Chulalongkorn University
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# Natural history and drug-resistant epilepsy

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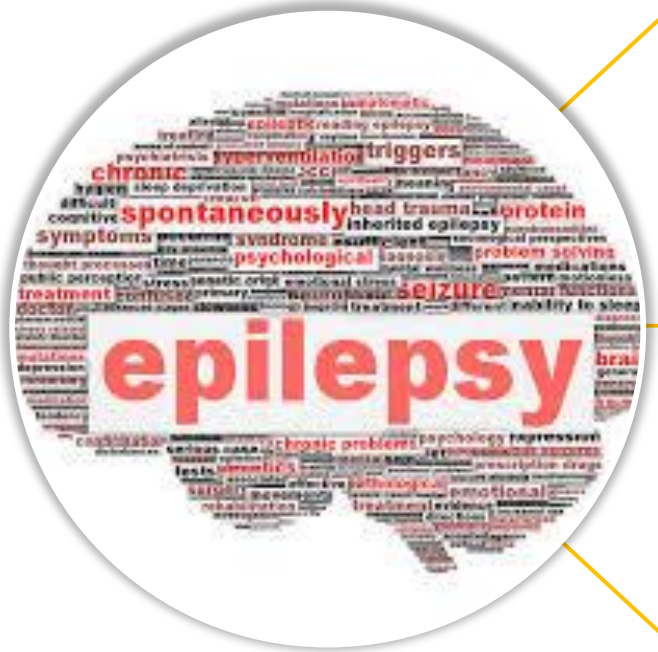
Febrile seizures

First unprovoked seizure




Untreated epilepsy

Treated epilepsy

Drug-resistant epilepsy

# Talk overview

- Natural course and prognosis  of
  - ❖ *Febrile seizures*
  - ❖ *First unprovoked seizure*
  - ❖ *Untreated epilepsy*
  - ❖ *Treated epilepsy*
- Patterns of treatment response in newly diagnosed epilepsy
- Defining drug-resistant epilepsy
- Predictors and consequences of drug-resistant epilepsy

# Natural course and prognosis of febrile seizures

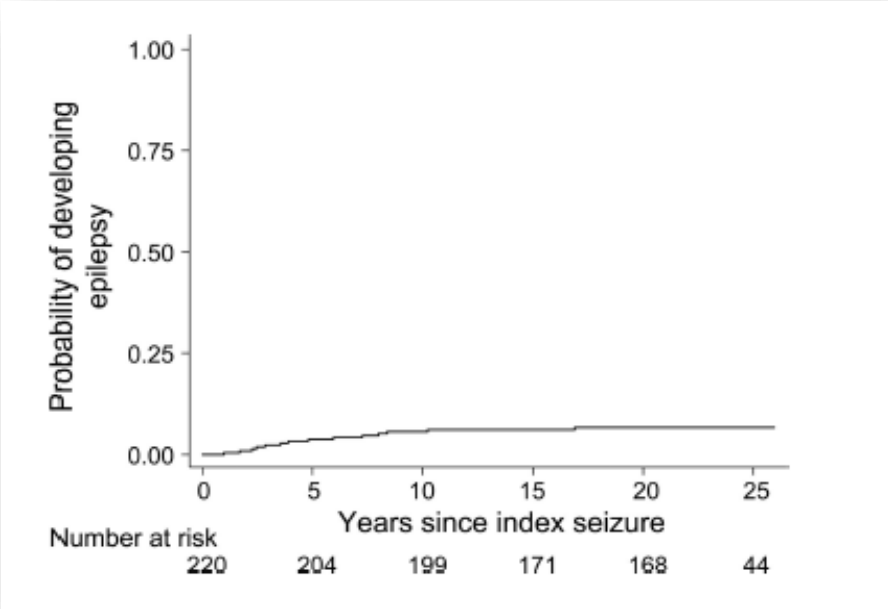
# Long-term prognosis of febrile seizures

- **Population-based studies: risk of later developing epilepsy between 2 and 7% (depending on duration of follow up)**

*Chungath M and Shorvon S; Nat Clin Pract Neurol 2008*

- **1980s to 2012, with a mean follow-up of 21.6 years**
  - **6% of the children developed subsequent epilepsy (compared with a population risk of 1.4%)**
  - **age-specific incidence risk of developing epilepsy is almost 10 times (SIR = 9.7, 95% CI 5.7-16.4)**

*Neligan A et.al; Neurology 2012*




  - **12-yr F/U: 1/3 simple febrile convulsions**
    **Risk factors: 1) number of FC:**
    **The more febrile convulsions that occurred, the more likely was subsequent epilepsy**
    **2) complex FC**

*MacDonald BK et,al; Eur Neurol 1999*

# Natural course and prognosis of first unprovoked seizure

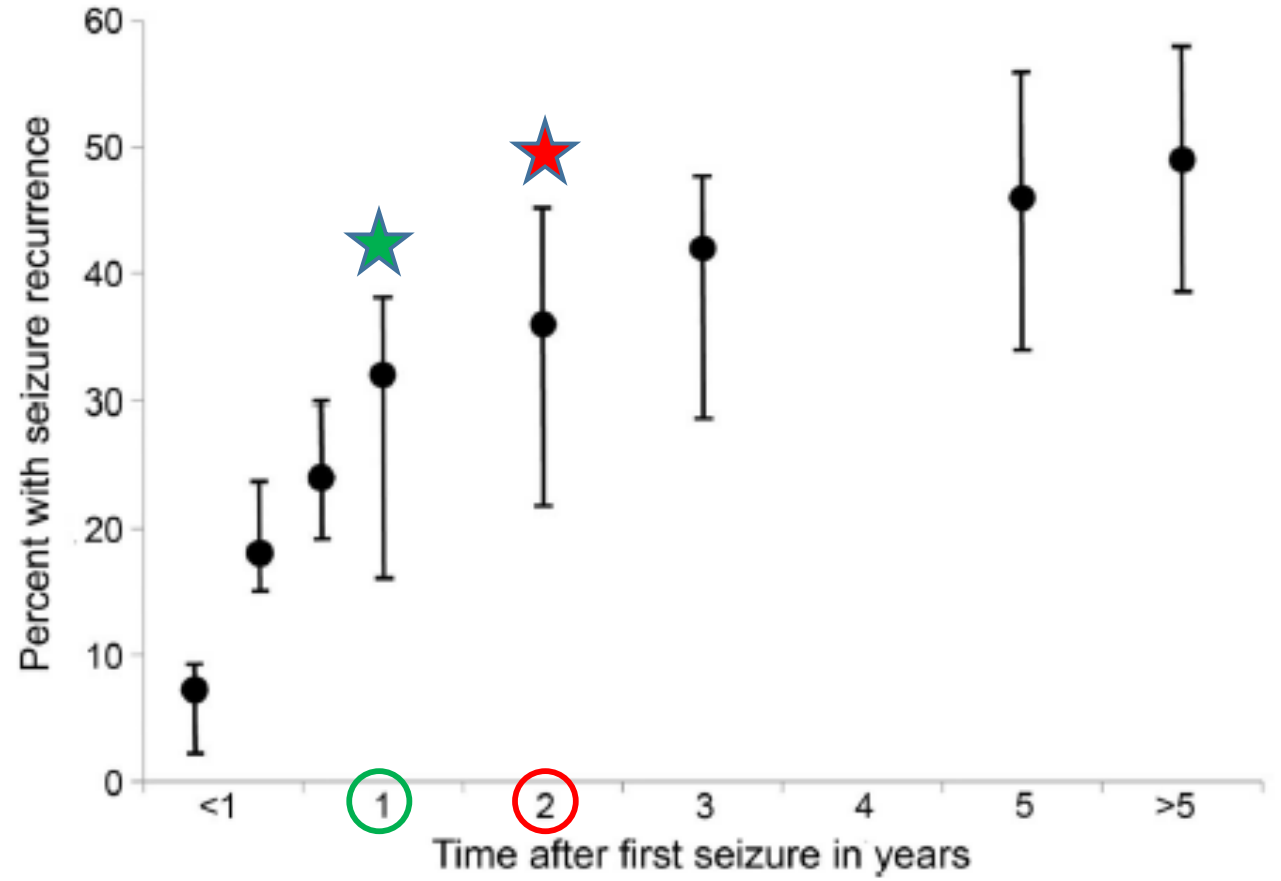
# An adult with an unprovoked first seizure is at greatest risk of a recurrence relatively early within the first 2 years (21-45%) and especially in the first year

**Table 1** Risk of seizure recurrence after an unprovoked first seizure in adults (Class I and II studies)

| | | | | Seizure recurrences at various times, n (%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ref. | Class | Age, y | No. | Treated | 1 mo | 3 mo | 6 mo | 1 y | 2 y | 3 y | 5 y | >5 y |
| 10, 11 | I | 70% >19 | 238 | 164 (69) | — | — | — | 38 (16) | 50 (21) | 60 (29) | 70 (34) | 81 (39) |
| 12, 13 | I | 72% >16 | 397 | 204 (51) | 24 (6) | 58 (15) | 75 (19) | 98 (25) | 111 (28) | — | — | — |
| 17 | II | ≥16 | 147 | 62 (42) | — | — | 39 (27) | 50 (34) | 60 (41) | 61 (41) | — | — |
| 18 | II | Mean >20 | 76 | 36 (47) | 2 (3) | 18 (24) | 20 (26) | 22 (29) | — | — | — | — |
| 16 | II | ≥16 | 306 | 41 (13) | | 55 (18) | 79 (26) | 111 (36) | 136 (44) | 144 (47) | — | — |
| 19 | II | 75% >15 | 424 | ? | 38 (9) | 89 (21) | 127 (30) | 153 (36) | 191 (45) | 204 (48) | 237 (56) | 244 (58) |
| 20 | II | 14-91 | 497 | 127 (26) | — | | — | 191 (38) | — | — | — | — |
| 15 | II | 60% >20 | 812 | 404 (50) | — | | 179 (22) | — | 288 (35) | — | 378 (46) | 398 (49) |
| 21 | II | ≥16 | 228 | 113 (50) | — | — | — | 68 (30) | — | — | — | — |
| 22 | II | 18-50 | 87 | 45 (52) | — | | — | 30 (34) | 37 (43) | 39 (45) | — | — |
| Total | | | 3,212 | 1,196 (43) | 64 (7) | 220 (18) | 519 (24) | 761 (32) | 873 (36) | 508 (42) | 685 (46) | 723 (49) |

