The American Clinical Neurophysiology Society Guideline on Indications for Continuous Electroencephalography Monitoring in Neonates

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Purpose: Continuous EEG (cEEG) monitoring is increasingly used in the management of neonates with seizures. There remains debate on what clinically relevant information can be gained from cEEG in neonates with suspected seizures, at high risk for seizures, or with definite seizures, as well as the use of cEEG for prognosis in a variety of conditions. In this guideline, we address these questions using American Clinical Neurophysiology Society structured methodology for clinical guideline development.

Methods: A working group was formed from American Clinical Neurophysiology Society membership with expertise in neonatal cEEG and a set of priority questions developed. We performed literature searches in PubMed and EMBASE to identify relevant studies. Evidence tables were compiled from extracted data and quality assessments performed. A modification of the GRADE process was used to evaluate the body of evidence and draft recommendations.

Results: Our working group identified six priority questions to evaluate the accuracy of cEEG for neonatal seizure diagnosis and the formulation of prognosis. An initial literature search yielded 18,167 results, which were distilled to a set of 217 articles. Overall, the quality of evidence for most priority questions was rated as very low and we provided conditional recommendations based on published literature and expert consensus. For each priority question, we also considered the benefits and harms of cEEG, with relative harms considered to be far less than the potential benefits across recommendations.

Conclusions: We present evidence-based clinical guidelines regarding indications for cEEG monitoring in neonates. Considering resource utilization and feasibility, when cEEG monitoring results have a likelihood of altering clinical decision making, the authors felt the resource investment was justifiable.

Key Words: EEG, Infant, Newborn, Guideline, Seizures, Intensive care units, Neonatal, Neonatal encephalopathy.

(J Clin Neurophysiol 2025;42: 1–11)

C. J. Wusthoff's research is supported by NIH and the Thrasher Research Fund. She has received a stipend for serving on data safety monitoring boards for PRA Health Sciences, ICON, and the University of Utah. She is on the editorial board for Epilepsy and Behavior Reports, the Journal of Clinical Neurophysiology, and is an associate editor for Neurology. She receives royalties from Cambridge University Press. A. D. Numis's research is supported by the NIH. He is on the editorial board for Seminars in Pediatric Neurology and Frontiers in Neurology. He has served as a consultant for Ambit, Inc. R. M. Pressler is an investigator for studies with UCB. She has served as a consultant, as a speaker, and/or on advisory boards for Natus, Esai, Kephala, GW, and UCB. Her research is supported by the National Institute of Health Research (NIHR) Biomedical Research Centre at Great Ormond Street Hospital and Cambridge University Hospital, NIHR, Thrasher Research Fund, and James Bradfield Memorial Grant (via the Evelyn Trust). She is on the editorial boards of Journal of Clinical Neurophysiology, Neurophysiologie Clinique, and European Journal of Pediatric Neurology and is an associate editor for Epilepsia Open. Dr. Chu receives research support from the NIH, the Epilepsy Foundation New England, Novartis, and Biogen. She is a site investigator for a clinical trial sponsored by Neuropace. She provides consulting services to Biogen, Ionis Pharmaceuticals, Novartis, Sun Pharmaceuticals, and Ovid Pharmaceuticals. S. Massey serves as a consultant for Sun Pharmaceuticals. S. Nguyen serves as a consultant for UCB. C. D. Hahn's research is supported by NIH and CIHR. He is an associate editor for the Journal of Clinical Neurophysiology and receives royalties from Cambridge University Press. He has served as a consultant on clinical trial design to Takeda Pharmaceuticals and UCB Pharma SRL. T. N. Tsuchida's research has been supported by NIH funding and had been a seizure drug trial advisor for Xenon and Hikma Pharmaceuticals. J. J. Riviello's spouse is a section editor for UpToDate. R. A. Shellhaas' research is supported by NIH. She receives royalties from UpToDate for authorship of topics related to neonatal seizures and serves as a consultant for the Epilepsy Study Consortium. She receives a stipend for her role as president of the Pediatric Epilepsy Research Foundation. The remaining authors have no conflicts of interest to disclose.

Funding sources for this work: American Clinical Neurophysiology Society.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's web site (www.clinicalneurophys.com).

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ISSN: 1537-1603/24/4201-0001
DOI 10.1097/WNP.0000000000001120

Seizures in a neonate often indicate acute neurologic injury and require urgent diagnosis and management. Yet, neonatal seizures are notoriously difficult to diagnose by clinical observation alone[1]; definitive diagnosis requires electroencephalography (EEG) confirmation.[2] Continuous EEG monitoring (cEEG) is often used in the management of seizures in newborns. At the same time, cEEG has uses beyond seizure detection in neonates, including to facilitate diagnosis of underlying conditions and to provide prognostic information. In 2011, recognizing increasing interest in cEEG, the American Clinical Neurophysiology Society (ACNS) issued "The ACNS Guideline on Continuous EEG Monitoring in Neonates".[3] That document relied on consensus among a group of experts to author recommendations regarding indications and technical standards for use of cEEG in newborns. It provided a set of goals for neonatal cEEG, while also recognizing that practical barriers may hinder implementation.

