echocardiogram.	C; Moderate
1H. Should not initiate home cardiorespiratory monitoring.	B; Moderate
2. Child abuse evaluation	
2A. Need not obtain neuroimaging (CT, MRI, or ultrasonography) to detect child abuse.	C; Weak
2B. Should obtain an assessment of social risk factors to detect child abuse.	C; Moderate
3. Neurologic evaluation	
3A. Should not obtain neuroimaging (CT, MRI, or ultrasonography) to detect neurologic disorders.	C; Moderate
3B. Should not obtain an EEG to detect neurologic disorders.	C; Moderate
3C. Should not prescribe antiepileptic medications for potential neurologic disorders.	C; Moderate
4. Infectious disease evaluation	
4A. Should not obtain a WBC count, blood culture, or cerebrospinal fluid analysis or culture to detect an occult bacterial infection.	B; Strong
4B. Need not obtain a urinalysis (bag or catheter).	C; Weak
4C. Should not obtain chest radiograph to assess for pulmonary infection.	B; Moderate
4D. Need not obtain respiratory viral testing if rapid testing is available.	C; Weak
4E. May obtain testing for pertussis.	B; Weak
5. Gastrointestinal evaluation	
5A. Should not obtain investigations for GER (eg, upper gastrointestinal tract series, pH probe, endoscopy, barium contrast study, nuclear scintigraphy, and ultrasonography).	C; Moderate
5B. Should not prescribe acid suppression therapy.	C; Moderate
6. IEM evaluation	
6A. Need not obtain measurement of serum lactic acid or serum bicarbonate.	C; Weak
6B. Should not obtain a measurement of serum sodium, potassium, chloride, blood urea nitrogen, creatinine, calcium, or ammonia.	C; Moderate
6C. Should not obtain a measurement of venous or arterial blood gases.	C; Moderate
6D. Need not obtain a measurement of blood glucose.	C; Weak
6E. Should not obtain a measurement of urine organic acids, plasma amino acids, or plasma acylcarnitines.	C; Moderate
7. Anemia evaluation	
7A. Should not obtain laboratory evaluation for anemia.	C; Moderate
8. Patient- and family-centered care	
8A. Should offer resources for CPR training to caregiver.	C; Moderate
8B. Should educate caregivers about BRUEs.	C; Moderate
8C. Should use shared decision-making.	C; Moderate

CPR, cardiopulmonary resuscitation; CT, computed tomography; GER, gastroesophageal reflux; WBC, white blood cell.

moderate, weak based on low-quality evidence, or weak based on balance between benefits and harms. Strong and moderate recommendations are associated with "should" and "should not" recommendation statements, whereas weak recommendation may be recognized by use of "may" or "need not" (Fig 2, Table 4).

A strong recommendation means that the committee's review of the evidence indicates that the benefits of the recommended approach clearly exceed the harms of that approach (or, in the case of a strong negative recommendation, that the harms clearly exceed the benefits) and that the quality of the evidence supporting this approach is excellent. Clinicians are advised to follow such guidance unless a clear and compelling rationale for acting in a contrary manner is present. A moderate recommendation means that the committee believes that the benefits exceed the harms (or, in the case of a negative recommendation, that the harms exceed the benefits), but the quality of the evidence on which this recommendation is based is not as strong. Clinicians are also encouraged to follow such guidance but also should be alert to new information and sensitive to patient preferences.

A weak recommendation means either that the evidence quality that exists is suspect or that well-designed, well-conducted studies have shown little clear advantage to one approach versus another. Weak recommendations offer clinicians flexibility in their decision-making regarding appropriate practice, although they may set boundaries on alternatives. Family and patient preference should have a substantial role in influencing clinical

1A. Clinicians Need Not Admit Infants Presenting With a Lower-Risk BRUE to the Hospital Solely for Cardiorespiratory Monitoring (Grade B, Weak Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce unnecessary testing and caregiver/infant anxiety Avoid consequences of false-positive result, health care–associated infections, and other patient safety risks
Risks, harm, cost	May rarely miss a recurrent event or diagnostic opportunity for rare underlying condition
Benefit-harm assessment	The benefits of reducing unnecessary testing, nosocomial infections, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for an underlying condition
Intentional vagueness	None
Role of patient preferences	Caregiver anxiety and access to quality follow-up care may be important considerations in determining whether a hospitalization for cardiovascular monitoring is indicated
Exclusions	None
Strength	Weak recommendation (because of equilibrium between benefits and harms)
Key references	31, 32

1B. Clinicians May Briefly Monitor Infants Presenting With a Lower-Risk BRUE With Continuous Pulse Oximetry and Serial Observations (Grade D, Weak Recommendation)

Aggregate Evidence Quality	Grade D
Benefits	Identification of hypoxemia
Risks, harm, cost	Increased costs due to monitoring over time and the use of hospital resources False-positive results may lead to subsequent testing and hospitalization False reassurance from negative test results
Benefit-harm assessment	The potential benefit of detecting hypoxemia outweighs the harm of cost and false results
Intentional vagueness	Duration of time to monitor patients with continuous pulse oximetry and the number and frequency of serial observations may vary
Role of patient preferences	Level of caregiver concern may influence the duration of oximetry monitoring
Exclusions	None
Strength	Weak recommendation (based on low quality of evidence)
Key references	33, 36

decision-making, particularly when recommendations are expressed as weak. Key action statements based on that evidence and expert consensus are provided. A summary is provided in Table 5.

The practice guideline underwent a comprehensive review by stakeholders before formal approval by the AAP, including AAP councils, committees, and sections; selected outside organizations; and individuals identified by the subcommittee as experts in the field. All comments were reviewed by the subcommittee and incorporated into the final guideline when appropriate.

This guideline is intended for use primarily by clinicians providing care for infants who have experienced a BRUE and their families. This guideline may be of interest to parents and payers, but it is not intended to be used for reimbursement or to determine insurance coverage. This guideline is not intended as the sole source of guidance in the evaluation and management of BRUEs but rather is intended to assist clinicians by providing a framework for clinical decision-making.

KEY ACTION STATEMENTS FOR LOWER-RISK BRUE

1. Cardiopulmonary

1A. Clinicians Need Not Admit Infants Presenting With a Lower-Risk BRUE to the Hospital Solely for Cardiorespiratory Monitoring (Grade B, Weak Recommendation)

Infants presenting with an ALTE often have been admitted for observation and testing. Observational data indicate that 12% to 14% of infants presenting with a diagnosis of ALTE had a subsequent event or condition that required hospitalization.[7,31] Thus, research has sought to identify risk factors that could be used to identify infants likely to benefit from hospitalization. A long-term follow-up study in infants hospitalized with an ALTE showed that no infants subsequently had SIDS but 11% were victims of child abuse and 4.9% had adverse neurologic outcomes (see 3. Neurology).[32] The ALTE literature supports that infants presenting with a lower-risk BRUE do not have an increased rate of cardiovascular or other events during admission and hospitalization may not be required, but close follow-up is recommended. Careful outpatient follow-up is advised (repeat clinical history and physical examination within 24 hours after the initial evaluation) to identify infants with ongoing medical concerns that would indicate further evaluation and treatment.

Al-Kindy et al[33] used documented monitoring in 54% of infants admitted for an ALTE (338 of 625) and identified 46 of 338 (13.6%) with "extreme" cardiovascular events (central apnea >30 seconds, oxygen saturation <80% for 10 seconds, decrease in heart rate <50–60/ minutes for 10 seconds on the basis

of postconceptional age). However, no adverse outcomes were noted for any of their cohort (although whether there is a protective effect of observation alone is not known). Some of the infants with extreme events developed symptoms of upper respiratory infection 1 to 2 days after the ALTE presentation. The risk factors for "extreme" events were prematurity, postconceptional age <43 weeks, and (presence of) upper respiratory infection symptoms. Importantly, infants with a postconceptional age >48 weeks were not documented as having an extreme event in this cohort. A previous longitudinal study also identified "extreme" events that occurred with comparable frequency in otherwise normal term infants and that were not statistically increased in term infants with a history of ALTE.[34]

Preterm infants have been shown to have more serious events, although an ALTE does not further increase that risk compared with asymptomatic preterm infants without ALTE.[34] Claudius and Keens[31] performed an observational prospective study in 59 infants presenting with ALTE who had been born at >30 weeks' gestation and had no significant medical illness. They evaluated factors in the clinical history and physical examination that, according to the authors, would warrant hospital admission on the basis of adverse outcomes (including recurrent cardiorespiratory events, infection, child abuse, or any life-threatening condition). Among these otherwise well infants, those with multiple ALTEs or age <1 month experienced adverse outcomes necessitating hospitalization. Prematurity was also a risk factor predictive of subsequent adverse events after an ALTE. Paroxysmal decreases in oxygen saturation in infants immediately before and during viral illnesses have been well documented.[33,35] However, the significance of these brief hypoxemic events has not been established.