*Krumholz et al; Neurology 2015*

**Figure 1** Percentages of patients with first seizure experiencing a recurrent seizure over time

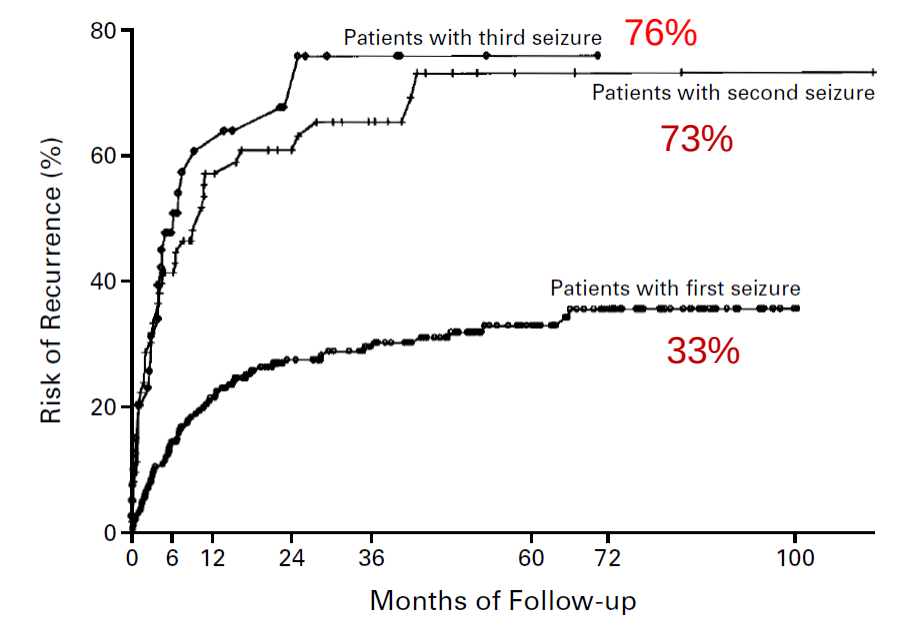



This graph is based on a fixed-effect pooled percentage model from data in table 1 and shows the cumulative average and the range for each time period from 1 month to more than 5 years.

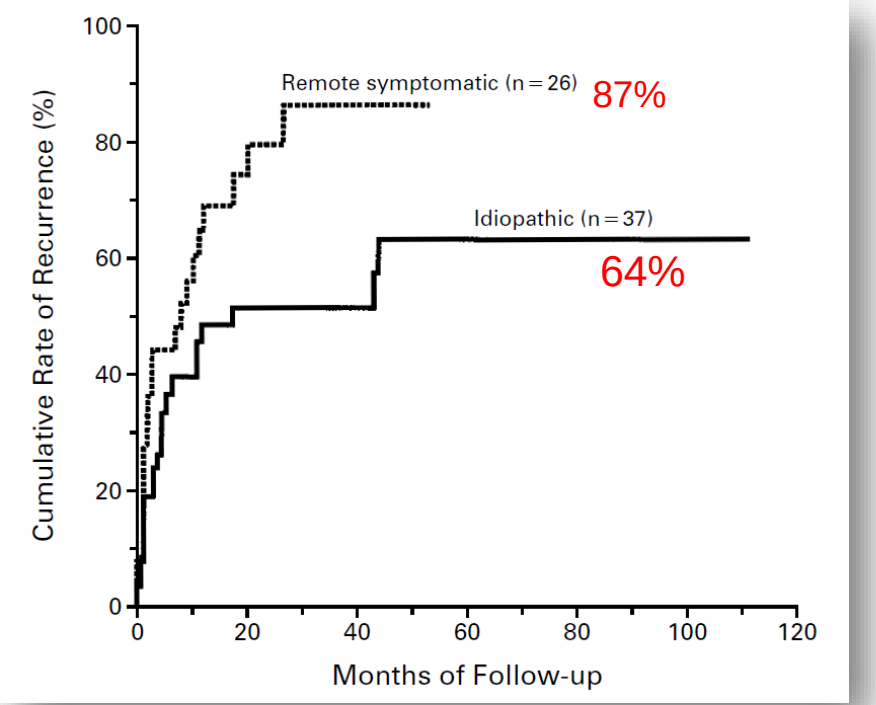
*Krumholz et al; Neurology 2015*

# Risk of recurrence

## After first, second and third seizure




## Etiology




*Hauser WA et.al; NEJM 1998*

# Prediction of risk of seizure recurrence

## MESS studies

| | Prognostic index |
|---|---|
| **Starting value** | |
| - 1 seizure prior to presentation | 0 |
| - 2 or 3 seizures prior to presentation | 1 |
| - 4 or more seizures prior to presentation | 2 |
| **Add if present** | |
| - Neurological disorder or deficit, *learning disability* or *developmental delay* | 1 |
| - Abnormal EEG | 1 |
| **Risk classification group for seizure recurrence** | |
| - Low risk | 0 |
| - Medium risk | 1 |
| - High risk | 2-4 |

"There is little benefit to immediate treatment in patients at low risk of seizure recurrence, but potentially worthwhile benefits are seen in those at **medium and high risk**"

**"Should treat"**

**First unprovoked seizure with**

- **Abnormal neurological signs**

**and/or**

- **Epileptiform discharges on EEG**

*Kim LG et al The Lancet 2006*

# Natural course and prognosis of untreated epilepsies

# Introduction

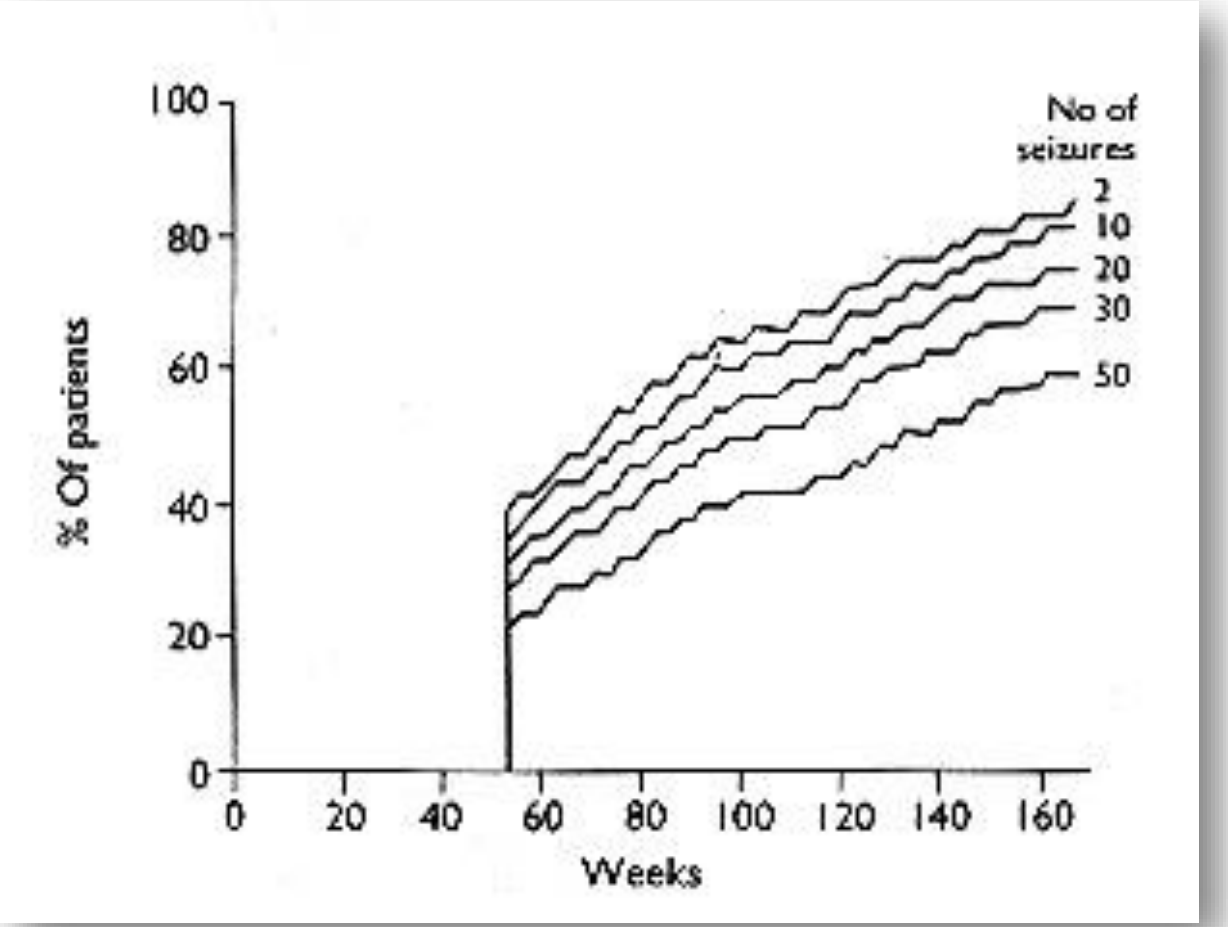
- **The course of disorders from onset to resolution, without interventions (Last, 1988)**
- **Evidence-based treatments with proven efficacy alter the natural course of disorders**
- **Prospective studies in untreated patients are thus not possible.**

# Effect of duration of epilepsy on long-term prognosis

**Gower's observation and Reynolds EH studies pointed out that the longer the history of epilepsy the worse the longer term prognosis**

