Q5: What is the added advantage of doing an electroencephalography (EEG) in people with convulsive epilepsy in non-specialist settings in low and middle income countries?

Background

The EEG is a technical instrument that can be used to support the diagnosis of seizures, classify epilepsy and to provide information on risk factors for seizure recurrence. Epilepsy is, by definition, a clinical condition characterized by two or more unprovoked seizures 24 hours apart (ILAE, 1993). However, this diagnostic and prognostic aid has several limitations which need to be emphasized in light of the available literature. An evidence-based approach is thus needed to put the EEG into a correct perspective. For this reason, the main indications of the EEG (i.e., use in support for the diagnosis of seizures and epilepsy, recognition of specific epilepsy syndromes to predict efficacy and tolerability of treatment, and prognostic value) must be assessed separately. In this light, the validity, reliability and overall utility of the EEG must be assessed with reference to different settings, especially LAMIC.

Population/Intervention(s)/Comparison/Outcomes (PICO)

Population:	children and adults with epilepsy from population-based and clinic-based settings
Interventions:	EEG
Comparison:	not applicable
Outcomes:	appropriate diagnosis
	management (seizure recurrence, mortality, adverse effects)
	sensitivity, specificity and predictive values of EEG for the diagnosis of epilepsy
	risk of seizure recurrence after the first unprovoked seizure

Search strategy

A Medline search was made for the diagnostic appropriateness and management separately; the diagnosis was addressed with the following key-words: EEG & epilepsy & appropriate diagnosis or diagnostic accuracy or misuse or useful tool; EEG & epilepsy & recurrence or seizure recurrence or risk of recurrence; the mortality was addressed with the key-words EEG & epilepsy & mortality or SUDEP; adverse effects of interventions were assessed with the key-words EEG & epilepsy & adverse effects. The abstract for the papers were examined first. Papers for which the abstract was not available were examined only if the title indicated an original article in line with the scoping question. Full text articles were examined when the corresponding abstracts were judged suitable and in accordance with the aims of the search. In addition, relevant papers included in the reference list of examined articles but not traced through the Medline search were retrieved and examined.

Inclusion and exclusion criteria: Included were studies done in humans; excluded were studies done in neonates, narrative reviews, case-reports, editorials, comments and papers without abstract and with title not fitting with the scoping question (see above). Only papers having these requisites were retained: study design; main demographic; diagnosis; EEG findings at least categorized as normal, slow or epileptiform.

Narrative description of the studies that went into the analysis

EEG and the diagnosis of epileptic seizure(s) / epilepsy (Table 1)

The first and foremost contribution of EEG in epilepsy to be evaluated is its utility for diagnostic purposes (i.e. the ascertainment of true epilepsy versus non-epileptic events and, to a lesser extent, the diagnosis of a specific epileptic syndrome). Most of the articles on diagnostic utility of EEG are from high income countries. These articles consider a standard EEG as a useful tool for diagnosis of a first seizure, provided that on the basis of a previous careful examination obvious non-epileptic events (syncope for instance) are ruled out. Indeed, EEG is not useful in the diagnosis of true syncope, while it could be positive in 30-50% of cases of true unprovoked first seizure, mainly due to the detection of epileptiform abnormalities (EA). Repeat EEG or activation procedures (hyperventilation, photic stimulation, sleep and sleep deprivation) may enhance EEG sensitivity up to 60-90 %. However, the additional diagnostic yield of EEG is virtually null after four tracings. The percentage of positive EEGs decreases with age. While EEG is not considered helpful in the management of febrile seizures, some guidelines recommend it in children with an apparent first unprovoked seizure; EEG abnormalities are more common in those with remote symptomatic seizures. Specificity of EEG can be considered high: false positive findings are detected only in 0.5-3.5% of cases, mostly in children. In summary, EEG could be recommended to support the diagnosis of epilepsy and help in defining epilepsies and epilepsy syndromes. Although epileptiform abnormalities tend to occur only in about 40-50% of children with status epilepticus, they help determine the nature and location of precipitating event.

Author	Title	Reference	Study design	Demographic features of examined	Clinical features of examined	EEG evaluator	EEG results	Diagnostic yield

				sample	**sample**			
Ajmone Marsan C, Zivin LS (1970)	Factors Related to the Occurrence of Typical Paroxysmal Abnormalities in the EEG Records of Epileptic Patients	*Epilepsia,*11: 361-381	Retrospective EEGs of epileptic patients selected from the first fourth of the alphabetically arranged files. Unquestionable epileptic seizure disorder and repeated (at least 3) EEGs				Sensitivity of EEG EA in the first EEG 55.5% EA after>1 year 92%	Percentage of positive EEGs decreased with age At least 1 positive EEG: <10 y 71.5% 10-19 69.5% 20-30 67.5% 31-40 55% >40 26.5%
Beghi E (2008)	Management of a first seizure: General conclusions and recommendations	*Epilepsia,* 49(Suppl. 1):58–61	Review				50% abnormal EEG after a first seizure	The diagnostic yield of the EEG in patients with a first seizure is moderate
Berg AT et al (2000)	How Well Can Epilepsy Syndromes Be Identified at Diagnosis?: A Reassessment 2 Years After Initial Diagnosis	*Epilepsia,* 41(10):1269-1275	Prospective cohort: 613 children recruited at the time of the initial diagnosis with epilepsy, reassessed after 2 years of follow-up	Median age at diagnosis 5.3y	Etiology at diagnosis: Idiopathic 185 Cryptogenic 317 Remote symptomatic 111 At follow-up: Etiology		Syndrome reassessment was due to a subsequent EEG in 45 cases (75%)	Syndrome reclassification due to EEG was mostly from a partial syndrome (e.g., cryptogenic localization-related or undetermined) to a more specific syndrome

					reassessed 28 Syndrome reassessed 84 (syndrome evolution 24 true reassessment 60)			
Berg AT et al (1999)	Classification of Childhood Epilepsy Syndromes in Newly Diagnosed Epilepsy: Inter-rater Agreement and Reasons for Disagreement	*Epilepsia,* 40:439-44	Prospective, community-based study. 613 children with newly diagnosed epilepsy. 3 pediatric neurologists independently classified epilepsy syndromes. Inter-rater agreement assessed with K. statistic	Median age at diagnosis 5.3y	Epilepsy syndrome: Localization-related 359 Generalized 178 Undetermined 76		Inter-rater agreement was extremely good, with K scores > 0.80 for almost all comparisons. Discrepancies between EEG and seizure information were associated with a tendency for more disagreement	Inter-rater agreement in EEG reading is more likely to be complete when raters indicate that the EEG is clearly contributory to a specific diagnosis; the K are higher than when raters indicate that there were problems with the EEG

Binnie CD, Stefan H (1999)	Modern electroencephalography: its role in epilepsy management	*Clinical Neurophysiology,* 110:1671-97..	Review				EEG sensitivity: wake 49% sleep 81% repeat wake and sleep 92% EEG specificity: false positive 0.4-3%	Proposed use of the EEG in epilepsy 1. support for the diagnosis of epilepsy 2. classification of epilepsies and epilepsy syndromes 3. excluding specific epilepsy syndromes with particular EEG abnormalities 4. classifying seizures (may require use of intensive monitoring) 5. differential diagnosis between epilepsy and other episodic phenomena
Camfield P et al (1995)	EEG results are rarely the same if repeated within six months in childhood epilepsy	*Canadian Journal of Neurological Sciences,* 22:297-300.	Retrospective EEG results of all children diagnosed in Nova Scotia with epilepsy onset between 1977-85. The results of the EEG at time of diagnosis (EEG1) were compared with those of a second EEG (EEG2) within 6 months				EEG1 and EEG2 were both normal in 23%. If EEG1 was abnormal, there was a 40-70% discordance for the type of abnormality on EEG2	Inter-ictal EEG in childhood epilepsy appears to be an unstable test. A repeat EEG within 6 months of a first EEG may yield different and conflicting information
Carpay JA et al (1997)	The Diagnostic Yield of a Second EEG After Partial Sleep Deprivation: A Prospective Study in Children with Newly Diagnosed Seizures	*Epilepsia,* 38:595-9.	Prospective, multicenter study: to assess the diagnostic yield of a repeated EEG after partial sleep deprivation	552 children and adolescents, mean age 6y (range 1 month to 16 y)	Newly diagnosed idiopathic or remote symptomatic seizures		Standard EEG (552): with EA 309(56%) without EA 243(44%) Repeated EEG after	Standard EEG shows EA in about fifty percent of patients with newly diagnosed seizures; sleep deprived EEG adds another 10%.

