

Outcomes of epilepsy surgery



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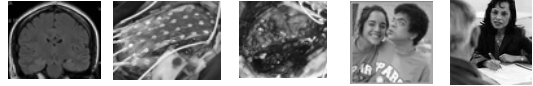
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Aims of epilepsy surgery

- The aim of epilepsy surgery is to improve patients' quality of life through obtaining seizure freedom or a substantial reduction of the seizure burden without disabling side effects



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Patients' aims beyond seizure freedom

- Desire for work
- Driving of motor vehicles
- Independence
- Socialising
- Freedom from drugs

Taylor et al 2001

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General considerations

- When you start a surgical program it is important to plan a prospective longitudinal follow-up program to evaluate the results
- In order to do a proper follow-up you must have a baseline
- In order to have a baseline you must decide which outcome domains to study and how to study them

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Outcome domains

- Seizure outcome
- Surgical complications
- Cognitive outcome
- Psychiatric outcome
- Psycho-social outcome
- Health-related quality of life (HRQL)

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Outline

- Seizure outcome
 - Outcome classifications
 - RCT or observational studies
 - Short vs long term seizure outcome
 - Resection type, etiology, IQ
- Psychosocial outcome
- Health-related quality of life (HRQL)

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Seizure outcome: Engel's outcome classification

- Class I: Seizure free
- Class II: Rare seizures ('almost seizure free')
- Class III: Worthwhile improvement
- Class IV: No worthwhile improvement

Engel 1993

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Seizure outcome: Engel's outcome classification

- Engel's Class I: Seizure free
 - A. Completely seizure free since surgery
 - B. Aura only since surgery
 - C. Some seizures after surgery, but seizure free for at least 2 years
 - D. Atypical GTCS with AED withdrawal only

Engel 1993

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Seizure outcome: ILAE classification

- 1. Completely seizure free, no auras
- 2. Only auras; no other seizures
- 3. 1-3 seizure days/year; \pm auras
- 4. Four seizure days/year to 50% reduction of baseline seizure days; \pm auras
- 5. Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; \pm auras
- 6. More than 100% increase of baseline seizure days; \pm auras

ILAE Commission report 2001

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RCTs of surgical treatments

- RCTs should not be performed too early since surgical treatments evolve rapidly and the technique may not yet be mature
- RCTs should not be performed too late when a procedure is already considered 'standard practice' by the medical community



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RCTs of surgical treatments

- RCTs for epilepsy surgery were proposed as early as 1963. The failure of an attempt in the early 90ies solidified the view that such trials are unfeasible.
- Nonetheless, RCTs of surgical procedures are feasible and have recently been performed even for such a standard practice as appendectomy

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RCTs in epilepsy surgery

- Wyler 1995
 - A randomised prospective study of the extent of MTL resection versus outcome from ATL
 - Single centre
 - 70 patients
 - Duration: 1 year
 - Single blind
 - Results: Better outcome with larger than with smaller MTL resections

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RCTs in epilepsy surgery

- Wiebe 2001
 - A randomised prospective study comparing surgical and medical treatment of TLE
 - Single centre
 - 80 patients
 - Duration: 1 year
 - Single blind

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RCT of surgery for TLE

- 80 patients with TLE were randomly assigned to surgery (40 patients) versus AED treatment for one year (40 patients)
- Optimal medical therapy and primary outcomes assessed by epileptologists unaware of treatment assignments
- Primary outcome: freedom from seizures with impairment of awareness

Wiebe et al 2001

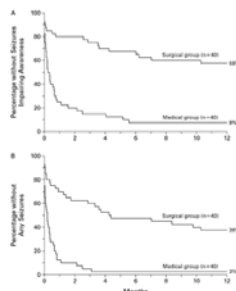
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RCT of surgery for TLE

- At one year 58% in the surgical group (64% of operated) vs 8% in the medical group were free from seizures with LOC ($p < 0.001$)
- Four patients (10%) had adverse effects of surgery. One patient in the medical group died



Wiebe et al 2001

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Problems with RCTs in epilepsy surgery

- Poor patient recruitment (10-50%)
- Patients are less willing to participate in surgical than medical RCTs
- Protocol deviations
- Surgical placebo
- Long term effects

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ILAE Commission on Neurosurgery

- Global survey on epilepsy surgery 1980-1990
- Responses from 46 epilepsy centres across the world
- 2 373 ATL – 57.3% seizure free
- 341 SAH – 60.1% seizure free
- 330 FLR – 41.2% seizure free

ILAE commission report 1997

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TLE – practice parameter

- Systematic review and analysis of the literature since 1990: 415 /1282 original citations, 2250 patients
 - 1 Class I RCT of TLE
 - 24 Class IV series of TLR resections (criteria for Class III were not met because outcome assessment was not independent of treatment)
 - Surgical outcome was consistent, differed little among stratifications and on average identical to those of the Class I study

Engel et al 2003

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RCT or OS?

