Texas Children's Hospital

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TEXAS CHILDREN'S HOSPITAL
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). The new term "is intended to better reflect the transient nature and lack of clear cause and removes the 'life-threatening' label." [(1)] The new term also specifies a clear age limit (<1 year of age). If there is an obvious reason for the event, it is not considered a BRUE.

Epidemiology: The incidence of BRUE is difficult to quantify because most studies report on the incidence of ALTE, which encompasses a broader scope than BRUE. The incidence of ALTE is 0.6 to 2.46 per 1,000 live births; accounts for 0.6%-0.8% of all emergency visits for children <1 year. [(2)]

Etiology: The most common reported causes of BRUE are gastroesophageal reflux (GER), seizures, lower respiratory tract infections; or greater than 50% of BRUEs are considered idiopathic. However, BRUEs can occur with metabolic and cardiac disorders.

Guideline Eligibility Criteria
Children <1 year

Guideline Exclusion Criteria
Children ≥1 year
Febrile infants
Comorbid diseases: known neurological disease, cardiac disease, metabolic disease, and tracheostomy/ventilated patients

Differential Diagnosis
Reflux
Seizures
Cardiac disease
Child abuse
Ingestion
Inborn error of metabolism
Poisoning

Diagnostic Evaluation: [(1,3)]
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*

Evidence Supports
- Admit higher-risk patients (i.e., age <2 months, born <32 weeks gestation *AND* corrected GA <45 weeks, CPR by *trained* medical provider, event lasted ≥1 minute, >1 event, abnormal physical exam) and place on continuous pulse oximetry. [4,5] – Weak recommendation, low quality evidence
- Consider toxicology screen if reported history of over-the-counter or prescribed medications to rule out ingestion. [6] – Weak recommendation, low quality evidence

Evidence Lacking/Inconclusive
- The following may be considered as part of initial diagnostic testing: Head CT and/or skeletal survey for patients in high-risk social situations; CXR if suspected cardiac etiology; urinalysis toxicology screen if history of medications being taken; viral studies, pertussis, and/or RSV if infectious etiology suspected. [1,7,8] – Weak recommendation, low quality evidence
- Discharge patient once symptom-free for 24 hours. – Consensus recommendation

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. [1,7,8] – Weak recommendation, low quality evidence
- Do not routinely utilize pH probe, multichannel OCRG, or upper GI contrast studies to rule out reflux. [1,9-11] – Weak recommendation, low quality evidence
- Do not routinely utilize MRI or EEG to rule out seizures; if clinician is concerned for seizures, consult Neurology. [1,12,13] – Weak recommendation, low quality evidence
- Do not routinely utilize ECHO to rule out cardiac disease. [1,14] – Weak recommendation, low quality evidence
- Do not routinely utilize skeletal survey or ophthalmology exam to rule out child abuse. [15-18] – Weak recommendation, low quality evidence
- Do not start empiric acid suppression pharmacotherapy in patients with suspected gastroesophageal reflux. [1,19-22] – Strong recommendation, low quality evidence