			when previous standard EEG does not show EA				sleep deprivation (177): with EA 61(35%)	
Flink R et al (2002)	Guidelines for the use of EEG methodology in the diagnosis of epilepsy	*Acta Neurologica Scandinavica,* 106:1-7	Review					Routine EEG can detect EA in 50% of epileptic patients Using activation procedures (hyperventilation, photic stimulation, sleep and sleep deprivation) EA are found in almost 90%
Fountain NB, Freeman JM (2006)	EEG Is an Essential Clinical Tool: Pro and Con	*Epilepsia,* 47(Suppl. 1):23–25	Expert opinion				Not considered (opinions not adequately supported by evidence)	
Hamiwka LD et al (2007)	Diagnostic Inaccuracy in Children Referred with "First Seizure": Role for a First Seizure Clinic	*Epilepsia,* 48:1062–66	Prospective cohort study: to determine the range of diagnoses, and the prevalence of previous seizures in children from a first seizure clinic.	127 children (67 M, 60 F; mean age 5, range 1-17)	94 children had epileptic events (58 first seizure, 36 at least 1 previous seizure)		EEG of 94 children with an epileptic event was abnormal in 44 cases (37 EA, 7 non EA). No difference between early and late (>48 h) EEG	EEG sensitivity 0.39
Hirtz D et al (2000)	Practice parameter: Evaluating a first non-febrile seizure in children	*Neurology,* 55:616–23	AAN Quality Standard on the basis of available evidence				The majority of evidence from Class I and Class II studies confirms that an EEG helps in determination of seizure type, epilepsy syndrome and may be helpful in determining the need for imaging	EEG is recommended as part of the diagnostic evaluation of the child with an apparent first unprovoked seizure (Standard)

							studies	
Jan MMS (2002)	Assessment of the utility of pediatric electroencephalography	Seizure, 11:99–103	Prospective: to examine the relationship between clinical indications and EEG results, and assess the predictability of normal results	438 consecutive pediatric EEGs performed in 438 children (mean age 5y, SD 4.2, range 1-17)	Established epilepsy 187 Probable seizure or 154 seizures of new onset Non-epileptic 40 paroxysmal event Acute CNS disorder 29 Chronic CNS disorder 28		45% of all EEGs were normal: 44/187 (24%) in established epilepsy; 95/154 (62%) in probable seizures or seizures of new onset; 39/40 (98%) in non-epileptic paroxysmal events	A normal EEG is highly predictable in children with non-epileptic paroxysmal events
King MA et al (1998)	Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients	*Lancet,* 352:1007-11	Prospective: 300 consecutive adults and children with unexplained seizures submitted to EEG within 24h. If EEG was negative, a sleep-deprived EEG was done				A generalized or partial epilepsy syndrome was clinically diagnosed in 141 (47%) patients. EEG data enabled to diagnose an epilepsy syndrome in 232 (77%) patients. EEG within 24 h was more useful in diagnosis of EA than later EEG (51 vs 34%).	The sensitivity of the EEG is fairly low when epilepsy must be confirmed; however, the diagnostic yield of an EEG done within 24h is higher and, when positive, the tracing helps diagnosing an epilepsy syndrome

Krumholz A et al (2007)	Practice Parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society.	*Neurology,* 69:1996-2007	AAN Quality Standard on the basis of available evidence				For adults presenting with a first seizure, a routine EEG revealed EA in approximately 23% of patients, and these were predictive of seizure recurrence.	EEG should be considered as part of the routine neurodiagnostic evaluation of adults presenting with an apparent unprovoked first seizure (Level B).
Kuyk J et al (1997)	The diagnosis of psychogenic non-epileptic seizures: a review	*Seizure,* 6:243-53	Review				Not considered: few data about the specific question (value of EEG in the differential diagnosis of ES vs PNES)	
Neufeld MY et al (2000)	The diagnostic aid of routine EEG findings in patients presenting with a presumed first-ever unprovoked seizure	*Epilepsy Research,* 42:197–202	Retrospective Patients >15 y admitted through the emergency room during 1991–1995 with first-ever unprovoked seizure submitted to EEG	91 patients (age 50y±24; 52 M)	66% with seizure of unknown origin 34% with presumed remote symptomatic seizures		Abnormal EEGs 69% EA 21% Slowing 58% EA and slowing 10%	Specific EA particularly helpful in supporting the clinical diagnosis of epileptic event mainly in younger patients with seizures of unknown origin
Panayiotopoulos CP (1998)	Significance of the EEG after the first afebrile seizure	*Archives of Disease in Childhood,* 78:575–7	Expert opinion				Not considered: review of studies already present in the list	

Perrig S, Jallon P (2008)	Management of a first seizure: Is the first seizure truly epileptic?	*Epilepsia,* 49(Suppl. 1):2–7	Review				Not considered: review of studies already present in the list	
Pillai J, Sperling MR (2006)	Interictal EEG and the Diagnosis of Epilepsy	*Epilepsia,* 47(Suppl. 1):14–22	Review				Sensitivity First EEG 29%-55% Repeat EEG 80%–90% Sleep deprivation increases the chance by 30%–70% Hyperventilation increases the yield <10% Specificity EA normal children 1.9–3.5% EA normal adults 0.2–0.5%	Sensitivity of first EEG is at best moderate but increases with repeat tracings, especially if sleep deprived; mild risk of false positive tracings especially in children
Pohlmann-Eden B, Newton M (2008)	First seizure: EEG and neuroimaging following an epileptic seizure	*Epilepsia,* 49(Suppl. 1):19–25	Review (summary of studies already present in the list)				The reported yield of EA in routine EEG ranged from 12% to 27% and increased to 23–50% in sleep EEG EA on the first EEG was significantly	EEG provides valuable information with regard to syndrome classification and seizure recurrence rates

							greater in children compared to patients >16 years	
Riviello JJ Jr et al (2006)	Practice parameter: diagnostic assessment of the child with status epilepticus (an evidence-based review)	*Neurology,* 67:1542-50.	AAN Quality Standard on the basis of available evidence				EA occurred in 43% of EEGs of children with SE and helped determine the nature and location of precipitating electroconvulsive events (8% generalized, 16% focal, and 19% both).	Although EA tend to occur only in about 40-50% of children with SE, they help determine nature and location of precipitating event
Salinsky M et al (1987)	Effectiveness of Multiple EEGs in Supporting the Diagnosis of Epilepsy: An Operational Curve	*Epilepsia,* 28:331-4	Retrospective To determine the probability of finding EA with serial EEGs reviewing data from 1,201 EEGs	504 patients followed at tertiary epilepsy center referred for the evaluation of probable epilepsy Mean age 45 (18-86)			EA are present in 50% of epileptic patients on the first record, in 84% by the third EEG, and in 92% by the fourth	The diagnostic yield of first EEG is modest but tends to increase with repeated tracings up to the fourth; little gain beyond this point
Shinnar S et al (1994)	EEG Abnormalities in Children with a First Unprovoked Seizure	*Epilepsia,* 35:471-6		347 children, 198 M-149 F Mean age 6.8y at time of first seizure Mean follow-up 47 month	291 (84%) with a first idiopathic seizure 56 (16%) with a first remote symptomatic seizure		EEGs available in 321/347 children (93%) 268/291 (92%) with an idiopathic seizure 53/56 (95%) with a remote symptomatic seizure Results: Abnormal EEG	EEG abnormalities are more common in children with partial seizures and those with remote symptomatic seizures. Abnormal EEGs occur at a higher rate after age 3 years than before

							135 Idiopathic 103(38%) Remote symptomatic 32(60%) Non-EA 33 Idiopathic 20 (7%) Remote Symptomatic 13(25%)	
Stores G (1991)	When does an EEG contribute to the management of febrile seizures?	*Archives of Disease in Childhood,* 66: 554-7	Expert opinion					An early postictal EEG will not be helpful in the following respects: (a) it will not distinguish between clinically simple and atypical seizures (b) it will not particularly help in the identification of a cerebral infective aetiology (c) EEG findings lack predictive value for the later occurrence of later febrile or afebrile seizures.
Storzbach D et al (2000)	Improved Prediction of Nonepileptic Seizures with Combined MMPI and EEG Measures	*Epilepsia,* 41:332-7	Prospective Consecutive patients referred for video-EEG underwent standard EEG and	167 pt >18y referred to a tertiary epilepsy center for suspected PNES or mixed			Overall classification accuracy was 74% for standard EEG, 71 % for MMPI-2 Hs scale, and 77% for MMPI-2 Hy scale. The model that best	EEG in combination with MMPI and symptom duration is a useful diagnostic tool. This model may be useful in order to distinguish ES and PNES and for screening candidates for video-EEG

			completed an MMPI-2 Patients were subsequently classified as having ES (91) or PNES (76) using standardized criteria Logistic regression was used to predict seizure type classification	ES/PNES			predicted diagnosis included standard EEG, MMPI-2, and number of years since the first spell, resulting in an overall classification accuracy of 86%	
van Donselaar CA et al (2006)	How Confident Are We of the Diagnosis of Epilepsy?	*Epilepsia,* 47(Suppl. 1):9–13	Expert opinion				Not considered: review of studies already present in the list	
Verity CM (1995)	The place of the EEG and imaging in the management of seizures.	*Archives of Disease in Childhood,* 73:557-62	Expert opinion				Not considered: review of studies already present in the list	
Worrell GA et al (2002)	Role and Limitations of Routine and Ambulatory Scalp Electroencephalography in Diagnosing and Managing Seizures	*Mayo Clinic Proceedings,* 77:991-8	Review				Not considered: review of studies already present in the list	

EEG as an indicator of seizure recurrence (Table 2)