- RCTs and OS!
- More RCTs are necessary
- Not all aspects of epilepsy surgery will be possible to study by RCT
- Important with high-quality OS as well, especially concerning long term effects



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Long-term seizure outcome – a systematic review

- No RCT, 1500 references, 142 eligible, 76 included
- Almost all studies without controls
- Seizure freedom >5 years after TLR median 58-65%
- Seizure freedom >5 years after FLR median 34%
- Few studies reported sustained seizure freedom!

Tellez-Zenteno et al 2005

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Long-term seizure outcome – the Swedish experience

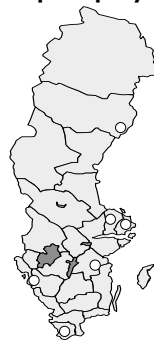
- Prospective longitudinal follow-up of seizure outcome and psychosocial variables 5 and 10 years after surgery
- Initiated 2005, sofar patients operated 1995-97 and 2000-2002 have been investigated
- A control group of patients evaluated for epilepsy surgery but not operated

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Epilepsy Surgery in Sweden



- Population 9 million
- No national epilepsy centre
- Six university hospitals
- Epilepsy care including epilepsy surgery at all regional centres
- A population based regional referral system, 800 000 – 1 800 000 per centre

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The Swedish National Epilepsy Surgery Register

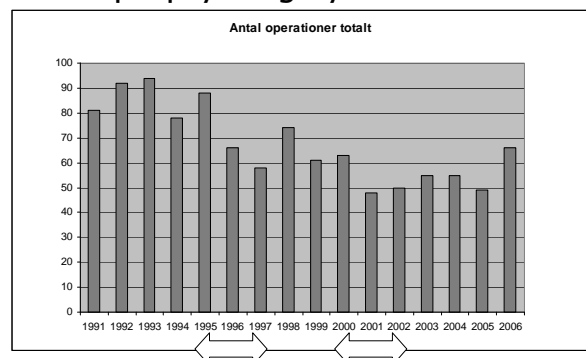
- Quality Control register (initiated by the Swedish National Board of Health and Welfare)
- Started 1990, prospective since 1995
- All epilepsy surgery centres participate
- Steering committee with participation from all centres
- The register contains data on patient history, seizure characteristics, presurgical investigations, surgical treatment, complications and prospective follow-up of all patients after 2, 5 and 10 years

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Epilepsy Surgery in Sweden



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Long-term seizure outcome – Seizure outcome classification

- Engel's Class I: Seizure free
 - A. Completely seizure free since surgery
 - B. Aura only since surgery
 - C. Some seizures after surgery, but seizure free for at least 2 years
 - D. Atypical GTCS with AED withdrawal only
- $\geq 75\%$ reduction of seizure frequency compared to baseline of 1 year before surgery
- 50-75% reduction of seizure frequency
- $<50\%$ reduction of seizure frequency
- Increased seizure frequency

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10 year follow-up of patients operated 1995-97 in Sweden

- 188 resective procedures: 133 TLR
- 144/188 patients 10 year follow-up:
 - 63% TLR seizure free (61% at 2 years)
29% sustained sz free (44% at 2 years)
 - 50% XTLR seizure free (40% at 2 years)
30% sustained sz free (36% at 2 years)
- Conclusion: Seizure free rates are similar at 10 year compared to 2 year follow-up, but lower proportion with sustained sz freedom

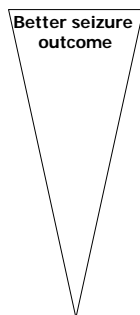
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Outcomes vs resection type

- Hemispherectomies
- Temporal lobe resections for MTLE
- Neocortical resections
- Multilobar resections



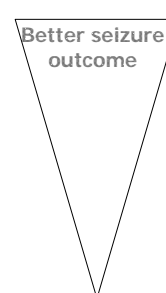
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Outcomes vs etiology

