Introduction

- Prognosis of epilepsy generally means probability of being seizure-free
  - after starting treatment
  - during treatment
  - after drug withdrawal
- Psychosocial outcomes of epilepsy is being paid attention on. (not including in my talk today)
- Prognosis of untreated epilepsy
  - There are only a few reports
  - Mostly from resource-poor countries

Methodologic issues

- Prognosis of epilepsy depends on
  - characteristics of patients
  - case definition
  - spectrum of severity of epilepsy
  - duration of follow-up
  - choice of prognostic predictors
  - choice of treatments

Ideal design of study on prognosis of epilepsy

- Well-defined inclusion criteria
- Homogenous definition on prognostic predictors and outcome measurements
- Adequate duration of follow-up and proper statistical methods to adjust for those lost to follow-up or limited periods of follow-up

Overall prognosis of epilepsy

- Incidence of epilepsy in health resource-poor countries are higher than that in industrialized countries
  - 30-60 per 100,000 Vs 70 per 100,000
- However the prevalence of epilepsy in health resource-poor countries are broadly similar to that in industrialized countries.
- Prevalence of active epilepsy are between 4-10 per 1,000.

Overall prognosis of epilepsy

- The increased mortality of epilepsy in resource-poor countries explains only part or the difference between incidence and prevalence.
- The most likely explanation for the similar prevalence rates between the resource-poor and the resource-rich countries is spontaneous remission in some patients.
- Therefore, overall prognosis of epilepsy is favorable in the majority of patients.


Prognosis after the first unprovoked seizures

- The reported risk of relapse after the 1st unprovoked seizure range from 14-68%.
- The reported relapse rate at 2 years are 21-69%.
- The reported relapse rate at 5 years are 34-71%.
- Population-based studies reported relapse rates:
  - at 1 year = 36-37%
  - at 2 years = 43-45%


Relapse risk factors of a 1st unprovoked seizure

- 2 most consistent predictors:
  - Brain pathology
  - Abnormal EEG (epileptiform and/or slow activity)


Prognosis after the first unprovoked seizures

- In a systematic review from 16 reports:
  - The average overall recurrence risk is 51% (95% CI, 49-53%).
  - The probability of relapse decreases with time.
  - About 50% of recurrences occur within the initial 6 months.
  - About 76-96% of recurrences occur within the 2 years.


Treatment, risk of recurrence, long-term prognosis of early epilepsy and 1st seizure

The Mess study

- Large pragmatic randomized European trial
- Comparing immediate and deferred AED for early epilepsy and 1st seizure
- Total 1,443 patients aged at least 1 month who and whose doctors were uncertain on starting AED were randomized.


<table>
<thead>
<tr>
<th>Immediate AED</th>
<th>Deferred AED</th>
<th>Stat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized No.</td>
<td>722</td>
<td>721</td>
</tr>
<tr>
<td>1st seizure</td>
<td>404</td>
<td>408</td>
</tr>
<tr>
<td>Time to the first relapse</td>
<td>prolonged</td>
<td>RR 1.5; 95% CI, 1.2-1.8</td>
</tr>
<tr>
<td>Seizure recurrence at 2-yr follow-up</td>
<td>32%</td>
<td>39%</td>
</tr>
<tr>
<td>2-yr remission at 2 yr</td>
<td>64%</td>
<td>52%</td>
</tr>
<tr>
<td>2-yr remission at 5 yr</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>2-yr remission at 8 yr</td>
<td>95%</td>
<td>96%</td>
</tr>
</tbody>
</table>
Immediate AED Rx of 1st seizure or early epilepsy
- It seems to reduce the risk of short-term relapse.
- Long-term prognosis is substantially unaffected.
- The comparative effects of immediate AED for 1st seizure and deferred AED until relapse on the chance of long-term remission after AED discontinuation have not yet been assessed.

The prognosis of untreated epilepsy come from resource-poor countries.
- A population-based study in Ecuador
  - Cumulative annual incidence rate 190 per 100,000
  - Prevalence rate of active of epilepsy 7 per 1,000
  - Imply a remission rate of at least 50%

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The prognosis of newly diagnosed epilepsy report cumulative 5-year remission rate:
- at 10 years = 58-65%
- at 20 years = 70%
- The 5-year remission rate at 10 years is 61% in adult patients.

Prognostic predictor of seizure remission
- Etiology of epilepsy is the strongest predictor.
  - Idiopathic epilepsy has better chance of remission than cryptogenic/symptomatic epilepsy.
- Absence of EEG epileptiform abnormalities
- Age and sex are not prognostic predictor of seizure remission.