Several articles examined the prognostic factors involved in seizure recurrence and the relative risk of recurrence associated with the presence of EEG abnormalities. The overall risk of recurrence after a first unprovoked seizure is commonly estimated to range from 26 to 56% at 1 year and varies according to

seizure etiology (being highest in remote symptomatic seizures). The estimated relative risk of recurrence in presence of an abnormal interictal EEG is 1.3-2.2.The relative risk is higher in idiopathic than in remote symptomatic seizures; in the former, epileptiform abnormalities (particularly generalized spike and wave discharges) are a significant prognostic factor; in the latter, the sole etiology seems to be the main factor contributing to the risk of recurrence. When assessing the correlation between EEG abnormalities and subsequent seizures, regardless of age, the sensitivity of an abnormal EEG varies from 0.29 to 0.77 and the specificity from 0.41 to 0.81; while some studies indicate higher sensitivity and specificity values with epileptiform EEGs, others conclude that epileptiform abnormalities (paroxysmal slow-wave abnormality with spiking) are no better predictors than reports of "any abnormality" (which includes slow-waves with or without spikes or sharp waves). Similar data can be found in studies conducted only in pediatric populations: the estimated relative risk of recurrence in children when the EEG is abnormal (whether epileptiform or focal or generalized slow) is 1.6-2.3; the predictive role of EEG abnormalities is higher in idiopathic and cryptogenic cases than in remote symptomatic, due to the aforementioned observations. EEG abnormalities tend to predict seizure recurrence in patients with untreated first seizures and in those discontinuing treatment after prolonged seizure remission.

Author	**Title**	**Reference**	**Study design**	**Demographic features of examined sample**	**Clinical features of examined sample**	**Results**	**EEG and risk of recurrence**	**Prognostic yield**
Annegers JF et al (1986)	Risk of Recurrence After an Initial Unprovoked Seizure	*Epilepsia*, 27:43-50	Retrospective Cohort of 424 patients examined to determine the patterns of risk for recurrence after an initial unprovoked seizure	204M,220F 247>55 y	287 idiopathic 122 remote symptomatic 15 cerebral palsy	Overall risk of recurrence: 36% 1 year 48% 3 years 56% 5 years Idiopathic: 26% 1 year 45% 5 years Remote symptomatic: 56% 1 year	1-y recurrence risk (idiopathic): Normal EEG 16% Abnormal 26% 1-y recurrence risk (remote symptomatic): Normal EEG 40% Abnormal 56% Estimated RR of recurrence if abnormal EEG:	Although the overall risk of recurrence is higher with an abnormal EEG associated with remote symptomatic seizures than with idiopathic seizures, the RR is higher with the latter

						77% 5 years Cerebral palsy: 92% 1 year	Idiopathic: 2.2 (1.1-4.3) Remote symptomatic: 1.3 (0.6-3.0)	
Arts WFM et al (1999)	The Early Prognosis of Epilepsy in Childhood: The Prediction of a Poor Outcome. The Dutch Study of Epilepsy in Childhood	*Epilepsia,* 40:726-34	Prospective Hospital-based cohort of 466 children with newly diagnosed epilepsy followed to determine good/poor outcome and to develop models to predict it	225M,241F Median age 5.5 y	Etiology: Idiopathic 235 Remote symptomatic 136 Cryptogenic 95		OR (CI 95%) for poor outcome (remission<6 mo): EEG at intake: EA vs normal 1.33 (0.71- 2.48) EEG at 6 mo EA vs normal 2.21 (1.12-4.36)	EA at six months are associated with a higher risk of seizure recurrence in children with newly diagnosed epilepsy
Beghi E (2008)	Management of a first seizure General conclusions and recommendations	*Epilepsia,* 49(Suppl. 1):58–61	Review			Not considered: review of studies already present in the list		
Berg AT, Shinnar S (1991)	The risk of seizure recurrence following a first unprovoked seizure: A quantitative review.	*Neurology,* 41:965-72	Meta-analysis of 16 reports			The average recurrence risk across the 16 studies was 51% (40% and 52% in prospective and retrospective studies) At 2 years following the first seizure, the recurrence risk	2-y seizure recurrence was 24% with normal EEG and unknown etiology, 48% with abnormal EEG and unknown etiology, and 65% with abnormal EEG and documented etiology	Seizure etiology and the EEG were the strongest predictors of recurrence of a first unprovoked seizure

						was 36% and 47% in prospective and retrospective studies		
Berg AT et al (2001)	Two-Year Remission and Subsequent Relapse in Children with Newly Diagnosed Epilepsy	*Epilepsia,* 42:1553-62	Cohort of 613 children with newly diagnosed epilepsy Minimum follow-up (2 years) in 594 (96.9%).	Median age at onset 5.3	Partial epilepsies 345 Idiopathic 57 Symptomatic 189 Cryptogenic 99 Generalized epilepsies 176 Idiopathic 124 Symptomatic 9 Cryptogenic 43	442 (74%) children achieved a 2-year remission in a median time of 2.3 years (2-6) After achieving a 2-year remission, 107 (24.2%) children experienced a relapse	Predictors associated with a decreased chance of attaining a 2-year remission: Any slowing on initial EEG: rate ratio 0.71 (0.54–0.93) Predictors associated with an increased risk of relapse after a 2-year remission: Focal slowing on initial EEG: rate ratio 2.13 (1.19–3.87)	Slowing of the EEG tracing is a marker for poor outcome in children with newly diagnosed epilepsy
Berg AT (2008)	Risk of recurrence after a first unprovoked seizure	*Epilepsia,* 49(Suppl. 1):13–8	Review			Not considered: review of studies already present in the list		
Camfield P, Camfield C (2008).	Special considerations for a first seizure in childhood and adolescence	*Epilepsia,* 49(Suppl. 1):40–4	Review			Not considered: review of studies already present in the list		
Camfield PR et al (1985)	Epilepsy after a first unprovoked seizure in childhood	*Neurology,* 35:1657–60				Overall, 51.8% recurred, and of those with a recurrence, 79% had additional	Children with generalized seizures, normal EEG and no neurological	The recurrence risk is increased by focal versus generalized seizures, spike discharge on EEG,

						seizures.	deficits have approximately a 20% chance of recurrence; children with focal seizures, abnormal EEGs, and concomitant neurological deficits have about an 80% risk of recurrence	and presence of concomitant neurological deficits.
Das CP et al (2000)	Risk of recurrence of seizures following Single Unprovoked Idiopathic seizure	*Neurology India,* 48:357-360	Prospective 76 pt with a first seizure excluding symptomatic and those with an abnormal CT scan were randomized to AED/not AED	56 M-20 F		22 (M=16, F=6) of the 76 patients (M=56, F=20) had a recurrence of seizure.	Recurrence (22/76) EEG normal 12 EEG abnormal 10 No recurrence (54/76) EEG normal 50 EEG abnormal 4 P<0.001	Abnormal EEG predicts risk of recurrence of a first unprovoked seizure
Dooley J et al (1996)	Discontinuation of anticonvulsant therapy in children free of seizures for 1 year: A prospective study	*Neurology,* 46:969-74	Prospective 97 children with 2 or more afebrile seizures, on AED monotherapy, seizure free for 1 year (excluded	50 M-47 F; mean seizure onset 65.9 ±45.89 months; mean age at attaining seizure control 86.95±49.2		The overall probability of remaining seizure free was 78% at 3 months (95% CI, 70, 87), 71% at 6 months (95% CI, 61, 81), 66% at 12 months (95% CI,	Pt without recurrence: EEG normal 45 EEG abnormal 5	The only EEG factor slightly predictive of recurrence is abnormal background activity

			those with juvenile myoclonic epilepsy) were followed for 32.4±13.1 months or until seizure recurrence	months.		57, 75), and 61% at 24 months (95% CI, 51, 71)	Pt with recurrence: EEG normal 27 EEG abnormal 8 p 0.074	
Fisher LS, Leppik I (2008)	Debate: When does a seizure imply epilepsy?	*Epilepsia,* 49(Suppl. 9):7–12	Review			Not considered: review of studies already present in the list		
Gilbert DL, Buncher CR (2000)	An EEG should not be obtained routinely after first unprovoked seizure in childhood	*Neurology,* 54:635-41	Systematic review			Not considered: review of studies already present in the list		
Gilbert DL et al (2003)	Meta-analysis of EEG test performance shows wide variation among studies	*Neurology,* 60:564–70	Meta-analysis of variation of EEG sensitivity and specificity in predicting future seizures	4,288 patients and EEGs (19 publications) relating epileptiform EEG and subsequent seizures. 1,856 patients and EEGs (12 publications) relating abnormal EEG and subsequent seizures			Risk of seizure recurrence: Epileptiform EEG Sensitivity 0.20–0.81 Specificity 0.41–0.99 Abnormal EEG Sensitivity 0.29–0.77 Specificity 0.42–0.81	The prognostic yield of EEG in predicting seizure recurrence is fairly low and varies across studies
Hauser WA et al	Risk of recurrent seizures after two unprovoked	*New England Journal of*	Prospective	142 M-62 F	Type of seizure:	Risk of 2nd recurrence within 5	In the univariate analysis EEG	

