

fable 2: Percentage	of types	of physic	ians respons	eds a	<b>dVICe!</b>	per hospital cate	90FV
note 21 Percentage	Center hospitals (n=12)	General hospitals (n=57)	Community hospitals (n=467)	University hospitals (n=7)	Hospitals under Department of Medical service (n=9)	Hospitals under Department of Mental Health (n=3)	Others' (n=4)
General Practitioners	9.7	35.1	91.5	8.7	27.3	40.7	0.0
Internists	25.8	29.8	3.7	17.4	27.3	0.0	50.0
Epileptologists	6.5	5.7	0.0	13.0	9.1	10.4	33.3
Neurologists	32.2	0.4	0.0	21.9	9.1	20.0	16.7
Pediatricians	16.1	23.7	2.0	17.4	13.6	0.0	0.0
Neurosurgeons	9.7	3.5	0.0	13.0	13.6	0.0	0.0
Psychiatrists	0.0	1.8	1.6	4.3	0.0	28.9	0.0
Ort	0.0	0.0	1.2	4.3	0.0	0.0	0.0

Why We Need Clinical Guidelines? Clinician needs advice!								
Table 7: Number and types and other countries	of physicians that	providing ca	re for persons	with epilepsy	y in Thailand			
	Thailand	Laos6	Mongolia <sup>s</sup>	Angola <sup>9</sup>	Zambia <sup>9</sup>			
Populations, million* Neurologists Neurosurgeons Psychiatrists	69.5 305 <sup>13</sup> 252 <sup>14</sup> 546 <sup>15</sup>	6.3 1 1 NA	2.8 200 NA NA	19.6 3 3 2	13.5 2 - 10			
*Populations based on report NA = Not available Tu L	of 2011 (Source: htt	tp://www.wo	rldbank.org/); 2007					



## Why We Need Clinical Guidelines? Clinician needs advice!

Table 9: Percentages of hospitals with specific antiepileptic drugs available in Thailand and other

	Thailand	Mongolia <sup>5</sup>	India <sup>10</sup>
502 - Million -			
Phenytoin	96.0	-	49
Carbarmazepine	97.9	86.2	67.6
Valproic acid	88.8	4.3	
Phenobarbital	99.9	3.3	· · ·
Topiramate	63.9	0.5	
Gabapentin	77.6	-	8.7
Lamotrigine	45.7	2	
Levetiracetam	46.0	-	-
Vigabatin	14.5		-
Pregabalin	33.6		
Oxacarbazepine	14.3		-

# What are the major Treatment Guidelines for Epilepsy?

- **ILAE** = International League Against Epilepsy (www.ilae.org)
- NICE = www.nice.org.uk- National Institute for Clinical Excellence (England and Wales)
- SIGN = www.sign.ac.uk- Scottish Intercollegiate Guidelines Network (Scotland). (Revision 2014)
- AAN = www.aan.com-American Academy of Neurology (USA) 2004









#### Searching the Evidences for the ILAE Review 2013

 The authors evaluated available evidence found through a structured literature review including Medline, Current Contents and The Cochrane Library for all aplicable articles from 1940 until July 2005 – 31 March 2012

• <u>Question</u>: best evidence to evaluate efficacy and effectiveness of AEDs in recently diagnosed patients.



## **Epilepsy Guidelines:**

#### • -ClassesRating 4

- Class I: A masked RCT, meeting all key variable criteria
- <u>Class II</u>: A masked prospective matched-group cohort study in a representative population that meets all key variable criteria OR an RCT in a representative population that lacks one of the key variable criteria
- <u>Class III</u>: All other controlled trials in a representative population, where outcome assessment is independent of patient treatment
- <u>Class IV</u>: Evidence from uncontrolled studies, case series, case reports or expert opinion