1B. Clinicians May Briefly Monitor Infants Presenting With a Lower-Risk BRUE With Continuous Pulse Oximetry and Serial Observations (Grade D, Weak Recommendation)

A normal physical examination, including vital signs and oximetry, is needed for a patient who has experienced a BRUE to be considered lower-risk. An evaluation at a single point in time may not be as accurate as a longer interval of observation. Unfortunately, there are few data to suggest the optimal duration of this period, the value of repeat examinations, and the effect of false-positive evaluations on family-centered care. Several studies have documented intermittent episodes of hypoxemia after admission for ALTE.[7,31,33] Pulse oximetry identified more infants with concerning paroxysmal events than cardiorespiratory monitoring alone.[33] However, occasional oxygen desaturations are commonly observed in normal infants, especially during sleep.[36] Furthermore, normative oximetry data are dependent on the specific machine, averaging interval, altitude, behavioral state, and postconceptional age. Similarly, there may be considerable variability in the vital signs and the clinical appearance of an infant. Pending further research into this important issue, clinicians may choose to monitor and provide serial examinations of infants in the lower-risk group for a brief period of time, ranging from 1 to 4 hours, to establish that the vital signs, physical examination, and symptomatology remain stable.

1C. Clinicians Should Not Obtain a Chest Radiograph in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Infectious processes can precipitate apnea. In 1 ALTE study, more than 80% of these infections involved the respiratory tract.[37] Most, but not all, infants with significant lower respiratory tract infections will be symptomatic at the time of ALTE presentation. However, 2 studies have documented pneumonia in infants presenting with ALTE and an otherwise noncontributory history and physical examination.[4,37] These rare exceptions have generally been in infants younger than 2 months and would have placed them in the higher-risk category for a BRUE in this guideline. Similarly, Davies and Gupta[38] reported that 9 of 65 patients (ages unknown) who had ALTEs had abnormalities on chest radiography (not fully specified) despite no suspected respiratory disorder on clinical history or physical examination. Some of the radiographs were performed up to 24 hours after presentation. Davies and Gupta further reported that 33% of infants with ALTEs that were ultimately associated with a respiratory disease had a normal initial respiratory examination.[38] Kant et al[18] reported that 2 of 176 infants discharged after admission for ALTE died within 2 weeks, both of pneumonia. One infant had a normal chest radiograph initially; the other, with a history of prematurity, had a "possible" infiltrate. Thus, most experience has shown that a chest radiograph in otherwise well-appearing infants rarely alters clinical management.[7] Careful follow-up within 24 hours is important in infants with a nonfocal clinical history and physical examination to identify those who will ultimately have a lower respiratory tract infection diagnosed.

1D. Clinicians Should Not Obtain Measurement of Venous or Arterial Blood Gases in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Blood gas measurements have not been shown to add significant clinical information in otherwise well-appearing infants presenting with an ALTE.[4] Although not part of

1C. Clinicians Should Not Obtain Chest Radiograph in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce costs, unnecessary testing, radiation exposure, and caregiver/infant anxiety
	Avoid consequences of false-positive results
Risks, harm, cost	May rarely miss diagnostic opportunity for early lower respiratory tract or cardiac disease
Benefit-harm assessment	The benefits of reducing unnecessary testing, radiation exposure, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for lower respiratory tract or cardiac disease
Intentional vagueness	None
Role of patient preferences	Caregiver may express concern regarding a longstanding breathing pattern in his/her infant or a recent change in breathing that might influence the decision to obtain chest radiography
Exclusions	None
Strength	Moderate recommendation
Key references	4, 37

1D. Clinicians Should Not Obtain Measurement of Venous or Arterial Blood Gases in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce costs, unnecessary testing, pain, risk of thrombosis, and caregiver/infant anxiety
	Avoid consequences of false-positive results
Risks, harm, cost	May miss rare instances of hypercapnia and acid-base imbalances
Benefit-harm assessment	The benefits of reducing unnecessary testing and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for hypercapnia and acid-base imbalances
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Moderate recommendation
Key reference	4

this guideline, future research may demonstrate that blood gases are helpful in select infants with a higher risk BRUE to support the diagnosis of pulmonary disease, control-of-breathing disorders, or inborn errors of metabolism (IEMs).

1E. Clinicians Should Not Obtain an Overnight Polysomnograph in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Polysomnography consists of 8 to 12 hours of documented monitoring, including EEG, electro-oculography, electromyography, nasal/oral airflow, electrocardiography, end-tidal carbon dioxide, chest/abdominal excursion, and oximetry. Polysomnography is considered by many to be the gold standard for identifying obstructive sleep apnea (OSA), central sleep apnea, and periodic breathing and may identify seizures. Some data have suggested using polysomnography in infants presenting with ALTEs as a means to predict the likelihood of recurrent significant cardiorespiratory events. A study in which polysomnography was performed in a cohort of infants with ALTEs (including recurrent episodes) reported that polysomnography may reveal respiratory pauses of >20 seconds or brief episodes of bradycardia that are predictive of ensuing events over the next several months.[40] However, without a control population, the clinical significance of these events is uncertain, because respiratory pauses are frequently observed in otherwise normal infants.[35] Similarly, Kahn and Blum[41] reported that 10 of 71 infants with a clinical history of "benign" ALTEs had an abnormal polysomnograph, including periodic breathing (7 of 10) or obstructive apnea (4 of 100), but specific data were not presented. These events were not found in a control group of 181 infants. The severity of the periodic breathing (frequency of arousals and extent of oxygen desaturation) could not be evaluated from these data. Daniëls et al[42] performed polysomnography in 422 infants with ALTEs and identified 11 infants with significant bradycardia, OSA, and/or oxygen desaturation. Home monitoring revealed episodes of bradycardia (<50 per minute) in 7 of 11 infants and concluded that polysomnography is a useful modality. However, the clinical history, physical examination, and laboratory findings were not presented. GER has also been associated with specific episodes of severe bradycardia in monitored infants.[43] Overall, most polysomnography studies have shown minimal or nonspecific findings in infants presenting with ALTEs.[44,45] Polysomnography studies generally have not been predictive of ALTE recurrence and do not identify those infants at risk of SIDS.[46] Thus, the routine use of polysomnography in infants presenting with a lower-risk BRUE is likely to have a low diagnostic yield and is unlikely to lead to changes in therapy.

OSA has been occasionally associated with ALTEs in many series, but not all.[39,47–49] The use of overnight polysomnography to evaluate for OSA should be guided by an assessment of risk on the basis of a

1E. Clinicians Should Not Obtain an Overnight Polysomnograph in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce costs, unnecessary testing, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss rare instances of hypoxemia, hypercapnia, and/or bradycardia that would be detected by polysomnography
Benefit-harm assessment	The benefits of reducing unnecessary testing and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for hypoxemia, hypercapnia, and/or bradycardia
Intentional vagueness	None
Role of patient preferences	Caregivers may report concern regarding some aspects of their infant's sleep pattern that may influence the decision to perform polysomnography
Exclusions	None
Strength	Moderate recommendation
Key reference	39

1F. Clinicians May Obtain a 12-Lead Electrocardiogram for Infants Presenting With Lower-Risk BRUE (Grade C, Weak Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	May identify BRUE patients with channelopathies (long QT syndrome, short QT syndrome, and Brugada syndrome), ventricular pre-excitation (Wolff-Parkinson-White syndrome), cardiomyopathy, or other heart disease
Risks, harm, cost	False-positive results may lead to further workup, expert consultation, anxiety, and cost False reassurance from negative results Cost and availability of electrocardiography testing and interpretation
Benefit-harm assessment	The benefit of identifying patients at risk of sudden cardiac death outweighs the risk of cost and false results
Intentional vagueness	None
Role of patient preferences	Caregiver may decide not to have testing performed
Exclusions	None
Strength	Weak recommendation (because of equilibrium between benefits and harms)
Key references	4, 16

comprehensive clinical history and physical examination.[50] Symptoms of OSA, which may be subtle or absent in infants, include snoring, noisy respirations, labored breathing, mouth breathing, and profuse sweating.[51] Occasionally, infants with OSA will present with failure to thrive, witnessed apnea, and/or developmental delay.[52] Snoring may be absent in younger infants with OSA, including those with micrognathia. In addition, snoring in otherwise normal infants is present at least 2 days per week in 11.8% and at least 3 days per week in 5.3% of infants.[53] Some infants with OSA may be asymptomatic and have a normal physical examination.[54] However, some studies have reported a high incidence of snoring in infants with (26%–44%) and without (22%–26%) OSA, making the distinction difficult.[55] Additional risk factors for infant OSA include prematurity, maternal smoking, bronchopulmonary dysplasia, obesity, and specific medical conditions including laryngomalacia, craniofacial abnormalities, neuromuscular weakness, Down syndrome, achondroplasia, Chiari malformations, and Prader-Willi syndrome.[34,56–58]

1F. Clinicians May Obtain a 12-Lead Electrocardiogram for Infants Presenting With Lower-Risk BRUE (Grade C, Weak Recommendation)

ALTE studies have examined screening electrocardiograms (ECGs). A study by Brand et al[4] found no positive findings on 24 ECGs performed on 72 patients (33%) without a contributory history or physical examination. Hoki et al[16] reported a 4% incidence of cardiac disease found in 485 ALTE patients; ECGs were performed in 208 of 480 patients (43%) with 3 of 5 abnormal heart rhythms identified by the ECG and the remaining 2 showing structural heart disease. Both studies had low positive-predictive values of ECGs (0% and 1%, respectively). Hoki et al had a negative predictive value of 100% (96%–100%), and given the low prevalence of disease, there is little need for further testing in patients with a negative ECG.

