

The rollercoaster perspective of epilepsy



# Prevention and Cure

## How to achieve the goal – European perspective\*

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\*1 in 26 individuals will have epilepsy at some point in their lifetime<sup>a</sup>. Epilepsy is like a rollercoaster.

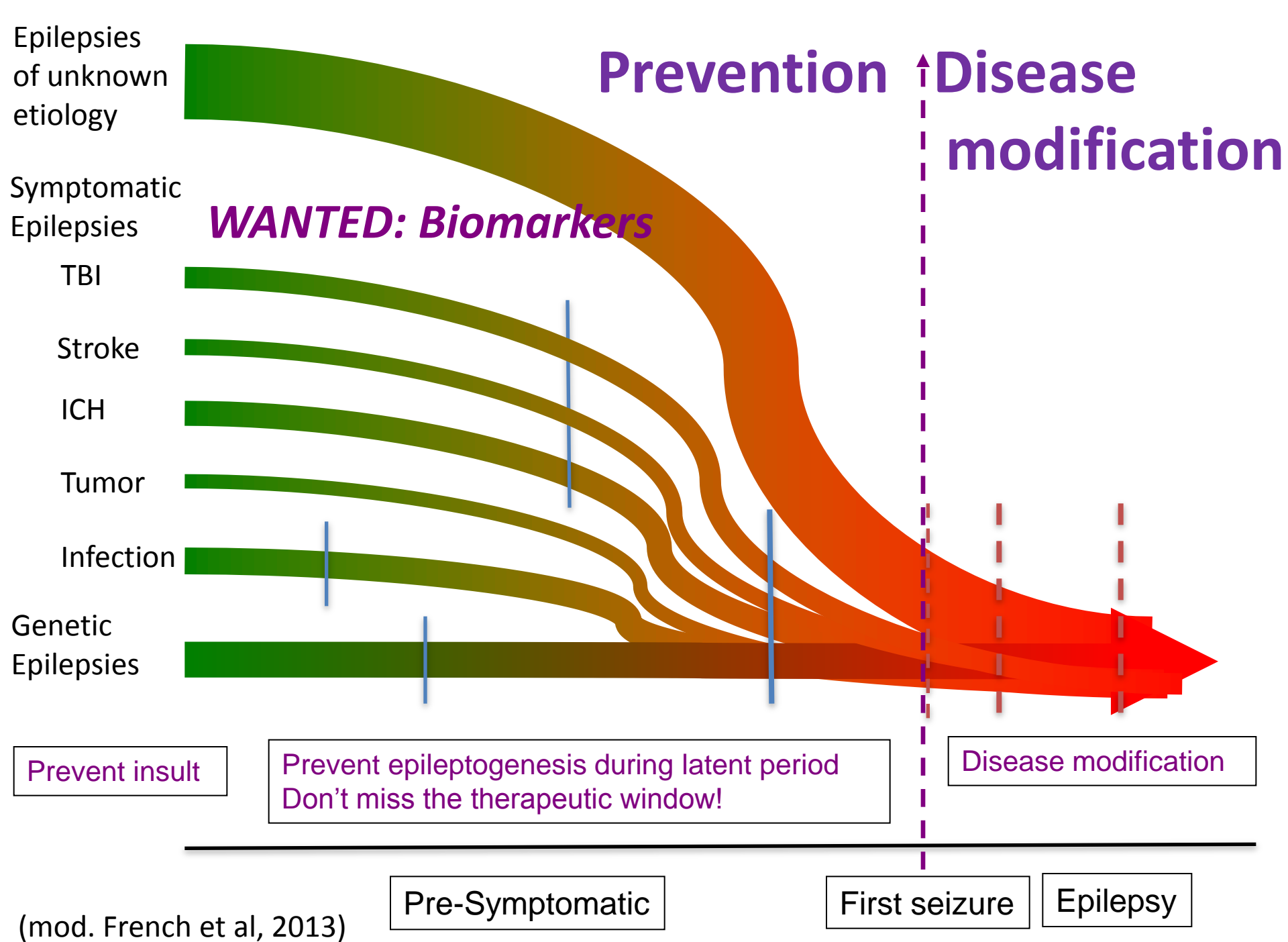
(Institute of Medicine. 2012).

