



**Mahidol University**  
Faculty of Medicine Siriraj Hospital

# Pragmatic Algorithm to Select Appropriate Antiseizure Medications

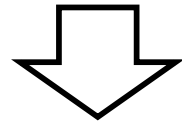
Kanokwan Boonyapisit, M.D.  
Department of Medicine  
Siriraj Hospital



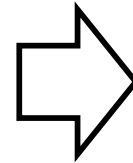
# **GOAL OF EPILEPSY TREATMENT**



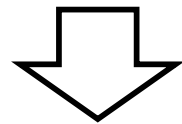
Diagnosis of epilepsy



Identify the  
underlying causes



Treat the  
underlying causes



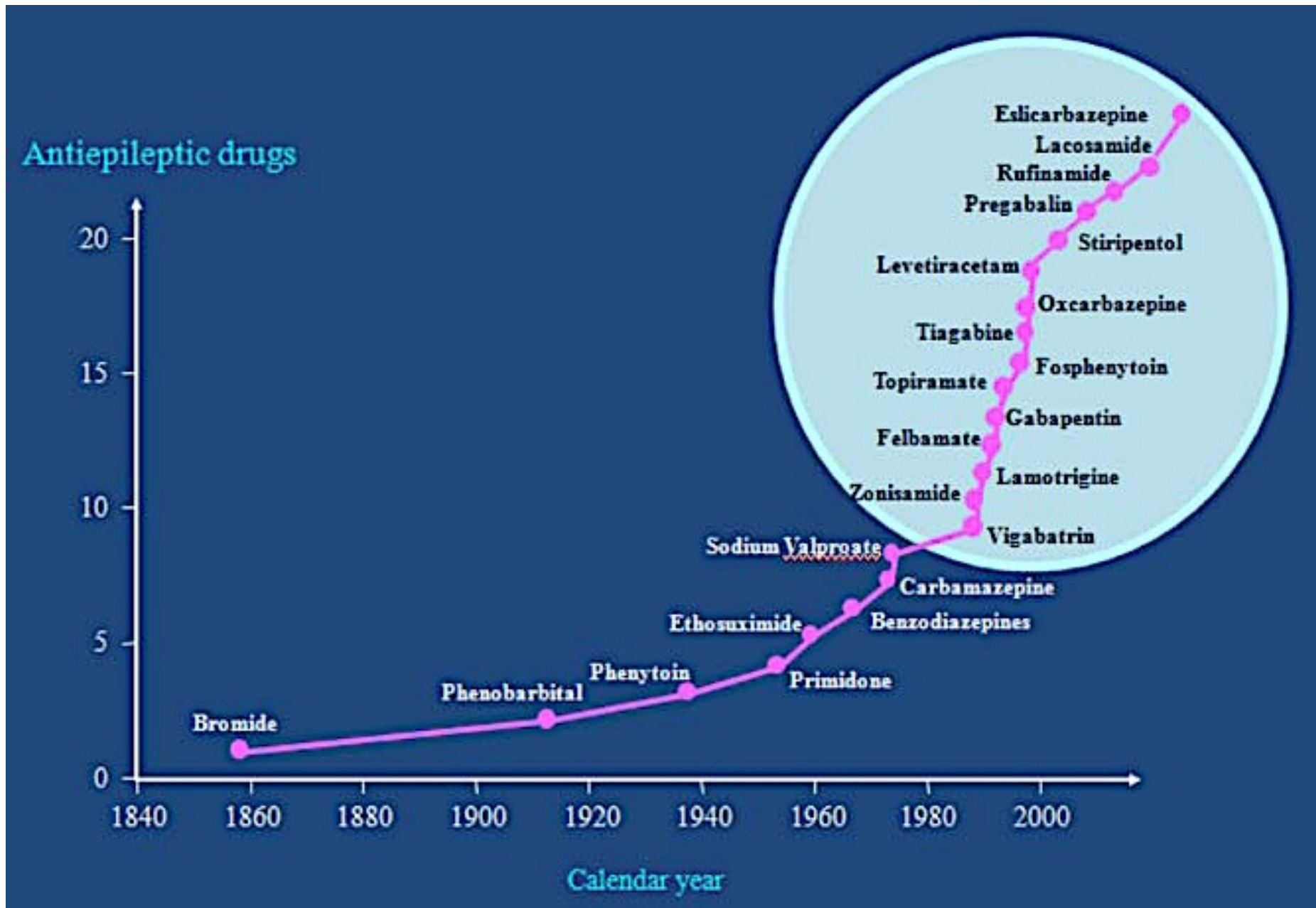
Control the  
seizures

With good  
quality of life

# THREE GENERATIONS OF AEDS



# Antiepileptic drug development



# Advantage of 2<sup>nd</sup> gen. AEDs

- Give clinician more choices of antiepileptic medications especially more choices of broad spectrum AEDs
- Better efficacy?
- Better tolerability?
- Better pharmacokinetic properties
- Low protein binding
- Most of the new AEDs are not strong hepatic enzyme inducers → fewer drug interaction
- Fewer serious adverse events

# Newest generation of antiepileptic medications: mechanism

Drugs	Related drugs	Mechanisms
Brivaracetam	Levetiracetam	10 fold higher affinity for SV2A than LEV
Eslicarbazepine	Carbamazepine	Less problem with drug interaction and toxic metabolites
Rufinamide	Lamotrigine	Acts on Na channels
Retigabine		Activate K current
Ganaxolone	Neurosteroids	Acts on postsynaptic and extrasynaptic GABA A receptors
Perampanel		Blocks AMPA receptors at “noncompetitive site”
Lacosamide		Block Na channel in slow inactivated state

