

AED choices in elderly patients



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When to start

- Usually > 1 unprovoked SZ
- After a single unprovoked SZ
 - brain lesion on imaging
 - an epileptiform on EEG
 - at patient's or family's request



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FIRST Seizure Trial Group

- Old age was found to be a significant predictor of seizure recurrence.

	No. pts.	Remissions			
		1 year		2 years	
		No. (%)	RR* (95% CI)†	No. (%)	RR* (95% CI)†
Treatment after first seizure					
No‡	204	170 (83.3)		122 (59.8)	
Yes	215	186 (86.5)	1.17 (0.95–1.45)	146 (67.9)	1.22 (0.97–1.56)
			1.03 (1.28–0.85)§		1.04 (1.30–0.82)§
Age (yrs)					
<16	114	95 (83.3)	0.80 (0.63–1.01)	72 (63.2)	0.90 (0.68–1.18)
16–60‡	277	241 (87.0)		182 (65.7)	
>60	28	20 (71.4)	0.67 (0.42–1.05)	14 (50.0)	0.69 (0.40–1.19)

Musicco M, et al. NEUROLOGY 1997;49:991-998



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What to start?

No seizure

- Efficacy

No side effects

- PK-PD
- Comorbidity
- Drug-drug interaction (polytherapy)
- Tolerability
- Cognitive SE

**Elderly are more prone to the adverse effects.
"Start low, go slow"**



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Efficacy: Treatment responding rate

Table 1 Pharmacological outcomes in newly diagnosed epilepsy by age at starting treatment

Patient groups	Age (years)	<i>n</i>	Remission (%)	Relapse (%)	Uncontrolled (%)
Adolescent	< 20	170	65*	12	23
Adult	20–64	520	53	4	43
Elderly	> 64	90	85**	1	14

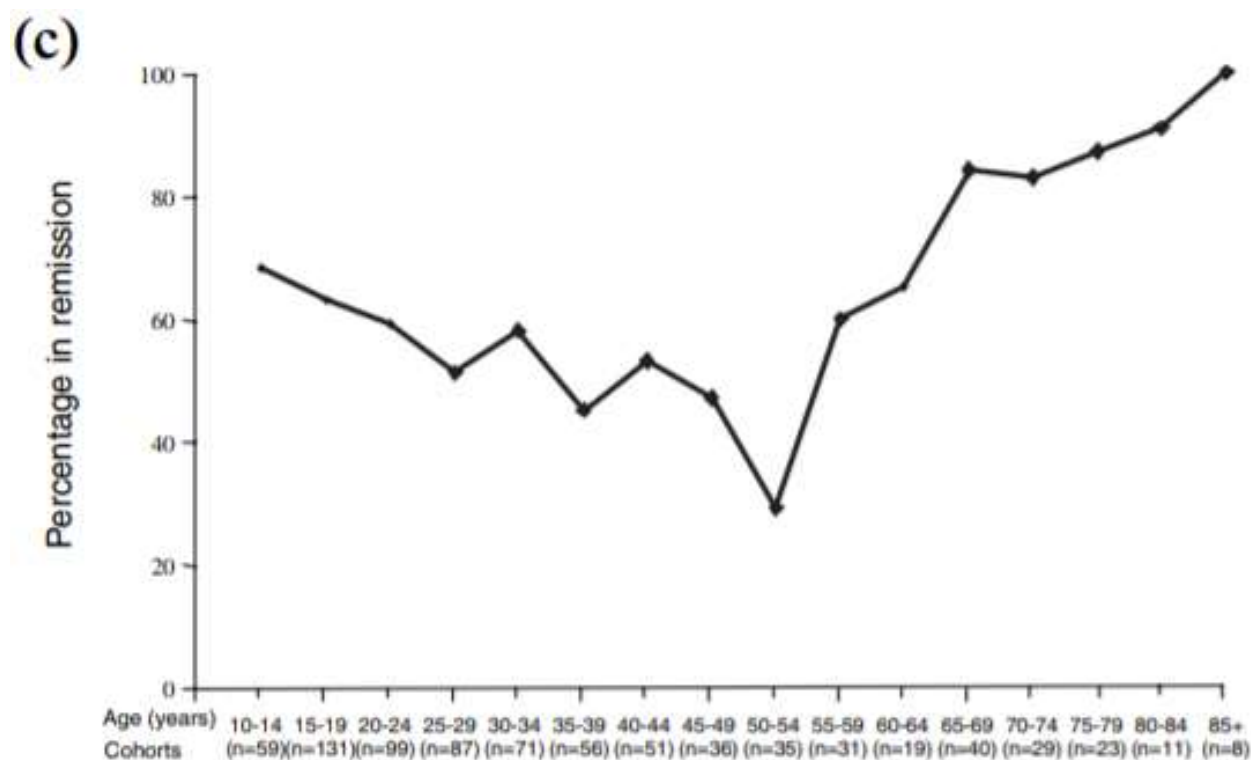
Up to 80% of elderly onset patients respond to AEDs.

