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Identifying serious underlying diagnoses among patients with brief resolved unexplained events (BRUEs): a Canadian cohort study

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ABSTRACT

Objective To describe the demographics and clinical outcomes of infants with brief resolved unexplained events (BRUE).

Design A retrospective cohort study.

Setting 11 centres within the Canadian Paediatric Inpatient Research Network.

Patients Patients presenting to the emergency department (ED) following a BRUE (2017–2021) were eligible, when no clinical cause identified after a thorough history and physical examination.

Main outcome measures Serious underlying diagnosis (requiring prompt identification) and event recurrence (within 90 days).

Results Of 1042 eligible patients, 665 were hospitalised (63.8%), with a median stay of 1.73 days. Diagnostic tests were performed on 855 patients (82.1%), and 440 (42.2%) received specialist consultations. In total, 977 patients (93.8%) were categorised as higher risk BRUE per the American Academy of Pediatrics guidelines. Most patients (n=551, 52.9%) lacked an explanatory diagnosis; however, serious underlying diagnoses were identified in 7.6% (n=79). Epilepsy/infantile spasms were the most common serious underlying diagnoses (2.0%, n=21). Gastro-oesophageal reflux was the most common non-serious underlying diagnosis identified in 268 otherwise healthy and thriving infants (25.7%). No instances of invasive bacterial infections, arrhythmias or metabolic disorders were found. Recurrent events were observed in 113 patients (10.8%) during the index visit, and 65 patients had a return to ED visit related to a recurrent event (6.2%). One death occurred within 90 days.

Conclusions There is a low risk for a serious underlying diagnosis, where the majority of patients remain without a clear explanation. This study provides evidence-based risk for adverse outcomes, critical information to be used when engaging in shared decision-making with caregivers.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous research, primarily from the USA, suggests a low risk of serious underlying diagnoses following a brief resolved unexplained event (BRUE) and limited benefit from extensive investigations. However, there is a notable lack of multicentre studies conducted outside of the USA, leaving an evidence gap in different healthcare settings.

WHAT THIS STUDY ADDS

⇒ In our analysis of a large Canadian cohort comprising over 1000 infants with BRUE, we found that only 8% had serious underlying conditions, primarily seizures and apnoeas, while the majority remained without an explanatory diagnosis.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This research offers evidence-based metrics that quantify the actual risks for critical clinical outcomes, informing shared decision-making with caregivers.

INTRODUCTION

Brief resolved unexplained events (BRUEs) in infancy often elicit concern among caregivers due to their unexplained and potentially life-threatening nature.[1–6] While most events are benign and self-limiting, they pose a diagnostic challenge for healthcare professionals tasked with identifying events rarely caused by a serious underlying condition.[7–12] Providers often find it difficult to convey the risk of serious aetiologies or event recurrence to caregivers,[10 13] resulting in uncertainty

that may lead to unwarranted hospitalisations for otherwise healthy infants.[14] This further increases caregivers' stress,[4 5] subjects infants to unnecessary harms associated with hospitalisation and procedures[9] and increases healthcare expenses.[15 16]

In 2016, the American Academy of Pediatrics (AAP) replaced the term apparent life-threatening event (ALTE) with BRUE to provide more precise diagnostic criteria focused on the clinical assessment by the provider, rather than just the presenting complaint, and to eliminate the alarming term 'life-threatening'.[1] Unlike ALTE, which included a broader range of presentations, including those with clear underlying aetiologies, BRUE specifically applies to events that are resolved and remain unexplained after a thorough evaluation. This distinction necessitated new research initiatives focusing on BRUE, as prior studies on ALTE may not be applicable to the narrower and more defined criteria of BRUE.[6 17] To date, only one large multicentre cohort of infants diagnosed with BRUE has been described, limited to hospitals within the USA.[7 8] Findings from this study suggest a low risk (5%) for a serious underlying diagnosis[9] and a limited utility in extensive investigations and consultations.[12 14 18] Notably, there is a gap in research as no comprehensive multicentre study has corroborated these findings in a different healthcare setting. The reliance on a single cohort study, while informative, presents limitations in terms of broader applicability and may not fully capture variations in clinical practice across different regions.