Principal prognostic predictors
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**Principal prognostic predictors**

- Early predictors of seizure intractability
  - Etiology of epilepsy
  - High initial seizure frequency
  - Focal EEG slowing

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**Prognosis of epilepsy and epilepsy syndromes**

- Epilepsy and epilepsy syndromes can be classified into 4 prognostic groups
  - Excellent prognosis (20-30%)
    - High probability of spontaneous remission
  - Good prognosis (30-40%)
    - Easy pharmacologic control and possibility of spontaneous remission
    - AED-dependent prognosis (10-20%)
      - Tend to relapse after AED withdrawal
    - Guarded prognosis (20%)
      - Tend to intractable to AEDs

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**Epilepsy and epilepsy syndrome with excellent prognosis**

- High probability of spontaneous remission
  - Including
    - Neonatal seizure
    - Benign partial epilepsies
    - Benign myoclonic epilepsy in infancy
    - Epilepsies provoked by specific modes of activation

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**Epilepsy and epilepsy syndrome with good prognosis**

- Easy pharmacologic control and possibility of spontaneous remission
  - Including
    - Infantile absence epilepsy
    - Epilepsies with generalized-tonic-clonic seizures secondary to specific conditions
    - Some partial epilepsies

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**Epilepsy and epilepsy syndrome with AED-dependent prognosis**

- May respond to AED
- Tend to relapse after AED withdrawal
  - Include
    - Juvenile myoclonic epilepsy
    - Most partial epilepsies (symptomatic or cryptogenic)

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**Epilepsy and epilepsy syndrome with guarded prognosis**

- Seizures tend to recur despite intensive treatment
  - Include
    - Epilepsies ass. with congenital neurologic defects
    - Progressive neurologic disorders
    - Some symptomatic or cryptogenic partial epilepsies
Antiepileptic drugs and seizure outcome

- AEDs do not alter long-term epilepsy outcome.
- There are no reports on the comparative efficacy of old and new AEDs on the long-term outcome of epilepsy.
- There is no evidence to suggest that the newer medications are more efficacious.
- The majority of seizure-free patients required only a moderate daily dose of AED.

Specchio LM and Beghi E reviewed 28 studies, total 4,615 patients, most patients had at least 2 years seizure remission, Proportion of seizure recurrence during or after AED discontinuation = 12-66%


Prognosis of epilepsy after AED withdrawal

<table>
<thead>
<tr>
<th>Cumulative probability of remaining seizure-free</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>at 1 year</td>
<td>66-96%</td>
<td>39-74%</td>
</tr>
<tr>
<td>at 2 years</td>
<td>61-91%</td>
<td>35-57%</td>
</tr>
</tbody>
</table>


Prognosis of epilepsy after AED withdrawal

- The relapse rate
  - Highest in the initial 12 months
  - especially initial 6 months
  - Tend to decrease with time
- A meta-analysis of 25 studies by Berg AT and Shinnar S in 1994, the pooled relapse rate was
  - at 1 year = 25% (95% CI, 21-30%)
  - at 2 years = 29% (95% CI, 24-34%)


Prognosis of epilepsy after AED withdrawal

- A randomized trial on the effects of AED withdrawal on seizure relapse
  - Relapse by 2 years:
    - on AED vs. off AED = 22% : 41%
  - The difference of relapse rate was
    - maximal between initial 1 and 2 years
    - decrease thereafter
  - After 2 years, risk of relapse was the same in both on AED and off AED gr.

The risk of seizure recurrence was similar in both patients who relapsed after off AEDs and those during on AEDs.


Factors predicting seizure relapse after AED withdrawal

- In the Medical Research Council AED withdrawal study, predictors of relapse are
  - Seizure types
    - Partial seizure
    - Primarily or secondarily generalized tonic-clonic seizure
    - Myoclonic seizure
  - Use of more than one AED
  - Seizures after treatment start
  - Shorter seizure-free period

- A meta-analysis of 25 studies by Berg AT and Shinnar S in 1994,
  - Adolescence onset had 1.34-fold increased risk of relapse (95%CI, 1.00-1.81) vs. adult onset
  - Remote symptomatic epilepsy had 1.55-fold increased risk of relapse (95%CI, 1.21-1.98)
  - Abnormal EEG prior to drug withdrawal associated with 1.45-fold increased risk of relapse (95%CI, 1.18-1.79)
  - 2-yr vs. 4-yr seizure-free interval was similar.

- A RCT comparing 6-week taper vs. 9-month taper after 2 year seizure remission in children with epilepsy showed no difference in recurrence risk at 2 years

References: