

# Ko darīt, kad nekas vairs nelīdz? Grūtu un sarežģītu epilepsiju ārstēšana.



Bērnu klīniskā  
universitātes  
slimnīca



RĪGAS STRADIŅA  
UNIVERSITĀTE

Jurģis Strautmanis, bērnu neirologs

BKUS Epilepsijas un miega medicīnas centra vadītājs

03.11.2023.

# EPILEPSY

## SYMPTOMS



Loss of  
Consciousness



Anxiety



Staring

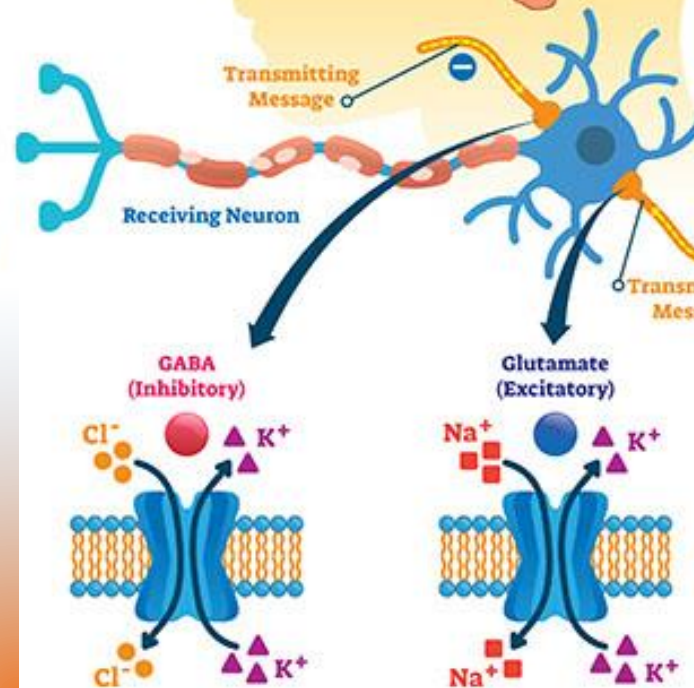
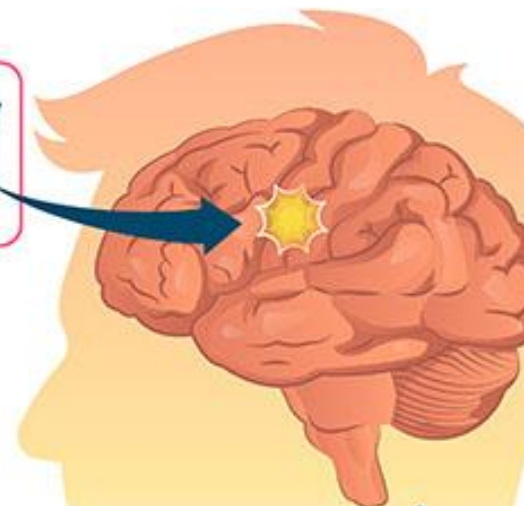