Our study aims to describe the demographics and clinical features of infants with BRUE, as well as identify rates and risk factors for serious underlying diagnoses and event recurrences, within a large Canadian multicentre cohort.[19] By doing so, we intend to equip clinicians with the necessary data to inform families about potential risks and guide subsequent management decisions, which may include hospitalisation or diagnostic testing.

METHODS

Study design

We conducted a retrospective cohort study across 11 centres within the *Canadian Paediatric Inpatient Research Network,* including eight children's hospitals and three general hospitals.[20] Annual emergency department (ED) visit volume was between 13 000 and 80 000 patients (median: 49 000). The study protocol has been previously published,[19] and the study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology statement for cohort studies (online supplemental table S1).[21]

Patients were identified using a previously validated approach,[22] based on the International Classification of Diseases, Tenth Revision, Canada admission or discharge codes. Health records spanning from 1 January 2017 to 31 December 2021 were reviewed to determine eligibility. Sampling included all cases within the specified date range, with a cap of 200 patients per site, to prevent the over-representation of any single site. At eight of the 11 sites, every identified patient was reviewed for eligibility. For the remaining three sites exceeding this limit, patients were selected sequentially from a randomised list until the predetermined maximum threshold was met.

Eligibility criteria

The study included infants aged 1–365 days of life who presented to the ED following a BRUE, with no identified clinical cause after a thorough history and physical examination.[1] Exclusion criteria were extreme prematurity (<28 weeks gestation), newborns on the first day of life, any known pre-existing comorbidity contributing to the BRUE, preceding symptoms, abnormal vital signs on ED presentation or physical examination findings inconsistent with a BRUE diagnosis.

Data collection

Each site designated one to three research assistants trained in data extraction. A sample of local charts (range: 10–37, online supplemental table S2) was assessed by all reviewers at each location, and inter-rater reliability was calculated for key variables (eg, patient eligibility and outcomes of interest), and used to provide further training. Patient and BRUE characteristics not documented in the patient's chart were assumed to be absent. Patients were risk stratified based on current AAP guidelines.

Study outcomes

The primary outcome was a serious underlying diagnosis, defined as a diagnosis requiring prompt identification that can otherwise lead to morbidity or mortality[8 23] (eg, bacterial infection requiring antibiotics, gastro-oesophageal reflux disease (GERD) leading to faltering growth) (online supplemental table S3).[19] Data were collected on any diagnoses attributed to the BRUE or identified during its evaluation, either at the index visit or within 90 days. The secondary outcome was event recurrence (during the initial hospitalisation, or on ED revisit). Additional secondary outcomes were ED revisits, hospital readmissions and mortality. Monitoring for all these outcomes was limited to 90 days after the index presentation. We also collected details on any documented complication during the initial hospitalisation (eg, false positive testing or non-clinically significant events on cardiorespiratory monitoring). False positive testing was defined as any diagnostic test that erroneously indicated an abnormal result, leading to additional testing or subspecialty consultation. This was categorised as a complication because it subjected infants to unnecessary further testing and prolonged their hospital stay.

Sensitivity analyses

Two sensitivity analyses were conducted. First, we excluded three hospitals where records for patients discharged directly from the ED were not available, as the admitted patients may represent those with more

Table 1 Demographic and clinical characteristics of patients with BRUE stratified by the presence of a serious underlying diagnosis

