



**THE SAHLGRENKA ACADEMY**

# **Implementation of Early Neurologist Evaluation after a First Epileptic Seizure**

Degree Project in Medicine

Therese Öqvist

Programme in Medicine

Gothenburg, Sweden 2018

Supervisor: Johan Zelano

Department of Clinical Neuroscience, Institute of Neuroscience and Physiology,  
Neuro Health Care at Sahlgrenska University Hospital

## Table of contents

<b>1</b>	<b>Abstract</b>	<b>3</b>
<b>2</b>	<b>Introduction</b>	<b>4</b>
2.1	First seizure clinic at Sahlgrenska University hospital	4
2.2	Definition of Epilepsy and Epileptic Seizure	5
2.3	Diagnosing Epilepsy	6
2.4	Risks of Epilepsy	7
<b>3</b>	<b>Aim</b>	<b>8</b>
<b>4</b>	<b>Material and Methods</b>	<b>8</b>
4.1	Study design	8
4.2	Study population	9
4.3	Data extraction	10
4.4	Definitions	10
4.5	Statistics	11
<b>5</b>	<b>Results</b>	<b>12</b>
5.1	Study population	12
5.2	Diagnosis	13
5.3	Time from seizure to neurologist visit	14
5.4	Time from seizure to MRI and EEG	16
5.4.1	Time from seizure to MRI	16
5.4.2	Time from seizure to EEG	18
5.5	Differences in the amount of MRI and EEG examinations	20
5.5.1	Differences in amount of MRI	20
5.5.2	Differences in amount of EEG	21
<b>6</b>	<b>Discussion</b>	<b>23</b>
6.1	Shorter wait-time	23
6.2	Ethical implication	24
6.3	No evidence showing a higher proportion of seizure patients or fewer unnecessary examinations	24
6.4	Other aspects to study	26
6.5	Methodological considerations	27
<b>7</b>	<b>Conclusions and Implications</b>	<b>28</b>
<b>8</b>	<b>Populärvetenskaplig sammanfattning</b>	<b>29</b>
<b>9</b>	<b>Acknowledgements</b>	<b>30</b>
<b>10</b>	<b>References</b>	<b>30</b>
<b>11</b>	<b>Appendices</b>	<b>32</b>
11.1	Appendix 1. Clinical report form	32
11.2	Appendix 2. Flowchart showing exclusion process	33

# 1 Abstract

Degree project, Programme in medicine

## **Implementation of Early Neurologist Evaluation after a First Epileptic Seizure**

Therese Öqvist, 2018, Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Neuro Health Care at Sahlgrenska University Hospital, Gothenburg, Sweden

**Introduction:** A seizure is a frightening experience and 10% of the population will experience one. A short wait-time from suspected seizure to neurologist visit is important both physically and psychologically. To shorten the wait-time at Sahlgrenska University hospital (SU) a new routine for managing first seizures at the emergency room (ER) was introduced in July 2016 and a first seizure clinic was established. Other prospects of the change were to increase the proportion of referrals from the ER leading to seizure diagnosis as opposed to differential diagnoses e.g. syncope and to reduce unnecessary examinations.

**Aim:** To evaluate the introduction of the first seizure clinic at SU in terms of efficient resource utilization.

**Method:** A retrospective medical chart review of 65 patients referred from the ER at SU to the neurologist at SU due to a suspected seizure.

**Results:** The time from suspected seizure to neurologist visit was significantly shorter in 2017 compared to 2016 ( $P=0.004$ ). There was no significant difference in diagnoses set after the neurologist visit, time from seizure to magnetic resonance imaging (MRI) or electroencephalography (EEG) or in amount of MRI and EEG examinations between 2016 and 2017.

**Conclusions:** The shorter wait-time from seizure to neurologist visit is important in minimizing the risk of seizure recurrence as patients are informed of prognosis and can, if

necessary, begin treatment. The streamline of the first seizure clinic shown in this study can hopefully aid in its establishment elsewhere.

**Keywords:** Epilepsy, First seizure clinic, wait-times

## **2 Introduction**

### **2.1 First seizure clinic at Sahlgrenska University hospital**

Epilepsy is one of our most common neurological diseases (1) with a prevalence of 0,5 – 1% (2). It is estimated that about 10% of the general population will experience a seizure in their lifetime (2-4). An epileptic seizure is a frightening experience with a fairly high risk of recurrence (21 – 45% within two years after the seizure) (5). The National Institute for Health and Care Excellence in the United Kingdom state that all patients with a recent onset suspected seizure should be seen by a specialist within two weeks (6). In Sweden the National Board of Health and Welfare recommends that an assessment by a neurologist should be made within four weeks (7). An early visit after a suspected seizure is important in order to give the patient an early diagnosis, information and, if necessary, begin treatment (6).

In July 2016 a new routine for management of first time epileptic seizures in the emergency room (ER) was introduced at Sahlgrenska University hospital (SU). One purpose of the new routine was to shorten the time to a first neurologist visit due to a suspected seizure, with the goal of patients to be offered a visit time within four weeks. In order to do so, special visit times were reserved at the neurologist office for patients with a suspected epileptic seizure. These reserved visit times were meant to function as a first seizure clinic, a concept that have been shown successful in shortening wait-times and is proposed to enable the decrease of unnecessary investigations (8). Two other hopes for the new routine were firstly that it would increase the amount of “right” patients who are referred to the neurologist i.e. patients who

after their neurologist visit were diagnosed with an epileptic seizure. This would mean a more efficient use of neurologists as a resource as their time to a higher extent would be used for patients in need of their expertise. Secondly the new routine was hoped to decrease the amount of unnecessary examinations, as magnetic resonance imaging (MRI) and electroencephalography (EEG) were recommended to be ordered by the neurologist upon necessity and not by the ER physician routinely. Fewer unnecessary examinations is in itself a better use of healthcare resources but also has further effects as it diminishes the crowding out of patients with an actual need of the examination.

## **2.2 Definition of Epilepsy and Epileptic Seizure**

Epilepsy was defined in 2005 by the International League Against Epilepsy (ILAE) as “a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure” (9). This definition was updated in 2014 by the ILAE. Since then, epilepsy is considered to be a disease and not a disorder as the preceding definition stated (10). In the classic definition of epilepsy, a patient is diagnosed if he or she had two or more unprovoked seizures more than 24 hours apart. In the new definition the ILAE presented two additional conditions to diagnose patients with epilepsy, namely “one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years” and “diagnosis of an epilepsy syndrome” (10). The first of the new conditions enables the diagnosis of epilepsy in patients with a greater risk of further seizures after a first unprovoked seizure than other patients e.g. patients with epileptiform activity on EEG (11).

As a result of the new definition in 2014, epilepsy is no longer regarded a lifelong condition. A patient's epilepsy is now considered "resolved" if either of the two following conditions are met, the patient has an age-dependent epilepsy syndrome and he or she is older than the age at which the syndrome is active or the patient has been seizure free for 10 or more years and has been off all anti-seizure medications for 5 or more years (10).

