

SYSTEMATIC REVIEW

Defining neonatal status epilepticus: A scoping review from the ILAE neonatal task force

Magda L. Nunes¹  | Elissa G. Yozawitz²  | Courtney J. Wusthoff³  |
 Renée A. Shellhaas⁴  | Efraín Olivas-Peña⁵ | Jo M. Wilmshurst⁶  |
 Ronit M. Pressler⁷  | Chahnez C. Triki⁸  | Hans Hartmann⁹ | Terrie Inder¹⁰ |
 Geraldine B. Boylan¹¹  | Kette Valente¹²  | Solomon L. Moshe^{13,14}  |
 Eli M. Mizrahi¹⁵ | Nicholas S. Abend¹⁶ 

Correspondence

Magda L. Nunes, School of Medicine and Brain Institute (BraIns), Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, RS, Brazil.
 Email: mlnunes@pucrs.br

Abstract

Objective: To review the available literature concerning the definition of neonatal status epilepticus (SE) and/or seizure burden.

Methods: The International League Against Epilepsy Neonatal Task Force performed a scoping review of the definitions of neonatal SE. Following a systematic literature review, articles were screened and data were abstracted regarding: (1) article characteristics (author identification, publication year, journal name, digital object identifier, title, objective, and study design); (2) cohort characteristics (sample size, gestational age, seizure etiology); (3) definition of SE and/or seizure burden; and (4) the method used to identify and classify SE, including routine EEG (EEG), continuous EEG monitoring (cEEG), amplitude-integrated EEG (aEEG), or clinical features.

Results: The scoping review yielded 44 articles containing a definition of neonatal SE. Studies mainly included infants with hypoxic-ischemic encephalopathy or neonates considered at risk for seizures. SE identification and classification most often relied on cEEG. The majority of studies based the definition of SE on seizure duration, including summed duration of seizures comprising ≥50% of any 1-h epoch, recurrent seizures for >50% of the total recording time, or either electrographic seizures lasting >30 min and/or repeated electrographic seizures totaling >50% in any 1-h period. Seizure burden was reported in 20 studies, and the most commonly used approach assessed total seizure burden, defined as total duration of EEG seizures in minutes. Sixteen studies assessed the relationship between seizure burden and outcomes, and most identified a significant association between higher seizure burden and unfavorable outcomes.

For affiliations refer to page 49.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Author(s). *Epilepsia Open* published by Wiley Periodicals LLC on behalf of International League Against Epilepsy.

Significance: This scoping review demonstrates a substantial variation in neonatal SE definitions across the literature. The most common definitions were based around a 30-min seizure duration criterion, but evidence was insufficient to support that 30 min was a cutoff defining prolonged seizures or that seizures exceeding this burden were more likely to be pharmacoresistant or associated with worse outcomes. As a next step, the Neonatal Task Force intends to develop a standardized approach to assessing and describing neonatal seizure burden and defining neonatal SE.

Plain Language Summary: Prolonged seizures are a neurologic emergency, if untreated, can lead to permanent injury or death. In adults and children, seizures lasting longer than 30 min are believed to cause brain damage. However, it is not clear if this definition can be applied to neonates. The International League Against Epilepsy Neonatal Taskforce performed a scoping literature review which identified 44 articles containing a definition of neonatal status epilepticus. In this article, the authors reviewed the current used definitions for prolonged seizures in neonates to establish a relationship between seizure duration and neurological outcome. As a next step, the Neonatal Task Force intends to develop a standardized approach to assessing and describing neonatal seizure burden and defining neonatal SE.

KEYWORDS

neonatal, neurocritical care, outcome, seizure burden, seizures, status epilepticus

1 | INTRODUCTION

Seizures are the most common neurological emergency in the neonatal period. Most seizures in neonates occur in the context of an acute brain injury, while 10%–15% occur in the context of an epilepsy syndrome.^{1–5} and may have distinct etiologies, clinical characteristics, and electroencephalographic (EEG) patterns.^{4,6,7} Neonatal seizures are associated with mortality, neuroimaging abnormalities, and subsequent epilepsy and neurobehavioral disorders.^{8,9}

Recent guidelines from the International League Against Epilepsy (ILAE) address the diagnosis and management of neonatal seizures, but details regarding neonatal status epilepticus (SE) were not addressed.^{3–5} The definition of SE among neonates varies within the related literature and has evolved (Figure 1).^{10–17} Many studies of neonates have extended the older 30-min time frame used to define SE in adults and older children has been extended to the neonatal period,^{18,19} including definitions focused on seizure duration (e.g., continuous seizure lasting 30 min) or seizure percentage within an EEG epoch (e.g., $\geq 50\%$ of 1-h epoch contains seizures) as proposed in the guidelines from the American Clinical Neurophysiology Society.²⁰ However, these definitions

Key Points

- There is a substantial variation on SE definition in neonates.
- Data are insufficient to support the 30 min seizure duration as a definition of SE in neonates.
- An evidence-based classification approach for neonatal seizure burden and a definition of neonatal SE is necessary.

might be arbitrary given there is limited evidence as to the duration at which seizures become more refractory to treatment, cause secondary brain injury, or impact outcome in neonates.^{18,19} Furthermore, the ILAE classification of SE in adults has become more nuanced and includes two operational dimensions. Time 1 (T1) is the duration at which a seizure is considered abnormally prolonged, and Time 2 (T2) is the duration of a seizure at which there is a risk of long-term consequences.²¹ The proposed T1 and T2 durations vary by seizure type, including: (1) tonic-clonic SE (T1 5 min; T2 30 min),

Neonatal Status Epilepticus is an evolving definition.

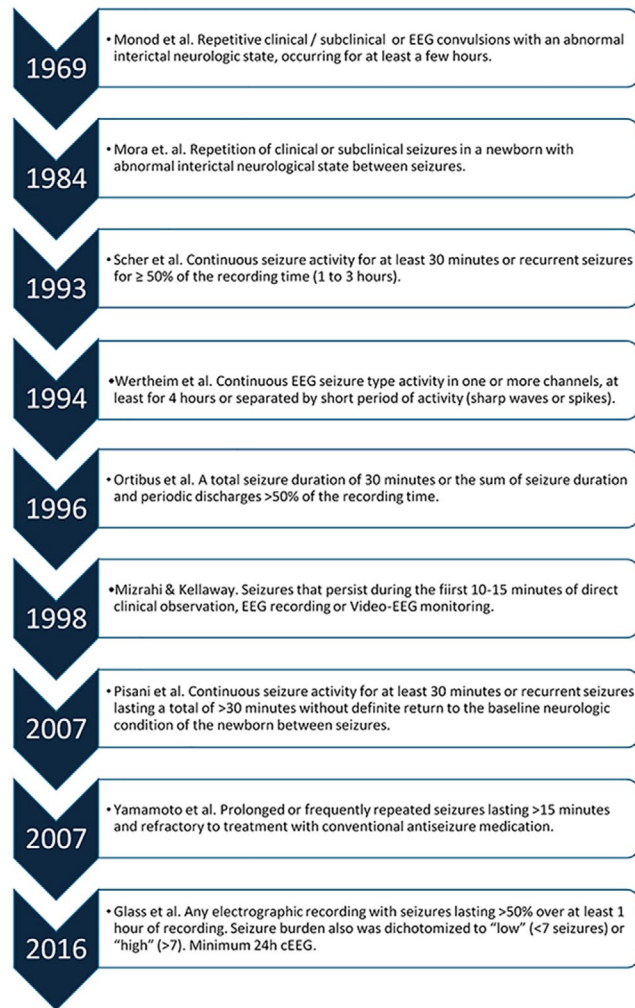


FIGURE 1 Neonatal Status Epilepticus is an evolving definition; this figure shows a timeline of previous definitions since 1969.

(2) focal SE with impaired awareness (T1 10 min; T2 >60 min), and (3) absence SE (T1 10–15 min; T2 unknown). The ILAE definitions of SE do not include neonates. Likewise, the American Clinical Neurophysiology Society has defined electrographic SE in critically ill children and adults as a continuous electrographic seizure lasting ≥ 10 min or electrographic seizures occurring for $>20\%$ of a 1-h epoch), but neonates were not included.²²

Understanding when a seizure or seizures constitute SE in a neonate may be clinically important given increasing data that longer seizure duration and greater seizure burden are associated with lower responsiveness to antiseizure medications, higher mortality, longer length of hospital stay, and higher rates of abnormalities in the neurological examination at discharge.^{1,7,9} Thus, seizure exposure may be a modifiable risk factor for unfavorable outcomes. A uniform definition of neonatal

SE could help standardize future research protocols and guide acute management. Given the lack of consensus in the literature for the definition of neonatal SE, the ILAE Neonatal Task Force performed a scoping review of the definitions of neonatal SE and associations with neurodevelopmental outcome. This is a critical initial step in establishing an evidence-based definition of neonatal SE.