## Diagnosis

- Check diagnosis: provoked seizure/ first unprovoked seizure/ epilepsy
- Etiology of epilepsy

## Starting AEDs

- Selecting the first AED

## Adjusting AEDs

- Switching AEDs
- Adding AEDs



## Diagnosis

- Check diagnosis: provoked seizure/ first unprovoked seizure/ epilepsy
- Etiology of epilepsy

## Starting AEDs

- Selecting the first AED

## Adjusting AEDs

- Switching AEDs
- Adding AEDs

# SELECTING THE FIRST AED



# Which medications?

- ลักษณะการชັกและประเภทของโรคลคมชັกของผู้ป่วย
- การบริหารยา
- ผลข้างเคียงของยากันชັก
- Drug interaction กรณีที่ผู้ป่วยได้ยาหลายชนิดพร้อมกัน
- Special situations/ other comorbidities
  - Reproductive age
  - Elderly
  - Hepatic impairment
  - Renal impairment

## AEDs

- Which AEDs are available?
- Cost
- Experience

## Patient's profile

- Type of seizures
- Age
- Weight
- Underlying diseases
- Current medication
- Occupation
- Psychological profiles

Drug administration  
Prone to which side effects  
Potential drug interaction

# CASE 1.1



AEDs available/ Patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	JME Myoclonic seizures, GTC	
Age	Age 18 F	
Weight	68 kg	
Underlying disease	None	
Occupation	Student	
Current medication	None	
Psychological profiles	Normal	
Payment plan		

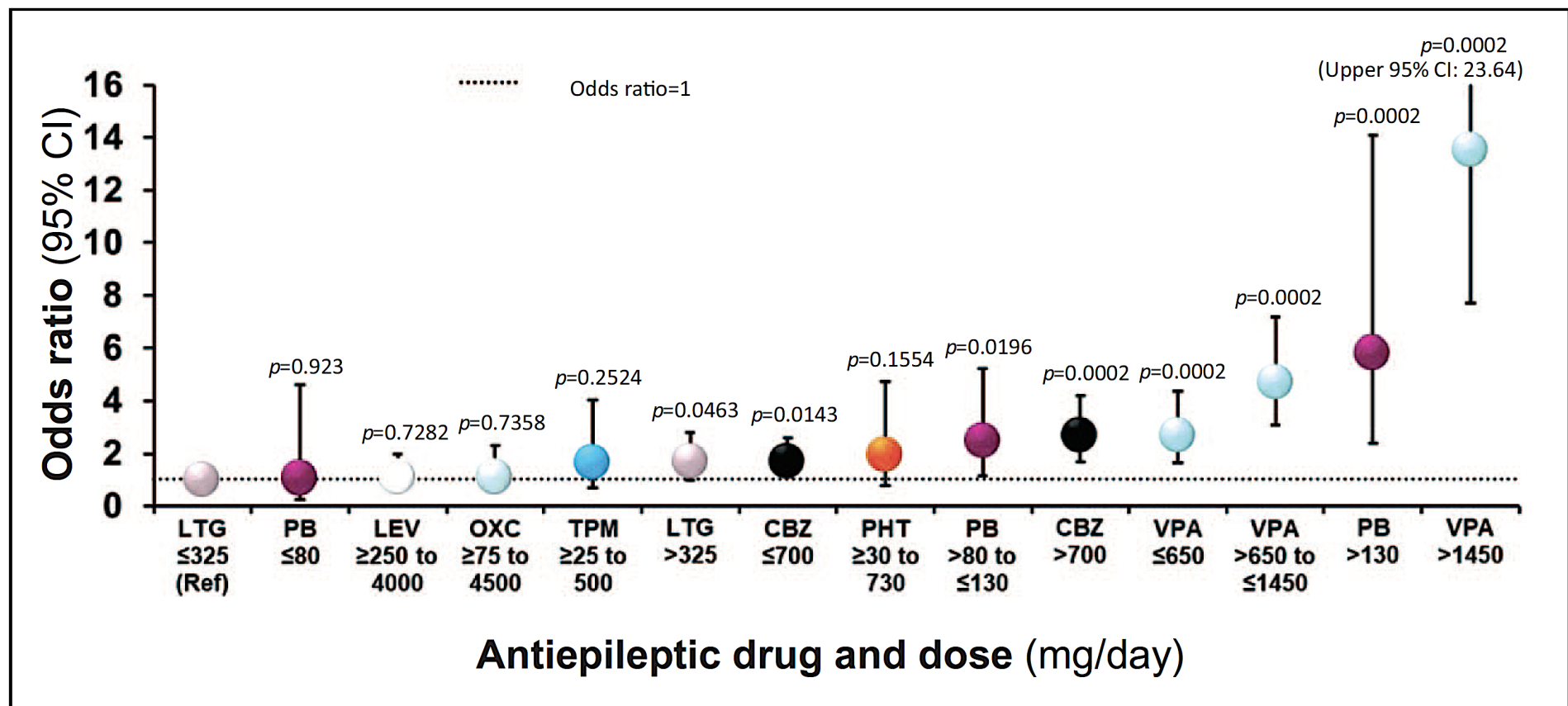
# Aggravation of seizures by AEDs

	CBZ	OXC	PHT	LTG	VPA	GBP	VGB	BDZ
Absence	+++	+	+++			+	++	
Myoclonic	+++	+	+++	+		+	+	
JME	++	+	++	+				
LGS/MAE	++	+	++	+		+	++	++
BECTS	+			+	+			
LKS/ESE S	+		+					
ULD			+					

