

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
EVIDENCE-BASED OUTCOMES CENTER
Diagnosis and Initial Management of Brief Resolved Unexplained Event (BRUE)
(Formerly Apparent Life-Threatening Event [ALTE])
Evidence-Based Guideline

Definition: A BRUE is defined as 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. ⁽¹⁾ In 2016, the American Academy of Pediatrics recommended replacement of the term "apparent life-threatening event" (ALTE) with "brief resolved unexplained event" (BRUE). BRUE "is intended to better reflect the transient nature and lack of clear cause and removes the 'life-threatening' label." ⁽¹⁾ BRUE also specifies a clear age limit (<1 year of age). If there is an obvious reason for the event, including choking or gagging related to feeding or congestion, it is not considered a BRUE.

Pathophysiology: The exact pathophysiology of a BRUE remains unknown as it is likely varied and multi-factorial.

Epidemiology: The incidence of BRUE is difficult to quantify because of the change of terminology from ALTE to BRUE; therefore most studies before 2016 reported on the incidence of ALTE, which encompassed a broader scope than BRUE. From a national representative sample, the incidence of BRUE is 4.28 per 1000 live births and 5.06 per 1000 infant emergency department encounters. ⁽²⁾

Etiology: The most common reported explanations of BRUE are gastroesophageal reflux (GER), and lower respiratory tract infections. More serious explanations may include seizures, airway abnormalities, or abusive head trauma, or cardiac disorder. However, for many children diagnosed with BRUE, no explanation can be found. ⁽³⁾

Inclusion Criteria

- Children <1 year

Exclusion Criteria

- Children ≥ 1 year
- Febrile or hypothermic infants
- Gagging and/or choking
- Comorbid diseases: known neurological disease, cardiac disease, metabolic disease, and tracheostomy/ventilated patients

Differential Diagnosis

Reflux
 Aspiration
 Seizures
 Cardiac disease
 Child abuse
 Ingestion
 Inborn error of metabolism
 Poisoning
 Unexplained or Idiopathic

Diagnostic Evaluation ⁽¹⁾

History: Assess for

- Details of the event
 - What alerted the caregiver to a problem?

- Behavioral state (awake or asleep)
- Color, color change during the event, tone, breathing, abnormal movements, eye movement, noise, fluid, and responsiveness
- Time and duration of event
- How did it stop? E.g., with no intervention, picking up, positioning, rubbing or clapping back, mouth-to-mouth, or chest compressions. Did it end abruptly or gradually? Was treatment provided by caregiver (e.g., glucose-containing drink or food)? 911 called?
- State after the event
- Circumstances and environment prior to the event
 - Recent illnesses (runny nose, cough, fever, vomiting, or diarrhea) or trauma
 - Sleep position (prone/supine/side) and sleeping arrangement/location (chair, lounger, crib, car seat, bed), as well as type of bedding and clothing
 - Environmental exposures (tobacco smoke, toxic substances, drugs, mold, water-damaged home)
- Considerations for possible abuse
 - Multiple or changing versions of the history/circumstances
 - History/circumstances inconsistent with child's developmental stage
 - History of unexplained bruising
 - Incongruence between caregiver's expectations and child's developmental stage, including assigning negative attributes to the child
 - Previous CPS or law enforcement involvement (e.g., domestic violence, animal abuse), alerts/reports for this child or others in the family
 - Physical exam finding of unexplained bruising or bleeding from mouth/nose or torn labial or lingual frenulum
- Consideration of feeding or choking causes
 - Feeding regimen
 - Anything in the mouth
 - Availability of choking hazards
 - Vomiting or spitting up
 - Choking or gagging noise
- Consideration of neurological causes
 - Muscle tone
 - Repetitive movements
 - Abnormal eye movement
- Consideration of infectious causes
 - Recent exposure to infectious illness, particularly URI, paroxysmal cough, pertussis
- Past medical history
 - Pre-/Perinatal and growth/development
 - Newborn screen results
 - Previous ER visits or hospitalizations
 - Prematurity
 - Surgical history
 - Previous apneic spells
- Medications
 - Homeopathic medications/vitamins

- Supplements
- Family history
 - SIDS or unexplained car accident or drowning in first- or second-degree family member before age 35, particularly in infant
 - BRUE in sibling
 - Long QT syndrome or arrhythmia
 - Inborn error of metabolism or genetic disease
 - Developmental delay
- Maternal history
 - Problems during pregnancy or delivery
 - Medications, if breastfeeding
 - Neurologic/metabolic disorders
- Social history
 - Family structure, individuals living in the home
 - Recent changes or stressors
- Support system/access to resources needed
- Current level of concern/anxiety, management of adverse situations
- Exposure to adults with history of mental illness or substance abuse