# Roadmap: How to achieve the goal

- Prevention of epileptogenic brain injury
- Discovery and preclinical development of antiepileptogenic drugs (AEG)
- Innovative clinical AEG trial design
- Summary and Conclusions

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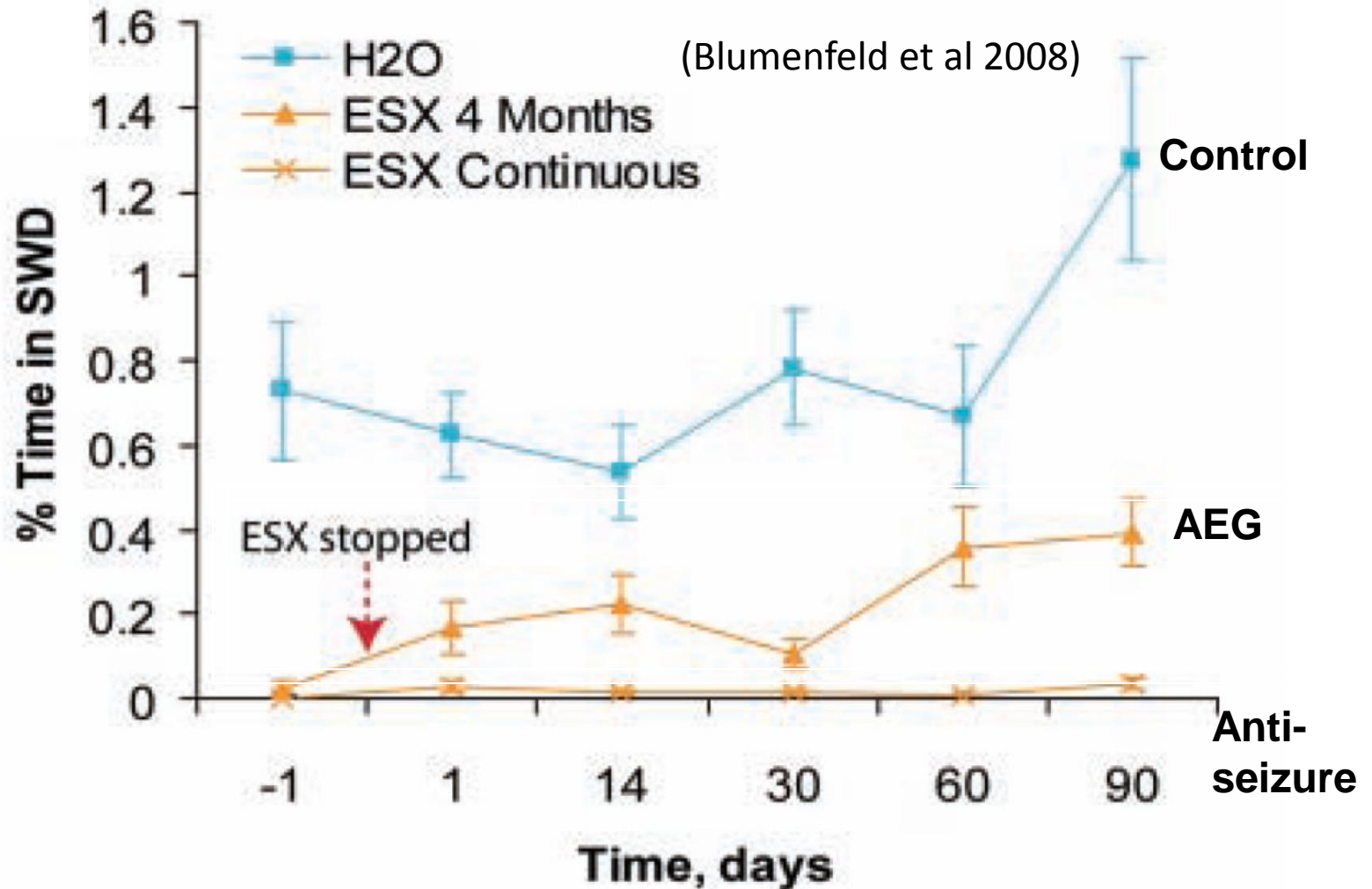


