Medicine by the Numbers
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The NNT Group rating system:

Green:	Benefits greater than harms
Yellow:	Unclear benefits
Red:	No benefits
Black:	Harms greater than benefits

Antiepileptic Drugs After First Unprovoked Seizure

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IMMEDIATE TREATMENT WITH ANTIEPILEPTIC DRUGS AFTER FIRST UNPROVOKED SEIZURE

Benefits	*Harms*
1 in 10 did not have a seizure recurrence within five years	1 in 10 had an adverse event No deaths were prevented

Details for This Review

Study Population: Patients of any age with any type of first unprovoked seizure[1]

Efficacy End Points: Seizure recurrence; seizure remission; mortality

Harm End Points: Tiredness or drowsiness; gastrointestinal symptoms; depression or anxiety; dizziness or unsteadiness; headache; injury

Narrative: The incidence of single unprovoked seizures ranges from 23 to 61 per 100,000 person-years[2] and affects approximately 4% of the population by 80 years of age.[3] The incidence of another unprovoked seizure after an initial seizure ranges from 30% to 50%[3,4] and would categorize a patient as epileptic. Prescribing an antiepileptic drug after an initial unprovoked seizure might lower the probability of a recurrent seizure; however, these drugs are not curative and have potential complications,[3] making the decision to start an antiepileptic drug after a first unprovoked seizure clinically challenging.

This summary discusses the benefits and harms of starting patients on antiepileptic drugs following an initial unprovoked seizure.[1] Six studies totaling 1,634 participants (two studies with adults only, one with children only, and three with adults and children) were included in this review, and the follow-up period ranged from nine months to 16 years. Patients in these studies were randomized to immediate treatment with a first-generation antiepileptic drug, placebo, deferred treatment, or no treatment.

Two studies of 1,212 participants reported on the primary outcome of seizure recurrence within five years after initiation of an antiepileptic drug immediately following an unprovoked seizure. Participants randomized to immediate treatment had a statistically significantly lower probability of repeat seizure at five years (relative risk [RR] = 0.78; 95% confidence interval [CI], 0.68 to 0.89), which yielded a number needed to treat of 10. A secondary outcome, seizure recurrence risk, was also statistically significantly lower in the immediate treatment group at one year (RR = 0.49; 95% CI, 0.42 to 0.58) and at two years (RR = 0.69; 95% CI, 0.59 to 0.80). As for the risk of recurrent seizure during the 24 months following treatment, there was no difference between immediate drug treatment and control in terms of five-year remission at any time (RR = 1.02; 95% CI, 0.87 to 1.21), reflecting the short-term effect of antiepileptic drugs. The median time to seizure recurrence after randomization to the control group was 736 days compared with 1,165 days in the immediate treatment group. Antiepileptic drugs did not significantly affect overall mortality after a first seizure (RR = 1.16; 95% CI, 0.69 to 1.95). When compared with deferred treatment, there was a higher risk of adverse events in the immediate treatment group (RR = 1.64; 95% CI, 1.37 to 1.97), with a number needed to harm of 10.

Caveats: Although six trials were included in this review, only two studies provided most of the long-term data used for the

primary outcome; the other studies were smaller and/or had short follow-up periods. Authors from the two main studies included in this review are also authors of this meta-analysis, which might suggest an inherent bias. All of the studies were pragmatic trials, and participants included had different types of seizures. Only first-generation antiepileptic drugs (except for lamotrigine [Lamictal]) were included, so results may be different if later-generation medications are administered.

Initiating antiepileptic drugs immediately following a first unprovoked seizure reduced the risk of a subsequent seizure, but did not affect the number of patients who achieved remission in the long term or impact overall mortality. Adverse events were more common in the treatment group, although this evidence was graded as low to moderate. Overall, the results of this meta-analysis support those reported in a previous meta-analysis,[5] as well as the clinical guideline recommendation from the American Academy of Neurology and American Epilepsy Society.[6] The decision about whether to start immediate drug therapy should be individualized based on shared decision making between the patient and the physician.

This series is coordinated by Dean A. Seehusen, MD, MPH, *AFP* Contributing Editor, and Daniel Runde, MD, from the NNT Group.

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