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CRITICAL REVIEW

Recurrence risk after a first remote symptomatic seizure in adults: Epilepsy or not?

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Abstract

The ILAE practical definition of epilepsy has a one seizure possibility to diagnose epilepsy after a first seizure if the recurrence risk is very high. The recurrence risk after a first seizure in brain disorders (first remote seizure) is often high, but varies with etiology, so more specific information is needed for clinical practice. This review describes etiology-specific recurrence risks in adults with a first remote seizure in stroke, traumatic brain injury, infections, dementia, multiple sclerosis, and tumors. Most studies are short, single center, and retrospective. Inclusion criteria, outcome ascertainment, and results vary. Few patient categories are clearly above the epilepsy threshold of recurrence risk, and there are surprisingly little data for important etiologies like brain infections. Beside stroke, severe TBI could have a sufficiently high recurrence risk for early epilepsy diagnosis, but more studies are needed, preferably prospective ones. The literature is uninformative regarding which seizures qualify as remote. The clinical implication of the low level of available evidence is that for other etiologies than stroke, seizure recurrence remains the most appropriate indicator of epilepsy for most patients with a first remote seizure. Nonetheless, there are worrying indications of a diagnostic drift, which puts patients with a preexisting brain disorder at risk of misdiagnosis. Although there are drawbacks to an intermediate term like "possible epilepsy," it could perhaps be useful in cases when the recurrence risk is high, but epilepsy criteria are not definitely met after a first remote seizure.

KEYWORDS

diagnosis, remote seizure, seizure recurrence, unprovoked seizure

1 | INTRODUCTION

In 2014, the ILAE introduced a practical definition of epilepsy, allowing a diagnosis to be made in cases of "One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years."[1] Previous stroke is specified as a clinical circumstance where a diagnosis can be motivated after a first remote seizure, because of the high recurrence risk demonstrated by Hesdorffer et al.[2] In other preexisting brain disorders, recurrence risks after a first unprovoked

seizure (remote seizure or remote symptomatic seizure) are less well known.

Etiology stratification is a reasonable approach to recurrence risk. Population-based or prospective studies have found recurrence risks after a first remote seizure at or just above the 60% threshold, but this is a composite result, and recurrence risks seem to differ between underlying etiologies.[2,3] Prior brain insults or abnormal brain imaging increase the risk of seizure recurrence twofold, but are not enough to put an individual clearly above the 60% risk threshold.[4] The ILAE emphasizes that epilepsy should not be diagnosed after a first seizure in the absence of clear information on a >60% recurrence risk, and that "a single seizure plus a lesion" does not satisfy criteria for epilepsy.[1] All first remote seizures cannot be treated the same.

This review aims to discuss (a) the available evidence on etiology-specific recurrence risks after a first remote seizure in adults, (b) the potential for systematic reviews or future studies, and (c) clinical implications of the current state of knowledge.

Key Points

- According to the ILAE, high recurrence risk after a first remote seizure can motivate diagnosis of epilepsy. Risks vary between etiologies
- After a first poststroke remote seizure, the risk is high. This review summarizes evidence on recurrence risk in several etiologies
- Most studies are small, single center, and retrospective. There is limited support for an early epilepsy diagnosis after first non-stroke remote seizures
- Severe traumatic brain injury could have a high risk, but more research is needed
- Clinicians should use the two-seizure rule in most cases. Education efforts are needed to prevent unintended diagnostic drift

2 | MEASURING RECURRENCE RISK

This is a narrative review, focusing on studies with at least 10 adult participants, but not populations with mixed causes of remote seizures, which do not provide enough detail for the present purpose.[3,4] In the literature, seizure recurrence risk is often reported as cumulative incidence (CI) or survival-adjusted risk. CI is the proportion of patients with recurrence. Survival-adjusted risk is often estimated by the Kaplan-Meier (KM) method. Both measurements have weaknesses. CI does not take participant time-at-risk into account and must be interpreted in relation to the follow-up time of each study. Risk in KM is an estimate of risk should no competing event (like death) occur. Competing risk is not a small problem in patients with brain disorders. The difference is illustrated by the pivotal Hesdorffer study cited in the ILAE epilepsy definition paper; 49% (72/148) of patients with a first remote seizure had a recurrence, but the KM risk was 65%.[2] KM can overestimate risks toward the end of an analysis; events with fewer cases get a heavier mathematical weight. CI is sometimes advocated if competing risks are present.[5] In this review, outcomes are presented as reported by the authors, with calculated CI if possible.