The definition of an epileptic seizure has not changed since 2005 (11) and is since then defined as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" (9). A seizure can be provoked (also called acute symptomatic) or unprovoked. A provoked seizure is transient in its nature and does not fall under the definition of epilepsy (12). Provoked seizures are "events, occurring in close temporal relationship with an acute CNS insult, which may be metabolic, toxic, structural, infectious, or due to inflammation" (13) and unprovoked seizures are defined as "seizures occurring in the absence of a potentially responsible clinical condition or beyond the interval estimated for the occurrence of acute symptomatic seizures" (13).

### **2.3 Diagnosing Epilepsy**

The diagnosis of epilepsy is complex and has extensive consequences for the patient, it should therefore be made by an epilepsy specialist (14). The patient's history and the description from potential eyewitnesses are of great importance when diagnosing epilepsy and eliminating its differential diagnoses (2, 15). Some differential diagnoses to epileptic seizures are vasovagal or cardiac syncope, non-epileptic attack disorder (14), migraine, transient ischemic attack and sleep disorders (16).

When an epileptic seizure is deemed the most probable cause the next questions to be answered are; was it a first time seizure and was the seizure provoked or unprovoked? (15)

Provoked seizures, including febrile, make up 55% of all seizures and anyone can be afflicted, regardless of having an epilepsy diagnosis or not (13). Provoked seizures are, as stated above, characterized by having a temporary cause, e.g. cerebral hypoxia or alcohol. A provoked seizure is not known for the risk of recurrence that defines epilepsy if the provocation does not recur and have a different prognosis compared to unprovoked seizures (13). Having epilepsy means having a predisposition for recurrent unprovoked seizures and therefore only the other 45% that is unprovoked seizures can lead to the diagnosis. Again, the patients' history is crucial in reaching the correct diagnosis.

Computed tomography (CT) has a role in the acute investigation of patients with suspected head injury or loss of consciousness (2), but not in the latter part of the investigation as CT is much inferior to MRI in finding lesions that could cause epilepsy (16, 17). EEG and MRI are frequently used in the investigation for a suspect first epileptic seizure.

EEG registers the electric activity of the brain and an abnormal or especially epileptiform EEG activity increases the likelihood of recurring seizures (18), and therefore epilepsy. EEG has a sensitivity of 50% and a high specificity of 98-99% (16), consequently 1-2% of EEG show a false positive result. Because of the risk of a false positive result EEG should not be used to rule out differential diagnoses (6). It is crucial with a good selection of patients in order to maintain the high specificity of the examination.

MRI is done in order to verify or eliminate the risk for structural brain disease or tumour as the cause of epilepsy (16) and is a part of almost every epilepsy evaluation.

## **2.4 Risks of Epilepsy**

There are many injuries linked to epileptic seizures e.g. cuts, bruises or head trauma from a fall and after a first seizure there is an increased risk of further seizures. The risk of recurrence after a single unprovoked seizure is 21-45% within the two first years (5) and the risk is

biggest soon after the first seizure (18). It has been shown that patients with epilepsy has an increased mortality rate compared to the general population, with a standardized mortality ratio (SMR) of 2.55 in a study with 20-25 years follow-up (19). The SMR is highest in close proximity of time to the first seizure (19). People with epilepsy also have a higher risk of psychiatric conditions such as depression (20). As if the risks that accompany epilepsy and the burden of the disease itself was not enough, people with epilepsy also have a long history of being the subject of prejudice and stigma (21).

### **3 Aim**

To evaluate the effect of the introduction of specific visit times at the neurologist office at Sahlgrenska University hospital for patients with first time seizures, in terms of efficient utilization of resources. The specific aim is to answer the three following questions:

1. Has the latency time from the suspected epileptic seizure to neurologist assessment and examinations shortened?
2. Has the proportion of patients who eventually are diagnosed with an epileptic seizure increased among the patients referred?
3. Has the amount of unnecessary examinations decreased?

## **4 Material and Methods**

### **4.1 Study design**

The study is a retrospective study of patients referred to a neurologist at SU for the first time due to a suspect first epileptic seizure during the two periods 1 January 2016 – 31 May 2016 and 1 January 2017 – 31 May 2017. The study was made on behalf of the head of the department at the neurologist SU and is a systematic follow up of health care. All patient



information was handled in accordance with the Patient Data Act. The inclusion criteria for the study were:

- Patients visiting the neurologist at SU for the first time.
- Patients with referrals to a neurologist sent from the ER at SU or medicinal emergency wards (ward 90 and 91) at SU due to a suspected epileptic seizure.

The exclusion criteria were:

- Patients who upon examination of their medical records were found to be previously diagnosed with epilepsy.
- Patients with protected identity and patients who themselves locked their medical records.

The outcome measures were diagnosis after first visit to the neurologist, proportion of patients who underwent MRI and EEG, time from seizure to MRI, time from seizure to EEG and time from seizure to neurologist assessment. The data was extracted using a clinical report form (CRF) shown in appendix 1.

## **4.2 Study population**

The patients were identified using an administrative system (ELVIS). All patients with the code F (first-time visit) and EP (suspected epilepsy) during the two periods mentioned above were examined. The medical records were then reviewed for inclusion/exclusion criteria and 65 patients were included. The 332 excluded patients and their reasons for exclusion are shown in a flowchart in appendix 2. There were 29 of the included patients who visited a neurologist in 2016 and the remaining 36 visited a neurologist in 2017. In 2016 there were 55,2% men (n=16) and 44,8% woman (n=13). In 2017 there were 58,3% men (n=21) and 41,7% woman (n=15) (Table 1). The age at the time of the visit among the included patients

ranged from 16 to 88 years. The mean age for the patients in 2016 was 41.52 years and the median 36 years while the mean age in 2017 was 50.72 years and the median 53 years.

### **4.3 Data extraction**

For included patients the information necessary for the study was transferred from the medical record to the CRF (Appendix 1) and anonymized prior to analysis. The information extracted was: year of birth, sex, date of first epileptic seizure, date of neurologist visit, date of eventual CT, MRI and/or EEG, date of results from eventual CT, MRI and/or EEG and the diagnosis set by the neurologist after visit. The diagnosis after the neurologist visit was divided into 5 categories: syncope, first unprovoked epileptic seizure, provoked epileptic seizure, others and unprovoked epileptic seizure with subsequent epilepsy diagnosis. Provoked epileptic seizure was subdivided into four categories, depending on the precipitating cause: alcohol, tramadol, other narcotics and others.

### **4.4 Definitions**

The date of the first seizure, thus the start of the latency time in the study, was defined as the date of the seizure that caused the referral to a neurologist. Some patients reported previous seizure-like events for which they had not sought medical attention or a referral to neurologist had not been sent even though the patient had sought medical attention. The phrase “Date of first epileptic seizure” used in the CRF (Appendix 1) was therefore in these cases used as “date of suspected epileptic seizure that led to referral to neurologist”.