*Gowers WR 1881*
*Reynolds EH; BMJ 1995*
*Reynolds EH et.al; Epilepsia 1989*

# Effect of number of seizure prior to treatment



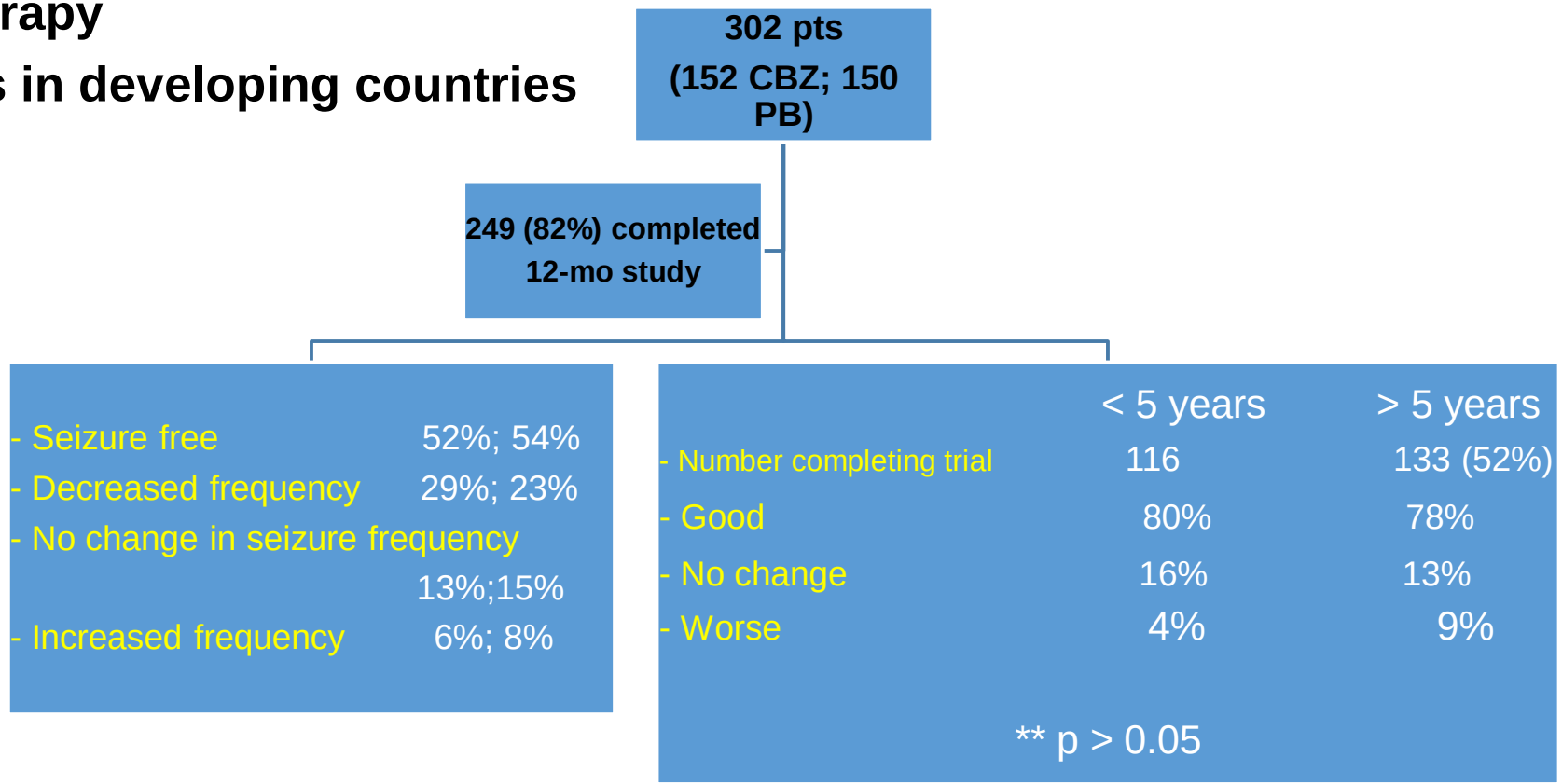

**Prospective study:**
**241 adults with newly diagnosed epilepsy treated with one drug**

*Gowers WR 1881*
*Reynolds EH; BMJ 1995*
*Reynolds EH et.al; Epilepsia 1989*

# The effects of AEDs on long-lasting untreated epilepsy

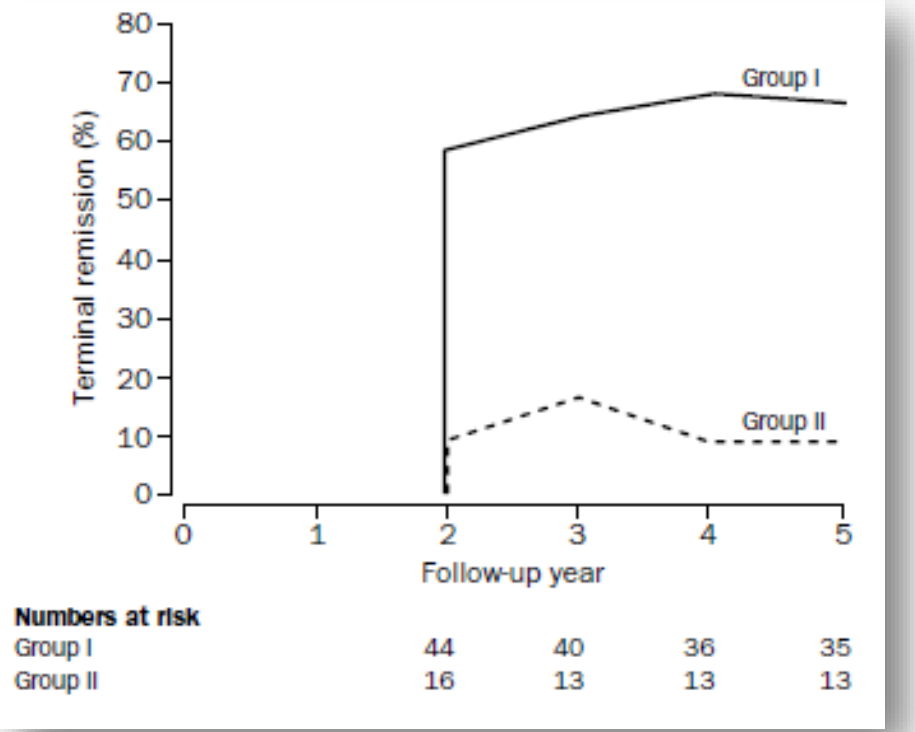
- **A study in Kenya (Lancet, 1991) : a finding that does not support the suggestion that the disorder becomes intractable if not treated early.**
- **Neither length of history of epilepsy nor number of seizures before treatment influenced effect of therapy**
- **Similar to other studies in developing countries**

  **(Malawi and Ecuador)**




*Feksi AT et.al; Lancet 1991*
*Watts AE; Br Med J 1989*
*Placencia et.al; JNNP 1994*

# Effect of number of seizure prior to treatment




**135 adult patients with partial seizure or GTCs**

- **Treated with either PB or PHT**
- **Primary outcome: 2-year seizure freedom**

**Group I: good compliance coupled with lifetime total of ≤ 30 GTCs**
**Group II: poor compliance and lifetime total ≥ 30 GTCs**

*Mani et.al; Lancet 2001*

# Natural course and prognosis of treated epilepsies

# Late prognosis

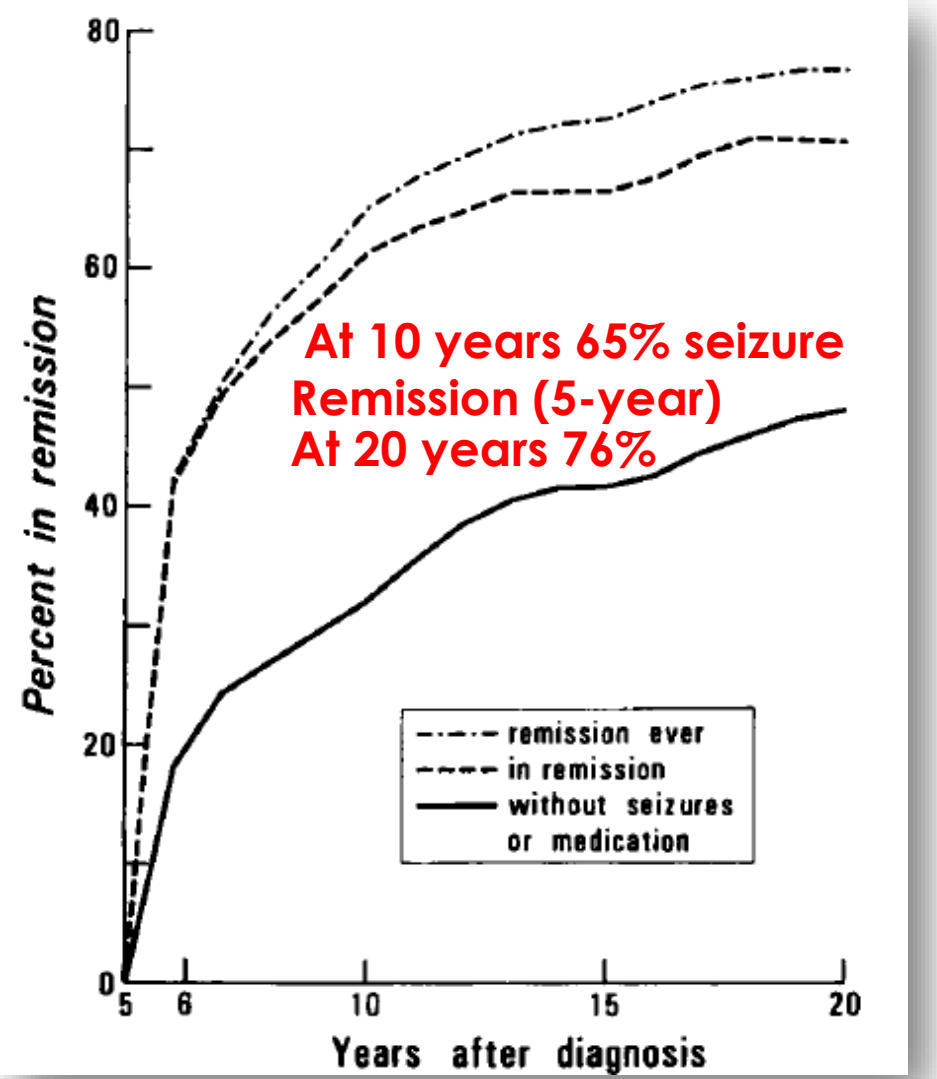
- **Based on 3 longitudinal community-based studies with long-term follow up**

