

## **Do antiepileptic drugs increase the risk of depression or suicidality? - Yes**

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Psychiatric adverse effects (PAEs), including depression, are reported in 15–20% of patients with epilepsy on antiepileptic drugs (AEDs). In 2008 the FDA issued a warning of increased risk for suicidal ideation and behavior during treatment with AEDs, based on findings of a meta-analysis of 199 trials of 11 AEDs. An expert consensus statement by an ILAE task force concluded that some (but not all) AEDs can be associated with PAEs which can lead to suicidal ideation and behavior. The actual suicidal risk was considered very low, but remained to be established. PAE risk varies considerably with different AEDs; GABAergic effects play an important part in depression. Barbiturates, vigabatrin, tiagabine, topiramate, levetiracetam, zonisamide and felbamate seem to be associated with higher risks compared with other AEDs. In a retrospective study 16% of 1394 outpatients on a second-generation AED experienced PAEs. The average rate for a single AED was 8.4%; 6.1% resulted in dosage change and 4.3% led to AED discontinuation. There were fewer PAEs with gabapentin and lamotrigine, and more with levetiracetam and tiagabine. Low rates of PAEs were seen with vigabatrin, felbamate, oxcarbazepine; intermediate rates with topiramate and zonisamide. Non-AED predictors, most significantly prior psychiatric history, affected the rates of AED-related PAEs, but when these were controlled for, relative PAE rates for the different AEDs remained similar. Patients with clinically relevant risk factors are relatively more vulnerable to AED PAEs, but the main finding reported in multiple studies remains robust: AEDs increase depression and suicidality risk.