French JA, Epilepsia 2004, 45(5):401-409 and 410-423



#### Guideline Methodology: Grading the evidence for each AED

- Recommendations 6 Levels
  - Level A: ≥1 Class I RCTs <u>OR</u> ≥2 Class II RCTs
  - Level B: 1 Class II RCTs <u>OR</u> ≥ 3 Class III RCTs
  - Level C: 2 Class III RCTs
  - Level D: Class III, or IV RCTs <u>OR</u> expert opinions
  - Level E: Absence of clinical evidence
  - Level F: Positive evidence of lack of efficacy <u>OR</u> Significant risk of seizure aggravation

Combination(s) of Clinical Trials Ratings	Level of Evidence	Conclusions	Recomendation (Based on efficacy and effectiviness data only)
≥ 1 Class I studies or meta- analysis meeting Class I criteria sources <u>OR</u> ≥ 2 Class II studies	A	AED established as efficacious or effective as initial monotherapy	AED should be considered for international states First mon rapy did
1 Class II study or meta- analysis meeting Class II criteria	В	AED probably efficacious or effective as initial monotherapy	
≥ 2 Class III double blind or openlabel studies	С	AED possibly efficacious or effective as initial monotherapy	AED may be d for initial monotherapy Ative first line monothe addidates
1 Class III double blind or open label study $QR \ge 1$ Class IV clinical studies <u>OR</u> Data from expert committee reports, opinions from experienced clinicians	D	AED potentially efficacious or effective as initial monotherapy	Weak efficacy available to y AED for i he use of the AED for i
Absence of directly applicable clinical evidence upon which to base a recommendation	E	No data available to assess if AED is effective as initial monotherapy	Either no da da sate efficacy or effecti da ullable to decide if A1 ald ullable for in 5000 cy
Positive evidence of lack of efficacy or effectiveness based on Class I to IV studies <u>OR</u> Significant risk of seizure aggravation based on Class I to IV studies	F	AED established as ineffective or significant risk of seizure aggravation	AED structure and the structure initial monotherapy

#### Partial Seizures: Adults Available Evidence

- A total of 33 (+6)randomized clinical trials (RCTs) and 5 (+4) meta-analyses examined initial monotherapy of adults with partial-onset seizures
- Division of trials
  - Class I (n=2+2=4)
  - Class II (n=1)
  - Class III (n=30+4=34)

#### Partial Seizures in Adults Listing of Class I-III Double-Blind RCTs Class I Mattson (1985) CBZ, PB, PHT, PRM Chadwick (99) CBZ, VGB Brodie (2007) LEV/CBZ, Baulac (2012) ZNS/ CBZ Class II Mattson (92) CBZ, VPA Class III ( Because of low power (DNIB) or forced exit) Brodie (95) CBZ, LTG Chadwick (98) GBP Brodie (02) GBP, LTG Sachdeo (00) TPM Christe (97) OXC, VPA Gilliam (03) TPM Bill (97) OXC, PHT Privitera (03) CBZ,TPM,VPA Dam (89) CBZ,OXC Arroyo (05) TPM Brodie (02) CBZ, REM Steiner (99) PHT, LTG Ramsay (83) CBZ, PHT Gibberd (82) PHT, PNT Mikkelsen (81) CBZ, CLP

#### Partial Seizures: Adults Recommendations

Level A: CBZ(n=23), PHT(n=12), LEV(n=1), ZNS(n=1) Level B: VPA (n=11) Level C: GBP, LTG, OXC, PB, TPM, VGB Level D: CZP, PRM Level E: Others Level F: None

#### Partial Seizures: Children Available Evidence

- A total of 25(+2) RCTs and 1(+4) meta-analysis examined initial monotherapy of children with partialonset seizures
- Division of trials
  - Class I (n=1)
  - Class II (n=0)
  - Class III (n=17+2)

#### Partial Seizures: Children Recommendations

Level A: OXC (no new AEDs) Level B: None Level C: CBZ, PB, PHT, TPM, VPA, VGB Level D: LTG, CLB, CLZ, ZNS Level E: Others Level F: None

#### Partial Seizures: Elderly Available Evidence

- A total of **30(+1)** RCTS with elderly participants included which examined initial monotherapy for partial-onset seizures
- Division of trials
  - Class I (n=1)
  - Class II (n=1)
  - Class III (n=2+1)

