

Brief resolved unexplained events (formerly apparent life-threatening events) and evaluation of lower-risk infants

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INFORMATION ABOUT CURRENT GUIDELINE

In May 2016, the American Academy of Paediatrics issued a clinical practice guideline on brief resolved unexplained events (BRUEs) in infancy, previously known as acute life-threatening events (ALTEs)

The aims of the guideline were threefold:

- Replace terminology and update the criteria for an ALTE.
- Provide an approach to patient evaluation that is based on the risk that the infant will have a repeat event.
- Provide management recommendations for infants deemed to be low risk.

This is the first clinical practice guideline from the Academy, which applies specifically to children who have experienced an ALTE (full reference [box 1](#)).

PREVIOUS GUIDANCE AND DEFINITIONS

The term BRUE is a new concept and has no previous guidelines. ALTE was first defined in 1986 by the National Institute of Health Consensus Development Conference of Infantile Apnoea and Home Monitoring as 'an episode that is frightening to the observer and that is characterised by some combination of apnoea, colour change, marked change in muscle tone, choking or gagging'.¹

The definition is open to interpretation and has made guideline development and research difficult.

KEY ISSUES

Definition of BRUE

The authors aimed to create a precise definition, which would aid in clinical care and research. It centred on the concept of a brief, resolved, unexplained event (BRUE, [box 2](#)). The term ALTE and the suggestion of a 'life-threatening event' has

Box 1 Resources

Tieder JS, Bonkowsky JL, Etzel RA, *et al*. Brief resolved unexplained events (formerly apparent life-threatening events) and evaluation of lower-risk infants. *Pediatrics* 2016;137:e20160590.

Box 2 Definition of BRUE—BRIEF: RESOLVED: UNEXPLAINED: EVENT

- ▶ **Brief:** duration <1 min; age <1 year
- ▶ **Resolved:** patient returned to their baseline state of health after the event
Normal observations, normal appearance
- ▶ **Unexplained:** not explained by an identifiable medical condition, eg, reflux, nasal congestion
- ▶ **Event:** ≥ 1 of the following cyanosis or pallor absent, decreased or irregular breathing, marked change in tone (hypertonia or hypotonia), altered responsiveness

purposefully been avoided as it was thought to cause undue anxiety in caregivers, lead to unnecessary testing and generate avoidable hospital admissions.

In comparison to the previous terminology of an ALTE:

- ▶ A strict age limit applies (<1 year).
- ▶ BRUE only diagnosed if no other likely explanation can be found.
- ▶ BRUE diagnosed based on clinician's characterisation of features of the event and not the caregivers' perception that the event was life threatening.
- ▶ Clinician needs to determine episodic pallor or cyanosis rather than just colour change. Redness in the face after prolonged coughing is not classed as a BRUE.
- ▶ Expands respiratory criteria beyond apnoea to include absent breathing and other respiratory abnormalities.