2 | METHODS

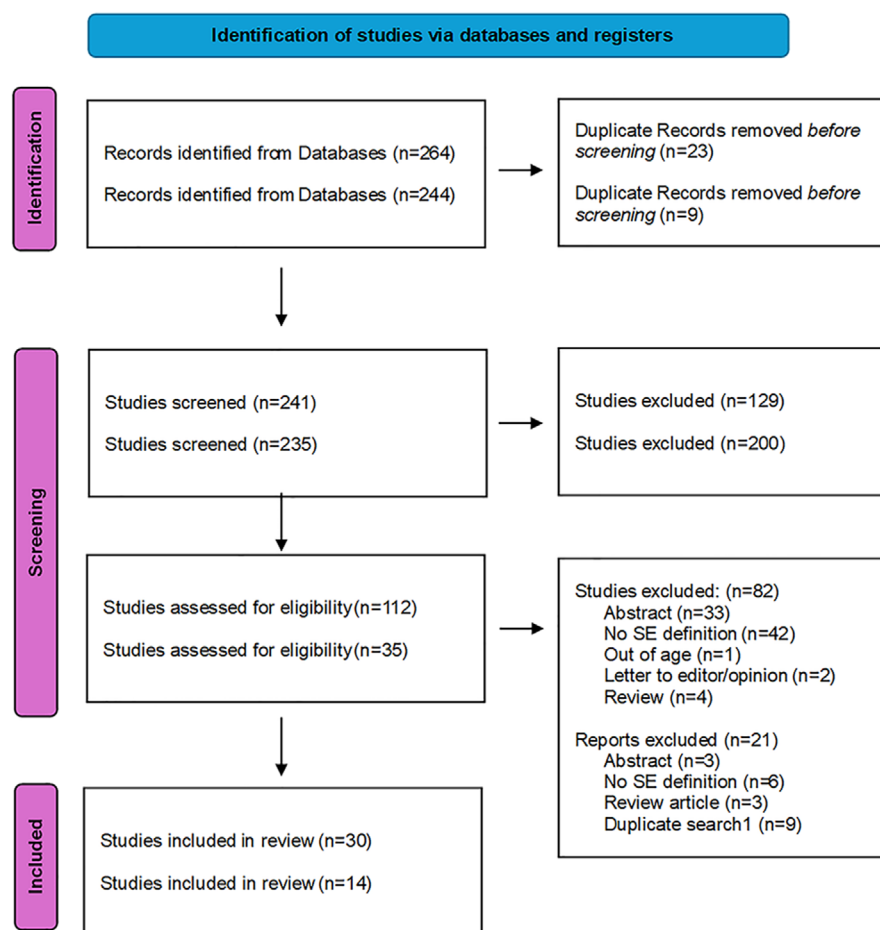
The ILAE Neonatal Task Force performed a scoping review focused on the definition of neonatal SE in a manner consistent with recent recommendations.^{23–27} The Task Force opted for scoping review rather than systematic review due to the scarce evidence providing high certainty of evidence for the definition of status epilepticus.²⁸ Articles were selected using a systematic approach, and results were reported according to the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses” (PRISMA) guidelines.²⁹

The task force searched four online databases (PubMed, Cochrane, Lilacs, and Embase) over ten years for relevant peer-reviewed articles that met our eligibility criteria. There was an initial search (July 2012 to July 2022) and then an updated search (August 2022 to November 2023). Appendix A provides the search strategy. The key words that defined the search strategy were “infant, newborn,” “infant, premature,” “term birth,” “neonate,” “preterm,” “SE,” “convulsive SE,” “non-convulsive SE,” “refractory SE,” “electrographic seizures,” and “seizures.” There were no language restrictions. The search results were merged, and duplicate articles were excluded.

Articles were screened for inclusion by two pediatric neurologists with neonatal neurology expertise (MLN, EGY) using independent review of titles and abstracts. Studies that did not assess SE or focused on non-neonatal cohorts were excluded. Abstracts, reviews, and editorials were excluded. Any disagreements about study characteristics or inclusion, including neonatal SE definitions, were resolved in consensus discussions with a third pediatric neurologist with neonatal neurology expertise (CJW). Figure 2 provides the PRISMA flow chart.

The full text of articles selected for inclusion was copied into an Excel (Microsoft 365) spreadsheet, and pairs of two members of the Task Force performed data extraction independently. Data were extracted using a standardized scoring form which included: (1) article characteristics (author identification, publication year, journal name, digital object identifier, title, objective, and study design);

FIGURE 2 PRISMA Flowchart for the initial search (top) and update search (bottom).



(2) cohort characteristics (sample size, gestational age, seizure etiology); (3) definitions of SE and/or seizure burden; and (4) the method used to identify and classify SE, including routine EEG, continuous EEG monitoring (cEEG), amplitude-integrated EEG (aEEG), or clinical features.

3 | RESULTS

The scoping review yielded 44 articles containing a definition of neonatal SE.^{1,16,30–71} Table 1 summarizes the article characteristics, cohort characteristics, SE and seizure burden definitions, and the methods used to identify and classify SE. Studies mainly included infants with hypoxic-ischemic encephalopathy (55%) or neonates considered at risk for seizures (e.g., extremely preterm or congenital heart defects). SE identification and classification most often relied on cEEG (with or without video) ($n = 21$, 48%), and less often used routine EEG (with or without video) ($n = 12$, 27%), aEEG alone ($n = 5$, 11%), or a combination of EEG/cEEG and aEEG ($n = 6$, 14%).

Most studies based the definition of SE on seizure duration (Table 1). Definitions included: (1) summed duration of seizures comprising $\geq 50\%$ of any 1-h

epoch,^{32,33,38–40,42,45–47,66,69,70} (2) recurrent seizures for $>50\%$ of the total recording time,^{1,33,44,47} or (3) either electrographic seizures lasting >30 min^{50,56,65} and/or repeated electrographic seizures totaling $>50\%$ in any 1-h period.^{16,52–54,59,62,63,67,68}

Among four studies that included clinical assessment of the neonate between recurrent seizures (specifically the return to baseline neurological condition),^{16,37,43,62} the duration of the seizure required to constitute SE was shorter than in other studies. Schoaib and Jacobwitz defined SE as >5 min of continuous seizure or recurrence of seizure without recovery to baseline between seizures.^{37,43} Pisani and Pavlidis defined SE as no return to the baseline neurologic condition between seizures after 30 minutes or recurrent seizures.^{16,62} Studies also used several other approaches to define SE. Jacobwitz et al. defined SE as persistent seizures despite the use of two antiseizure medications.³¹ Tarocco et al. defined super refractory SE as electroclinical seizures that continued for >24 h.⁶⁵ Two studies based the definition of SE on aEEG features.^{50,68} Chen et al.⁵⁰ described that regular patterns of increased cortical activity with sawtooth pattern were suggestive of SE, and Mastrangelo et al.⁶⁸ defined SE as a continuous/prolonged increase of the lower and upper margin.

TABLE 1 Summary of the 44 articles included.

Author/year	Population (n) % term/preterm	Definition of SE	Definition of SB	Based on	Etiology
Eberhard et al. 2024	(1) 100/0	Recurrent focal seizures of 1.5 to 2.5 min duration independently over the left and right posterior regions, without clear clinical change, occupying up to 55% of the recording	-	cEEG	Infection—meningitis (group B Streptococcus)
Jacobowitz et al. 2023	(28) Term and preterm	Persistent seizures despite two appropriately dosed antiseizure medications	-	EEG + clinical	Variety
Pin et al. 2023	(1) 0/100	Electrographic seizure activity totaling more than 30 min in any 1-h period (i.e., 50% seizure burden)	-	cEEG	HIE
Castro Conde et al. 2023	(39) 0/100	-	TSB	cEEG + video	HIE + others
Glass et al. 2023	(46) Term or late preterm	Summed duration of seizures comprising $\geq 50\%$ of any 1-h epoch of recording	-	cEEG	HIE
Alharbi et al. 2023	(98) Term or late preterm (>36 weeks)	-	TSB and MHSB	cEEG for 48 h	HIE and others
Shoaib et al. 2023	(28 neonates—14 with SE) Term and preterm	Five minutes or more of continuous seizure activity or recurrence of seizure activity without recovery to baseline between seizures	-	EEG	Variety
Moeller et al. 2023	(107) Term and preterm	Total seizure burden adding up to ≥ 30 min of any given hour	LSB = ≤ 2 seizures per hour or total burden adding up to < 20 min of any given hour. MSB = > 2 seizures/hour or total burden adding up to ≥ 20 min and < 30 min of any given hour	EEG	HIE and others
Danzer et al. 2023	(75) 0/100	Electrographic seizure activity totaling more than 30 min in any 1-h period (i.e., 50% seizure burden)	-	cEEG	ECMO Congenital diaphragmatic hernia
Bättig et al. 2023	(108) 18/82	The summed duration of seizures comprised $\geq 50\%$ 1-h epoch.	-	EEG or aEEG	HIE and others
Simmons et al. 2022	(132) 4/96	Continuous seizure activity or recurrent seizures for more than 50% of 1–3 h of recording time	-	cEEG	Congenital brain malformation
Chen et al. 2022	(71) 39.5/60.5	Continuous electrographic seizures lasting at least 30 min or repeated electrographic seizures totaling more than 30 min in any 1-h period	-	cEEG + video	HIE and others
Nyman et al. 2022	(85) Term or late preterm (>36 weeks)	Seizures covering $> 50\%$ of the given 1-h epoch.	TSB and MHSB	aEEG	HIE