ชนิดของอาการชัก	Traditional AEDs	New AEDs
Absence	Sodium valproate	Lamotrigine Clonazepam
Myoclonic, atonic	Sodium valproate	Lamotrigine Topiramate Clonazepam Levetiracetam
Generalized tonic clonic	Phenobarbital Phenytoin Carbamazepine Sodium valproate	Lamotrigine Topiramate Oxcarbazepine Levetiracetam Gabapentin Clonazepam



AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	JME Myoclonic seizures, GTC	Avoid Na channel blocker	VPA, LEV, (TPM), (LTG) <b>Avoid PHT, CBZ, OXC</b>
Age, Sex	Age 18 F	WWE	
Weight	68 kg	Weight issue	
Underlying disease	None	-	
Occupation	Student	Drug administration	
Current medication	None		
Psychological profiles	Normal		
Payment plan			



**FIGURE 3.** Risk of major congenital malformations (odds ratios with 95% confidence intervals) with different antiepileptic drug treatments compared with lamotrigine 325 mg/day or less. CBZ, carbamazepine; LEV, levetiracetam; LTG, lamotrigine; OXC, oxcarbazepine; PB, phenobarbital; PHT, phenytoin; Ref, reference; TPM, topiramate; VPA, valproate. Based on Data from [5<sup>11</sup>].

Tomson T, Battino D, Bonizzoni E, et al. Comparative risk of major congenital malformations with eight different antiepileptic drugs: a prospective cohort study of the EURAP registry. *Lancet Neurol* 2018; 17:530–538.

# Skin and cosmetic side effects

Side effects	AEDs	Time frame	Incidence	Reversible
Alopecia	VPA		0.5-4%/ up to 6%	
	CBZ, OXC	2-3 months		
Gum hypertrophy	PHT	Chronic use	10-40%	/
Hirsutism, hypertrichosis	PB			
	PHT			
Acne	VPA			
	PHT			
Dupuytren's Contracture, plantar fibromatosis	PB	Chronic use	Up to 5%	/

# Body weight changes with AEDs

Side effects	AEDs	Time frame	Incidence	Extent
Weight gain	VPA	2-3 months and may be continue	Up to 30-40%	1-3% of BW Up to 8% of BW (with high dose)
	GBP		23%	
	PGB		18%	
	RTG			
Weight loss	TPM	Stabilize after 12-18 months	6-17% in leaflet (upto 60% in review)	Up to 7.5% of BW Dose dependent
	ZNS		3%	
	FBM			
	STP			

AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	JME Myoclonic seizures, GTC	Avoid Na channel blocker	VPA, LEV, (TPM), (LTG) <del>Avoid PHT, CBZ, OXC</del>
Age, Sex	Age 18 F	WWE	LEV, (TPM), (LTG) (VPA)
Weight	68 kg	Weight issue	LEV, (TPM), (LTG) (VPA)
Underlying disease	None	-	
Occupation	Student	Drug administration	
Current medication	None	-	
Psychological profiles	Normal	-	
Payment plan			

AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	JME Myoclonic seizures, GTC	Avoid Na channel blocker	VPA, LEV, (TPM), (LTG) <del>Avoid PHT, CBZ, OXC</del>
Age, Sex	Age 18 F	WWE	LEV, (TPM), (LTG) (VPA)
Weight	68 kg	Weight issue	LEV, (TPM), (LTG) (VPA)
Underlying disease	None	-	LEV, (TPM), (LTG) (VPA)
Occupation	Student	Drug administration	LEV, (TPM), (LTG) (VPA)
Current medication	None	-	LEV, (TPM), (LTG) (VPA)
Psychological profiles	Normal	-	LEV, (TPM), (LTG) (VPA)
Payment plan			

# CASE 1.2



AEDs available	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	JME Myoclonic seizures, GTC	Avoid Na channel blocker	VPA, LEV, (TPM), (LTG) <del>Avoid PHT, CBZ, OXC</del>
Age	Age 18 M	-	VPA, LEV, (TPM), (LTG)
Weight	58 kg	-	VPA, LEV, (TPM), (LTG)
Underlying disease	Migraine		
Occupation	Student		
Current medication	None		
Psychological profiles	Depression		
Payment plan			



# Matching AEDs with other comorbidities

	Avoid/ caution	Prefer
Migraine		VPA, TPM
Mood lability/ bipolar disorder	-	LTG, CBZ, OXC, PHT, VPA
Pain		CBZ, PGB, GBP
Anxiety	FLB, LEV, LTG, TGB	BZD, GBP, PGB
Depression	Barbiturates, LEV, PGB, TGB, TPM, VGB, ZNS	LTG
On warfarin	Enzyme inducing AEDs	
On OCP	Enzyme inducing AEDs	
HLA 1502 +ve	CBZ	
Sulfa allergy	ZNS	

# Consider about psychiatric side effects in pts. with psychiatric comorbidities

Psychiatric comorbidities	Avoid	Consider
Mood lability/ bipolar disorder	-	LTG, CBZ, OXC, PHT, VPA
Anxiety	FLB, LEV, LTG, TGB	BZD, GBP, PBG
Depression	Barbiturates, LEV, PGB, TGB, TPM, VGB, ZNS	LTG
Psychosis	ETX, FLB, LEV, PHT, TGB, TPM, VGB, ZNS	-