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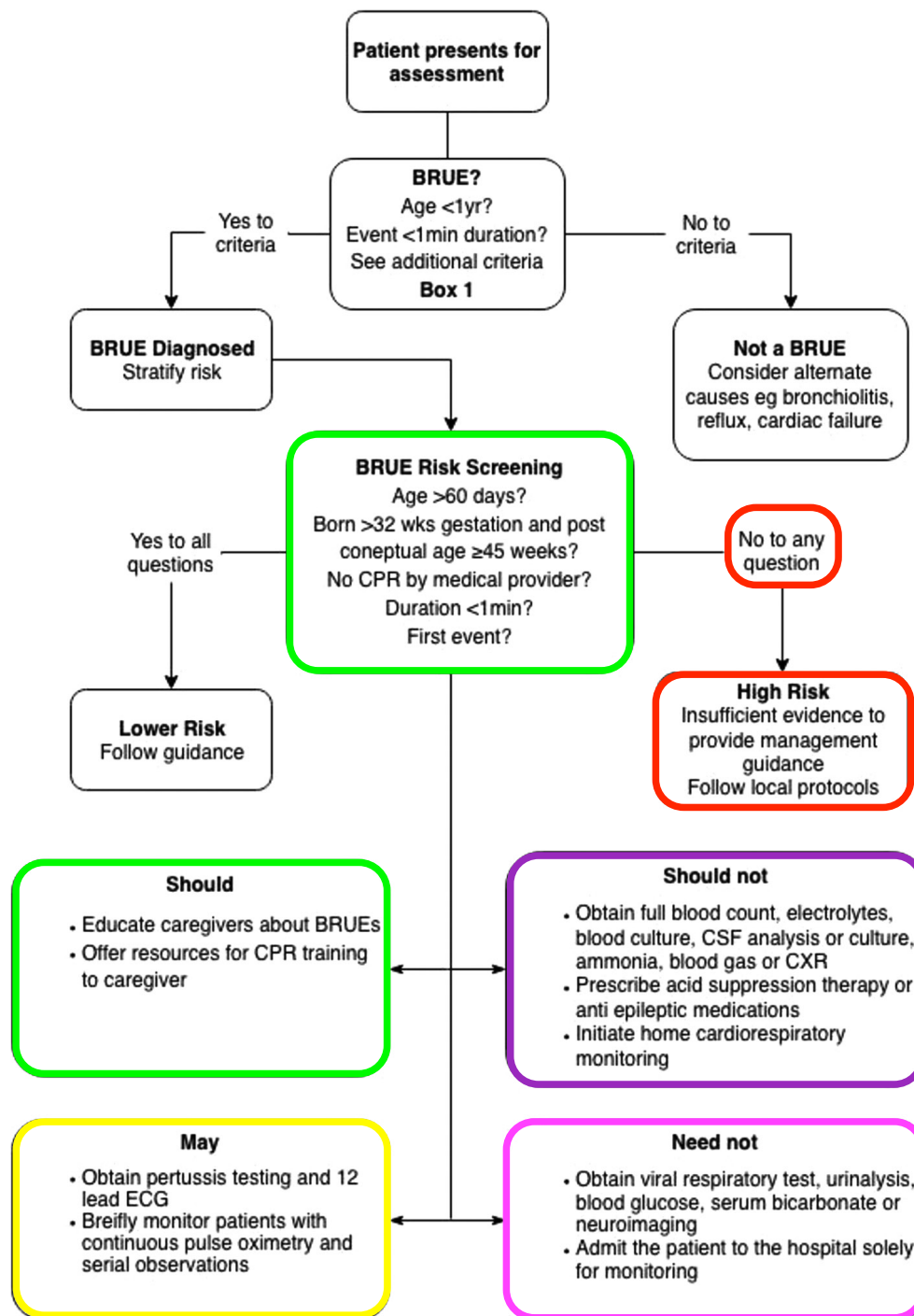


Figure 1 BRUE, brief resolved unexplained event; CXR, chest X-ray.

Box 3 Definition of low-risk brief resolved unexplained event

Age **>60 days**, gestational age **≥32 weeks** and postconceptual age **≥45 weeks**, **first BRUE**, **no cardiopulmonary resuscitation by trained medical provider**, **no concerning features in history or examination**, eg, family history of sudden cardiac death.

- Choking or gagging in history precludes the diagnosis of a BRUE.

HISTORY AND CLINICAL EXAMINATION

During assessment of the child, the clinician needs to determine if the history or examination suggests a diagnosis other than BRUE. In BRUE, a patient should have a resolved and unexplained event. History

of failure to thrive, enlarged head circumference or abnormal breathing all suggest an underlying medical condition and cannot be classified as a BRUE. Observations outside of normal parameters for age such as tachypnoea, tachycardia or fever all preclude a diagnosis of BRUE. Additionally, clinicians should be vigilant for evidence of non-accidental injury or conditions such as infantile spasms which could present in a similar manner to a BRUE.

High risk versus low risk

During the review of existing ALTE literature, a subset of patients were identified who met the BRUE criteria and were unlikely to have a recurrent event or a serious underlying condition. These patients were categorised as 'low risk' and met the criteria in (box 3).

Management of low-risk BRUE

In cases identified as low risk, the authors were able to create key action statements based on a systematic review of existing ALTE data, which could be applied to the new BRUE definition. In cases classed as high risk (ie, not meeting the criteria above), insufficient evidence was available to guide practice and the clinician is advised to follow local guidance.

Management recommendations based on strong-to-moderate evidence are as follows (figure 1):

In low-risk BRUEs clinicians should

- ▶ **Educate** caregivers about BRUEs and engage in shared decision making to guide management and follow-up.
- ▶ **Offer CPR training to caregiver.**

Clinicians should not

- ▶ Obtain full blood count, electrolytes, blood or CSF culture, metabolic tests including ammonia or amino acids or blood gasses.
- ▶ Perform a chest X-ray, echocardiogram, EEG or studies for reflux.
- ▶ Initiate home cardiorespiratory monitoring.
- ▶ Prescribe acid suppression therapy or antiepileptic medication.

RECOMMENDATIONS BASED ON WEAK EVIDENCE:

Clinicians may

- ▶ Briefly monitor patients with continuous pulse oximetry and serial observations.
- ▶ Obtain pertussis testing and 12-lead ECG.