In the subsequent years, cEEG use has expanded, as has the medical literature regarding neonatal cEEG. In addition, the ACNS has since adopted structured methodology requirements for the development of clinical guidelines.[4] For these reasons, an update of the 2011 guidance was needed to provide an evidence-based guideline regarding indications for neonatal cEEG. Updated guidance regarding technical standards for recording and reporting of neonatal cEEG will be presented separately in a forthcoming document.

This guideline discusses the use of cEEG in neonates, defined as those of postmenstrual age less than 48 weeks. The focus is on cEEG of hospitalized neonates; this guideline does not suggest indications for outpatient neonatal EEG or "routine" EEG of duration less than 60 minutes. Practical barriers to performing cEEG remain in many settings. As such, these guidelines provide recommendations regarding which patients would most benefit from cEEG, but do not constitute a universal standard of care, nor are they exhaustive for all the patients who might benefit from cEEG.

METHODS

In 2022, a working group was formed to update the 2011 ACNS Guideline on Continuous EEG Monitoring in Neonates. Members were invited based on their expertise in neonatal cEEG and availability for this work. All working group members were required to hold active ACNS membership (with the exception of a medical librarian), and to adhere to ACNS standards regarding conflicts of interest. Financial disclosures were required before the start of work and updated annually. American Clinical Neurophysiology Society provided meeting space for the working group but there was no other funding.

The group developed a set of priority questions to address in this guideline. These were drafted using the PICO format (Patients, Intervention, Comparison group, and Outcome under consideration) for each question.[5] These questions and their associated outcomes of interest were used as the basis for a subsequent systematic literature review. While seven priority questions were originally developed, the systematic review found highly overlapping evidence for two questions (PICOs 1 and 2), which were subsequently jointly addressed in Recommendation 1.

Throughout this process, an EEG seizure was defined as a paroxysmal, rhythmic, evolving event on EEG lasting 10 seconds or longer.[6] Electrographic-only (EEG-only) seizures were defined as seizures evident only on EEG without clear accompanying clinical signs, often referred to as subclinical or nonconvulsive seizures. Electroclinical seizures were defined as those with both ictal evolution on EEG and simultaneous clinical signs. Where literature discussed clinical seizures without EEG confirmation, this was noted in data extraction.

A medical librarian assisted in the development of a search strategy to identify published literature relevant to our priority questions. The systematic review was registered with PROSPERO before the first search (CRD42022331639). A search was performed in PubMed and EMBASE on April 29, 2022, and updated on March 20, 2023. (see **Supplemental Material**, **Supplemental Digital Content 1**, http://links.lww.com/JCNP/A284, http://links.lww.com/JCNP/A285) Results were included if full text was available in English, German, or French (all languages for which at least two authors had proficiency), with publication before the search date. Titles and abstracts were screened independently by two members of the author group for relevance to the priority questions and the following inclusion criteria: human studies, primary research, EEG recorded with eight or more electrodes, EEG recorded for greater than 60 minutes duration, and with or without concurrent video. Exclusion criteria were animal and *in vitro* studies, studies with fewer than five neonates, abstracts or conference proceedings, review articles, editorials, and those that did not address a priority question. If there was disagreement between two reviewers, then a third reviewer resolved conflicts. Articles were screened by reviewers with fluency in the language of each article. Those articles included after title and abstract screening underwent full text review using the same process. Covidence systematic review software (Melbourne, Australia) was used to perform article screening, full text review, and data extraction.

Data extraction was performed by two independent reviewers, with discrepancies resolved by a third reviewer. Extracted data included author, year of publication, study design, study period, inclusion and exclusion criteria, participant characteristics, EEG findings, and adverse events. Risk of bias and quality assessments were performed independently by two reviewers, with disagreements resolved by a third reviewer using the QUADAS-2 tool for studies of diagnostic tests, and the QUIPS tool for studies of prognosis.[7] Data were synthesized in evidence profiles taking the form of tables and summarized using a narrative approach. In recognition of the heterogeneity of data and limited evidence for some questions, meta-analysis was not planned.

The GRADE process modified for diagnostic tests[8–10] was used to evaluate the body of evidence for each priority question. Evidence tables for each priority question were synthesized, compiling the extracted components of articles relevant to each priority question. The overall quality of evidence for each PICO was reached by group consensus.[8] The writing group developed recommendations and stated the strength of each recommendation based on the overall quality of evidence. For each

recommendation, quality of evidence, balance of benefits to harms, values and preferences of the target population, and resource use were considered. Recommendations were made for or against cEEG in each situation (direction) and described in strength (strong or conditional).[8] Strong recommendations are those for which most patients should receive the recommended course of action, while conditional recommendations are those for which the majority of patients/families would want the recommended course of action while some may not, or where resource or feasibility considerations might limit the recommended course of action in some situations. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for diagnostic test accuracy studies checklists is provided in **Supplemental Digital Content 1** (**Prisma DTA Checklist**, http://links.lww.com/JCNP/A290).[11]

A draft guideline was sent to the ACNS Guidelines Committee for review and comment by an internal review panel, and then by the ACNS Executive Committee, with revision based on feedback. A draft was posted for public comment for 30 days on the ACNS web site, with comment requested from stakeholder groups. Comments were reviewed individually and the guideline was revised as appropriate. The final manuscript was approved by the ACNS Council before submission for publication.