#### Partial Seizures: Elderly Recommendations

#### Level A: GBP, LTG (no new AED)

Level B: None Level C: CBZ Level D: TPM, VPA Level E: Others Level F: None

#### Generalized Tonic Clonic Seizures: Adults Available Evidence

- A total of 23 (+4) RCTs and 5 (+4) meta-analyses examined initial monotherapy of adults with generalized-onset tonic clonic seizures
- Division of trials
  - Class I (n=0)
  - Class II (n=0)
  - Class III (n=10+4):CBZ, GBP, LTG, OXC, PB, PHT, TPM, VPA

#### Generalized Tonic Clonic Seizures: Adults Recommendations

#### Level A: None

Level B: None Level C: CBZ\*,LTG,OXC\*,PB, PHT\*,TPM,VPA Level D: GBP,VGB Level E: Others Level F: None

 \*=may aggravate tonic clonic seizures and more commonly other generalized seizure types, should be used with caution

#### Generalized Tonic Clonic Seizures: Children Available Evidence

- A total of 20 (+0) RCTs examined initial monotherapy of children with generalized onset tonic clonic seizures
- Division of trials
  - Class I (n=0)
  - Class II (n=0)
  - Class III (n=14): CBZ, CLB, OXC, PB, PHT, TPM, VPA

#### Generalized Tonic Clonic Seizures: Children Recommendations

#### Level A: None

Level B: None Level C: CBZ\*,PB, PHT\*,TPM,VPA Level D: OXC\* Level E: Others Level F: None

\*may aggravate tonic clonic seizures and more commonly other generalized seizure types, should be used with caution

#### Childhood Absence Epilepsy: Available Evidence

- A total of 6 (+2) RCTs examined initial monotherapy of children with Childhood Absence Epilepsy
- Division of trials
  - Class I (n=0+1)
  - Class II (n=0)
  - Class III (n=6+1) -3 Double Blinded ETX, LTG, VPA

#### Childhood Absence Epilepsy: Recommendations

#### Level A: None- (ESM, VPA)

Level B: None Level C: LTG Level D: None Level E: Others Level F: CBZ, GBP, OXC, PB, PHT,TGB,VGB

### BECTS:

## Available Evidence

- A total of 3 (+1)RCTs examined initial monotherapy of children with BECTS, 2 were DB
- Division of trials
  - Class I (n=0)
  - Class II (n=0)
  - Class III (n=2+1)

## BECTS:

Recommendations

#### Level A: None

Level B: None Level C:CBZ, VPA Level D: GBP,STM, LEV, OXC Level E: Others Level F: None

#### Juvenile Myoclonic Epilepsy: Available Evidence

- A total of 0 (+1) RCTs examined initial monotherapy of children with Juvenile Myoclonic Epilepsy
- Division of trials
  - Class I (n=0)
  - Class II (n=0)
  - Class IIII (n=0+1)

#### Juvenile Myoclonic Epilepsy : Recommendations

#### Level A: None

Level B: None Level C: None Level D: TPM, VPA Level E: Others Level F: CBZ\*, GBP, OXC\*, PHT\*, TGB, VGB

\*may aggravate myoclonic seizure types, should be used with caution

#### Juvenile myoclonic epilepsy

- Drugs to be avoided
- Clinical evidence has been provided that PHT, CBZ, OXC, VGB, TGB, GBP (PRE?) may aggravate absence and myoclonic seizures
- LTG has been shown to aggravate severe myoclonic epilepsies in infancy and in JME Level of Evidence III-IV,

Recommendation C

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, VP/ Level D: GBP, LEV, VGB
Children with generalized-onset tonic–clonic seizures	0	0	14	Level A: None Level B: None Level C: CBZ, PB, PHT, TPM, VPA Level D: CXC
Children with absence seizures	1	0	7	Level A: ESM, VPA Level B: None Level C: LTG Level D: None
Benign epilepsy with centrotemporal spikes (BECTS)	0	0	3	Level A: None Level B: None Level C: CBZ, VPA Level D: CBP, LEV, OXC, STM
Juvenile myoclonic epilepsy (JME)	0	0	I	Level A: None Level B: None Level C: None Level C: None

