



MANAGEMENT OF AN UNPROVOKED FIRST SEIZURE IN ADULTS

This is a summary of the American Academy of Neurology (AAN) and American Epilepsy Society (AES) evidence-based guideline regarding the management of an unprovoked first seizure in adults.

Please refer to the full guideline at AAN.com/guidelines for more information, including definitions of the classifications of evidence and recommendations.

Risk of Seizure Recurrence

For the adult who presents with an unprovoked first seizure, what are the risks for seizure recurrence?

Strong evidence	Adults presenting with an unprovoked first seizure should be informed that the chance for a recurrent seizure is greatest within the first two years after a first seizure (21 percent to 45 percent) (Level A).
	Clinicians should also advise such patients that clinical factors associated with an increased risk for seizure recurrence include a prior brain insult such as a stroke or trauma (Level A) and an EEG with epileptiform abnormalities (Level A).
Moderate evidence	Clinicians should also advise such patients that clinical factors associated with an increased risk for seizure recurrence include a significant brain-imaging abnormality (Level B) and a nocturnal seizure (Level B).

Management

For the adult presenting with an unprovoked first seizure, does immediate treatment with an antiepileptic drug (AED) change the short-term (2-year) prognosis for seizure recurrence?

Moderate evidence	Clinicians should advise patients that immediate AED therapy, as compared with delay of treatment pending a second seizure, is likely to reduce the risk for a seizure recurrence in the two years subsequent to a first seizure (Level B).
Weak evidence	Clinicians should advise patients that immediate AED therapy, as compared with delay of treatment pending a second seizure, may not improve quality of life (QOL) (Level C).

For the adult presenting with an unprovoked first seizure, does immediate treatment with an AED as compared with delay pending a seizure recurrence influence prognosis such as the potential for seizure remission over the longer term (> 3 years)?

Moderate evidence	Clinicians should advise patients that over the longer term (> 3 years) immediate AED treatment is unlikely to improve the prognosis for sustained seizure remission (Level B).
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Risks of AED Treatment

For the adult who presents with an unprovoked first seizure, what are the nature and frequency of adverse events (AEs) with AED treatment?

Moderate evidence	Patients should be advised that their risk for AED AEs ranges from 7 percent to 31 percent (Level B) and that these AEs are predominantly mild and reversible.
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Clinical Context

For an adult with a first seizure, the risk of a recurrence poses major concerns and raises the question of whether immediate AED treatment is advisable. It is a proposed and now generally accepted principle that when a patient with a first seizure suffers one or more ensuing seizures, an AED should be initiated because the risk for yet additional seizures is very high (57 percent by one year and 73 percent by four years), with risk increasing proportionally after each subsequent recurrence as the time interval between seizures decreases. In contrast, immediate AED treatment at the time of the first unprovoked seizure is not well accepted and is debated.

For a patient with a first unprovoked seizure, the chance for a seizure recurrence can be estimated and stratified on the basis of clinical factors, with greater risk associated with a prior brain insult or lesion as the cause of the seizure, an EEG with epileptiform abnormalities, a significant brain-imaging abnormality, or a nocturnal seizure. Such risk stratification may help guide physicians counseling patients about their risks for seizure recurrence and options for management. In some instances, a patient's statistical risk for a seizure recurrence may approach that of patients for whom immediate AED treatment is generally accepted, such as those who have already experienced multiple seizures. A recent report from the International League Against Epilepsy (ILAE) promotes a new practical clinical definition of epilepsy that emphasizes the importance of estimating recurrence risk for individuals with a first unprovoked seizure.¹ The ILAE expanded the diagnosis of epilepsy beyond the prior standard requiring at least two unprovoked seizures, to encompass people with an unprovoked seizure and a high (at least 60 percent) risk for seizure recurrence over the subsequent 10 years. However, as our analysis indicates and the ILAE cautions, the lack of evidence with regard to specific risk factors and their interactions poses limitations.

Some of these risk factors may be independent predictors for risk of recurrence, whereas others (e.g., a prior brain lesion as a seizure cause, or a brain-imaging abnormality) likely are related. The relatively small numbers of subjects in studies addressing this issue limit the strength of evidence. Only two studies analyze evidence specifically with regard to additive effects or covariance of the risk factors for seizure recurrence after a first seizure, and come to somewhat different conclusions. One study noted that the only independent risk factor for seizure recurrence was an EEG with epileptiform abnormalities, and the other reported a remote symptomatic seizure etiology as the only independent risk factor. Because of this lack of evidence, caution is urged as regards the calculation of additive risk for seizure recurrence after a first unprovoked seizure. The ILAE report states as much: "No formula can be applied for additive risks since data are lacking on how such risks combine; such risks will have to be decided by individualized considerations."¹ Such caution also applies to decisions as regards AED treatment.¹

Indications for immediate AED treatment are based largely, but not only, on estimations of an individual's risk for a seizure recurrence.¹ Physicians planning to prescribe an AED for treatment should also carefully consider the drug's specific therapeutic and AE profiles on an individualized basis. Evidence indicates that immediate AED therapy is likely to reduce seizure recurrence risk for individuals with an unprovoked first seizure, particularly within the first two years. Such seizure recurrence prevention, even in the short term, may be important, with potentially greater implications for adults than for children. For adults, seizure recurrences may cause such serious psychological and social consequences as loss of driving privileges and limitations on employment. Still, one controlled Class II study comparing immediate AED treatment with treatment deferred until after a seizure recurrence found no significant difference in standard 2-year QOL measures. However, that study also noted that patients who were not immediately treated with AEDs were more likely to be restricted from driving.

The longer-term prognosis for patients with a first seizure as measured by whether patients maintain seizure freedom demonstrates no benefit for immediate AED treatment. Moreover, although individual seizure recurrences pose some risk for physical harm and even death, there is no evidence that immediate AED treatment reduces that risk or improves QOL. Also, the only study appraising the incidence of sudden unexplained death after an unprovoked first seizure demonstrates no advantage with immediate AED therapy.

¹ Fisher RS, Acevedo C, Arzimanoglou A, et al. A practical clinical definition of epilepsy. *Epilepsia* 2014;55:475–482.

This guideline was endorsed by the American Neurological Association and the World Federation of Neurology.

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