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# Prevention of epilepsy: animal model

AEG = antiepileptogenic



**Issues:**

**Control: Active drug? Epilepsy model? Counting seizures?**

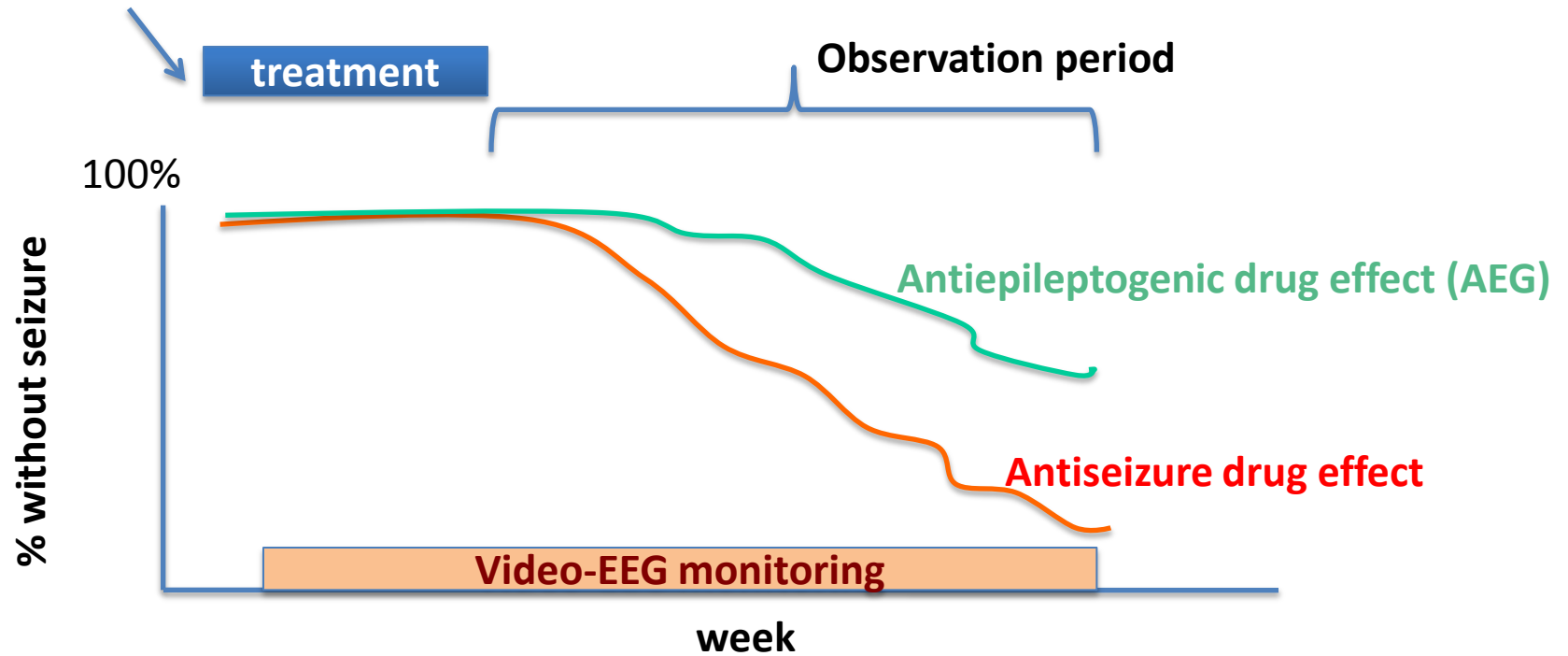
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# Prevention: Clinical proof-of-concept(target) trial

(Schmidt and Friedmann, 2012)

Epileptogenic insult



Issues: Controls-active drug?

Issues: Biomarkers

Issues: Remote seizure count?