Some cardiac conditions that may present as a BRUE include channelopathies (long QT syndrome, short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia), ventricular pre-excitation (Wolff-Parkinson-White syndrome), and cardiomyopathy/myocarditis (hypertrophic cardiomyopathy, dilated cardiomyopathy). Resting ECGs are ineffective in identifying patients with catecholaminergic polymorphic ventricular tachycardia. Family history is important in identifying individuals with channelopathies.

Severe potential outcomes of any of these conditions, if left undiagnosed or untreated, include sudden death or neurologic injury.[59] However, many patients do not ever experience symptoms in their lifetime and adverse outcomes are uncommon. A genetic autopsy study in infants who died of SIDS in Norway showed an association between 9.5% and 13.0% of infants with abnormal

1G. Clinicians Should Not Obtain an Echocardiogram in Infants Presenting With Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, caregiver/infant anxiety, and sedation risk
	Avoid consequences of false-positive results
Risks, harm, cost	May miss rare diagnosis of cardiac disease
Benefit-harm assessment	The benefits of reducing unnecessary testing and sedation risk, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for cardiac causes
Intentional vagueness	Abnormal cardiac physical examination reflects the clinical judgment of the clinician
Role of patient preferences	Some caregivers may prefer to have echocardiography performed
Exclusions	Patients with an abnormal cardiac physical examination
Strength	Moderate recommendation
Key references	4, 16

1H. Clinicians Should Not Initiate Home Cardiorespiratory Monitoring in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce costs, unnecessary testing, and caregiver/infant anxiety
	Avoid consequences of false-positive results
Risks, harm, cost	May rarely miss an infant with recurrent central apnea or cardiac arrhythmias
Benefit-harm assessment	The benefits of reducing unnecessary testing and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for recurrent apnea or cardiac arrhythmias
Intentional vagueness	None
Role of patient preferences	Caregivers will frequently request monitoring be instituted after an ALTE in their infant; a careful explanation of the limitations and disadvantages of this technology should be given
Exclusions	None
Strength	Moderate recommendation
Key reference	34

or novel gene findings at the long QT loci.[60] A syncopal episode, which could present as a BRUE, is strongly associated with subsequent sudden cardiac arrest in patients with long QT syndrome.[61] The incidence and risk in those with other channelopathies have not been adequately studied. The incidence of sudden cardiac arrest in patients with ventricular pre-excitation (Wolff-Parkinson-White syndrome) is 3% to 4% over the lifetime of the individual.[62]

1G. Clinicians Should Not Obtain an Echocardiogram in Infants Presenting With Lower-Risk BRUE (Grade C, Moderate Recommendation)

Cardiomyopathy (hypertrophic and dilated cardiomyopathy) and myocarditis could rarely present as a lower-risk BRUE and can be identified with echocardiography. The cost of an echocardiogram is high and accompanied by sedation risks.

In a study in ALTE patients, Hoki et al[16] did not recommend echocardiography as an initial cardiac test unless there are findings on examination or from an echocardiogram consistent with heart disease. The majority of abnormal echocardiogram findings in their study were not perceived to be life-threatening or related to a cause for the ALTE (eg, septal defects or mild valve abnormalities), and they would have been detected on echocardiogram or physical examination. Brand et al[4] reported 32 echocardiograms in 243 ALTE patients and found only 1 abnormal echocardiogram, which was suspected because of an abnormal history and physical examination (double aortic arch).

1H. Clinicians Should Not Initiate Home Cardiorespiratory Monitoring in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

The use of ambulatory cardiorespiratory monitors in infants presenting with ALTEs has been proposed as a modality to identify subsequent events, reduce the risk of SIDS, and alert caregivers of the need for intervention. Monitors can identify respiratory pauses and bradycardia in many infants presenting with ALTE; however, these events are also occasionally observed in otherwise normal infants.[34,40] In addition, infant monitors are prone to artifact and have not been shown to improve outcomes or prevent SIDS or improve neurodevelopmental outcomes.[63] Indeed, caregiver anxiety may be exacerbated with the use of infant monitors and potential false alarms. The overwhelming majority of monitor-identified alarms, including many with reported clinical symptomatology, do not reveal abnormalities on cardiorespiratory recordings.[64–66] Finally, there are several studies showing a lack of correlation between ALTEs and SIDS.[24,32]

Kahn and Blum[41] monitored 50 infants considered at "high risk" of SIDS and reported that 80% had alarms at home. All infants with alarms had at least 1 episode of parental intervention motivated by the alarms, although the authors acknowledged that some cases of parental intervention may have been attributable to parental anxiety. Nevertheless, the stimulated infants did not die of SIDS or require rehospitalization and therefore it was concluded that monitoring

resulted in successful resuscitation, but this was not firmly established. Côté et al[40] reported "significant events" involving central apnea and bradycardia with long-term monitoring. However, these events were later shown to be frequently present in otherwise well infants.[34] There are insufficient data to support the use of commercial infant monitoring devices marketed directly to parents for the purposes of SIDS prevention.[63] These monitors may be prone to false alarms, produce anxiety, and disrupt sleep. Furthermore, these machines are frequently used without a medical support system and in the absence of specific training to respond to alarms. Although it is beyond the scope of this clinical practice guideline, future research may show that home monitoring (cardiorespiratory and/or oximetry) is appropriate for some infants with higher-risk BRUE.

2. Child Abuse

2A. Clinicians Need Not Obtain Neuroimaging (Computed Tomography, MRI, or Ultrasonography) To Detect Child Abuse in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

2B. Clinicians Should Obtain an Assessment of Social Risk Factors To Detect Child Abuse in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Child abuse is a common and serious cause of an ALTE. Previous research has suggested that this occurs in up to 10% of ALTE cohorts.[3,67] Abusive head trauma is the most common form of child maltreatment associated with an ALTE. Other forms of child abuse that can present as an ALTE, but would not be identified by radiologic evaluations, include caregiver-fabricated illness (formally known as Münchausen by proxy), smothering, and poisoning.

Children who have experienced child abuse, most notably abusive head trauma, may present with a

2A. Clinicians Need Not Obtain Neuroimaging (Computed Tomography, MRI, or Ultrasonography) To Detect Child Abuse in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Decrease cost
	Avoid sedation, radiation exposure, consequences of false-positive results
Risks, harm, cost	May miss cases of child abuse and potential subsequent harm
Benefit-harm assessment	The benefits of reducing unnecessary testing, sedation, radiation exposure, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for child abuse
Intentional vagueness	None
Role of patient preferences	Caregiver concerns may lead to requests for CNS imaging
Exclusions	None
Strength	Weak recommendation (based on low quality of evidence)
Key references	3, 67

2B. Clinicians Should Obtain an Assessment of Social Risk Factors To Detect Child Abuse in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Identification of child abuse
	May benefit the safety of other children in the home
	May identify other social risk factors and needs and help connect caregivers with appropriate resources (eg, financial distress)
Risks, harm, cost	Resource intensive and not always available, particularly for smaller centers
	Some social workers may have inadequate experience in child abuse assessment
	May decrease caregiver's trust in the medical team
Benefit-harm assessment	The benefits of identifying child abuse and identifying and addressing social needs outweigh the cost of attempting to locate the appropriate resources or decreasing the trust in the medical team
Intentional vagueness	None
Role of patient preferences	Caregivers may perceive social services involvement as unnecessary and intrusive
Exclusions	None
Strength	Moderate recommendation
Key reference	68

BRUE. Four studies reported a low incidence (0.54%–2.5%) of abusive head trauma in infants presenting to the emergency department with an ALTE.[22,37,67,69] If only those patients meeting lower-risk BRUE criteria were included, the incidence of abusive head trauma would have been <0.3%. Although missing abusive head trauma can result in significant morbidity and mortality, the yield of performing neuroimaging to screen for abusive head trauma is extremely low and has associated risks of sedation and radiation exposure.[32,70]

Unfortunately, the subtle presentation of child abuse may lead to a delayed diagnosis of abuse and result in significant morbidity and mortality.[70] A thorough history and physical examination is the best way to identify infants at risk of these

conditions.[67,71] Significant concerning features for child abuse (especially abusive head trauma) can include a developmentally inconsistent or discrepant history provided by the caregiver(s), a previous ALTE, a recent emergency service telephone call, vomiting, irritability, or bleeding from the nose or mouth.[67,71]

Clinicians and medical team members (eg, nurses and social workers) should obtain an assessment of social risk factors in infants with a BRUE, including negative attributions to and unrealistic expectations of the child, mental health problems, domestic violence/intimate partner violence, social service involvement, law enforcement involvement, and substance abuse.[68] In addition, clinicians and medical team members can help families identify and use resources that may expand and strengthen their network of social support.