	Total n (%)	No serious underlying diagnosis	Serious underlying diagnosis	P value
Patient characteristics				
Number of patients	1042	963	79	
Age, days [IQR]	41 [13, 84]	43 [14, 86]	31 [8, 63]	0.03
Sex				0.91
Female	529 (50.8)	488 (50.7)	41 (51.9)	
Male	513 (49.2)	475 (49.3)	38 (48.1)	
Patient risk factors				
Gestational age				0.11
Term (≥37 weeks)/not indicated	890 (85.4)	828 (86.0)	62 (78.5)	
Late preterm (34–36+ weeks)	102 (9.8)	89 (9.2)	13 (16.5)	
Moderate preterm (32–33+ weeks)	26 (2.5)	25 (2.6)	1 (1.3)	
Very preterm (28–31+ weeks)	24 (2.3)	21 (2.2)	3 (3.8)	
Prematurity (<32 weeks) or corrected <45 weeks*	180 (17.3)	159 (16.5)	21 (26.6)	0.03
Age ≤60 days	658 (63.1)	600 (62.3)	58 (73.4)	0.05
Family history concerning for serious condition	133 (12.8)	111 (11.5)	22 (27.8)	<0.001
Social history concerning for abuse	48 (4.6)	43 (4.5)	5 (6.3)	0.40
Abnormal medical history	320 (30.7)	288 (29.9)	32 (40.5)	0.06
Conditions related to prematurity	128 (12.3)	113 (11.7)	15 (19.0)	0.07
Neonatal respiratory disorders	99 (9.5)	87 (9.0)	12 (15.2)	0.11
Gastro-oesophageal reflux or feeding-related conditions	78 (7.5)	69 (7.2)	9 (11.4)	0.18
Jaundice	77 (7.4)	68 (7.1)	9 (11.4)	0.18
Other medical conditions	97 (9.3)	89 (9.2)	8 (10.1)	0.84
BRUE characteristics†				
Abnormal breathing	686 (65.8)	626 (65.0)	60 (75.9)	0.05
Tone change	607 (58.3)	558 (57.9)	49 (62.0)	0.55
Colour change	514 (49.3)	472 (49.0)	42 (53.2)	0.49
Altered responsiveness	377 (36.2)	346 (35.9)	31 (39.2)	0.55
Event duration ≥1 min	354 (34.0)	325 (33.7)	29 (36.7)	0.62
History of similar event	343 (32.9)	296 (30.7)	47 (59.5)	<0.001
History of multiple events or event clusters	325 (31.2)	285 (29.6)	40 (50.6)	<0.001
CPR performed and indicated	44 (4.2)	40 (4.2)	4 (5.1)	0.57
Higher risk BRUE as defined by the AAP guidelines	977 (93.8)	898 (93.3)	79 (100.0)	0.01

*Defined as per the AAP higher risk BRUE criteria.
†Patients may present with BRUE episodes including multiple characteristics.
AAP, American Academy of Pediatrics; BRUE, brief resolved unexplained event; CPR, cardiopulmonary resuscitation.

concerning features on history, physical examination or investigations, thereby potentially inflating the prevalence of the outcomes of interest. Second, we excluded patients transferred in or out, for a similar rationale, as well as the potential for incomplete data collection for patients transferred in, or the ascertainment of outcomes for those transferred out.

Statistical analysis

Descriptive statistics were used for baseline demographic characteristics and study outcomes, including frequency and percentage for binary and categorical outcomes, and median and IQR for continuous outcomes. Fisher's test and Mann-Whitney tests compared characteristics for infants with and without outcomes of interest. To account for the multicentre nature of the study and clustering by hospital, mixed-effects logistic regression models were conducted for the outcomes of interest, serious underlying diagnosis and event recurrence. Covariates included patient and BRUE characteristics, as well as previously described

Table 2 Clinical management and outcomes of patients with BRUE

	n (%)
Clinical management	
Hospital admission	665 (63.8)
Length of stay, days [IQR]	1.73 [1.00, 3.00]
ICU admission	67 (10.1)
Length of stay, days [IQR]	3.00 [1.50, 6.50]
Treatments	
Antiepileptics	17 (1.6)
Antimicrobials	80 (7.7)
Acid suppression or antireflux medications	160 (15.4)
Nasogastric feeds	16 (1.5)
Intravenous fluids	59 (5.7)
Caffeine	24 (2.3)
Oxygen (low-flow nasal prongs, or high flow)	29 (2.8)
Positive pressure ventilation (CPAP or BiPAP)	12 (1.2)
CPR training offered	140 (13.4)
Complications	162 (15.5)
False positive testing	127 (12.2)
Non-clinically significant events on monitors	43 (4.1)
Intravenous extravasation	2 (0.2)
Significant surgical complications	1 (0.1)
Other	11 (1.1)
Diagnostic testing*	855 (82.1)
Consultations†	440 (42.2)
Clinical outcomes	
Underlying diagnosis‡	
Serious	79 (7.6)
Non-serious	412 (39.5)
N/A (unexplained)	551 (52.9)
Recurrent event	163 (15.6)
During index visit	113 (10.8)
After discharge‡	65 (6.2)
Return visit‡	216 (20.7)
Return visit‡—related to BRUE	92 (8.8)
Rehospitalisation‡	64 (6.1)
Death‡	1 (0.1)