- Epileptogenic lesions
- Mesial Sclerosis
- Cortical dysplasias
- Gliosis



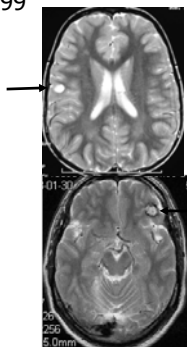
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Epilepsies due to Lesions Sweden 1990-1999

- 109 Lesionectomies
 - 36 low-grade gliomas
 - 37 gangliogliomas
 - 3 DNET
 - 27 cavernomas
 - 6 other vascular lesions
- 79% seizure free at 2 year follow-up:
 - 84% of temporal lesions (N=80)
 - 79% of frontal lesions (N=14)
 - 78% of parietal lesions (N=9)
- Hence, pathological substrate more important for outcome than anatomical localisation



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Outcomes vs IQ: The Swedish series

- Data from the population based Swedish National Epilepsy Surgery Register over a ten year period 1990-99 were analysed
- Outcome data at the two-year follow-up were related to preoperative IQ categories and to neuropathological diagnoses
- Aim: to verify or refute the hypothesis that patients with $IQ < 70$ have a worse seizure outcome than patients with $IQ > 70$

Malmgren et al, Brain 2008

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Temporal lobe resections in relation to IQ

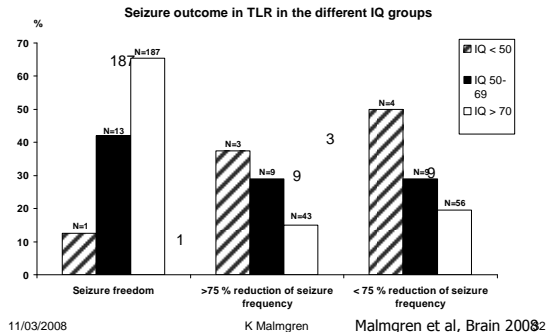
- 250 adults, mean age at surgery 35 yrs (19-61)
 - 231 had IQ>70 (92%)
 - 19 had IQ 50-69 (7.6%)
 - 1 had IQ<50 (0.4%)
 - 8% of adults had IQ<70
- 75 children, mean age at surgery 11 yrs (2-18)
 - 55 had IQ>70 (73.3%)
 - 13 had IQ 50-69 (17.3%)
 - 7 had IQ<50 (9.3%)
 - 26.6% of children had IQ<70

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Malmgren et al, Brain 2008₃₁

Seizure outcome in TLR related to IQ category



Psychosocial outcome

- Employment
- Driving status
- Relationships and social behaviour

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Employment status

- US prospective multicentre study
- 375 adults included, 2 year employment data for 299, i e 80%
- Results:
 - 47% working full or part time preoperatively
 - 55% working full or part time after 2 years
- Conclusions: Net employment gains were modest and higher with better seizure outcomes

Chin et al 2007

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Long-term employment status: The Göteborg series

- 70 adult patients with long-term follow-up mean 12 years after epilepsy surgery
- Seizure free patients continued to work:
 - 82% preoperatively
 - 74% at longterm follow-up
- Patients with seizures worked less:
 - 63% preoperatively
 - 30% at longterm follow-up

Asztély et al 2007

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Employment and rehabilitation

- Short term rehab unit launched in Bethel 1997
- Rehab group (N=167) were compared with historical non-rehab group (N=103)
- 2 years after TLR 75% of rehab pats were employed compared to 61% of non-rehab (p=0.01)
- Conclusions: A rehab program can improve postop employment

Thorbecke et al AES 2007

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Indicators of Quality of Life

- Many items (or domains) in QoL inventories assess factors such as:
 - physical function
 - social function
 - health status
 - vocational status
- Improvement in such domains is not a good in itself, but only instrumentally good in that it tends to promote a good life

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Health Related Quality of Life

The term is used with several meanings, e.g.:

- QoL in so far as it is (objectively) dependent on health
- QoL in so far as the patient judges it to be dependent on her health
- Objective functioning in so far as the patient judges it of be affected by her illness

Malmgren & Malmgren 2000

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Health-related Quality of Life

- Despite the conceptual confusion, HRQL has become a generally accepted name for a set of measures which aim at capturing many of the psychosocial and subjective aspects of chronic diseases
- Measuring the HRQL indicators is often a reasonable way of assessing the effect of a treatment on the patients' HRQL