Most etiology-stratified studies of recurrence risk have shorter follow-up time than 10 years. Population-based studies are rare and antiseizure medication (ASM) treatment often not described in detail. Categorization into early and late seizures varies between studies. A common method is retrospective medical records review at a single center. This is a study design with risk of selection bias and better detection of epilepsy than single seizures. Already in 1991, Berg and Shinnar found that recurrence risks are higher in retrospective studies than prospective ones.[6] For the purpose of this review, short or retrospective studies can still be informative, if the recurrence risk exceeds or falls short, respectively, of the ILAE epilepsy threshold.

Selected studies for non-stroke etiologies are summarized in Table 1 and stroke studies in Table 2. Reported risks in studies with more than two years of follow-up are illustrated in Figure 1.

3 | DEMENTIA

Three studies have reported quite different recurrence risks in dementia (Table 1). One is a retrospective review of autopsy-verified Alzheimer disease (AD), in which 69% of 77 patients had more than one seizure, but only 29% had more than two seizures.[7] The second is a prospective study of persons with AD that found a CI of 29%, but it had just 14 participants and short follow-up.[8] The third is a large register-based (but not population-wide) study that found a 32% survival-adjusted risk of epilepsy five years after a first seizure.[9] Subgroups with higher risks were patients with dementia onset <70 years of age (48%), and early-onset AD (50%).

TABLE 1 Studies describing recurrence risks in patients with dementia, multiple sclerosis, CNS infections, traumatic brain injury (TBI)

Author, year	Subgroup	Design	n	Men	Women	Age	Follow-up	n recu	C Inc (%)	Surv-adj risk (95%CI)	Comment
Dementia											
Mendez 1994[7]	AD	Retrospective, single center	77	30	47	71	≈3 y	53	69		Only 29% had >2 sz
Baker 2019[8]	AD	Prospective, single center	14			79	1 y	3	21		
Mahamud, 2020[9]	All	Retrospective	1039	446	573					5 y: 32% (27-37)	
	<70		215							48% (37-59)	
	>70		824							26% (21-30)	
	Early AD		130							50% (33-67)	
Multiple sclerosis											
Langenbruch, 2019[10]	All	Retrospective, single center	62	17	45	40	82 mo	38	61		
	1-y follow-up		52				>12 mo	31	60		
	RRMS		29				>12 mo	17	59		
	1st sz at relapse		11				>12 mo	6	55		
	1 st not at relapse		10				>12 mo	1	10		
Mahamud, 2018[15]	All	Retrospective	289	92	197	48				10 y:51 (44-59)	
	SE		18							86 (68-100)	
	RRMS		121							46 (35-57)	
	SPMS		90							61 (47-75)	
Catenoix, 2011[11]	All	Retrospective, single center	67	23	44	33	7 y	38	57		
Nyquist, 2001[12]	All	Retrospective, single center	51				1-8 y	33	65		
Engelsen, 1997[13]	All	Retrospective, population-wide	17	6	11	33	>4 y	16	94		
Kinnunen, 1986[14]	All	Retrospective, population-wide	13	5	8	38	13 y	11	85		
CNS infections											
Elafros, 2018[21]	HIV, all	Prospective, multi-center	72			37	8 mo	21	30		Death significant competing risk.
	Survivors		58				11 mo	20	34		WHO stage III or IV in most
Olajumoke, 2013[22]	HIV	Retrospective, single center	20	6	14	34	1 y	13	65		Limited workup, etiology not clear

(Continues)