If the patient had experienced several seizures before the index seizure, it was sometimes possible to diagnose the patient with epilepsy on the first visit. In these cases the outcome “epilepsy diagnosis” was registered in the CRF. Patients who received epilepsy diagnosis were also, by implication, assessed to have had an unprovoked epileptic seizure, according to the criteria for epilepsy diagnosis described in the introduction. Therefore the outcome

“epilepsy diagnosis” in the CRF could be equated with unprovoked epileptic seizure with subsequent epilepsy diagnosis in the analysis.

Patients may experience further seizures as they wait for their appointment with the neurologist. In these cases it was sometimes possible for the neurologist to diagnose the patient with epilepsy on the first visit. These patient was registered in the form as both “first unprovoked epileptic seizure” and “epilepsy diagnosis” as the seizure that led to the referral of the patient to a neurologist, the index seizure, was assessed by the neurologist to be the first the patient had experienced and the patient was diagnosed with epilepsy.

If the neurologist’s assessment was “possible seizure” and there were no provocative factors the patient was registered in the CRF as “first unprovoked epileptic seizure”.

Time is often presented as weeks in the results. Week one is defined as day one through seven after the suspected epileptic seizure. Any examinations executed on day zero, and therefore in association with the ER visit, are presented separately.

During the analysis the categories “first unprovoked seizure” and “epilepsy diagnosis” seen in the CRF were merged together to “epileptic seizure”.

## **4.5 Statistics**

SPSS version 25 (IBM Corp., Armonk, New York) was used when performing Chi-square and Mann-Whitney U tests. Chi-squared tests were used to analyse differences between the sexes and Mann-Whitney U tests were used to compare distributions of age groups and wait-times. Fisher’s exact test was used when comparing proportion and was preformed using Graphpad QuickCalcs, Web site: <https://www.graphpad.com/quickcalcs/contingency1/> (accessed April 2018). The data was examined prior to analysis using histograms and was found not to be normally distributed. The assumed level of significance used was 0.05.

## 5 Results

### 5.1 Study population

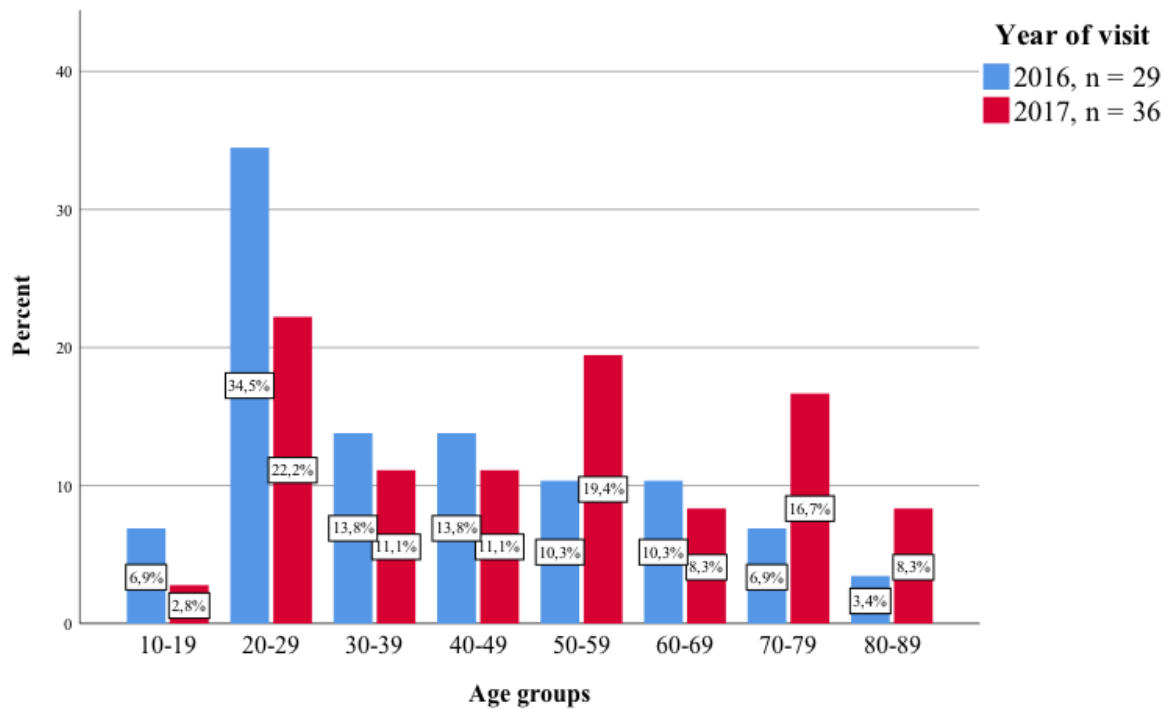
There was no significant difference between the sexes in the study population ( $P = 0.264$ ), although there were a predominant proportion of men in absolute numbers, 37 men (56.9%) and 28 women (43.1%). There was no significant difference between the sexes when the patients were grouped with regards to their year of visit either ( $P = 0.577$  for 2016 and  $P = 0.317$  for 2017), though there was a higher count of men in each group both years (Table 1).

**TABLE 1. Gender differences amongst included patients in the two years examined**

Year of visit			Sex		Total
			Man	Woman	
2016	Count		16	13	29
	% within Year of visit		55,2%	44,8%	100,0%
2017	Count		21	15	36
	% within Year of visit		58,3%	41,7%	100,0%
Total	Count		37	28	65
	% within Year of visit		56,9%	43,1%	100,0%

The mean age amongst the participants from 2016 was 41.52 years (SD 19.15) and the median 36 years, the mean age 2017 was 50.72 years (SD 21.72) and the median 53 years.