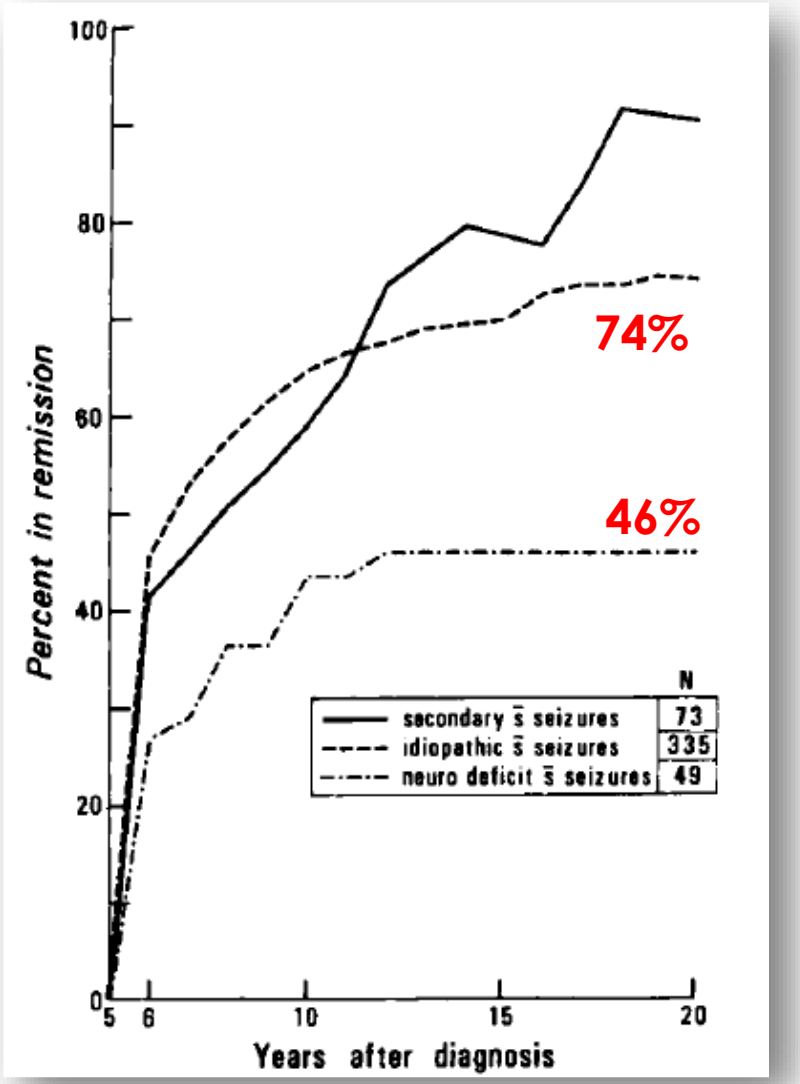
  **- Mayo Clinic Record linkage study (US)**

