EST 30th ANNIVERSARY ANNUAL MEETING

Epilepsy in the elderly:

Diagnostic complexity and treatment consideration

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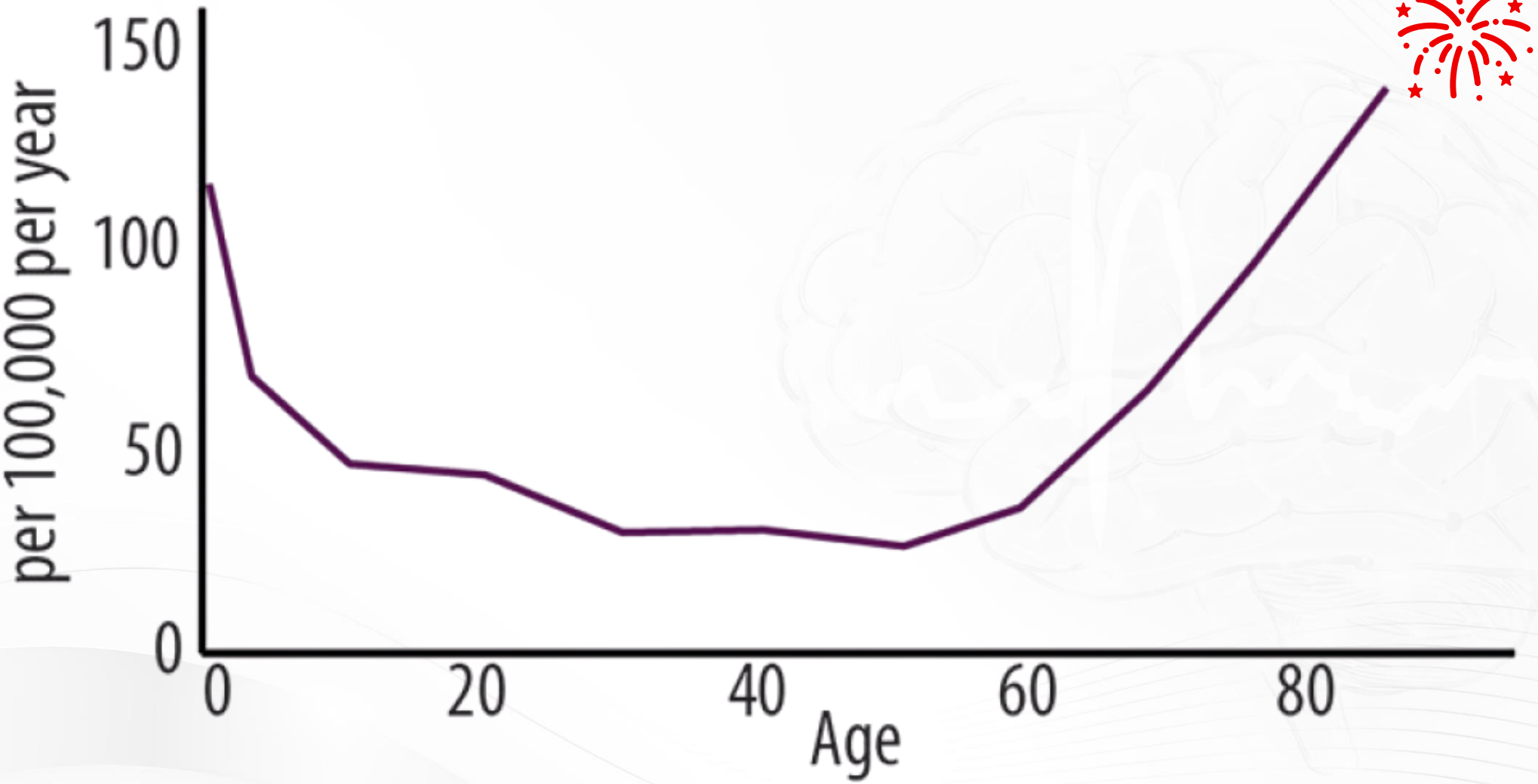
Why elderly epilepsy matter?

Diagnostic complexity

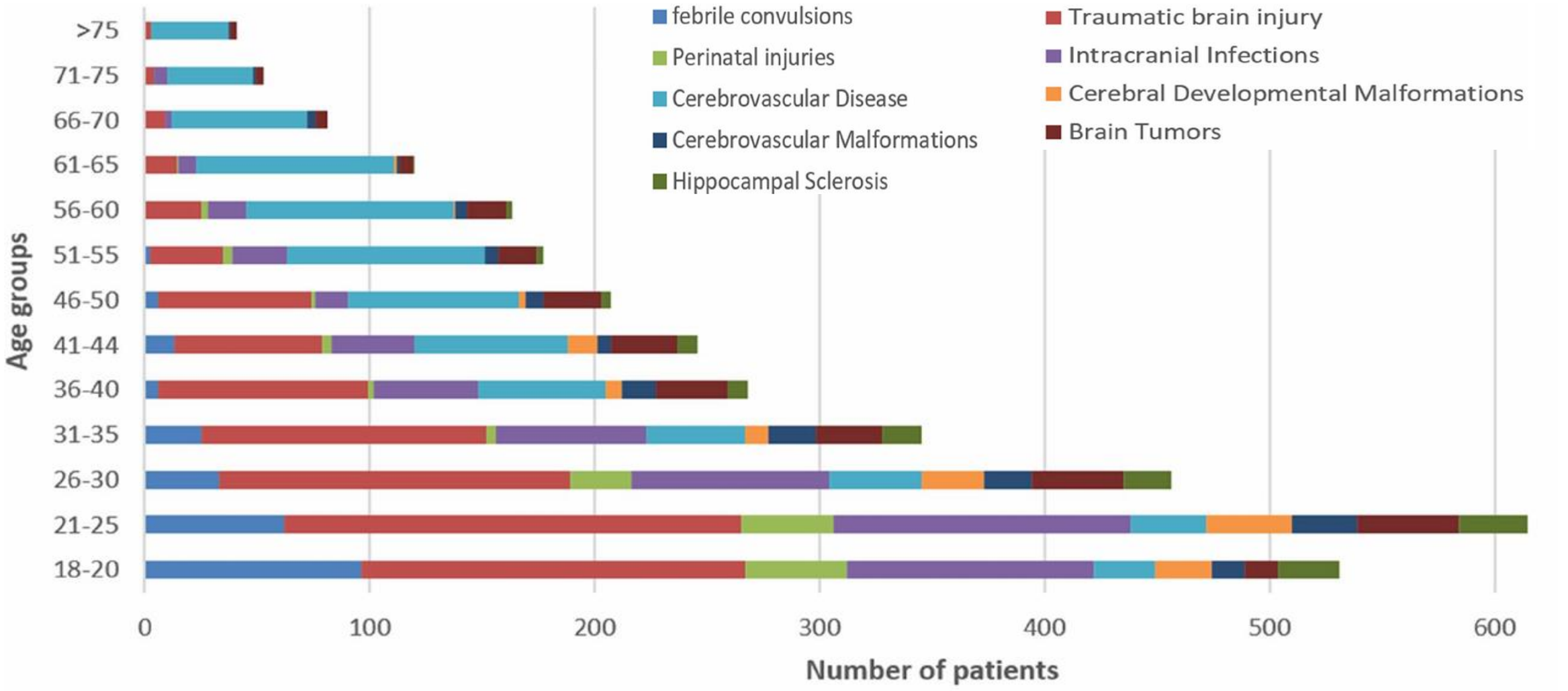
Treatment consideration

Why elderly epilepsy matter?



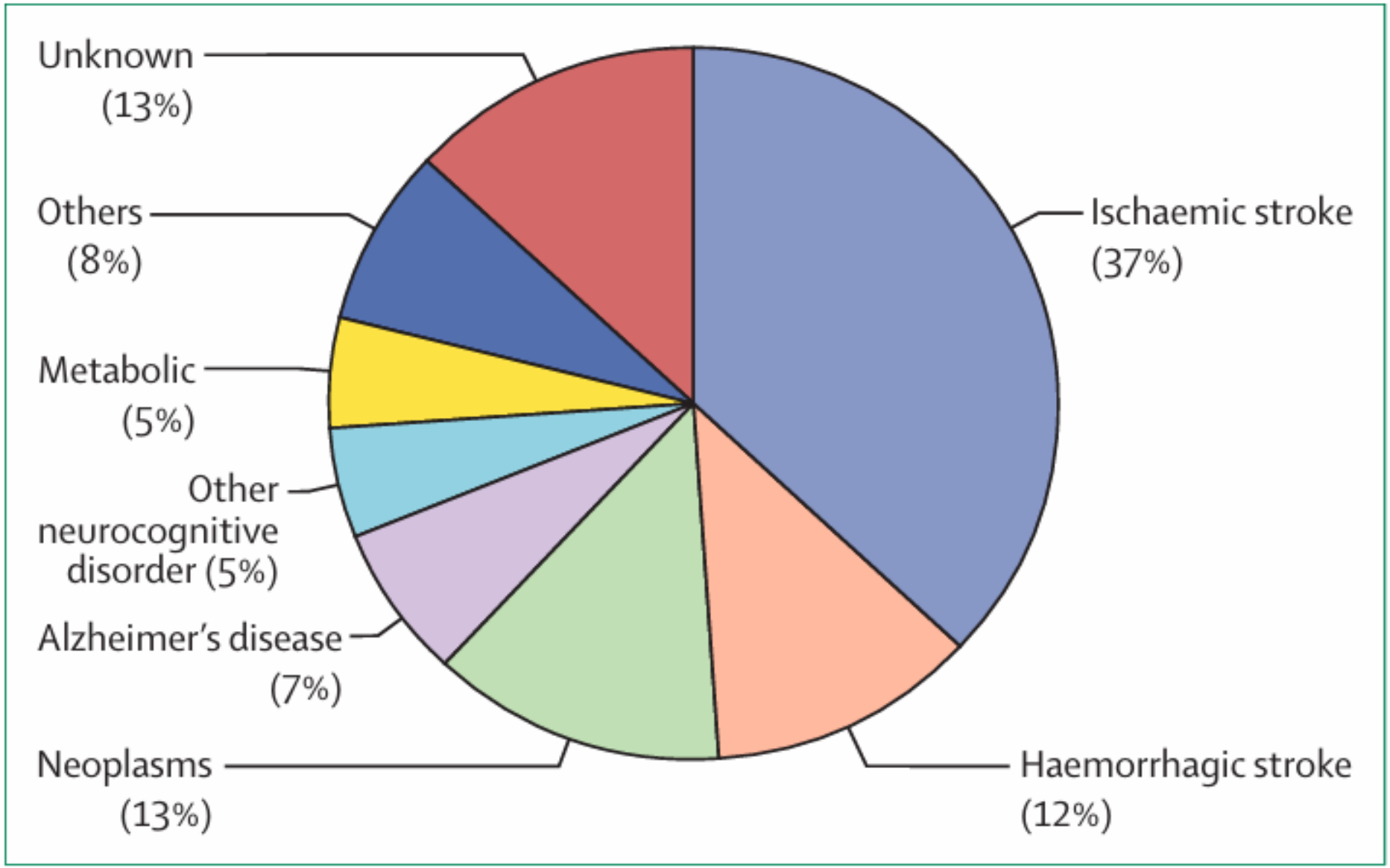
Practical neurology, October 2022

Distribution of the Main Potential Causes among Adult-Onset Epilepsy Patients Across Different Age Groups