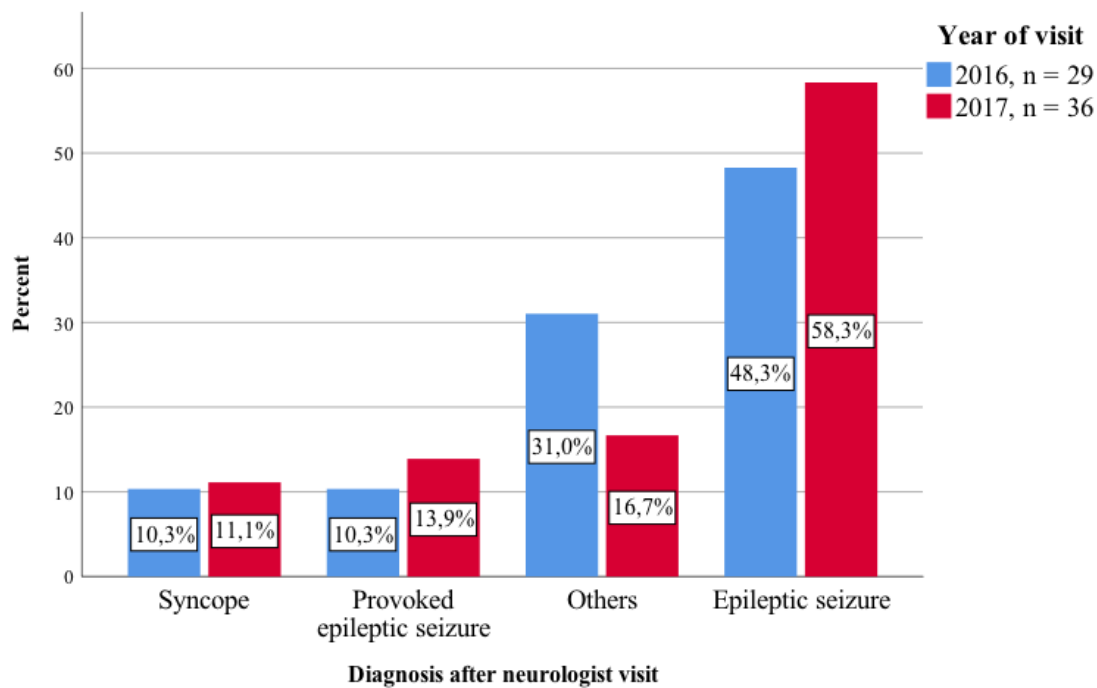
The age at the time of visit ranged from 18 – 84 years in the 2016 group and ranged from 17 – 89 years in the 2017 group. The patients' ages were divided into age groups of 10 years and are displayed below (Figure 1). There was no significant difference in the distribution of age groups between the two years ( $P = 0.071$ ). The age group with the highest percentage of patients in both 2016 and 2017 was 20-29 years (34.5% in 2016 and 22.2% in 2017).



**FIGURE 1. Age of the included patients divided into subgroups of 10 years**

## 5.2 Diagnosis

No significant differences were found when comparing any of the diagnoses between the years. There were 48.3% of cases diagnosed with “epileptic seizure” in 2016 and 58.3% in 2017 ( $P = 0.461$ ). “Others” was the outcome in 31.0% of the cases in 2016 and 16.7% in 2017 ( $P = 0.238$ ). Syncope constituted 10.3% of the diagnoses in 2016 and 11.1% of diagnoses in 2017 ( $P = 1.000$ ). There were 10.3% provoked epileptic seizures in 2016 and 13.9% in 2017 ( $P = 0.723$ ) (Figure 2).



**FIGURE 2. Diagnosis after the first neurologist visit due to a suspected epileptic seizure**

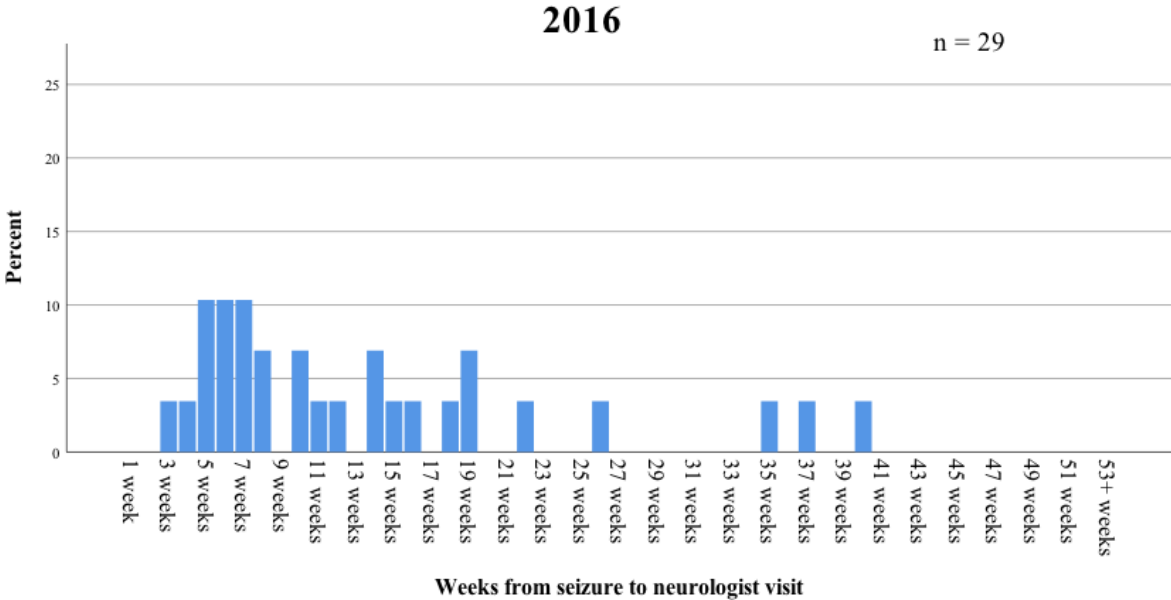
### 5.3 Time from seizure to neurologist visit

The time from the suspected epileptic seizure to the patients neurologist visit was significantly shorter in 2017 compared to 2016 ( $P = 0.004$ ). The mean time in 2016 was 92.31 days (SD 70.09) and the median 70.00 days. The mean time from suspected seizure to neurologist visit in 2017 was 70.31 days (SD 103.95) and the median 35.50 days.

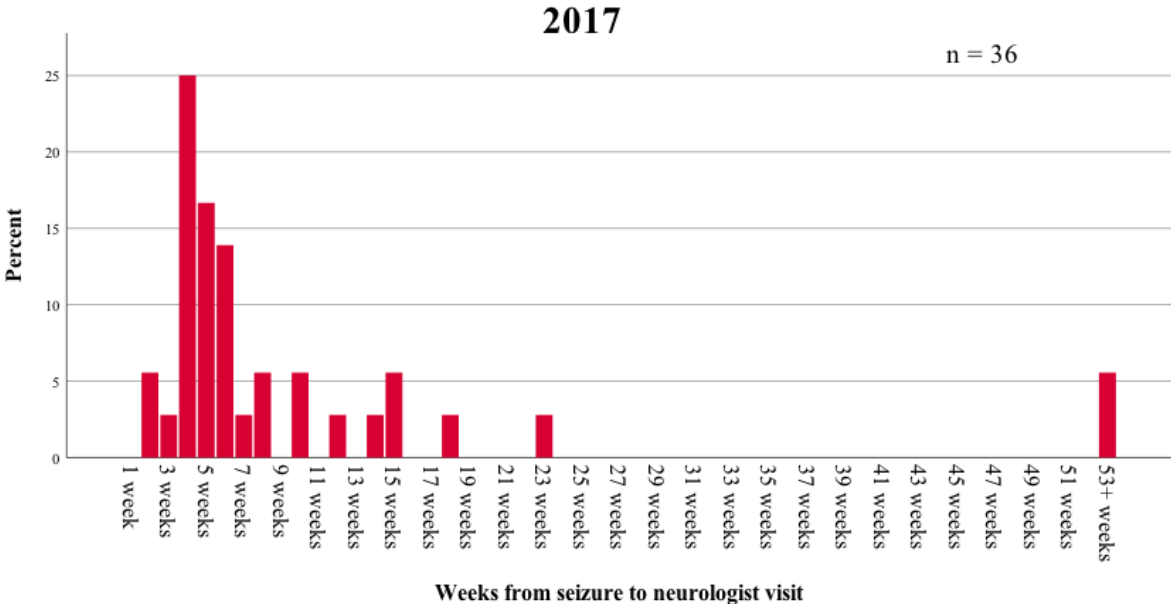
The shortest latency time in 2016 was visit within the third week after the suspected seizure (Figure 3) and was represented by 3.4% ( $n = 1$ ) of the included patients 2016. There were 6.8% of patients who had their visit within the first four weeks after the suspected seizure in 2016. Visit within the fifth, sixth or seventh week was the most common in 2016 with 10.3% of the patients in each of these three categories.

The shortest latency time in 2017 was visit within week two (Figure 4) and was the case for 5.6% ( $n = 2$ ) of the included patients 2017. Within the first four weeks of the seizure in 2017 had 33.4% of the patients been to their visit. The most common week of visit in 2017 was the

fourth week after the suspected seizure (25%). There were 5.6% (n = 2) of patients in 2017 who waited 53 or more weeks for their neurologist visit.



**FIGURE 3. Time from suspected epileptic seizure to neurologist visit in 2016 divided into weeks**



**FIGURE 4. Time from suspected epileptic seizure to neurologist visit in 2017 divided into weeks**

## 5.4 Time from seizure to MRI and EEG

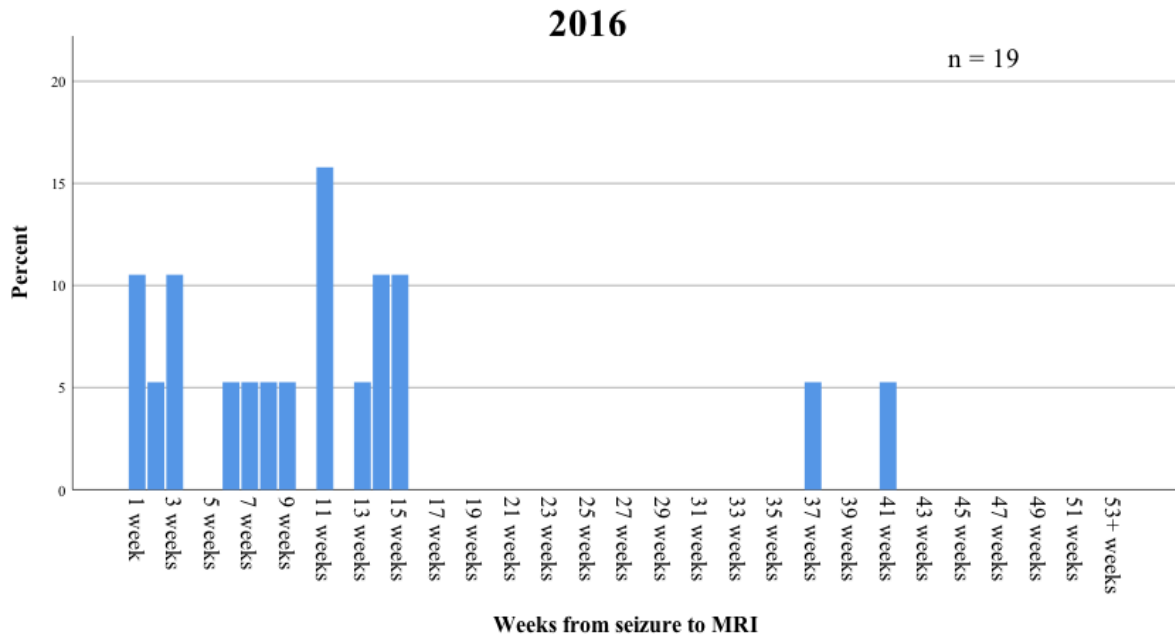
### 5.4.1 Time from seizure to MRI

There was no significant difference between the times from the suspected epileptic seizure to MRI the two years examined ( $P = 0.178$ ). The mean time from seizure to MRI in 2016 was 74.60 days (SD 75.40) and the median 67.00 days. In 2017 the mean time was 44.87 days (SD 45.83) and the median 30.00 days.

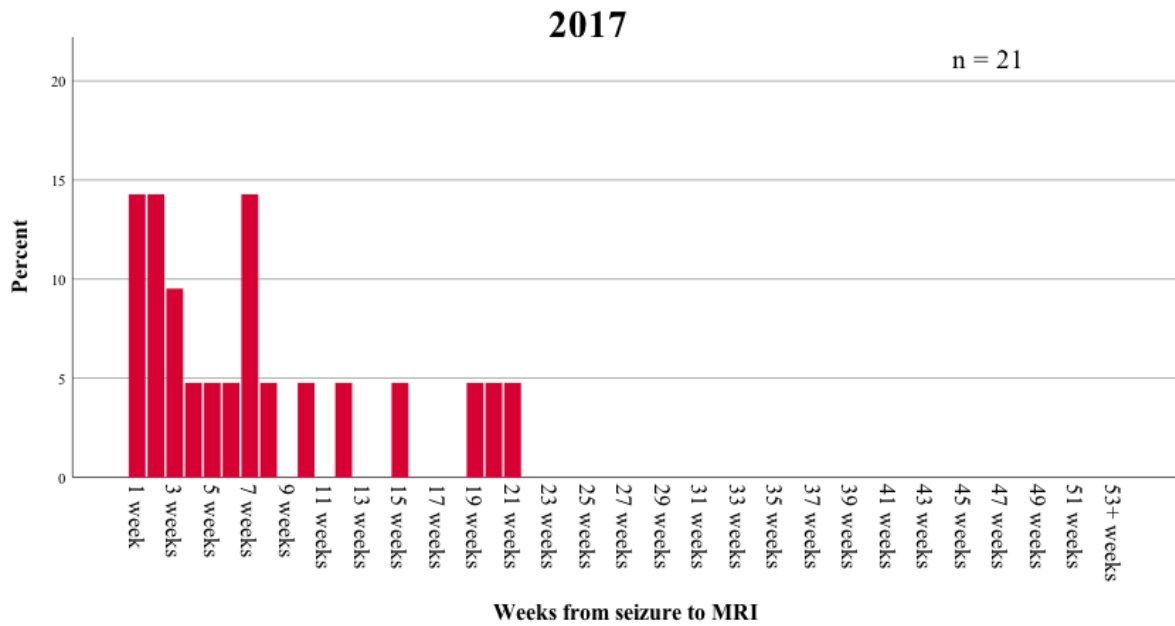
Among the patients in 2016, 19 underwent an MRI from day one and forward and 10.5% of them did so within the first week of their seizure (Figure 5). 5.3% had their examination within the second week. The most common week of examination in 2016 was within the 11th week (15.8%). The longest time to MRI was 41 weeks, which was the case for one patient (5.3%). There was one patient who had an MRI on the day of his or hers suspected epileptic seizure, day zero. Nine patients in 2016 did not go through an MRI.

In 2017 there was one patient who went through a MRI on day zero. Among the other 21 patients who went through a MRI 14.3% did it within the first week of their suspected seizure (Figure 6). The same amount, 14.3% had their MRI carried out within the second week. Equally common was examination in the seventh week (14.3%). The longest time to examination was 21 weeks ( $n = 1$ , 4.8%). In 2017 there were 13 patients who did not go through a MRI and there was one patient who, for some reason, did an MRI 5 days prior to the suspected epileptic seizure.





**FIGURE 5. Time from suspected epileptic seizure to magnetic resonance imaging (MRI) in 2016 divided into weeks**



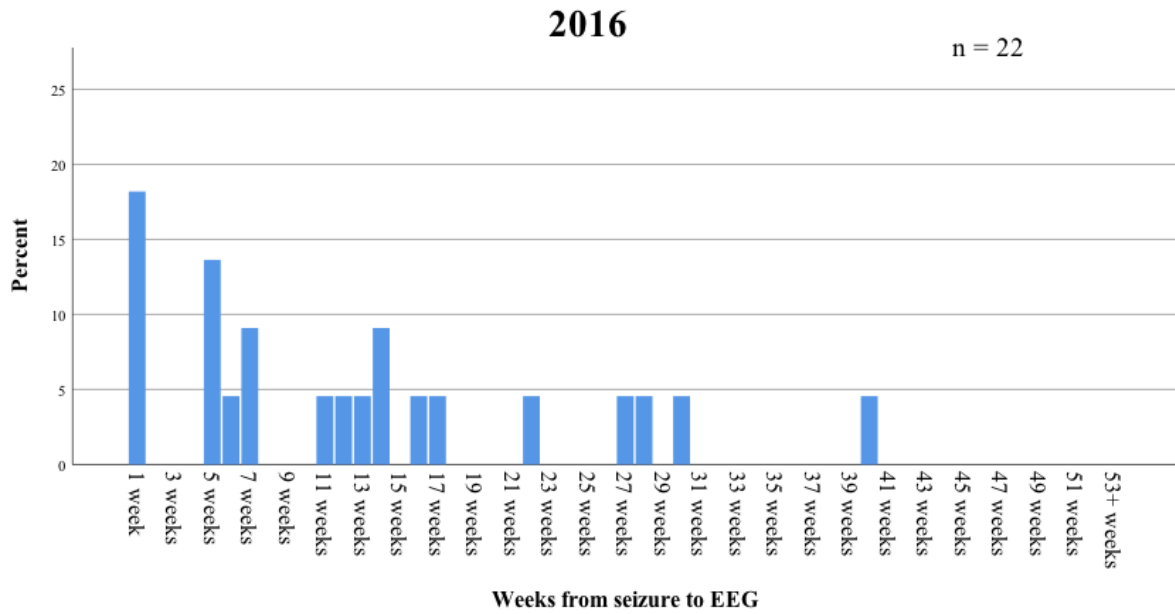
**FIGURE 6. Time from suspected epileptic seizure to magnetic resonance imaging (MRI) in 2017 divided into weeks**

#### **5.4.2 Time from seizure to EEG**

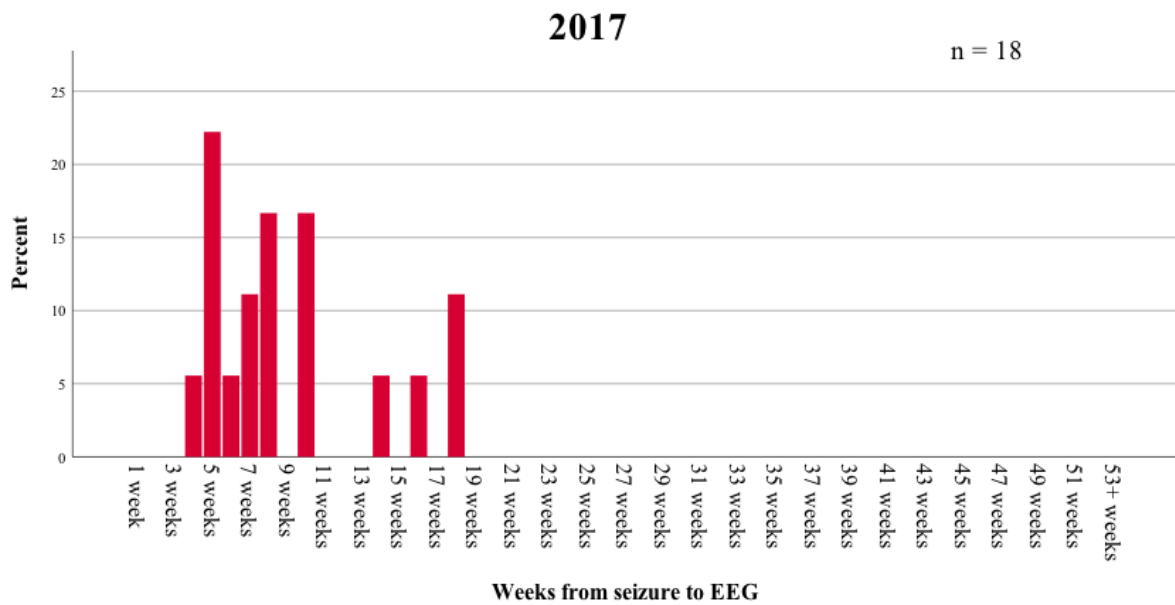
The difference in time from the suspected epileptic seizure to EEG between the two years was not significant ( $P = 0.545$ ). The mean time from seizure to EEG in 2016 was 87.23 days (SD 75.840) and the median was 79.50 days. The mean time in 2017 was 51.24 days (SD 37.61) and the median 47.00 days.

None of the patients in 2016 had an EEG performed on day zero. Amongst the 22 patients who had an EEG there were 18.2% who had their examination within the first week (Figure 7), which makes week one the most common. The second most common week of examination was week 5 with 13.6% of the patients. The longest wait-time for examination was 40 weeks and was the case for one patient (4.5%). Seven patients in 2016 did not go through an EEG.

Two patients had an EEG performed on day zero in 2017 and one patient had an EEG prior to his or hers suspected epileptic seizure. There were 18 patients who had an EEG from day one and forward. The earliest week of examination in 2017 was week four with 5.6% ( $n = 1$ ) (Figure 8). Week five was the most common week of examination with 22.2% of the patients. The second most common weeks were week eight and ten with 16.7% each. The latest week of examination was week 18 with 11.1% of patients. There were 15 patients who did not do an EEG in 2017.