Seizure type or epilepsy syndrome	Class I	Class II	Class III	Level of efficacy and effectiveness evidence (alphabetic order)
POS: Adults	2 (+2)	1	30(*4)	Level A: CBZ, PHT, LTV, 2018 Level B: VPA Level C: GBP, LTG, OXC, PB, TPM, VGB Level D: C22, FMB
POS: Children	1	0	17(* 2)	Level A: OXC Level B: None Level C: CBZ, PHT, TPM, VPA Level D: CLB: CZP, LTD, 2006
POS: Elderly	1	1	2(*1)	Level A: GBP, LTG Level B: None Level C: CBZ Level D: 1998, 1999

### 6

Seizure type or epilepsy syndrome	Class I	Class II	Class III	Level of efficacy and effectiveness evidence (alphabetic order)
TCGS: Adults	0	0	23+ 4	Level A: None Level B: None Level C: CBZ, LTG, OXC, PB, PHT, TPM, VPA Level D: CBTF (LTC, VPB)
TCGs: Children	0	0	14	Level A: None Level B: None Level C: CBZ, PB, PHT, TPM, VPA Level D: CMC
Absence		0	6+ 1	Level A: VPA, ESM
seizure				Level B: None Level C: 155 Level D: None

AED-specific variables	Patient-specific variables	Nation-specific variable
Seizure type or epilepsy syndrome	*Genetic background	•AED availability
effectiveness	*Age	*AED cost
*Dose-dependent	*Gender	*Insurance coverage
	*Comedications	
	*Comorbidities	
*Chronic toxicities	*Insurance coverage	
	*Ability to swallow	
Carcinogenicity	pills/tablets	



Table 5: Percentage of hospitals having standard antiepileptic drugs available classified by hospital types

	Center hospitals	General hospitals	Community hospitals	University hospitals	Hospitals under Department of Medical Service	Hospitals under Department of Mental Health	Others*
	(n=12)	(n=57)	(n=467)	(n=7)	(n=9)	(n=3)	(n=4)
Phenobarbital	100.0	100.0	99.1	100.0	100.0	100.0	100.0
Phenytoin	100.0	94.5	88.5	100.0	88.9	100.0	100.0
Carbamazepine	100.0	98.2	86.9	100.0	100.0	100.0	100.0
Valproic acid	100.0	89.1	45.1	100.0	87.5	100.0	100.0

Tiamkao S, Neurology Asia2013







สารบัญ		
	หน้า	
สำนัญน	n	
efnih	π	
รายนามพณะประว	n	
ข้อแนะนำการใช้	4	
บทย่า	1	
บทที่ 1 การวิบิจฉัดอาการซัก : การซักประวัติและการตรวจร่างกาย	10	
บทที่ 2 การจัดจำนวยประเทศของการจัดและโรงชมจัด	14	
บทที่ 3 แนวทางการสืบคันในผู้ป่วยที่มีอาการจักและโรคลมจัก	21	
บทที่ 4 การวินิจฉัยแอกอาการซักและโรคณะชักจากการะชิ้น ๆ	24	
บทที่ 5 แนวทางการวักษาผู้ป่วยชักหรั้งแรกและชักฟ้า	31	
บทที่ 6 แนวทางการบริหารยากันจัก	34	
บทที่ 7 แนวทางการคูแลผู้ป่วยโรคสมชักชนิดไม่คอบสนองค่อการรักษา	64	
นทที่ 8 การชุมสร้างกลาวะชักต่อเนื่อง (Status epilepticus)	48	
บทที่ 9 แนวทางการปฏิบัติในการคุณแต๊กที่มีอาการอักจากไข้ (Febrie seizure)	58	
unif 10 Infantile spasms & West syndrome	63	
บทที่ 11 การผ่าดีครักษาผู้ป่วยโรคณาร์ก (Epileptic surgery)	66	
บทที่ 12 อาการจักจากการสรวณติดปกติหรือโรคของระบบต่างๆ พรงอายุรกรรม	69	
newen		
ภาคณวกที่ 1 การปฐมพยาบาลเปื้อเดิน	78	
ภาคมนวกที่ 2 การให้ความรู้แก่ผู้ปวยและผู้ปกครอง	79	
ภาคณวกที่ 3 การอดไข้ในเด็ก	81	
ภาคณวกที่ 4 การให้ความรู้เรื่อกกันธุกรรมของโรคณชัก	82	
ภาคมนวกที่ 5 การต่อต่อผู้ป่วยเพื่อการรักษา	84	
ภาครณวกที่ 6 โรคสมพักในผู้หญิง	85	
ภาคณวกที่ 7 โรคณาจักในผู้อุขายุ	87	
ภาคมนากที่ 8 โรคสมรักไมเด็ก	88	
messuanil 9 Ketogenic diet	90	
ภาคณวกที่ 10 บัญชียาหลักแห่งชาติ	92	