BMC Neurology (2025) 25:512

Causes of new-onset epilepsy in older people



Lancet 2020; 395: 735–48

Factors that increase risk of late onset epilepsy

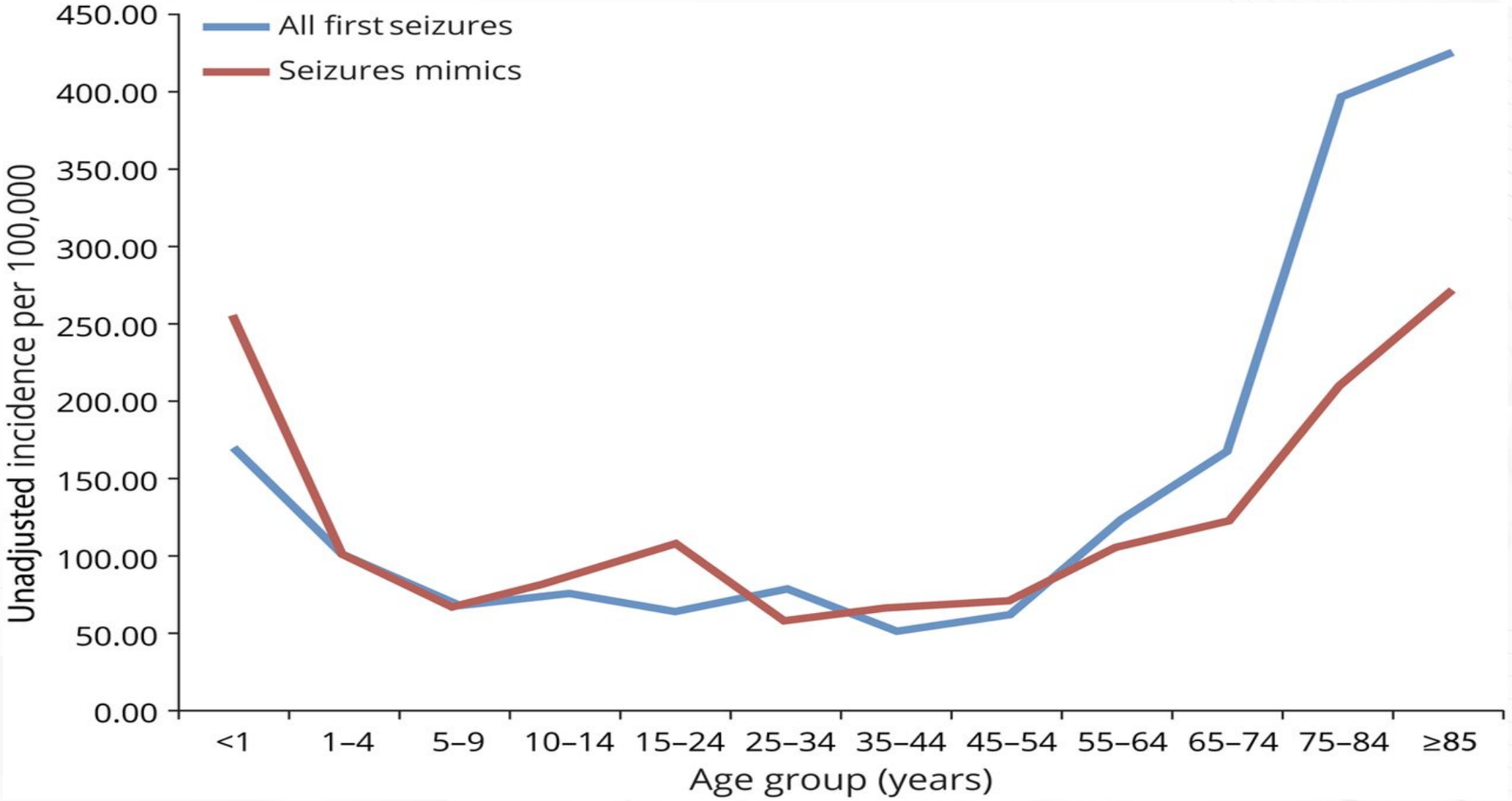
Risk factor		Hazard ratio (95 % confidence interval)
Diabetes*		1.43 (1.14 – 1.80)
Hypertension		1.26 (1.05 – 1.51)
Smoking		1.09 (1.01 – 1.17)
Dementia		2.68 (2.19 – 3.28)
Apolipoprotein E e4 allele	1 copy	1.22 (1.02 – 1.46)
	2 copies	1.93 (1.32 – 2.81)
White matter hyperintensities		1.28 (1.06 – 1.54)
Cortical Atrophy#		1.87 (1.16 – 3.02) ˆ
Reduction in plasma $A\beta_{42}/A\beta_{40}$ over time		2.30 (1.27 – 4.17)

Legend: *Statistically significant among Black population. # measured as total cortical volume. ˆ Odds ratio. Above risk estimates from.

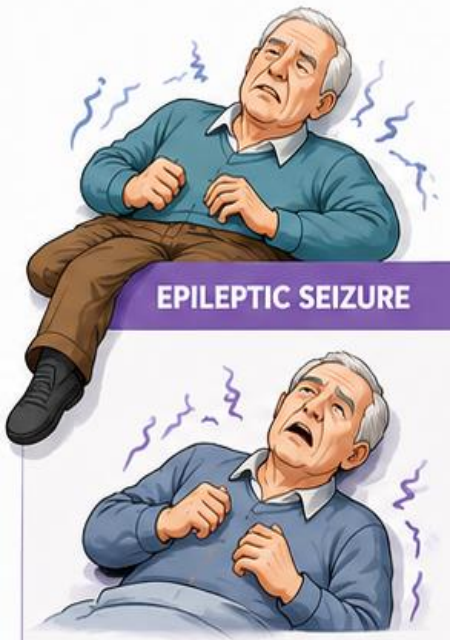
Seizure: European Journal of Epilepsy 128 (2025) 68–73

Diagnostic complexity

Incidence of first seizures and seizure mimics



Neurology. August 4, 2020 issue95 (5) e576-e590



COMMON DIFFERENTIAL DIAGNOSIS OF SEIZURES IN OLDER ADULTS

Not all paroxysmal events are seizures. Careful history and targeted evaluation are key.

Always consider seizure if event is stereotyped, recurrent, and unexplained.

EPILEPTIC SEIZURE

Sudden, uncontrolled abnormal electrical discharge in the brain

Features
- Stereotyped
- Brief (seconds–minutes)
- Often with postictal confusion, drowsiness, or fatigue
- May have tongue bite, incontinence, injury

Types in Older Adults
- Focal aware (simple partial)
- Focal impaired awareness (complex partial)
- Focal to bilateral tonic–clonic
- Generalized onset

Clues
- Occurs with standing, dehydration, pain, or emotion
- Hypotension, bradycardia, arrhythmia
- Trigger identifiable

Check BP, ECG, orthostatic vitals

TRANSIENT ISCHEMIC ATTACK (TIA)

Transient neurological dysfunction due to focal cerebral ischemia

Features
- Sudden focal deficit (weakness, numbness, speech difficulty, visual loss)
- No loss of consciousness
- Symptoms resolve within minutes–hours (usually < 1 hour)

Clues
- Vascular risk factors (HTN, DM, AF, HLP, smoking)
- Negative motor phenomena (loss of function)
- ABCD² score helps risk stratification

Urgent evaluation to prevent stroke

PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES)

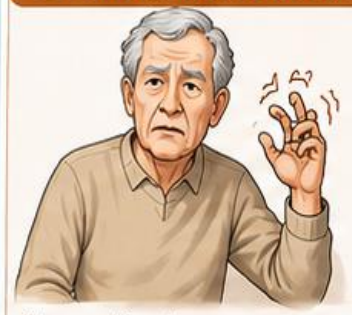
Events that resemble seizures but are psychological in origin

Features
- Longer duration
- Asynchronous or side-to-side movements
- Eyes closed during event
- No postictal confusion (may be emotional)
- Recall may be preserved

Clues
- History of psychiatric disorders
- Multiple ED visits with normal tests
- Events triggered by stress or conflict
- Video-EEG is the gold standard

Video-EEG is the gold standard

MOVEMENT DISORDERS (e.g., TREMOR, MYOCLONUS, DYSTONIA, PARKINSONISM)



Abnormal involuntary movements that may mimic seizures

Features
- Variable movements
- Often stimulus-sensitive
- No alteration in consciousness
- Long-standing history
- May occur in specific body parts

Clues
- Known movement disorder (e.g., Parkinson's disease)
- Movements are suppressible
- No postictal state

Careful observation and exam

METABOLIC DISTURBANCES

Electrolyte imbalance, hypoglycemia, hepatic or uremic encephalopathy

Features
- Altered mental status
- May have asterixis, myoclonus, or stiffness
- Fluctuating course
- Often with systemic illness

Clues
- History of kidney, liver, or endocrine disease
- Abnormal labs
- Medication toxicity

Check labs: glucose, Na, Ca, renal, liver function

PARASOMNIAS (e.g., REM SLEEP BEHAVIOR DISORDER)

Abnormal behaviors arising from sleep, not epilepsy

Features
- Occur during sleep or sleep–wake transition
- Confusion or dream enactment
- No postictal state
- Often in REM sleep behavior disorder

Clues
- History from bed partner
- Associated with neurodegenerative diseases (e.g., PD, DLB, MSA)
- Polysomnography helps diagnosis

Consider sleep study if suspected

Differential Diagnosis Matrix

Clinical Features	Focal Seizure	Syncope	Limb-Shaking TIA	Delirium / Dementia
Stereotypical nature of events	✓	✗	✗	✗
Prolonged post-event confusion	✓	✗	✗	✓
Provoked by posture / micturition	✗	✓	✗	✗
Presence of headaches post-event	✓	✗	✗	✗
Focal motor signs present	✓	✗	✓	✗

CRITICAL WARNING: Non-convulsive status epilepticus must be suspected in any older patient presenting with unexplained fluctuating awareness and behavioral changes.