RESULTS

The initial literature search yielded 18,167 results, which were distilled to a set of 217 articles for data extraction [Fig. 1]. (see **Supplemental Material**, **Supplemental Digital Content 1**, http://links.lww.com/JCNP/A284, http://links.lww.com/JCNP/A285) Evidence tables compiled extracted data and quality assessments for each priority question, allowing synthesis into profiles, and summarized in narrative form (listed in Fig. 2). Priority questions 1 and 2 had highly overlapping evidence and, therefore, considered jointly for recommendation 1. Standardized evidence to recommendation templates and checklists was used to facilitate development of each recommendation (see **Supplemental Material**, **Supplemental Digital Content 1**, http://links.lww.com/JCNP/A284, http://links.lww.com/JCNP/A285).

The systematic review did not find reports of direct harm from cEEG for any priority question. There is, however, a known risk for skin irritation and injury that may occur with the application or prolonged use of recording electrodes. Longer duration of cEEG, higher number of electrodes, and younger postmenstrual age of the patient each increases this risk. The risk of skin injury can be mitigated by technique,[12–14] including regular inspection of skin for early signs of irritation and repositioning of electrodes when needed, but the risk is never completely removed. Similarly, although not reported in the results of our systematic review, cEEG electrodes and related equipment may complicate positioning and holding of the neonate. These relative potential harms were considered far outweighed by the potential benefits in each recommendation.

Conclusions regarding feasibility and resource use of cEEG similarly applied to each indication. Continuous EEG is recognized to be a high-resource tool because of the required equipment and skilled personnel to initiate and interpret recordings. Availability of cEEG varies widely. In some cases, transfer to another center may be required to obtain cEEG. Where cEEG is available, some sites are limited in how long cEEG can continue or how many patients can have cEEG simultaneously. A formal cost–benefit analysis was not performed.

Recommendations

1. We Suggest cEEG Use in Neonates to Improve Accuracy of Seizure Diagnosis in Clinically Suspected Seizures, as Compared With Clinical Observation Alone, aEEG Alone, or Routine/Spot EEG. (Conditional Recommendation, Very Low Quality of Evidence)

Consistently across 57 studies including both term and preterm neonates with clinically suspected seizures due to heterogeneous etiologies, cEEG substantially improved the accuracy of seizure diagnosis. This was true when cEEG was compared with clinical diagnosis, aEEG alone, or to routine/spot EEG. However, few studies directly compared EEG modalities simultaneously in the same neonates. The overall quality of evidence was very low.

Clinical observation alone

In studies of neonates with a clinical diagnosis of seizure, 33 to 85% of neonates clinically thought to have seizures did not have seizures confirmed on cEEG, with most reports describing more than half of neonates found not to have cEEG seizures. This was as high as 96% in a series of neonates undergoing cEEG on ECMO,[15] 90% in a small series of newborns with HIE,[16] and 100% in a mixed group.[17] Similarly, even among neonates with confirmed epilepsy or brain injury, myoclonus and/or tremor were sometimes inaccurately thought to be seizures; cEEG identified these episodes as nonseizure in critically ill patients.[18,19] Among neonates with clinical seizures that were confirmed by EEG, cEEG often identified a far greater seizure burden or number of seizures than were recognized clinically. In some studies, as many as 80 to 90% of seizures were subclinical.[20,21] There was an association between higher seizure burden and the likelihood of seizures being subclinical/nonconvulsive.[22] One small series reported that clinical observation had a sensitivity for individual seizures of 13% and specificity of 38%.[23]

aEEG alone

There was a wide range of reported accuracy compared with cEEG, with sensitivity ranging from 0 to 70%, and specificity ranging from 64 to 82%. The benefit of cEEG beyond aEEG may vary depending on the risk of seizures for an individual patient and by aEEG interpreters' skill, though there was consistently higher accuracy reported for cEEG than for aEEG. In one of the few studies that compared with simultaneous cEEG, aEEG was reported to identify individual seizures with a sensitivity of 13% and specificity of 46%.[23] Across studies, the limited electrode array of aEEG was more likely than cEEG to miss seizures localized to the frontal or occipital regions.[3,21] Seizures were also more likely to be missed on aEEG if they were of brief duration, or of lower voltage. Conversely, artifact was more likely to result in a false positive with aEEG than with cEEG.