Mohanraj R, Brodie MJ. European Journal of Neurology 2006, 13: 277–282



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Efficacy: Remission rate



Epilepsy in the elderly generally responds well to treatment.

Mohanraj R, Brodie MJ. European Journal of Neurology 2006, 13: 277–282



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AED: Old generation

	Advantages	Disadvantages
Phenobarbital (PB)	Broad spectrum Once daily Cheapest	Sedation Cognitive impairment Behavioral problems Enzyme induction, Bone loss
Phenytoin (PHT)	Once daily No titration Cheap	Sedation Rash **Saturation kinetics Enzyme induction, Bone loss
Carbamazepine (CBZ)	Goal standard for focal SZ Studied in elderly Relatively cheap	Rash Enzyme induction, Bone loss **HypoNa **Slow titration
Na Valproate (VPA)	Broad spectrum Rapid titration Relatively cheap	Tremor Weight gain Enzyme inhibition, Bone loss **Parkinsonism



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Bone health in epilepsy

- ↑1.3-3.8 RR of osteopenia
- ↑1.7-3.8 RR of osteoporosis
- EIAEDs
 - ↓ serum Vit D
 - Among EIAEDs, CBZ have the least effect to bone.
- VPA also ↓ serum Vit D
- Newer AEDs have had no evidence of impairing bone health.
- Long term use >12 years -- ↑ bone disease



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Bone loss

Recommendation (limited available data)

- Screening DEXA scan in high risk AEDs; EIAEDs & VPA (no clear interval of the screening)
- Supplement both calcium and Vit D
 - (Ideal dosage is still lacking)
 - Calcium 1000 – 1500 mg/d
 - High dose Vit D 4000u/d



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AED: New generation

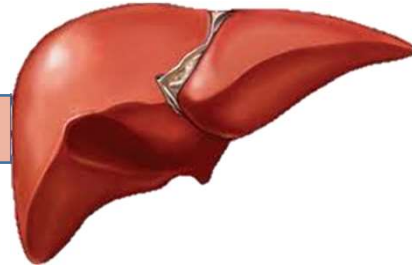
	Advantages	Disadvantages
Lamotrigine	Broad spectrum Good tolerability Few interactions	Slow titration Rash
Topiramate	Broad spectrum Weight loss	Slow titration Cognitive impairment Renal stone
Oxcarbazepine	Good tolerability	Rash HypoNa
Levetiracetam	Broad spectrum No interactions Rapid titration	Behavioral problems
Zonisamide	Broad spectrum Once daily No interactions	Slow titration Rash Renal stones