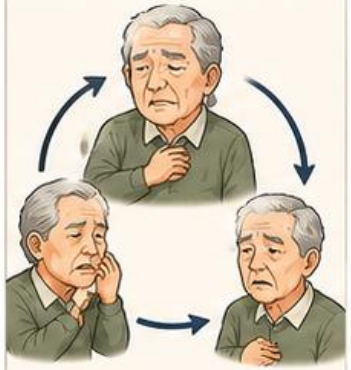
RED FLAGS FOR SEIZURE

These features increase the likelihood that an event is an **epileptic seizure** rather than a non-epileptic mimic.

KEY MESSAGE

Careful history from patient and witness is crucial to identify true seizures and underlying causes.

1 Stereotyped events

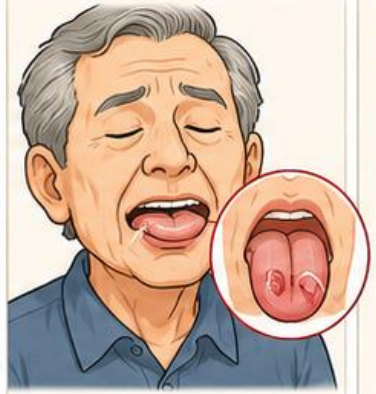


- Events look the same every time in semiology, duration and recovery.
- Reproducible pattern suggests epileptic seizure.

2 Recurrent and unexplained

- Occurs more than once without clear provocation.
- Recurrent unexplained events raise concern for seizure.

3 Tongue bite (lateral)



- Lateral tongue bite is highly specific for generalized tonic–clonic seizures.
- Tip-of-tongue bite is less specific.

4 Incontinence

- Urinary incontinence during the event supports generalized seizure.
- Not specific alone, but important when present with other features.

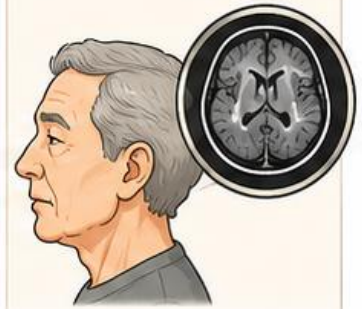
5 Postictal confusion or fatigue

- Confusion, disorientation, or extreme sleepiness after the event (minutes to hours).
- Reflects postictal state and supports seizure.

6 Focal onset with progression

- Starts in one part of the body or with a focal symptom, then spreads.
- Suggests focal aware seizure progressing to focal or bilateral tonic–clonic seizure.

7 New onset in older adult (evaluate for (structural cause)



- New seizures after age ~60 years are more likely to have an underlying structural cause.
- Neuroimaging is essential.

IMPORTANT

No single feature is 100% diagnostic. The combination of these red flags plus careful history increases the probability of true seizure.

ALWAYS CONSIDER

- Detailed history from patient and witness
- Review medical history and medications
- Rule out provoking factors (metabolic, infection, drugs)
- Neuroimaging in new onset or focal seizures
- EEG to support diagnosis and classification

GOAL

Identify true seizures early, address underlying causes, and reduce risk of recurrence and complications.

Drugs Reported as Possible Causes of Seizures

(from LICE – SIMG Guidelines)

CLASS OF DRUGS	EXAMPLES OF MOLECULES	
Opiate analgesics	Tramadol, morphine, pentazocine	
Anti-asthmatics	Theophylline, salbutamol	
Antibiotics	Cephalosporins, fluoroquinolones, erythromycin, penicillins, gentamicin	
Antidepressants	Tricyclics, SSRIs, bupropion, mianserin, trazodone, venlafaxine	
Antimalarials	Chloroquine, mefloquine	
Antineoplastics	Busulfan, cisplatin, chlorambucil, methotrexate, vinblastine, vincristine	
Antipsychotics	• **Typical**	Haloperidol, chlorpromazine, fluphenazine
	• **Atypical**	Clozapine, olanzapine, risperidone
Antihistamines	Chlorphenamine, diphenhydramine	
Antivirals	Acyclovir	
Cardiovascular	Digoxin, beta-blockers (metoprolol, propranolol), quinidine, disopyramide, mexiletine	
NSAIDs	Diclofenac, ibuprofen, indomethacin, ketoprofen, naproxen, piroxicam	
Drugs of abuse	All, in particular ethanol and cocaine	
Immunosuppressants	Azathioprine, corticosteroids, cyclosporine, interferon-A, tacrolimus	
Hypoglycemic agents	Chlorpropamide, glipizide, insulin	
Sympathomimetics	Amphetamines, ephedrine, phenylephrine	
Others	Baclofen, cimetidine, cycloserine, dantrolene, desmopressin, disulfiram, domperidone, erythropoietin, fampridine, flumazenil, probenecid	

ⓘ **NSAIDs:** Non-steroidal anti-inflammatory drugs.

Table 1

Clinically observed signs in convulsive syncope and convulsive seizures.

Common features	Convulsive syncope	Convulsive seizure
Number of Myoclonic Jerks*^	<10	>20
Rhythmic myoclonic jerks*	Absent (sporadic)	Present
Bilateral myoclonic jerks	Present in 78 % patients	Present in all patients
Loss of body tone*	Always	Never
Tonic Posturing	Present in 65 % patients	Present in all patients

Legend: * Features that can help differentiate the two conditions with high certainty. ^ 10/20 rule: Less than 10 myoclonic jerks indicate syncope and more than 20 a convulsive seizure.

Investigation in late onset epilepsy

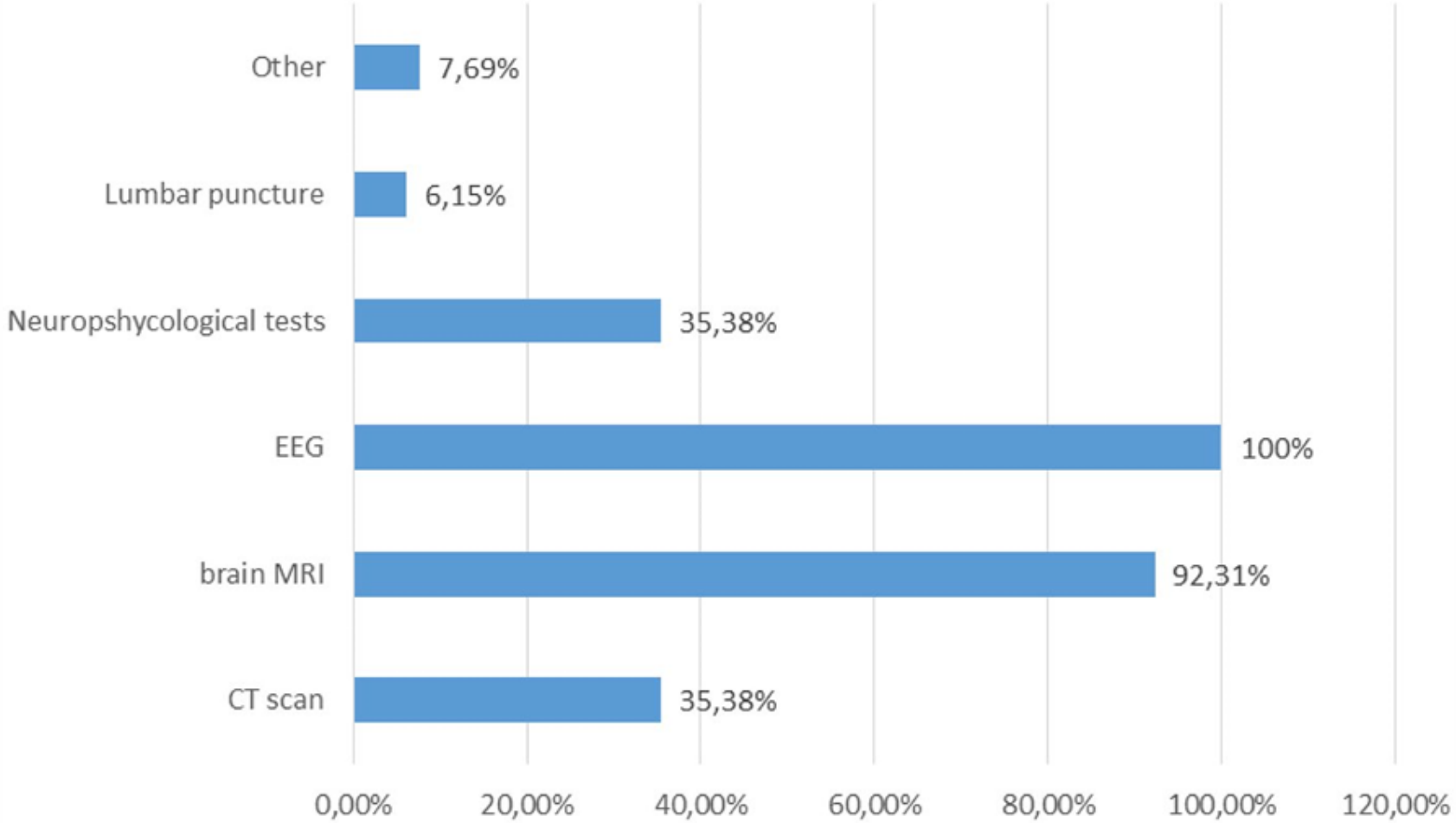


FIGURE 2 Answers to question 3 (multiple choice available): *Which kind of instrumental and laboratory diagnostic tools do you use in patients with LOE during the first evaluation at your center?*