# Opportunities for disease modification: natural history of treated new-onset epilepsy

37 years of follow-up from the first seizure on

- 48% Terminal remission from the start
- 19% Late remission (Relapsing-remitting course)

= *67% Good outcome with terminal remission*

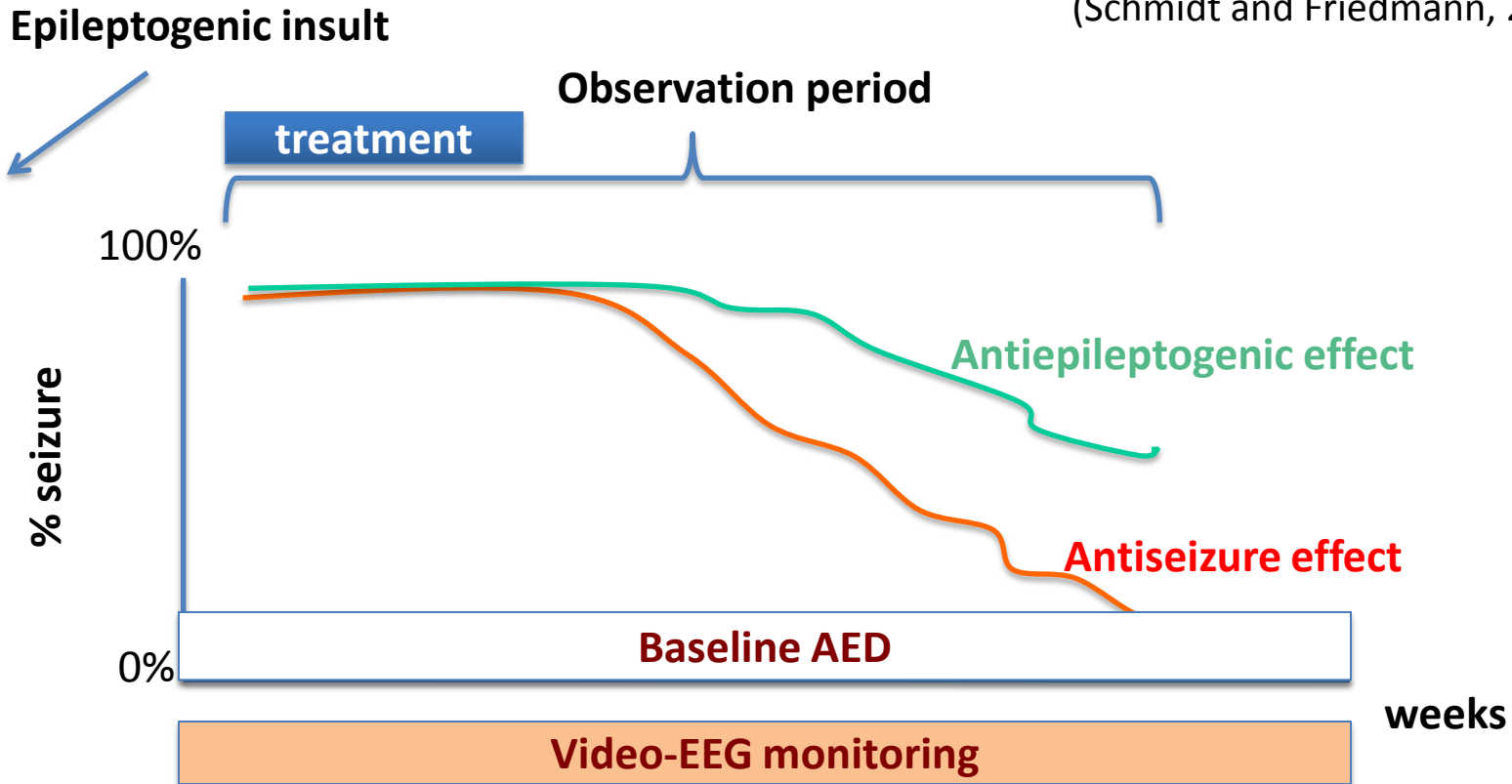
- 14% Worsening course (Remitting-relapsing)
- 19% Drug resistant epilepsy from the start

= *33% Poor outcome without remission*

(Sillanpää and Schmidt, Brain, 2006)

# Disease modification: Clinical proof-of-concept(target) trial

(Schmidt and Friedmann, 2012)



Issues: Control by active drug?

Issues: Biomarkers?

Issues: Remote seizure count?