In previously described ALTE cohorts, abnormal physical findings were associated with an increased risk of abusive head trauma. These findings include bruising, subconjunctival hemorrhage, bleeding from the nose or mouth, and a history of rapid head enlargement or head circumference >95th percentile.[67,70–74] It is important to perform a careful physical examination to identify subtle findings of child abuse, including a large or full/bulging anterior fontanel, scalp bruising or bogginess, oropharynx or frenula damage, or skin findings such as bruising or petechiae, especially on the trunk, face, or ears. A normal physical examination does not rule out the possibility of abusive head trauma. Although beyond the scope of this guideline, it is important for the clinician to note that according to the available evidence, brain neuroimaging is probably indicated in patients who qualify as higher-risk because of concerns about abuse resulting from abnormal history or physical findings.[67]

A social and environmental assessment should evaluate the risk of intentional poisoning, unintentional poisoning, and environmental exposure (eg, home environment), because these can be associated with the symptoms of ALTEs in infants.[75–78] In 1 study, 8.4% of children presenting to the emergency department after an ALTE were found to have a clinically significant, positive comprehensive toxicology screen.[76] Ethanol or other drugs have also been associated with ALTEs.[79] Pulmonary hemorrhage can be caused by environmental exposure to moldy, water-damaged homes; it would usually present with hemoptysis and thus probably would not qualify as a BRUE.[80]

3. Neurology

3A. Clinicians Should Not Obtain Neuroimaging (Computed Tomography, MRI, or Ultrasonography) To Detect Neurologic Disorders in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Epilepsy or an abnormality of brain structure can present as a lower-risk BRUE. CNS imaging is 1 method for evaluating whether underlying abnormalities of brain development or structure might have led to the BRUE. The long-term risk of a diagnosis of neurologic disorders ranges from 3% to 11% in historical cohorts of ALTE patients.[2,32] One retrospective study in 243 ALTE patients reported that CNS imaging contributed to a neurologic diagnosis in 3% to 7% of patients.[4] However, the study population included all ALTEs, including those with a significant past medical history, non–well-appearing infants, and those with tests ordered as part of the emergency department evaluation.

In a large study of ALTE patients, the utility of CNS imaging studies in potentially classifiable lower-risk BRUE patients was found to be low.[32] The cohort of 471 patients was followed both acutely and long-term for the development of epilepsy and other neurologic disorders, and the sensitivity and positive-predictive value of abnormal CNS imaging for subsequent development of epilepsy was 6.7% (95% confidence interval [CI]: 0.2%–32%) and 25% (95% CI: 0.6%–81%), respectively.

The available evidence suggests minimal utility of CNS imaging to evaluate for neurologic disorders, including epilepsy, in lower-risk patients. This situation is particularly true for pediatric epilepsy, in which even if a patient is determined ultimately to have seizures/epilepsy, there is no evidence of benefit from starting therapy after the first seizure compared with starting therapy after a second seizure in terms of achieving seizure remission.[81–83] However, our recommendations for BRUEs are not based on any prospective studies and only on a single retrospective study. Future work should track both short- and long-term neurologic outcomes when considering this issue.

3B. Clinicians Should Not Obtain an EEG To Detect Neurologic Disorders in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Epilepsy may first present as a lower-risk BRUE. The long-term risk of epilepsy ranges from 3% to 11% in historical cohorts of ALTE patients.[2,32] EEG is part of the typical evaluation for diagnosis of seizure disorders. However, the utility of obtaining an EEG routinely was found to be low in 1 study.[32] In a cohort of 471 ALTE patients followed both acutely and long-term for the development of epilepsy, the sensitivity and positive-predictive value of an abnormal EEG for subsequent development of epilepsy was 15% (95% CI: 2%–45%) and 33% (95% CI: 4.3%–48%), respectively. In contrast, another retrospective study in 243 ALTE patients reported that EEG contributed to a neurologic diagnosis in 6% of patients.[4] This study

3A. Clinicians Should Not Obtain Neuroimaging (Computed Tomography, MRI, or Ultrasonography) To Detect Neurologic Disorders in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce unnecessary testing, radiation exposure, sedation, caregiver/infant anxiety, and costs
	Avoid consequences of false-positive results
Risks, harm, cost	May rarely miss diagnostic opportunity for CNS causes of BRUEs
	May miss unexpected cases of abusive head trauma
Benefit-harm assessment	The benefits of reducing unnecessary testing, radiation exposure, sedation, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for CNS cause
Intentional vagueness	None
Role of patient preferences	Caregivers may seek reassurance from neuroimaging and may not understand the risks from radiation and sedation
Exclusions	None
Strength	Moderate recommendation
Key references	2, 32, 81

3B. Clinicians Should Not Obtain an EEG To Detect Neurologic Disorders in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce unnecessary testing, sedation, caregiver/infant anxiety, and costs
	Avoid consequences of false-positive or nonspecific results
Risks, harm, cost	Could miss early diagnosis of seizure disorder
Benefit-harm assessment	The benefits of reducing unnecessary testing, sedation, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for epilepsy
Intentional vagueness	None
Role of patient preferences	Caregivers may seek reassurance from an EEG, but they may not appreciate study limitations and the potential of false-positive results
Exclusions	None
Strength	Moderate recommendation
Key references	32, 84, 85

population differed significantly from that of Bonkowsky et al[32] in that all ALTE patients with a significant past medical history and non–well-appearing infants were included in the analysis and that tests ordered in the emergency department evaluation were also included in the measure of EEG yield.

A diagnosis of seizure is difficult to make from presenting symptoms of an ALTE.[30] Although EEG is recommended by the American Academy of Neurology after a first-time nonfebrile seizure, the yield and sensitivity of an EEG after a first-time ALTE in a lower-risk child are low.[86] Thus, the evidence available suggests no utility for routine EEG to evaluate for epilepsy in a lower-risk BRUE. However, our recommendations for BRUEs are based on no prospective studies and on only a single retrospective study. Future work should track both short- and long-term epilepsy when considering this issue.

Finally, even if a patient is determined ultimately to have seizures/epilepsy, the importance of an EEG for a first-time ALTE is low, because there is little evidence that shows a benefit from starting therapy after the first seizure compared with after a second seizure in terms of achieving seizure remission.[81–83,85]

3C. Clinicians Should Not Prescribe Antiepileptic Medications for Potential Neurologic Disorders in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Once epilepsy is diagnosed, treatment can consist of therapy with an antiepileptic medication. In a cohort of 471 ALTE patients followed both acutely and long-term for the development of epilepsy, most patients who developed epilepsy had a second event within 1 month of their initial presentation.[32,87] Even if a patient is determined ultimately to have seizures/epilepsy, there is no evidence of benefit from starting therapy after the first seizure compared with starting therapy after a second seizure in terms of achieving seizure remission.[81–83,85] Sudden unexpected death in epilepsy (SUDEP) has a frequency close to 1 in 1000 patient-years, but the risks of SUDEP are distinct from ALTEs/BRUEs and include adolescent age and presence of epilepsy for more than 5 years. These data do not support prescribing an antiepileptic medicine for a first-time possible seizure because of a concern for SUDEP. Thus, the evidence available for ALTEs suggests lack of benefit for starting an antiepileptic medication for a lower-risk BRUE. However, our recommendations for BRUEs are based on no prospective studies and on only a single retrospective study. Future work should track both short- and long-term epilepsy when considering this issue.

4. Infectious Diseases

4A. Clinicians Should Not Obtain a White Blood Cell Count, Blood Culture, or Cerebrospinal Fluid Analysis or Culture To Detect an Occult Bacterial Infection in Infants Presenting With a Lower-Risk BRUE (Grade B, Strong Recommendation)

Some studies reported that ALTEs are the presenting complaint of an invasive infection, including bacteremia and/or meningitis

3C. Clinicians Should Not Prescribe Antiepileptic Medications for Potential Neurologic Disorders in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce medication adverse effects and risks, avoid treatment with unproven efficacy, and reduce cost
Risks, harm, cost	Delay in treatment of epilepsy could lead to subsequent BRUE or seizure
Benefit-harm assessment	The benefits of reducing medication adverse effects, avoiding unnecessary treatment, and reducing cost outweigh the risk of delaying treatment of epilepsy
Intentional vagueness	None
Role of patient preferences	Caregivers may feel reassured by starting a medicine but may not understand the medication risks
Exclusions	None
Strength	Moderate recommendation
Key references	32, 85, 87

4A. Clinicians Should Not Obtain a White Blood Cell Count, Blood Culture, or Cerebrospinal Fluid Analysis or Culture To Detect an Occult Bacterial Infection in Infants Presenting With a Lower-Risk BRUE (Grade B, Strong Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce unnecessary testing, pain, exposure, caregiver/infant anxiety, and costs Avoid unnecessary antibiotic use and hospitalization pending culture results Avoid consequences of false-positive results/contaminants
Risks, harm, cost	Could miss serious bacterial infection at presentation
Benefit-harm assessment	The benefits of reducing unnecessary testing, pain, exposure, costs, unnecessary antibiotic use, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for a bacterial infection
Intentional vagueness	None
Role of patient preferences	Caregiver concerns over possible infectious etiology may lead to requests for antibiotic therapy
Exclusions	None
Strength	Strong recommendation
Key references	4, 37, 88

detected during the initial workup. However, on further review of such cases with serious bacterial infections, these infants did not qualify as lower-risk BRUEs, because they had risk factors (eg, age <2 months) and/or appeared ill and had abnormal findings on physical examination (eg, meningeal signs, nuchal rigidity, hypothermia, shock, respiratory failure) suggesting a possible severe bacterial infection. After eliminating those cases, it appears extremely unlikely that meningitis or sepsis will be the etiology of a lower-risk BRUE.[2–4,37,88,89] Furthermore, performing these tests for bacterial infection may then lead the clinician to empirically treat with antibiotics with the consequent risks of medication adverse effects, intravenous catheters, and development of resistant organisms. Furthermore, false-positive blood cultures (eg, coagulase negative staphylococci, *Bacillus* species, *Streptococcus viridans)* are likely to occur at times, leading to additional testing, longer hospitalization and antibiotic use, and increased parental anxiety until they are confirmed as contaminants.