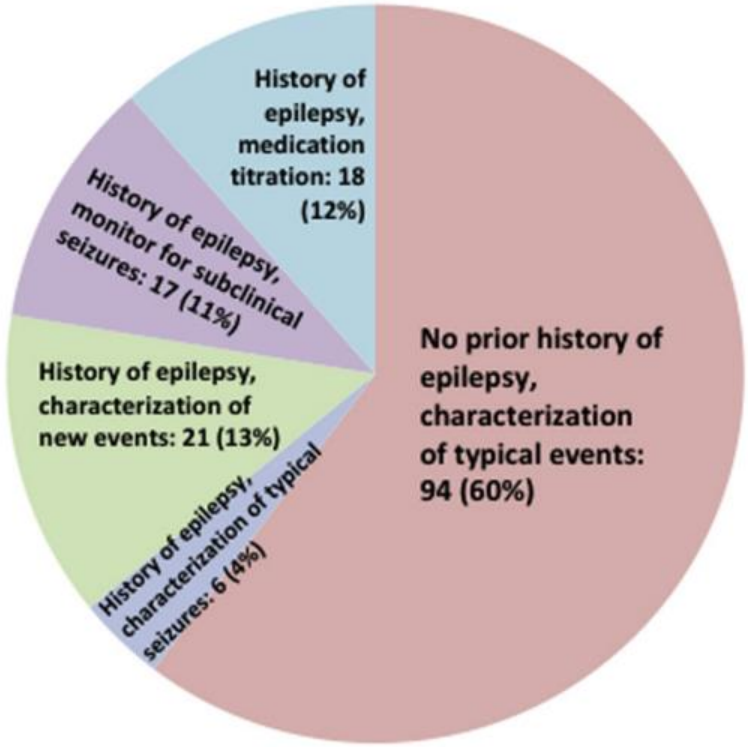
Epilepsia Open. 2025;10:1639–1647.

Investigation in late onset epilepsy

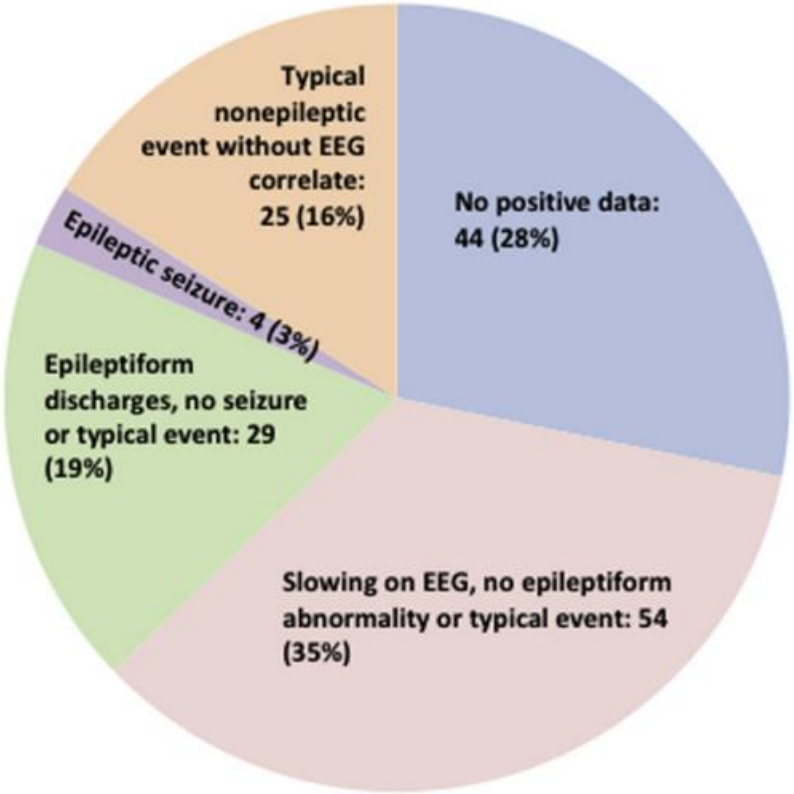
Diagnostic yield of ambulatory EEGs in the elderly

Benjamin Tolchin, Jong Woo Lee, Milena Pavlova, Barbara A. Dworetzky, Rani A. Sarkis *

Department of Neurology, The Edward B. Bromfield Epilepsy Program, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA



Reasons for obtaining ambulatory EEGs



Breakdown of findings on ambulatory EEG

Clin Neurophysiol. 2017 Jul;128(7):1350-1353.

Investigation in late onset epilepsy

Table 1
Ambulatory EEG results. Studies were performed for patients with or without a known history of epilepsy. Studies performed on patients with a known history of epilepsy were obtained to characterize a new event type or to monitor epileptic activity before or after down-titration of an anti-seizure medication.

	Patients without known history of epilepsy (%)	Patients with known history of epilepsy (%)	Total (%)
Total	94 (100)	62 (100)	156 (100)
Abnormal	60 (64)	52 (84)	112 (72)
Focal slowing	53 (56)	45 (73)	98 (63)
Epileptiform	15 (16)	27 (44)	42 (27)
Seizure	2 (2)	2 (3)	4 (3)
Typical nonepileptic event	18 (19)	7 (11)	25 (16)
Diagnostic finding: epileptiform discharge, epileptic seizure, and/or typical nonepileptic event	30 (32)*	28 (45)*	58 (37)*
Changed management	15 (16)	18 (29)	33 (21)

* Some patients had both typical nonepileptic events and epileptiform abnormalities on EEG.

Table 2
Diagnostic yield broken down by age category (patients aged 60–74 vs. patients aged 75 and up). Fisher's exact test yields a two-sided *p*-value of 0.825, indicating no statistically significant difference between yields in different age groups.

EEG findings	Patients aged 60–74 (%)	Patients aged 75+ (%)	All patients (%)
No positive data	26 (27)	18 (31)	44 (28)
Focal slowing only	34 (35)	20 (34)	54 (35)
Epileptiform discharges, no seizures or typical events	18 (18)	11 (19)	29 (19)
Epileptic seizures	2 (2)	2 (3)	4 (3)
Typical nonepileptic event	18 (18)	7 (12)	25 (16)
Total	98 (100)	58 (100)	156 (100)

Clin Neurophysiol. 2017 Jul;128(7):1350-1353.

Investigation in late onset epilepsy

Video-EEG Monitoring in the Elderly: A Review of 94 Patients 18 hr

*Alexandra E. McBride, †Tina T. Shih, and †Lawrence J. Hirsch

TABLE 1. *Reasons for admission*

Diagnosis of paroxysmal events	56%
Characterization of known seizures	20%
Evaluation for subclinical seizures or nonconvulsive status epilepticus	15%
Presurgical evaluation	6%
Medication adjustment or toxicity	3%

TABLE 2. *Results*

Epileptic seizures	46
Partial onset ± secondary generalization	45
Generalized onset	1
Nonepileptic seizures	27
Physiologic	14
Cataplexy	1
Hypotensive episode	1
Nocturnal confusion	1
Episodic vomiting	1
Myoclonic jerks	2
TIA	2
Behavioral spell[a]	6
Psychogenic	13
No events	30

N = 99 patient admissions. Of note, four patients had both epileptic events and nonepileptic events.

TIA, transient ischemic attack.

Epilepsia. 2002 Feb;43(2):165-9.

Investigation in late onset epilepsy

- Electroencephalography
  - 17% - 83% of neurologically healthy seniors show abnormal EEG.
  - Focal and diffuse slowing is common.
  - In epileptic seniors, routine EEG is normal up to 52% of the time

An abnormal EEG in an older adult **does not** guarantee epilepsy;
A normal EEG does not rule it out.
Context is everything

Seizure: European Journal of Epilepsy 128 (2025) 90–121

Investigation in late onset epilepsy

- Electroencephalography
  - Up to 45% of captured clinical events in geriatric long-term monitoring (LTM) are psychogenic non-epileptic seizure (PNES) or physiological non-epileptic events
  - Geriatric PNES signature
    - Duration: frequently lasts > 5 minutes
    - Motor presentation: often presents as fine, low-amplitude tremors or alternating movements rather than aggressive thrashing
    - Responsiveness: features prolonged blank spells with variable, fluctuating unresponsiveness, mimicking focal impaired awareness

Seizure: European Journal of Epilepsy 128 (2025) 90–121

Neuroimaging (CT/MRI) Features in Elderly Patients with Seizures

Structural brain abnormalities are common, with vascular lesions and atrophy being the most frequent findings.

CT (n = 201) — 201 patients

MRI (n = 43) — 43 patients

Overall Focal Lesions
CT: 48.8%
MRI: 55.8%

1 Types of Focal Lesions (% of patients)

	CT (n=201)	MRI (n=43)
Ischemic stroke	45.9%	28.0%
Intracranial hemorrhage (ICH)	18.4%	24.0%
Granuloma	17.3%	24.0%
Space occupying lesion	15.3%	20.0%
Gliosis	3.1%	4.0%

Space Occupying Lesions – Subtypes (% of patients)

Low grade glioma	1.0% / 2.0%	Metastases	1.0% / 1.0%
High grade glioma	1.5% / 1.0%	Arachnoid cyst	1.5% / 0%
Meningioma	2.5% / 1.0%	Diffuse edema	10.4% / 9.3%

2 Vascular Lesions

Ischemic Stroke – Type (% of patients)

	CT (n=201)	MRI (n=43)
Old infarction	12.4%	57.2%
Fresh infarction	9.0%	42.8%
Old + Fresh infarction	1.0%	–

Type of ICH (% of patients)

Acute cerebral hemorrhage	5.0%	2.3%
Subarachnoid hemorrhage	1.5%	0%
Subdural hemorrhage	1.0%	0%
Extradural hemorrhage	0.5%	0%
SAH + SDH	0.5%	0%
Old cerebral hemorrhage	0.5%	11.6%

Type of Granuloma (% of patients)

Calcified granuloma	5.0%	7.0%
Cysticercal granuloma	3.0%	4.7%
Tuberculoma	0.5%	0%

3 Atrophy & White Matter Changes

Type of Atrophy (% of patients)

	CT (n=201)	MRI (n=43)
Cortical	34.8%	46.5%
Sub-cortical	3.0%	2.3%
Diffuse	30.8%	20.9%
Hemispheric atrophy	0.5%	2.3%

Grade of Atrophy (% of patients)

Mild	38.8%	41.9%
Moderate	21.4%	18.6%
Severe	9.0%	11.6%

White Matter Changes & Others (% of patients)

White matter changes	37.3%	46.5%
UBO (Unidentified Bright Objects)	0%	27.9%
VR spaces (Virchow Robin spaces)	0%	16.3%

KEY TAKEAWAY

Structural abnormalities are common in elderly patients with seizures. Focal lesions in ~50% of CT and ~56% of MRI.