*Diagnostic testing included laboratory testing (bloodwork, urine or cerebral spinal fluid studies, imaging and ancillary testing).
†Consultations included evaluation by specialists or allied healthcare providers.
‡At or within 90 days of index presentation.
BiPAP, bilevel positive airway pressure; BRUE, brief resolved unexplained event; CPAP, continuous positive airway pressure; CPR, cardiopulmonary resuscitation; ICU, intensive care unit.

potential risk factors[1 7 8]: age <60 days, prematurity (<32 weeks or corrected <45 weeks), abnormal family, medical or social histories, change in colour, breathing pattern, tone or responsiveness, duration ≥1 min and presenting with multiple events (prior history or event cluster). R V.4.3.1 (Vienna, Austria) was used for data analyses, with the mixed-effects models fitted using the lme4 package (version 1.1-35.5).[24]

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Cohort description

A total of 1042 patients meeting the diagnostic criteria for BRUE were identified (online supplemental figure S1), with a median age of 41 days (IQR: 13–84 days) (table 1). Prematurity was observed in 152 patients (14.6%), and 320 patients (30.7%) had an abnormal medical history. Abnormal breathing pattern was the most common presentation (65.8%), followed by a change in tone (58.3%). A history of a similar prior event was reported in 343 patients (32.9%). Using the AAP guideline criteria, 977 patients (93.8%) were classified as higher risk BRUE.

Clinical management

Of the studied cohort, 665 patients were hospitalised (63.8%), with a median length of stay of 1.7 days (IQR: 1.0–3.0 days) (table 2). 67 (10.1%) of hospitalised patients were admitted to the paediatric/neonatal intensive care unit (ICU), including 63 (94%) who were directly admitted from the ED, despite being asymptomatic at the time of presentation. Among the cohort, complications were documented in 162 (15.5%), with false positive testing being the most common (n=127, 12.2%). A total of 855 patients (82.1%) underwent diagnostic testing, and specialist consultations were conducted with 440 patients (42.2%).

Primary outcome: serious underlying diagnosis

The majority of patients did not have an explanatory diagnosis (n=551, 52.9%); serious diagnoses were identified in 7.6% (n=79) (table 2, online supplemental figure S2). When excluding transferred patients or hospitals reporting only on admitted patients, serious underlying diagnoses were made in 6.7% and 5.4%, respectively (online supplemental tables S4 and S5).

Epilepsy/infantile spasms were the most common serious underlying diagnoses (2.0%, n=21/1042) (table 3). Apnoea requiring ICU care, oxygen, ventilatory support or caffeine was the second most common aetiology among patients with a serious underlying diagnosis (1.9%, n=20), with an additional 39 cases of apnoea not meeting the serious diagnosis threshold.

Gastro-oesophageal reflux and associated laryngospasm were the most common non-serious underlying diagnoses, identified in 268 otherwise healthy and thriving infants (25.7%). In contrast, 11 patients had severe GERD resulting in failure to thrive. Among the cohort, 160 patients (15.4%) were discharged home on acid suppression therapy. Meanwhile, oropharyngeal

Table 3 Identified serious and non-serious diagnoses among patients with a brief resolved unexplained event (BRUE)

	Patients (n)
Serious diagnoses (n=79)	
Seizure/epilepsy or infantile spasms	21
Apnoea (*requiring treatment*)	20
GERD (*leading to faltering growth*)	11
Urinary tract infection	6
Cow's milk protein allergy	5
Viral respiratory tract infection	4
Oropharyngeal dysphagia or feeding difficulties (*leading to faltering growth or serious aspiration*)	4
Severe periodic breathing	4
Genetic disorders	3
Anaemia	2
Upper airway abnormality	2
Hypoglycaemia	2
Brain tumour	2
Other*	6
Non-serious diagnoses (n=412)	
GER and associated laryngospasm	268
Oropharyngeal dysphagia or feeding difficulties	66
Apnoea	39
Viral respiratory tract infection	29
Breath holding spell	28
Periodic breathing	15
Upper airway abnormality	7
Cow's milk protein allergy	7
Normal reflex or movement	4
Myoclonic jerks	4
Problems with growth	2
Genetic disorders	2
Other†	15