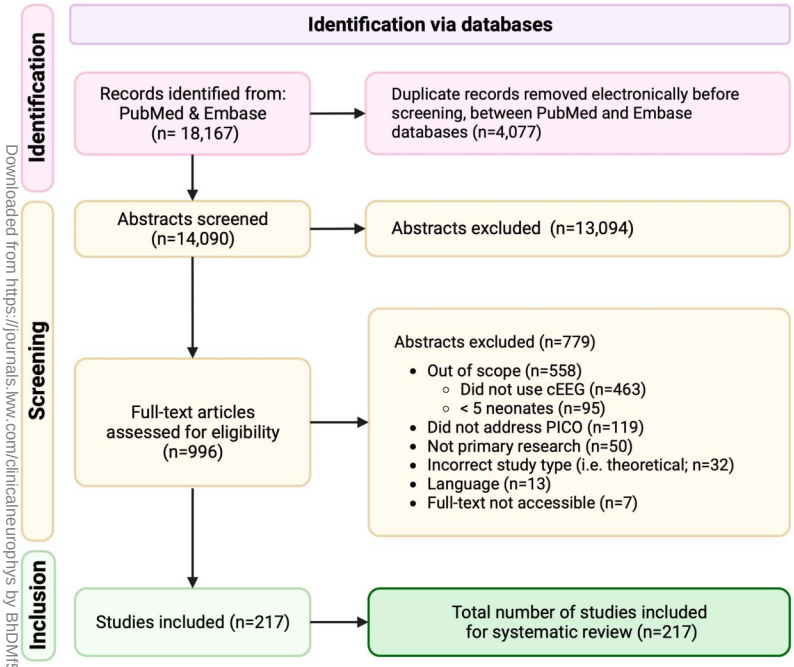

FIG. 1. PRSIMA flowchart. Created with BioRender.com.

Routine/spot EEG

Several studies indirectly examined the accuracy of cEEG for the diagnosis for neonatal seizures as compared with routine/spot EEG. A retrospective study compared two periods before and after the availability of cEEG. During the first period, routine/spot EEG confirmed electrographic seizures in 12 of 35 infants with clinically suspected seizures (34%).[24] Once cEEG was available, electrographic seizures were confirmed in 18 of 34 infants (53%) with clinically suspicious events. Furthermore, 5 of 37 infants (14%) who had cEEG without clinically suspected seizures were discovered to have electrographic seizures. In a similar series before and after the implementation of cEEG, seizures were confirmed electrographically in 10 of 50 infants (20%) with routine/spot EEG versus 17 of 50 infants (34%) with cEEG.[25] With the availability of cEEG, the detection of EEG-only seizures increased. One single-center study evaluating seizure detection in the era of routine/spot EEG versus cEEG use demonstrated that with routine/spot EEG, seizures were first detected by clinical manifestations in 85% of neonates, whereas after cEEG was available, seizures were detected first on EEG in 33% of neonates. In that study, neonates with EEG-only seizures were diagnosed almost exclusively after cEEG became available (27 vs. 2%).[26] Finally, in a study of 98 neonates with seizures on cEEG monitoring, only 50 of 98 neonates (51%) had their first seizure in the first hour of cEEG monitoring, with the remainder only diagnosed with prolonged monitoring.[27]

Even though the overall quality of evidence was very low, in considering the balance of benefits and harms, the body of evidence strongly favors benefits of cEEG over clinical observation alone, aEEG alone, or routine/spot EEG alone to improve accuracy of seizure diagnosis in neonates with clinically suspected seizures. In weighing values and preferences, it was recognized that neonates' families typically value a definitive diagnosis of seizures, or definitive confirmation that an event is not a seizure.[28,29] We acknowledge that misdiagnosis of seizures could lead to over- or undertreatment with potential for harm. Some families may identify concerns that cEEG can interfere with holding, utilization of family-centered care principles can decrease the impact of skin-to-skin time loss. In general, the information obtained from cEEG is regarded as important enough that families wish to proceed. Given that cEEG is resource intensive and not feasible in all settings and the overall quality of evidence was very low, this recommendation is conditional.

2. We Suggest cEEG Use in Neonates to Confirm Diagnosis of aEEG Events Suspected to Be Seizures. (Conditional Recommendation, Very Low Quality of Evidence)

We reviewed 13 studies with evidence comparing the accuracy of cEEG to aEEG in neonates with suspected seizures based on aEEG evaluation.[20,30–32] These studies included neonates with clinically suspected seizures and those diagnosed with seizures solely on aEEG (without clinical signs); details comparing accuracy for just the subgroup of neonates who presented only with aEEG seizures (and without clinical suspicion for seizures) were not reported. The available evidence was, therefore, indirect, taken from cohorts of neonates with suspected seizures based on either aEEG evaluation or clinical observation alone.

Among neonates with suspected seizures diagnosed by aEEG, aEEG was reported to detect between 13% and 80% of the seizures confirmed by simultaneous cEEG recording, whereas the reported specificity of aEEG ranged from 46 to 93%. False positive seizures identified on aEEG were most often attributed to movement artifacts.[20,30–32]