Vascular lesions are leading causes, especially ischemic stroke (old infarction) seen more often on MRI.

Age-related changes are frequent: cortical atrophy and white matter changes are common, particularly on MRI.

Source:
Adapted from the data in Table 1: Neuroimaging (CT/MRI) features in elderly patients with seizures

Ann Indian Acad Neurol 2012;15:273-80

Investigation in late onset epilepsy

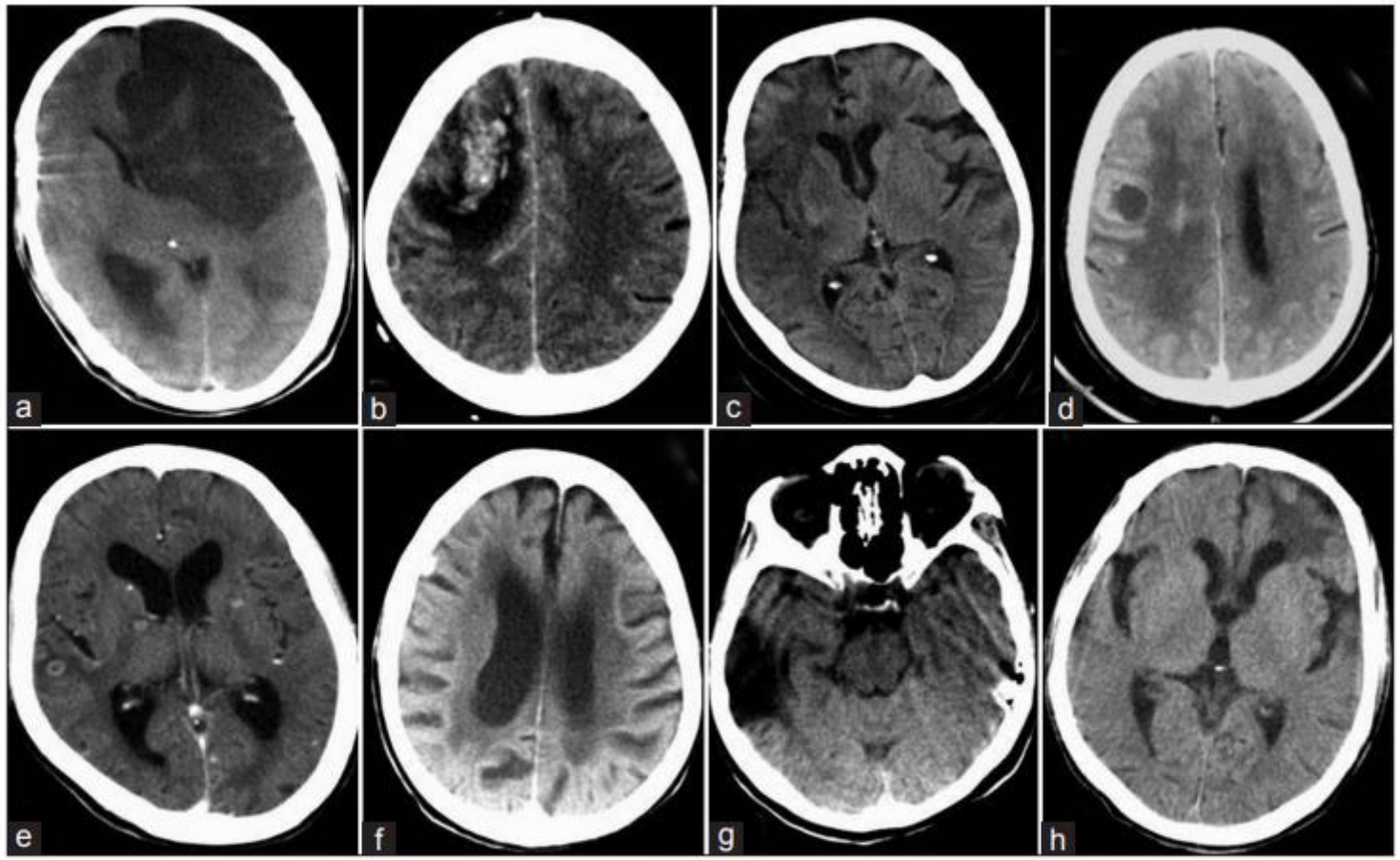


Figure 1: CT scan findings of elderly patients with new onset seizures (a) acute ischemic infarct involving left frontal region (ICA) with mass effect and transfalcine herniation (b) right frontal hemorrhagic infarct possibly due to cerebral sino-venous thrombosis (c) right temporal and frontal hypodensity in patient with suspected herpes simplex encephalitis (d) right frontal single large metastatic lesion with mass effect (e) Multiple small ring enhancing lesion suggestive neurocysticercosis (f) periventricular hypodensity with diffuse cerebral atrophy suggesting leukoaraiosis (g) Gliosis due to old infarct involving right temporal region; and (h) left frontal post-traumatic gliotic changes

Ann Indian Acad Neurol 2012;15:273-80

Investigation in late onset epilepsy

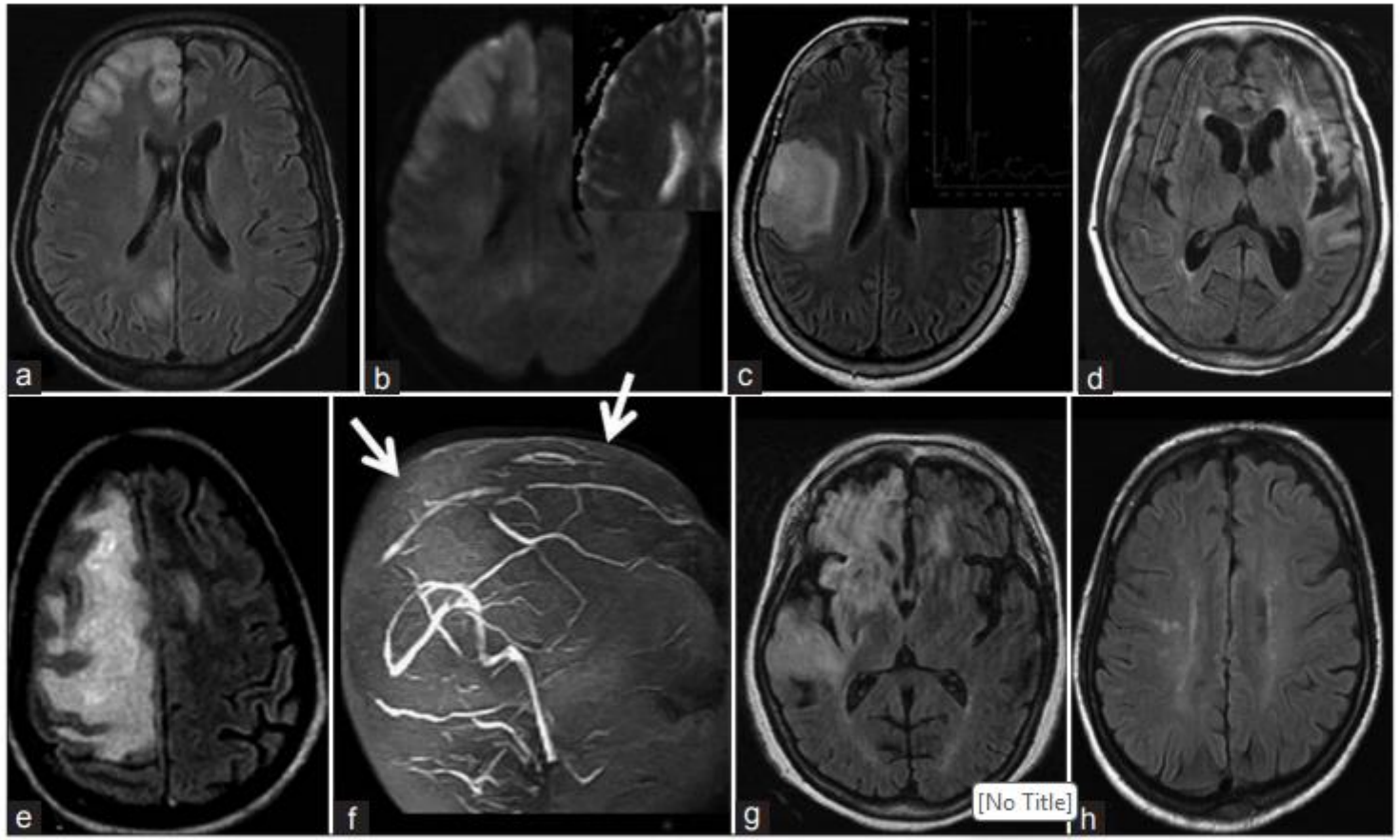
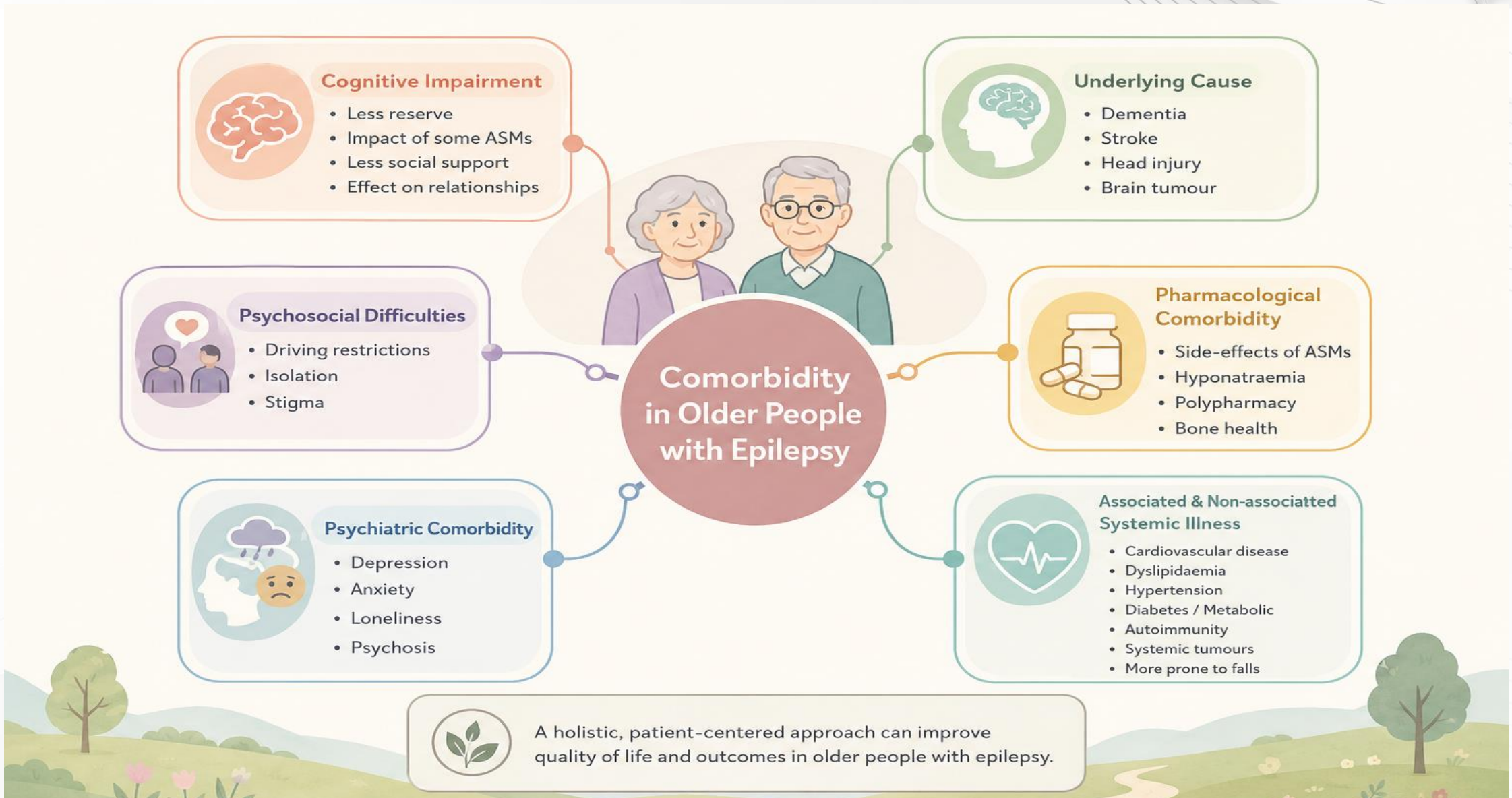