This table outlines the probable or confirmed diagnoses deemed by the providers to explain the BRUE, identified either during the index visit or within 90 days. Diagnoses are classified as 'Serious' (where delay in prompt diagnosis and treatment may have caused significant morbidity or mortality).
*Serious—other: problems with growth (1), hypoxia (1), HSV encephalitis (1), hypertrophic cardiomyopathy (1), cardiac arrest (no identified aetiology) (1), gastroenteritis/vomiting (1).
†Non-serious—other: congestion/rhinitis (4), shuddering spells (3), cutis marmorata (1), hypotonia due to deep sleep (1), neonatal withdrawal (1), partial airway obstruction (1), smothering event (1), spasmus nutans (1), vasovagal (1), seizure/epilepsy (*no treatment*) (1), gastroenteritis/vomiting (1), purple crying (1), hypoxaemia (1), viral meningitis (1), tracheomalacia (1).
GER, gastro-oesophageal reflux; GERD, gastro-oesophageal reflux disease.HSV, Herpes simplex virus;

dysphagia, choking and feeding difficulties were identified as explanatory in 66 patients, with an additional four patients meeting the serious criteria. Urinary tract infection was the sole bacterial infection found as an explanatory diagnosis in six patients. No instances of invasive bacterial infections, such as bacteraemia or meningitis, or pertussis were noted. One case of hypertrophic cardiomyopathy was identified as an underlying diagnosis. There were no identified arrhythmias or inborn errors of metabolism diagnoses.

After adjusting for covariates, a serious underlying diagnosis was more common among patients with multiple events prior to presentation (adjusted OR (aOR): 3.07 (1.70–5.56)), those with events ≥1 min (aOR: 2.10 (1.18–3.75)) and those with event recurrence after the index presentation (aOR: 6.43 (3.73–11.08)) (figure 1, online supplemental table S6). Patient's age at index presentation was not associated with a serious underlying diagnosis considered as a continuous or a dichotomous (<60 days vs ≥60 days) variable.

Secondary outcomes

A total of 163 patients (15.6%) experienced a recurrent event (table 2), including 113 patients (10.8%) who had an in-hospital recurrent event during the index visit. Among hospitalised patients, observation of the recurrent event by a healthcare provider provided an explanatory diagnosis in only 4.8% (n=32/665).

A return visit within 90 days occurred in 216 patients (20.7%), including 92 visits (8.8%) directly related to the BRUE episode, and 65 patients (6.2%) having experienced a recurrent event following discharge. 64 patients (6.1%) were rehospitalised, and a single death was reported within 90 days of the index visit secondary to hypertrophic cardiomyopathy.

In mixed-effects multivariable analysis, a recurrent event was more likely among infants younger than 60 days (aOR: 1.87 (1.24–2.84)), patients with a concerning family history (aOR: 2.32 (1.40–3.84)) and patients with multiple events prior to presentation (aOR: 2.98 (2.02–4.40)) (figure 1, online supplemental table S6).

DISCUSSION

In this large Canadian cohort of over 1000 patients with BRUE, the vast majority of which were classified as 'higher-risk', we found that most infants did not have an explanatory diagnosis and only 8% had serious underlying conditions, where delayed treatment could have increased morbidity or mortality. Serious diagnoses primarily included seizures/infantile spasms and apnoea. Gastrointestinal diagnoses were predominant among non-serious aetiologies. Our findings support the growing body of evidence indicating a low likelihood of serious diagnoses presenting as BRUE,[7 11 14] and provide clinicians and caregivers with metrics to guide management.

Infants with BRUE are commonly admitted and undergo diagnostic testing to identify serious underlying diagnoses.[14 25–29] While these practices are intended to be reassuring, they can inadvertently increase caregiver anxiety, risk for harm due to testing cascades as well as elevate costs.[2–5 30] The low prevalence and heterogeneity