(1998)	seizures	*Medicine,* 338:429-34	The risk of a second, third, and fourth seizure was estimated in 204 patients with a first unprovoked seizure followed from the day of the initial seizure	Mean age 36 ys	Generalized 134 Partial 67 Unclassified 3 Etiologic category: Idiopathic or cryptogenic 145 Rem sympt 59	years of the first seizure 33% (95% CI, 26-40%) Among those with a 2nd recurrence the risk of 3rd at 4 years was 73% (95 % CI, 59-87%) Among those with a 3rd recurrence the risk of a 4th at 3 years was 76% (95% CI, 60-91%)	findings were not associated with the risk of recurrence	
Hauser WA et al (1990)	Seizure recurrence after a 1st unprovoked seizure: An extended follow-up	*Neurology,* 40:1163-70	Prospective 208 patients identified on the day of their 1st unprovoked seizure were followed for a mean duration of 4 years			Recurrence risks were estimated to be 14%, 29%, and 34% at 1, 3, and 5 years following the 1st seizure	Among idiopathic cases, a generalized spike and wave EEG increased risk for recurrence	Interictal generalized spike-wave EEGs are associated with increate risk of recurrence of a first unprovoked seizure

Hirtz D et al (2000)	Practice parameter: Evaluating a first nonfebrile seizure in children	*Neurology,* 55:616–23	AAN Quality Standard on the basis of available evidence				The majority of evidence from Class I and Class II studies confirms that an EEG helps in determination of the risk for recurrence, and therefore may affect further management decisions. Experts commonly recommend that an EEG be performed after all first nonfebrile seizures. It is not clear what the optimal timing should be for obtaining an EEG	EEG is recommended as part of the diagnostic evaluation of the child with an apparent first unprovoked seizure (Standard)
Hirtz D et al (2003)	Practice parameter: Treatment of the child with a first unprovoked seizure	*Neurology*, 60:166–75				Not considered: recommendations based on studies already present in the list		
Hopkins A et al (1988)	The first seizure in adult life. Value of clinical features, electroencephalography, and computerized tomographic scanning in prediction of seizure recurrence	*Lancet,* 1:721-726	Prospective 408 adults (age 16y and over) were followed up after their initial seizure			Risk of recurrence was 52% by the end of 3 years	In univariate analysis, EEG features were not of predictive value	EEG findings do not seem to predict the recurrence of a first seizure in adult life

Kho LK et al (2006)	First seizure presentation: Do multiple seizures within 24 hours predict recurrence?	*Neurology,* 67:1047–49	Prospective prognosis of 72 adults with first-ever multiple discrete seizures within 24 hours compared to 425 patients presenting with a single seizure			The overall seizure recurrence rate at 1 year was 38% The only variable independently predictive of seizure recurrence at 1 year on stepwise logistic regression was remote symptomatic etiology (OR 2.2, CI 1.4- 3.4; p= 0.0006)		EEG findings do not seem to predict the recurrence of a first seizure in adult life
Kim LG et al (2006)	Prediction of risk of seizure recurrence after a single seizure and early epilepsy: further results from the MESS trial	*Lancet Neurology,* 5: 317–22	Prospective to assess the role of patients' characteristics and treatment in the prediction of seizure recurrence 1420 patients were randomly assigned either immediate treatment with an AED or delayed treatment Median follow-up 4·4 years	815 M - 605 F Mean age at randomisation 31.2y (SD 19.1)	Neurological disorder 254 (18%) Abnormal EEG 618 (44%) Epilepsy syndrome 63 (4%)	Individuals with 2 or 3 seizures, a neurological disorder, or an abnormal EEG were identified as the medium-risk group, those with 2 of these features or more than 3 seizures as the high-risk group, and those with a single seizure only as the low-risk group No significant difference was observed between treatments for low-risk individuals (Log-rank test χ^2=1·7, p=0·2), but there was an indication of	Hazard ratio for recurrence if abnormal EEG (defined as specific focal or generalised epileptiform or slow wave abnormality) 1·54 (1·27–1·86) p<0·0001 EA on the EEG (paroxysmal slow-wave abnormality with spiking) added no greater specificity than the variable "any abnormality", which included also slow-wave disturbance	An abnormal EEG (regardless of the presence of EA) indicates an increased risk of recurrence in patients with a first unprovoked seizure and call for early treatment

			(3·0–6·3)			improvement with immediate AED treatment for medium-risk and high-risk individuals (7·0, p=0·008; 21·9, p<0·0005, respectively)	without spikes or sharp waves	
Lindsten H et al (2001)	Remission of Seizures in a Population-Based Adult Cohort with a Newly Diagnosed Unprovoked Epileptic Seizure	*Epilepsia,* 42:1025-30.	Prospective 107 pts with a newly diagnosed unprovoked epileptic seizure in 1985 through 1987 were followed up until the date of death or to the end of 1996. The proportion of cases that attained a 1-y, 3-y, 5-y remission was calculated by actuarial analyses	Median age at diagnosis 52 ys (17-83)	Etiologic groups: Cryptogenic 42 (39%) Remote symptomatic 65 (61%)	Cumulative 1-yr remission calculated from epilepsy diagnosis 68% Cumulative 5-yr remission calculated from epilepsy diagnosis 58%	Focal spikes (25 patients) or generalized spike–wave activity (9 patients) on the EEG at inclusion had a tendency to be a good predictor of not achieving a 5-year remission (p = 0.06)	Focal spikes or generalized spike-wake activity are negative prognostic predictors for 5-y remission in newly diagnosed epileptic seizures in adults
Marson A et al	Immediate versus deferred antiepileptic drug treatment for early	*Lancet,* 365: 2007–13	Prospective: 722 pt were			Immediate AED treatment reduces the occurrence of	No information about EEG data and	

(2005)	epilepsy and single seizures: a randomised controlled trial		assigned immediate treatment with AEDs and 721 were assigned deferred treatment			seizures in the next 1–2 years, but does not affect long-term remission in individuals with single or infrequent seizures	risk of recurrence	
Martinovic Z, Jovic N (1997)	Seizure recurrence after a first generalized tonic-clonic seizure in children, adolescents and young adults	*Seizure,* 6:461-465	Prospective 78 patients who had a first unprovoked generalized tonic-clonic seizure between the age of 3 and 21y	Sex (M/F) 46 / 32 Age at first GTCS: Mean 9.3 ys (3-21) Follow-up period: Mean 4.1 ys (2-10)	Seizure aetiology: Idiopathic 50 (64. 1 %) Cryptogenic 16 (20.5%) Remote symptomatic 12 (15.4%)	Number of patients with recurrent seizures 54 (68.3%) Seizure recurrence: Idiopathic 32 41.0% Cryptogenic 12 15.4% Symptomatic 10 12.8%	Seizure recurrence (54) Epileptiform EEG 51 Normal EEG 3 No recurrence (24) Epileptiform EEG 14 Normal EEG 10 p<0.001	The presence of epileptiform EEG patterns in the first two EEGs (including prolonged monitoring and/or sleep after sleep deprivation in 22 patients) is predictive for seizure recurrence
Musicco M et al (1997)	Treatment of first tonic-clonic seizure does not improve the prognosis of epilepsy. First Seizure Trial Group (FIRST Group)	*Neurology,* 49:991-8	Prospective 419 randomized to evaluate the probability of achieving 1 or 2 years of complete seizure control in pts treated at first seizure (215) vs those (204) treated only in the event of	236 M, 183 F		In treated pts the cumulative probability of recurrence was 17% after 1 year and 26% after 2 years; the corresponding probabilities in initially untreated patients were 37% and 45%.	An epileptiform EEG was one of the significant predictors of the risk of recurrence. However it did not influence the probability of remaining seizure free for 1 or 2 years	Epileptiform interictal EEG findings predict early seizure recurrence but do not affect long-term prognosis of a first unprovoked seizure

			seizure recurrence					
Pohlmann-Eden B et al (2006)	The first seizure and its management in adults and children	*British Medical Journal,* 332:339–42	Review			Not considered: review of studies already present in the list		
Ramos Lizana J et al (2000)	Seizure Recurrence After a First Unprovoked Seizure in Childhood: A Prospective Study	*Epilepsia,* 41:1005-13	Prospective Consecutive patients aged less than 14 years with one or more unprovoked seizures followed to study the risk of recurrence	217 children 133 M- 84 F Mean age 7.4 y Age: 0-3y 53 3-10y 107 10-14y 57	Etiology: Symptomatic 47 Idiopathic 48 Cryptogenic 122	Recurrence risk was 58% (±3.4), 65% (±3.3), 74% (±3.1), 74% (±3.1), 76% (±3.1), and 79% (±3.2) at 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years, respectively	RR of recurrence in different etiologic groups if EEG abnormal Overall cohort 1.6 (1-2.7) p=0.057 Idiopathic/cryptogenic 2 1.(1-3.5) p=0.0262 Symptomatic 0.7 (0.3-1.9) p=0.5186	An abnormal EEG is an important predictor of recurrence risk, but only in patients with idiopathic/cryptogenic seizures
Schreiner A, Pohlmann-Eden B (2003)	Value of the early electroencephalogram after a first unprovoked seizure	*Clinical Electroencephalography,* 34:140-4	Prospective The predictive value of the standard EEG and EEG with sleep deprivation for seizure relapse was studied in 157 adult patients				The standard EEG was abnormal in 70.7% and significantly associated with an increased risk of seizure recurrence (risk ratio 4.5, 95% CI 1.8-11.3, p=0.001). Subgroup analysis	The abnormal EEG is a highly significant predictor for seizure recurrence. An additional EEG with sleep deprivation is helpful in cases when standard EEG does not reveal epileptiform

			presenting with a first unprovoked seizure. EEGs were performed within the first 48 hours of the first seizure				revealed the highest recurrence rates for patients with focal EA (risk ratio 2.2, CI 95% 1.2-4.2, p=0.01).	discharges.
Shafer SQ et al (1988)	EEG and Other Early Predictors of Epilepsy Remission: A Community Study	*Epilepsia,* 29:590-600	Retrospective From 1935 through 1982, 731 new cases of epilepsy among residents of Rochester were followed, with 432 with at-least 5 years of follow-up 306/432 had an EEG after the first seizure and before remission. Outcome: remission (5 years seizure-free with or without prescription of AED)			Of the 432 new cases, 283 (66%) achieved 5-y remission	Hazard ratio for 5-y remission if no generalized spike-wave: 1.58, p<0.01	Absence of generalized spike-wave activity in the interictal EEG predicts 5-y remission in patients with newly diagnosed epilepsy