TABLE 1 (Continued)

Author/year	Population (n) % term/ preterm	Definition of SE	Definition of SB	Based on	Etiology
Jacobowitz et al. 2022	(69 /13 neonates) 0/100	(1) as > 5 min of continuous and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures, (2) brief seizures totaling > 5 min in an hour, seizure(s) > 5 min, or both	-	EEG or aEEG	HIE and others
Massey et al. 2022	(354) 0/100	Summed duration of seizures comprising ≥50% of any 1-h epoch	-	EEG	Congenital heart/pulmonary disorders
Herzberg et al. 2022	(112) 71.4/28.6	Any electrographic recording with seizures lasting > 50% over at least 1 h of recording	LSB (< 7 EEG seizures/hour) or HSB (> 7)	cEEG + video	Vascular hemorrhage
Pavel et al. 2022	(154) 0/100	Seizure burden in a minimum of 30 min within 1 h	TSB	EEG	Variety
Pittet et al. 2022	(31) Late preterm and term	> 30 min of electrographic seizure activity occurring during a 1-h epoch	TSB and MHSB	cEEG	Congenital heart disease
Chalak et al. 2021	(364) 0/100	Multiple seizures with overall cumulative duration greater than 30 min and/or status epilepticus	-	aEEG	HIE
Basti et al. 2020	(32) 0/100	≥ 30 min continuously seizure	HSB (seizure present > 15 min in total per 1-h period) LSB (< 15 min/hour)	aEEG	HIE
Chen et al. 2020	(23) Late preterm > 35 weeks	Regular patterns of increased cortical activity with sawtooth pattern	-	aEEG	HIE
Rennie et al. 2019	(240) 0/100	-	TSB and MHSB	cEEG	HIE
Lloyd et al. 2017	(120) 100/0	Continuous or accumulative electrographic seizures present in > 50% of a 1-h period	TSB	cEEG	Variety
Lin et al. 2017	(99) Not available	Continuous 30 min electrographic seizures or electrographic seizures > 30 min/hour	-	cEEG	ECMO
Buraniqi et al. 2016	(52) 100/0	> 30 min of continuous intermittent seizures in 1-h epoch	-	cEEG	Vascular hemorrhage
Elshorbagy et al. 2016	(39) 0/100	> 30 min	-	cEEG + video	HIE
Kharoshankaya et al. 2016	(47) 0/100	-	TSB and MHSB	cEEG	HIE
Glass et al. 2016	(426) 22/88	Any electrographic seizure lasting > 50% over at least 1-h recording	LSB (< 7 seizures) HSB (isolated EEG seizure, > 7)	cEEG + video	HIE
Low et al. 2016	(19) 0/100	-	Hourly SB and MHSB	cEEG	HIE

(Continues)

TABLE 1 (Continued)

Author/year	Population (n) % term/ preterm	Definition of SE	Definition of SB	Based on	Etiology
Pressler et al. 2015	(14) 0/100	-	TSB	cEEG	HIE
Naim et al. 2015	(161) Term and preterm	Any single seizure >30 min or if recurrent seizures together lasted for more than 30 min in any 1-h epoch (50% SB)	-	cEEG + video	Congenital cardiopathy
Srinivasakumar et al. 2015	(72) 0/100	-	Cumulative SB	Video EEG	HIE
Lynch et al. 2015	(23) 0/100	-	TSB and MHSB	cEEG + aEEG	HIE
Pavlidis et al. 2015	(n = 47) 40.5/59.5	Continuous seizure activity ≥30 min or recurrent seizures lasting a total of >30 min without definite return to the baseline neurologic condition of the newborn between seizures or (hourly seizure burden range: ≥50%–100%)	-	Video EEG	Variety
Low et al. 2014	(9) 0/100	Continuous or accumulative electrographic seizure activity lasting ≥50% of a 1-h period	-	EEG aEEG+ clinical observation	Vascular- stroke
Glass et al. 2014	(90) 0/100	Continuous electrographic seizure lasting at least 30 min, or recurrent electrographic seizures for at least 50% of 1–3 h of recording time	-	cEEG	HIE
Vesoulis et al. 2014	(95) 100/0	A single ictal episode with a duration greater than 30 min	Cumulative daily SB	aEEG	Vascular hemorrhage
Tarocco et al. 2014	(1) 100/0	Super refractory SE defined as electroclinical seizures continue more than 24 h	-	Video EEG	Genetic + Structural (migration disorder)
Shah et al. 2014	(85) 0/100	Seizure >30 min in any 1-h period	HSB (seizures >15 min in total/1-h period) LSB (<15)	EEG + aEEG	HIE
Mastrangelo et al. 2013	(28) 0/100	(a) continuous seizure activity for at least 30 min, or (b) recurrent seizures for >50% of the recording time ranging from 1 to 3 h or (c) a continuous electrographic seizure longer than 15 min and/or more than 1 electrographic seizure over a 10-min period on the EEG. aEEG = status epilepticus was depicted as continuous increase of the lower and upper margin	-	EEG+ aEEG	HIE and others

TABLE 1 (Continued)

Author/year	Population (n) % term/ preterm	Definition of SE	Definition of SB	Based on	Etiology
Srinivasakumar et al. 2013	(69) 0/100	Continuous or cumulative electrographically documented seizure activity lasting for at least one-half of each 1-h period	SB= total duration of EEG seizures in seconds	Video EEG	HIE
Low et al. 2012	(107) 0/100	Continuous or cumulative electrographic seizure activity lasting $\geq 50\%$ of each 1-h period	TSB	EEG	HIE
Pisani et al. 2007	(160/ 26 with SE) Preterm and term	Continuous seizure activity for ≥ 30 min or recurrent seizures lasting a total of > 30 min without definite return to the baseline neurologic condition of the newborn between seizures	-	Video EEG	Variety
Scher et al. 2002	(1) 0/100	Eight electrographic/clinical events over a 40-min recording	-	Video EEG	Vascular – stroke

Abbreviations: aEEG, amplitude integrated EEG; cEEG, continuous EEG; ECMO, extracorporeal membrane oxygenation; HIE, hypoxic ischemic encephalopathy; HSB, high seizure burden; HSB, hourly seizure burden; LSB, low seizure burden; MHSB, maximum hourly seizure burden; MSB, moderate seizure burden; SE, status epilepticus; TSB, total seizure burden.

Seizure burden was reported in 20 studies. The most commonly used approach assessed total seizure burden, defined as total duration of EEG seizures in minutes (11 studies, 55%). Other approaches included maximum hourly seizure burden (8 studies),^{36,38,42,47,51,56,57,61} cumulative seizure burden defined as the total duration of electrographic seizures in seconds (2 studies),^{60,69} hourly seizure burden (1 study),⁵⁸ and daily seizure burden (1 study).⁶⁵ High/moderate and low seizure burden were categorized in five studies^{1,38,44,49,66} which used varied definitions for the number of seizures classified as high/moderate or low (Table 1).

Table 2 summarizes 16 studies which assessed the relationship between seizure burden and a variety of outcomes, including brain injury and response to antiseizure medication.^{1,34,36,38,42,46,49,51,52,56,57,60,64,66,69,70} The relationship between seizure burden and neurodevelopment outcomes at ages from 18 to 48 months was assessed in eight studies.^{1,34,36,42,49,56,60,63} Except for one report,⁶⁴ these studies identified a significant association between higher seizure burden and unfavorable outcomes. Three studies assessed etiology, and a high seizure burden occurred with stroke, severe hypoxic-ischemic encephalopathy, intraventricular hemorrhage type III-IV, and structural lesions on neuroimage.^{51,53,66} Five studies used seizure burden to assess the effectiveness of treatment (pharmacological and therapeutic hypothermia).^{38,46,57,68,70}

4 | DISCUSSION

A previous ILAE report on SE definitions and classification noted that in the neonatal period (0 to 30 days for term babies), SE may be difficult to recognize, but it did not explore further aspects among neonates.²¹ Thus, to expand work addressing common terminology and classification approaches for SE, this scoping review aimed to assess and categorize the definitions of neonatal SE available in the literature as an initial step in establishing an evidence-based definition of neonatal SE. The review indicated that: (1) studies have used variable definitions of SE; (2) most SE definitions rely on assessment using EEG (most often cEEG but sometimes aEEG); and (3) most studies define SE in relation to 30 min, including continuous seizure activity lasting 30 min or brief seizures totaling 30 min within a 1-h epoch (50% seizure burden).^{32,33,38–40,42,44–48,67,70,71} The validity of criteria focused on return to a normal neurological state is questionable in critically ill neonates who may be sedated and/or paralyzed and who are often encephalopathic or comatose given the underlying acute brain injury etiology causing the SE.

TABLE 2 Relationship of seizure burden and different outcomes (*n* = 16 studies).

Study	Outcome measured
Castro-Conde et al. 2023	Abnormal neurodevelopment was significantly associated with total SB >25 min (odds ratio 95% 1.72–142.86, <i>p</i> = 0.026)
Alharbi et al. 2023	Higher SB during neonatal encephalopathy was independently associated with worse cognitive and language scores at 18 months
Moeller et al. 2023	The standardized, SB-based protocol for the treatment of neonatal seizures improved short-term patient outcomes. The use of a continuous midazolam infusion was reduced by 53.7%, duration of EEG monitoring decreased, the proportion of infants discharged without antiseizure medications increased by 68%
Nyman et al. 2022	Although neonatal SB was associated with post neonatal epilepsy at group level, at individual level aEEG background is more accurate for prediction of epilepsy
Pavel et al. 2022	Significantly lower SB burden and fewer seizures were noted in the infants treated with antiseizure medication within 1 h of seizure onset (<i>p</i> = 0.029 and 0.035, respectively)
Basti et al. 2020	A high SB correlates with a persistent abnormal aEEG trace, tissue injury on MRI and abnormal developmental outcome at age 18–24 months
Rennie et al. 2019	Neonates with stroke and severe HIE tended to have the largest SB
Lloyd et al. 2017	An association among higher SB and severe IVH (grade III–IV) in preterm infants was suggested
Low et al. 2016	Phenobarbitone immediately reduced SB but the effect was not significant within 4 h of treatment. Doses of phenobarbitone at 20 mg/kg, rather than 10 mg/kg, were significantly more effective in reducing SB
Kharoshankaya et al. 2016	In HIE, a high electrographic SB is significantly associated with abnormal outcome (at 24–48 months), independent of HIE severity or treatment with hypothermia. The odds of an abnormal outcome increased over ninefold if a neonate had a total seizure burden of more than 40 min (<i>p</i> = 0.001), and eightfold if a neonate had a MHSB >13 min per hour (<i>p</i> = 0.003)
Glass et al. 2016	High SB was associated to need of ≥2 antiseizure medications, death or abnormal examination at discharge. Greater seizure burden was associated with increased morbidity and mortality
Srinivasakumar et al. 2015	EEG monitoring and treatment of electrographic seizures results in significant reduction in SB. SB is associated with more severe brain injury and significantly lower performance scores across all neurodevelopment domains on Bayley III
Vesoulis et al. 2014	No association was found between high SB on either day 1, 2 or 3 and children’s subsequent motor, cognitive and language scores at age 2 years
Shah et al. 2014	In multivariate logistic regression, high SB was independently associated with greater injury on MRI (OR 5.00, 95% CI 1.47 to 17.05 <i>p</i> = 0.01)
Srinivasakumar et al. 2013	Therapeutic hypothermia was associated with reduced electrographic SB in mild neonatal HIE and in the ones with mild and moderate MRI injuries.
Low et al. 2012	A decreased SB burden was seen in neonates with moderate HIE who received cooling.

Abbreviations: aEEG, amplitude integrated EEG; CI, confidence interval; HIE, hypoxic ischemic encephalopathy; IVH, intraventricular hemorrhage; MHSB, maximum hourly seizure burden; MRI, magnetic resonance image; SB, seizure burden.

The generalizability and validity of any of the neonatal SE definitions are unknown. Further, there is little evidence that the definitions used in the studies, including the 30-min cutoff to define SE, provide an evidence-based approach to defining an abnormally prolonged seizure (T1 in the ILAE definition for adults), identifying a seizure duration which might reduce responsiveness to antiseizure medications, or identifying a seizure duration associated with secondary brain injury and worse outcomes (T2 in the ILAE definition for adults).²¹ Although higher seizure burden has been associated with unfavorable outcomes,^{1,33,36,42,49,56,60,63} the definition of “high” seizure burden has not been uniform. Several studies have been published after the inclusion search for this article. In a study of 39 neonates with moderate–severe

hypoxic–ischemic encephalopathy enrolled in a clinical trial undergoing cEEG undergoing cEEG, maximal pre-treatment seizure burden predicted successful response to seizure treatment better than other seizure burden measures.⁷² In a study if 70 neonates with hypoxic–ischemic encephalopathy, seizures were not associated with death or neurodevelopmental impairment after adjustment for clinical and imaging variables, including for severe seizures.⁷³

Experimental studies provide insight on the importance of defining the seizure duration which could impact neurodevelopmental outcomes.^{74–76} Data suggest that the immature brain is more resistant to structural damage as a result of seizures.⁷⁵ Furthermore, etiology may impact the relationship between seizure burden and brain injury;

a rat model of ischemic stroke indicated that the harmful effect of kainic acid on brain injury was not related to duration of SE.⁷⁶ These findings suggest that the context related to prior insults and underlying etiology may influence the seizure burden which in turn contributes to secondary brain injury.

In conclusion, this scoping review demonstrated substantial variation in neonatal SE definitions across the literature, in the methods used for recognition of SE (EEG, cEEG with and without video, aEEG), and in the population studied. The most common definitions were based around 30-min duration criteria. However, evidence was insufficient that seizures exceeding 30 min were more likely to be pharmacoresistant or associated with worse outcomes. Given the variability in neonatal SE definitions identified in this scoping review, there is an urgent need to develop a standardized and evidence-based classification approach for neonatal seizure burden and a definition of neonatal SE that could be applied rigorously in research studies and extended to clinical practice. Similar to adults and non-neonatal children,²² a uniform approach and definitions will enable comparison of data across studies and translation of data from studies into clinical practice. This approach may help establish T1 and T2 timepoints aligned with the ILAE approach for non-neonates. As a next step, the ILAE Neonatal Task Force intends to develop a standardized approach to assessing and describing neonatal seizure burden and defining neonatal SE using an inter-disciplinary team of selected experts providing consensus-recommendations through a structured and rigorous Delphi process.

AFFILIATIONS

¹School of Medicine and Brain Institute (BraIns), Pontifical Catholic University of Rio Grande Do Sul, Porto Alegre, Rio Grande do Sul, Brazil

²Isabelle Rapin Division of Child Neurology of the Saul R Korey Department of Neurology and Pediatrics, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, New York, USA

³Department of Neurology, University of California, Davis, Sacramento, California, USA

⁴Division of Pediatric Neurology, Department of Neurology, Washington University in St Louis School of Medicine, St Louis, Missouri, USA

⁵Department of Neurosciences, National Institute of Perinatology, Mexico City, Mexico. Department of Pediatrics, Women's Hospital, Yautepec Morelos, Mexico

⁶Department of Paediatric Neurology, Red Cross War Memorial Children's Hospital, Neuroscience Institute, University of Cape Town, Cape Town, South Africa

⁷Clinical Neuroscience, UCL GOS Institute of Child Health and Department of Clinical Neurophysiology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

⁸Child Neurology Department, Hedi Chaker Hospital, LR19ES15, University of Sfax, Sfax, Tunisia

⁹Department of Pediatric Kidney, Liver, Metabolic and Neurological Diseases, Hannover Medical School, Hannover, Germany

¹⁰Department of Pediatrics, University of California, Irvine; Director, Center for Newborn Research, Children's Hospital of Orange County, California, USA

¹¹INFANT Research Centre and Department of Paediatrics & Child Health, University College Cork, Cork, Ireland

¹²Department of Psychiatry and Pediatrics, Research Center for Complex and Rare Epilepsies, Faculty of Medicine of the University of São Paulo (FMUSP), São Paulo, Brazil

¹³Laboratory of Clinical Neurophysiology and LIM 21, Department of Psychiatry, Clinics Hospital, University of São Paulo (HC FMUSP), São Paulo, Brazil

¹⁴Isabelle Rapin Division of Child Neurology, Saul R. Korey Department of Neurology, and Department of Neuroscience and Pediatrics, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York, USA

¹⁵Department of Neurology and Pediatrics, Baylor College of Medicine, Houston, Texas, USA

¹⁶Department of Neurology and Pediatrics, Children's Hospital of Philadelphia and University of Pennsylvania, Philadelphia, Pennsylvania, USA

ACKNOWLEDGMENTS

We acknowledge gratefully Ms. Alessandra Pinto Fagundes, Librarian from the Pontifical Catholic University of Rio Grande do Sul- Brazil, for the construction of the search strategy across the different databases.

CONFLICT OF INTEREST STATEMENT

M.L.N. is supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq)-Brazil (PQ 306338/2017-3). C.J.W. receives royalties from Cambridge Publishing, receives a stipend as Associate Editor for Neurology, and receives honoraria from ICON and University of Utah for service on Data Safety Monitoring Boards. R.A.S. receives royalties from UpToDate for authorship of topics related to neonatal seizures; serves as a consultant for the Epilepsy Study Consortium; and receives a stipend for her role as President of the Pediatric Epilepsy Research Consortium®. G.B.B. is founder and co-director of Kephala Ltd. and CergenX Ltd. She has a consultancy agreement through University College Cork with Nihon Kohden. R.M.P. is an associate editor for Epilepsia-Open; acts as an Investigator for studies with UCB Pharma; has received honoraria from Longboard, Natus, and UCB Pharma for services on advisory boards, teaching, or consultancy work; is supported by the National Institute of Health Research (NIHR) Biomedical Research Centre at Great Ormond Street Hospital, Evelyn Trust, Cambridge

Biomedical Research Centre, and NIHR. K.V. receives a stipend as Associate Editor of Epilepsy & Behavior and research grants from FAPESP and CNPq. She receives honorarium as the Director and Coordinator of Clinical Research Center for Clinical Trials in Complex and Rare Epilepsies. JMW is an associate editor for Epilepsia, chief Editor of Pediatric Neurology subsection of Frontiers in Neurology and is on the South African national advisory boards for Sanofi, Roche, and Novartis. She receives honoraria for work related to these activities. S.L.M. is the Charles Frost Chair in Neurosurgery and Neurology and partially funded by grants from NIH U54 NS100064 (EpiBioS4Rx), RO1-NS43209 and RO1- NS127524, US Department of Defense (W81XWH-22-1-0510, W81XWH-22-1-0210), a pilot grant from the NICHD center grant (P50 HD105352) for the Rose F. Kennedy Intellectual and Developmental Disabilities Research Center (RFK-IDDRC), and the Heffer Family and the Segal Family Foundations, and the Abbe Goldstein/Joshua Lurie and Laurie Marsh/Dan Levitz families. E.M.M. receives royalties from Springer Publishing Company, Princeton, NJ, USA. T.E.I. is a scientific advisor for Aspect Imaging, Realta, and Chiese Pharmaceutical. C.C.T., E.O.P., and N.S.A. no conflict of interest to declare. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Magda L. Nunes  <https://orcid.org/0000-0002-3402-6810>

Elissa G. Yozawitz  <https://orcid.org/0000-0001-8230-8364>

Courtney J. Wusthoff  <https://orcid.org/0000-0002-1882-5567>

Renée A. Shellhaas  <https://orcid.org/0000-0002-3175-3908>

Jo M. Wilmschurst  <https://orcid.org/0000-0001-7328-1796>

Ronit M. Pressler  <https://orcid.org/0000-0002-2905-6839>

Chahnez C. Triki  <https://orcid.org/0000-0003-2918-3819>

Geraldine B. Boylan  <https://orcid.org/0000-0003-0920-5291>

Kette Valente  <https://orcid.org/0000-0002-5008-0809>

Solomon L. Moshe  <https://orcid.org/0000-0001-9427-9476>

Nicholas S. Abend  <https://orcid.org/0000-0001-6166-2663>

REFERENCES

1. Glass HC, Shellhaas RA, Wusthoff CJ, Chang T, Abend NS, Chu CJ, et al. Contemporary profile of seizures in neonates: a prospective cohort study. *J Pediatr*. 2016;174:98–103. <https://doi.org/10.1016/j.jpeds.2016.03.035>
2. Pellegrin S, Munoz FM, Padula M, Heath PT, Meller L, Top K, et al. Neonatal seizures: case definition & guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*. 2019;37(52):7596–609.
3. Zuberi SM, Wirrell E, Yozawitz E, Wilmschurst JM, Specchio N, Riney K, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: position statement by the ILAE task force on nosology and definitions. *Epilepsia*. 2022;63(6):1349–97. <https://doi.org/10.1111/epi.17239>
4. Pressler RM, Cilio MR, Mizrahi EM, Moshé SL, Nunes ML, Plouin P, et al. The ILAE classification of seizures and the epilepsies: modification for seizures in the neonate. Position paper by the ILAE task force on neonatal seizures. *Epilepsia*. 2021;62(3):615–28. <https://doi.org/10.1111/epi.16815>
5. Pressler RM, Abend NS, Auvin S. Treatment of seizures in the neonate: guidelines and consensus-based recommendations—special report from the ILAE task force on neonatal seizures. *Epilepsia*. 2023;00:1–21. <https://doi.org/10.1111/epi.17745>
6. Nunes ML, Yozawitz EG, Zuberi S, Mizrahi EM, Cilio MR, Moshé SL, et al. Neonatal seizures: is there a relationship between ictalelectroclinical features and etiology? A critical appraisal based on a systematic literature review. *Epilepsia Open*. 2019;4:10–29. <https://doi.org/10.1002/epi4.12298>
7. Shellhaas RA. Neonatal seizures reach the mainstream: the ILAE classification of seizures in the neonate. *Epilepsia*. 2021;62(3):629–31. <https://doi.org/10.1111/epi.16857>
8. Pisani F, Facini C, Pavlidis E, Spagnoli C, Boylan G. Epilepsy after neonatal seizures: literature review. *Eur J Paediatr Neurol*. 2015;19(1):6–14. <https://doi.org/10.1016/j.ejpn.2014.10.001>
9. Pinchefskey EF, Hahn CD. Outcomes following electrographic seizures and electrographic status epilepticus in the pediatric and neonatal ICUs. *Curr Opin Neurol*. 2017;30(2):156–64.
10. Monod N, Dreyfus-Brisac C, Sfaello Z. Detection and prognosis of the neonatal mal according to the electroclinical study of 150 cases. *Arch Fr Pediatr*. 1969;26(10):1085–102.
11. Udaeta Mora E, Olmos-Garcia de Alba G, Villanueva Garcia D, Malagon VJ. Neonatal status epilepticus I: clinical aspects. *Clin Electroencephalogr*. 1984;15(4):193–6. <https://doi.org/10.1177/155005948401500402>
12. Scher MS, Hamid MY, Steppe DA, Beggarly ME, Painter MJ. Ictal and interictal electrographic seizure durations in preterm and term neonates. *Epilepsia*. 1993;34(2):284–8.
13. Wertheim D, Mercuri E, Faundez JC, Rutherford M, Acolet D, Dubowitz L. Prognostic value of continuous electroencephalographic recording in full term infants with hypoxic ischaemic encephalopathy. *Arch Dis Child Fetal Neonatal Ed*. 1994;71(2):F97–F102. <https://doi.org/10.1136/fn.71.2.f97>
14. Ortibus E, Sum J, Hahn J. Predictive value of EEG for outcome and epilepsy following neonatal seizures. *Electroencephalogr Clin Neurophysiol*. 1996;98(3):175–85. [https://doi.org/10.1016/0013-4694\(95\)00245-6](https://doi.org/10.1016/0013-4694(95)00245-6)
15. Mizrahi EM, Kellaway P. Diagnosis and Management of Neonatal Seizures. Philadelphia: Lipincott-Raven; 1998.
16. Pisani F, Cerminara C, Fusco C, Sisti L. Neonatal status epilepticus vs recurrent neonatal seizures: clinical findings and