TABLE 1 (Continued)

Author, year	Subgroup	Design	n	Men	Women	Age	Follow-up	n recu	C Inc (%)	Surv-adj risk (95%CI)	Comment
Chadha, 2000[23]	HIV	Not clear, single center	23	23		32		15	65		7 toxoplasmosis, 3 TB
Singh, 2017[24]	NCC	Prospective, single center	54	26	28	20	1 y	13	24		Single calcification, all treated with OXC, KM risks 20% without edema 1 y and 65% with edema 1 y
Lachuriya, 2016[25]	NCC	Prospective, single center	109	77	32	19	1 y	34	31		All treated with OXC
Sharma, 2011[26]	NCC	Prospective, single center	74	36	38	18	6 mo	13	18	6 mo ≈ 35%	All treated with OXC.
Calliauw, 1984[27]	Abscess		21				5.8 y	17	81		
TBI											
Thapa, 2010[16]	Severe	Prospective, single center	14				1 y	11	79		Neurosurgery inpatients, 10/14 adults
Haltiner, 1997[17]	Severe	Prospective, single center	63	50	13	31	2 y	49	78	2 y: 86%	Participants selected for high risk of PTE: 1 of depressed skull fracture, penetrating head injury, cortical contusion, acute hematoma on CT, GCS ≤10, early seizure
Hauser, 1982[20]		Prospective, multi-center	24							20 mo: 46%	LOC/amnesia 30 min, skull fracture, or intracranial bleeding
Hesdorffer, 2009[2]		Retrospective, population-wide	37	23	14					10 y: 47% (30-66)	

TABLE 1 (Continued)

Author, year	Subgroup	Design	n	Men	Women	Age	Follow-up	n recu	C Inc (%)	Surv-adj risk (95%CI)	Comment
Angeleri 1999[18]		Prospective, single center	18			15-65	1 y	18	100		15/18 moderate/severe. First remote sz >4 wk after TBI.
SALAZAR, 1985[70]	Penetrating	Retrospective, single center	217	217	0		15 y	200	92		Vietnam war injuries

≈ indicates read from graph. Follow-up is mean, median, or minimum/maximum as indicated by <>.
Abbreviations: 95%CI, 95% confidence interval; C Inc, cumulative incidence.

4 | MULTIPLE SCLEROSIS

Reported CI of recurrence after a first seizure in multiple sclerosis (MS) ranges from 57% to 94%, with lower estimates in the larger studies.[10–14] In a Swedish register-based study, the survival-adjusted 10-year risk of epilepsy after a first seizure was 52%, with no difference between relapsing-remitting MS and age- and sex-matched controls.[15] A higher risk was seen in MS patients with initial status epilepticus (86%), but the subgroup was small and the study based purely on administrative data.

5 | TRAUMA

Several studies on very severe TBI have reported high CI of recurrence; 78%-100%,[16–19] and the survival-adjusted risk after 2 years was 86% in one of these.[17] Importantly, the populations were neurosurgical inpatients with severe trauma or war veterans with penetrating head injury. For more "normal" TBI, two population-based studies from Minnesota reported survival-adjusted recurrence risks after 2 or 10 years, respectively, of approximately 45%.[2,20] One of these states inclusion criteria suggestive of at least moderate TBI (unconsciousness/amnesia >30 minutes, skull fracture, or intracranial bleeding).[20]

6 | INFECTIONS

Most studies describing recurrence risks in CNS infections have either very short follow-up or few adult patients. Reported CI of seizure recurrence in specific etiologies is for HIV 30%-65%,[21–23] neurocysticercosis 18%-31%,[24–26] and brain abscess 81%.[27]

7 | STROKE

Cumulative incidence of recurrence ranges between 18% and 73% in mixed stroke cohorts after variable follow-up, 42%-81% in ischemic stroke cohorts, and 28%-84% in ICH.[2,28–48] Long-term survival-adjusted risks (3-10 years) have been reported at >70% for mixed and ischemic stroke populations (Table 2). One study reported 70% CI of recurrence after a remote seizure in central venous thrombosis.[48]