Shinnar S et al (1994b)	Discontinuing antiepileptic drugs in children with epilepsy: a prospective study	*Annals of Neurology,* 35:534-45	Prospective AED were discontinued in 264 children with epilepsy after a mean seizure-free interval of 2.9 years and then followed for a mean of 58 months to ascertain recurrence			Seizures recurred in 95 (36%) of the children	Slowing on the EEG prior to medication withdrawal was a significant predictor of recurrence in the idiopathic group (RR = 2.4)	Slowing of interictal EEG predicts recurrence after treatment discontinuation in children in long-term remission with AED
Shinnar S et al (1994a)	EEG Abnormalities in Children with a First Unprovoked Seizure	*Epilepsia,* 35(3):471-6	Prospective 347 children with a first unprovoked afebrile seizure	347 children, 198 M - 149 F Mean age 6.8y at the time of first seizure Mean follow-up 47 month	291 (84%) with an idiopathic first seizure 56 (16%) with a remote symptomatic first seizure	EEGs were available in 321/347 children (93%) Risk of recurrence: Normal EEGs 42/165 (25%) Abnormal EEG 56/103(54%) p<0.001	EEG abnormalities were more common in children with partial seizures and those with remote symptomatic seizures. Abnormal EEGs occur at a higher rate after age 3 years than before	Abnormal EEG predicts recurrence of a first unprovoked seizure in children
Shinnar S et al (2000)	Predictors of Multiple Seizures in a Cohort of Children Prospectively Followed from the Time of Their First Unprovoked Seizure	*Annals of Neurology,* 48:140–7	Prospective 407 children followed from the time of their first unprovoked seizure to assess the risk of	407 children 234 M - 173 F Mean age at first seizure 6.8y	Etiology: Cryptogenic/Idiopathic 342 Remote symptomatic	182/407 (45%) experienced a recurrence The overall risk of recurrence was 29% at 1 year (25-33%), 37% at 2	An abnormal EEG was associated with an increased recurrence risk after a first and a second seizure, but not with an increased risk of	Abnormal interictal EEG predicts recurrence after a first and a second unprovoked seizure but not multiple seizures

			multiple recurrences after an initial seizure Mean follow-up after first seizure 9.6 (yr)		65	years (33-42%), 43% at 5 years (38-48%), and 46% at 10 years (41-51%) The risk of a third seizure was 57%, 63%, and 72% at 1, 2, and 5 years, respectively, after the second seizure After a third seizure, the cumulative risk of another seizure was 66%, 70%, and 81% at 1, 2, and 5 years, respectively.	multiple seizures after a second seizure (RR = 1.08; 95% CI: 0.81,1.67; p = 0.41). Risk of 2nd seizure with abnormal EEG was 2.16 (1.60-2.91, p<0.0001), and risk of 3rd seizure was 2.15 (1.51-3.05, p<0.0001)	
Shinnar S et al (1996)	The Risk of Seizure Recurrence After a First Unprovoked Afebrile Seizure in Childhood: An Extended Follow-up	*Paediatrics,* 98;216-25	Prospective 407 children who presented with a first unprovoked seizure were then followed to assess the long-term recurrence risks after a first unprovoked seizure Mean follow-up period was 6.3 years	407 children 234 M - 173 F Mean age at first seizure 6.8y	Etiology: Cryptogenic/Idiopathic 342 Remote symptomatic 65	171/407 (42%) had recurrences The overall estimate of recurrence was 22% at 6 months (18-26%), 29% at 1 year (25-33%), 37% at 2 years (32-42%), 42% at 5 years (37-47%), and 44% at 8 years (39-49%)	Abnormal EEG and risk of recurrence: Overall RR 2.3 (1.7-3.2, p <.0001) Cryptogenic RR 2.6 (1.8-3.7, p <.0001) Remote Symptomatic RR 1.1 (0.6-2.0, p=0.78	Abnormal EEG predicts long-term recurrence of a first unprovoked afebrile seizure but only in children with cryptogenic seizures

Stroink H et al (1998)	The first unprovoked, untreated seizure in childhood: a hospital based study of the accuracy of the diagnosis, rate of recurrence, and long term outcome after recurrence. Dutch study of epilepsy in childhood	*Journal of Neurology, Neurosurgery & Psychiatry,* 64:595–600	Prospective 156 children aged 1 month to 16 years after a first seizure followed up to assess the accuracy of the diagnosis, the recurrence rate within two years, the risk factors for recurrence, and the long term outcome two years after recurrence	156 children 70 M – 86 F median age at intake 6.9y; range 0.2–15.6y	Etiology: Idiopathic/cryptogenic 129 Remote symptomatic 27	The overall recurrence rate was 40% (33–48%) at six months; 46% (38–53%) at one year; and 54% (46–62%) at two years	Children with epileptic discharges in their first EEG (n=68; 44%) had a recurrence rate of 71% at two years (60–81%); in children with a normal first EEG (57) the rate was 40% (28–53%)	An epileptiform EEG is the most important predictive factor for seizure recurrence in children with a first unprovoked seizure in a full model multivariate analysis
van Donselaar CA et al (1992)	Value of the Electroencephalogram in Adult Patients With Untreated Idiopathic First Seizures	*Archives of Neurology,* 49:231-7	Prospective To assess the reliability and accuracy of the EEG as a predictor of the risk of recurrence within 2 years in 157 patients with untreated idiopathic first seizures				The finding of epileptic discharges was associated with a risk of recurrence of 83% (CI 95% , 69% to 97%) vs 41% (CI 95%, 29% to 53%) in patients with nonepileptic abnormalities	EA predict recurrence in adults with a first untreated idiopathic seizure

Wiebe S et al (2008)	Management of a first seizure: An evidence-based approach to the first seizure	*Epilepsia*, 49(Suppl. 1):50–7	Review			Not considered: review of studies already present in the list		

EEG as a predictor of mortality (Table 3)

Another important issue is the overall risk of mortality in epilepsy and the incidence of sudden unexplained death in epilepsy (SUDEP). Some clinical factors are commonly identified as potentially increasing the risk of death: symptomatic etiology (both remote and acute), comorbid neurologic disease and, particularly for SUDEP, seizure severity and high frequency. On the contrary, no detailed data are available for a possible contribution of EEG to the definition of mortality risk, with a notable exception: few articles deal with the possible role of cardiac asystolia provoked by epileptic seizures and ictal hypoxemia and hypercapnia (possibly implied in SUDEP).

Author	Title	Reference	Study design	Demographic features of examined sample	Clinical features of examined sample	Results	EEG and risk of SUDEP/mortality	Prognostic yield
Bateman LM et al (2008)	Ictal hypoxemia in localization-related epilepsy: analysis of incidence, severity and risk factors	*Brain,* 131(Pt 12):3239-45	Prospective: to determine the incidence and severity of ictal hypoxemia in patients with localization-related epilepsy undergoing video-EEG		304 seizures with accompanying oxygen saturation data were recorded in 56 consecutive patients with intractable localization-related epilepsy	Desaturations below 90% were significantly correlated with seizure localization (p = 0.005; OR of temporal versus extratemporal = 5.202; [1.665, 16.257]), seizure lateralization (p = 0.001; OR of right versus left = 2.098; [1.078, 4.085]), contralateral spread of seizures (p = 0.028; OR of contralateral spread versus no spread = 2.591; [1.112, 6.039])		Ictal hypoxemia occurs often in patients with localization-related epilepsy and may be pronounced and prolonged. Ictal hypoxemia and hypercapnia may contribute to SUDEP