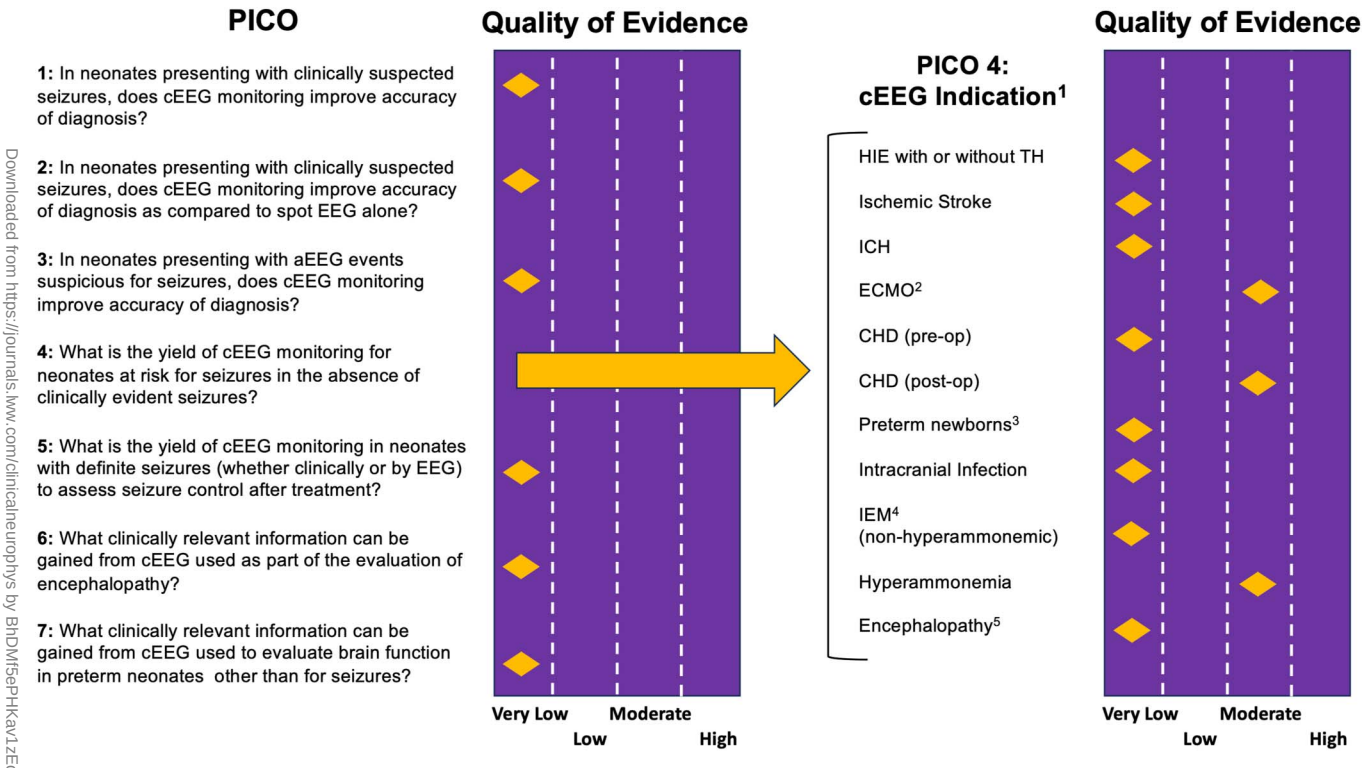

FIG. 2. Quality of evidence for each PICO (Population, Intervention, Comparison, and outcome) priority question. CHD, Congenital heart disease; ECMO, Extracorporeal membrane oxygenation; HIE, Hypoxic-ischemic encephalopathy; ICH, Intracerebral hemorrhage; TH, Therapeutic hypothermia. 1. The following indications had insufficient evidence for GRADE: Congenital brain and/or spine malformation, intraventricular hemorrhage in term neonates, neonatal systemic inflammatory syndrome, preterm neonates without seizure risk factors, sepsis, sinovenous thrombosis, transient metabolic disturbances, therapeutic paralysis. 2. Includes cardiac, pulmonary, and other indications. 3. Very preterm (28 to <32 weeks gestation) and extreme preterm infants (<28 weeks gestation) with seizure risk factors (i.e., intraventricular hemorrhage). 4. Inborn errors of metabolism. 5. Owing to multiple congenital anomalies and high-risk respiratory conditions (CDH, omphalocele, pulmonary HTN, CCAM/CPAM), encephalopathy NOS/unknown cause.

Across all studies, cEEG improved the accuracy of seizure diagnosis as compared with aEEG. Although the overall quality of evidence was very low, there was consistency in the direction of reported findings. In considering the balance of benefits and harms, the body of evidence strongly favors the benefits of cEEG used for detection of seizure in neonates. In weighing values and preferences, considerations were the same as in the first recommendation. Given that cEEG is resource intensive and not feasible in all settings and the overall quality of evidence was very low, this recommendation is conditional.

3. We Suggest cEEG Use to Monitor Neonates at Risk for Seizures in the Absence of Clinically Evident Seizures. (Conditional Recommendation, Quality of Evidence Ranging From Very Low to Moderate for Specific Subgroups)

We reviewed 91 studies (2 RCTs, 34 prospective observational, and 55 retrospective studies) to evaluate cEEG in neonates at risk for seizures in the absence of clinically evident seizures stratified by 14 prespecified indications. The number of studies analyzed varied by seizure etiology and ranged from 64 studies of term neonates with HIE to 2 studies of neonates requiring ECMO. There were also several seizure etiologies that had insufficient or no evidence to address this question, precluding our ability to make a formal recommendation.