  **- Tonbridge study (UK)**

  **- Turku study (Finland) (childhood-onset epilepsy)**

# Mayo clinic study (20 years follow up)

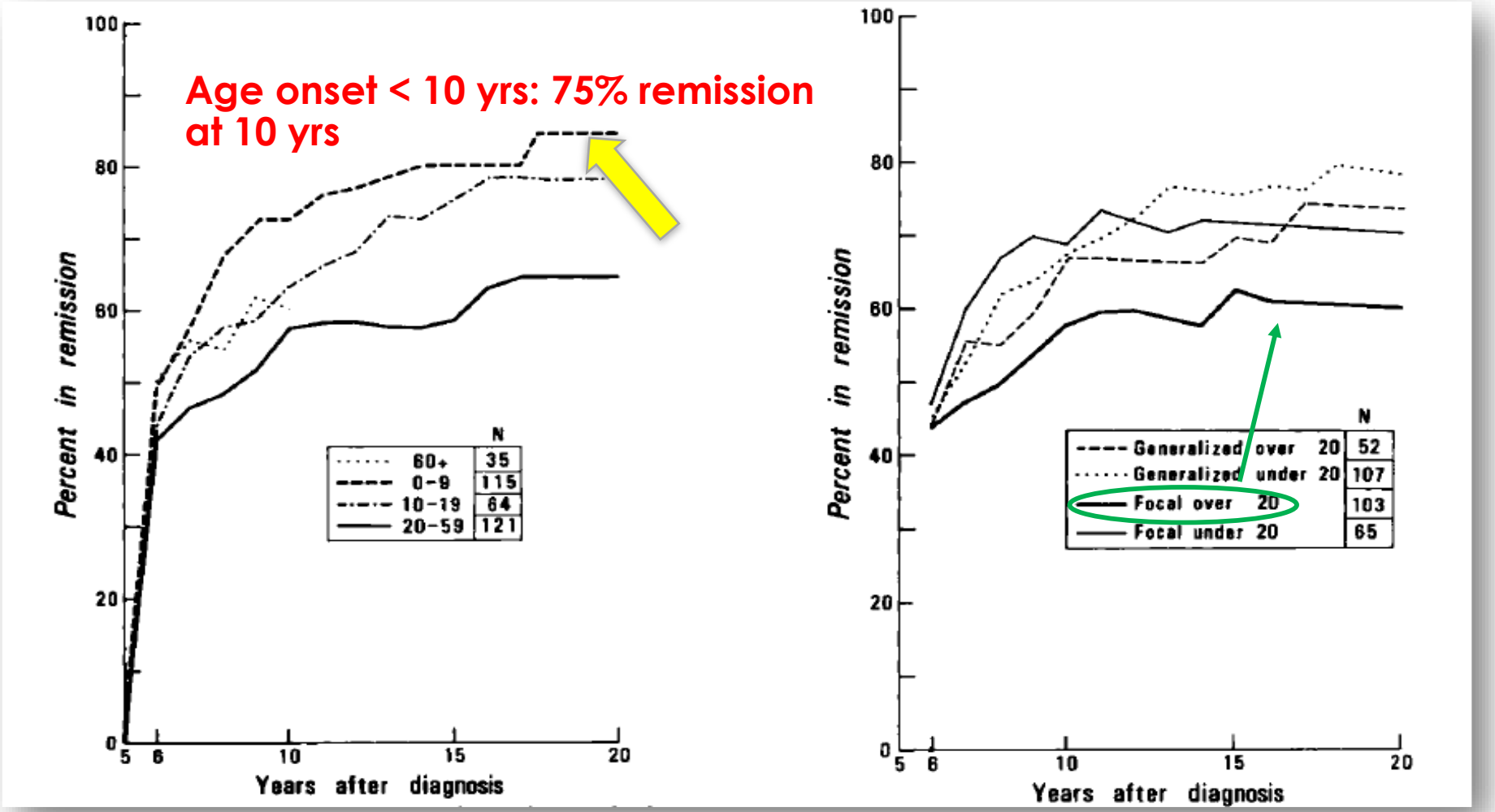



- 475 pts followed at least 5 yrs
- 141 pts > 20 yrs

*Annegers et.al; Epilepsia 1979*

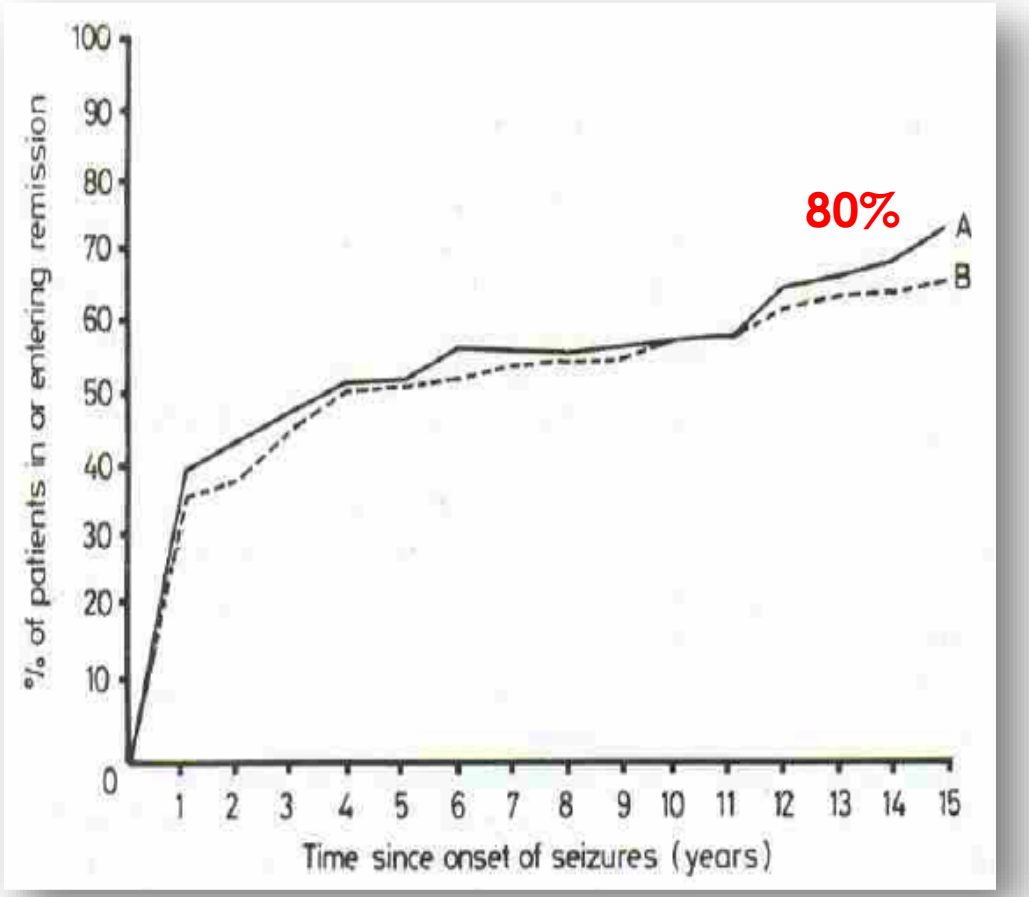
# Mayo clinic study

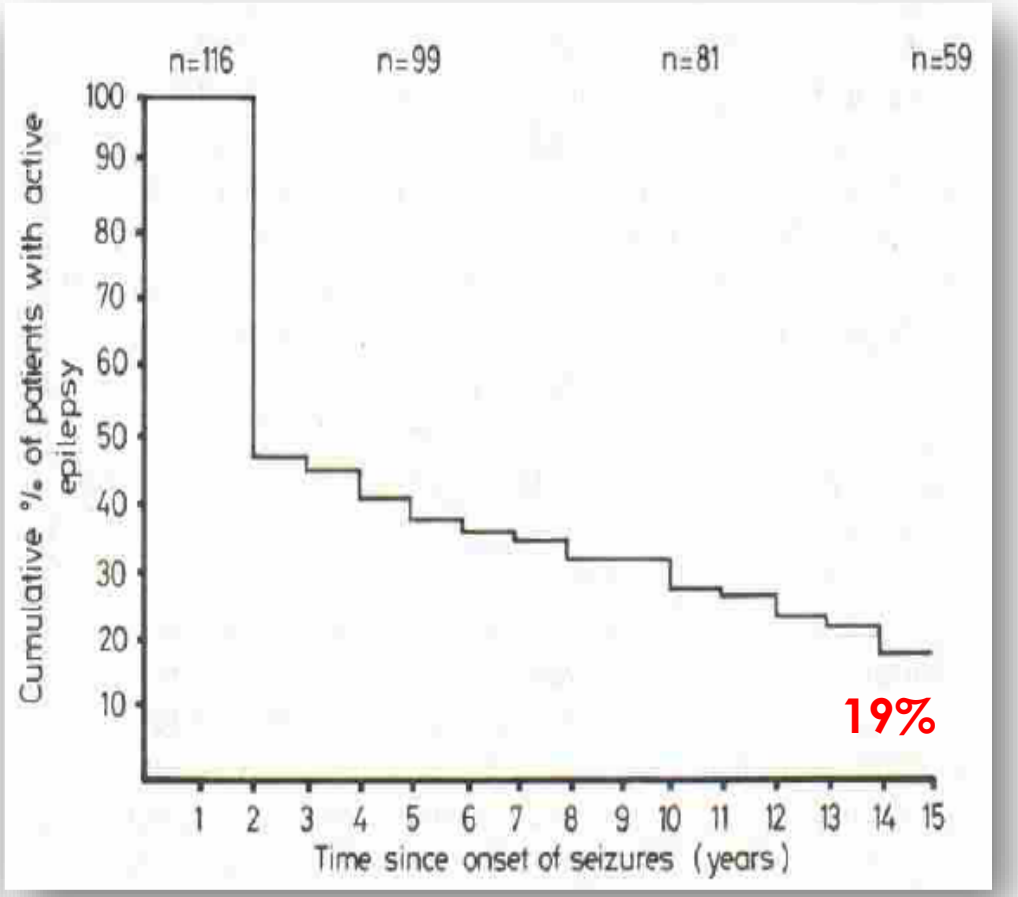



**Higher remission: generalized-onset seizure diagnosed < 10 yrs**

**Lower remission: CPS with adult onset**

# Tonbridge study (15 years follow up)




**About one fifth (20%) of the patients continued to have seizure (chronic epilepsy)**

*Goodridge and Shorvon; BMJ 1983*

# Tonbridge study

- **At 5 years after the first seizure**

  **- of those whose epilepsy was still active, only 21% achieved subsequent terminal remission as compared with 96% of those who were already in remission**

**“ the longer seizure continues to occur, the lower the probability for subsequent remission”**

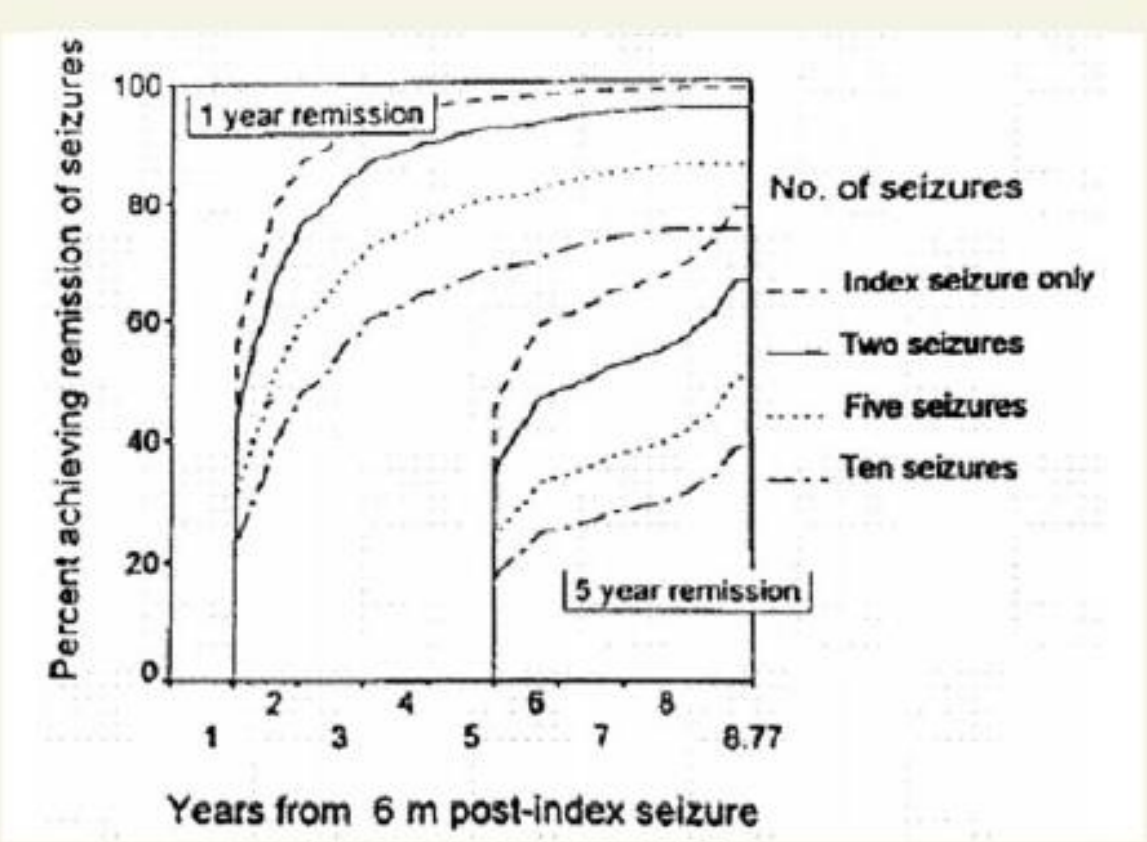


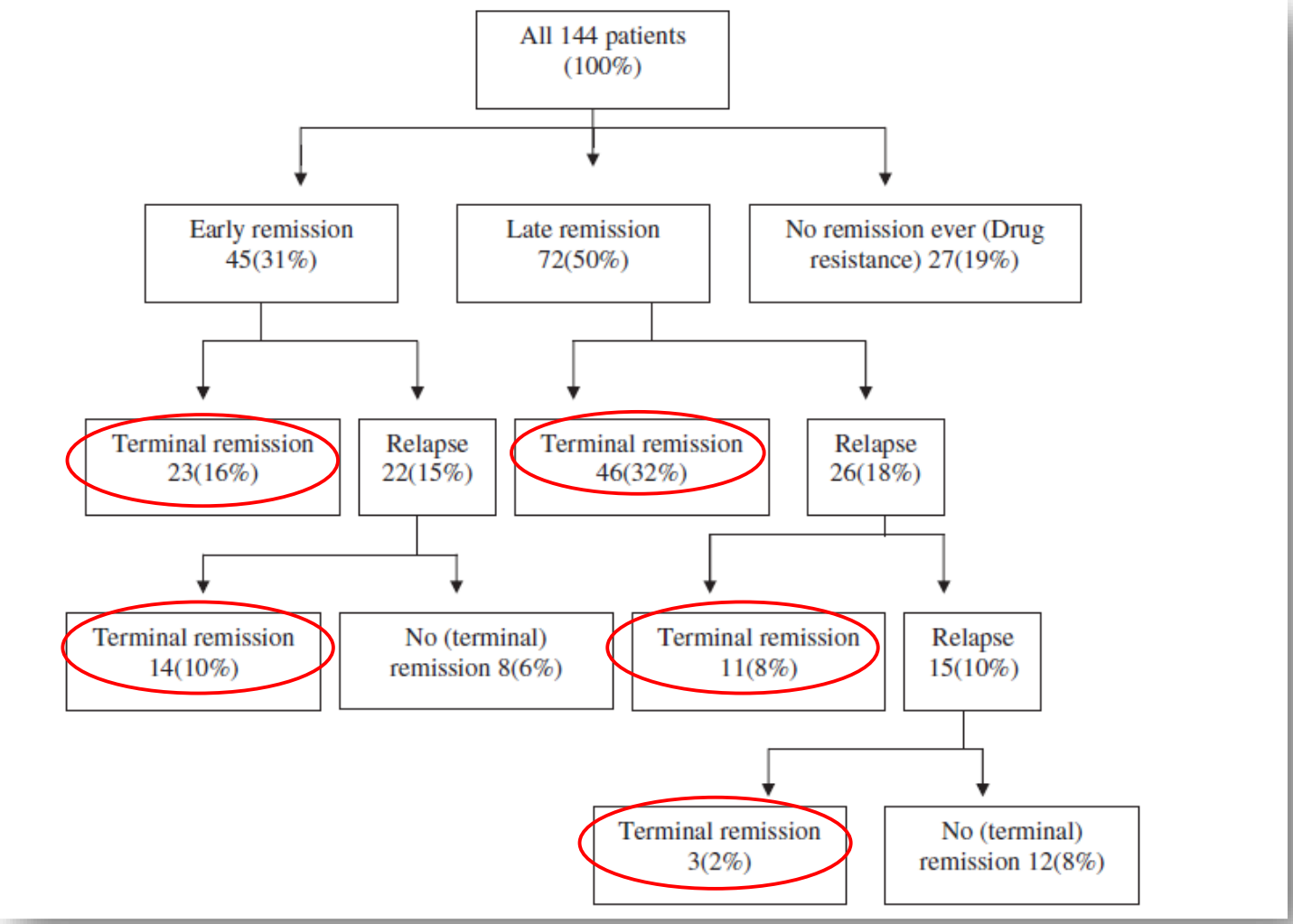

Figure 2 NGPSE: the influence of seizure density on long-term remission. The percentage of patients achieving remission in those who had experienced one (dashed line), two (solid line), five (dotted line), or 10 (dashed and dotted line) seizures in the period from the index seizure to 6 months.