AEDs available	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	JME Myoclonic seizures, GTC	Avoid Na channel blocker	VPA, LEV, (TPM), (LTG) <del>Avoid PHT, CBZ, OXC</del>
Age	Age 18 M		VPA, LEV, (TPM), (LTG)
Weight	58 kg		VPA, LEV, (TPM), (LTG)
Underlying disease	Migraine	Prefer migraine prophylaxis	VPA, TPM, (LEV), (LTG)
Occupation	Student		
Current medication	None		
Psychological profiles	Depression	Avoid AEDs that can ↑depression	VPA, (TPM), (LEV), (LTG)
Payment plan			

# CASE 2



AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Mesial temporal sclerosis Automotor seizure,GTC		
Age, Sex	Age 25 M	-	
Weight	65 kg	-	
Underlying dis	None	-	
Occupation	Factory worker	Drug administration	
Current medication	None	-	
Psychological profiles	Normal	-	
Payment plan	ต้องการรักษาใกล้บ้าน		

## SPECIAL REPORT

# Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes

**\*Tracy Glauser, †Elinor Ben-Menachem, ‡Blaise Bourgeois, §Avital Cnaan, ¶Carlos Guerreiro, #Reetta Kälviäinen, \*\*Richard Mattson, ††Jacqueline A. French, ‡‡Emilio Perucca, §§Torbjorn Tomson for the ILAE subcommission of AED Guidelines**

**\*Comprehensive Epilepsy Center, Division of Neurology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio, U.S.A.; †Institution for Clinical Neuroscience, Sahlgrenska Academy, University of Göteborg, Göteborg, Sweden; ‡Department of Neurology, The Children's Hospital and Harvard Medical School, Boston, Massachusetts, U.S.A.; §Division of Biostatistics and Study Methodology, Center for Translational Science, Children's National Medical Center, Washington, District of Columbia, U.S.A.; ¶Department of Neurology, University of Campinas (UNICAMP), Hospital das Clínicas, Campinas, Sao Paulo, Brazil; #Department of Neurology, Kuopio Epilepsy Center, Kuopio University Hospital, Kuopio, Finland; \*\*Department of Neurology, Yale University School of Medicine, Yale New Haven Hospital, New Haven, Connecticut, U.S.A.; ††Comprehensive Epilepsy Center, New York University Langone Medical Center, New York, New York, U.S.A.; ‡‡Clinical Pharmacology Unit, Institute of Neurology, IRCCS C. Mondino Foundation, University of Pavia, Pavia, Italy; and §§Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden**

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**Table 4. Summary of studies and level of evidence for each seizure type and epilepsy syndrome**

Seizure type or epilepsy syndrome	Class I studies	Class II studies	Class III studies	Level of efficacy and effectiveness evidence (in alphabetical order)
Adults with partial-onset seizures	4	1	34	Level A: CBZ, LEV, PHT, ZNS Level B: VPA Level C: GBP, LTG, OXC, PB, TPM, VGB Level D: CZP, PRM
Children with partial-onset seizures	1	0	19	Level A: OXC Level B: None Level C: CBZ, PB, PHT, TPM, VPA, VGB Level D: CLB, CZP, LTG, ZNS
Elderly adults with partial-onset seizures	1	1	3	Level A: GBP, LTG Level B: None Level C: CBZ Level D: TPM, VPA
Adults with generalized onset tonic-clonic seizures	0	0	27	Level A: None Level B: None Level C: CBZ, LTG, OXC, PB, PHT, TPM, VPA Level D: GBP, LEV, VGB

AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Mesial temporal sclerosis Automotor seizure, GTC		PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Age, Sex	Age 25 M	-	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Weight	65 kg	-	
Underlying dis	None	-	
Occupation	Factory worker	Drug administration	
Current medication	None	-	
Psychological profiles	Normal	-	
Payment plan	ต้องการรักษาใกล้บ้าน		



AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Mesial temporal sclerosis Automotor seizure,GTC		PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Age, Sex	Age 25 M	-	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Weight	65 kg	-	
Underlying dis	None	-	
Occupation	Factory worker	Drug administration	PHT, PB, ZNM, PER, VPA, CBZ, TPM, LEV, LTG, OXC, (GBP, PGB), LCM
Current medication	None	-	
Psychological profiles	Normal	-	
Payment plan	ต้องการรักษาใกล้บ้าน		PHT, PB, CBZ, VPA

# CASE 3



AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Post stroke epilepsy Focal clonic seizure GTC		PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Age, Sex	Age 75 M	-	
Weight	65 kg	-	
Underlying dis	HT, DM, CAD, CKD AF on warfarin	CKD, warfarin	
Occupation	Retired		
Current medication	Warfarin Other meds	Drug interaction	
Psychological profiles	Normal	-	
Payment plan		-	

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# Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes

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Children with partial-onset seizures	1	0	19	Level A: OXC Level B: None Level C: CBZ, PB, PHT, TPM, VPA, VGB Level D: CLB, CZP, LTG, ZNS
Elderly adults with partial-onset seizures	1	1	3	Level A: GBP, LTG Level B: None Level C: CBZ Level D: TPM, VPA
Adults with generalized onset tonic-clonic seizures	0	0	27	Level A: None Level B: None Level C: CBZ, LTG, OXC, PB, PHT, TPM, VPA Level D: GBP, LEV, VGB