**FIGURE 7. Time from suspected epileptic seizure to electroencephalography (EEG) in 2016 divided into weeks**

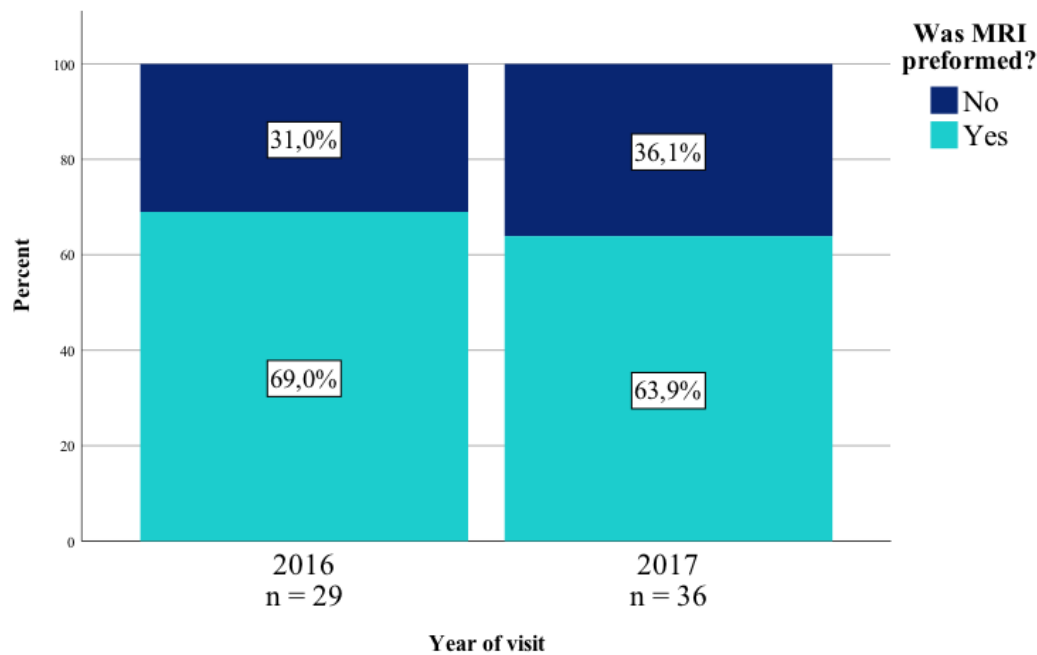


**FIGURE 8. Time from suspected epileptic seizure to electroencephalography (EEG) in 2017 divided into weeks**

## 5.5 Differences in the amount of MRI and EEG examinations

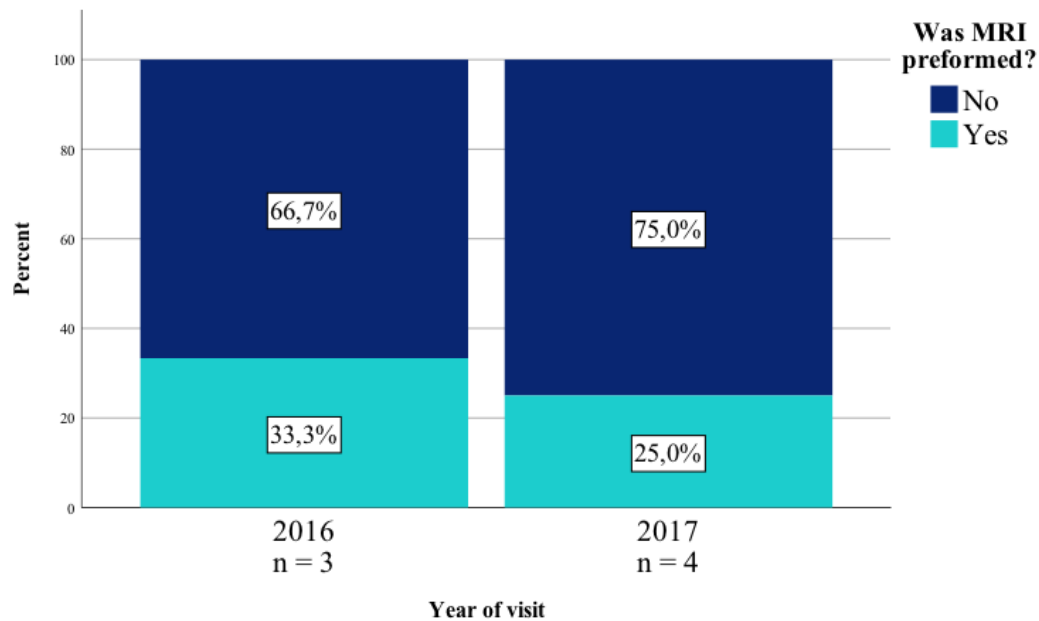
### 5.5.1 Differences in amount of MRI

There were no significant difference in the amount of MRI examinations between 2016 and 2017 ( $P = 0.794$ ). Among the included patients in 2016 there were 69.0% who were examined using MRI (Figure 9). In 2017 there were 63.9% who did go through an MRI.



**FIGURE 9. Percentage of patients who did or did not go through magnetic resonance imaging (MRI) divided by year of visit**

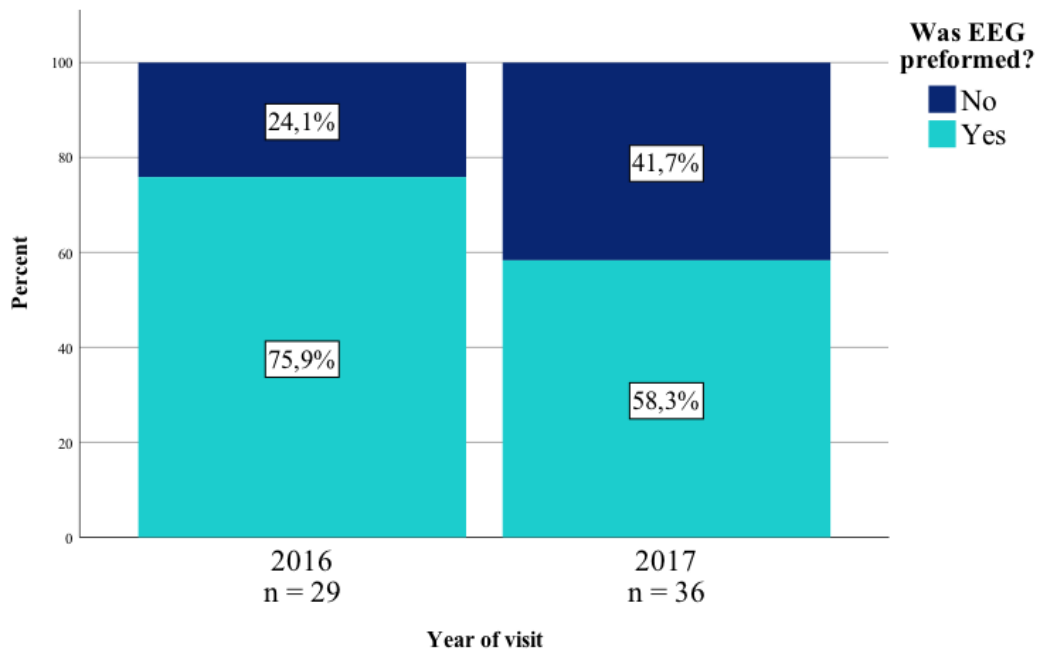
There was no significant difference in amount of MRI examinations between the years when comparing the groups diagnosed with syncope ( $P = 1.000$ ). There were 33.3% of patients diagnosed with syncope who went through an MRI in 2016 compared to 25.0% who did the same in 2017 (Figure 10).