None of which have superior efficacy to the old gen



AED to avoid in liver/renal failure

► Hepatic Failure



Benzodiazepines

Carbamazepine

Felbamate

Phenytoin

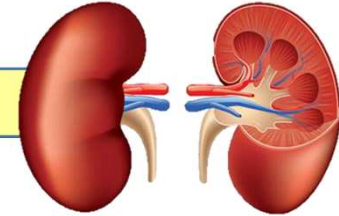
Phenobarbital

Primidone

Rufinamide

Valproic acid and its derivatives

► Renal Failure



Gabapentin

Levetiracetam

Pregabalin

Vigabatrin



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Hyponatremia

- Oxcarbazepine > Carbamazepine
- Esp. combination w/ thiazide or other diuretics
- Usually asymptomatic



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Double-blind, RCT

References	Investigated drugs	Main findings
Brodie et al.	LTG vs. IR-CBZ	LTG equally effective and better tolerated than CBZ
Saetre et al.	LTG vs. CR-CBZ	Equal efficacy and tolerability
Werhahn et al.	LTG vs. LEV vs CR-CBZ	Equal efficacy; CBZ less tolerated
Ramsay et al.	TPM 50 mg/day vs. 200 mg/day	Good efficacy; sufficient tolerability for both dosages



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Open label studies

References	Investigated drugs	Main findings
Kutlu et al.	LEV	Good efficacy and tolerability
Belcastro et al. (2008)	LEV	Good efficacy and tolerability
Belcastro et al. (2007)	LEV	Good efficacy and tolerability



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Neurology[®]

April 18, 2017; 88 (16 Supplement) APRIL 27, 2017

Efficacy and tolerability of lacosamide monotherapy in elderly patients with newly diagnosed epilepsy: subgroup analysis of a non-inferiority trial versus controlled-release carbamazepine (P5.232)

Felix Rosenow, Manuel Toledo, Michel Baulac, Kiyohito Terada, Ting Li, Melissa Brock, Simon Borghs, Marc De Backer, Konrad Werhahn

- Efficacy: LCM similar to CBZ-CR
- Tolerability: better than CBZ-CR



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Zonisamide in the management of epilepsy in the elderly

This article was published in the following Dove Press journal:

Clinical Interventions in Aging

8 June 2015

Number of times this article has been viewed

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- Patients aged ≥ 65 years
- no new/unexpected side effects.
- ZNS may be effective and well tolerated as monotherapy or adjunctive AEDs in the elderly

Keywords: zonisamide, elderly, epilepsy, safety, efficacy

Romigi A, et al. Clinical Interventions in Aging 2015:10 931–7



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Efficacy and safety of perampanel in the subgroup of elderly patients included in the phase III epilepsy clinical trials



Ilo E. Leppik^{a,*}, Robert T. Wechsler^b, Betsy Williams^c,
Haichen Yang^d, Sharon Zhou^c, Antonio Laurenza^d