# European Study of Epilepsy Prevention (ESEP) and Disease Modification (ESDM)

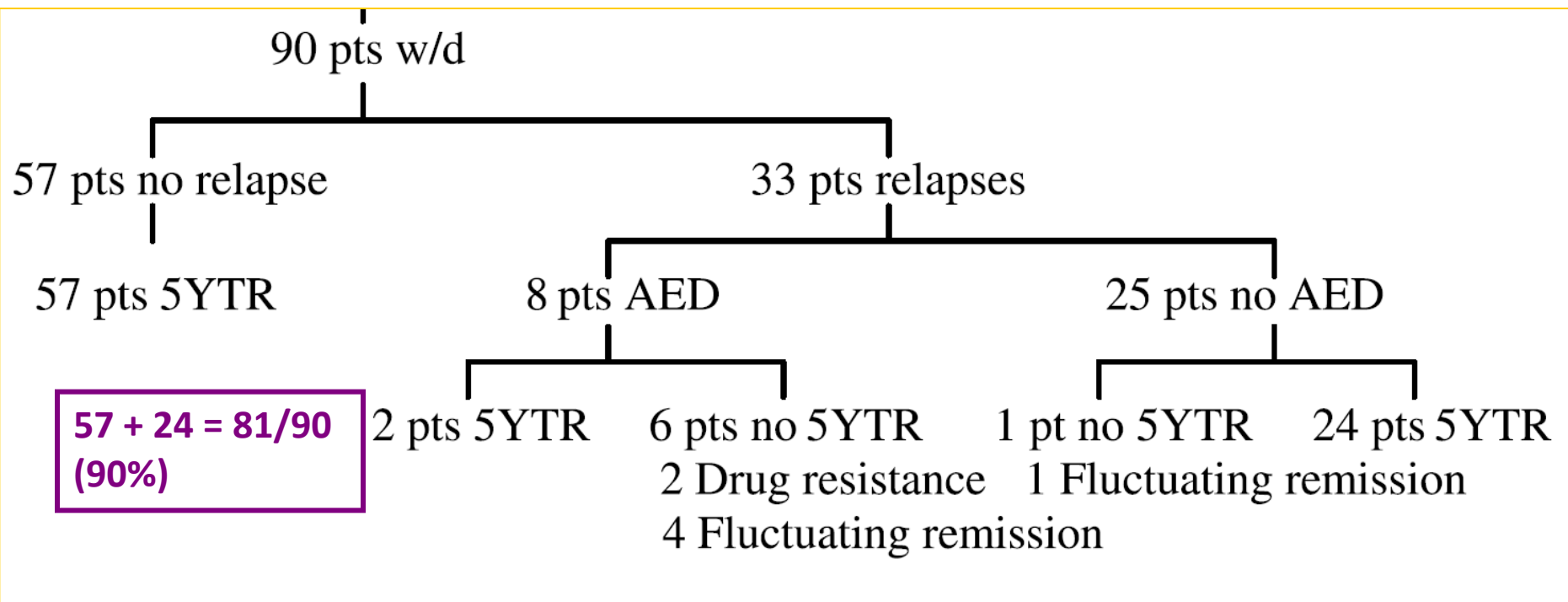
- *Prevent insult*: stroke, cancer, injury etc
- *Prevent epilepsy in latent period*
- Comparative preclinical and clinical proof of concept (target) studies of antiepileptogenic drugs using biomarkers for the risk of epilepsy
- *Prevent epilepsy after first seizure (Disease modification)*
- Comparative preclinical and clinical proof of concept (target) studies of antiepileptogenic drugs using biomarkers for the risk of worsening of epilepsy
- Identify better methods to follow the course of epilepsy

# European Study of Epilepsy Cure (ESEC)

- Prevent or control drug resistant epilepsy
- Prevent or control relapse following remission on AEDs and off AEDs
- Prevent or control relapse following surgical remission on and off AEDs