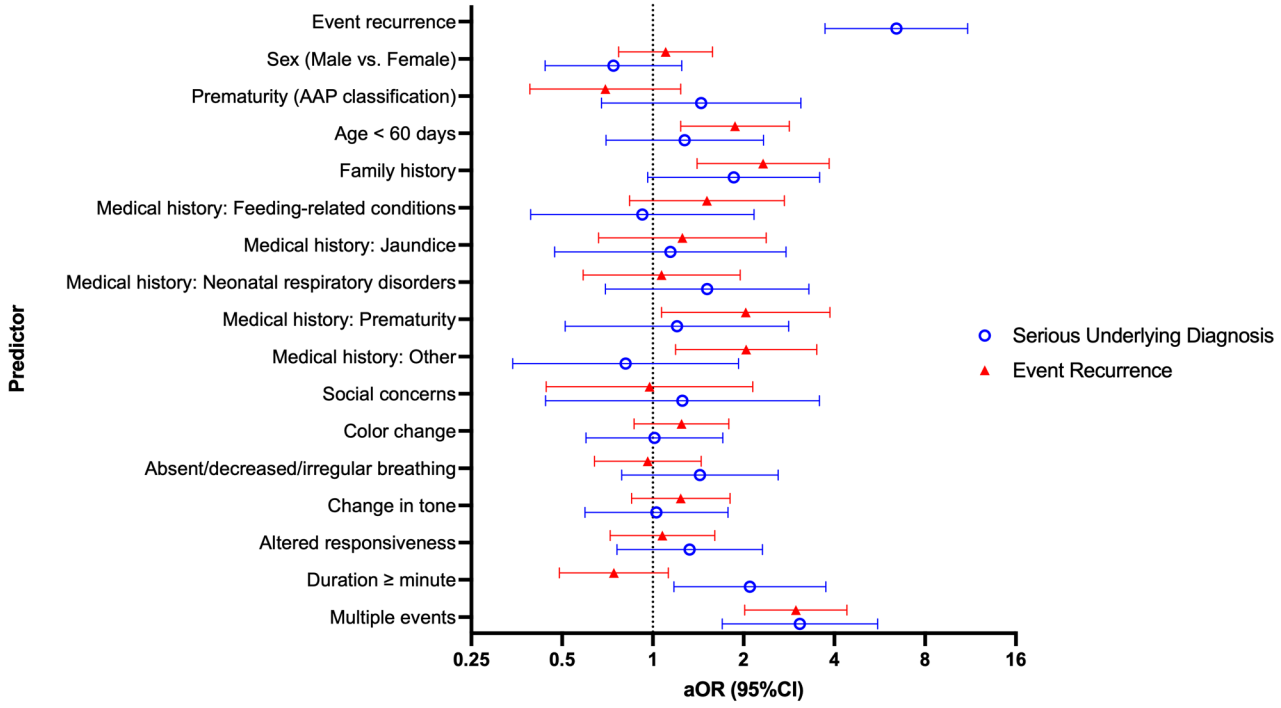

Figure 1 Multivariable mixed-effects logistic regression analysis of risk factors for serious underlying diagnosis and event recurrence. AAP, American Academy of Pediatrics; aOR, adjusted OR.

of serious underlying diagnoses contribute to a low diagnostic yield. Routine tests frequently unveil incidental or clinically insignificant findings (eg, haemolysed samples requiring multiple repeats), rather than explaining the index event.[14] The AAP recommends consideration of pertussis testing and an ECG for lower risk patients.[1] However, combining data from our cohort with the BRUE Quality Improvement and Research Collaborative from 15 US children's hospitals,[7] a total of 4325 patients, revealed that only six had pertussis, and four had a serious underlying cardiac diagnosis. This calls into question the value of routine ECG and pertussis testing unless specific clinical concerns exist. While some may perceive ECG as a simple non-invasive test to provide reassurance, research has shown that this often leads to a diagnostic cascade where non-specific ECG findings lead to prolonged hospital stay for further testing or cardiology consultation, inadvertently increasing parental anxiety.[14] Epilepsy was the most common serious underlying diagnosis. Patients exhibiting red flags for neurological conditions or experiencing recurrent events—identified as a significant risk factor for serious illness in both our study and others[8 12]—might benefit from a close outpatient neurological evaluation to assess the need for an electroencephalogram.[31–33]

Apart from serious diagnoses, non-serious underlying conditions are prevalent, and identifying them could offer an explanation and potentially bring reassurance.[4] The majority of these diagnoses relate to feeding and gastrointestinal issues.[7] Having a specialist provider or service observe feeding can help identify issues like reflux or oropharyngeal dysphagia. However, providers should exercise caution when prescribing reflux medications, given the mounting evidence of their limited benefits and potential side effects.[34–37] Despite the lack of worrisome signs in most infants with reflux (eg, no failure to thrive), we noted a high number of patients being discharged on reflux medications, presenting an area for quality improvement and provider and caregiver education.