# Caution of SE of AEDs in elderly

AEDs	Special precautions
Phenobarbital	Drowsiness, cognitive dysfunction May reduce effects of other drugs (enzyme inducer)
Phenytoin	Reduced metabolism and clearance Reduced protein binding → increased free fraction Increase incidence of adverse effects PHT level may be increased by amiodarone, cimetidine, isoniazid, trazodone May reduce effects of other drugs (enzyme inducer)
Carbamazepine	Increase incidence of adverse effects May reduce effects of other drugs (enzyme inducer) Hyponatremia
Sodium valproate	Drowsiness, parkinsonism Thrombocytopenia
Oxcarbazepine	Increase incidence of adverse effects Hyponatremia
Topiramate	Cognitive side effects at higher dosage (can be avoided by slow titration)

AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Post stroke epilepsy Focal clonic seizure GTC		PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Age, Sex	Age 75 M	-	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Weight	65 kg	-	
Underlying dis	HT, DM, CAD, CKD AF on warfarin	CKD, warfarin	
Occupation	Retired		
Current medication	Warfarin Other meds	Drug interaction	
Psychological profiles	Normal	-	
Payment plan		-	

# Drug interaction with warfarin

- Metabolites through CYP3A4, 2C9
- **Phenytoin, phenobarbital and carbamazepine** reduce the concentration of warfarin by up to 50-65%
- Phenobarbital and carbamazepine also reduce the anticoagulation effects of warfarin metabolites
- Newer AEDs do not have significant interaction with anticoagulant





**ESC**

European Society  
of Cardiology

Europace (2021) **00**, 1–65  
doi:10.1093/europace/euab065

**POSITION PAPER**  
*EHRA PRACTICAL GUIDE*

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# 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation

**Jan Steffel<sup>1\*</sup>, Ronan Collins<sup>2</sup>, Matthias Antz<sup>3</sup>, Pieter Cornu<sup>4</sup>, Lien Desteghe<sup>5,6</sup>,  
Karl Georg Haeusler<sup>7</sup>, Jonas Oldgren<sup>8</sup>, Holger Reinecke<sup>9</sup>,  
Vanessa Roldan-Schilling<sup>10</sup>, Nigel Rowell<sup>11</sup>, Peter Sinnaeve<sup>12</sup>, Thomas Vanassche<sup>12</sup>,  
Tatjana Potpara<sup>13</sup>, A. John Camm<sup>14</sup>, and Hein Heidbüchel<sup>5,6</sup>**

Steffel J, et al. Europace 2021; 0:1-65

	Via <sup>426, 539-541</sup>	Dabigatran etexilate	Apixaban	Edoxaban	Rivaroxaban
P-gp substrate		Yes	Yes	Yes	Yes
CYP3A4 substrate		No	Yes (≈25%)	No (<4%)	Yes (≈18%)
Drug					
Brivaracetam	–	No relevant interaction known/assumed			
Carbamazepine	Strong CYP3A4/P-gp induction; CYP3A4 competition	-29% <sup>542</sup>	-50% (SmPC)	SmPC	SmPC
Ethosuximide	CYP3A4 competition	No relevant interaction known/assumed			
Gabapentin	–	No relevant interaction known/assumed			
Lacosamide	–	No relevant interaction known/assumed			
Lamotrigine	P-gp competition	No relevant interaction known/assumed			
Levetiracetam	P-gp induction; P-gp competition				
Oxcarbazepine	CYP3A4 induction; P-gp competition				
Phenobarbital	Strong CYP3A4/possible P-gp induction		SmPC	SmPC	SmPC
Phenytoin	Strong CYP3A4/P-gp induction; P-gp competition	SmPC <sup>543</sup>	SmPC	SmPC	SmPC
Pregabalin	–	No relevant interaction known/assumed			
Topiramate	CYP3A4 induction; CYP3A4 competition				
Valproic acid	CYP3A4/P-gp induction/inhibition				Ref 544
Zonisamide	CYP3A4 competition; weak P-gp inhibition	No relevant interaction known/assumed (SmPC)			

AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Post stroke epilepsy Focal clonic seizure GTC		PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Age, Sex	Age 75 M	-	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Weight	65 kg	-	
Underlying dis	HT, DM, CAD, CKD AF on warfarin	CKD, warfarin	VPA, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER (TPM, LEV, LTG, GBP, PGB May need dose adjustment) Avoid PHT, PB, CBZ
Occupation	Retired		
Current medication	Warfarin Other meds	Drug interaction	
Psychological profiles	Normal	-	
Payment plan	ประกันสุขภาพถ้วนหน้า	-	

AEDs available/ patient's profile	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER	Consideration	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, GBP, PGB, LCM, PER
Diagnosis, seizure type	Post stroke epilepsy Focal clonic seizure GTC		PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Age, Sex	Age 75 M	-	PHT, PB, VPA, CBZ, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER
Weight	65 kg	-	
Underlying dis	HT, DM, CAD, CKD AF on warfarin	CKD, warfarin	VPA, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER (TPM, LEV, LTG, GBP, PGB May need dose adjustment) Avoid PHT, PB, CBZ
Occupation	Retired		
Current medication	Warfarin Other meds	Drug interaction	
Psychological profiles	Normal	-	
Payment plan	ประกันสุขภาพถ้วนหน้า	-	VPA, TPM, LEV, LTG, ZNM, OXC, (GBP, PGB), LCM, PER (TPM, LEV, LTG, GBP, PGB May need dose adjustment)

**IF THE 1<sup>ST</sup> AED DOES NOT  
WORK, WHAT TO DO NEXT?**



Monotherapy: starting dose



Increase dosage if seizure persists, no side effects

Monotherapy: maximal tolerated dose



Second monotherapy with different mechanism of action



Two drugs combination (select drugs with different mechanism of action and least drug interaction)

# How to adjust the medications?

- ก่อนจะพิจารณาเปลี่ยนหรือปรับยาในแต่ละขั้นตอนต้องคำนึงถึงสิ่งต่อไปนี้เสมอ
  - Is the diagnosis correct?
  - ยากันชักที่เลือกใช้เหมาะสมกับชนิดของการชักของผู้ป่วยหรือไม่?
  - Compliance
  - Avoid precipitating factors
  - Drug interaction

## REFRACTORY SEIZURES

# Rational polytherapy

\*Jacqueline A. French and †Edward Faught

\*New York University School of Medicine, New York, New York, U.S.A.; and †Birmingham Department of Veterans' Affairs Medical Center,  
The University of Alabama School of Medicine, Birmingham, Alabama, U.S.A.