**The more number of seizure in the 6 months after the first seizure, the lesser is the chance of long-term remission**

*MacDonald BK et.al; Ann Neurol 2000*

# Turku study (37 years follow up)

- **Seizure before the age of 16 years**




- **67% achieved terminal remission (5-year seizure freedom at the end of follow up)**
- **19% drug resistant**
- **19% entered terminal remission after a relapse**

*Sillanpaa M and Schmidt D; Brain 2006*

# Conclusion

- **2/3 of the patients (58-65%) achieved 5-year cumulative terminal remission at 7-10 years follow up**

- **3/4 of the patients (67-78%) with childhood-onset epilepsy achieved 3-5 year remission at 12-37 years follow up**

**Factors which influence on long-term remission rate**

- ✓ **Neurological deficits**
- ✓ **Age onset**
- ✓ **Seizure type**
- ✓ **Number of early seizure**

# Patterns of treatment response in newly diagnosed epilepsy

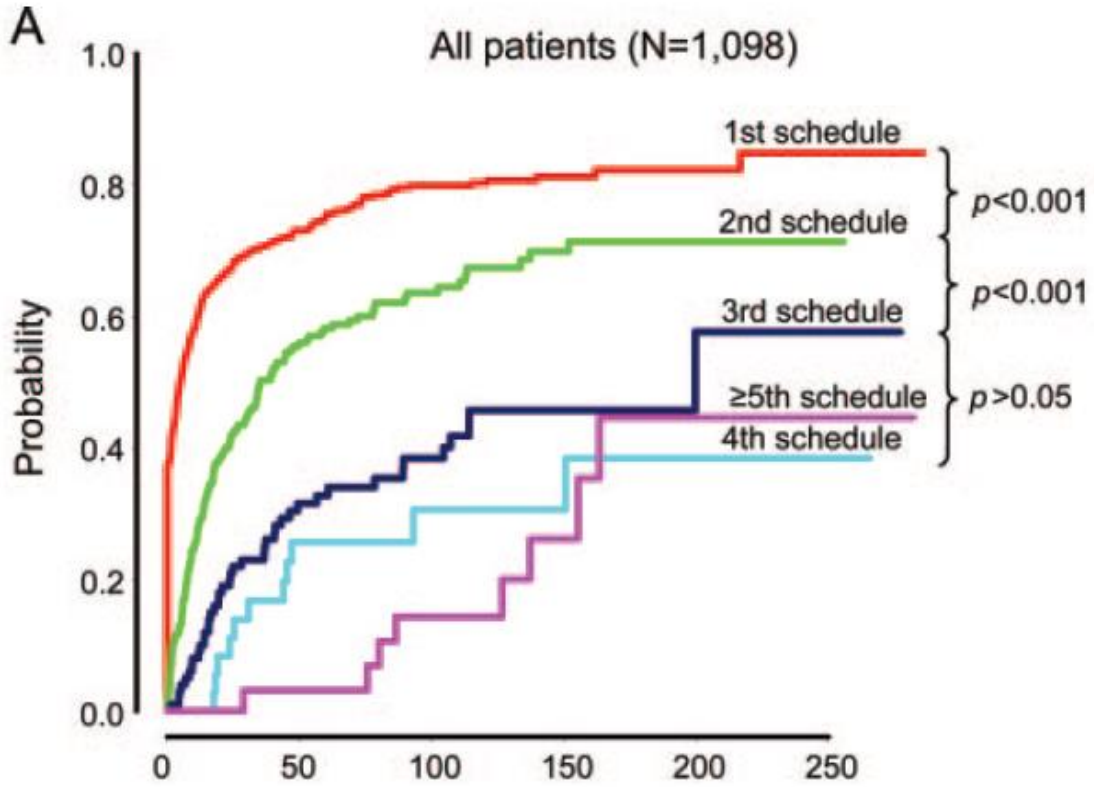
# Seizure-free rates with successive AED regimens

There was a higher probability of seizure freedom in patients receiving 1 compared to 2 drug regimens, and 2 compared to 3 regimens ($p < 0.001$)

**Table 1** Seizure-

| Drug regimens | No. of patients | % Seizure-free on regimen |
|---|---|---|
| First | 1,098 | 49.5 |
| Second | 398 | 36.7 |
| Third | 168 | 24.4 |
| Fourth | 68 | 16.2 |
| Fifth | 32 | 12.5 |
| Sixth | 16 | 12.5 |
| Seventh | 9 | 22.2 |
| Eighth | 3 | 0.0 |
| Ninth | 2 | 0.0 |

**Figure 2** Cumulative probability of being seizure-free by time from start of treatment and number of antiepileptic drug regimens tried




*Brodie MJ et al.; Neurology 2012*

# 4 patterns of treatment response (1,098 pts)

| | |
|---|---|
| A) Early and sustained seizure freedom | **37%** |
| B) Delayed but sustained seizure freedom | **22%** |
| C) Fluctuation between periods of seizure freedom and relapse | **16%** |
| D) Seizure freedom never attained | **25%** |

Seizure freedom was defined as no seizures for 1 year at last follow-up

**Drug responsiveness of a patient's epilepsy should be regarded as a**
**"dynamic process rather than a fixed state"**

The classification of a patient's epilepsy as drug resistant at a given point in time is valid only at the time of the assessment and does not necessarily imply that the patient will never become seizure-free on further manipulation of AED therapy

*Brodie MJ et al.; Neurology 2012*

# Defining drug-resistant epilepsy

# Defining Intractability: Comparisons among Published Definitions

- **Individual studies use different definitions, creating difficulties for comparisons of results across studies**
- **This study was designed to detect the appearance of intractable seizures early in the course of the disorder**
- Study subjects are members of the **Connecticut Study** of Epilepsy, a prospective**, community-based cohort of 613 children** who were recruited during 1993 through 1997 at the time they were **first diagnosed with epilepsy**

*Berg AT & Kelly MM; Epilepsia 2006*

# Definitions of intractable epilepsy

**TABLE 1.** *Published criteria used for determining intractable epilepsy*

| Study/Citation | Criteria | | Comments/qualifications |
|---|---|---|---|
| | Minimum AEDs failed | Seizures | |
| Connecticut (2) | 2 | 1 seizure per mo for ≥18 mo and ≤3 mo seizure free during that time | The outcome had to be met within 3 years of diagnosis |
| Holland (1) | Not specified | At 6 mo after diagnosis, failure to be ≥3 mo seizure free | Published criteria were not modified. This is an indicator of risk and not a criterion for intractability per se. |
| Philadelphia (3) | 2 | At 2 yr after diagnosis, failure to be ≥6 mo seizure free | Criteria were used as published without modification |
| Canada (5) | 3 | ≥1 seizure every 2 mo in last year of follow-up | Modified to be assessed at 5 yr after initial diagnosis |
| Scotland (6) | 2 | <1 yr seizure free at last follow-up | Modified to be assessed at 5 yr after initial diagnosis |
| Surgery (4) | 2 | Not explicitly stated | The outcome had to be met within 3 yr of diagnosis |

*Berg AT & Kelly MM; Epilepsia 2006*

# Definitions of intractable epilepsy

**TABLE 2.** *Proportion of children who met each of the different definitions of intractability or poor outcome*

| Criteria (n = number with unclassified outcomes due to insufficient follow-up) | Did not meet criteria | Met criteria |
|---|---|---|
| Connecticut (n = 10) | 546 (91%) | 57 (9%) |
| Dutch (n = 4) | 461 (76%) | 148 (24%) |
| Philadelphia (n = 14) | 530 (88%) | 69 (12%) |
| Canadian (n = 48) | 514 (91%) | 51 (9%) |
| Scottish (n = 48) | 491 (87%) | 74 (13%) |
| Surgery (n = 0) | 510 (83%) | 103 (17%) |

- The epilepsy of **9–24%** of children was considered intractable
- Kappa ranged from low of **0.45 to 0.79**

*Berg AT & Kelly MM; Epilepsia 2006*

**TABLE 4.** *Associations between intractability criteria and longer-term outcomes of 2- and 5-year remission*

| Criteria | In 2-yr remission at last follow-up for those followed up for ≥7 yr (n = 549) | In 5-yr remission at last follow-up for those followed up for ≥10 yr (n = 210) |
|---|---|---|
| Connecticut | | |
| Not intractable | 386/502 (77%) | 133/193 (69%) |
| Intractable | 4/47 (9%) | 1/17 (6%) |
| RR | 9.0 (8.3–9.9) | 11.7 (10.3–13.3) |
| Holland | | |
| Not at increased risk | 340/424 (80%) | 122/173 (71%) |
| At increased risk | 50/125 (40%) | 12/37 (32%) |
| RR | 2.0 (1.8–2.2) | 2.2 (1.8–2.6) |
| Philadelphia | | |
| Not intractable | 377/489 (77%) | 131/189 (69%) |
| Intractable | 13/60 (22%) | 3/21 (14%) |
| RR | 3.6 (3.2–4.0) | 4.9 (4.1–5.7) |
| Canadian | | |
| Not intractable | 388/499 (77%) | 134/195 (69%) |
| Intractable | 2/50 (4%) | 0/15 (0) |
| RR | 14.4 (13.5–15.5) | ~20.6 (18.4–23.1) |
| Scotland | | |
| Not intractable | 380/478 (79%) | 134/190 (71%) |
| Intractable | 10/71 (14%) | 0/20 (0) |
| RR | 5.6 (5.2–6.2) | ~28.2 (25.7–31.0) |
| Surgery | | |
| Not intractable | 364/459 (79%) | 130/184 (71%) |
| Intractable | 26/90 (29%) | 4/26(15%) |
| RR | 2.7 (2.5–3.0) | 4.6 (3.9–5.4) |

**1 seizure per mo for ≥18 mo and ≤3 mo seizure free during that time**
**2 Minimum AEDs failed**

**≥ 1 seizure every 2 mo in last year of follow-up**
**3 Minimum AEDs failed**

*Berg AT & Kelly MM; Epilepsia 2006*

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

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

*Kwan P et al.; Epilepsia 2010*

## Goals

- Aid nonspecialists in recognizing patients with drug resistant epilepsy for prompt referral to specialist centers for evaluation

- Facilitate comparison and meaningful synthesis of results across studies

**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

**The consensus to adopt the failure of two (rather than greater numbers)** AED schedules in the definition represents a testable hypothesis and aims to avoid unnecessary delay in evaluation, and **may be revised as more high quality data become available**

**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

## Appropriately chosen

**For instance, ethosuximide would usually not be considered an appropriate intervention for focal seizures**.

Under most circumstances, a trial of this drug in a patient with focal epilepsy would not "count" toward being defined as "drug resistance."