Thus, the available evidence suggests that a complete blood cell count, blood culture, and lumbar puncture are not of benefit in infants with the absence of risk factors or findings from the patient's history, vital signs, and physical examination (ie, a lower-risk BRUE).

4B. Clinicians Need Not Obtain a Urinalysis (Bag or Catheter) in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Case series of infants with ALTEs have suggested that a urinary tract infection (UTI) may be detected at the time of first ALTE presentation in up to 8% of cases.[3,4,37,88] Claudius et al[88] provided insight into 17 cases of certain (n = 13) or possible (n = 4) UTI. However, 14 of these cases would not meet the criteria for a lower-risk BRUE on the basis of age younger than 2 months or being ill-appearing and/or having fever at presentation.

Furthermore, these studies do not always specify the method of urine collection, urinalysis findings, and/or the specific organisms and colony-forming units per milliliter of the isolates associated with the reported UTIs that would confirm the diagnosis. AAP guidelines for the diagnosis and management of UTIs in children 2 to 24 months of age assert that the diagnosis of UTI requires "*both* urinalysis results that suggest infection (pyuria and/or bacteruria) *and* the presence of at least 50 000 colony-forming units/mL of a uropathogen cultured from a urine specimen obtained through catheterization or suprapubic aspirate."[90] Thus, it seems unlikely for a UTI to present as a lower-risk BRUE.

Pending more detailed studies that apply a rigorous definition of UTI to infants presenting with a lower-risk BRUE, a screening urinalysis need not be obtained routinely. If it is decided to evaluate the infant for a possible UTI, then a urinalysis can be obtained but should only be followed up with a culture if the urinalysis has

4B. Clinicians Need Not Obtain a Urinalysis (Bag or Catheter) in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce unnecessary testing, pain, iatrogenic infection, caregiver/infant anxiety, and costs Avoid consequences of false-positive results Avoid delay from time it takes to obtain a bag urine
Risks, harm, cost	May delay diagnosis of infection
Benefit-harm assessment	The benefits of reducing unnecessary testing, iatrogenic infection, pain, costs, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for a urinary tract infection
Intentional vagueness	None
Role of patient preferences	Caregiver concerns may lead to preference for testing
Exclusions	None
Strength	Weak recommendation (based on low quality of evidence)
Key references	4, 88

4C. Clinicians Should Not Obtain a Chest Radiograph To Assess for Pulmonary Infection in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Reduce costs, unnecessary testing, radiation exposure, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss early lower respiratory tract infection
Benefit-harm assessment	The benefits of reducing unnecessary testing, radiation exposure, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for pulmonary infection
Intentional vagueness	None
Role of patient preferences	Caregiver concerns may lead to requests for a chest radiograph
Exclusions	None
Strength	Moderate recommendation
Key references	4, 18, 37

abnormalities suggestive of possible infection (eg, increased white blood cell count, positive nitrates, and/or leukocyte esterase).

4C. Clinicians Should Not Obtain a Chest Radiograph To Assess for Pulmonary Infection in Infants Presenting With a Lower-Risk BRUE (Grade B, Moderate Recommendation)

Chest radiography is unlikely to yield clinical benefit in a well-appearing infant presenting with a lower-risk BRUE. In the absence of abnormal respiratory findings (eg, cough, tachypnea, decreased oxygen saturation, auscultatory changes), lower respiratory tract infection is unlikely to be present.

Studies in children presenting with an ALTE have described occasional cases with abnormal findings on chest radiography in the absence of respiratory findings on history or physical examination.[4,37] However, the nature of the abnormalities and their role in the ALTE presentation in the absence of further details about the radiography results make it difficult to interpret the significance of these observations. For instance, descriptions of increased interstitial markings or small areas of atelectasis would not have the same implication as a focal consolidation or pleural effusion.

Kant et al,[18] in a follow-up of 176 children admitted for an ALTE, reported that 2 infants died within 2 weeks of discharge and both were found to have pneumonia on postmortem examination. This observation does not support the potential indication for an initial radiograph. In fact, one of the children had a normal radiograph during the initial evaluation. The finding of pneumonia on postmortem examination may reflect an agonal aspiration event. Brand et al[4] reported 14 cases of pneumonia identified at presentation in their analysis of 95 cases of ALTEs. However, in 13 of the patients, findings suggestive of lower respiratory infection, such as tachypnea, stridor, retractions, use of accessory muscles, or adventitious sounds on auscultation, were detected at presentation, leading to the request for chest radiography.

4D. Clinicians Need Not Obtain Respiratory Viral Testing If Rapid Testing Is Available in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Respiratory viral infections (especially with respiratory syncytial virus [RSV]) have been reported as presenting with apnea or an ALTE, with anywhere from 9% to 82% of patients tested being positive for RSV.[2,4,37,88] However, this finding was observed predominantly in children younger than 2 months and/or those who were born prematurely. Recent data suggest that apnea or an ALTE presentation is not unique to RSV and may be seen with a spectrum of respiratory viral infections.[90] The data in ALTE cases do not address the potential role of other respiratory viruses in ALTEs or BRUEs.

In older children, respiratory viral infection would be expected to present with symptoms ranging from upper respiratory to lower respiratory tract infection rather than as an isolated BRUE. A history of respiratory symptoms and illness exposure; findings of congestion and/or cough, tachypnea, or lower respiratory tract abnormalities; and local epidemiology regarding currently circulating viruses are

4D. Clinicians Need Not Obtain Respiratory Viral Testing If Rapid Testing Is Available in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, and caregiver/infant discomfort
	Avoid false-negative result leading to missed diagnosis and false reassurance
Risks, harm, cost	Failure to diagnose a viral etiology
	Not providing expectant management for progression and appropriate infection control interventions for viral etiology
Benefit-harm assessment	The benefits of reducing unnecessary testing, pain, costs, false reassurance, and false-positive results, as well as alleviating caregiver and infant anxiety and challenges associated with providing test results in a timely fashion, outweigh the rare missed diagnostic opportunity for a viral infection
Intentional vagueness	"Rapid testing"; time to results may vary
Role of patient preferences	Caregiver may feel reassured by a specific viral diagnosis
Exclusions	None
Strength	Weak recommendation (based on low-quality evidence)
Key references	4, 37, 91

4E. Clinicians May Obtain Testing for Pertussis in Infants Presenting With a Lower-Risk BRUE (Grade B, Weak Recommendation)

Aggregate Evidence Quality	Grade B
Benefits	Identify a potentially treatable infection
	Monitor for progression of symptoms, additional apneic episodes
	Potentially prevent secondary spread and/or identify and treat additional cases
Risks, harm, cost	Cost of test
	Discomfort of nasopharyngeal swab
	False-negative results leading to missed diagnosis and false reassurance
	Rapid testing not always available
	False reassurance from negative results
Benefit-harm assessment	The benefits of identifying and treating pertussis and preventing apnea and secondary spread outweigh the cost, discomfort, and consequences of false test results and false reassurance; the benefits are greatest in at-risk populations (exposed, underimmunized, endemic, and during outbreaks)
Intentional vagueness	None
Role of patient preferences	Caregiver may feel reassured if a diagnosis is obtained and treatment can be implemented
Exclusions	None
Strength	Weak recommendation (based on balance of benefit and harm)
Key reference	93

considerations in deciding whether to order rapid testing for respiratory viruses. Because lower-risk BRUE patients do not have these symptoms, clinicians need not perform such testing.

In addition, until recently and in reports of ALTE patients to date, RSV testing was performed by using antigen detection tests. More recently, automated nucleic acid amplification-based tests have entered clinical practice. These assays are more sensitive than antigen detection tests and can detect multiple viruses from a single nasopharyngeal swab. The use of these tests in future research may allow better elucidation of the role of respiratory viruses in patients presenting with an ALTE in general and whether they play a role in BRUEs.

As a cautionary note, detection of a virus in a viral multiplex assay may not prove causality, because some agents, such as rhinovirus and adenovirus, may persist for periods beyond the acute infection (up to 30 days) and may or may not be related to the present episode.[92] In a lower-risk BRUE without respiratory symptoms testing for viral infection may not be indicated, but in the presence of congestion and/or cough, or recent exposure to a viral respiratory infection, such testing may provide useful information regarding the cause of the child's symptoms and for infection control management. Anticipatory guidance and arranging close follow-up at the initial presentation could be helpful if patients subsequently develop symptoms of a viral infection.

4E. Clinicians May Obtain Testing for Pertussis in Infants Presenting With a Lower-Risk BRUE (Grade B, Weak Recommendation)

Pertussis infection has been reported to cause ALTEs in infants, because it can cause gagging, gasping, and color change followed by respiratory pause. Such infants can be afebrile and may not develop cough or lower respiratory symptoms for several days afterward.