*Epilepsy & Behavior* 21 (2011) 331–341

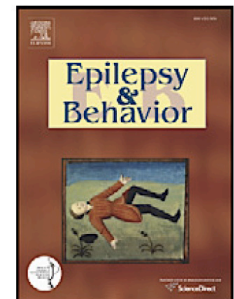


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Review

### Antiepileptic drug therapy: Does mechanism of action matter?

Martin J. Brodie <sup>a,\*</sup>, Athanasios Covanis <sup>b</sup>, Antonio Gil-Nagel <sup>c</sup>, Holger Lerche <sup>d</sup>, Emilio Perucca <sup>e,f</sup>,  
Graeme J. Sills <sup>g</sup>, H. Steve White <sup>h</sup>



# Add or switch AEDs

		Add	Switch
Failed single monotherapy			✓
1 <sup>st</sup> AED has side effects or disadvantage or cannot tolerate 1 <sup>st</sup> AED			✓
First AED provided partial or near complete control		✓	
Inadequate control with two sequential monotherapies		✓	
Risk of seizure exacerbation	High	✓	
	Low		✓
Potential drug interaction	Yes		✓
	No	✓	
Total score			

# Add or switch AEDs

		Add	Switch
Failed single monotherapy			<input checked="" type="checkbox"/>
1 <sup>st</sup> AED has side effects or disadvantage or cannot tolerate 1 <sup>st</sup> AED			<input checked="" type="checkbox"/>
First AED provided partial or near complete control		✓	
Inadequate control with two sequential monotherapies		✓	
Risk of seizure exacerbation	High	✓	
	Low		<input checked="" type="checkbox"/>
Potential drug interaction	Yes		✓
	No	<input checked="" type="checkbox"/>	
Total score		0	3

# Add or switch AEDs

		Add	Switch
Failed single monotherapy			✓
1 <sup>st</sup> AED has side effects or disadvantage or cannot tolerate 1 <sup>st</sup> AED			✓
First AED provided partial or near complete control, tolerate 1 <sup>st</sup> AED well		✓	
Inadequate control with two sequential monotherapies		✓	
Risk of seizure exacerbation	High	✓	
	Low		✓
Potential drug interaction	Yes		✓
	No	✓	
Total score		2	

# Which AEDs combination?

	AEDs	Added AEDs
Focal epilepsy	Na channel blocker PHT, CBZ, LTG, OXC, LCM	Broad spectrum AEDs VPA, TPM, LEV, ZNM
	Na channel blocker PHT, CBZ, LTG, OXC, LCM	Other specific mech PB, PGB, PER
Generalized epilepsy, myoclonic	Broad spectrum AEDs VPA, LEV, (TPM, ZNM)	Broad spectrum AEDs VPA, LEV, (TPM, ZNM)
Generalized+focal epilepsy Rapidly generalized sz.	VPA	LTG

**“- Several duotherapy combinations should be tested before considering the addition of a third drug.  
- Larger numbers of drugs should be avoided as it is unlikely that this strategy will produce a useful seizure reduction”**

## AEDs

- Which AEDs are available?
- Cost
- Experience

## Patient's profile

- Type of seizures
- Age
- Weight
- Underlying diseases
- Current medication
- Occupation
- Psychological profiles

Drug administration  
Prone to which side effects  
Potential drug interaction

# DRUG RESISTANCE EPILEPSY



## SPECIAL REPORT

# Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies

\*<sup>1</sup>Patrick Kwan, †Alexis Arzimanoglou, ‡Anne T. Berg, §Martin J. Brodie, ¶W. Allen Hauser, #<sup>2</sup>Gary Mathern, \*\*Solomon L. Moshé, ††Emilio Perucca, ‡‡Samuel Wiebe, and §§<sup>2</sup>Jacqueline French

**Drug resistant epilepsy may be defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.**

# What to consider before declaring that the patient is medical refractory?

- Is the diagnosis correct?
- ยากันชักที่เลือกใช้เหมาะสมกับชนิดของการชักของผู้ป่วยหรือไม่?
- Compliance
- Avoid precipitating factors
- Drug interaction



# Treatment of medical refractory epilepsy

- Epilepsy surgery
- Neurostimulation
  - Vagal nerve stimulation
  - Deep brain stimulation
  - Trigeminal nerve stimulation
  - Closed loop stimulation
- Other modalities: ketogenic diet