Physical Examination

- Height, weight, and head circumference
- Vital signs
- Detailed physical exam (plus assess for trauma, upper airway obstruction, or facial dysmorphism)
- Developmental assessment

Critical Points of Evidence*

TCH Evidence-Based Recommendations

Evidence Supports

- Consider admission for patients with the following criteria: age <2 months, born <32 weeks gestation AND corrected GA <45 weeks, CPR by trained medical provider, chronic medical condition, recurring event and/or history of events presenting to the Emergency Center related to BRUE, or infants who present to the Emergency Center for BRUE and parents have been provided anticipatory guidance but continue to feel uncomfortable with discharge from the Emergency Center.⁽⁴⁻⁸⁾ - Weak recommendation, low quality evidence

Evidence Against

- The following should not be *routinely* performed as part of initial diagnostic testing: ECHO, ECG, CBC, urinalysis, chemistry, LP, MRI, viral panel, blood culture, lactate, or ammonia.⁽⁹⁻¹⁴⁾ – Strong recommendation, moderate quality evidence
- Do not routinely utilize pH probe, multichannel OCRG, or upper GI contrast studies to rule out reflux.^(1,15-18) – Weak recommendation, low quality evidence
- Do not routinely utilize skeletal survey or ophthalmology exam to rule out child abuse.^(10,12) – Weak recommendation, low quality evidence
- Do not start empiric acid suppression pharmacotherapy in patients with suspected gastroesophageal reflux.^(1,16,17,19) – Strong recommendation, low quality evidence

Evidence Lacking/Inconclusive

- Discharge hospitalized patient once symptom-free for 24 hours from last recent event. – Consensus recommendation

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

General: A BRUE is defined as 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. BRUE is a diagnosis by exclusion, and many times, no explanation can be found.

Treatment Recommendations: According to the 2016 BRUE American Academy of Pediatrics Guideline, no routine testing or treatment is recommended for BRUE. If concerned regarding specific finding, may consult specialists.

Admission Criteria

- Consider admission for patients with the following criteria: age <2 months, born <32 weeks gestation AND corrected GA <45 weeks, CPR by trained medical provider, chronic medical condition, recurring event and/or history of events presenting to the Emergency Center related to BRUE, or infants who present to the Emergency Center for BRUE and parents have been provided anticipatory guidance but continue to feel uncomfortable with discharge from the Emergency Center.^(1,20)

Discharge Criteria

- Discharge hospitalized patient once symptom-free for 24 hours from last recent event

Consults/Referrals

In addition to routine care,

- Consider Social Work consult for high-risk social situations.
- Consult Cardiology if suspected cardiac etiology and consider obtaining ECG or ECHO.
- Consult Neurology if concerned for seizures.
- Consult GI if concerned for growth deficiency or recurrent events
- Consider speech language pathology, occupational therapy, lactation, or nutrition if concern for feeding difficulty
- Call poison control, obtain UA toxicology screen, and consult Toxicology if suspicion of ingestion.
- Provide CPR training for caregiver(s).⁽¹⁾