Figure 2: MRI observations in elderly patients with new onset seizures (a, b), (b) Acute ischemic infarct involving right frontal and occipital region as shown in FLAIR (a) and DWI (b) and ADC (b) sequences (c) right temporo-parietal glioma with increased choline: creatine peak in the MRS study (c) (d) left perisylvian hyperintensity with ipsiplateral hemiatrophy in a elderly patient with histopathologically proven Rasmussens' encephalitis (e,f) Superior sagittal sinus thrombosis (absence of flow- arrows) and venous infarct involving right frontal region (g) Herpes simplex encephalitis involving right temporal and basi-frontal region (h) unidentified bright objects (UBOs) in FLAIR images

Ann Indian Acad Neurol 2012;15:273-80

Treatment consideration



Lancet 2020; 395: 735–48

Physiological Changes During Aging

Affecting Pharmacokinetics and Pharmacodynamics of AEDs

PHARMACOKINETIC CHANGES

Parameter	Decreased ↓	Increased ↑
Gastrointestinal motility, secretion	+/–	
Serum albumin	+	
Body fat / lean mass ratio		+
Total body water	+	
Liver mass and blood flow	+	
Cytochrome P450 enzyme activity	+	
Renal blood flow and weight	+	
Glomerular filtration rate	+	
Filtration fraction		+

PHARMACODYNAMIC CHANGES

Parameter	Decreased ↓	Increased ↑
Receptor number	+	
Receptor sensitivity	+	

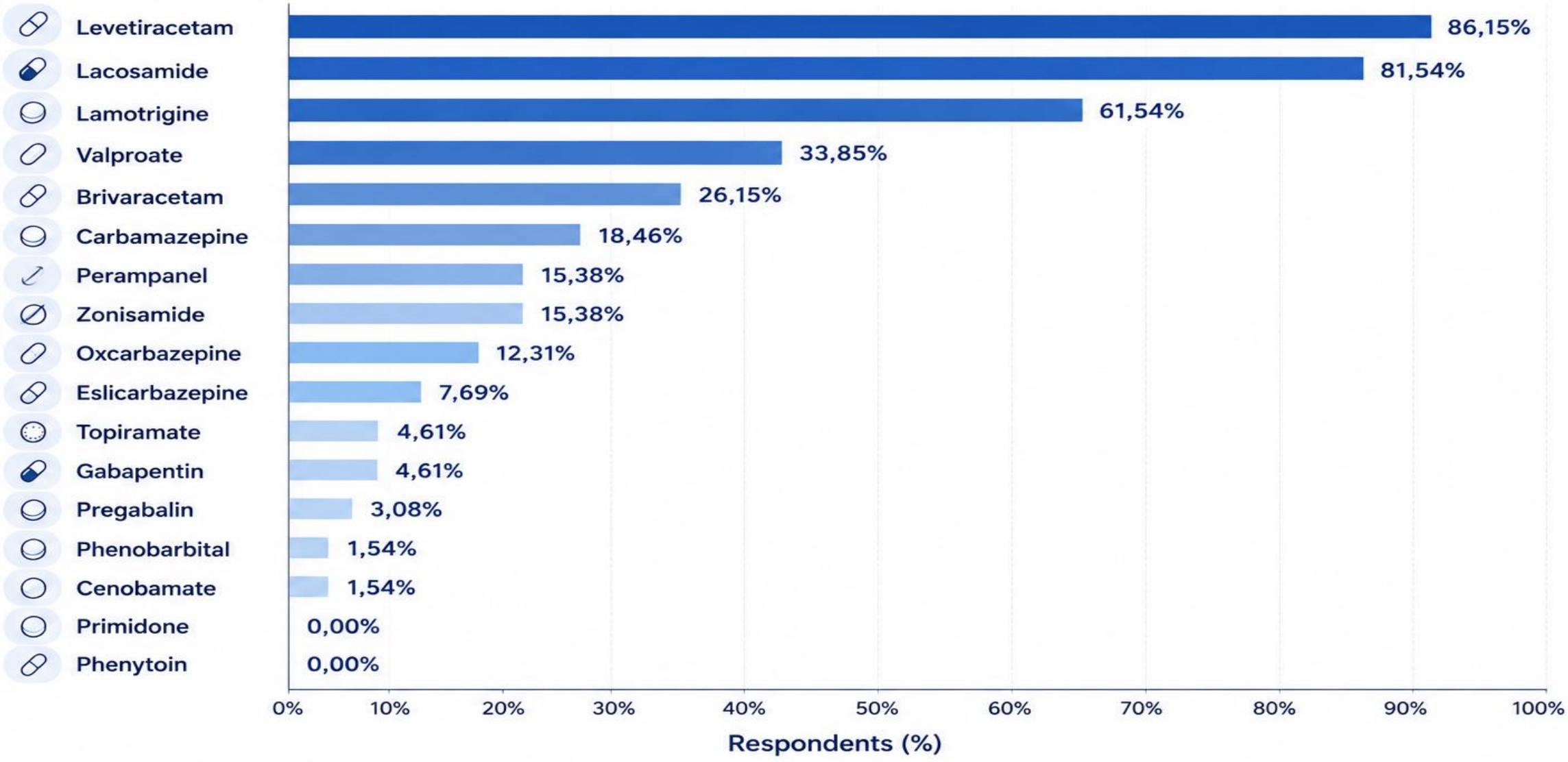
KEY TAKEAWAY

Aging is associated with multiple physiological changes that can alter the absorption, distribution, metabolism, excretion, and response to AEDs.

Consider these changes when selecting and dosing antiepileptic medications in older adults.

Note: "+" indicates a clinically relevant decrease; "+" in the Increased column indicates a clinically relevant increase; "+ / –" indicates variable or inconsistent effects.

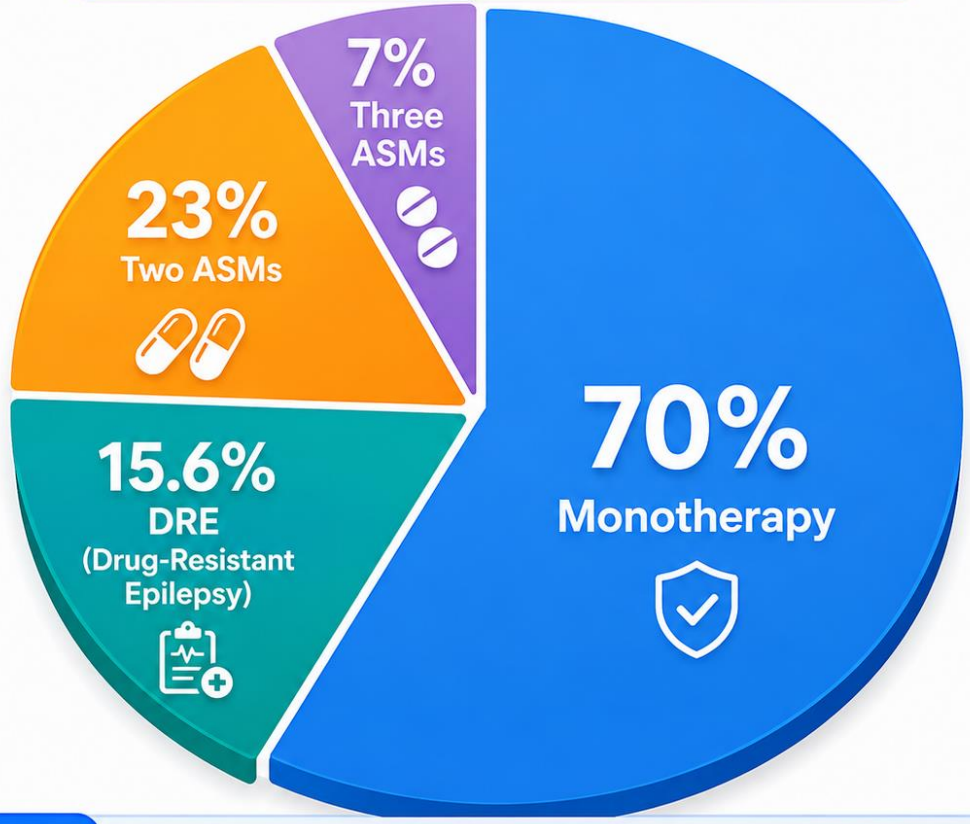
Which ASMs are you used to adopt in patient with LOE?