The decision to test a lower-risk BRUE patient for pertussis should consider potential exposures, vaccine history (including intrapartum immunization of the mother as well as the infant's vaccination history), awareness of pertussis activity in the community, and turnaround time for results. Polymerase chain reaction testing for pertussis on a nasopharyngeal specimen, if available, offers the advantage of rapid turnaround time to results.[94] Culture for the organism requires selective media and will take days to yield results but may still be useful in the face of identified risk of exposure. In patients in whom there is a high index of suspicion on the basis of

the aforementioned risk factors, clinicians may consider prolonging the observation period and starting empirical antibiotics while awaiting test results (more information is available from the Centers for Disease Control and Prevention).[95]

5. Gastroenterology

5A. Clinicians Should Not Obtain Investigations for GER (eg, Upper Gastrointestinal Series, pH Probe, Endoscopy, Barium Contrast Study, Nuclear Scintigraphy, and Ultrasonography) in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

5A. Clinicians Should Not Obtain Investigations for GER (eg, Upper Gastrointestinal Series, pH Probe, Endoscopy, Barium Contrast Study, Nuclear Scintigraphy, and Ultrasonography) in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce unnecessary testing, procedural complications (sedation, intestinal perforation, bleeding), pain, radiation exposure, caregiver/infant anxiety, and costs
	Avoid consequences of false-positive results
Risks, harm, cost	Delay diagnosis of rare but serious gastrointestinal abnormalities (eg, tracheoesophageal fistula)
	Long-term morbidity of repeated events (eg, chronic lung disease)
Benefit-harm assessment	The benefits of reducing unnecessary testing, complications, radiation, pain, costs, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for a gastrointestinal abnormality or morbidity from repeat events
Intentional vagueness	None
Role of patient preferences	Caregiver may be reassured by diagnostic evaluation of GER
Exclusions	None
Strength	Moderate recommendation
Key references	96, 97

GER occurs in more than two-thirds of infants and is the topic of discussion with pediatricians at one-quarter of all routine 6-month infant visits.[96] GER can lead to airway obstruction, laryngospasm, or aspiration. Although ALTEs that can be attributed to GER symptoms (eg, choking after spitting up) qualify as an ALTE according to the National Institutes of Health definition, importantly, they do not qualify as a BRUE.

GER may still be a contributing factor to a lower-risk BRUE if the patient's GER symptoms were not witnessed or well described by caregivers. However, the available evidence suggests no utility of routine diagnostic testing to evaluate for GER in these patients. The brief period of observation that occurs during an upper gastrointestinal series is inadequate to rule out the occurrence of pathologic reflux at other times, and the high prevalence of nonpathologic reflux that often occurs during the study can encourage false-positive diagnoses. In addition, the observation of the reflux of a barium column into the esophagus during gastrointestinal contrast studies may not correlate with the severity of GER or the degree of esophageal mucosal inflammation in patients with reflux esophagitis. Routine performance of an upper gastrointestinal series to diagnose GER is not justified and should be reserved to screen for anatomic abnormalities associated with vomiting (which is a symptom that precludes the diagnosis of a lower-risk BRUE).[98] Gastroesophageal scintigraphy scans for reflux of ^{99m}Tc-labeled solids or liquids into the esophagus or lungs after the administration of the test material into the stomach. The lack of standardized techniques and age-specific normal values limits the usefulness of this test. Therefore, gastroesophageal scintigraphy is not recommended in the routine evaluation of pediatric patients with GER symptoms or a lower-risk BRUE.[97] Multiple intraluminal impedance (MII) is useful for detecting both acidic and nonacidic reflux, thereby providing a more detailed picture of esophageal events than pH monitoring. Combined pH/MII testing is evolving into the test of choice to detect temporal relationships between specific symptoms and the reflux of both acid and nonacid gastric contents. In particular, MII has been used in recent years to investigate how GER correlates with respiratory symptoms, such as apnea or cough. Performing esophageal pH +/- impedance monitoring is not indicated in the routine evaluation of infants presenting with a lower-risk BRUE, although it may be considered in patients with recurrent BRUEs and GER symptoms even if these occur independently.

Problems with the coordination of feedings can lead to ALTEs and BRUEs. In a study in Austrian newborns, infants who experienced an ALTE had a more than twofold increase in feeding difficulties (multivariate relative risk: 2.5; 95% CI: 1.3–4.6).[99] In such patients, it is likely that poor suck-swallow-breathe coordination triggered choking or laryngospasm. A clinical speech therapy evaluation may help to evaluate any concerns for poor coordination swallowing with feeding.

5B. Clinicians Should Not Prescribe Acid Suppression Therapy for Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

The available evidence suggests no proven efficacy of acid suppression therapy for esophageal reflux in patients presenting with a lower-risk BRUE. Acid suppression therapy with H2-receptor antagonists or proton

5B. Clinicians Should Not Prescribe Acid Suppression Therapy for Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce unnecessary medication use, adverse effects, and cost from treatment with unproven efficacy
Risks, harm, cost	Delay treatment of rare but undiagnosed gastrointestinal disease, which could lead to complications (eg, esophagitis)
Benefit-harm assessment	The benefits of reducing medication adverse effects, avoiding unnecessary treatment, and reducing cost outweigh the risk of delaying treatment of gastrointestinal disease
Intentional vagueness	None
Role of patient preferences	Caregiver concerns may lead to requests for treatment
Exclusions	None
Strength	Moderate recommendation
Key reference	98

pump inhibitors may be indicated in selected pediatric patients with GER disease (GERD), which is diagnosed in patients when reflux of gastric contents causes troublesome symptoms or complications.[98] Infants with spitting up or throat-clearing coughs that are not troublesome do not meet diagnostic criteria for GERD. Indeed, the inappropriate administration of acid suppression therapy may have harmful adverse effects because it exposes infants to an increased risk of pneumonia or gastroenteritis.[100]

GER leading to apnea is not always clinically apparent and can be the cause of a BRUE. Acid reflux into the esophagus has been shown to be temporally associated with oxygen desaturation and obstructive apnea, suggesting that esophageal reflux may be one of the underlying conditions in selected infants presenting with BRUEs.[101] Respiratory symptoms are more likely to be associated with GER when gross emesis occurs at the time of a BRUE, when episodes occur while the infant is awake and supine (sometimes referred to as "awake apnea"), and when a pattern of obstructive apnea is observed while the infant is making respiratory efforts without effective air movement.[102]

Wenzl et al[103] reported a temporal association between 30% of the nonpathologic, short episodes of central apnea and GER by analyzing combined data from simultaneous esophageal and cardiorespiratory monitoring. These findings cannot be extrapolated to pathologic infant apnea and may represent a normal protective cessation of breathing during regurgitation. Similarly, Mousa et al[104] analyzed data from 527 apneic events in 25 infants and observed that only 15.2% were temporally associated with GER. Furthermore, there was no difference in the linkage between apneic events and acid reflux (7.0%) and nonacid reflux (8.2%). They concluded that there is little evidence for an association between acid reflux or nonacid reflux and the frequency of apnea. Regression analysis revealed a significant association between apnea and reflux in 4 of 25 infants. Thus, in selected infants, a clear temporal relationship between apnea and ALTE can be shown. However, larger studies have not proven a causal relationship between pathologic apnea and GER.[105]

As outlined in the definition of a BRUE, when an apparent explanation for the event, such as GER, is evident at the time of initial evaluation, the patient should be managed as appropriate for the clinical situation. However, BRUEs can be caused by episodes of reflux-related laryngospasm (sometimes referred to as "silent reflux"), which may not be clinically apparent at the time of initial evaluation. Laryngospasm may also occur during feeding in the absence of GER. Measures that have been shown to be helpful in the nonpharmacologic management of GER in infants include avoiding overfeeding, frequent burping during feeding, upright positioning in the caregiver's arms after feeding, and avoidance of secondhand smoke.[106] Thickening feedings with commercially thickened formula for infants without milk-protein intolerance does not alter esophageal acid exposure detected by esophageal pH study but has been shown to decrease the frequency of regurgitation. Given the temporal association observed between GER and respiratory symptoms in selected infants, approaches that decrease the height of the reflux column, the volume of refluxate, and the frequency of reflux episodes may theoretically be beneficial.[98] Combined pH/MII testing has shown that, although the frequency of reflux events is unchanged with thickened formula, the height of the column of refluxate is decreased. Studies have shown that holding the infant on the caregiver's shoulders for 10 to 20 minutes to allow for adequate burping after a feeding before placing the infant in the "back to sleep position" can decrease the frequency of GER in infants. In contrast, placing an infant in a car seat or in other semisupine positions, such as in an infant carrier, exacerbates esophageal reflux and should be avoided.[98] The frequency of GER has been reported to be decreased in breastfed compared with formula-fed infants. Thus, the benefits of breastfeeding are preferred over the theoretical effect of thickened formula feeding, so exclusive breastfeeding should be encouraged whenever possible.

6. Inborn Errors of Metabolism

6A. Clinicians Need Not Obtain Measurement of Serum Lactic Acid or Serum Bicarbonate To Detect an IEM in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

6B. Clinicians Should Not Obtain a Measurement of Serum Sodium, Potassium, Chloride, Blood Urea Nitrogen, Creatinine, Calcium, or Ammonia To Detect an IEM on Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

6C. Clinicians Should Not Obtain a Measurement of Venous or Arterial Blood Gases To Detect an IEM in Infants Presenting With Lower-Risk BRUE (Grade C, Moderate Recommendation)

6D. Clinicians Need Not Obtain a Measurement of Blood Glucose To Detect an IEM in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

6E. Clinicians Should Not Obtain Measurements of Urine Organic Acids, Plasma Amino Acids, or Plasma Acylcarnitines To Detect an IEM in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

IEMs are reported to cause an ALTE in 0% to 5% of cases.[2,27,38,99,107,108] On the basis of the information provided by the authors for these patients, it seems unlikely that events could have been classified as a lower-risk BRUE, either because the patient had a positive history or physical examination or a recurrent event. The most commonly reported disorders include fatty acid oxidation disorders or urea cycle disorders.[107,109] In cases of vague or resolved symptoms, a careful history can help determine whether the infant had not received previous treatment (eg, feeding after listlessness for suspected hypoglycemia). These rare circumstances could include milder or later-onset presentations of IEMs.