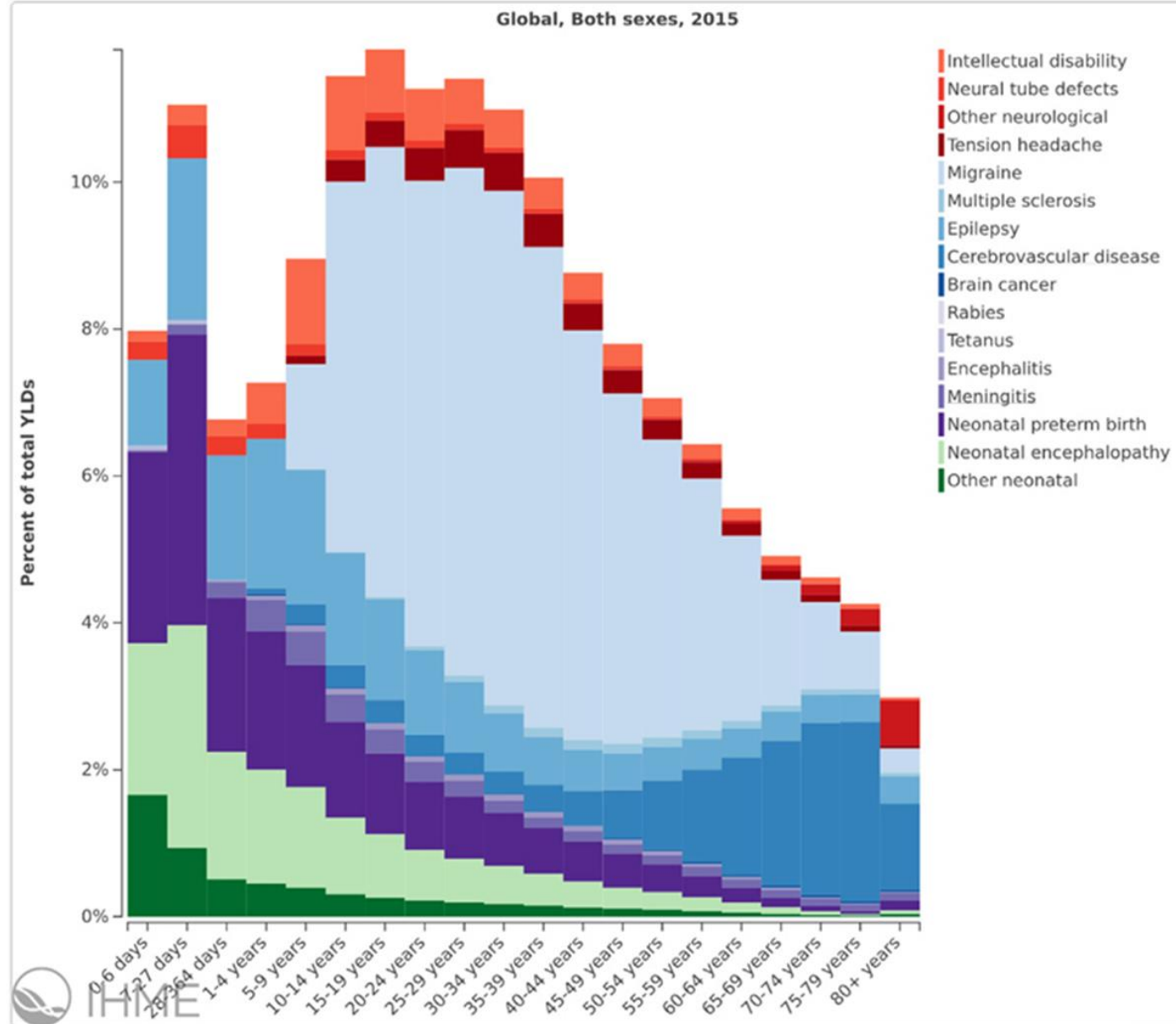
Weakness



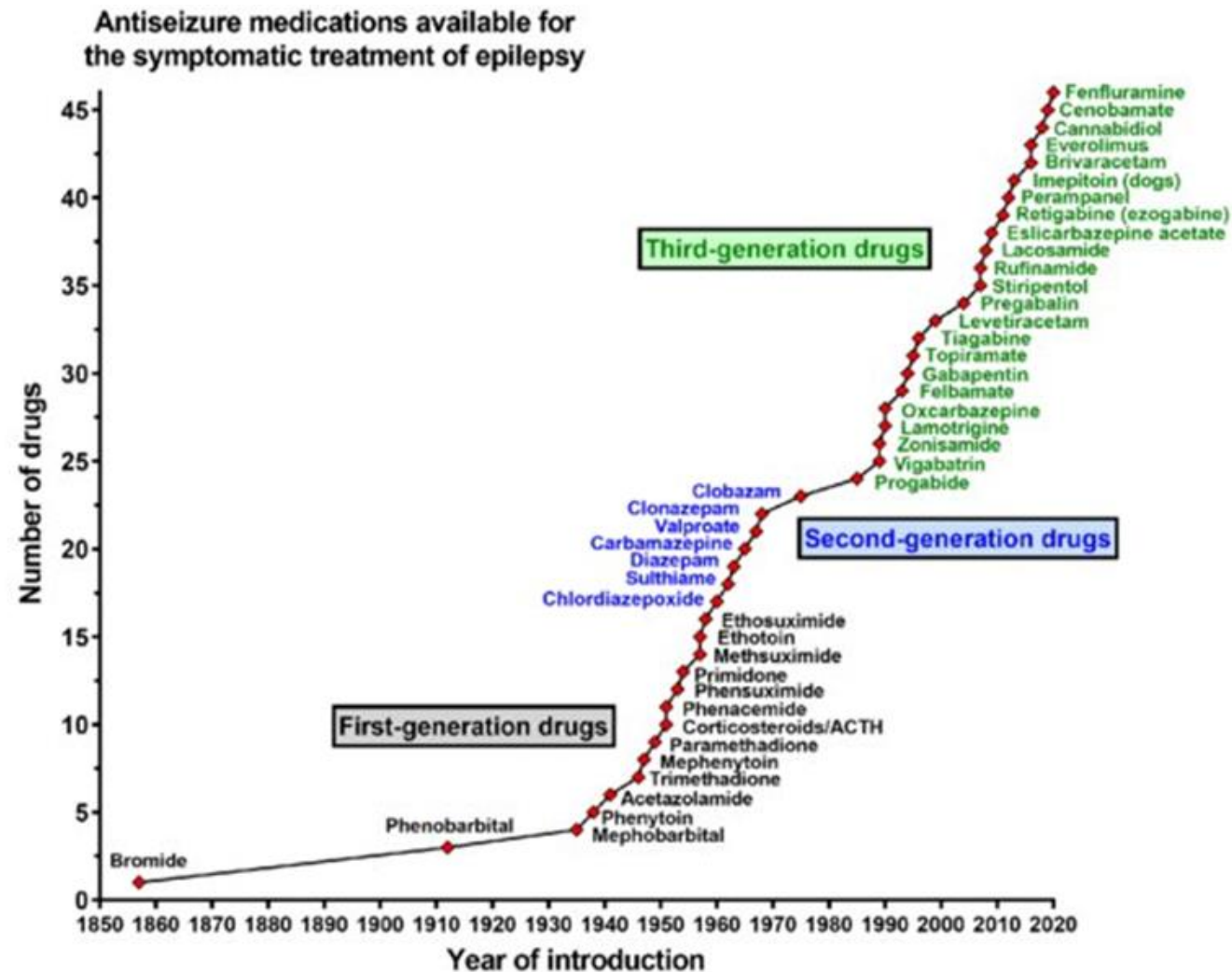
Muscle Contraction  
and Jerking

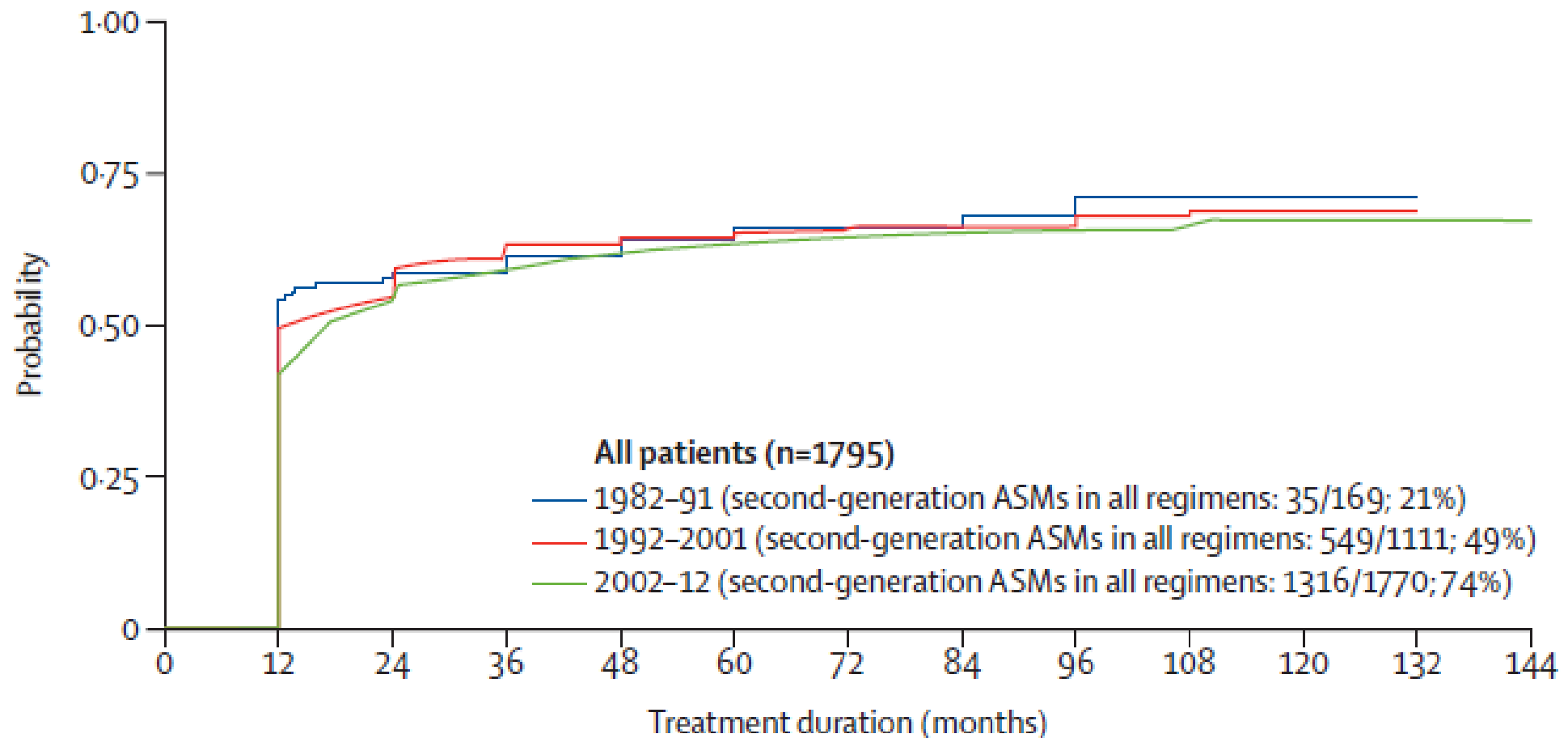
Epilepsy is a Disorder Marked by  
**DISTURBED ELECTRICAL  
RHYTHMS** in the Central  
Nervous System





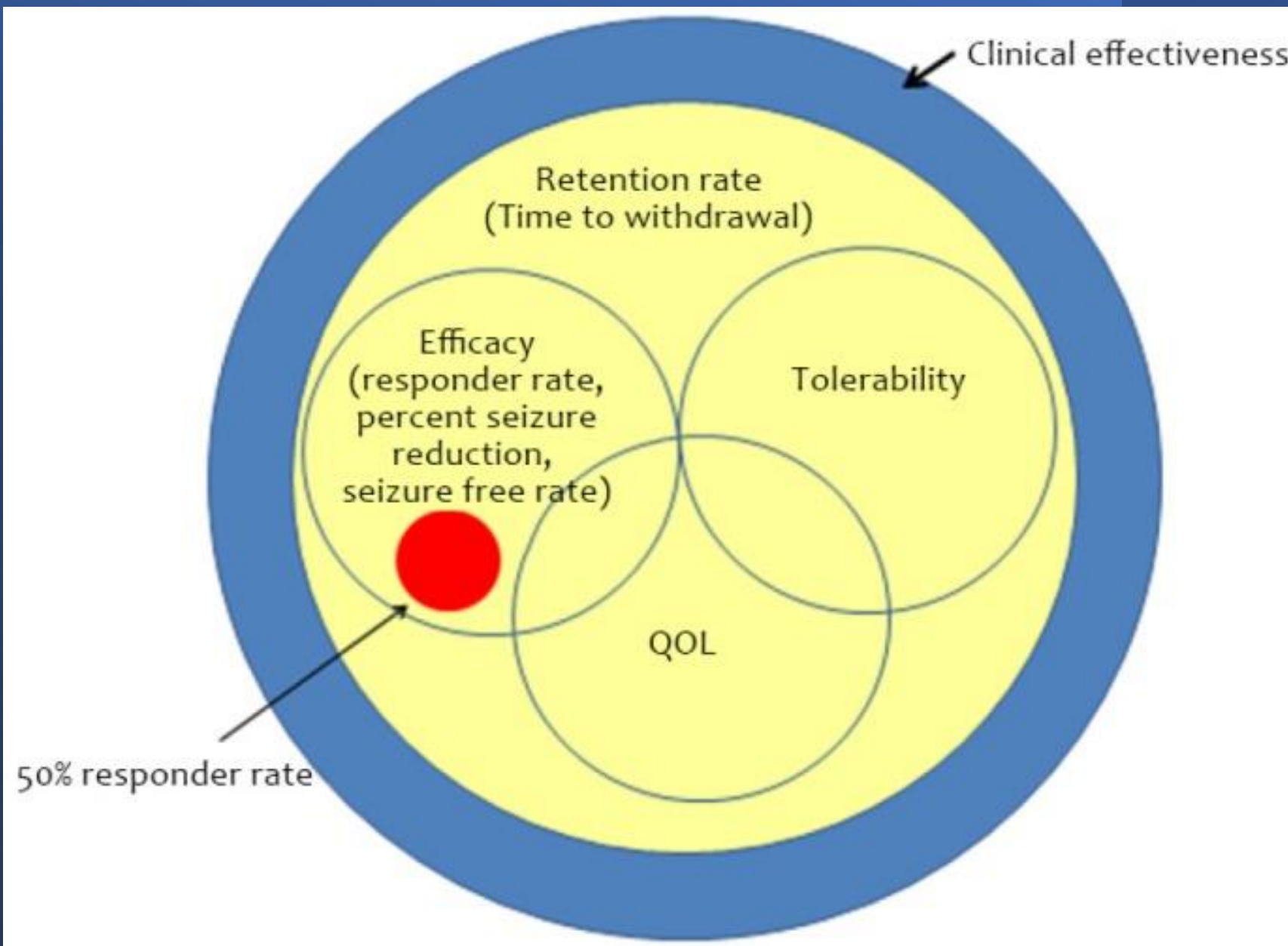
Medikamentu  
rezistenta  
epilepsija  
20-40%.