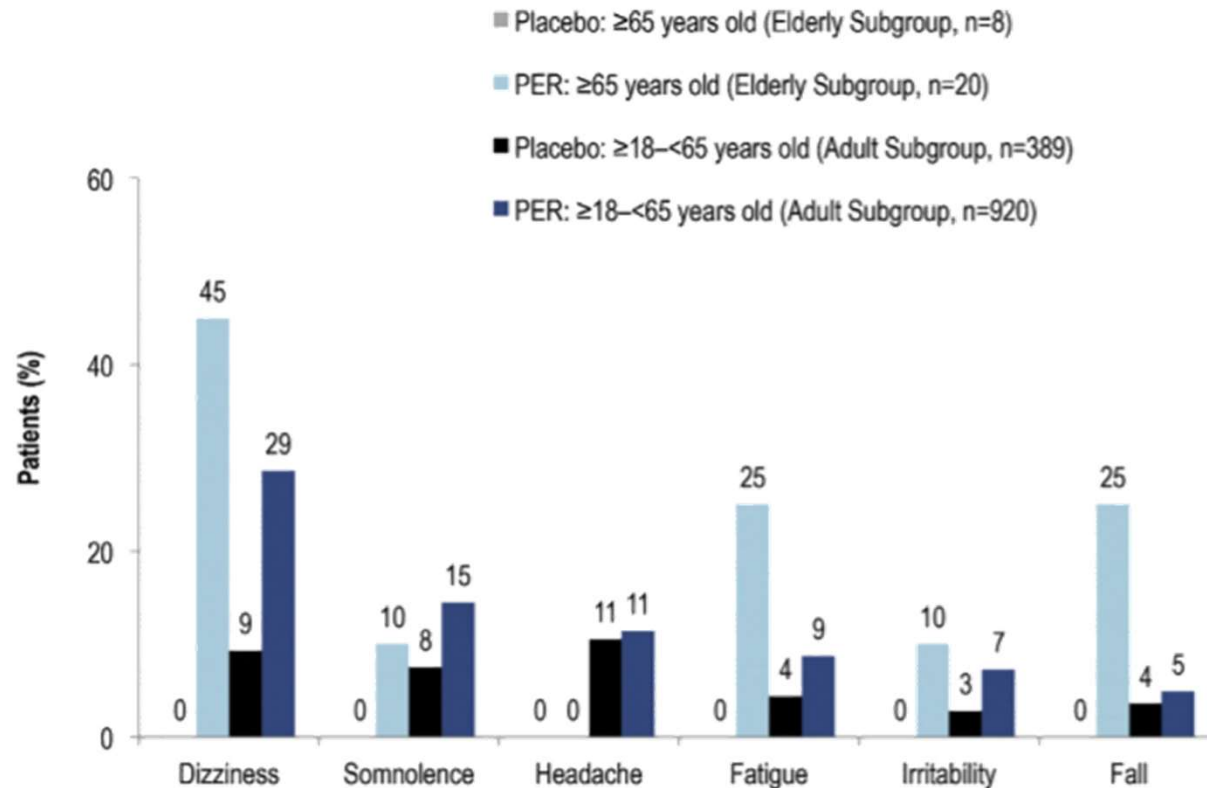
Summary Clinical data regarding use of antiepileptic drugs in the elderly are generally scarce. Therefore, a subanalysis of subjects aged ≥ 65 years who participated in the 3 phase III perampanel studies was undertaken to determine efficacy and safety in these patients. Efficacy (change in seizure frequency/28 days and 50% responder rate) in the elderly subgroup was found to be consistent with the adult population. Adverse event rates were also largely similar, with some exceptions. Because risks of falls, dizziness, and fatigue were greater in the elderly, careful titration of perampanel in patients aged ≥ 65 years is suggested, especially at higher

P: subgroup aged > 65
I: phase III perampanel study
C: determined efficacy and safety in elderly compare to adult population and placebo

Leppik IE, et al. Epilepsy Research (2015) 110, 216-20



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O: efficacy similar to adult population
Side effect of dizziness, fall, fatigue are greater than in young adults

Leppik IE, et al. Epilepsy Research (2015) 110, 216-20



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Summary from trials

- Efficacy: NO significantly different between old (CBZ-CR) and new generation (LTG, LEV, LCS, PER).
- Tolerability:
 - seems to be better in new generation AEDs.
- New generation AEDs need further RCT studies to compare efficacy and side effects.



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Strategic recommendation

- No seizure and no (minimal) side effects
- PK-PD, comorbidity, drug-drug interaction should be 1st considered
- **Slow titration** to an initial maintenance of LTG 50 mg bid or LEV 500 mg bid.
- If do not tolerated to 1st drug → switch to 2nd AEDs
- If SZs continue, 2nd monotherapy with a different MOA should be tried.



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- If AED causes neurotoxicity (eg, dizziness, unsteadiness, tremor), a small ↓ dose back to previous tolerated dose is recommended.
- Surgical treatment for refractory epilepsy can also be an option for older people.
- Treatment is usually lifelong as any causes in old age are not likely to remit.



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Thank you for your attention



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