Healthcare providers commonly express concern regarding the risk for an underlying diagnosis, while caregivers are similarly anxious about event recurrence.[5 10] Notably, our results show a strong association between the two outcomes, with the odds of a serious underlying diagnosis being more than three times higher in patients with multiple events prior to presentation. Hospital monitoring for event recurrence has been suggested as a potential advantage of admission.[5 23] However, it is important to note that such recurrences are infrequent, and rarely do they contribute to reaching a diagnosis, given that the majority of BRUE events remain unexplained without an underlying aetiology. In our study, a mere 5% of hospitalised patients experienced a recurrent event while in the hospital, which then led to an explanatory diagnosis. This observation aligns with findings from Bochner *et al*, where only 7% of cases noted a similar outcome.[9] Conveying these findings may allow caregivers to assess whether hospital admission aligns with their individual values. Some caregivers might value the observation period, while others may question the benefits of hospitalisation.[2–5] This highlights the need for personalised BRUE management centred on shared decision-making (SDM). The successful application of SDM in paediatric

conditions like traumatic brain injury has reduced low-yield investigations and improved parental satisfaction.[38] SDM benefits in the context of BRUE have been acknowledged by caregivers,[4 5] clinicians[10] and researchers.[1 7 13] A critical piece in SDM is the discussion of risk. Our study results can guide these discussions, helping providers and caregivers understand potential BRUE outcomes on a population level. Other strategies that focus on individual risk factors and estimate specific patient's risk have been explored but remain to be validated.[7] These approaches may offer more precise risk estimates than the current AAP higher risk stratification, which categorises most patients as higher risk,[7 17 39 40] and has been increasingly questioned for its effectiveness and utility.[7 8 41] Despite the overall low risk of serious underlying diagnoses and event recurrence during hospitalisation, we observed a relatively high rate of ICU admissions, predominantly for observation, consistent with trends reported in single-centre studies in the USA.[27 42] Additionally, there was variability between hospital practices. ICU care should be reserved for patients requiring high-acuity interventions, such as respiratory support, vasoactive medications or continuous close monitoring. Patients presenting with BRUE who are asymptomatic on admission generally do not warrant ICU-level care, representing another area for targeted quality improvement efforts.

The study strengths include its large sample size, and multisite involvement across a vast geographical area (spanning different Canadian regions) and including diverse hospital settings. A limitation is the potential for missing patients who might have had a serious diagnosis but lack specific BRUE-related International Classification of Diseases codes. However, our selection approach has been validated with 99% sensitivity, and it is unlikely that patients meeting the BRUE criteria will have a clear explanatory diagnosis coded at the time of admission.[22] Given the retrospective nature of our study, there is also a possibility that patients may have subsequently sought care at a different hospital or healthcare system, which our review might have missed. However, our study covered major paediatric centres, where critically ill patients are likely to receive both inpatient and outpatient care. Moreover, several provinces in our study have a shared data system within the province, ensuring comprehensive data capture. Finally, in three hospitals where the number of patients approached 200, our sampling approach may have reduced our power, with potential differences between the cases sampled and those not sampled. However, the randomisation process implemented is anticipated to significantly mitigate this potential bias.

In conclusion, our study, describing a large BRUE cohort, demonstrates a low risk for a serious underlying diagnosis, where the majority of patients remain without a clear explanation. This provides evidence-based risk for adverse outcomes, critical information to be used when engaging in SDM with caregivers, to convey the pros and cons of different management approaches, understand the family's values and risk tolerance and offer reassurance. Future research should focus on operationalising how to share these data with caregivers and how to engage in SDM, along with evaluating its benefits.

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Contributors NN, ZL, KP, FJ, JNB, JT and PG planned and conceived the study. ZL, KP, JQ, JF, JAG, CN, BP, MD, RDG, AS, RK, JH, PK, NK, IO, ÉH, AS, EF-P, PR, PH, MW, SA, PN, Marie-Pier Goupil, Shawn Lee, Emy Philibert, Juliette Dufresne, Raman Chawla and Martin Ogwuru acquired study data. NN drafted the first version of the manuscript. All authors critically revised the manuscript, approved the final draft and agreed to be accountable for all aspects of the work. NN is responsible for the overall content as guarantor.

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