

## Brief Communication

## Why are antiepileptic drugs continued after successful epilepsy surgery in adults?

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## ABSTRACT

**Objective:** Studies have demonstrated that a substantial number of patients continue treatment with antiepileptic drugs (AEDs) for many years after epilepsy surgery despite seizure freedom. In this study, we aimed to investigate why AED treatment is maintained in patients three and seven years after successful epilepsy surgery. To our knowledge, an analysis of this specific subgroup of completely seizure-free patients has not been done before. **Material and methods:** Danish patients with medically refractory epilepsy and histopathologically proven hippocampal sclerosis operated between 1995 and 2014 who were reported seizure-free at one-year postsurgery were contacted by telephone in 2017 and retrospectively asked about the reasons to continue or taper AED at three and seven years after the operation.

**Results:** Fifty patients were completely seizure-free three years after the operation. Of those, 31 (62%) were still taking AEDs at three years, thereof 10 (20%) in the same dose and number and half of those on their own wish. At seven years, nine patients were still taking AEDs, two in unchanged number and dose, both on their own wish. Fear of relapse was the most common reason not to withdraw medication. Presurgery seizure frequency for patients taking AEDs at three and seven years was not higher than for those who had discontinued taking AEDs.

**Conclusions:** A large portion of completely seizure-free patients still take AEDs even seven years after epilepsy surgery. This seems to be largely due to the patients' own wishes and fear of relapse, and unrelated to presurgery seizure frequency. Our results could aid in counseling patients on the decision to withdraw AEDs after successful epilepsy surgery.

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## 1. Introduction

The ultimate goal of epilepsy surgery is to eliminate epileptic seizures without using antiepileptic drugs (AEDs). In many patients with drug-resistant epilepsy, adverse effects of AEDs have been shown to have a more negative influence on health-related quality of life than the seizures themselves [1], and the hope of AED discontinuation is one of the major motives for undergoing epilepsy surgery [2–4]. Child neurologists will generally recommend early discontinuation of AEDs because of the potential risk of neurodevelopmental delay related to the medication [5,6] but for adults, no consensus exists and a substantial number of patients continue AED treatment even many years after complete seizure freedom has been achieved [7,8]. In this study, we aimed to investigate why AED treatment is maintained in adult patients three and seven years following

successful epilepsy surgery. To our knowledge, an analysis of this specific subgroup of completely seizure-free patients has not been done before.

## 2. Material and methods

## 2.1. Patients

In total, 159 Danish patients with medically refractory epilepsy and histopathologically proven hippocampal sclerosis who were operated with either temporoamygdalahippocampotomy (TAH) or selective amygdalahippocampotomy (AH) between 1995 and 2014 (>16 years) were evaluated. The surgical approach was determined by the operating neurosurgeon in collaboration with the entire Danish epilepsy surgery group. Patients (n = 93) who were reported seizure-free The International League Against Epilepsy (ILAE class IA) at one-year follow-up visit after surgery were retrospectively identified and contacted by telephone.

At three-year postsurgery, 50 patients (TAH, n = 12; AH, n = 38) remained completely seizure-free (ILAE IA) and were included in the

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**Table 1**  
Basic characteristics.

Variable	
Sex	
Female	28 (56%)
Male	22 (44%)
Average age at debut of epilepsy (median)	12.3 (9)
Average age at surgery (median)	38.1 (39)
Side of surgery	
Right	26 (52%)
Left	24 (48%)

study. Twenty-six patients had experienced seizure recurrence, and 17 patients could not be evaluated (seven patients were lost to follow-up; three did not want to participate; two had emigrated; four had died; and one was psychotic at the time of the telephone interview). Out of the 50 patients analyzed three years after surgery, 13 were operated after 2010, and information regarding their seven-year outcomes was thus not available. Nine patients had seizure recurrence since three-year postsurgery, leaving 28 patients that remained completely seizure-free for evaluation at seven-year postsurgery.

## 2.2. Data

Basic information regarding age at surgery, gender, surgical approach, side of surgery, and amount of seizures before surgery was collected from the medical records (Table 1). Information regarding seizure outcome at one, three, and seven years and AEDs taken at three and seven years after surgery was also collected from the medical records and supplemented by a telephone interview. Information regarding the reasons to continue or taper AED was collected by a semistructured telephone interview performed by MTF and MB in

2017. The patients were asked to explain the reasons or concerns they had to continue or taper AED at three years and seven years, respectively, after surgery. Contacting the patients by telephone was approved by the Danish Safety Authority.