8 | TUMORS

Seizure recurrence risk in brain tumors is very complex. A recent prospective study found tumors to confer the

TABLE 2 Studies describing recurrence risks in patients with stroke

Author, year	Subgroup	Design	n	Men	Women	Age	Follow-up	N recur	C inc (%)	Surv-adj risk	Comment
Mixed stroke populations											
Hesdorffer, 2009[2]		Retrospective, population-wide	101							10 y: 72% (60-82)	
Tomari, 2017[28]		Retrospective, single center	61	34	27	72		25	41	3 y ≈ 70%	
Tanaka, 2015[29]		Retrospective, single center	104	71	33	74	1 y	31	30	1.6 y ≈ 33%	
Berges, 2000[30]		Retrospective, single center	94				47 mo	54	57		
Conrad, 2013[31]		Prospective, single center	26	14	12	59	30 mo	19	73		
Jungehulsing, 2013[32]		Prospective, population-wide	84	38	46		2 y	34	40		
Okuda, 2012[33]		Single center, retrospective	18	14	4	60	4 mo	6	33		
Alvarez-Sabin, 2002[34]		Prospective, single center	71	39	32	64	>1 y	13	18	2 y ≈ 15%–30%	all treated with GBP
Arntz, 2013[34]	Age 18-50	Prospective, single center	53	31	23		<30 y	31	57		
Ischemic stroke											
Zhang, 2020[36]		Retrospective single center	124			65	>1 y			4 y ≈ 80%	
Kim, 2016[37]		Retrospective, single center	76	40	36	69	30 mo	37	49		
De Reuck, 2008[38]		Retrospective, single center	161				3 y	86	53		
Gilad, 2007[39]		Prospective, single center	64	46	18	67	1 y	27	42	1 y ≈ 30%–55%	5 early sz, all LTG or CBZ
So, 1996[40]		Retrospective, population-wide	27				<16 y	18	67	5 y ≈ 90%	
Louis, 1967[41]		Retrospective, single center	27				2-4 y	22	81		
Bladin, 2000[42]		Prospective, multi-center	62					34	55		
Zhu, 2021[43]		Prospective, single center	45				18 mo	21	47		Trial of high-dose statin
Lamy, 2003[44]	Age 18-55	Prospective, multi-center	20	11	9	42	26 mo	11	55		
Intracerebral hemorrhage											
Qian, 2014[44]		Retrospective, population-wide	58	32	26	63	<15 y	49	84		
Biffi, 2016[46]		Prospective, single center	77	39	40	73	4 y	30	38		
Yang, 2009[47]		Retrospective, single center	11	7	4	55	>3 y	3	27		
Other											
Sánchez v Kammen, 2020[48]	CSVT	Retrospective, multi-center	123		83	42	2.6 y	85	70		

≈, indicates read from graph. Follow-up is mean, median, or minimum/maximum as indicated by <>.

Abbreviations: 95%CI, 95% confidence interval; C Inc, cumulative incidence.