Follow-Up Care

- PRN follow-up as needed based upon provider preference

Measures

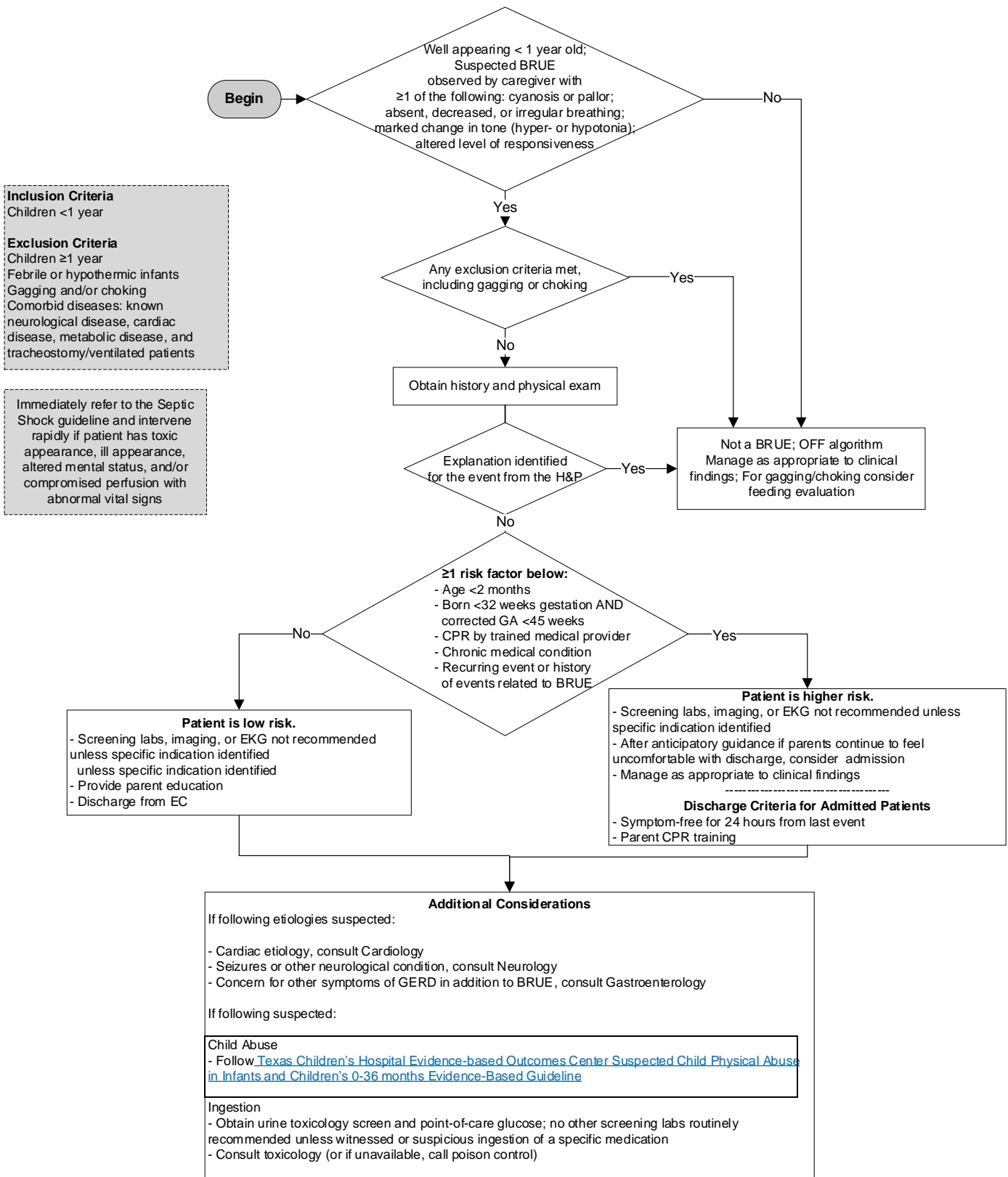
Process

- Percentage of: chest x-rays, head imaging, ECGs, EEGs, pH probes, multichannel OCRGs, upper GI contrast studies
- Percentage of consults

Outcome

- Mortality
- Total adjusted charges
- Length of stay
- Readmission within 30 days
- Return presentation to care in the EC

TCH Evidence-Based Outcomes Center
Clinical Algorithm for Brief Resolved Unexplained Event (BRUE)
(Formerly Apparent Life-Threatening Event [ALTE])



Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
 - PICO questions established
 - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
 - Unexplained Events (Formerly Apparent Life-Threatening Events) and Evaluation of Lower-Risk Infants (2016), AAP Diagnosis and Management of Gastroesophageal Reflux in Preterm Infants (2018), North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Pediatric Gastroesophageal Reflux Clinical Practice Guidelines (2018)
3. Literature Review of Relevant Evidence
 - Searched: PubMed, Cochrane
4. Critically Analyze the Evidence
 - 21 nonrandomized studies
5. Summarize the Evidence
 - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a brief resolved unexplained event (BRUE) evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides evidence to support an intervention

"Evidence Against" provides evidence against an intervention.

"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of brief resolved unexplained event (BRUE) in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content experts are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner should use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

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Version History

Date	Comments
Jul 2015	Originally completed
Feb 2019	Incorporated the AAP's 2016 guideline and 2 guidelines from other children's hospitals that were developed via the Pediatric Initiative for Clinical Standards (PICS) collaborative; Reaffirmed practice recommendations
Nov 2024	Updated Literature Review and references; Updated guideline and algorithm