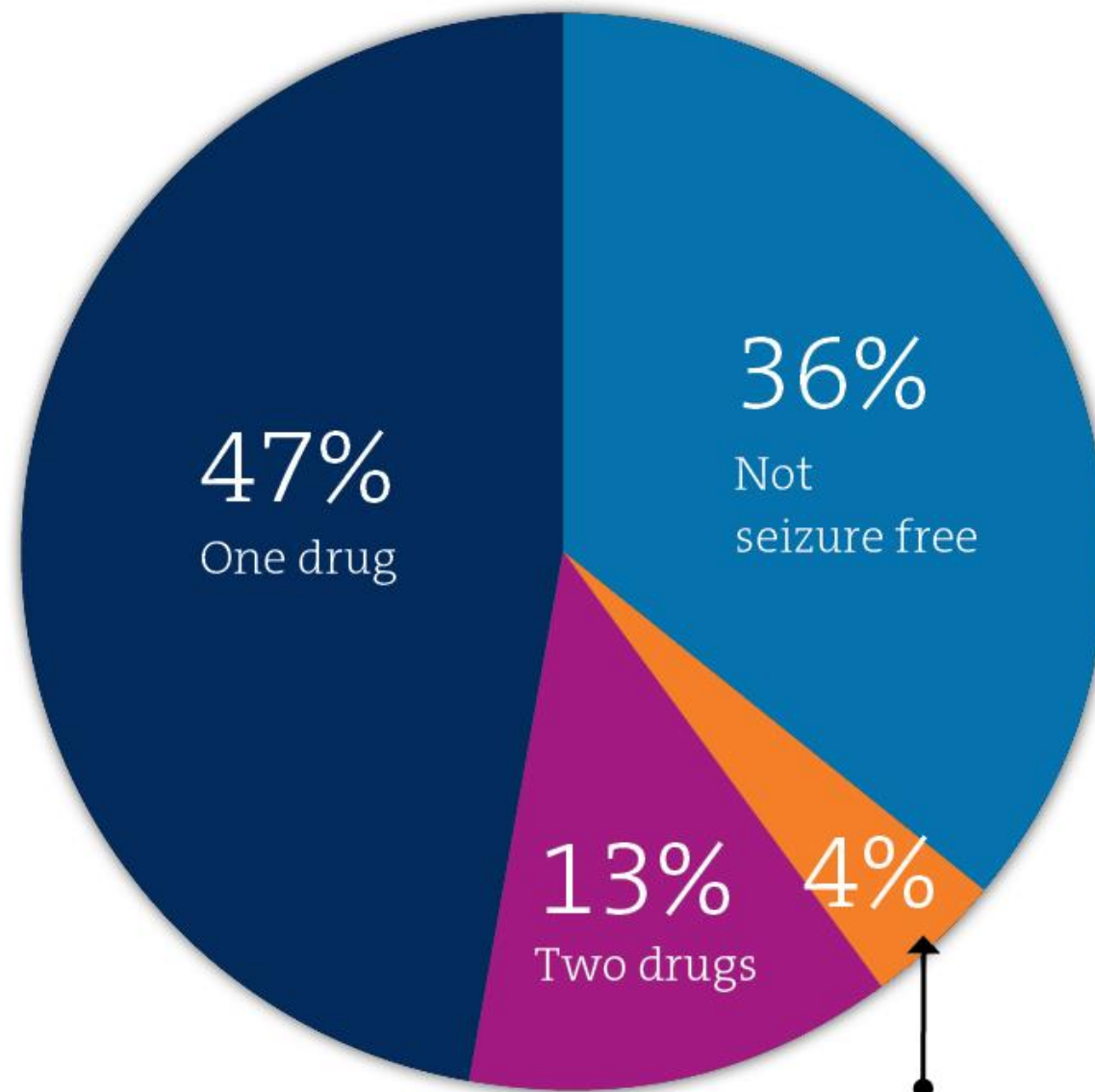




**Number at risk**

|           |     |     |     |     |     |     |     |     |     |    |    |    |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|
| 1982-91   | 142 | 57  | 43  | 27  | 21  | 18  | 16  | 10  | 3   | 1  | 1  | 0  |
| 1992-2001 | 684 | 301 | 229 | 197 | 156 | 123 | 106 | 74  | 42  | 21 | 8  | 0  |
| 2002-12   | 969 | 389 | 312 | 261 | 228 | 202 | 175 | 148 | 119 | 98 | 69 | 29 |





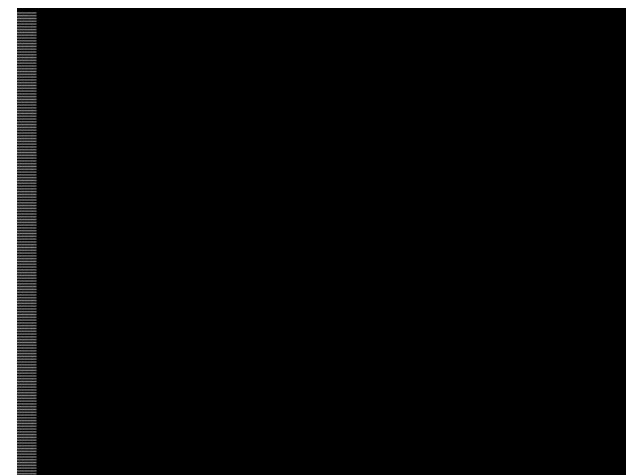
Three or more drugs



Ko darīt?

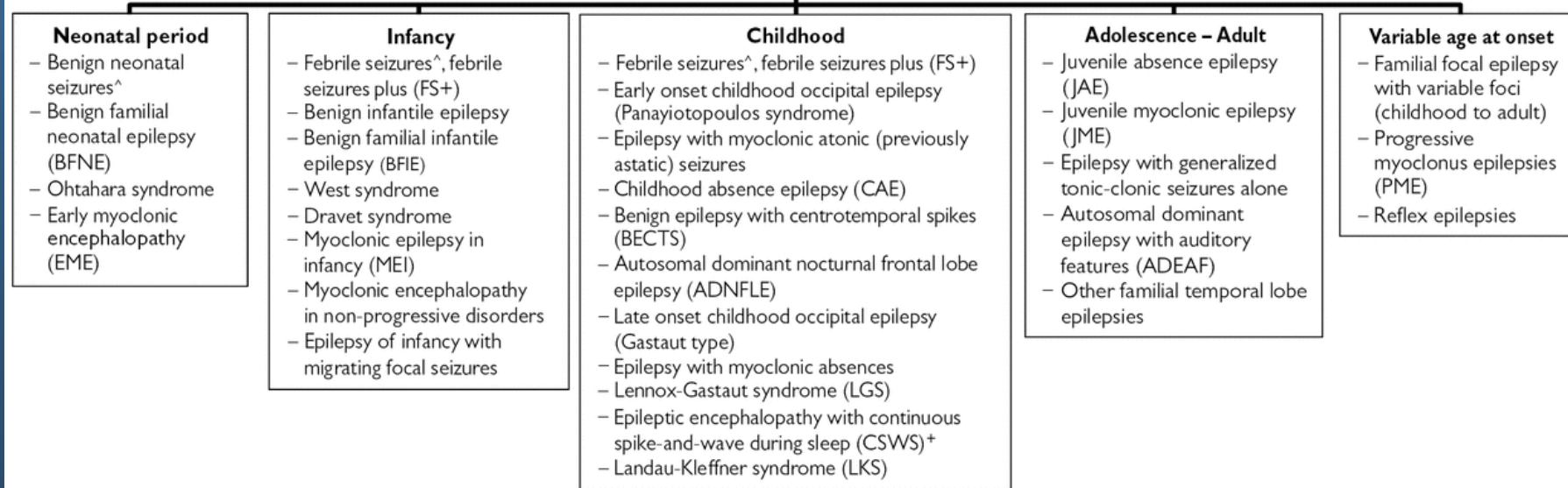
# Vai diagnoze ir pareiza?

- 25% zāļu rezistentas epilepsijas pacientiem nav epilepsijas.
  - Ģībonis (ANAMNĒZE).
  - Funkcionālas lēkmes.
  - Miega traucējumi.
- Video EEG novērošana!
- Mājas video!



## Electroclinical syndromes

One example of how syndromes can be organized:  
Arranged by typical age at onset\*



### Distinctive constellations/surgical syndromes

- Distinctive constellations/Surgical syndromes**
- Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
  - Rasmussen syndrome
  - Gelastic seizures with hypothalamic hamartoma
  - Hemiconvulsion-hemiplegia-epilepsy

### Non-syndromic epilepsies\*\*

- Epilepsies attributed to and organized by structural-metabolic causes**
- Malformations of cortical development (hemimegalencephaly, heterotopias, etc.)
  - Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber, etc.)
  - Tumour, infection, trauma, angioma, antenatal and perinatal insults, stroke, etc.

**Epilepsies of unknown cause**

\* The arrangement of electroclinical syndromes does not reflect aetiology.

<sup>^</sup> Not traditionally diagnosed as epilepsy

<sup>+</sup> Sometimes referred to as Electrical Status Epilepticus during Slow Sleep (ESES)

\*\* Forms of epilepsies not meeting criteria for specific syndromes or constellations

*This Proposal is a work in progress.....*

**We welcome your thoughts on this proposal. Please visit our Classification & Terminology Discussion Group at: <http://community.ilae-epilepsy.org/home/> to login and register your comments.**

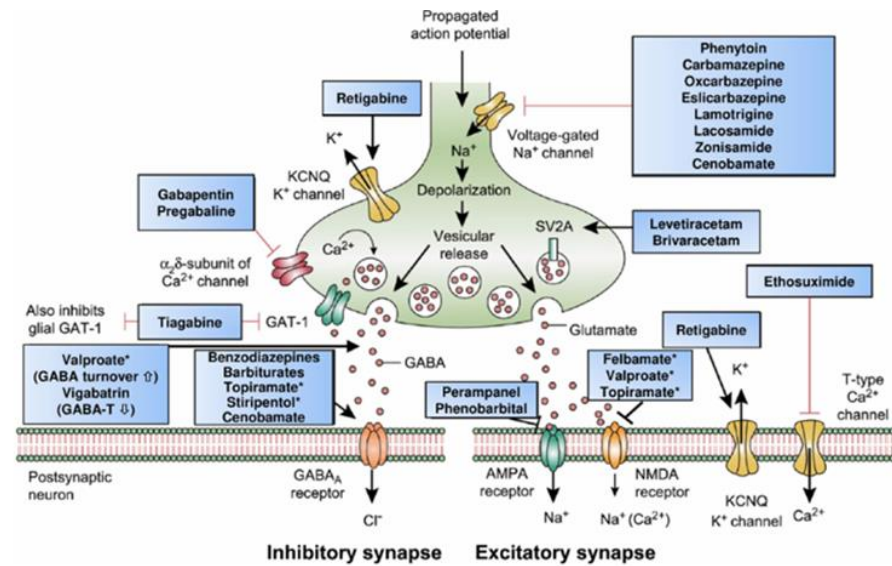
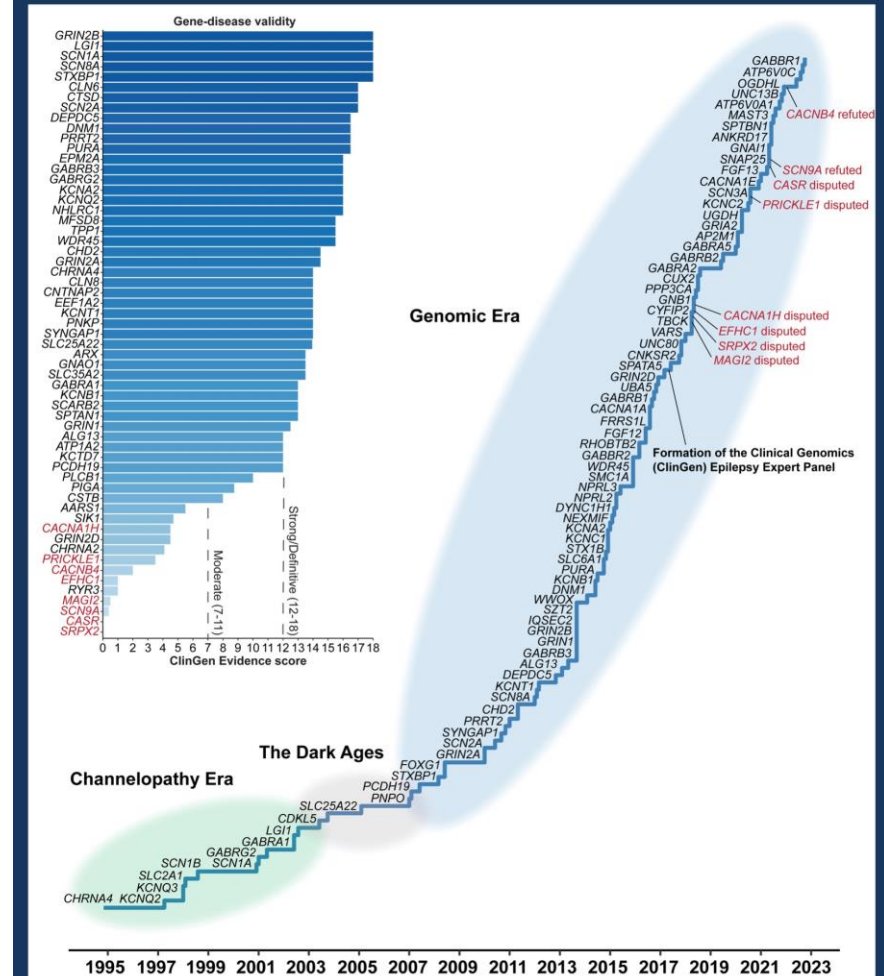
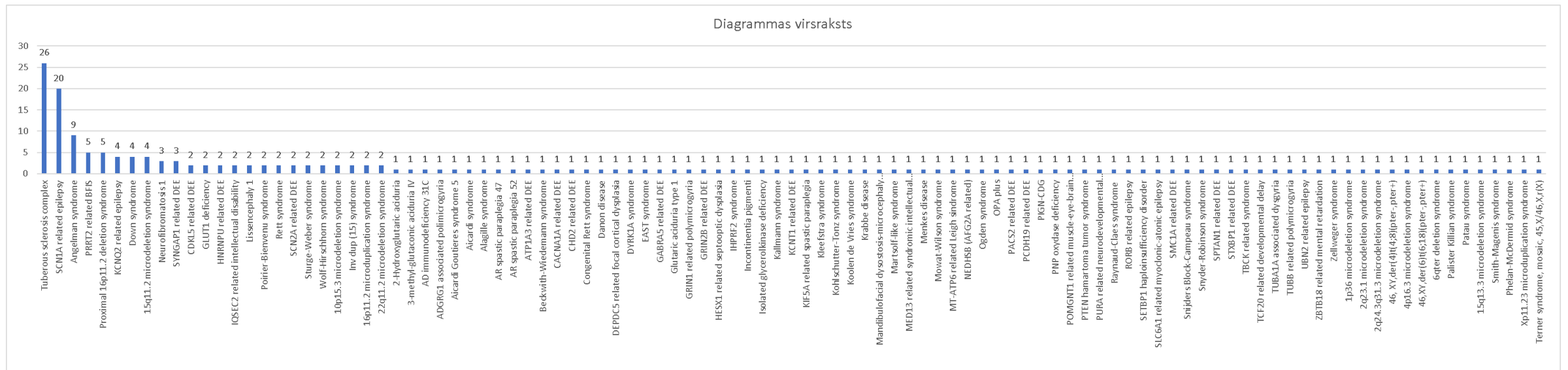