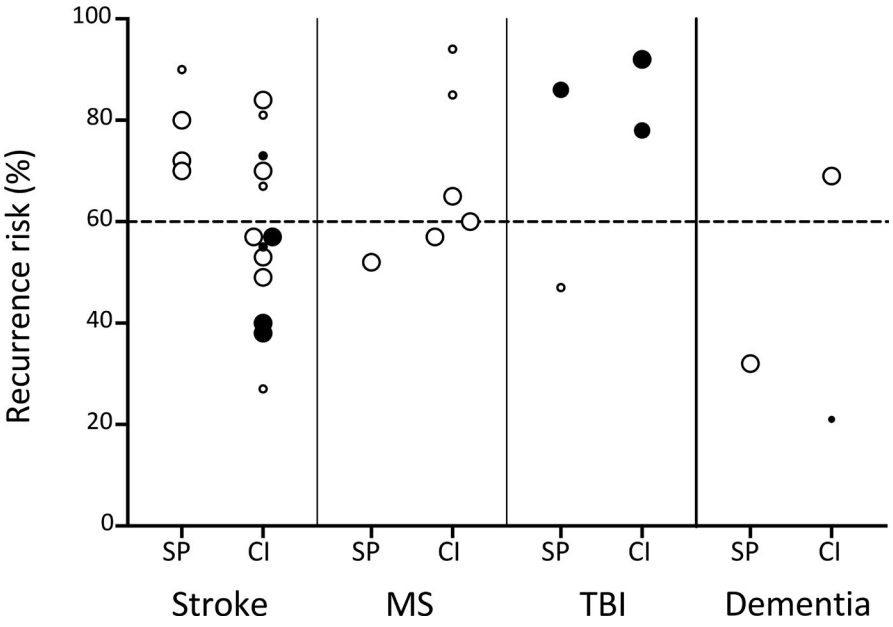

FIGURE 1 Illustration of identified studies with more than 2 years of follow-up. Large points represent studies with more than 50 participants, filled points indicate prospective studies. The dotted line indicates recurrence risk motivating an epilepsy diagnosis according to the ILAE. CI, cumulative incidence; SP, survival-adjusted probability

highest recurrence risk among remote etiologies, at the level of the 60% threshold.[3] Recurrence risks probably differ between tumor types,[49] so composite findings do not help individual prediction. Studies describing first seizure recurrence risks per tumor type are rare. Surgically treated series provide some guidance, but are not really first seizure studies and the risk of bias toward recurrence is substantial (more seizures could be an argument for surgery). One such study reported that 38% of patients with seizures before resection of meningiomas had more than one preoperative seizure.[50] The recurrence risk after a first postoperative seizure after meningioma surgery is not well characterized.[51] In gliomas, seizure risks are related to tumor histology and progression.[52–54] In surgically treated patients with seizures in glioma, more than one preoperative seizure has been reported in >60%.[55,56]

9 | POTENTIAL FOR SYSTEMATIC REVIEWS AND NEED FOR FUTURE STUDIES

In summary, the etiology-stratified literature on recurrence risks after a first remote seizure is very heterogeneous. Retrospective single-center studies dominate, in which bias is likely.

Single centers seem to struggle to recruit significant number of participants for many etiologies.

Can more precise recurrence risk estimates be obtained through systematic reviews and meta-analyses? Judging by the studies discussed in this review, such attempts would be difficult and could be premature. Systematic reviews could perhaps be possible for stroke, severe TBI, and MS, but the low level of evidence and imprecise methodological descriptions in many studies will be a problem for meaningful syntheses of results.

Surprisingly, there are very little data on recurrence risk in adults after important CNS infections, like herpes encephalitis and bacterial meningitis. The Hesdorffer study cited in the ILAE epilepsy definition found a survival-adjusted recurrence risk of 64% after all CNS infections, but the 95% confidence interval was 21%-99% and 6/10 in the cohort were 1-19 years old.[2] Young age is generally a risk factor for symptomatic epilepsy, so the risk estimate is not clinically useful in adult neurology. The lack of knowledge about late seizures after herpes encephalitis was noted in a review more than ten years ago.[57] A review on bacterial meningitis in 2008 stated that "Unprovoked seizures following bacterial meningitis tend to be recurrent (Rosman et al, 1985; Annegers et al, 1988; Pomeroy et al, 1990)"[58] but the cited articles are predominantly pediatric.[59–61] Recent large studies describing seizures after brain infections combine acute symptomatic and unprovoked seizures and do not report recurrence risks after one remote seizure.[62–66]

Prospective studies are needed for better information on recurrence risks. Advances in big data can perhaps facilitate generation of such knowledge. Methods allowing prediction based on multifactorial models incorporating age, lesion severity like cortical involvement in stroke (perhaps even several brain diseases?) would be ideal. Paradoxically, ASM treatment resulting from improved knowledge on the high recurrence risk after many first remote seizures will make it harder and harder to determine whether the natural course equals epilepsy. What is really needed for earlier epilepsy diagnoses are biomarkers of epilepsy.

10 | CLINICAL IMPLICATIONS

Currently, few patient categories are clearly above the 60% threshold after a first remote seizure. Stroke is the most studied etiology. Although the findings are heterogeneous, several studies agree with the ILAE position that a remote poststroke seizure can motivate an epilepsy diagnosis.[1] Nonetheless, clinicians should be aware of limitations in the literature. Many studies include only clinical stroke.[1,2] Whether the findings extend to minor stroke or silent brain infarctions detected in the workup of a first seizure is less clear. The literature is not informative on how closely linked a seizure needs to be to a stroke in terms of timing or semiology to qualify as remote. Most late seizures after stroke occur within 1-2 years.[67] A longer latency is more common in poststroke seizures that are not followed by recurrence.[38] Cortical damage and stroke severity are important epilepsy risk factors after ICH or IS[68,69] and can sometimes, together with timing, help link a first seizure to a previous stroke.

There are other etiologies in which many patients probably reach the ILAE threshold. Severe TBI is a strong candidate, but the injury characteristics in the studies reporting high risk limit generalizability (skull fracture/low GCS, penetrating war injuries, etc).[17,19] A high recurrence risk could also exist for patients with a first unprovoked seizure after a brain abscess[27] or new-onset status epilepticus in MS,[15] but more studies are needed before this is taken to clinical practice.

The studies on recurrence risk in dementia have divergent results, presumably because of differences in inclusion criteria and methodology. The authors of the AD study with the highest recurrence risk commented that "The typical patient was institutionalized, had severe memory loss, was unable to solve problems, had little independent function, and required a great deal of assistance in activities of daily living."[7] Extrapolation to less severe AD or other forms of dementia seems difficult.

There are little or no data supporting that dementia in general, MS in general, or other CNS infections than a brain abscess would put patients with first remote seizures clearly above a 60% recurrence risk. Whether epilepsy is present or not after a first seizure in a patient with glioma is often an academic question, overshadowed by other concerns related to the neoplastic disease, managed by ASM treatment, and often resolved by seizure recurrence. This is not the case in meningiomas, for which more information is needed on recurrence risks after a first seizure. Currently, the literature does not seem to support a diagnosis of epilepsy after a first seizure simply because the workup reveals a meningioma.

Overall, there is only low-grade evidence, which is an unsatisfactory basis for a life-changing diagnosis as epilepsy. Caution is needed. Two seizures still seem like the most appropriate indicator of epilepsy for most patients.

11 | TREATMENT

ASM treatment should always be considered after a first seizure, after an individual assessment of risks associated with recurrence versus ASM side effects. The treatment decision is "distinct from a diagnosis" according to the ILAE.[1] In the reviewed studies, ASM treatment was common after a first remote seizure, but not universal. The authors of a paper on recurrence risks in AD wrote in 1994: "Moreover, the frequent occurrence of one or two seizures in advanced dementia often leads to unnecessary treatment with anticonvulsant medications."[7] The authors of a MS paper discuss that the relatively high chance of seizure freedom after just one seizure could be an argument against ASM treatment, whereas the risk of status epilepticus could be an argument for, the sort of nuanced decision-making advocated by the ILAE.[10]

12 | THE RISK OF MISDIAGNOSIS

An erroneous epilepsy diagnosis is costly and hard to remove,[70] so implementation of the "one seizure-possibility" needs to be closely monitored. Clearly, it can have a huge impact. When applied by a panel of neurologists to 283 suspected new-onset seizures in a population-wide study, 34% were considered as epilepsy based on the new definition.[71] The authors reported substantial discordance among the neurologists involved about the 60% threshold and called for more studies on patients at the "margin of this risk threshold."[71] The report highlights how relying on clinical judgment in application of the 60% threshold could increase subjectivity.