Berg AT et al (2004)	Mortality in Childhood-Onset Epilepsy	*Archives of Pediatric &Adolescent Medicine,* 158:1147-52	Prospective: to evaluate mortality in children with newly diagnosed epilepsy, to determine the risk of death, and to identify predictors of death from the point of diagnosis. Median follow-up 7.9 years	613 children were recruited 307 M – 306 F The median age at study entry was 6.1 years (age range, 1 month to 16 years).	13 had died 7 months to 7 years (median, 4.2 y) after diagnosis	In a multivariable Cox proportional hazards model, remote symptomatic etiology (RR, 10.2;2.1-49.6; P=.004) and epileptic encephalopathy (RR, 13.3; 3.4-51.7; P<.001) were independently associated with mortality	No data on possible contribution of EEG to the definition of mortality risk	
Brodie MJ, Gregory LH (2008)	Should all patients be told about sudden unexpected death in epilepsy (SUDEP)? Pros and Cons	*Epilepsia,* 49(Suppl. 9):99–101	Review			Factors associated with the greatest risk of SUDEP are generalized tonic–clonic seizures, high seizure frequency, concomitant learning disabilities, AED polypharmacy, and frequent changes in dosing	No data on possible contribution of EEG to the definition of mortality risk	
Callenbach PMC et al (2001)	Mortality Risk in Children With Epilepsy: The Dutch Study of Epilepsy in Childhood	*Pediatrics,*107: 1259 –63	Prospective: 472 children, aged 1 month to 16 years, with 2 or more newly diagnosed unprovoked seizures were enrolled. All children were followed for 5 years or			9 children died during follow-up, amounting to a mortality rate of 3.8/1000 person-years, sevenfold higher than expected (95% CI 2.4 –11.5). All deceased children had epilepsy that was caused by a static or progressive neurologic disorder	No data on possible contribution of EEG to the definition of mortality risk	

			until death			(mortality risk = 22.9; CI 95% 7.9 –37.9). None of them died from SUDEP		
Camfield P, Camfield C (2008)	Special considerations for a first seizure in childhood and adolescence	*Epilepsia,* 49(Suppl. 1):40–4	Review				Not considered: review of studies already present in the list	
Camfield CS et al (2002)	Death in children with epilepsy: a population-based study	*Lancet,* 359:1891–5	Prospective: population-based cohort study including all children who developed epilepsy during 1977–85 to assess the frequency and causes of death of children with epilepsy			Children with epilepsy have more than five times the risk of dying than the general population in the first 15–20 years after diagnosis. Most deaths are related to comorbid neurological disorders sufficient to cause functional neurological deficit and not to the epilepsy	No data on possible contribution of EEG to the definition of mortality risk	
Forsgren L et al (2005)	Mortality of Epilepsy in Developed Countries: A Review	*Epilepsia,* 46(Suppl. 11):18–27	Review				Not considered: review of studies already present in the list	
Hauser WA, Beghi E (2008)	First seizure definitions and worldwide incidence and mortality	*Epilepsia,* 49(Suppl. 1):8–12	Review				Not considered: review of studies already present in the list	
Hauser WA et al (1980)	Mortality in Patients with Epilepsy	*Epilepsia,* 21:399-412	Retrospective: 618 residents with first diagnosis of epilepsy between 1935 and 1974 were observed for 8,233 person-years.			During the period of follow-up, there were 187 deaths. SMR for the total group was 2.3 (1.9 – 2.6 through 29 years of follow-up)	No data on possible contribution of EEG to the definition of mortality risk	

Hitiris N et al (2007b)	Mortality in epilepsy	*Epilepsy & Behavior,* 10 : 363–76	Review				Not considered: review of studies already present in the list	
Hitiris N et al (2007a)	Sudden unexpected death in epilepsy: A search for risk factors	*Epilepsy & Behavior,* 10: 138–41	Retrospective: case–control study of SUDEP within a large cohort of adult patients followed up over a 23-year period to investigate the association between clinical characteristics and SUDEP, focusing on likely risk factors				No data on possible contribution of EEG to the definition of risk of SUDEP	
Jehi L, Najm IM (2008)	Sudden unexpected death in epilepsy: Impact, mechanisms, and prevention	*Cleveland Clinical Journal of Medicine,*75 (suppl 2): S66-S70	Review				No data on possible contribution of EEG to the definition of risk of SUDEP	
Langan Y et al (2005)	Case-control study of SUDEP		154 cases with a postmortem examination were investigated. Each case had 4 controls with epilepsy from the community. To examine the influence of various factors on the risk of SUDEP in epilepsy OR for risk and protection were determined				No data on possible contribution of EEG to the definition of risk of SUDEP	

Langan Y (2000)	Sudden unexpected death in epilepsy (SUDEP): risk factors and case control studies	*Seizure,* 9:179–83	Review				Not considered: review of studies already present in the list	
Lhatoo SD et al (2001)	Mortality in Epilepsy in the First 11 to 14 Years after Diagnosis: Multivariate Analysis of a Long-Term, Prospective, Population-Based Cohort	*Annals of Neurol ogy,* 49:336–44	Prospective, population-based study of newly diagnosed epilepsy. A cohort of 792 patients was followed for up to 14 years (median follow-up 11.8 years, range 10.6 –11.7 years), a total of 11,400 person-years			214 deaths occurred in the entire cohort (SMR 1.9; CI 95% CI = 1.6, 2.2; p< 0.001) In the idiopathic group SMR 1.3 (CI 95% = 0.9,1.9) In the remote symptomatic SMR 3.7 (CI 95% 2.9, 4.6) and in the acute symptomatic group SMR 3.0 (CI 95% 2.0, 4.3).	No data on possible contribution of EEG to the definition of mortality risk	
Lindsten H et al (2000)	Mortality Risk in an Adult Cohort with a Newly Diagnosed Unprovoked Epileptic Seizure: A Population-Based Study	*Epilepsia,* 41:1469-73	Prospective: 107 patients >17 yr with newly diagnosed unprovoked epileptic seizures were followed until the date of death or the end of 1996. SMR was analyzed. The influences on the SMR of time since diagnosis, sex, age at diagnosis, seizure cause, seizure type, and cause of death were also investigated			The total cohort mortality risk was significantly increased (SMR, 2.5; 1.2-3.2) Patients with remote symptomatic cause had a significantly elevated risk of death (SMR, 3.3; 2.4-4.5)	No data on possible contribution of EEG to the definition of mortality risk	

Loiseau P et al (2005)	One-Year Mortality in Bordeaux Cohort: the value of syndrome classification	*Epilepsia,* 46(Suppl. 11):11–4	Retrospective: Date and cause of death in an incidence study of first afebrile seizures were classified by epilepsy syndrome. 804 pts were included. SMR were calculated			Cryptogenic SMR = 1.7, 95% CI 0.1–9.7 Remote symptomatic SMR = 6.4, 95% CI 3.6–10.3 Acute symptomatic SMR=10.3, 95% CI 8.3–12.7	No specific data on possible contribution of EEG to the definition of mortality risk	Although a syndromic diagnosis is important for treatment decisions and some prognostic aspects of seizure disorders, its value in mortality studies is limited
Montè CP et al (2007)	Sudden unexpected death in epilepsy patients: Risk factors A systematic review	*Seizure,* 16: 1-7	Review				No data on possible contribution of EEG to the definition of risk of SUDEP	
Olafsson E et al (1998)	Long-Term Survival of People with Unprovoked Seizures: A Population-Based Study	*Epilepsia,* 39:89-92	Prospective: 224 incidence cases of unprovoked seizures in Iceland. Survivorship status and date of death was collected. SMR was calculated			30 years after diagnosis, there were 45 deaths among the index cases (SMR=1.6,1.2-2.1) In the remote symptomatic group SMR was 2.3,1.4-3.5 In the idiopathic group SMR was 1.3, 0.8-1.9	No data on possible contribution of EEG to the definition of mortality risk	
Rocamora R et al (2003)	Cardiac Asystole in Epilepsy: Clinical and Neurophysiologic Features	*Epilepsia,* 44:179–85	Retrospective analysis of the clinical records of hospitalized patients who underwent long-term video-EEG monitoring to determine the frequency of cardiac asystole provoked by epileptic seizures (possibly implied			Seizure-induced asystole is a rare complication. The event appeared only in 5 cases of focal epilepsy (3 frontal and 2 left-temporal)	EEG may contribute to identify ictal patterns at risk for seizure-induced asystolia	

			in SUDEP) and to analyze the correlation between EEG, ECG, and clinical features obtained from long-term video-EEG monitoring.					
Schuele SU et al (2007)	Video-electrographic and clinical features in patients with ictal asystole	*Neurology,*69:434-41	Retrospective: Ictal asystole (IA) is a rare event mostly seen in patients with temporal lobe epilepsy (TLE) and a potential contributor to SUDEP A database search was performed of 6,825 patients undergoing long-term video-EEG monitoring for episodes of IA			IA was recorded in 0.27% of all patients with epilepsy, 8 with TLE, 2 with extratemporal (XTLE), and none with generalized epilepsy	Clinical predisposing factors for IA, including cardiovascular risk factors or ECG or EEG abnormalities were not identified	
Tèllez-Zenteno JF et al (2005)	Sudden unexpected death in epilepsy: Evidence-based analysis of incidence and risk factors	*Epilepsy Research,* 65:101–15	Evidence-based review				No data on possible contribution of EEG to the definition of risk of SUDEP	
Tomson T et al (2008)	Sudden unexpected death in epilepsy: current knowledge and future directions	*Lancet Neurology,* 7: 1021–31	Review				No data on possible contribution of EEG to the definition of risk of SUDEP	
Tomson T et al (2005)	Sudden Unexpected Death in Epilepsy: A Review of Incidence and Risk Factors	*Epilepsia,* 46(Suppl. 11):54–61	Review				No data on possible contribution of EEG to the definition of risk of SUDEP	