The overall quality of evidence was *moderate* for postoperative neonates who required newborn heart surgery for severe congenital heart disease (CHD),[33–43] those receiving ECMO for any indication,[15,44] and those with hyperammonemia.[45] Moderate quality of evidence denotes that the true effect of cEEG use to monitor neonates at risk for seizures is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. The quality of evidence was *very low* for neonates with HIE with or without therapeutic hypothermia, ischemic stroke, intracranial hemorrhage, preterm gestation <32 weeks with additional risk factors, intracranial infection, encephalopathy (beyond HIE), and with nonhyperammonemic inborn errors of metabolism. There was *insufficient or no evidence* to provide a recommendation for term neonates with intraventricular hemorrhage, sinovenous thrombosis, sepsis, neonatal systemic inflammatory syndrome, congenital brain and/or spine malformations, pharmacologic paralysis, and with simple transient metabolic disturbance. Although there was also insufficient evidence to make a recommendation for neonates with

a known genetic diagnosis with high risk for seizures, these infants typically present with clinical seizures and, therefore, would not be covered by this priority question[26,46,47] (Fig. 3).

Overall, for the above conditions with moderate and very low-quality evidence, the balance of benefits versus harms is in favor of cEEG for neonates at risk for seizures in the absence of clinically evident seizures.

In general, there was insufficient evidence to make a formal recommendation on the timing of cEEG to evaluate for electrographic seizures in the absence of clinically evident seizures for specific conditions. There was indirect evidence for neonates with acute brain injury due to HIE demonstrating that 24 or more hours of cEEG to screen for seizures is superior to EEG of less than 60 minutes.[17,27,48–57] For the three conditions with moderate-quality evidence supporting cEEG in the absence of clinically evident seizures, there was limited data on optimal timing of cEEG. Among neonates with CHD in the postoperative period after repair, seizures typically appear as soon as 6 hours postoperatively, as perioperative medications are cleared and median time to seizure is just more than 24 hours postoperatively.[37] Thus, cEEG would be of highest yield within 6 hours and up to 48 hours postoperatively. For neonates undergoing ECMO, seizure risk varies; cEEG should be initiated as soon as possible after cannulation with duration based on ongoing risk for seizures and any clinical evolution of neurologic status. Similarly, for neonates with hyperammonemia, seizure risk is associated with higher plasma ammonia levels.[45] Continuous EEG should be initiated at diagnosis with duration based on plasma levels and ongoing risk for seizures.

In considering values and preferences, while there may be variation in family preferences regarding whether to have cEEG placed or replaced, there is not substantial variation in how families value accurate diagnosis or substantial variation by indication.[58,59] In addition to prognosis, families usually do want to know whether their child is experiencing seizures, and having that information is important to communicate. As described above, cEEG is resource intensive and not feasible in all settings. Given the relatively higher quality of evidence for cEEG in neonates with congenital heart disease postoperatively, on ECMO, or with hyperammonemia, it may be especially helpful to develop clinical pathways for cEEG that optimize resources for particular populations. Given the overall quality of evidence and variability in cEEG feasibility, this recommendation for cEEG to monitor for seizures in high-risk neonates is conditional.

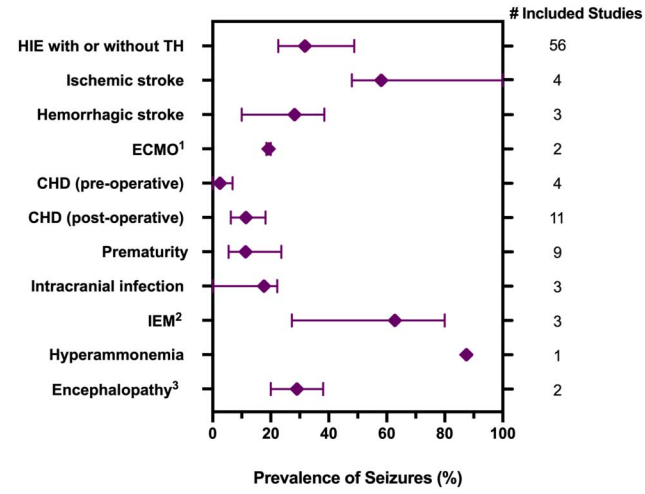

FIG. 3. Prevalence estimates of neonates at risk for seizures but without clinically evident seizures by indication. Data are median and interquartile range for cEEG indications with >3 studies and median and range for cEEG indications with ≤ 3 studies.

4. We Suggest cEEG Use in Neonates With Definite Seizures to Assess for Seizure Control After Treatment. (Conditional Recommendation, Very Low Quality of Evidence) There was insufficient evidence to make a recommendation for or against cEEG after weaning or discontinuing antiseizure medications.

We reviewed 34 studies (3 RCTs, 13 prospective observational studies, and 18 retrospective studies) to evaluate cEEG in neonates to confirm the seizure control. Three studies reported that cEEG was superior to clinical diagnosis alone to confirm seizure control after treatment with antiseizure medications (ASMs).[60–62] Another study indirectly confirmed that cEEG was superior to clinical diagnosis alone.[63] The overall quality of evidence was very low.