The one seizure possibility also aggravates the consequences if acute symptomatic or unrelated seizures are mislabeled as remote. This problem is probably small when the risk of epilepsy is high, like in the first year after stroke.[72] When the risk of epilepsy is low, like long after mild TBI, in multiple sclerosis, or dementia,[73-75] more first seizures could be chance occurrences.

13 | DIAGNOSTIC DRIFT?

There are worrying indications that the one seizure possibility puts patients with brain disorders at risk of being prematurely diagnosed with epilepsy after a single seizure. In research articles, inclusive interpretations of the one seizure possibility are becoming more common. Examples include epilepsy being defined as "...one unprovoked seizure with an increased risk of recurrent seizures (Fisher et al, 2014), as evidenced by the presence of epileptiform activity on electroencephalography (EEG)."[76] and "Recently the International League Against Epilepsy

(ILAE) Commission on Classification and Terminology has established that a diagnosis of epilepsy can be made after a single unprovoked seizure when there is high risk for recurrence, as in presence of a structural brain lesion, including a tumor."[77] The authors of an article on seizure recurrence in AD refer to the ILAE definition to argue that their findings support a diagnosis of epilepsy after a first seizure. But by a recurrence risk of 70%, they mean that 38/54 patients were classified as "seizures happened in the last year or still require active management" both at baseline and at follow-up.[78] This is a broad interpretation of the ILAE definition. In research, definitions of epilepsy must sometimes be sensitive rather than specific, but it would probably be beneficial with more communication from the ILAE on the level of certainty required in clinical practice.

The ILAE definition is relatively clear to epileptologists, who are aware of the damage that can be inflicted by epilepsy misdiagnosis. But the definition is also read and interpreted outside the epilepsy field. The new European Academy of Neurology guideline on dementia states that "A first seizure after a patient has been diagnosed with dementia may be interpreted as structural epilepsy (if no other competing factors which may lower the threshold of a seizure are identified), requiring consideration of institution of treatment."[79] The evidence motivating an epilepsy diagnosis after one seizure in dementia is not extensive, and linking diagnosis to ASM treatment contrasts with the ILAE view.[1] The EAN guideline does not mandate an epilepsy diagnosis after a first seizure and continues with a good discussion of pros and cons of ASM treatment.[79] Nonetheless, the wording illustrates how the one seizure possibility can lead to unintended diagnostic drift.

Whether the 60% threshold is appropriate or not is not the topic of this review. One elegant study found that a recurrence risk of 60% after a first remote seizure does not equal the recurrence risk after two unprovoked seizures.[3] If so, the threshold for an epilepsy diagnosis could be inappropriately low for patients with preexisting brain disease.

14 | NEED FOR A NEW TERM?

A recent study examining when early ASM treatment is motivated to maximize quality of life found a recurrence risk above 40% to be a reasonable threshold.[80] Many patient groups in this review reach that level; ASM treatment seems appropriate, but an epilepsy diagnosis is not motivated. Even with better data for prediction of recurrence risk, there will always be patients that fall short of the epilepsy threshold. A unifying term to capture this clinical scenario could perhaps be of value.

Has the time come for "possible epilepsy"? "Possible epilepsy" could be used for circumstances when clinicians feel that there is a high recurrence risk, but are uncertain about the 60% threshold. A possible diagnosis could be easier to remove should no recurrence occur. There are of course drawbacks. Pending more information, the ILAE should enhance education efforts to prevent an unintended widening of the epilepsy term among patients with preexisting brain disorders.

15 | CONCLUSION

There are very little robust data on recurrence risks over 60% after a first remote seizure for most patients with other preexisting brain disorders than stroke. If clinicians do not adhere strictly to the ILAE definition and reserve the epilepsy diagnosis for when recurrence risks are known to be very high—patients with brain disorders could be at risk of misdiagnosis.

CONFLICT OF INTERESTS

Dr Zelano reports speaker honoraria for non-branded educations from UCB and Eisai and being investigator in clinical trials sponsored by UCB, GW Pharma, Bial, and SK Life Science as an employee of Sahlgrenska University Hospital (no personal compensation). I confirm that I have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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