Walczak TS et al (2001)	Incidence and risk factors in sudden unexpected death in epilepsy: A prospective cohort study	*Neurology,*56:519-25	Prospective: 3 epilepsy centers enrolled 4,578 patients and prospectively followed these patients for 16,463 patient-years to determine incidence of and risk factors for SUDEP			Overall incidence of SUDEP was 1.21/1,000 patient-years, highest in patients aged 50 to 59. Incidence in F (1.45/1,000 patient-years) was higher than in M (0.98/1,000 patient-years, p=0.0512) 3 independent risk factors for SUDEP were identified: 1) exposure to tonic-clonic seizures, 2) mental retardation, and 3) the number of anticonvulsant drugs used	No data on possible contribution of EEG to the definition of risk of SUDEP	

EEG and prevention of adverse effects of treatment

No specific data were found about a possible role of EEG in preventing adverse effects of treatment. However, as some adverse effects of AEDs may be related to inappropriate diagnoses, the indirect contribution of EEG could be relevant for this issue.

Relevant to above points

It is critical to recognize that virtually all data cited in support of the diagnostic and prognostic value of EEG was obtained under optimal conditions with regard to several critical factors including:

1. EEG equipment/facilities-There are established expert recommendations (e.g. American Clinical Neurophysiology Society Guidelines, European Guidelines) regarding minimal acceptable quality for recordings in terms of number of electrodes, montages, etc.

2. EEG technical ascertainment-There are minimal training standards and qualification for EEG technicians required for ABRET-certified laboratories. Again, these minimal standards were almost certainly met in all labs or clinics where the data to support EEG was obtained. Technical qualifications of the person obtaining the recording are even more critical where analog (rather than digital) recordings are still in use.

3. EEG interpretation-The data cited in support of EEGs value was almost certainly obtained in setting where the EEG was interpreted by an epileptologist (i.e. a neurologist with additional training in epilepsy/clinical neurophysiology).

It is important to note that there is a reasonable body of data to suggest that in fact when EEG is obtained under suboptimal conditions, the value of EEG for diagnostic purposes is substantially less. There is some limited data to indicate that EEG can be harmful and lead to overdiagnosis and unnecessary treatment when used for diagnostic confirmation by less experienced readers. There is a general agreement among epileptologists that over-reading is more harmful than under-reading and that less experienced readers are more likely to over-interpret benign patterns and variants as epileptic(Engel 1984; Chadwick 1990)

See below for details of evidence

Williams et al, 1985: This study took a random sample of 100 active electroencephalographers in the US and showed them selected EEGs to determine inter-rater variability and correct responses. Reader characteristics such as board certification, number of EEGs reviewed annually and percent of time in EEG work determined reader responses.

Gilbert et al, 2003: A meta-analysis of 25 studies involving 4,912 EEGs revealed a wide range of inter-reader variation in terms of sensitivity and specificity with regard to whether or not the EEG could predict seizure recurrence. The largest proportion of this variability (37% of variability) was accounted for by the interpretation threshold of the neurologist reader. Higher specificity readers had greater diagnostic accuracy.

Benbadis & Lin, 2008: This retrospective review from a single epilepsy center looked at EEGs from patients referred for epilepsy management who were ultimately determined NOT to suffer from epilepsy. The EEGs of interest were those obtained by non-epilepsy experts and interpreted as having epileptiform discharges by the local EEG reader who was not expert in EEG interpretation. The retrospective review identified 37 patients who met the following criteria—(1) had been referred for epilepsy management (2) had an outside EEG available for review that had been reported as having epileptiform discharges, and (3) the patient was ultimately determined NOT to have epilepsy. Expert review of these 37 EEGs determined that none of them actually had epileptiform discharges (EDCs) but in fact had benign patterns commonly mistaken for EDCs by naive readers.

Benbadis & Tatum, 2003: This is a retrospective review of the EEG tracings (obtained and interpreted by the referring physician) of patients referred to an epilepsy center with a diagnosis of epilepsy who were ultimately determined to have psychogenetic, non-epileptic seizures (PNES). Subjects identified with PNES from January 1999-June 2001 were included. EEGs obtained and interpreted by the referring physicians were reviewed by a board-certified electroencephalographer specializing in epilepsy. The referring physicians were general neurologists. Of 127 PNES patients, 41 had a history of epileptiform discharges on their referring EEGs—and 15 of these 41 EEGs were available for expert review. On review, 0/15 EEGs showed epileptiform discharges. Normal variants and benign wave patterns mistaken for EDCs were identified.

Role of EEG in management of convulsive epilepsy

Smith et al, 1999: This retrospective analysis of 184 patients referred to a single epilepsy center with a diagnosis of intractable epilepsy identified an overall misdiagnosis rate (meaning the patient did not have epilepsy) of 26.1% (46/184). Nineteen of the 46 misdiagnoses were based upon EEGs obtained and interpreted by non-epileptologists that were interpreted as having epileptiform discharges but which on expert review had no EDCs evident but only normal variants. Essentially, poor EEG interpretation by a general neurologist contributed to almost half of the misdiagnosed cases. Importantly, most of these patients had been treated unnecessarily with AEDs for long periods of time.

Tuan et al, 2008: This field survey done in northern Vietnam identified 1,338 positive responses to a questionnaire on seizure disorders. On clinical examination, 190 patients met the criteria for active epilepsy. All considered to fulfil the criteria for active epilepsy, were offered an EEG examination (not feasible in 10 patients). EEG was without abnormalities in 149 (78%) of 190 cases (artifact in 6 patients), whereas epileptiform activity was recorded in only 21 patients (11%).

Tekle-Haimanot et al, 1997: This community-based study identified 139 incident cases in a door-to-door survey in a rural area of central Ethiopia. This corresponded to an annual incidence of 64 in 100,000 (95% CI 44-84). EEG was recorded in 53 patients; it was normal in 38%, and demonstrated epileptiform activity in 34%, non-specific abnormalities in 18%, and paroxysmal rhythms in 11%. Of those with abnormal EEG recordings, 20% had focal unilateral or nonfocal unilateral abnormalities suggestive of a lateralized lesion (partial epilepsy). In some subjects who clinically had only generalized convulsive seizures, the EEG showed focal epileptiform activity. These patients were classified as having partial seizures secondarily generalized.

Given the above (i.e. that all data cited in support of EEG's utility was obtained under ideal circumstances in terms of equipment, technical support and interpretators' qualifications) recommendations can only be made in support of EEG under similar circumstances/conditions. Furthermore, there should be some notes of caution issued about the use of EEG in the absence of well-qualified technicians and interpreters.

Engel 1984: This study looks at the EEG being an aid for the diagnostic process of epilepsy and not a diagnosis itself. When used to help differentiate between generalized and partial epileptic conditions and to Identify benign epileptic syndromes, the EEG has prognostic and therapeutic implications. Also, the EEG can be used to determine whether a patient is deteriorating due to increased seizure activity or increased side effects. The study also discussed how healthy young adults with medically intractable partial complex seizures with unilateral or bilaterally independent interictal anterior temporal EEG spike foci are the best candidates for resective surgical therapy while those with multifocal or bilaterally synchronous interictal EEG spikes combined with mental retardation are less likely to benefit from resective surgery.

Benbadis SR, Tatum WO (2003). "Overintepretation of EEGs and misdiagnosis of epilepsy." *Journal of Clinical Neurophysiology,* **20**(1): 42-4.
The overinterpretation of EEGs is a known problem that has not been reported specifically. The authors report a series of EEGs on patients who were diagnosed eventually with psychogenic nonepileptic seizures and who had an EEG read as epileptiform. Of the 15 actual records available for review, the overread patterns were wicket spikes (n = 1), hypnagogic hypersynchrony (n = 1), and hyperventilation-induced slowing (n = 1). In the other 12 records, the overread

patterns were simple fluctuations of sharply contoured background rhythms or fragmented alpha activity. Rather than well-described normal variants, the overinterpreted patterns tend to be normal fluctuations of background activity

Benbadis SR and Lin K, 2008: "Errors in EEG interpretation and misdiagnosis of epilepsy. Which EEG patterns are overread?" *European Neurology,* **59**(5): 267-71. The overinterpretation of EEGs is common and is an important contributor to the misdiagnosis of epilepsy. The authors reviewed their experience in order to clarify which EEG patterns are commonly overread as epileptiform. They identified patients who were seen at our epilepsy clinic and were ultimately diagnosed as having conditions other than epilepsy. They selected those who had previously had an EEG read as showing epileptiform discharges and whose EEG was available for their own re-review. 37 patients met the above criteria. Eventual diagnoses were psychogenic nonepileptic seizures (10), syncope (7), other miscellaneous diagnoses (5) and unexplained nonspecific symptoms (15). None of the EEGs had epileptiform discharges. The descriptions of the abnormalities included 'temporal sharp waves' in 30, 'frontal sharp waves' in 2 and 'generalized spike-wave complexes' in 2. Three had no reports available to identify the alleged abnormality. The benign patterns mistaken for temporal (30) and frontal (2) sharp waves were simple fluctuations of background activity with temporal phase reversals. The authors concluded that by far the most common patterns overread as epileptiform are nonspecific fluctuations of background in the temporal regions, which are misread as temporal sharp waves.