Infants may be classified as being at a higher risk of BRUE because of a family history of an IEM, developmental disabilities, SIDS, or a medical history of abnormal newborn screening results, unexplained infant death, age younger than 2 months, a prolonged event (>1 minute), or multiple events without an explanation. Confirmation that a newborn screen is complete and is negative is an important aspect of the medical history, but the clinician must consider that not all potential disorders are included in current newborn screening panels in the United States.

6A. Clinicians Need Not Obtain Measurement of Serum Lactic Acid or Serum Bicarbonate To Detect an IEM in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce unnecessary testing, caregiver/infant anxiety, and costs Avoid consequences of false-positive or nonspecific results
Risks, harm, cost	May miss detection of an IEM
Benefit-harm assessment	The benefits of reducing unnecessary testing, cost, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for an IEM
Intentional vagueness	Detection of higher lactic acid or lower bicarbonate levels should be considered to have a lower likelihood of being a false-positive result and may warrant additional investigation
Role of patient preferences	Caregiver concerns may lead to requests for diagnostic testing
Exclusions	None
Strength	Weak recommendation (based on low-quality evidence)
Key reference	38

6B. Clinicians Should Not Obtain a Measurement of Serum Sodium, Potassium, Chloride, Blood Urea Nitrogen, Creatinine, Calcium, or Ammonia To Detect an IEM on Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, pain, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss detection of an IEM
Benefit-harm assessment	The benefits of reducing unnecessary testing, cost, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for an IEM
Intentional vagueness	None
Role of patient preferences	Caregiver concerns may lead to requests for diagnostic testing
Exclusions	None
Strength	Moderate recommendation
Key reference	4

Lactic Acid

Measurement of lactic acid can result in high false-positive rates if the sample is not collected properly, making the decision to check a lactic acid problematic. In addition, lactic acid may be elevated because of metabolic abnormalities attributable to other conditions, such as sepsis, and are not specific for IEMs.

Only 2 studies evaluated the specific measurement of lactic acid.[27,38] Davies and Gupta[38] reported 65 infants with consistent laboratory evaluations and found that 54% of infants had a lactic acid >2 mmol/L but only 15% had levels >3 mmol/L. The latter percentage of infants are more likely to be clinically significant and less likely to reflect a false-positive result. Five of 7 infants with a lactic acid >3 mmol/L had a "specific, serious diagnosis," although the specifics of these diagnoses were not included and no IEM was

6C. Clinicians Should Not Obtain a Measurement of Venous or Arterial Blood Gases To Detect an IEM in Infants Presenting With Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, pain, risk of thrombosis, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss detection of an IEM
Benefit-harm assessment	The benefits of reducing unnecessary testing, cost, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for an IEM
Intentional vagueness	None
Role of patient preferences	Caregiver concerns may lead to requests for diagnostic testing
Exclusions	None
Strength	Moderate recommendation
Key reference	4

6D. Clinicians Need Not Obtain a Measurement of Blood Glucose To Detect an IEM in Infants Presenting With a Lower-Risk BRUE (Grade C, Weak Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, pain, risk of thrombosis, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss rare instances of hypoglycemia attributable to undiagnosed IEM
Benefit-harm assessment	The benefits of reducing unnecessary testing, cost, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for an IEM
Intentional vagueness	Measurement of glucose is often performed immediately through a simple bedside test; no abnormalities have been reported in asymptomatic infants, although studies often do not distinguish between capillary or venous measurement
Role of patient preferences	Caregiver concerns may lead to requests for diagnostic testing
Exclusions	None
Strength	Weak recommendation (based on low-quality evidence)
Key reference	4

confirmed in this study. This study also reported a 20% positive yield of testing for a bicarbonate <20 mmol/L and commented that there was a trend for lower bicarbonate and higher lactic acid levels in those with a recurrent event or a definitive diagnosis. The second publication[27] found no elevations of lactate in 4 of 49 children who had an initial abnormal venous blood gas, of which all repeat blood gas measurements were normal.

Serum Bicarbonate

Abnormal serum bicarbonate levels have been studied in 11 infants, of whom 7 had a diagnosis of sepsis or seizures.[38] Brand et al[4] studied 215 infants who had bicarbonate measured and found only 9 abnormal results, and only 3 of these contributed to the final diagnosis. Although unknown, it is most likely that the event in those infants would not have been classified as a BRUE under the new classification, because those infants were most likely symptomatic on presentation.

Serum Glucose

Abnormal blood glucose levels were evaluated but not reported in 3 studies.[4,38,110] Although abnormalities of blood glucose can occur from various IEMs, such as medium-chain acyl–coenzyme A dehydrogenase deficiency or other fatty acid oxidation disorders, their prevalence has not been increased in SIDS and near-miss SIDS but could be considered as a cause of higher-risk BRUEs.[111] It is important to clarify through a careful medical history evaluation that the infant was not potentially hypoglycemic at discovery of the event and improved because of enteral treatment, because these disorders will not typically self-resolve without intervention (ie, feeding).

Serum Electrolytes and Calcium

ALTE studies evaluating the diagnostic value of electrolytes, including sodium, potassium, blood urea nitrogen, and creatinine, reported the rare occurrence of abnormalities, ranging from 0% to 4.3%.[4,38,110] Abnormal calcium levels have been reported in 0% to 1.5% of infants with ALTE, although these reports did not provide specific causes of hypocalcemia. Another study reported profound vitamin D deficiency with hypocalcemia in 5 of 25 infants with a diagnosis of an ALTE over a 2-year period in Saudi Arabia.[4,21,38,110] In lower-risk BRUE infants, clinicians should not obtain a calcium measurement unless the clinical history raises suspicion of hypocalcemia (eg, vitamin D deficiency or hypoparathyroidism).

Ammonia

Elevations of ammonia are typically associated with persistent symptoms and recurring events, and therefore testing would not be indicated in lower-risk BRUEs. Elevations of ammonia were reported in 11 infants (7 whom had an IEM) in a report of infants with recurrent ALTE and SIDS, limiting extrapolation to

lower-risk BRUEs.[109] Elevations of ammonia >100 mmol/L were found in 4% of 65 infants, but this publication did not document a confirmed IEM.[38] Weiss et al[27] reported no abnormal elevations of ammonia in 4 infants with abnormal venous blood gas.

Venous or Arterial Blood Gas

Blood gas abnormalities leading to a diagnosis have not been reported in previous ALTE studies. Brand et al[4] reported 53 of 60 with positive findings, with none contributing to the final diagnosis. Weiss et al[27] reported 4 abnormal findings of 49 completed, all of which were normal on repeat measurements (along with normal lactate and ammonia levels). Blood gas detection is a routine test performed in acutely symptomatic patients who are being evaluated for suspected IEMs and may be considered in higher-risk BRUEs.

Urine Organic Acids, Plasma Amino Acids, Plasma Acylcarnitines

The role of advanced screening for IEMs has been reported in only 1 publication. Davies and Gupta[38] reported abnormalities of urine organic acids in 2% of cases and abnormalities of plasma amino acids in 4% of cases. Other reports have described an "unspecified metabolic screen" that was abnormal in 4.5% of cases but did not provide further description of specifics within that "screen."[4] Other reports have frequently included the descriptions of ALTEs with urea cycle disorders, organic acidemias, lactic acidemias, and fatty acid oxidation disorders such as medium chain acyl–coenzyme A dehydrogenase deficiency but did not distinguish between SIDS and near-miss SIDS.[107,109,111] Specific testing of urine organic acids, plasma amino acids, or plasma acylcarnitines may have a role in patients with a higher-risk BRUE.

6E. Clinicians Should Not Obtain Measurements of Urine Organic Acids, Plasma Amino Acids, or Plasma Acylcarnitines To Detect an IEM in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, pain, risk of thrombosis, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss detection of an IEM
Benefit-harm assessment	The benefits of reducing unnecessary testing, cost, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the rare missed diagnostic opportunity for an IEM
Intentional vagueness	Lower-risk BRUEs will have a very low likelihood of disease, but these tests may be indicated in rare cases in which there is no documentation of a newborn screen being performed
Role of patient preferences	Caregiver concerns may lead to requests for diagnostic testing
Exclusions	None
Strength	Moderate recommendation
Key references	4, 38

7A. Clinicians Should Not Obtain Laboratory Evaluation for Anemia in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Reduce costs, unnecessary testing, pain, risk of thrombosis, and caregiver/infant anxiety Avoid consequences of false-positive results
Risks, harm, cost	May miss diagnosis of anemia
Benefit-harm assessment	The benefits of reducing unnecessary testing, cost, and false-positive results, as well as alleviating caregiver and infant anxiety, outweigh the missed diagnostic opportunity for anemia
Intentional vagueness	None
Role of patient preferences	Caregivers may be reassured by testing
Exclusions	None
Strength	Moderate recommendation
Key reference	22

7. Anemia

7A. Clinicians Should Not Obtain Laboratory Evaluation for Anemia in Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Anemia has been associated with ALTEs in infants, but the significance and causal association with the event itself are unclear.[38,112,113] Normal hemoglobin concentrations have also been reported in many other ALTE populations.[69,112,114] Brand et al[4] reported an abnormal hemoglobin in 54 of 223 cases, but in only 2 of 159 was the hemoglobin concentration associated with the final diagnosis (which was abusive head injury in both). Parker and Pitetti[22] also reported that infants who presented with ALTEs and ultimately were determined to be victims of child abuse were more likely to have a lower mean hemoglobin (10.6 vs 12.7 g/dL; $P = .02$).