LOE = Late-Onset Epilepsy

Epilepsia Open. 2025;10:1639–1647.

OVERALL ASM THERAPY PATTERNS



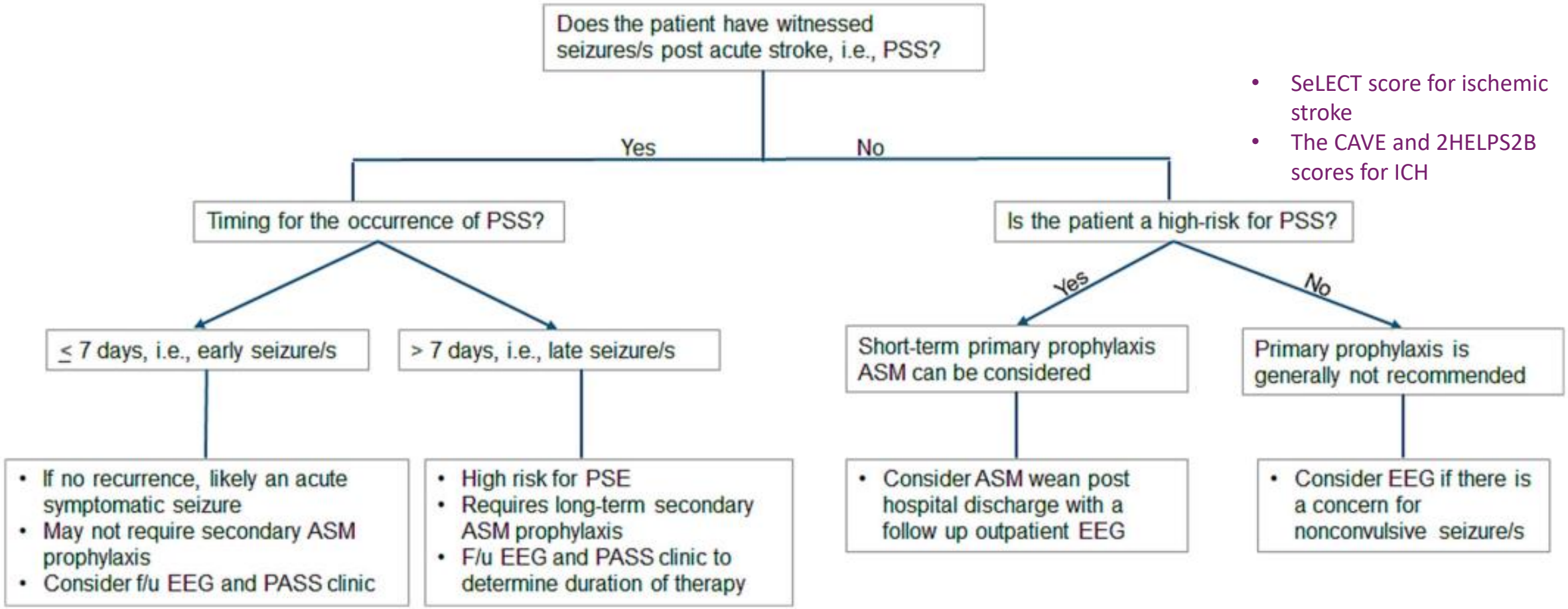
70%	Monotherapy	Patients controlled with a single ASM
23%	Two ASMs	Patients requiring two ASMs
15.6%	DRE (Drug-Resistant Epilepsy)	Patients with DRE on multiple ASMs
7%	Three ASMs	Patients requiring three ASMs

IMAJ 2023;25:412-415.

Table 1
Summary of most relevant clinical recommendations for antiepileptic drugs in older people with epilepsy [102].
Source. Modified from a similar table in Pugh et al. [102] and used with permission.

Guideline	Date	Specific geriatric AED recommendation	Level of evidence
Scottish Intercollegiate Guideline Network (SIGN)	1997 2001 2003	Lamotrigine may be advantageous because of its favorable adverse event profile, few drug interactions	1
National Institute of Health and Clinical Excellence (NICE)	2004	Same as for younger adults	1
International League Against Epilepsy (ILEA)	2006	Lamotrigine and gabapentin preferred first-line; carbamazepine as an alternative first-line	1

Proposed algorithm for decision-making regarding primary and secondary ASM prophylaxis in patient presenting with post stroke seizure



- SeLECT score for ischemic stroke
- The CAVE and 2HELPS2B scores for ICH

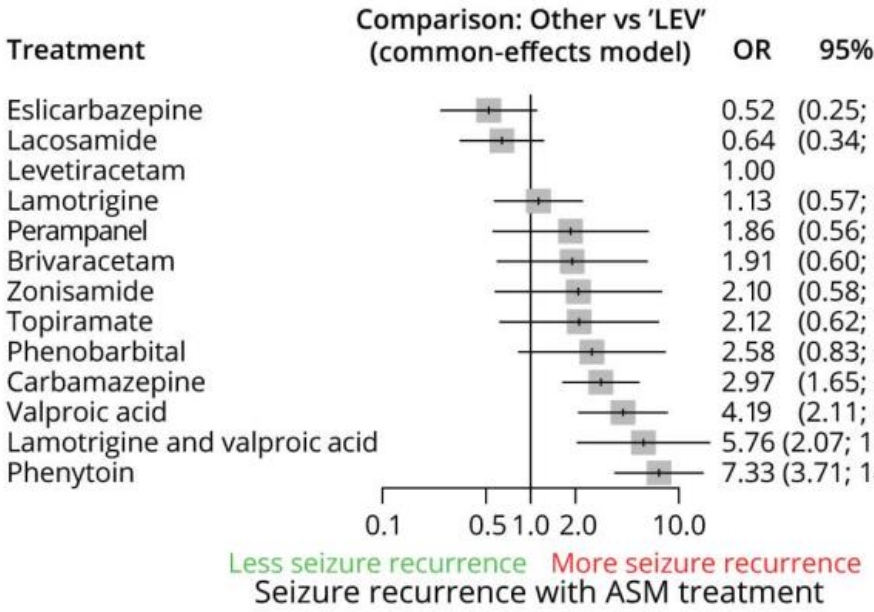
Front. Neurol. 16:1648064.

EST 30th ANNIVERSARY ANNUAL MEETING

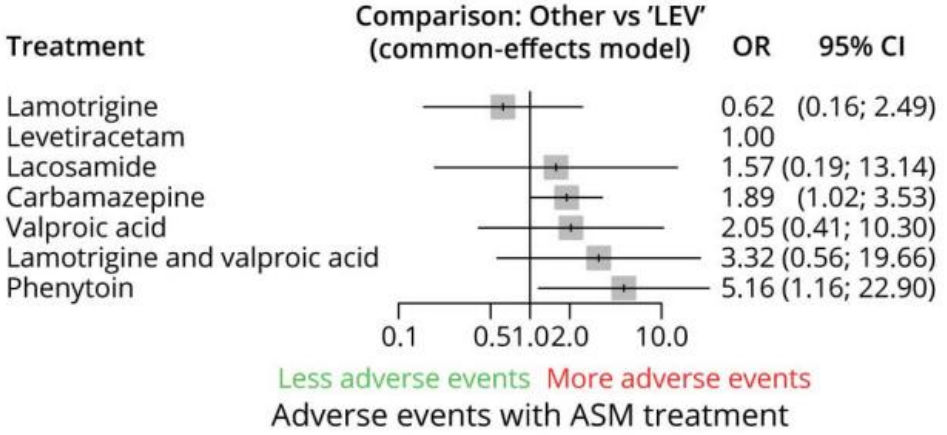
Antiseizure Medications in Poststroke Seizures