Any statistical summaries

The best review of evidence available about the contribution of EEG to diagnosis is AAN Quality Standard (Hirtz et al, 2000) about evaluation of first nonfebrile seizures in children, concluding that the majority of evidence from Class I and Class II studies confirms that an EEG helps in determination of seizure type, epilepsy syndrome and may be helpful in determining the need for imaging studies. A number of meta-analyses deal with EEG and the risk of seizure recurrence following a first unprovoked seizure: Berg & Shinnar, 1991, (meta-analysis of 16 reports) concludes that seizure etiology and the EEG are the strongest predictors of recurrence; Gilbert & Buncher, 2000 (meta-analysis of 31 publications relating epileptiform or abnormal EEG and subsequent seizures) indicates a wide range of values for both sensitivity (0.20-0.81) and specificity (0.41-0.99) in a previous systematic review of 4 studies involving 831 children. Gilbert & Buncher, 2000 stated that the pretest probability of recurrence was less than the lower limit of the range for rational testing, concluding that EEG should be ordered selectively, not routinely, after first unprovoked seizure in childhood. On the contrary, the aforementioned AAN Quality Standards on the basis of available evidence (Hirtz et al, 2000; Krumholz et al, 2007) recommends EEG as part of the diagnostic evaluation of the child with an apparent first unprovoked seizure.

Methodological limitations

Methodological limitations have to be considered, some of them intrinsic to the EEG recording and interpretation and some depending on the quality of the study designs. The major intrinsic limitations are the low sensitivity of interictal EEG, which can be moderately increased only by prolonging the duration of the recording (generally through repeat testing), and the poor interrater reliability. Besides the well known subjectivity of EEG reporting, some publications support

the concept that interictal EEG in childhood epilepsy appears an unstable test *per se*, so a repeated EEG could yield different and conflicting information; on the contrary, others (dealing with interrater agreement in classification of childhood epilepsy syndromes) conclude that when an abnormal EEG is clearly contributory to a specific diagnosis, interrater agreement is extremely good. A possible interpretation is that some EEG patterns are unequivocal and less prone to differing interpretations and others, perhaps the majority, are ill-defined and subjected to differing interpretations. However, these apparently conflicting results also reflect the limitations of the EEG technology, which in spite of standard recording and interpretation techniques, is time-dependent and may be profoundly affected by the variability of the bioelectric patterns in the epileptic brain. For this reason, repeat tracings and use of activation techniques may explain at least in part the differing results across studies and the increasing diagnostic yield with a more intensive investigation. Another important flaw is that EEG readers are often unblinded. This is even more important, given the fair and sometimes poor reliability of the EEG readings. Other limitations include the retrospective design, the small sample size, the differing study populations, and the duration of the follow-up.

Directness (in terms of population, outcome, intervention and comparator)

The largest body of information on the diagnostic and prognostic yield of EEG has been obtained from clinic-based observational studies done in selected referral populations (mostly children and adolescents and – to a lesser extent – adults) which were investigated using different technologies and modalities for recording and interpretation. Lesser studies were performed in population-based samples. Most of these studies have been carried out in high income countries. However, given the purposes of these latter surveys (mostly interested in broad EEG findings), there were few or no attempts in assessing the diagnostic contribution of the EEG tracings depending on the intensity of the investigation and in classifying patients into precise syndromic categories. As well, regarding the prognostic yield of interictal EEG, population-based studies only assessed the results of the first tracing disregarding the possible contribution of repeat EEGs. Although the results of electrophysiological investigations and neuroimaging have been repeatedly compared in surgical candidates to assess the outcome of epilepsy surgery and the comparative value of EEG and neuroimaging has been assessed in patients with a first seizure, to our knowledge there are no reports on the evidence-based diagnostic contribution of the EEG tracings compared to other diagnostic techniques. Only indirect comparisons are available between EEG and other prognostic indicators in studies on the risk of seizure relapse and mortality of epilepsy. There are virtually no reports on the diagnostic yield of interictal EEG in resource-poor countries. In this light, given the fairly low sensitivity of this diagnostic technique, about 50% of cases with true epileptic seizures may go undetected unless repeat tracings and/or activation procedures are performed.

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From evidence to recommendations

Factor	Explanation
Narrative summary of the evidence base	Diagnosis – Seven prospective and four retrospective studies, usually descriptive, plus reviews. It is important to use clinical judgement in the diagnosis of possible epileptic events – EEG is not helpful in the diagnosis of, for example, syncope. Initial EEG is likely to be positive in up to half of

	cases of unprovoked seizures and this yield may be improved by repeat EEG or activation procedures (although there is little to be gained beyond the fourth EEG). The percentage of positive EEG recordings obtained decreases with increasing age, but EEGs are not useful in the management of febrile seizures. They may be useful in determining the nature and location of precipitating events in children with status epilepticus. It is critical to recognize that virtually all data cited in support of the diagnostic and prognostic value of EEG was obtained under optimal conditions with regard to several critical factors including: a) EEG equipment/facilities-There are established expert recommendations (e.g. American Clinical Neurophysiology Society Guidelines, European Guidelines) regarding minimal acceptable quality for recordings in terms of number of electrodes, montages, etc. b) EEG technical ascertainment-There are minimal training standards and qualification for EEG technicians required for ABRET-certified laboratories. Again, these minimal standards were almost certainly met in all labs or clinics where the data to support EEG was obtained. Technical qualifications of the person obtaining the recording are even more critical where analog (rather than digital) recordings are still in use. c) EEG interpretation-The data cited in support of EEGs value was almost certainly obtained in setting where the EEG was interpreted by an Epileptologist (i.e. a Neurologist with additional training in epilepsy/clinical neurophysiology). When EEG is obtained under suboptimal conditions, the value of EEG for diagnostic purposes is substantially less. There is some limited data to indicate that EEG can be harmful and lead to overdiagnosis and unnecessary treatment when used for diagnostic confirmation by less experienced readers. There is a general agreement among epileptologists that over-reading is more harmful than under-reading and that less experienced readers are more likely to over-interpret benign patterns and variants as epileptic. Risk of recurrence. Nineteen prospective and two retrospective studies contribute to the

	evidence, plus reviews. Usually internal comparisons. The overall risk of recurrence after a first unprovoked seizure is about 26 to 56% at one year and is highest among those with remote symptomatic seizures. Overall the presence of an abnormal EEG is associated with an increased relative risk of recurrence, but the RR is greater in people with idiopathic epilepsy than in those with remote symptomatic seizures. Most studies shows that recurrence, or poor outcome, is predicted by an abnormal EEG but the results are heterogeneous and some studies show no predictive value while others show positive findings only in people with certain seizure types. Mortality. Only 3 studies considered the evidence. Two were retrospective. The prospective study used internal comparisons. Most studies did not look at evidence regarding EEG and mortality. A prospective study involving EEG and oxygen saturation data found desaturations significantly correlated with seizure location – this may be of relevance to SUDEP. A retrospective study found that EEG may sometimes contribute to identification of ictal patterns at risk for asystole, while another retrospective study found no associations.
Summary of the quality of evidence	Most of these studies are from high income countries done in specialist settings - LOW or VERY LOW quality evidence
Balance of benefits versus harms	Most published evidence in support of the diagnostic and prognostic value of EEG was obtained under optimal conditions regarding facilities, technical procedures and interpretation. There are limited data to suggest that EEG can be harmful and lead to overdiagnosis and unnecessary treatment when used for diagnostic confirmation by less experienced people.
Values and preferences including any variability and human rights issues	Diagnostic accuracy may contribute to the treatment and management of people with epilepsy. It may help to differentiate those whose risk of recurrence is lower. It may also contribute to the correct treatment of those whose risk of recurrence is higher, thus increasing the chances of seizure freedom and reducing stigma.

Role of EEG in management of convulsive epilepsy

Costs and resource use and any other relevant feasibility issues	Whilst standard EEG may in itself be a fairly inexpensive treatment aid, it is important that certain technical and interpretive standards are met so that over-diagnosis and treatment are avoided. The expertise required may be expensive. Multiple retesting is resource intensive.

Final recommendation(s)

EEG should not be used routinely for diagnosis of epilepsy in non-specialized health care in low and middle income countries. If there is clinical evidence for the diagnosis of convulsive epilepsy, treatment should be started without EEG. EEG may be a useful tool to support diagnosis and classify epileptic syndromes particularly in young, but should be done in specialized facilities under optimum technical conditions and with adequate expertise for interpretation of the data and results.
Strength of recommendation: STRONG

Update of the literature search – June 2012

In June 2012 the literature search for this scoping question was updated. No new systematic reviews were found to be relevant.