## 3. Results

### 3.1. Three-year outcomes

The main results at three-year postsurgery are summarized in Fig. 1. None of the patients increased the number or dose of AEDs.

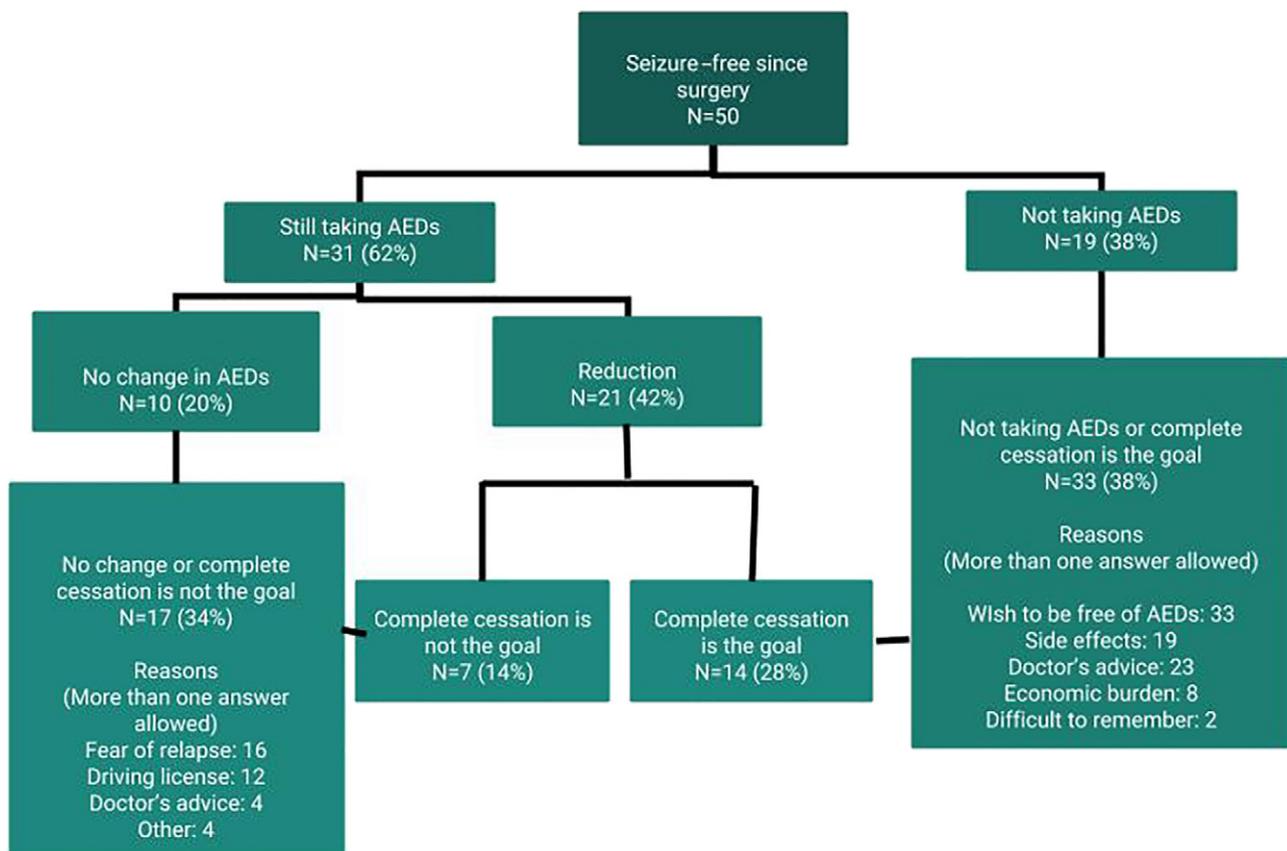
#### 3.1.1. Reasons to continue AED therapy

At three-year postsurgery, 31 (62%) were still taking AEDs. For a third of those patients, there had been no change in the AED treatment at all (dose or number of drugs). All these patients claimed that complete cessation of AED treatment never had been the goal, and that the initiative not to withdraw medication came from the neurologist in five cases (50%). For the rest of the patients who were still taking AEDs postsurgery, their dose or number of drugs had been reduced, and for most of these patients (14/21), complete cessation was still the goal.

#### 3.1.2. Reasons to withdraw AED therapy

At three-year postsurgery, 19 of 50 patients (38%) were not taking any AEDs, and of these, ten (53%) replied that the initiative to withdraw medication came specifically from the neurologist, whereas the rest (47%) replied that medication was discontinued mainly on their own wish.