Fig. 5 Mechanism of action of clinically approved antiepileptic medi- mechanism(s) of action are described in Table 2. *AMPA* α-amino-3-

## The history of gene discovery in the epilepsies (Xian and Helbig, 2023)

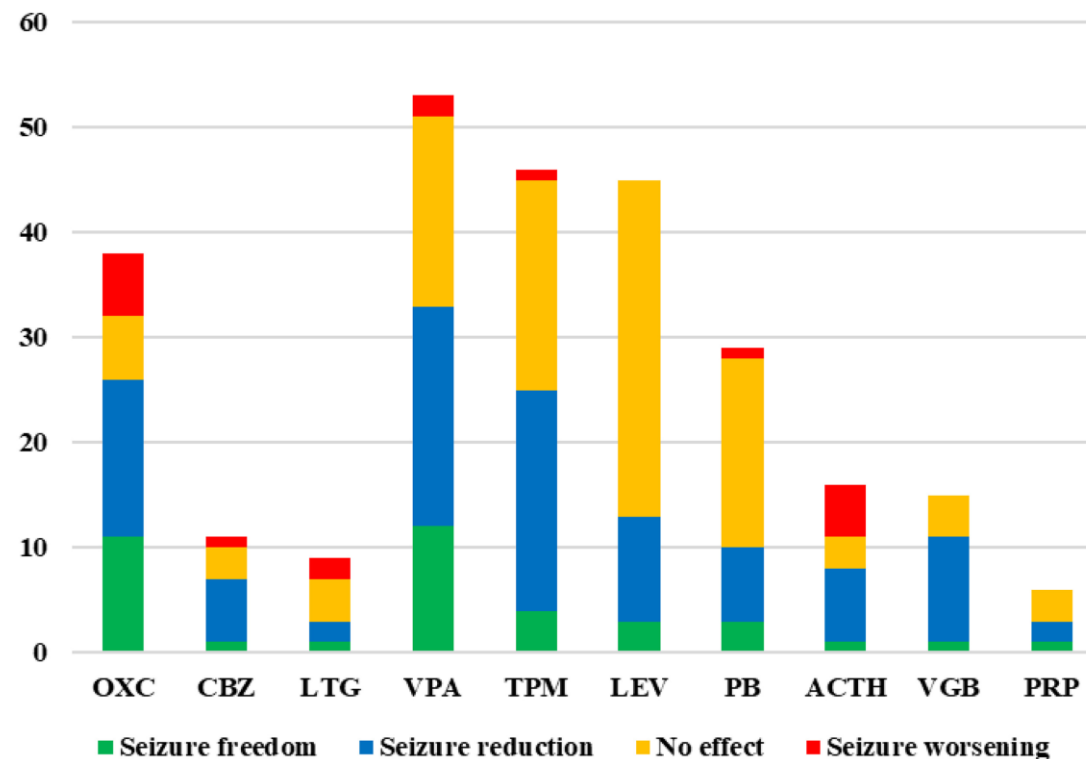


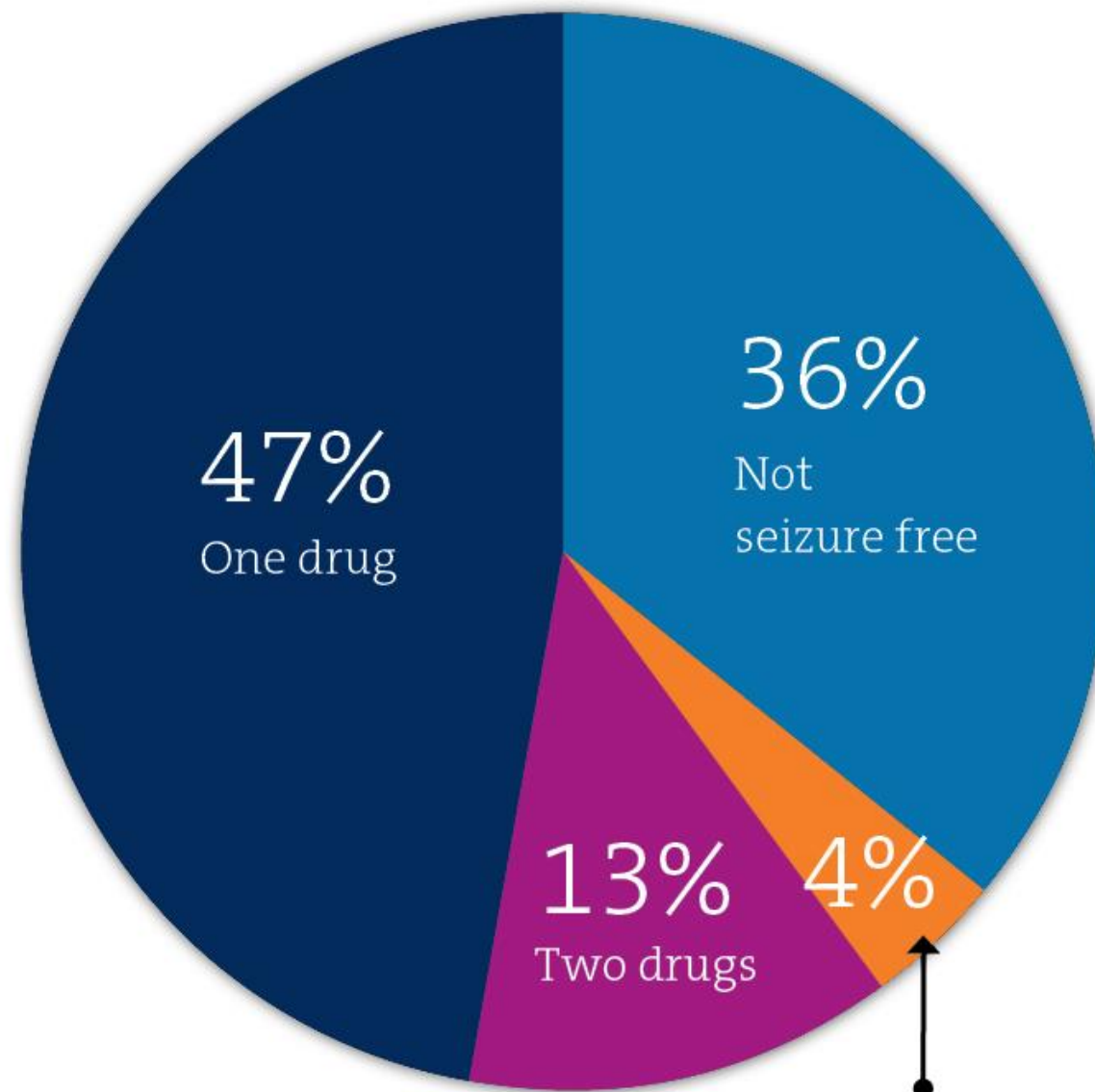
# BKUS atklātās ģenētiskās epilepsijas.



# Precīzijas terapija.

- Klīniskais gadījums.
  - Paciente 9 g.
  - Lēkmes - pamostas, iekliezās, sastingst, raustās 20 sek. Uzreiz iemieg, tad pamostas un 1-1.5 h nesakarīga. Vairākas lēkmes ned. LEV neefektīvs.
  - Garīgās attīstības traucējumi, ataksija.
  - SCN2A pozit.
  - 05.2021. OXC 300 mg x2.
  - Lēkmju brīva >2 gadi.