Given the high prevalence of EEG-only seizures in neonates, particularly after treatment is initiated,[64] cEEG is the most accurate method to objectively confirm resolution of seizures regardless of the number or burden of seizures. There are few studies that indirectly confirm that 24 hours or more of cEEG after ASM treatment is superior to EEG of 1 hour or shorter duration to confirm resolution of seizures.[45,65–72]

One study reported difficulty in administration of respiratory support during cEEG related to head positioning of the infant.[25] We acknowledge that in children undergoing selective head cooling, there could be positional and mechanical interference with equipment. At the same time, the benefits of cEEG were found to outweigh potential harms.

There may be situations in which families prefer not to have cEEG placed (or replaced) for ongoing detection of electrographic seizures in neonates with definite seizures.[58,59] However, most families would prefer accurate diagnosis confirming resolution of seizures without significant variability by seizure etiology. As previously discussed, cEEG is resource intensive, and not universally available. Given this, and the very low quality of evidence, the recommendation of cEEG for to assess for seizure control after treatment and to confirm resolution of seizures is conditional.

5. We Suggest cEEG Use in Neonates With Encephalopathy for Assessment of Interictal Background Patterns as Part of Risk Stratification for Evolving Brain Injury and Prediction of Acute Seizures, Death, or Neurodevelopmental Disability. (Conditional Recommendation, Very Low Quality of Evidence)

We reviewed 106 studies to evaluate the use of cEEG in neonatal encephalopathy for purposes other than seizure detection. Progression of EEG background patterns can highlight evolving

brain injury and offer the possibility of acute preventative or supportive interventions. Among neonates with encephalopathy, moderately and severely abnormal cEEG background and cEEG-confirmed seizures (especially high seizure burden) were independent predictors of death and abnormal development. Background asynchrony and asymmetry have each been associated with poor developmental outcome.[73,74] The reappearance of sleep–wake cycling was predictive of normal developmental outcome,[75,76] while persistently abnormal sleep–wake cycling into the second week of life was associated with poor neurodevelopmental outcome.[77,78] Abnormal cEEG background was also associated with other aspects of illness severity, including multiorgan dysfunction and slow progress toward oral feeding.[79]

Initially abnormal EEG background patterns can improve, or even normalize, for hours or days. These rapid dynamics require repeated, extended observations to detect.[80,81] Multiple studies demonstrated that some early abnormal EEG findings in the presence or absence of therapeutic hypothermia can recover and, therefore, had limited predictive value for long-term neurodevelopmental outcome.[80,82–86] However, early normal EEG findings (6–8 hours) predicted good outcome.[63,82,84,85,87] Conversely, later (>24 hours or midpoint of therapeutic hypothermia) severe abnormalities[63,80,82,83,85–89] or absence of sleep–wake cycling at 48 hrs[84] was associated with poor outcome. Markedly depressed EEG backgrounds that persisted beyond 1 week[82,83,90–92] or mildly depressed backgrounds that persisted beyond 3 weeks[78,93] were associated with unfavorable outcome.

A markedly abnormal cEEG background was associated with a higher risk for seizures.[27,94,95] Seizures on cEEG, particularly cEEG-confirmed status epilepticus, were associated with severe brain injury[54,83] and postneonatal epilepsy.[96]

For neonates with congenital heart disease, abnormal EEG background and EEG-confirmed seizures were independently associated with abnormal neurodevelopment.[36,97,98] Real-time cEEG for critically ill neonates may provide opportunities to predict physiologic decompensation associated with impending cardiac arrest.[38]

Given the evidence, the balance of benefits versus harms favors cEEG use among neonates with encephalopathy for assessment of interictal background patterns as part of risk stratification for evolving brain injury and prediction of acute seizures, death, or neurodevelopmental disability. However, the quality of evidence is very low. In considering family values and preferences, there may be variability in how families and clinicians value information from cEEG because it relates to prognosis or risk stratification for evolving brain injury.[58,59] Although many families welcome information on prognosis, some families do not wish to receive prognostic information. cEEG that aims only to provide prognostic information may not be universally desired.

As discussed above, cEEG is known to be resource intensive. When cEEG results have a likelihood of altering clinical decision making, the authors considered the resource investment was justifiable. Clinically relevant examples of altering clinical decision making include neuroimaging in cases of asymmetry or evolving deterioration of the interictal background, initiation of antiseizure medication, counseling around goals of care, or referral to early intervention therapies. At the same time, cEEG is not feasible in all settings. Given this, and the very low quality of evidence, this recommendation is conditional.

6. We Suggest cEEG Use in Preterm Neonates for Assessment of Interictal Background Patterns as Part of Risk Stratification for Evolving Brain Injury and Prediction of Death or Neurodevelopmental Disability. (Conditional Recommendation, Very Low Quality of Evidence)