# **ILAE Reports & Guidelines**

#### Antiepileptic Drugs

- <u>Antiepileptic drugs and suicidality: an expert consensus</u> <u>statement</u> (2013)
- Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. (2013)
- <u>Antiepileptic drug selection for people with HIV/AIDS:</u> <u>Evidence-based guidelines from the ILAE and AAN</u> (2012)
- Antiepileptic drugs Best practice guidelines for therapeutic drug monitoring: (2008)
- ILAE Treatment Guidelines (2006) • Treatment Guidelines Excel spreadsheet
  - Guidelines PPT Presentation

# **ILAE Reports & Guidelines**

- Antiepileptic Drugs (Pediatric)
- Diagnostic test utilization in evaluation for resective epilepsy surgery in children Report from The Task Force for Paediatric Epilepsy Surgery, Commission for Paediatrics, and the Diagnostic Commission (2014)
- Guidelines for imaging infants and children with recentonset epilepsy (2009)
- Guidelines on Neonatal Seizures (WHO, ILAE) (2011)

# **ILAE Reports & Guidelines**

#### • Other ILAE Guidelines

- <u>Cavernoma-related epilepsy: Review and recommendations</u> for management (2013)
- Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: A staged approach(2013)
- Identification of new epilepsy treatments: issues in preclinical methodology (2012)
- Epilepsy imaging study guideline criteria: Commentary on diagnostic testing study guidelines and practice parameters (2011)

## **ILAE Reports & Guidelines**

#### • Other ILAE Guidelines

- <u>Standards for epidemiologic studies and surveillance of</u> <u>epilepsy</u> (2011)
- <u>Genetic testing in the epilepsies: Report of the ILAE Genetics</u> <u>Commission</u> (2010)
- <u>Recommendation for a definition of acute symptomatic</u> <u>seizure</u>: Report from the ILAE Commission on Epidemiology (2009)
- <u>Definition of drug resistant epilepsy:</u> Consensus proposal by the ad hoc task force of the ILAE Commission on Therapeutic Strategies (2009)

## **ILAE Reports & Guidelines**

- Other ILAE Guidelines
- Guidelines for Neuroimaging Evaluation of Patients with <u>Uncontrolled Epilepsy Considered for Surgery</u>. Commission on Neuroimaging of the ILAE (1998)
- Recommendations for Neuroimaging of Patients with Epilepsy; ILAE Commission on Neuroimaging (1997)

## **Conclusion about Guidelines**

- When selecting a patient's AED, all relevant variables and not just efficacy and effectivenes should be considered.

- Guidelines or evidence reviews can be seen as

additional tool, not the only tool in the clinical decision. – Most guidelines actually not guidelines but more recommendations based largely by "expert opinion"

and common practice

\_Totally pointless if not circulated, read, and widely available

## **Conclusion about Guidelines**

- It must ultimately remain for the individual physician to use his judgement aqnd expertise when deciding on the most appropriate drugs for the specific patients (ILAE)

**Thank You Very Much**