Research

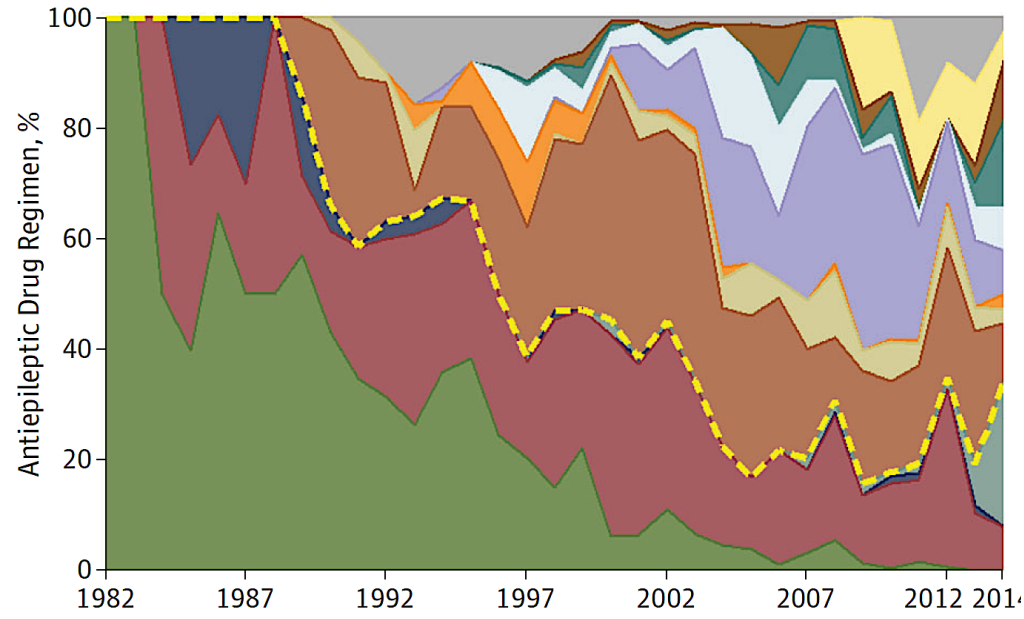
JAMA Neurology | **Original Investigation**

# Treatment Outcomes in Patients with Newly Diagnosed Epilepsy Treated With Established and New Antiepileptic Drugs A 30-Year Longitudinal Cohort Study

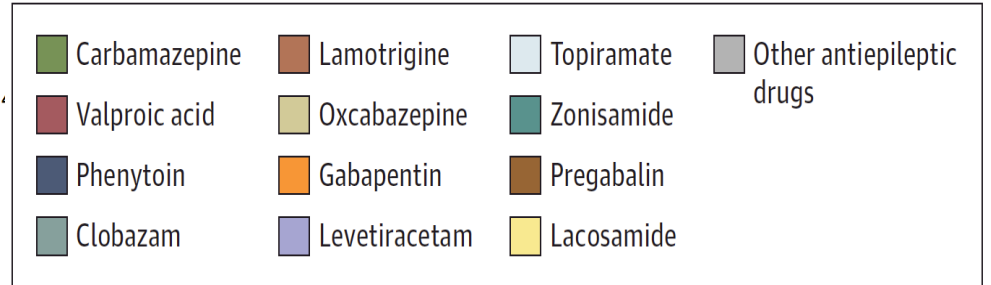
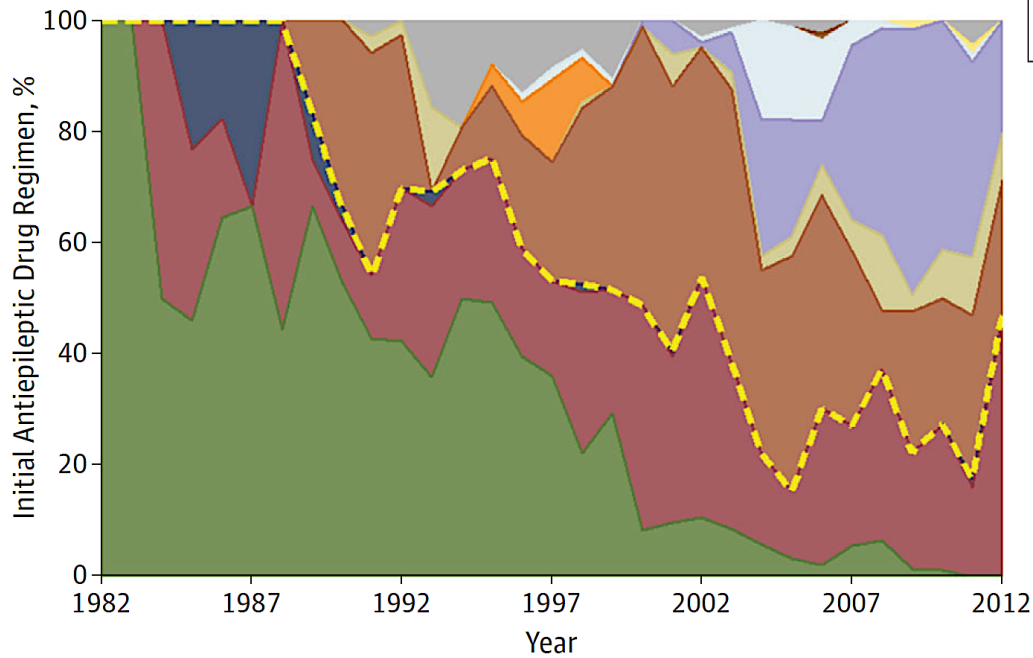
Zhibin Chen, PhD; Martin J. Brodie, MD; Danny Liew, MD, PhD; Patrick Kwan, MD, PhD

**DESIGN, SETTING, AND PARTICIPANTS** This longitudinal observational cohort study was conducted at the Epilepsy Unit of the Western Infirmary in Glasgow, Scotland. A total of 1795 individuals who were newly treated for epilepsy with AEDs between July 1, 1982, and October 31, 2012, were included in this analysis. All patients were followed up for a minimum of 2 years (until October 31, 2014) or until death, whichever came sooner. Data analysis was completed between March 2015 and May 2016.