- outcome. *Neurology*. 2007;69(23):2177–85. <https://doi.org/10.1212/01.wnl.0000295674.34193.9e>
17. Yamamoto H, Aihara M, Nijima S, Yamanouchi H. Treatments with midazolam and lidocaine for status epilepticus in neonates. *Brain and Development*. 2007;29(9):559–64. <https://doi.org/10.1016/j.braindev.2007.02.003>
 18. Wusthoff CJ. Diagnosing neonatal seizures and status epilepticus. *J Clin Neurophysiol*. 2013;30(2):115–21.
 19. Abend NS, Wusthoff CJ, Goldberg EM, Dlugos DJ. Electrographic seizures and status epilepticus in critically ill children and neonates with encephalopathy. *Lancet Neurol*. 2013;12(12):1170–9. [https://doi.org/10.1016/S1474-4422\(13\)70246-1](https://doi.org/10.1016/S1474-4422(13)70246-1)
 20. Tsuchida TN, Wusthoff CJ, Shellhaas RA, et al. American clinical neurophysiology society standardized EEG terminology and categorization for the description of continuous EEG monitoring in neonates: report of the American clinical neurophysiology society critical care monitoring committee. *J Clin Neurophysiol*. 2013;30(2):161–73. <https://doi.org/10.1097/WNP.0b013e3182872b24>
 21. Trinka E, Cock H, Hesdorffer D, et al. A definition and classification of status epilepticus—report of the ILAE task force on classification of status epilepticus. *Epilepsia*. 2015;56(10):1515–23. <https://doi.org/10.1111/epi.13121>
 22. Hirsch LJ, Fong MWK, Leitinger M, LaRoche SM, Beniczky S, Abend NS, et al. American clinical neurophysiology society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol*. 2021;38(1):1–29. <https://doi.org/10.1097/WNP.0000000000000806>
 23. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol*. 2018;18(1):143. <https://doi.org/10.1186/s12874-018-0611-x>
 24. Colquhoun HL, Levac D, O'Brien KK, Straus S, Tricco AC, Perrier L, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *J Clin Epidemiol*. 2014;67(12):1291–4. <https://doi.org/10.1016/j.jclinepi.2014.03.013>
 25. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol*. 2005;8(1):19–32. <https://doi.org/10.1080/1364557032000119616>
 26. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci*. 2010;5:69. <https://doi.org/10.1186/1748-5908-5-69>
 27. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc*. 2015;13(3):141–6. <https://doi.org/10.1097/XEB.0000000000000050>
 28. Jetté N, Kirkpatrick M, Lin K, Fernando SMS, French JA, Jehi L, et al. What is a clinical practice guideline? A roadmap to their development. Special report from the guidelines task force of the international league against epilepsy. *Epilepsia*. 2022;63:1920–9. <https://doi.org/10.1111/epi.17312>
 29. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. <https://doi.org/10.1136/bmj.n71>
 30. Eberhard R, Paquette K, Garfinkle J, Myers KA. Response to hydrocortisone in an extremely preterm neonate with late-onset sepsis, meningoencephalitis, and drug-resistant seizures. *Clin EEG Neurosci*. 2024;55(2):252–6. <https://doi.org/10.1177/15500594221147138>
 31. Jacobowitz M, Mulvihill C, Kaufman MC, Gonzalez AK, Resendiz K, Francoeur C, et al. A comparison of ketamine and midazolam as first-line anesthetic infusions for pediatric status epilepticus. *Neurocrit Care*. 2023;40:984–95. <https://doi.org/10.1007/s12028-023-01859-2>
 32. Pin JN, Leonardi L, Nosadini M, Cavicchiolo ME, Guariento C, Zarpellon A, et al. Efficacy and safety of ketamine for neonatal refractory status epilepticus: case report and systematic review. *Front Pediatr*. 2023;11:1189478. <https://doi.org/10.3389/fped.2023.1189478>
 33. Danzer E, Massey SL, Flohr SJ, Mathew L, Hoffman C, Abramson A, et al. Extracorporeal membrane oxygenation for neonates with congenital diaphragmatic hernia: prevalence of seizures and outcomes. *Pediatr Crit Care Med*. 2023;24(5):e224–e235. <https://doi.org/10.1097/PCC.0000000000003197>
 34. Castro Conde JR, González Campo C, González Barrios D, Reyes Millán B, Díaz González CL, Jiménez SA. High effectiveness of midazolam and lidocaine in the treatment of acute neonatal seizures. *J Clin Neurophysiol*. 2023;41:450–7. <https://doi.org/10.1097/WNP.0000000000001013>
 35. Glass HC, Wusthoff CJ, Comstock BA, Numis AL, Gonzalez FF, Maitre N, et al. Risk of seizures in neonates with hypoxic-ischemic encephalopathy receiving hypothermia plus erythropoietin or placebo. *Pediatr Res*. 2023;94(1):252–9. <https://doi.org/10.1038/s41390-022-02398-w>
 36. Alharbi HM, Pinchevsky EF, Tran MA, Salazar Cerda CI, Parokaran Varghese J, Kamino D, et al. Seizure burden and neurologic outcomes after neonatal encephalopathy. *Neurology*. 2023;100(19):e1976–e1984. <https://doi.org/10.1212/WNL.000000000000207202>
 37. Shoaib AB, Machie M, Thomas JM, Dolce A. Lacosamide for the treatment of seizures in neonates and infants: a retrospective assessment of efficacy and tolerability. *Pediatr Neurol*. 2023;149:176–81. <https://doi.org/10.1016/j.pediatrneurol.2023.09.021>
 38. Moeller AA, Stefanescu AR, Stefanescu BM, Golomb MR, Boyle FA, Buss WF, et al. A standardized, 3-tiered, seizure burden-based protocol for the treatment of neonatal seizures. *J Child Neurol*. 2023;38(3–4):142–52. <https://doi.org/10.1177/08830738231164704>
 39. Bättig L, Dünner C, Cserpan D, Rüegger A, Hagmann C, Schmitt B, et al. Levetiracetam versus phenobarbital for neonatal seizures: a retrospective cohort study. *Pediatr Neurol*. 2023;138:62–70. <https://doi.org/10.1016/j.pediatrneurol.2022.10.004>
 40. Simmons R, Martinez AB, Barkovich J, Numis AL, Cilio MR, Glenn OA, et al. Disorders of neuronal migration/organization convey the highest risk of neonatal onset epilepsy compared with other congenital brain malformations. *Pediatr Neurol*. 2022;127:20–7. <https://doi.org/10.1016/j.pediatrneurol.2021.11.005>
 41. Chen WH, Chan OW, Lin JJ, Chiang MC, Hsia SH, Wang HS, et al. Electrographic seizures in neonates with a high risk of encephalopathy. *Children (Basel)*. 2022;9(6):770. <https://doi.org/10.3390/children9060770>
 42. Nyman J, Mikkonen K, Metsäranta M, Toiviainen-Salo S, Vanhatalo S, Lauronen L, et al. Poor aEEG background recovery after perinatal hypoxic ischemic encephalopathy