A Systematic Review and Network Meta-Analysis

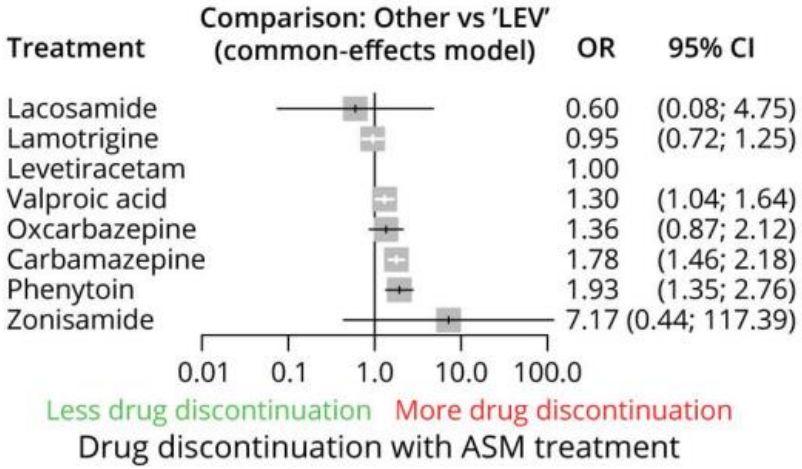
A Seizure Recurrence



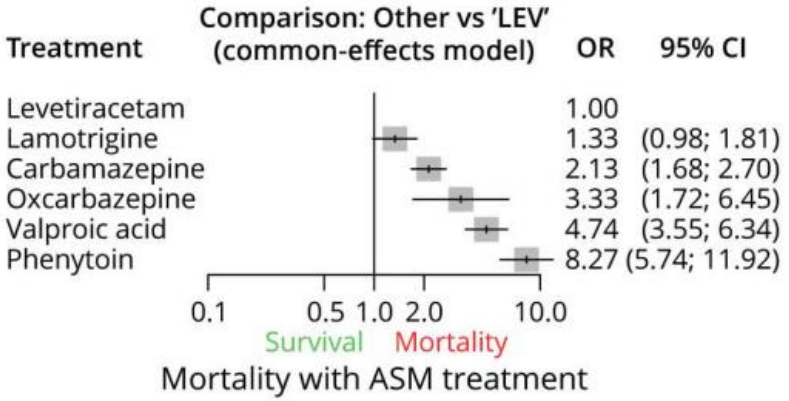
B Adverse events



C Drug discontinuation

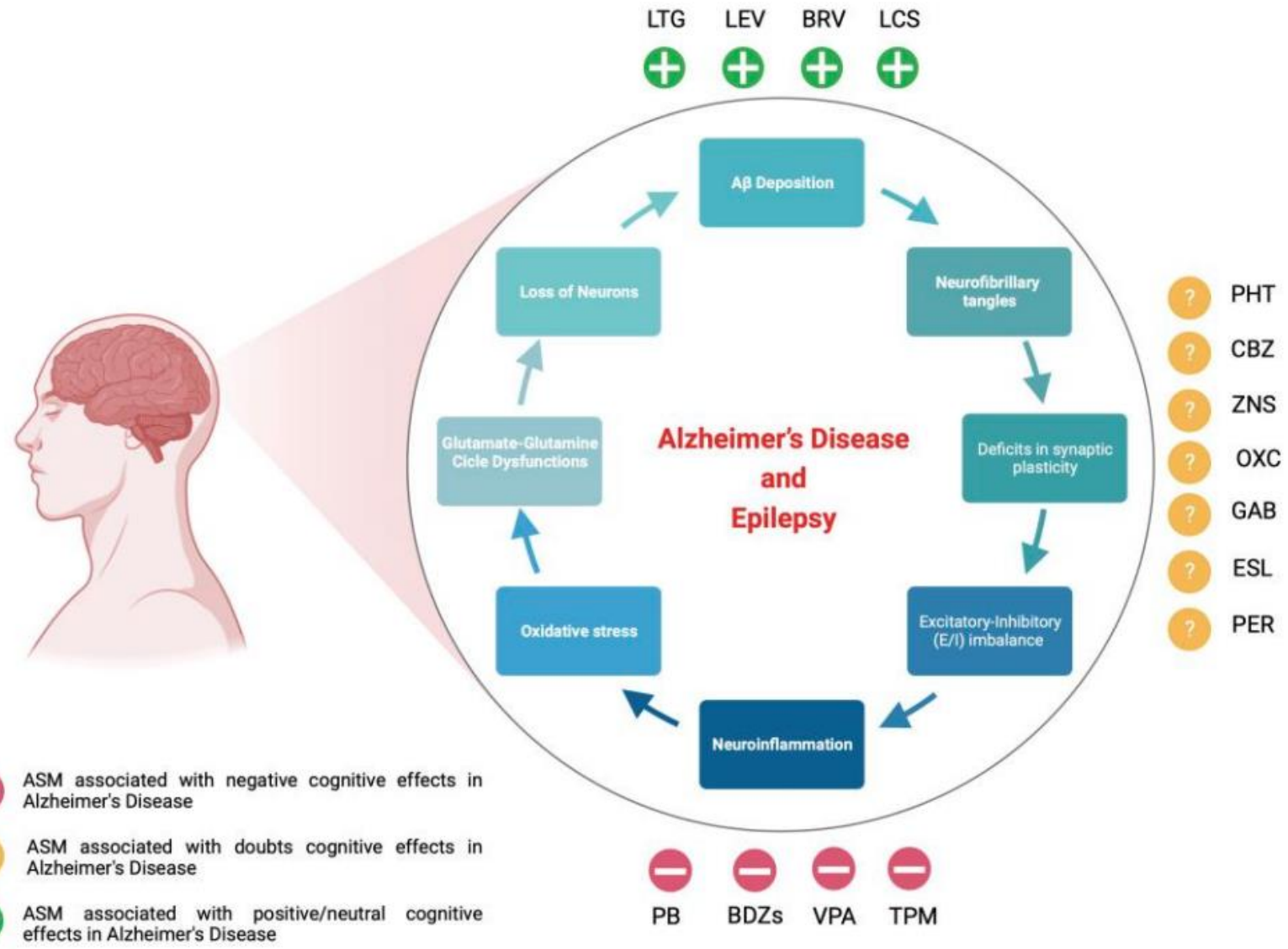


D Mortality



Neurology. 2025 Feb 11;104(3):e210231.

Diagram depicting the main molecular pathways involved in Alzheimer's disease–epilepsy comorbidity and ASM effects on cognitive trajectory in Alzheimer's



Int J Mol Sci. 2023 Aug 10;24(16):12639.

Antiseizure Medications in Alzheimer's Disease

✅ PREFERRED
(Often Considered)

Levetiracetam
- Minimal drug interactions
- Monitor behavioral adverse effects

Lamotrigine
- Favorable cognitive profile
- Slow titration

Lacosamide
- Relatively low interaction potential
- Consider cardiac conduction issues

⚠ CAUTION
(Use With Caution)

Gabapentin / Pregabalin
- Sedation, dizziness
- Renal dose adjustment

Valproate
- Cognitive/behavioral & systemic adverse effects
- Not preferred solely for seizure prophylaxis

🛑 AVOID
(Generally Avoid / Less Favorable)

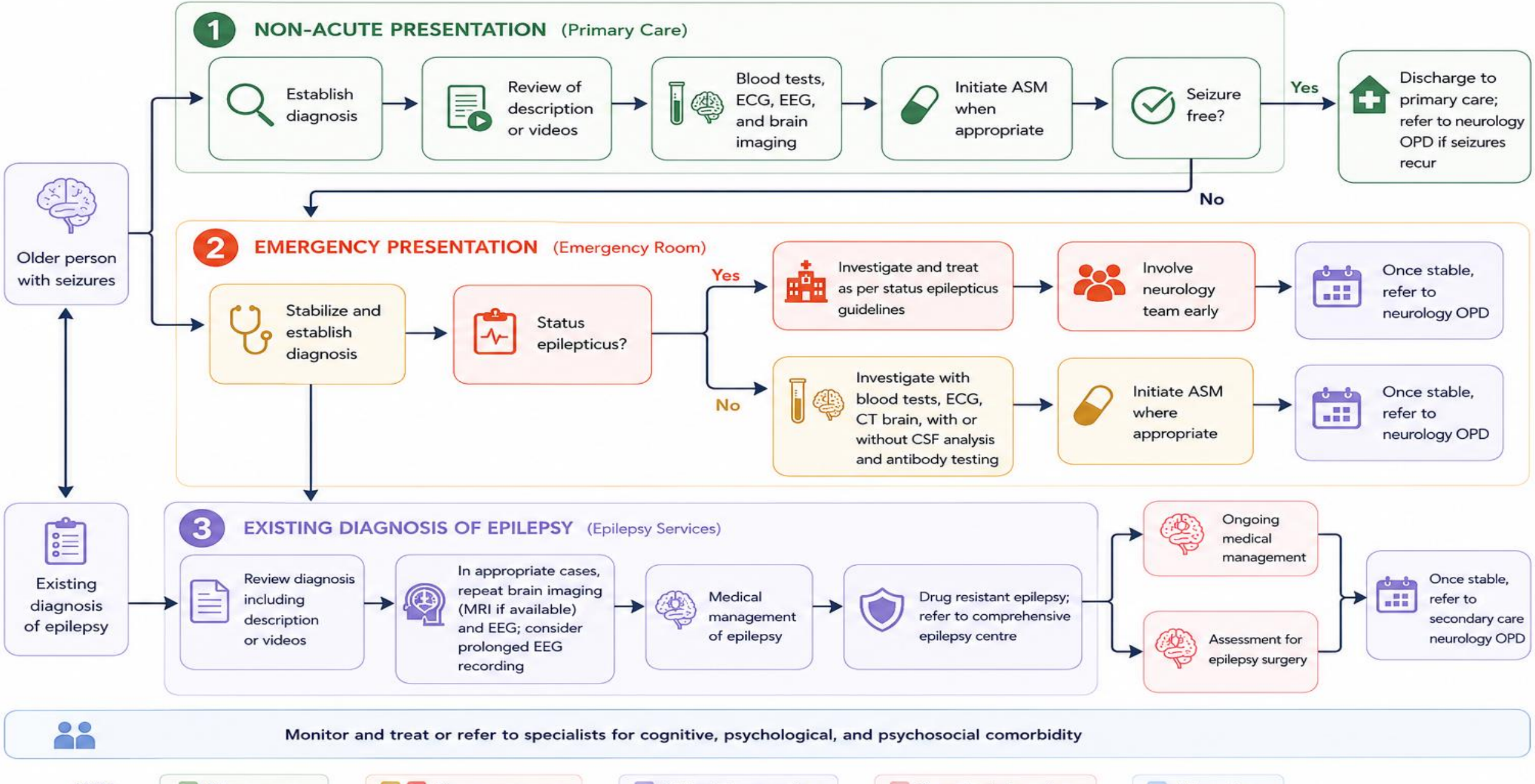
Phenobarbital
- Cognitive impairment
- Sedation

Phenytoin
- Cognitive effects, interactions
- Pharmacokinetic complexity

Carbamazepine
- Interactions, hyponatremia
- Tolerability concerns

BOTTOM LINE: In Alzheimer's disease, prioritize seizure control while minimizing cognitive, behavioral, sedative, and drug–drug interactioction burden.

Management Pathway for an Older Person with Seizures



Lancet 2020; 395: 735–48

Take home messages

- Think beyond seizures- diagnosis requires a broad differential
- A new onset seizure – search for an underlying cause
- EEG is supportive- normal EEG does not exclude epilepsy
- Treat the patient, not just the seizure
- ASM selection must account for aging
- Start low, go slow-but aim for seizure freedom