## Adequate

- Application of the intervention at adequate strength/dosage for a sufficient length of time

- This **may not be the case** in some circumstances, for example**, when a drug is withdrawn before it has been titrated to its clinically effective dose range because of an adverse effect**

For adults, reference may be made to the **World Health Organization (WHO)'s defined daily dose (DDD),** which is the assumed average maintenance dose per day for a drug used for its main indication (World Health Organization, 2008)

*Kwan P et al.; Epilepsia 2010*


**https://www.whocc.no/atc_ddd_index/**

**Drug-responsive epilepsy**
Epilepsy in which the patient receiving the current AED regimen has been **seizure-free for a minimum of three times the longest preintervention interseizure interval or 12 months**, **whichever is longer**

**Seizure freedom**
Freedom from all types of seizures for 12 months or three times the preintervention interseizure interval, whichever is longer

A patient was newly started on **carbamazepine after two partial seizures in 9 months**. He has had no seizures for **12 months** since

**Undefined**
**The pretreatment interseizure interval was 9 months**.
**Although the patient has had no seizure for 12 months, the duration is less than three times the pretreatment interseizure interval**, hence outcome to treatment is undetermined and drug responsiveness of epilepsy is **undefined**

A patient had **one seizure in January 2006 and two seizures in October 2006**. After starting treatment in November 2006 he has been **seizure free for 30 months** with no adverse effect

**Drug responsive**
**The longest pretreatment interseizure interval was 9 months (January–October 2006).**
The patient has had no seizure for more than three times the pretreatment interseizure interval and for more than 12 months

*Kwan P et al.; Epilepsia 2010*

# Predictors of drug-resistant epilepsy

# Predictors of refractory epilepsy (multivariate analysis)

A total of **780 patients living in the West of Scotland** diagnosed with epilepsy and prescribed their first AED in the Epilepsy Unit of the Western Infirmary in Glasgow, Scotland, between July 1982 and May 2001 were included in this analysis

| Predictors | Odds ratio | 95% CI |
|---|---|---|
| **Family history** | 1.89 | 1.15 – 3.00 |
| **Febrile convulsions in infancy** | 3.36 | 1.58 – 7.18 |
| **Traumatic brain injury** | 2.73 | 1.59 – 4.69 |
| **Psychiatric comorbidity (particularly depression)** | 2.17 | 1.33 – 3.55 |
| **Recreational drug use** | 4.26 | 2.03 – 8.94 |
| **More than 10 seizures before treatment** | 2.77 | 1.98 – 3.89 |

*Hitiris N et al.; Epilepsy Res 2007*

# Consistent predictors of refractory epilepsy

- Early response to medication
- Underlying etiology
  - ✓ Epilepsies relating to structural brain abnormalities are less likely to enter remission compared that occurring in patients with structurally normal brains
  - ✓ Lower remission rate for symptomatic epilepsies (both partial and generalised) compared to idiopathic epilepsy syndromes in children
- Number of seizure prior to treatment

*Mohanraj R & Brodie M; Seizure 2013*

# Consequences of drug-resistant epilepsy

# Increased mortality

**Table 1**
Risks of premature death in individuals with epilepsy compared with those in population controls and unaffected siblings.


| | Odds ratio for death compared with population controls (aOR [95% CI]) | Odds ratio for death compared with unaffected sibling controls (aOR [95% CI]) |
|---|---|---|
| All-cause mortality | 11.1 (10.6–11.6) | 11.4 (10.4–12.5) |
| Natural causes | 15.5 (14.6–16.4) | 16.7 (14.9–18.7) |
| Neoplasms | 11.2 (10.3–12.2) | 11.3 (9.4–13.7) |
| Nervous system | 71.1 (57.3–88.4) | 86.9 (54.3–139.1) |
| External causes | 3.6 (3.3–4.0) | 3.2 (2.7–3.7) |
| Suicide | 3.7 (3.3–4.2) | 2.9 (2.4–3.6) |
| All accidents | 3.6 (3.1–4.1) | 3.6 (2.9–4.5) |
| Vehicle | 1.4 (1.1–1.8) | 1.5 (1.1–2.2) |
| Other | 5.5 (4.7–6.5) | 6.3 (4.6–8.8) |
| Drug poisoning | 5.1 (3.9–6.5) | 5.7 (3.3–9.7) |
| Fall | 8.5 (5.3–13.7) | 10.0 (2.9–33.8) |
| Drowning | 7.7 (4.7–12.7) | 9.5 (3.5–25.7) |
| Other and unspecified | 4.9 (3.6–6.5) | 5.2 (3.2–8.5) |
| Assault | 2.8 (1.6–4.8) | 1.7 (0.9–3.3) |

Data are adjusted odds ratios (aOR) of external deaths compared with population controls (matched for age and sex, and adjusted for income, and marital and immigration status) or unaffected sibling controls (adjusted for age and sex).

*Laxer KD et al.; Epilepsy & Behav 2014*

Mortality is greater for those with epilepsy than for those without

**Within epilepsy, mortality is greatest for those with refractory epilepsy**

**SUDEP (sudden, unexplained death in epilepsy)**

- The average incidence is **1/1,000** patients with epilepsy per year

- In **refractory epilepsy**, the incidence is **6 /1,000** patients per year, and the lifetime incidence is 7% to 35%, with the greater end of this range applying to childhood-onset refractory epilepsy

- Risk of SUDEP in those with epilepsy is approximately **16-times** that of the general population, after adjustment for multiple factors, including age, sex, and psychiatric and neurologic disease

# Increased risk of neuropsychiatric impairment

# How are epilepsy and neuropsychiatric conditions related ?

## Could be

### 1) Seizure activity itself

Patients with **chronic seizures** experience greater rates of cognitive deficits, emotional problems, physical and psychiatric disease, health care utilization, educational and occupational underachievement, failure in fulfilling normal social roles, and reduced quality of life

### 2) Structural and functional abnormalities often precede the onset of seizures and medication use

It is increasingly clear that **neuropsychiatric comorbidities are evident prior to the onset of observable seizure activity**, or sufficiently soon after onset that they are unlikely to have been caused by seizure activity itself.

Conditions with greater degree present at, before, or soon after onset of seizures

- ADHD
- Depression
- Behavioral problems
- Cognitive difficulties

*Laxer KD et al.; Epilepsy & Behav 2014*

# Neuroimaging of drug resistance in epilepsy

# Memory circuit reorganization in the pre-op and post-op periods in drug-resistant TLE

Clinical study

## Memory loss and memory reorganization patterns in temporal lobe epilepsy patients undergoing anterior temporal lobe resection, as demonstrated by pre-versus post-operative functional MRI

Chusak Limotai [a,b,c,1], Richard S. McLachlan [a], Susan Hayman-Abello [a], Brent Hayman-Abello [a], Suzan Brown [a], Frank Bihari [a], Seyed M. Mirsattari [a,d,e,f,*]

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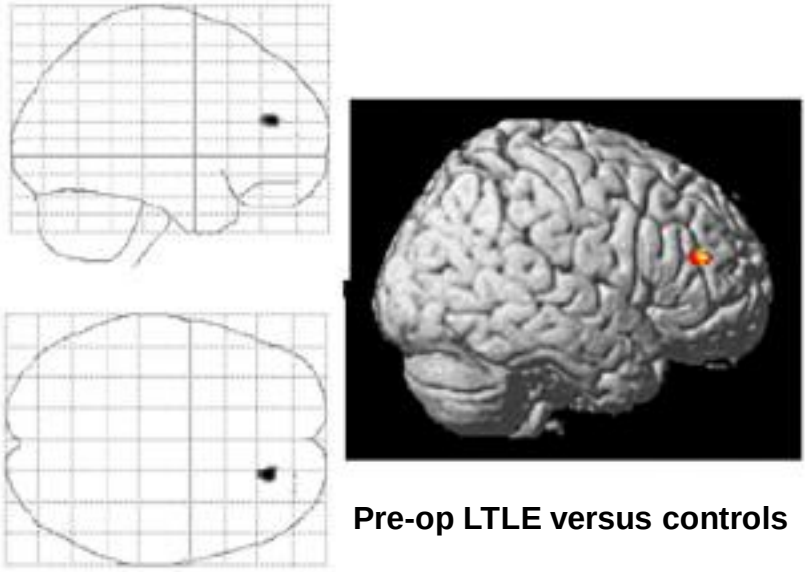
[d] Department of Medical Imaging, Western University, London, Ontario, Canada
[e] Department of Medical Biophysics, Western University, London, Ontario, Canada
[f] Department of Psychology, Western University, London, Ontario, Canada