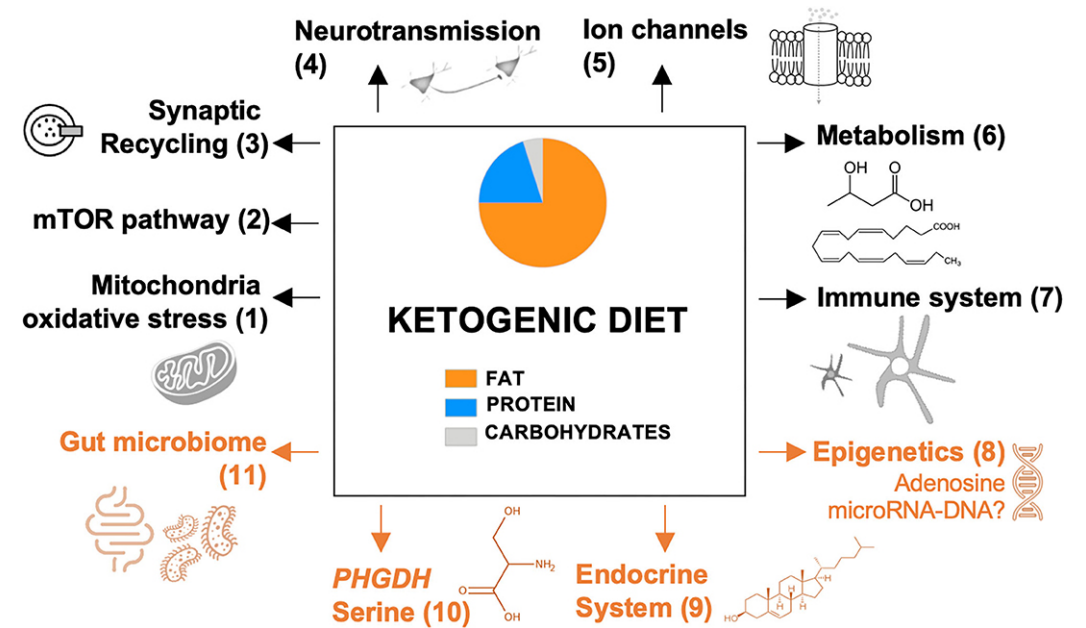




Three or more drugs

# Ketogēna diēta.

- Stingri matemātiski aprēķināta, ārsta un uztura speciālista uzraudzīta diēta!
- Augsts taukvielu saturs.
- Ierobežots ogļhidrātu saturs.
- Taukskābju oksidācija - aknu mitohondrijos ketonvielas - tiek izmantotas glikozes vietā enerģijas iegūšanai – pretkrampju efekts.



Efficacy for  $\geq 50\%$  seizure reduction

Month-3 53% (95% CI: 42, 63)

Month-6 46% (95% CI: 36, 56)

Month-12 41% (95% CI: 27, 55)

Efficacy for  $\geq 90\%$  seizure reduction

Month-3 27% (95% CI: 20, 34)

Month-6 26% (95% CI: 19, 33)

Month-12 23% (95% CI: 17, 30)

Efficacy for seizure free

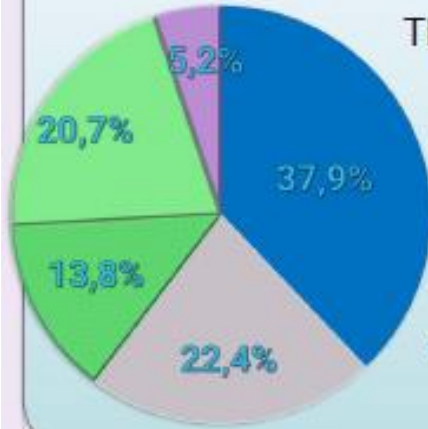
Month-3 10% (95% CI: 05, 16)

Month-6 11% (95% CI: 06, 15)

Month-12 11% (95% CI: 06, 16)

Ketogēnas  
diētas  
efektivitātes  
metanalīze.

The diet was used for at least 6 months  
by 36 patients.

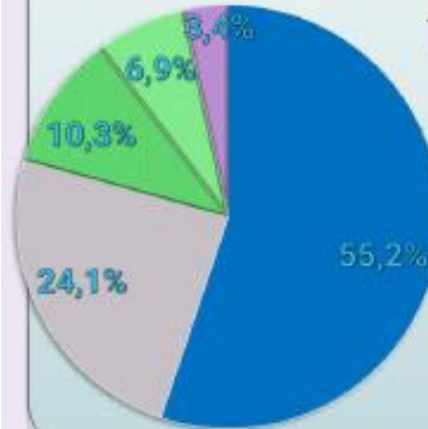


There were 20/58 (34,5%) **responders**,  
including 8/58 (13,8%) **best responders**.  
3/58 (5,2%) patients were **non-responders**.

13/58 (22,4%) patients had **not enough data**  
available to estimate the seizure reduction level.

22/58 (37,9%) patients had used diet for **less than  
6 months** by the moment of data gathering.

The diet was used for at least 12 months  
by 26 patients.



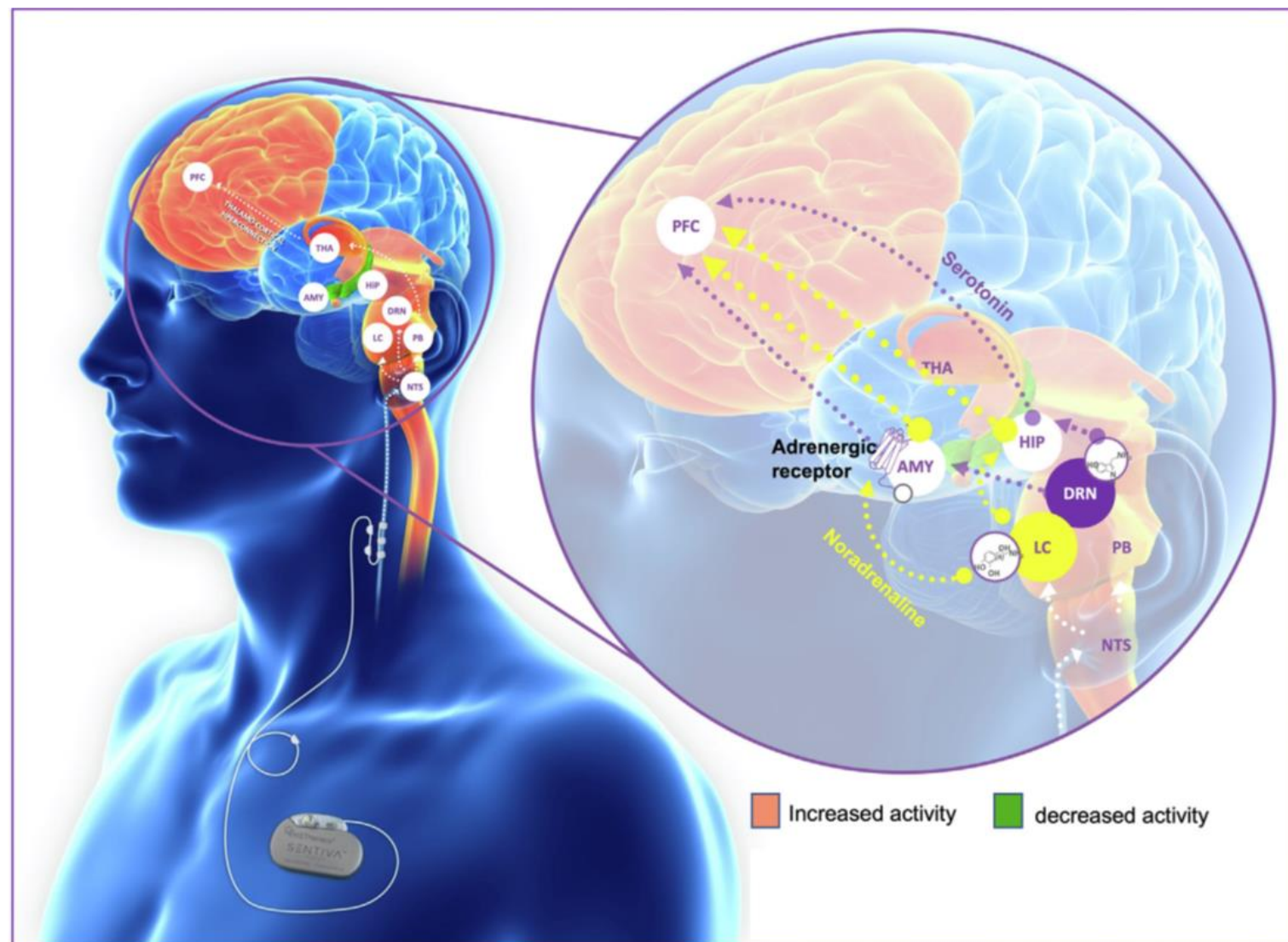
There were 10/58 (17,2%) **responders**,  
including 6/58 (10,3%) **best responders**.  
2/58 (3,4%) patients were **non-responders**.

14/58 (24,1%) patients had **not enough data**  
available to estimate the seizure reduction level.

32/58 (55,2%) patients had used diet for **less than  
12 months** by the moment of data gathering.

BKUS dati  
(2021.g.) – 58  
pacienti.