8. Patient- and Family-Centered Care

8A. Clinicians Should Offer Resources for CPR Training to Caregivers (Grade C, Moderate Recommendation)

The majority of cardiac arrests in children result from a respiratory deterioration. Bystander CPR has been reported to have been conducted in 37% to 48% of pediatric out-of-hospital cardiac arrests and

in 34% of respiratory arrests.[116] Bystander CPR results in significant improvement in 1-month survival rates in both cardiac and respiratory arrest.[117–119]

Although lower-risk BRUEs are neither a cardiac nor a respiratory arrest, the AAP policy statement on CPR recommends that pediatricians advocate for life-support training for caregivers and the general public.[115] A technical report that accompanies the AAP policy statement on CPR proposes that this can improve overall community health.[115] CPR training has not been shown to increase caregiver anxiety, and in fact, caregivers have reported a sense of empowerment.[120–122] There are many accessible and effective methods for CPR training (eg, e-learning).

8B. Clinicians Should Educate Caregivers About BRUEs (Grade C, Moderate Recommendation)

Pediatric providers are an important source of this health information and can help guide important conversations around BRUEs. A study by Feudtner et al[123] identified 4 groups of attributes of a "good parent": (1) making sure the child feels loved, (2) focusing on the child's health, (3) advocating for the child and being informed, and (4) ensuring the child's spiritual well-being. Clinicians should be the source of information for caregivers. Informed caregivers can advocate for their child in all of the attribute areas/domains, and regardless of health literacy levels, prefer being offered choices and being asked for information.[124] A patient- and family-centered care approach results in better health outcomes.[125,126]

8C. Clinicians Should Use Shared Decision-Making for Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Shared decision-making is a partnership between the clinician and the patient and family.[125,126] The general principles of shared decision-making are as follows: (1) information sharing, (2) respect and honoring differences, (3) partnership and collaboration, (4) negotiation, and (5) care in the context of family and community.[125] The benefits include improved care and outcomes; improved patient, family, and clinician satisfaction; and better use of health resources.[126] It is advocated for by organizations such as the AAP and the Institute of Medicine.[126,127] The 5 principles can be applied to all aspects of the infant who has experienced a BRUE, through each step (assessment, stabilization, management, disposition, and follow-up). Shared decision-making will empower families and foster a stronger clinician-patient/family alliance as they make decisions together in the face of a seemingly uncertain situation.

8A. Clinicians Should Offer Resources for CPR Training to Caregivers (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Decrease caregiver anxiety and increase confidence Benefit to society
Risks, harm, cost	May increase caregiver anxiety Cost and availability of training
Benefit-harm assessment	The benefits of decreased caregiver anxiety and increased confidence, as well as societal benefits, outweigh the increase in caregiver anxiety, cost, and resources
Intentional vagueness	None
Role of patient preferences	Caregiver may decide not to seek out the training
Exclusions	None
Strength	Moderate recommendation
Key reference	115

8B. Clinicians Should Educate Caregivers About BRUEs (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Improve caregiver empowerment and health literacy and decrease anxiety May reduce unnecessary return visits Promotion of the medical home
Risks, harm, cost	Increase caregiver anxiety and potential for caregiver intimidation in voicing concerns Increase health care costs and length of stay
Benefit-harm assessment	The benefits of decreased caregiver anxiety and increased empowerment and health literacy outweigh the increase in cost, length of stay, and caregiver anxiety and intimidation
Intentional vagueness	None
Role of patient preferences	Caregiver may decide not to listen to clinician
Exclusions	None
Strength	Moderate recommendation
Key references	None

DISSEMINATION AND IMPLEMENTATION

Dissemination and implementation efforts are needed to facilitate guideline use across pediatric medicine, family medicine, emergency medicine, research, and patient/family communities.[128] The following general approaches and a Web-based toolkit are proposed for the dissemination and implementation of this guideline.

8C. Clinicians Should Use Shared Decision-Making for Infants Presenting With a Lower-Risk BRUE (Grade C, Moderate Recommendation)

Aggregate Evidence Quality	Grade C
Benefits	Improve caregiver empowerment and health literacy and decrease anxiety May reduce unnecessary return visits Promotion of the medical home
Risks, harm, cost	Increase cost, length of stay, and caregiver anxiety and intimidation in voicing concerns
Benefit-harm assessment	The benefits of decreased caregiver anxiety and unplanned return visits and increased empowerment, health, literacy, and medical home promotion outweigh the increase in cost, length of stay, and caregiver anxiety and information
Intentional vagueness	None
Role of patient preferences	Caregiver may decide not to listen to clinician
Exclusions	None
Strength	Moderate recommendation
Key references	None

1. Education

Education will be partially achieved through the AAP communication outlets and educational services (*AAP News, Pediatrics,* and PREP). Further support will be sought from stakeholder organizations (American Academy of Family Physicians, American College of Emergency Physicians, American Board of Pediatrics, Society of Hospital Medicine). A Web-based toolkit (to be published online) will include caregiver handouts and a shared decision-making tool to facilitate patient- and family-centered care. Efforts will address appropriate disease classification and diagnosis coding.

2. Integration of Clinical Workflow

An algorithm is provided (Fig 1) for diagnosis and management. Structured history and physical examination templates also are provided to assist in addressing all of the relevant risk factors for BRUEs (Tables 2 and 3). Order sets and modified documents will be hosted on a Web-based learning platform that promotes crowd-sourcing.

3. Administrative and Research

International Classification of Diseases, 9th Revision, and International Classification of Diseases, 10th Revision, diagnostic codes are used for billing, quality improvement, and research; and new codes for lower- and higher-risk BRUEs will need to be developed. In the interim, the current code for an ALTE (799.82) will need to be used for billing purposes. Efforts will be made to better reflect present knowledge and to educate clinicians and payers in appropriate use of codes for this condition.

4. Quality Improvement

Quality improvement initiatives that provide Maintenance of Certification credit, such as the AAP's PREP and EQIPP courses, or collaborative opportunities through the AAP's Quality Improvement Innovation Networks, will engage clinicians in the use and improvement of the guideline. By using proposed quality measures, adherence and outcomes can be assessed and benchmarked with others to inform continual improvement efforts. Proposed measures include process evaluation (use of definition and evaluation), outcome assessment (family experience and diagnostic outcomes), and balancing issues (cost and length of visit). Future research will need to be conducted to validate any measures.

FUTURE RESEARCH

The transition in nomenclature from the term ALTE to BRUE after 30 years reflects the expanded understanding of the etiology and consequences of this entity. Previous research has been largely retrospective or observational in nature, with little long-term follow-up data available. The more-precise definition, the classification of lower- and higher-risk groups, the recommendations for the lower-risk group, and the implementation toolkit will serve as the basis for future research. Important areas for future prospective research include the following.

1. Epidemiology

- Incidence of BRUEs in all infants (in addition to those seeking medical evaluation)
- Influence of race, gender, ethnicity, seasonality, environmental exposures, and socioeconomic status on incidence and outcomes

2. Diagnosis

- Use and effectiveness of the BRUE definition
- Screening tests and risk of UTI
- Quantify and better understand risk in higher- and lower-risk groups
- Risk and benefit of screening tests
- Risk and benefit and optimal duration of observation and monitoring periods
- Effect of prematurity on risk
- Appropriate indications for subspecialty referral
- Early recognition of child maltreatment
- Importance of environmental history taking
- Role of human psychology on accuracy of event characterization

- Type and length of monitoring in the acute setting

3. Pathophysiology

- Role of abnormalities of swallowing, laryngospasm, GER, and autonomic function

4. Outcomes

- Patient- and family-centered outcomes, including caregiver satisfaction, anxiety, and family dynamics (eg, risk of vulnerable child syndrome)
- Long-term health and cognitive consequences

5. Treatment

- Empirical GER treatment on recurrent BRUEs
- Caregiver education strategies, including basic life support, family-centered education, and postpresentation clinical visits

6. Follow-up

- Strategies for timely follow-up and surveillance

SUBCOMMITTEE ON BRIEF RESOLVED UNEXPLAINED EVENTS (FORMERLY REFERRED TO AS APPARENT LIFE THREATENING EVENTS) (OVERSIGHT BY THE COUNCIL ON QUALITY IMPROVEMENT AND PATIENT SAFETY)

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ALTE: apparent life-threatening event
BRUE: brief resolved unexplained event
CI: confidence interval
CNS: central nervous system
CPR: cardiopulmonary resuscitation
ECG: electrocardiogram
GER: gastroesophageal reflux
IEM: inborn error of metabolism
MII: multiple intraluminal impedance
OSA: obstructive sleep apnea
RSV: respiratory syncytial virus
SIDS: sudden infant death syndrome
SUDEP: sudden unexpected death in epilepsy
UTI: urinary tract infection

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