Chulalongkorn Comprehensive Epilepsy Centre

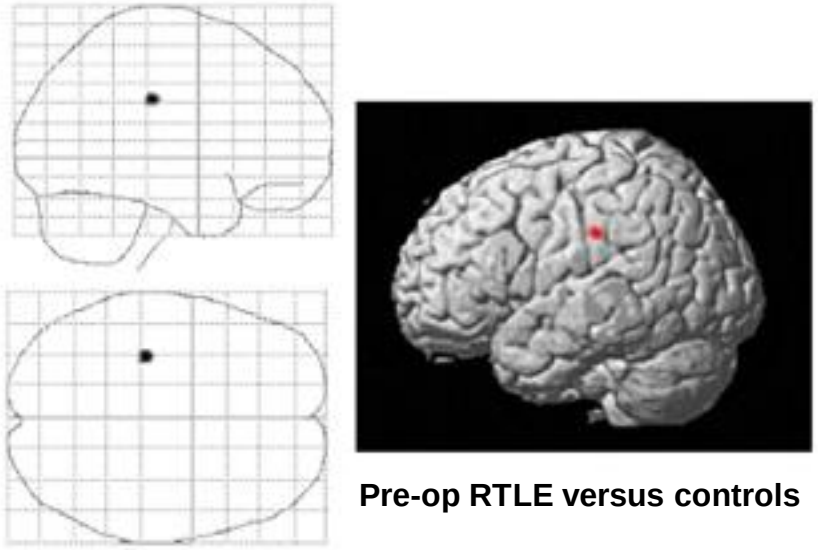
Western UNIVERSITY · CANADA

*Limotai C et al.; J Clin Neurol 2018*



Pre-op LTLE versus controls

(A)



Pre-op RTLE versus controls

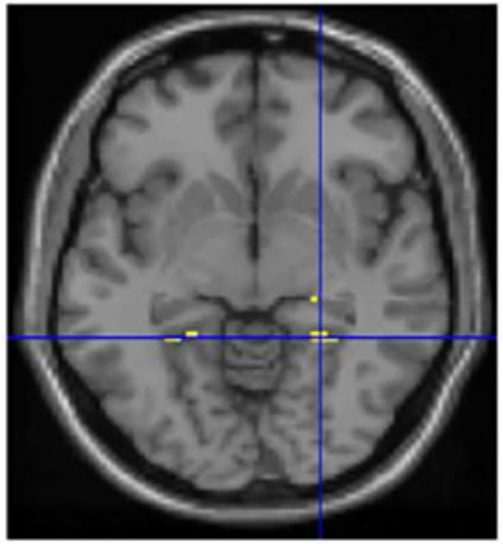
Nineteen patients with medically-intractable TLE (10 left TLE, 9 right TLE) and 15 healthy controls were enrolled

Group analyses were conducted pre- and post-ATL of a **novelty complex scene-encoding paradigm** comparing areas of BOLD signal activations on fMRI

**Extra-temporal activations** were detected pre-operatively in both LTLE and RTLE, particularly in the frontal lobe

*Limotai C et al.; J Clin Neurol 2018*

L

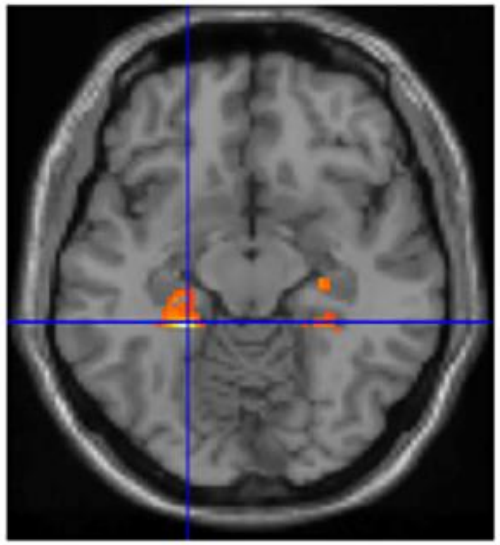


R

Pre-op LTLE versus controls

(E)

L



R

Pre-op RTLE versus controls

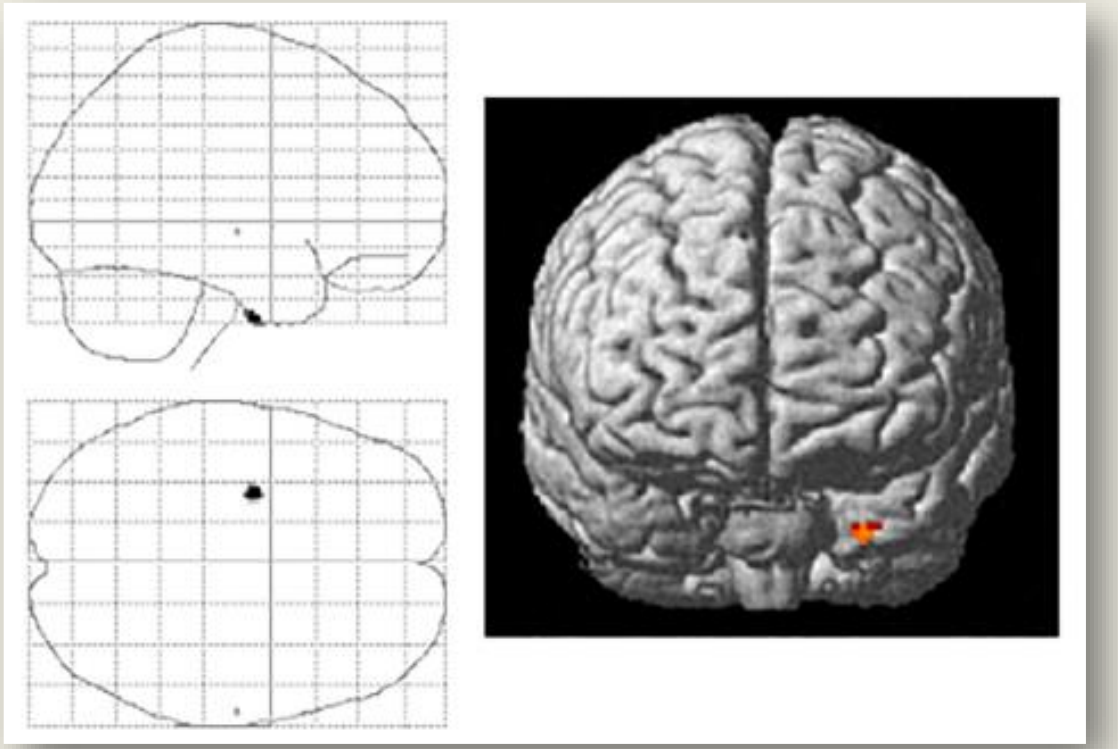
Greater activations also were noted in the contralateral hippocampus and parahippocampus in LTLE and RTLE

**Signal changes in the left HC/PHC ($R^2$ = 0.513 (p = 0.025) for verbal memory (AdDel score)**

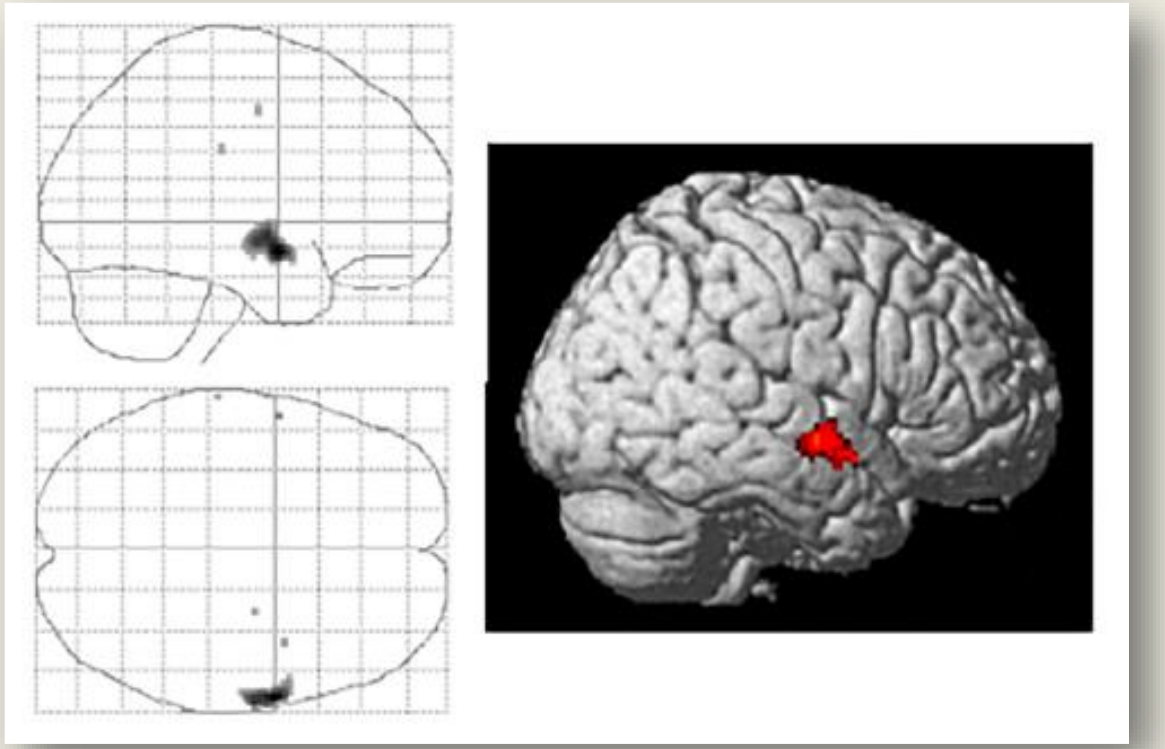
fMRI provides evidence for importance of **"Functional adequacy of ipsilateral structures"** rather than functional reserve of the contralateral hemisphere

*Limotai C et al.; J Clin Neurol 2018*
*Koepp MJ; Curr Opin Neurol 2014*

# Whole-brain memory circuit reorganization at post-operative period



LTLE Post-op versus Pre-op



RTLE Post-op versus Pre-op

**Pronounced temporal activations, particularly in the ipsilateral temporal area**

*Limotai C et al.; J Clin Neurol 2018*

# Thank you