We reviewed 34 articles to evaluate the use of cEEG in preterm neonates for purposes other than seizure detection. Preterm birth is associated with a risk of brain dysfunction. cEEG can provide prognostic information and identify risk for evolving brain injury for preterm infants. Interictal background patterns, including presence or absence of sleep–wake cycling,[81,99–101] degree of discontinuity,[102–104] asynchrony,[105,106] asymmetry,[105–107] presence or absence of normal graphoelements,[108] and excessive positive sharp waves[106,109] all inform risk prediction. In particular, positive sharp waves in the central and vertex regions were shown to have high specificity for underlying white matter injury (specificity 100%, sensitivity 32% for white matter lesions; specificity 83%, sensitivity 27% for intraventricular hemorrhage in an autopsy study of 39 preterm infants).[106,109] Evolution of EEG background abnormalities over time (especially the result of EEG at 36 weeks PMA or greater) has been predictive of neurodevelopmental outcomes at 12 to 36 months.[78,81,100,102,105,107,110–115] In addition, cEEG-confirmed seizures, especially status epilepticus, are associated with a high risk for unfavorable outcomes (e.g., death, cerebral palsy, and postneonatal epilepsy).[74,107,112,116–118] Limited studies directly compare serial routine/spot EEG with cEEG for these uses. The balance of benefits versus harms favors cEEG use for assessment of interictal background patterns as part of risk stratification for evolving brain injury and prediction of death or neurodevelopmental disability. However, the quality of evidence is very low.

There is variability in how families and clinicians value information from cEEG as related to prognosis or risk stratification for evolving brain injury. Many families wish to receive prognostic information for death or neurodevelopmental outcomes.[58,59] Evolving EEG background patterns can highlight evolving brain injury and offer the possibility of acute preventative or supportive interventions. Yet, some families do not wish to receive prognostic information.

As discussed above, cEEG is known to be resource intensive. When cEEG results have a likelihood of altering clinical decision making, the authors considered the resource investment justified. Examples of altering clinical decision making include neuroimaging in cases of asymmetry or evolving deterioration of the interictal background, initiation of antiseizure medication, counseling around goals of care, or referral to early intervention therapies.

DISCUSSION

This document presents an evidence-based clinical guideline regarding indications for cEEG in neonates. In some settings, such as "Neuro-Neonatal Intensive Care Units" and tertiary level

NICUs, cEEG should be available as a component of specialized care. In other settings, cEEG may be only intermittently available or not available. In recognition of this limited availability, the recommendations in this guideline are all conditional.

Although the systematic review identified many publications describing the accuracy of cEEG for seizure diagnosis and prognosis formulation in a variety of conditions, there were gaps in evidence directly demonstrating that cEEG use improves long-term outcomes for neonates. cEEG has facilitated a shift in practice away from reactive confirmation of seizures after suspicious events to more proactive identification of seizures among those at high risk. In the newborn, there is preliminary evidence that seizures identified by screening and treated early have a better treatment response.[17,119] Some evidence using cEEG suggests that seizure burden impacts clinical outcomes and is reflected by severity of injury on MRI.[57,120] Concurrently, further study is needed to determine whether cEEG utilization and seizure management improve clinically meaningful long-term outcomes. Such research is inherently complex given the interdependent impact of seizure detection and optimal and appropriately timed seizure management, but is much needed to guide future practice.

We do not specify here the timing or duration of cEEG for every condition. For seizure detection and diagnosis, the 2011 ACNS guideline suggested a minimum duration of 24 hours or until seizures were controlled for at least 24 hours.[3] This duration was based on expert consensus; there remains a lack of direct evidence comparing varying durations of cEEG for this indication. Similarly, for conditions such as prematurity with risk factors or suspected HIE, it may be reasonable to perform cEEG for the first 72 hours and then discontinue cEEG if no concerning features are found. It may be possible to tailor the duration of cEEG based on the interictal patterns in the first 24 to 48 hours in some cases.[52,56,94,121] There is insufficient evidence to make specific recommendations for all relevant conditions. Further recommendations regarding the technical standards for acquisition of cEEG in neonates are beyond the scope of this document.

We endeavored to follow transparent and rigorous methodology in the development of this guideline. Although this conferred many strengths, there are also clear limitations. First, this work was strengthened by the formation of an expert work group that included representation of multiple practice settings both within and beyond the United States. Although four countries were represented among the author group, there was not robust global representation. This reflects the requirement that all coauthors be active ACNS members, and that ACNS is based in the United States. Yet, these guidelines may be useful beyond the United States, with adaptation as needed based on practice location and setting. Second, these guidelines further benefited from a thorough systematic review of the medical literature using accepted methodology under the oversight of a medical librarian. A specific challenge inherent to our topic is that cEEG is widely considered the gold standard for diagnosis of neonatal seizures. Therefore, it was not possible to apply traditional approaches to synthesizing and grading evidence comparing cEEG with other modalities with lower diagnostic accuracy. Third, this guideline did not include a patient/family representative from the outset, which we intend to remedy in future revisions. Input from family groups was sought during the public comment period. Finally, this guideline did not address cEEG recording and interpretation of cEEG because these topics will be summarized in a forthcoming ACNS guideline on technical standards for cEEG in neonates.

This guideline presents recommendations based on the overall body of evidence at the time of publication. In accordance with ACNS standards, we expect the guideline will be updated every 5 years to include additional available evidence. Our hope is that this work may facilitate high-quality and equitable care using cEEG for neonates, as well as focused research to address remaining knowledge gaps.

ACKNOWLEDGMENTS

The authors thank the ACNS guidelines committee, and the ACNS internal review panel members (Nicholas Abend, Ankita Prasad, and Dragos Sabau) for their suggestions for this manuscript.

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