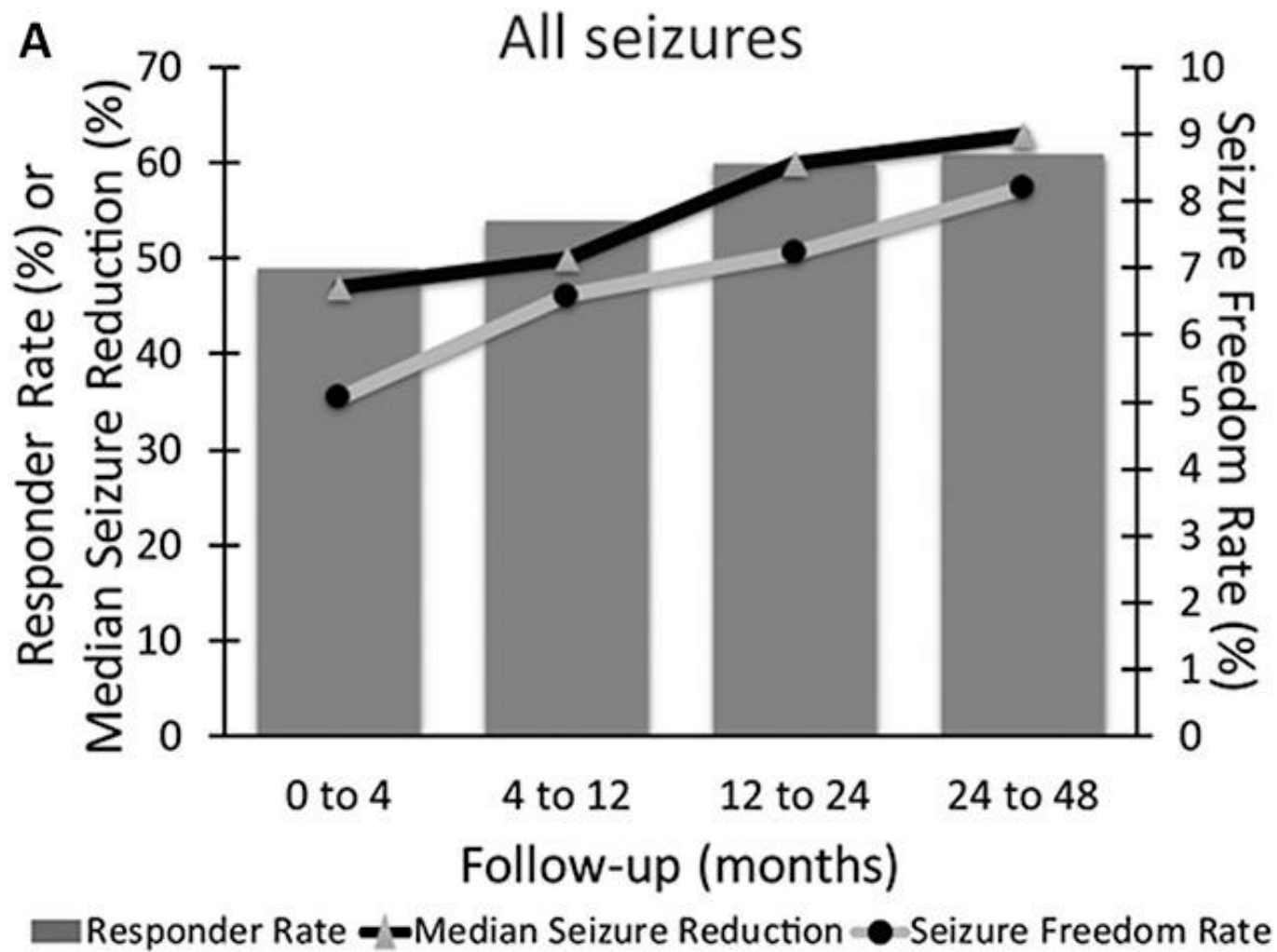
Klejtājnera  
stimulācijas  
terapija (VNS) -  
neimodulācija.



# Klejotājnerva stimulācijas terapija (VNS).

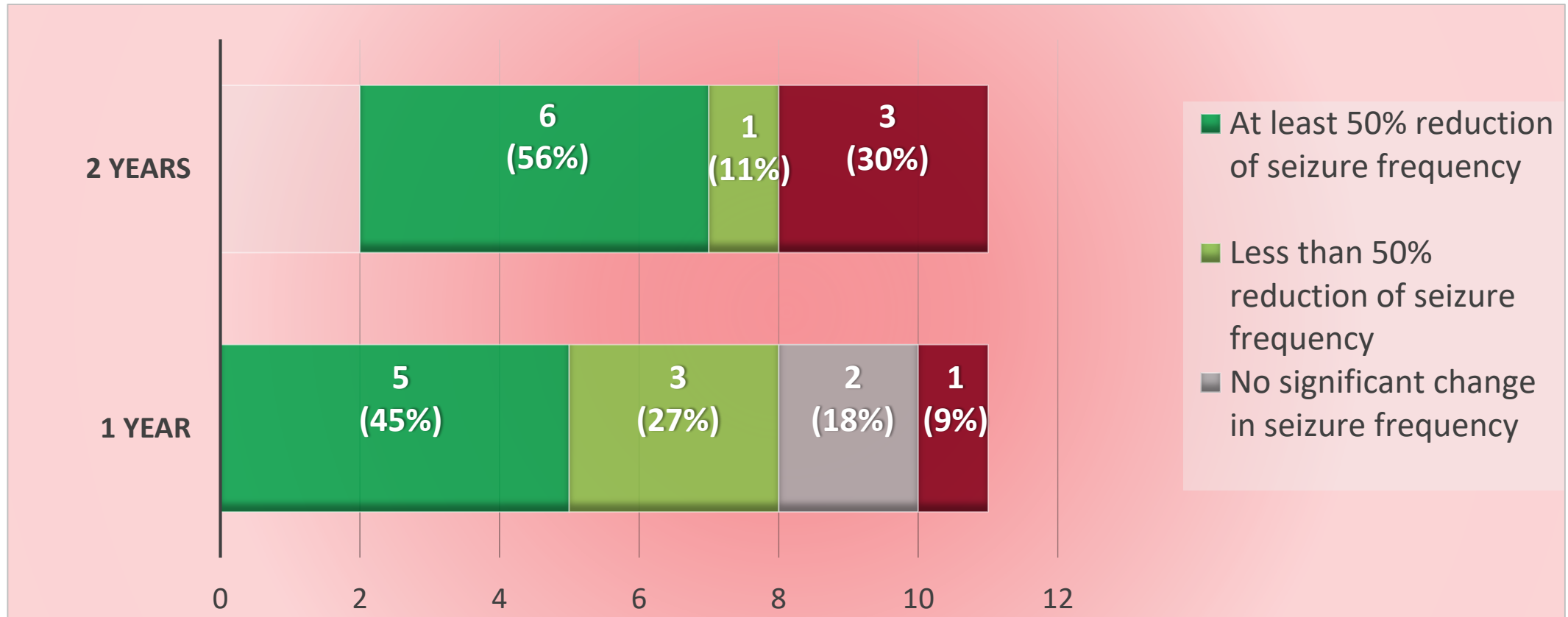
- Normāla stim. – ieslēdzas uz 30 sek. ik 5 min.
- Autostim. – ieslēdzas uz 60 sek. lēkmes gadījumā (tahikardija).
- Magnēta stim. – pacients ieslēdz papildus stim. lēkmes gadījumā.





VNS  
efektivitāte.

# VNS efektivitāte. BKUS dati (2018.-2021.g. 11 pacienti).



# Epilepsija ir saistīta ar paaugstinātu mirstību (līdz 11 reizēm).

**Table 1**

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

Copyright © 2013 Lancet. Reproduced with permission to be obtained from Elsevier Inc. [55].

|                       | 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)                                                                 |

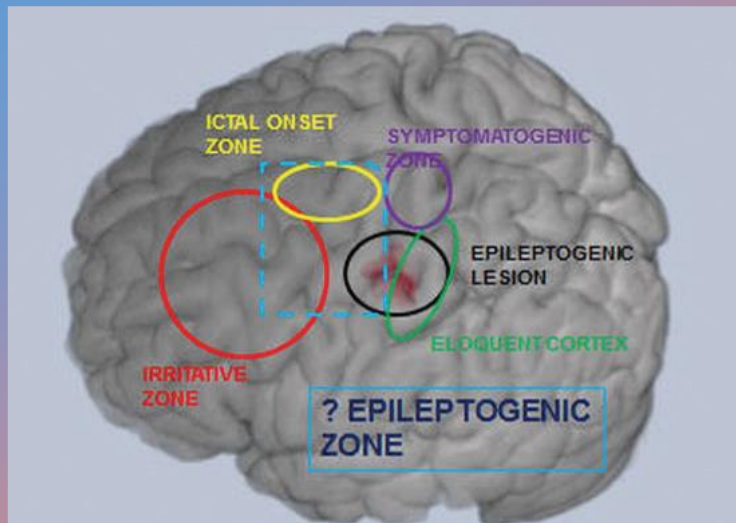
Data are adjusted odds ratios (aOR) of external deaths compared with population controls (matched for age and sex, and adjusted for income, and marital and immigration status) or unaffected sibling controls (adjusted for age and sex).

**Table 3. Predictors of Death.\***

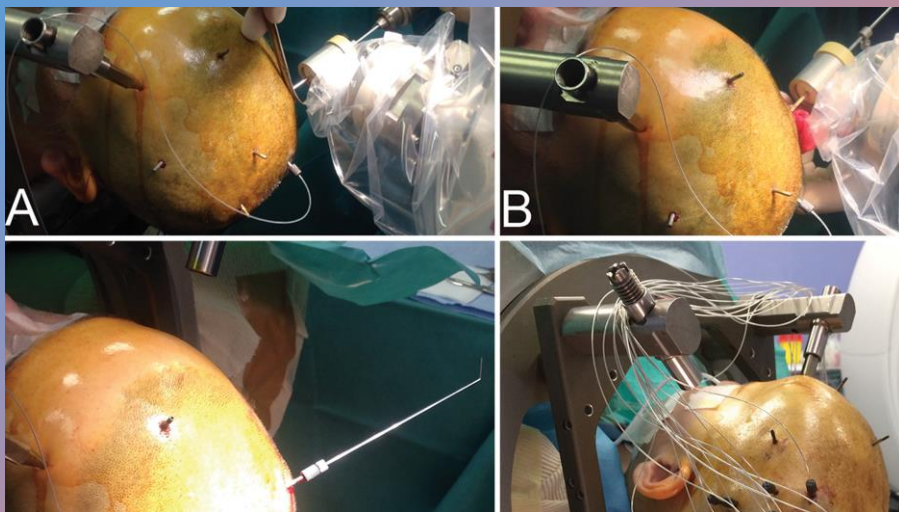
| Risk Factor                          | Univariate Analysis   |         | Multivariate Analysis |         |
|--------------------------------------|-----------------------|---------|-----------------------|---------|
|                                      | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value |
| All deaths                           |                       |         |                       |         |
| Absence of 5-yr terminal remission   | 5.3 (2.6–11.0)        | <0.001  | 4.7 (1.5–14.9)        | 0.007   |
| Remote symptomatic cause of epilepsy | 3.4 (1.9–6.1)         | <0.001  | 1.5 (0.7–3.6)         | 0.31    |
| Prior status epilepticus             | 1.9 (1.2–3.2)         | 0.01    | 1.5 (0.7–3.0)         | 0.28    |
| Age at onset <2 yr                   | 1.4 (0.8–2.3)         | 0.20    | 1.7 (0.8–3.5)         | 0.13    |
| Epilepsy-related deaths              |                       |         |                       |         |
| Absence of 5-yr terminal remission   | 6.4 (2.2–18.8)        | <0.001  | 4.7 (1.5–14.9)        | 0.007   |
| Remote symptomatic cause of epilepsy | 3.1 (1.4–6.7)         | 0.004   | 1.5 (0.7–3.6)         | 0.31    |
| Prior status epilepticus             | 2.1 (1.1–4.2)         | 0.03    | 1.5 (0.7–3.0)         | 0.28    |
| Age at onset <2 yr                   | 1.9 (0.96–3.8)        | 0.06    | 1.7 (0.8–3.5)         | 0.13    |
| Sudden, unexplained deaths           |                       |         |                       |         |
| Absence of 5-yr terminal remission   | 5.2 (1.4–18.5)        | 0.01    | 5.0 (1.2–20.1)        | 0.02    |
| Prior status epilepticus             | 2.8 (1.1–7.0)         | 0.03    | 2.6 (0.9–7.5)         | 0.07    |
| Age at onset <2 yr                   | 2.1 (0.8–5.5)         | 0.11    | 1.9 (0.7–5.2)         | 0.20    |
| Remote symptomatic cause of epilepsy | 1.9 (0.7–4.8)         | 0.20    | 0.8 (0.3–2.4)         | 0.72    |
| Localization-related epilepsy        | 0.8 (0.3–2.0)         | 0.60    | 0.5 (0.2–1.5)         | 0.21    |

\* A Cox proportional-hazards model was used to assess the risk of death associated with an absence of 5-year terminal remission, with remission status treated as a time-dependent covariate. A remote symptomatic cause of epilepsy indicates epilepsy associated with a major neurologic abnormality or insult. CI denotes confidence interval.