# Cure of childhood-onset epilepsy: now

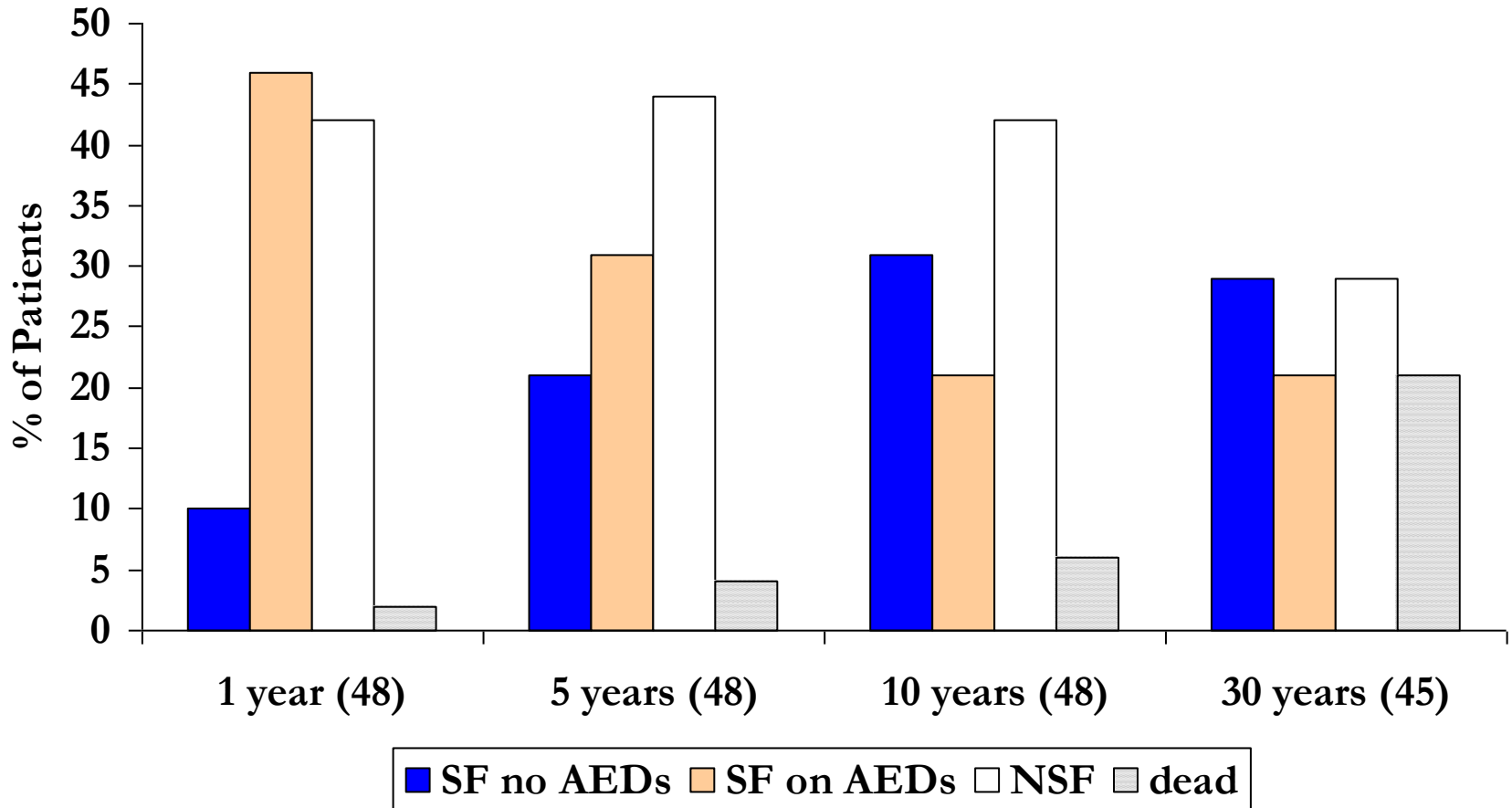
Cure = sustained remission off AEDs



*M. Sillanpää, D. Schmidt / Epilepsy & Behavior 8 (2006) 713–719*

# Surgical cure: Seizure free off AEDs after temporal lobe surgery

Kelley and Theodore 2005



- 104 of 365 (28%) seizure-free adults had discontinued AEDs after epilepsy surgery (de Tisi et al. 2011)

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# Roadmap: How to achieve the goal of prevention and cure of epilepsy

- Establish a European Consortium for Prevention of Epilepsy Studies: preclinical and clinical
- Establish a European Consortium for Cure and Disease Modification of Epilepsy Studies: preclinical and clinical
- Support target-driven discovery and development of antiepileptogenic drugs (AEG)
- Support innovative clinical AEG trial design