Difference in presurgery seizure frequency between those taking and not taking AEDs at three-year postsurgery is summarized in Table 2. Patients taking AEDs at three-year postsurgery did not have higher presurgery seizure frequency than those not taking AEDs.



**Fig. 1.** Results at three-year postsurgery.

**Table 2**  
Number of seizures before surgery in patients taking AEDs versus patients not taking AEDs at three-year postsurgery.

Preoperative seizure frequency	Whole group (n = 50)	Three-year postsurgery			Seven-year postsurgery		
		Taking AEDs (n = 31)	Not taking AEDs (n = 19)	p-Value	Taking AEDs (n = 9)	Not taking AEDs (n = 19)	p-Value
SP <sup>a</sup> /month	14.6	14.9	13.8	0.43	10.2	9.2	0.39
CP <sup>a</sup> /month	7.7	6.8	9.2	0.18	8.2	7.4	0.39
GTC <sup>a</sup> /month	2.3	1.2	3.9	0.16	3.05	1.3	0.28

<sup>a</sup> Terminology used for seizure classification used in the records. SP = simple partial seizure, CP = complex partial seizure, GTC = generalized tonic-clonic seizure.

3.2. 7-Year outcomes

The main results at seven-year postsurgery are summarized in Fig. 2.

3.2.1. Reasons to continue AED therapy

Nine patients were still taking AEDs at seven-year postsurgery. Two were still taking AEDs in unchanged dose and number, both on their own wish and for fear of relapse and loss of driving license. The average number of presurgery seizure frequency in these two patients was 27.5 simple partial seizures and 7.7 complex partial seizures per month, and 0.25 generalized tonic-clonic seizures per year, respectively. Four of the nine patients (44%) who were still taking AEDs at seven-year postsurgery were disappointed still to do so.

3.2.2. Reasons to withdraw AED therapy

Nineteen patients were not taking AEDs at seven-year postsurgery. Ten (53%) and four (21%) of these patients claimed that the initiative to stop was the neurologists or mutual, respectively. Of the 14 who claimed that AED reduction or stop was the goal at three-year

postsurgery, seven were still followed at seven years; five were still seizure-free; and two had managed to stop taking AEDs.

Presurgery seizure frequency difference between those taking and not taking AEDs at seven-year postsurgery is summarized in Table 2. Patients still taking AEDs at that time did not have a significantly higher seizure frequency than those who had discontinued the treatment. Of note, one of the patients still taking AEDs had 24 generalized tonic-clonic seizures per month presurgery.

4. Discussion

This small study demonstrated consistently with other studies [9], that a large proportion of adult seizure-free patients are still taking AEDs many years after successful epilepsy surgery. In our study, 62% of patients continued AED at three years after surgery and 32% of patients at seven-year postsurgery. This is, however, somewhat lower than previously reported. A retrospective meta-analysis of 506 seizure-free patients [8] and a prospective population-based study [7] found that as many as 81% of adult patients were still taking AED at 6.5 years after surgery and 57% of patients continued AEDs even 10 years after surgery, respectively. The difference may be explained