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Major approaches to QoL assessment

- Standardised descriptive instruments
 - Generic
 - Disease specific
- Utility (preference-based) measures
- Individualised approaches

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Some epilepsy specific scales for assessing aspects of HRQL

Acronym	Name/domains
WPSI	Washington Psycho-social inventory
ESI-55	Epilepsy Surgery Inventory – 55
QOLIE 89	Quality of Life in Epilepsy
Liverpool Battery (HRQOL)	Liverpool Seizure Severity Scale, self-esteem, stigma, adverse effects of drugs
QOLAS	Quality of Life Assessment Schedule
SHE	Subjective Handicap of Epilepsy
PeSoS	Comprehensive Care Inventory

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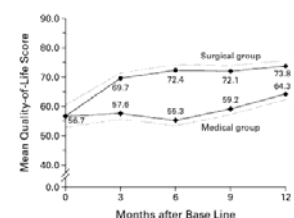
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RCT of surgery for TLE

- Patients in the surgical group had significantly better HRQL than the medical group on the mean global score of QOLIE-89 ($p < 0.001$ for both comparisons)

Wiebe et al 2001



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HRQL over time since surgery

- US prospective multicentre study
- 396 patients who underwent resective epilepsy surgery completed QOLIE-89 preoperatively and postoperatively
- QOLIE-89 scores increased significantly, changes over time were sensitive to seizure free status
- QOLIE-89 scores stabilized at 2 years and were unrelated to duration of epilepsy or continued AED use

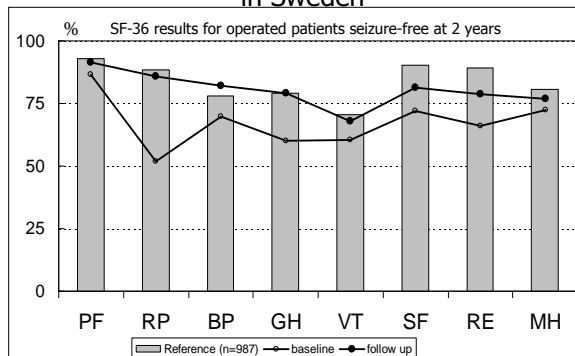
Spencer et al 2007

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HRQL two years after epilepsy surgery in Sweden

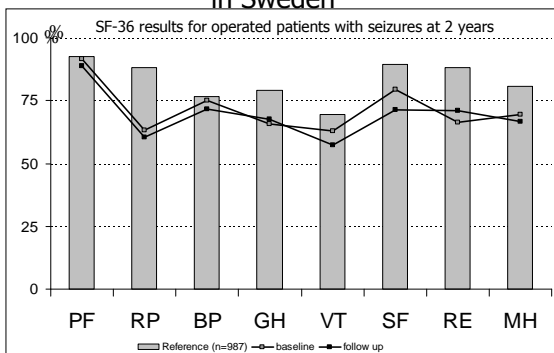


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Sager Magnusson et al 2006

HRQL two years after epilepsy surgery in Sweden



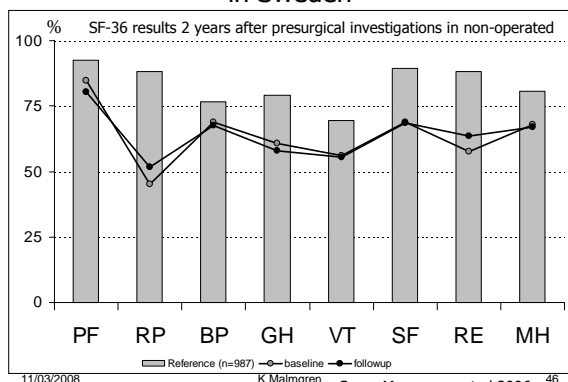
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Sager Magnusson et al 2006

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HRQL two years after epilepsy surgery in Sweden



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Sager Magnusson et al 2006

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General considerations

- When you start a surgical program it is important to plan a prospective longitudinal follow-up program to evaluate the results
- In order to do a proper follow-up you must have a baseline
- In order to have a baseline you must decide which outcome domains to study and how to study them

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Conclusions

- Seizure outcome is one of many outcome variables in epilepsy surgery
- Seizure free patients improve in HRQL but not necessarily in employment
- It is important to individualise our aims in relation to patient needs
- Detailed outcome knowledge improves patient counselling and may be instrumental in the planning of postoperative rehabilitation

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