# Epilepsijas ķirurģijas principi.

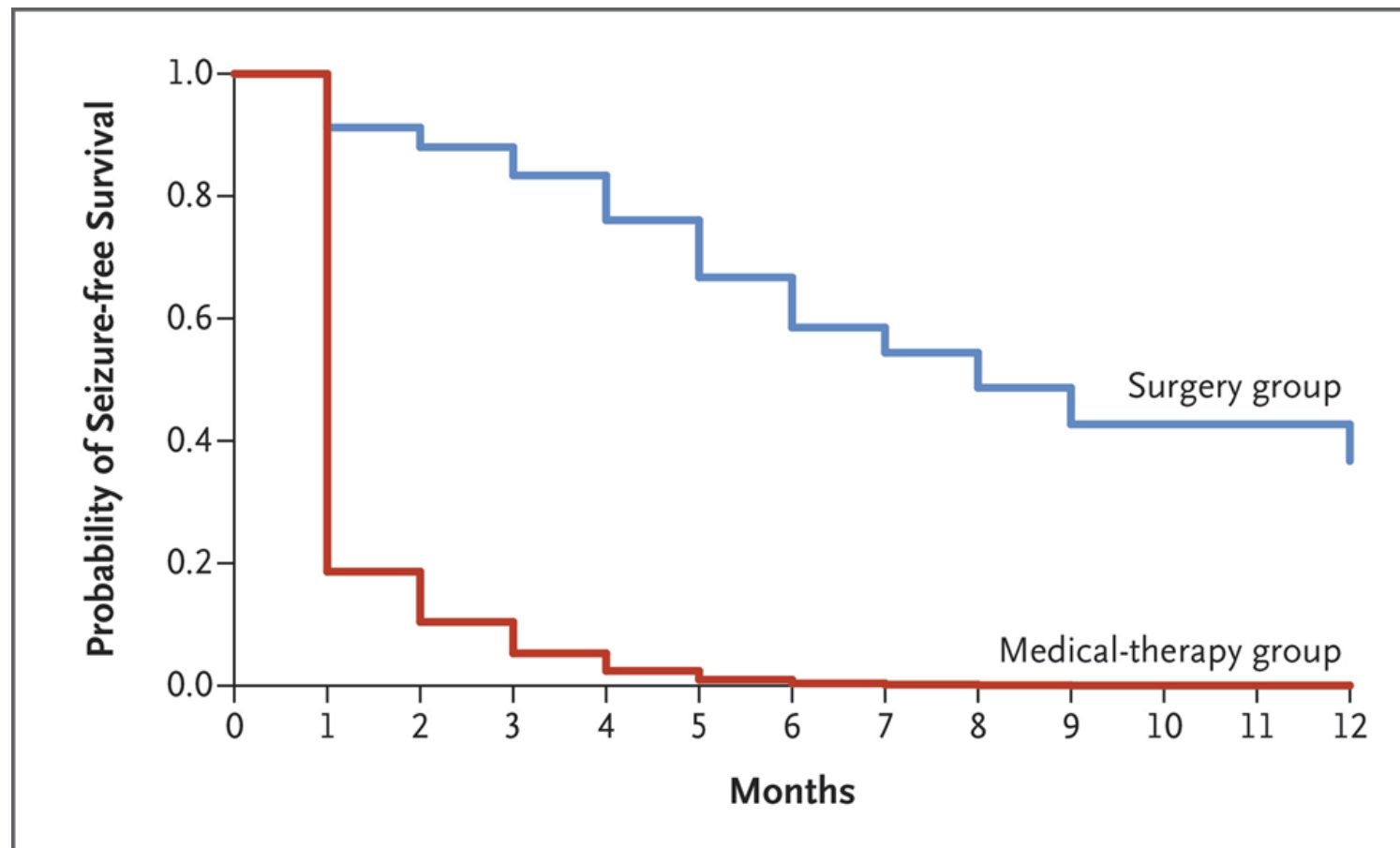


- Epileptogēna zona (smadzeņu daļa, kuru izoperējot pazūd lēkmes):
  - Simptomatogēna zona (kā lēkme izpaužas?);
  - Iritatīva zona (EEG starp lēkmēm, EEG avota lokalizācija);
  - Lēkmes sākuma zona (EEG lēkmes laikā, avota lokalizācija);
  - Funkcionāla deficīta zona (parēze, atmiņas un domāšanas traucējumi, PET);
  - Epileptogēns bojājums (MRI, pēcapstrāde, ne vienmēr jābūt).
- Elokventa garoza – neizbēgams kritiski svarīgu funkciju zudums (redze, kustības, valoda).

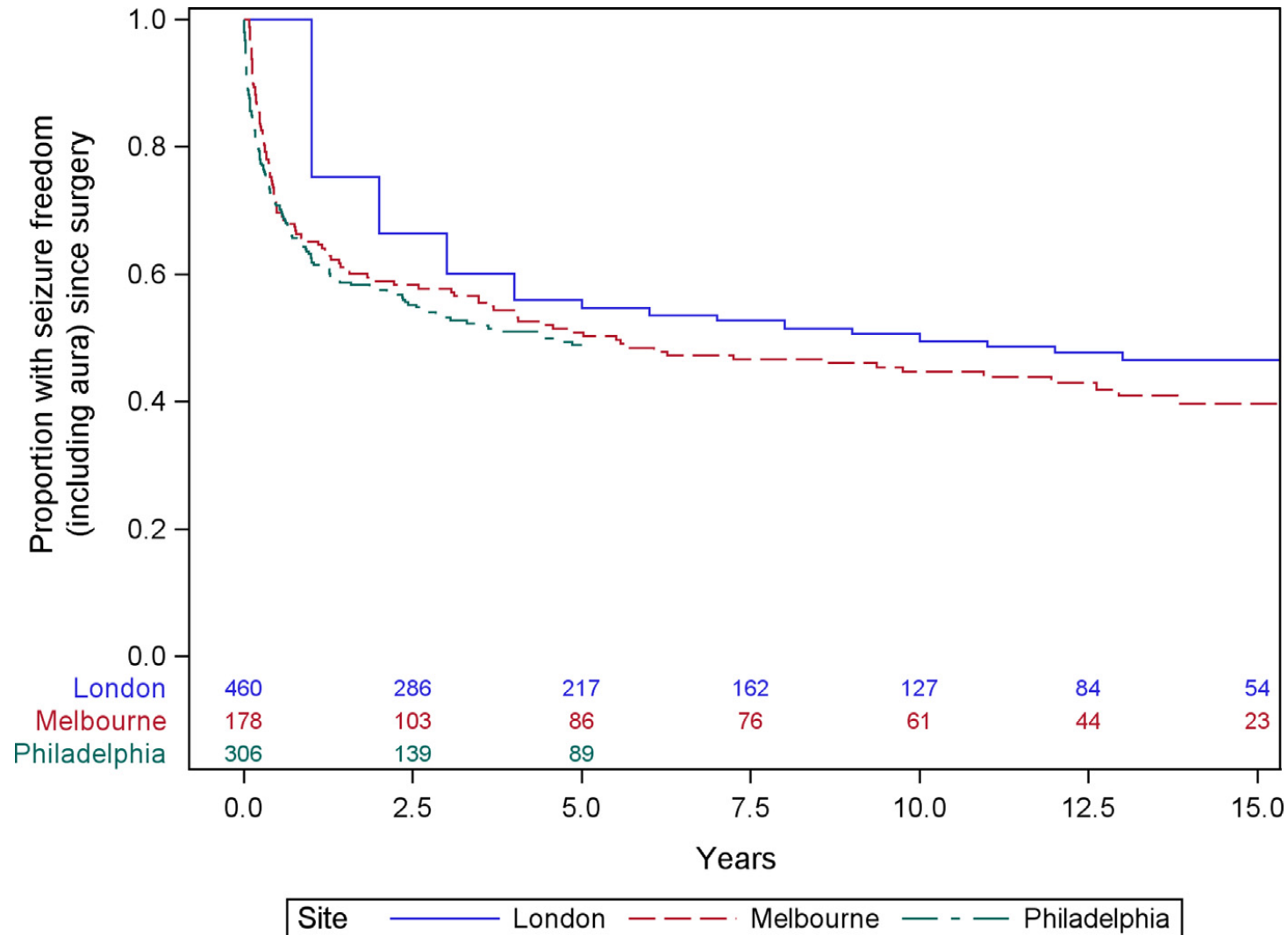


# Epilepsijas ķirurģiska ārstēšana – visefektīvākā zāļu rezistentas epilepsijas ārstēšana.

Randomizēts kontrolēts prospektīvs pētījums (refraktāras epilepsijas bērni, kam ķirurģiska ārstēšana iespējama): ķirurģija vs medikamenti. Lēkmju brīvu bērnu proporcija.