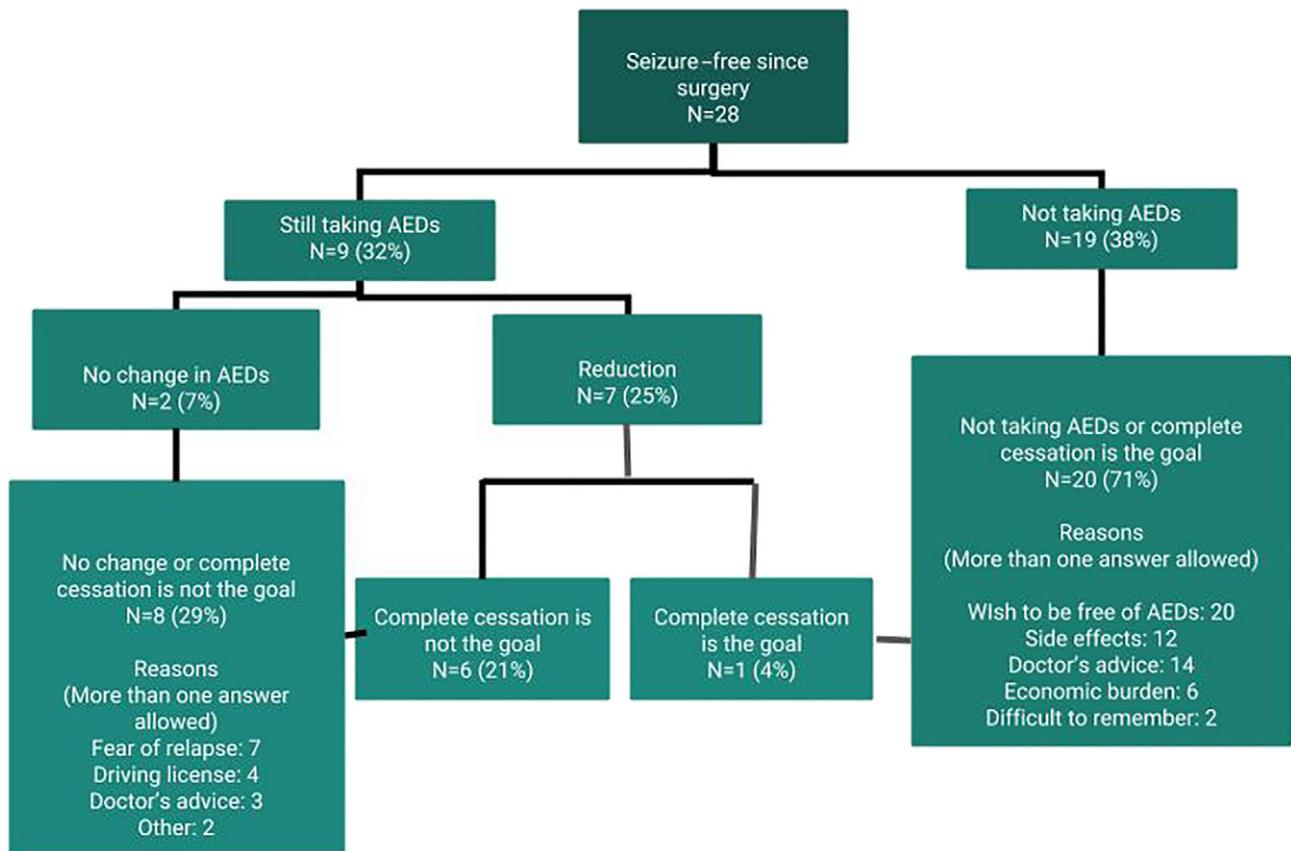


Fig. 2. Results at seven-year postsurgery.

by the fact that we evaluated only patients who had been completely seizure-free throughout the period since surgery and did not include patients that had seizure relapse and regained seizure control following reintroduction of AEDs. To our knowledge, an analysis of this specific subpopulation having not had any seizures since surgery has not been done before.

There are no existing international standardized guidelines regarding in whom, when, and how to discontinue AED after successful surgery [9]. According to the Danish epilepsy surgery protocol, adults in general continue stable AEDs the first two-year postsurgery. Further decisions about withdrawal is taken individually but patients are generally in the preoperative phase informed that drug tapering two years after surgery will be considered. A systematic approach toward AED discontinuation may be worthwhile as described by Rathore et al. who succeeded to discontinue AED in around 2/3 of patients with mesial temporal lobe epilepsy when discontinuation was planned prior to surgery [10].

The decision for continuing or discontinuing AEDs in the adult population depends on various psychosocial and cultural factors and is influenced by economy, presence, or absence of adverse effects, stigmatization related to the diagnosis, and to vocational and driving issues [2–4]. In our study population, continuing AEDs was largely done due to the patients' own wish and fear of relapse whereas the presurgery seizure frequency appeared not to influence the decision. Specific concerns related to the risk of loss of driving were reported as a cause for continuing AED in more than half of the patients even after seven years of seizure freedom whereas adverse effects related to the drugs were the reason for AED discontinuation in up to 60% of patients.

The limitations of the study were the relatively small number of patients included and that patients were retrospectively asked about the reasons and concerns they had three and seven years after the surgery. Information about the role of the neurologist in the decision-making was also gathered retrospectively from the patients themselves. The study's strengths are that only completely seizure-free patients were evaluated and they all shared the same histopathology.

## 5. Conclusion

Our study suggests that a large portion of completely seizure-free patients still take AEDs even seven years after the surgery, largely due

to the patients' own wishes and fear of relapse and unrelated to seizure frequency before the surgery. These results might aid in counseling patients on the decision to withdraw medication after successful surgery.

## Declaration of Competing Interest

Anne Sabers received consultancy or lecture fees from Eisai Denmark and UCB Nordic.

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