- predicts postneonatal epilepsy by age 4 years. *Clin Neurophysiol.* 2022;143:116–23. <https://doi.org/10.1016/j.clinph.2022.09.005>
43. Jacobwitz M, Mulvihill C, Kaufman MC, Gonzalez AK, Resendiz K, MacDonald JM, et al. Ketamine for Management of Neonatal and Pediatric Refractory Status Epilepticus. *Neurology.* 2022;99(12):e1227–e1238. <https://doi.org/10.1212/WNL.0000000000200889>
 44. Herzberg EM, Machie M, Glass HC, Shellhaas RA, Wusthoff CJ, Chang T, et al. Seizure severity and treatment response in newborn infants with seizures attributed to intracranial hemorrhage. *J Pediatr.* 2022;242:121–128.e1. <https://doi.org/10.1016/j.jpeds.2021.11.012>
 45. Massey SL, Glass HC, Shellhaas RA, Bonifacio S, Chang T, Chu C, et al. Characteristics of neonates with cardiopulmonary disease who experience seizures: a multicenter study. *J Pediatr.* 2022;242:63–73. <https://doi.org/10.1016/j.jpeds.2021.10.058>
 46. Pavel AM, Rennie JM, de Vries LS, Blennow M, Foran A, Shah DK, et al. Neonatal seizure management: is the timing of treatment critical? *J Pediatr.* 2022;243:61–8. <https://doi.org/10.1016/j.jpeds.2021.09.058>
 47. Pittet MP, Marini D, Ly L, Au-Young SH, Chau V, Seed M, et al. Prevalence, risk factors, and impact of preoperative seizures in neonates with congenital heart disease. *J Clin Neurophysiol.* 2022;39(7):616–24. <https://doi.org/10.1097/WNP.0000000000000825>
 48. Chalak LF, Pappas A, Tan S, das A, Sánchez PJ, Laptook AR, et al. Association between increased seizures during rewarming after hypothermia for neonatal hypoxic ischemic encephalopathy and abnormal neurodevelopmental outcomes at 2-year follow-up: a nested multisite cohort study. *JAMA Neurol.* 2021;78(12):1484–93. <https://doi.org/10.1001/jamaneurol.2021.3723>
 49. Basti C, Maranella E, Cimini N, Catalucci A, Ciccarelli S, del Torto M, et al. Seizure burden and neurodevelopmental outcome in newborns with hypoxic-ischemic encephalopathy treated with therapeutic hypothermia: a single center observational study. *Seizure.* 2020;83:154–9. <https://doi.org/10.1016/j.seizure.2020.10.021>
 50. Chen YJ, Chiang MC, Lin JJ, Chou IJ, Wang YS, Kong SS, et al. Seizures severity during rewarming can predict seizure outcomes of infants with neonatal hypoxic-ischemic encephalopathy following therapeutic hypothermia. *Biom J.* 2020;43(3):285–92. <https://doi.org/10.1016/j.bj.2020.06.008>
 51. Rennie JM, de Vries LS, Blennow M, Foran A, Shah DK, Livingstone V, et al. Characterization of neonatal seizures and their treatment using continuous EEG monitoring: a multicenter experience. *Arch Dis Child Fetal Neonatal Ed.* 2019;104(5):F493–F501. <https://doi.org/10.1136/archdischild-2018-315624>
 52. Lloyd RO, O'Toole JM, Pavlidis E, Filan PM, Boylan GB. Electrographic seizures during the early postnatal period in preterm infants. *J Pediatr.* 2017;187:18–25. <https://doi.org/10.1016/j.jpeds.2017.03.004>
 53. Lin JJ, Banwell BL, Berg RA, Dlugos DJ, Ichord RN, Kilbaugh TJ, et al. Electrographic seizures in children and neonates undergoing extracorporeal membrane oxygenation. *Pediatr Crit Care Med.* 2017;18(3):249–57. <https://doi.org/10.1097/PCC.0000000000001067>
 54. Buraniqi E, Sansevere AJ, Kapur K, Bergin AM, Pearl PL, Loddenkemper T. Electrographic seizures in preterm neonates in the neonatal intensive care unit. *J Child Neurol.* 2017;32(10):880–5. <https://doi.org/10.1177/0883073817713918>
 55. Elshorbagy HH, Azab AA, Kamal NM, Barseem NF, Bassiouny MM, Elsayed MA, et al. Value of electroencephalographic monitoring in newborns with hypoxic-ischemic encephalopathy treated with hypothermia. *J Pediatr Neurosci.* 2016;11(4):309–15. <https://doi.org/10.4103/1817-1745.199467>
 56. Kharoshankaya L, Stevenson NJ, Livingstone V, Murray DM, Murphy BP, Ahearne CE, et al. Seizure burden and neurodevelopmental outcome in neonates with hypoxic-ischemic encephalopathy. *Dev Med Child Neurol.* 2016;58(12):1242–8. <https://doi.org/10.1111/dmcn.13215>
 57. Low E, Stevenson NJ, Mathieson SR, Livingstone V, Ryan AC, Rennie JM, et al. Short-term effects of phenobarbitone on electrographic seizures in neonates. *Neonatology.* 2016;110(1):40–6. <https://doi.org/10.1159/000443782>
 58. Pressler RM, Boylan GB, Marlow N, Blennow M, Chiron C, Cross JH, et al. Bumetanide for the treatment of seizures in newborn babies with hypoxic ischaemic encephalopathy (NEMO): an open-label, dose finding, and feasibility phase 1/2 trial. *Lancet Neurol.* 2015;14(5):469–77. [https://doi.org/10.1016/S1474-4422\(14\)70303-5](https://doi.org/10.1016/S1474-4422(14)70303-5)
 59. Naim MY, Gaynor JW, Chen J, Nicolson SC, Fuller S, Spray TL, et al. Subclinical seizures identified by postoperative electroencephalographic monitoring are common after neonatal cardiac surgery. *J Thorac Cardiovasc Surg.* 2015;150(1):169–80. <https://doi.org/10.1016/j.jtcvs.2015.03.045>
 60. Srinivasakumar P, Zempel J, Trivedi S, Wallendorf M, Rao R, Smith B, et al. Treating EEG seizures in hypoxic ischemic encephalopathy: a randomized controlled trial. *Pediatrics.* 2015;136(5):e1302–e1309. <https://doi.org/10.1542/peds.2014-3777>
 61. Lynch NE, Stevenson NJ, Livingstone V, Mathieson S, Murphy BP, Rennie JM, et al. The temporal characteristics of seizures in neonatal hypoxic ischemic encephalopathy treated with hypothermia. *Seizure.* 2015;33:60–5. <https://doi.org/10.1016/j.seizure.2015.10.007>
 62. Pavlidis E, Spagnoli C, Pelosi A, Mazzotta S, Pisani F. Neonatal status epilepticus: differences between preterm and term newborns. *Eur J Paediatr Neurol.* 2015;19(3):314–9. <https://doi.org/10.1016/j.ejpn.2015.01.002>
 63. Low E, Mathieson SR, Stevenson NJ, Livingstone V, Ryan CA, Bogue CO, et al. Early postnatal EEG features of perinatal arterial ischaemic stroke with seizures. *PLoS One.* 2014;9(7):e100973. <https://doi.org/10.1371/journal.pone.0100973>
 64. Vesoulis ZA, Inder TE, Woodward LJ, Buse B, Vavasseur C, Mathur AM. Early electrographic seizures, brain injury, and neurodevelopmental risk in the very preterm infant. *Pediatr Res.* 2014;75(4):564–9. <https://doi.org/10.1038/pr.2013.245>
 65. Tarocco A, Ballardini E, Garani G. Use of ketamine in a newborn with refractory status epilepticus: a case report. *Pediatr Neurol.* 2014;51(1):154–6. <https://doi.org/10.1016/j.pediatrneurol.2014.03.006>
 66. Shah DK, Wusthoff CJ, Clarke P, Wyatt JS, Ramaiah SM, Dias RJ, et al. Electrographic seizures are associated with brain injury in newborns undergoing therapeutic hypothermia. *Arch Dis Child Fetal Neonatal Ed.* 2014;99(3):F219–F224. <https://doi.org/10.1136/archdischild-2013-305206>
 67. Glass HC, Wusthoff CJ, Shellhaas RA, Tsuchida TN, Bonifacio SL, Cordeiro M, et al. Risk factors for EEG seizures in

- neonates treated with hypothermia: a multicenter cohort study. *Neurology*. 2014;82(14):1239–44. <https://doi.org/10.1212/WNL.0000000000000282>
68. Mastrangelo M, Fiocchi I, Fontana P, Gorgone G, Lista G, Belcastro V. Acute neonatal encephalopathy and seizures recurrence: a combined aEEG/EEG study. *Seizure*. 2013;22(9):703–7. <https://doi.org/10.1016/j.seizure.2013.05.006>
 69. Srinivasakumar P, Zempel J, Wallendorf M, Lawrence R, Inder T, Mathur A. Therapeutic hypothermia in neonatal hypoxic ischemic encephalopathy: electrographic seizures and magnetic resonance imaging evidence of injury. *J Pediatr*. 2013;163(2):465–70. <https://doi.org/10.1016/j.jpeds.2013.01.041>
 70. Low E, Boylan GB, Mathieson SR, Murray DM, Korotchikova I, Stevenson NJ, et al. Cooling and seizure burden in term neonates: an observational study. *Arch Dis Child Fetal Neonatal Ed*. 2012;97(4):F267–F272. <https://doi.org/10.1136/archdischild-2011-300716>
 71. Scher MS, Redline RW, Bangert BA. Delayed onset of status epilepticus after transient asphyxia in an asymptomatic full-term neonate. *J Child Neurol*. 2002;17(10):780–3. <https://doi.org/10.1177/08830738020170101806>
 72. Numis AL, Glass HC, Comstock BA, Gonzalez F, Maitre NL, Massey SL, et al. Relationship of neonatal seizure burden before treatment and response to initial antiseizure medication. *J Pediatr*. 2024;268:113957. <https://doi.org/10.1016/j.jpeds.2024.113957>
 73. Langeslag JF, Onland W, Groenendaal F, de Vries LS, van Kaam AH, de Haan TR, et al. Association between seizures and neurodevelopmental outcome at two and five years in asphyxiated newborns with therapeutic hypothermia. *Pediatr Neurol*. 2024;153:152–8. <https://doi.org/10.1016/j.pediatrneurol.2024.01.023>
 74. Katsarou A-M, Galanopoulou AS, Moshé SL. Epileptogenesis in neonatal brain. *Semin Fetal Neonatal Med*. 2018;23:159–67. <https://doi.org/10.1016/j.siny.2017.12.004>
 75. Molinero I, Galanopoulou AS, Moshé SL. Rodent models: where it all started with these “truths”. *Eur J Paediatr Neurol*. 2020;24:61–5. <https://doi.org/10.1016/j.ejpn.2019.12.011>
 76. Hasson H, Malhotra S, Giorgi FS, Rosenbaum DM, Moshé SL. Harmful effect of kainic acid on brain ischemic damage is not related to duration of status epilepticus. *Neurol Sci*. 2010;31:103–5. <https://doi.org/10.1007/s10072-009-0115-x>

How to cite this article: Nunes ML, Yozawitz EG, Wusthoff CJ, Shellhaas RA, Olivas-Peña E, Wilmschurst JM, et al. Defining neonatal status epilepticus: A scoping review from the ILAE neonatal task force. *Epilepsia Open*. 2025;10:40–54. <https://doi.org/10.1002/epi4.13090>

ANNEX A

SEARCH STRATEGY

Aim: review definitions of status epilepticus in neonates.