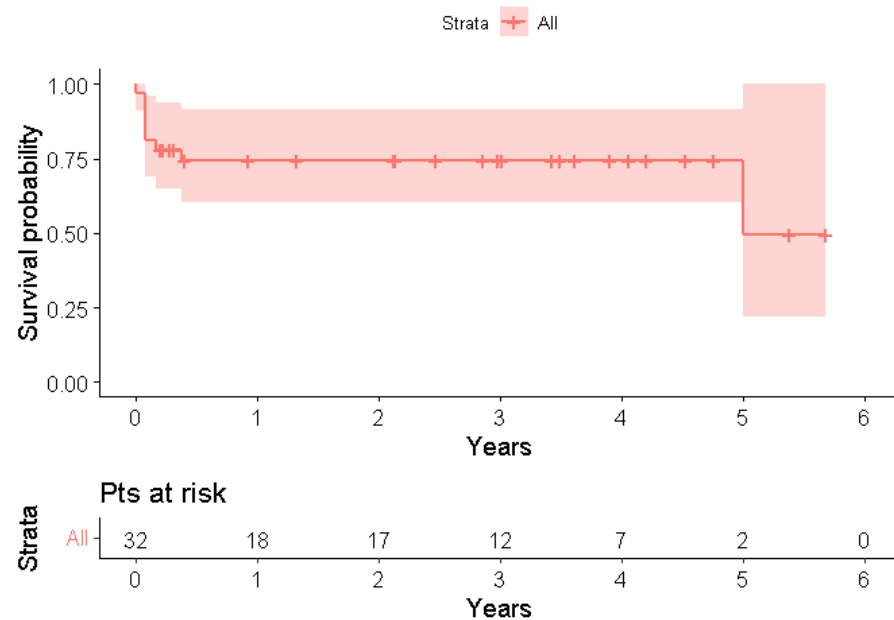


# Eilepsijas ķirurģiskas ārstēšanas ilgtermiņa rezultāti.



# Epi ķirurģija BKUS (kopš 2017. gada).

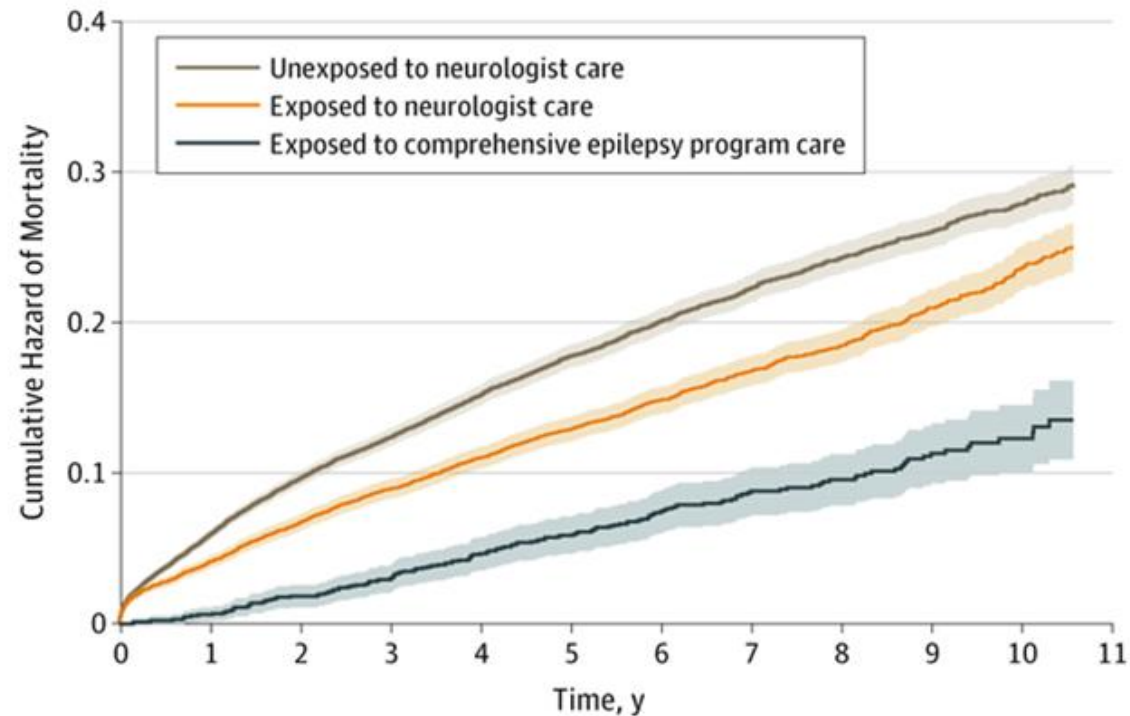
- 44 pacienti:
  - 37 rezekcijas, 2 hemisferotomijas, 3 kallozotomijas, 1 MST.
- 2 stereotaktiskas EEG.



| Characteristic | N = 32   |
|----------------|----------|
| Seizure free   |          |
| yes            | 23 (72%) |
| No             | 9 (28%)  |
| n (%)          |          |

| Characteristic | 1 Years        | 2 Years        | 3 Years        | 4 Years        | 5 Years         | 6 Years  |
|----------------|----------------|----------------|----------------|----------------|-----------------|----------|
| Overall        | 74% (61%, 91%) | 74% (61%, 91%) | 74% (61%, 91%) | 74% (61%, 91%) | 50% (22%, 100%) | — (—, —) |

Visaptveroša  
epilepsijas  
terapija  
samazina  
mirstību.



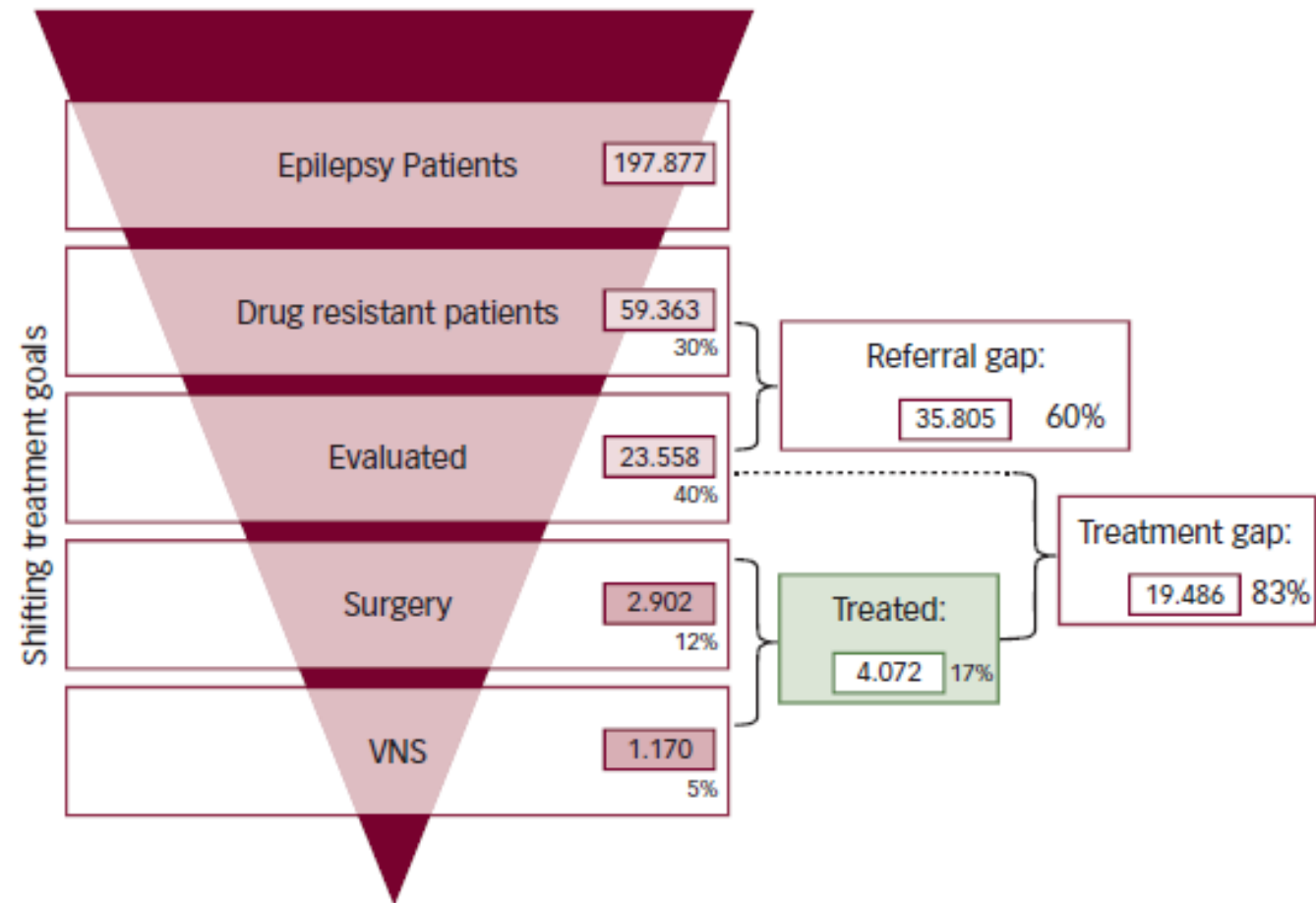
No. at risk by time

|                                                |       |       |       |       |      |      |      |      |      |      |      |
|------------------------------------------------|-------|-------|-------|-------|------|------|------|------|------|------|------|
| Unexposed to neurologist care                  | 16865 | 13200 | 11829 | 10648 | 9258 | 7970 | 6875 | 5889 | 4615 | 3277 | 2040 |
| Exposed to neurologist care                    | 5746  | 7167  | 6997  | 6772  | 6128 | 5262 | 4462 | 3679 | 2916 | 2120 | 1450 |
| Exposed to comprehensive epilepsy program care | 683   | 1284  | 1498  | 1608  | 1586 | 1443 | 1244 | 1033 | 805  | 598  | 355  |

# BKUS iespējas epileptoloģijā atbilst labāko centru standartiem.

- Diagnostika (epileptologu konsultācijas, standarta EEG, videoEEG novērošana, EEG pēcapstrāde, MRI ar epilepsijas protokolu, MRI pēcapstrāde, ģenētiska izmeklēšana).
- Stereotaktiska EEG (EEG elektrodu implantācija galvas smadzenēs).
- Medikamentoza ārstēšana (individuāla kompensācija!). Precīzijas terapija.
- Ketogēna diēta.
- VNS terapija.
- Ķirurģiska ārstēšana (visa veida operācijas, neironavigācija, intraoperatīva neiromonitorēšana).

## Figure 2: Drug-resistant Epilepsy Treatment Gap



VNS = vagus nerve stimulation.

BKUS Epilepsijas  
un miega  
medicīnas centra  
būvniecība.