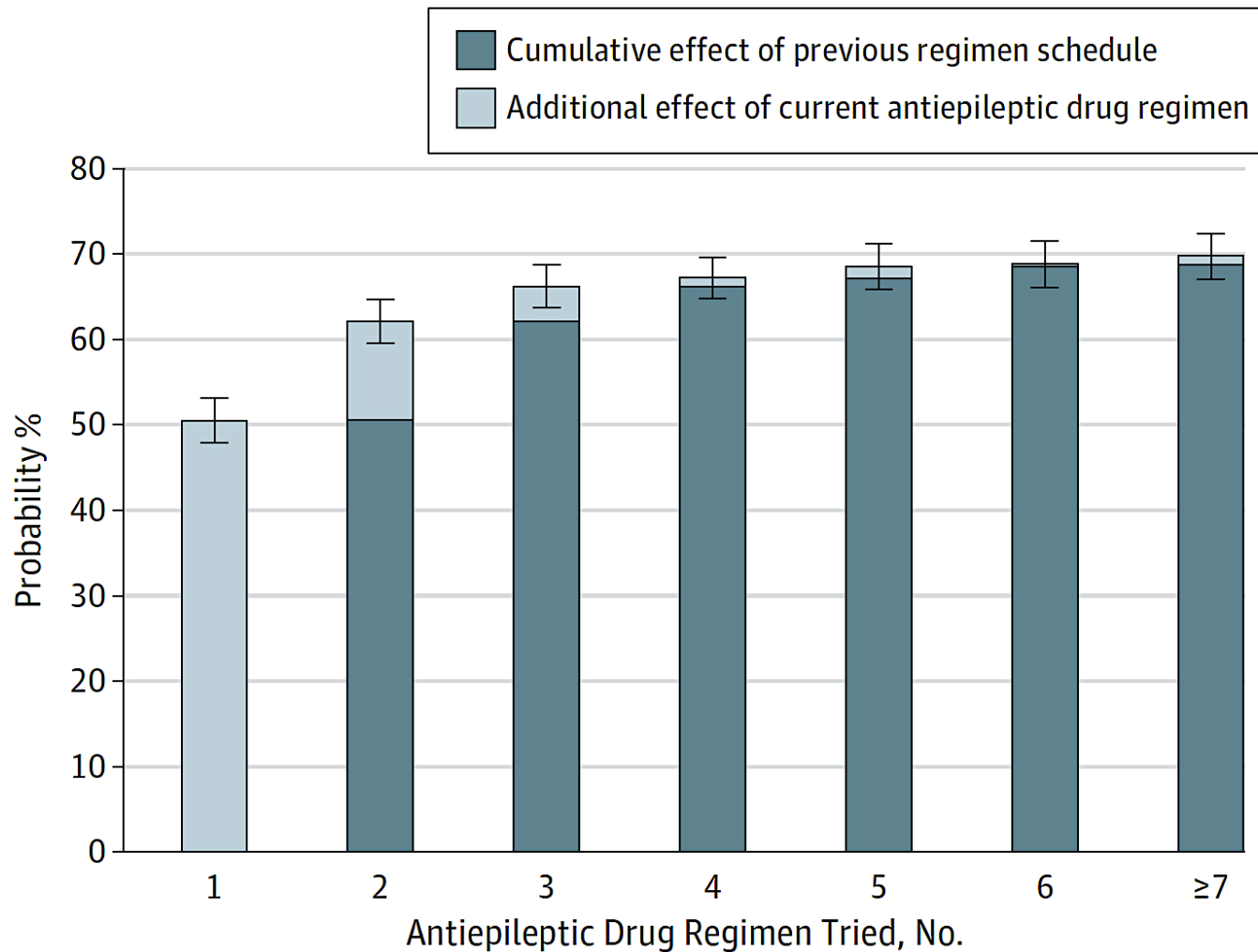
**A** All AED prescriptions



**B** Antiepileptic drugs prescribed as initial monotherapy



## Increases in Probability of 1-Year Seizure Freedom for Each Additional Antiepileptic Drug Regimen Tried



The percentage of patients achieving seizure freedom via the first, second, third, fourth, fifth, sixth, and seventh AED regimens were 50.5%, 11.6%, 0.99%, 1.34%, 0.28%, and 0.94%, respectively. Please see Table 2 for numbers of patients achieving seizure freedom and total patients in each subgroup.

## Diagnosis

- Check diagnosis: provoked seizure/ first unprovoked seizure/ epilepsy
- Etiology of epilepsy

## Starting AEDs

- Selecting the first AED

## Adjusting AEDs

- Switching AEDs
- Adding AEDs

## AEDs

- Which AEDs are available?
- Cost
- Experience

## Patient's profile

- Type of seizures
- Age
- Weight
- Underlying diseases
- Current medication
- Occupation
- Psychological profiles

Drug administration  
Prone to which side effects  
Potential drug interaction

## Diagnosis

- Check diagnosis: provoked seizure/ first unprovoked seizure/ epilepsy
- Etiology of epilepsy

## Starting AEDs

- Selecting the first AED

## Adjusting AEDs

- Switching AEDs
- Adding AEDs

## Consider drug resistant

- Failure of adequate trial of two AEDs regimen