Time frame: 10 years.

Key words and search terms

Infant, Newborn", "Infant, Premature", Term Birth"
 # Neonate # Preterm
 # status epilepticus
 # convulsive status epilepticus
 # non convulsive status epilepticus
 # refractory status epilepticus
 # electrographic seizures

EMBASE

("Absence Status" OR "Complex Partial Status Epilepticus" OR "Electrographic Status Epilepticus" OR "Generalized Convulsive Status Epilepticus" OR "Generalized Status Epilepticus" OR "Grand Mal Status Epilepticus" OR "Non Convulsive Status Epilepticus" OR "Non-Convulsive Status Epilepticus" OR "Petit Mal Status" OR "Simple Partial Status Epilepticus" OR "Status Epilepticus, Complex Partial" OR "Status Epilepticus, Electrographic" OR "Status Epilepticus, Generalized" OR "Status Epilepticus, Generalized Convulsive" OR "Status Epilepticus, Grand Mal" OR "Status Epilepticus, Non Convulsive" OR "Status Epilepticus, Non-Convulsive" OR "Status Epilepticus, Simple Partial" OR "Status Epilepticus, Subclinical" OR "Status, Absence" OR "Status, Petit Mal" OR "Subclinical Status Epilepticus" OR "electrographic seizures" OR "refractory status epilepticus") AND ("Infant, Newborn" OR "Infants, Newborn" OR "Neonate" OR "Neonates" OR "Newborn" OR "Newborn Infant" OR "Newborn Infants" OR "Newborns" OR "Infant, Preamture" OR "Infant, Preterm" OR "Infants, Premature" OR "Infants, Preterm" OR "Neonatal Prematurity" OR "Premature Infant" OR "Premature Infants" OR "Prematurity, Neonatal" OR "Preterm Infant" OR "Preterm Infants" OR "Term Birth" OR "Birth of Full Term Infant" OR "Birth of Full Term Newborn" OR "Birth of Full-Term Infant" OR "Birth of Full-Term Newborn" OR "Birth, Fullterm" OR "Birth, Term" OR "Births, Fullterm" OR "Full-Term Infant Births" OR "Fullterm Birth" OR "Fullterm Births" OR "Term Births" OR Preterm)

PUBMED

("Absence Status" OR "Complex Partial Status Epilepticus" OR "Electrographic Status Epilepticus" OR "Generalized Convulsive Status Epilepticus" OR "Generalized Status Epilepticus" OR "Grand Mal Status Epilepticus" OR "Non Convulsive Status Epilepticus" OR "Non-Convulsive Status Epilepticus" OR "Petit Mal Status" OR "Simple Partial Status Epilepticus" OR "Status Epilepticus, Complex Partial" OR "Status Epilepticus, Electrographic" OR "Status Epilepticus, Generalized" OR "Status Epilepticus, Generalized Convulsive" OR "Status Epilepticus, Grand Mal" OR "Status Epilepticus, Non Convulsive" OR "Status Epilepticus, Non-Convulsive" OR "Status Epilepticus, Simple Partial" OR "Status Epilepticus, Subclinical" OR

“Status, Absence” OR “Status, Petit Mal” OR “Subclinical Status Epilepticus” OR “electrographic seizures” OR “refractory status epilepticus”) AND (“**Infant, Newborn**” OR “Infants, Newborn” OR “Neonate” OR “Neonates” OR “Newborn” OR “Newborn Infant” OR “Newborn Infants” OR “Newborns” OR “**Infant, Premature**” OR “Infant, Preterm” OR “Infants, Premature” OR “Infants, Preterm” OR “Neonatal Prematurity” OR “Premature Infant” OR “Premature Infants” OR “Prematurity, Neonatal” OR “Preterm Infant” OR “Preterm Infants” OR “**Term Birth**” OR “Birth of Full Term Infant” OR “Birth of Full Term Newborn” OR “Birth of Full-Term Infant” OR “Birth of Full-Term Newborn” OR “Birth, Fullterm” OR “Birth, Term” OR “Births, Fullterm” OR “Full-Term Infant Births” OR “Fullterm Birth” OR “Fullterm Births” OR “Term Births” OR Preterm)

LILACS

(“Absence Status” OR “Complex Partial Status Epilepticus” OR “Electrographic Status Epilepticus” OR “Generalized Convulsive Status Epilepticus” OR “Generalized Status Epilepticus” OR “Grand Mal Status Epilepticus” OR “Non Convulsive Status Epilepticus” OR “Non-Convulsive Status Epilepticus” OR “Petit Mal Status” OR “Simple Partial Status Epilepticus” OR “Status Epilepticus, Complex Partial” OR “Status Epilepticus, Electrographic” OR “Status Epilepticus, Generalized” OR “Status Epilepticus, Generalized Convulsive” OR “Status Epilepticus, Grand Mal” OR “Status Epilepticus, Non Convulsive” OR “Status Epilepticus, Non-Convulsive” OR “Status Epilepticus, Simple Partial” OR “Status Epilepticus, Subclinical” OR “Status, Absence” OR “Status, Petit Mal” OR “Subclinical Status Epilepticus” OR “electrographic seizures” OR “refractory status epilepticus”) AND (“Infant, Newborn” OR “Infants, Newborn” OR “Neonate” OR “Neonates” OR “Newborn” OR “Newborn Infant” OR “Newborn Infants” OR “Newborns” OR “Infant, Premature” OR “Infant, Preterm” OR “Infants, Premature” OR “Infants, Preterm” OR “Neonatal Prematurity” OR “Premature Infant” OR

“Premature Infants” OR “Prematurity, Neonatal” OR “Preterm Infant” OR “Preterm Infants” OR “Term Birth” OR “Birth of Full Term Infant” OR “Birth of Full Term Newborn” OR “Birth of Full-Term Infant” OR “Birth of Full-Term Newborn” OR “Birth, Fullterm” OR “Birth, Term” OR “Births, Fullterm” OR “Full-Term Infant Births” OR “Fullterm Birth” OR “Fullterm Births” OR “Term Births” OR Preterm)

COCHRANE

(“Absence Status” OR “Complex Partial Status Epilepticus” OR “Electrographic Status Epilepticus” OR “Generalized Convulsive Status Epilepticus” OR “Generalized Status Epilepticus” OR “Grand Mal Status Epilepticus” OR “Non Convulsive Status Epilepticus” OR “Non-Convulsive Status Epilepticus” OR “Petit Mal Status” OR “Simple Partial Status Epilepticus” OR “Status Epilepticus, Complex Partial” OR “Status Epilepticus, Electrographic” OR “Status Epilepticus, Generalized” OR “Status Epilepticus, Generalized Convulsive” OR “Status Epilepticus, Grand Mal” OR “Status Epilepticus, Non Convulsive” OR “Status Epilepticus, Non-Convulsive” OR “Status Epilepticus, Simple Partial” OR “Status Epilepticus, Subclinical” OR “Status, Absence” OR “Status, Petit Mal” OR “Subclinical Status Epilepticus” OR “electrographic seizures” OR “refractory status epilepticus”) AND (“Infant, Newborn” OR “Infants, Newborn” OR “Neonate” OR “Neonates” OR “Newborn” OR “Newborn Infant” OR “Newborn Infants” OR “Newborns” OR “Infant, Premature” OR “Infant, Preterm” OR “Infants, Premature” OR “Infants, Preterm” OR “Neonatal Prematurity” OR “Premature Infant” OR “Premature Infants” OR “Prematurity, Neonatal” OR “Preterm Infant” OR “Preterm Infants” OR “Term Birth” OR “Birth of Full Term Infant” OR “Birth of Full Term Newborn” OR “Birth of Full-Term Infant” OR “Birth of Full-Term Newborn” OR “Birth, Fullterm” OR “Birth, Term” OR “Births, Fullterm” OR “Full-Term Infant Births” OR “Fullterm Birth” OR “Fullterm Births” OR “Term Births” OR Preterm)