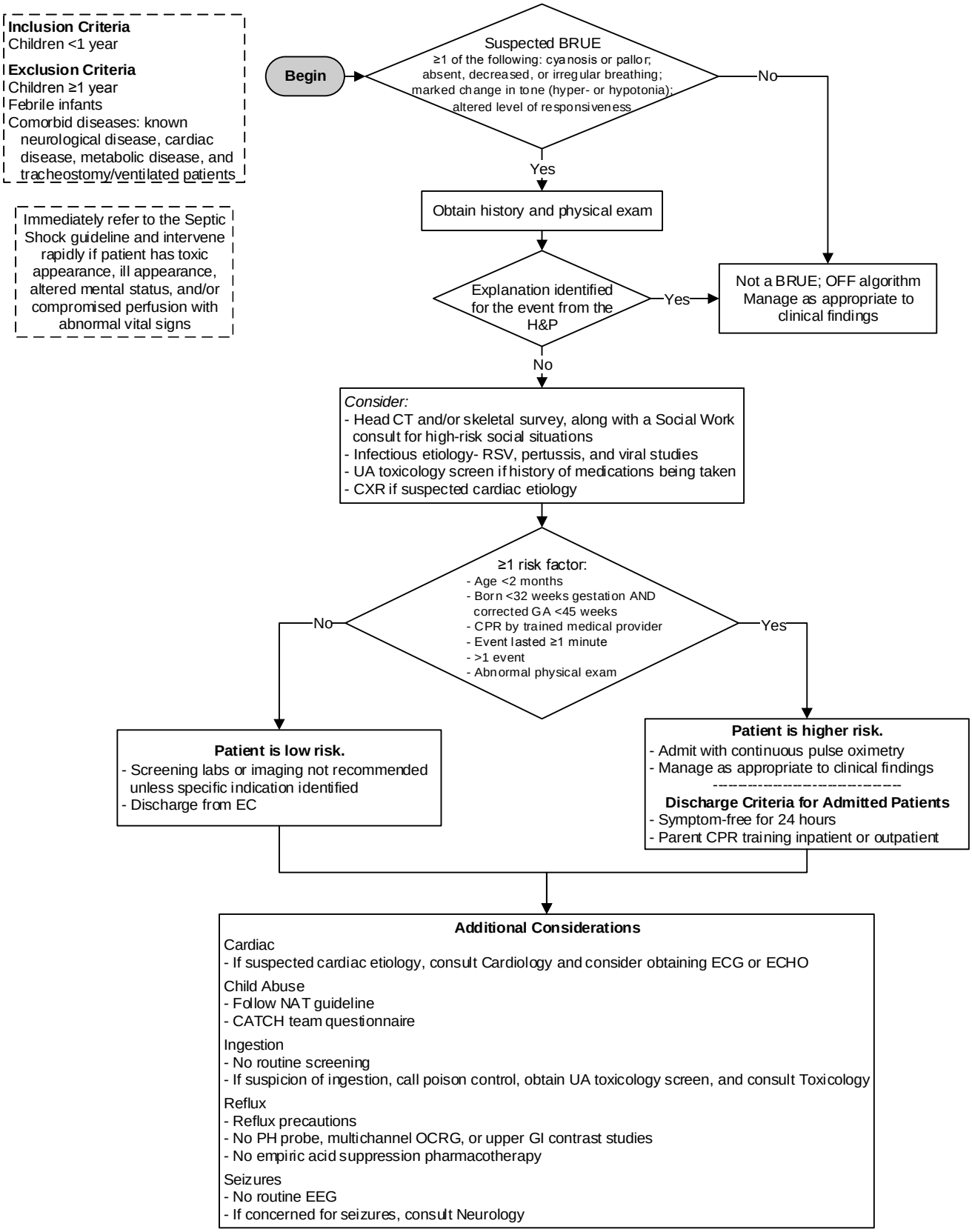
*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

In addition to routine care,
- Consider Social Work consult for high-risk social situations.
- Call poison control, obtain UA toxicology screen, and consult Toxicology if suspicion of ingestion.
- Consult Cardiology if suspected cardiac etiology and consider obtaining ECG or ECHO.
- Consult Neurology if concerned for seizures.
- PCP follow-up within 3 days.
- Provide inpatient/outpatient CPR training for caregiver(s). [1]

Measures
- Mortality
- Admission rate
- Total adjusted charges
- Length of stay
- Percentage of consults
- Readmission within 30 days
- Time to discharge
- Percentage of: chest x-rays, CTs, ECGs, EEGs, pH probes, multichannel OCRGs, upper GI contrast studies

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



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Guideline Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Portions of it were adapted from Nationwide Children's Hospital's and Children's Hospital of Orange County's submissions to the Pediatric Initiative for Clinical Standards (PICS) collaborative. 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.

BRUE Content Expert Team
Mark Riccioni, CPNP PC/AC, Critical Care, Co-Chair
Jenilea Thomas, CPNP PC/AC, Critical Care, Co-Chair
Beth Bubolz, MD, Emergency Medicine
Eric Chiou, MD, Gastroenterology
Jimmy Holder, MD, Neurology
Lucila Marquez, MD, Infectious Disease
Mona McPherson, MD, Critical Care
Ernestina Portillo, MD, Pulmonary
Joe Tran, MD, Pediatric Hospital Medicine
Shabana Yusuf, MD, Emergency Medicine

EBOC Team
Jennifer Loveless, MPH, Evidence-Based Practice Specialist
Janelle Smith, MSN, RN, CPN, Evidence-Based Practice Specialist
Charles Macias, MD, MPH, Director

Additional EBOC Support
Tom Burke, Research Assistant
Sherin Titus, Research Assistant
Karen Gibbs, MSN/MPH, RN, Evidence-Based Practice Specialist
Andrea Jackson, MBA, RN, Evidence-Based Practice Specialist
Betsy Lewis, MSN, RN, CNL, Evidence-Based Practice Specialist
Sheesha Porter, MSN, RN, Evidence-Based Practice Specialist
Monica Lopez, MD, MS, Associate Medical Director
Anne Dykes, MSN, RN, Assistant Director
Warren Boudreau, MSN, RN, Director

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
   - American Academy of Pediatrics (AAP) Brief Resolved 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: EBSCO, PubMed, CINAHL

4. Critically Analyze the Evidence
   - 17 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 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 and initial management of BRUE in infants. 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 Expert Teams 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 must 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.

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