Clinicians need not

- ▶ **Admit the patient to hospital solely for cardiorespiratory monitoring.**
- ▶ **Obtain viral respiratory test,** urinalysis, blood glucose, serum bicarbonate, lactic acid.
- ▶ **Obtain neuroimaging.**

UNRESOLVED CONTROVERSIES

Quality of available evidence

The authors have presented their analysis in terms of the quality of available evidence and the perceived risk/benefit of excluding an investigation from the low-risk BRUE guideline. They have attempted to translate this approach to clinical practice by way of suggesting clinicians 'should, should not, may and need not' perform a particular investigation. Although this detailed guidance is welcomed, the more uncertain recommendations under the categories 'may and need not' are harder to apply at the bedside and are discussed further below.

BRUE has a more precise definition than its predecessor, which in turn allows the clinician to make an easier judgement as to whether their patient is high or low risk. The authors are clear that guidance is only offered for low-risk patients. More work needs to be done to identify those who are high risk and what investigations are necessary as a starting point.

No meta-analyses or 'well-designed and conducted trials' were available to guide the authors in their analysis. Recommendations were based on trials with minor limitations or observational studies. This is in no doubt due to the ambiguity of the ALTE definition, which has hindered research and prompted the transition to the new term BRUE.

DISCUSSION OF WEAK RECOMMENDATIONS

Duration of observation

The authors concede that no specific evidence exists which identifies the ideal duration of observations after a BRUE. The authors suggest a **period of 1–4 hours may be necessary in some cases to establish that the patient and their observations remain stable.** Pulse oximetry has been identified as preferable to cardiorespiratory monitoring in identifying paroxysmal events, although it is also noted that healthy infants can have occasional desaturations when asleep.²

Blood glucose

Detailed review of the evidence base regarding glucose testing suggests that inborn errors of metabolism (IEM) cause an ALTE in only 0%–5% of cases.³ Individual papers are divided on the value of blood glucose as a universal screening tool in ALTE. The BRUE panel argue that patients who frequently attend with unexplained events or a family history of IEM will be categorised as high risk and therefore are not in the scope of the guideline. Blood glucose testing is inexpensive and a relatively non-invasive procedure and can point the clinician in the direction of occult metabolic conditions such as a fatty oxidation disorder. Despite newborn screening, IEMs are diagnosed during periods of illness. Due to differences of opinion and evidence in this matter, individual units should consider whether to make it their unit policy to include blood glucose measurement during initial assessment of patients presenting with BRUE-like symptoms.

Guideline review

12-Lead ECG

The evidence base for performing an ECG in a low-risk BRUE is weak. The authors recognise the low positive predictive values of ECG in ALTE^{4 5} and additionally comment that an isolated resting ECG may not pick up some serious cardiac pathologies. With this in mind, it is reasonable to consider an ECG on an individual case-by-case basis but it is not recommended as a routine assessment in a low-risk BRUE.

Pertussis

Pertussis can produce symptoms of an ALTE in view of paroxysmal cough, colour change and pauses in breathing. The authors highlight that performing pertussis testing in a low-risk BRUE should be based on clinical history, immunisation status and degree of suspicion from the assessing clinician. If suspicion of pertussis is strong enough, we suggest the case can no longer be considered as a BRUE, empirical antibiotics are recommended along with admission for observation beyond 1–4 hours.

WHAT DO I NEED TO KNOW?

What should I **stop doing**?

- ▶ **Stop using the term ALTE.**
- ▶ **Avoid admitting infants** to hospital for observation beyond 1–4 hours in low-risk BRUE.
- ▶ **Routinely performing a blood gas** or other blood tests in low-risk BRUEs.

What should I **start doing**?

- ▶ **Reassure** parents and be confident in conservative management.
- ▶ Recognise that the BRUE definition is more precise. Cough, fever, reflux, symptoms of viral upper respiratory tract infection, unresolved episodes or significant family history needs managing separately from these guidelines.

What can I continue to do as before?

- ▶ Consider alternative diagnoses throughout assessment.
- ▶ Continue to be vigilant to child protection concerns.

Clinical bottom line

- ▶ BRUE is the new term for an ALTE.
- ▶ Patients with BRUE are classified as high or low risk based on history and clinical examination.
- ▶ Low-risk BRUEs can be conservatively managed by avoiding all of blood tests, admission for observation >4 hours and radiological investigations.
- ▶ Parental communication and agreed management plans are paramount in successful treatment.

- ▶ Continue to involve parents in agreed management plans.
- ▶ **Continue to offer life support training to parents.**

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