**FIGURE 10. Percentage of patients who did or did not go through magnetic resonance imaging (MRI) in the group diagnosed with Syncope divided by year of visit**

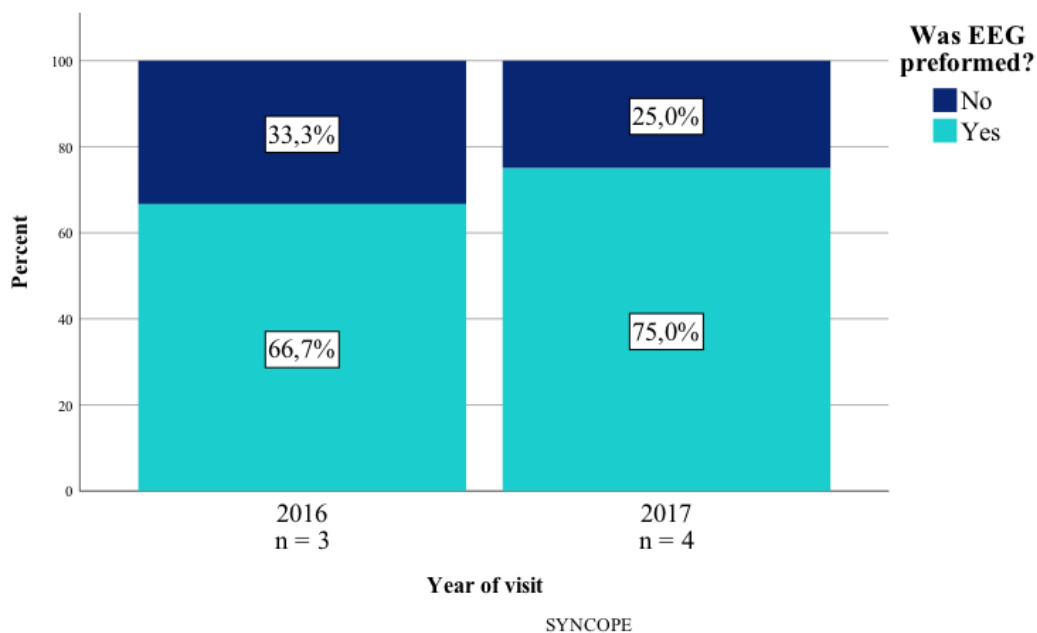
### 5.5.2 Differences in amount of EEG

The difference in amount of EEG examinations was not significant between the two years ( $P = 0.189$ ). A total of 75.9% of all included patients in 2016 went through an EEG examination whereas 58.3% of patients did the same in 2017 (Figure 11).



**FIGURE 11. Percentage of patients who did or did not go through electroencephalography (EEG) divided by year of visit**

There was no significant difference in amount of EEG examinations between the years when comparing the groups diagnosed with syncope ( $P = 1.000$ ). EEG was preformed in 66.7% of the cases diagnosed with syncope in 2016 and in 75.0% of the cases diagnosed with syncope in 2017 (Figure 12).



**Figure 12. Percentage of patients who did or did not go through electroencephalography in the group diagnosed with Syncope divided by year of visit**

## 6 Discussion

### 6.1 Shorter wait-time

The time from the suspected epileptic seizure to neurologist visit was significantly shorter in 2017 compared to 2016 ( $P = 0.004$ ). This result advocates that the new routine at SU with reserved visit times that act as a first seizure clinic was effective in shortening wait-times after a suspected epileptic seizure. This result is consistent with results from other evaluations of first seizure clinics (8). To keep wait-times short is important in order to minimize the risk of recurring seizures (18). A recently published Canadian study showed that there is a higher prevalence of depression in people with an unprovoked first seizure but also that prevalence of depression increases with time for people with undiagnosed epilepsy (20).

In 2017 there were 33.4% (Figure 4) of patients who had their visit within the first 4 weeks after their suspected seizure, which is in accordance with the Swedish National Board of Health and Welfares recommendations (7). The same number for 2016 is only 6.8% (Figure 3). Since the Swedish guidelines recommend a visit within 4 weeks 33.4% of patients might not seem sufficient. It is possible that more patients were managed in accordance with the guidelines, as their beginning of the latency time is the date when the patient first sought medical attention for the suspected seizure whereas in this study the latency time starts at the date of the patients suspected seizure. To what extent the dates differed is not reviewed in this study. The end of the latency time in this study was the date of the patients' neurologist visit, if a patient was initially offered an earlier appointment but declined or failed to attend was not taken into consideration. One study of a first seizure clinic estimated that patients failed to attend or made a late cancellation in 35-40% of appointments (22). If that estimation is transferable to this study, the result is largely impacted by attendance rates.

First seizure clinics have been shown to reduce wait-times to investigations such as MRI and EEG (8), which could not be shown in this study. Whilst the mean time was shortened from suspected seizure to MRI (from 74.60 days to 44.87 days) and EEG (from 87.23 days to 51.24 days) the difference was not statistically significant. One may hypothesize that the difference could be significant given a bigger study population.

## **6.2 Ethical implication**

The shorter wait-time shown in this study is beneficial for seizure patients, how other groups of patients with neurological issues are impacted was not examined. When the routine for managing seizure patients was changed in July 2016 and the first seizure clinic was established there were specific visit times reserved for seizure patients. These visit times were previously used for patients with all kinds of neurological disorders and diseases. By shortening wait-times for patients with epileptic seizures wait-times must inevitably lengthen for other patients waiting for a neurologist appointment, as visit times are limited. Which patients were affected was not examined in this study and whether their neurological issues were urgent or not is therefore unknown.

## **6.3 No evidence showing a higher proportion of seizure patients or fewer unnecessary examinations**

No significant results were found that prove that a higher proportion of patients eventually diagnosed with a seizure were referred or that unnecessary examinations decreased. Although one may discuss the non-significant results with results from other studies in mind.

The percentage of seizure diagnoses in 2017 was 58.3% (Figure 2), which is consistent with findings from another first seizure clinic in Scotland (59%) (22). In an Australian study also examining a first seizure clinic with referrals from the ER there were 83% (including 9% provoked seizures) of patients who were diagnosed with a seizure (23). Adding the provoked



seizures to this study's result makes a total of 72.2%. The Australian results could suggest a room for improvement at SU in referring the "right" patients from the ER.

The increase in absolute numbers in the diagnose epileptic seizure (from 48.3% to 58.3%) combined with the decrease in "others" (from 31.0% to 16.7%) (Figure 2) seen in this study, could support the idea of an increase in the proportion of "right" patients being referred to the neurologist. Although these are speculations as neither of the results were significant.

In 2016 there were 18.2% of patients who were examined with an EEG in the first week after their suspected seizure. These examinations can probably not be explained by being acute as EEGs carried out on day zero, i.e. the day of the suspected seizure, were not included in that percentage. Maybe the lack of EEGs in the earliest weeks in 2017 could be explained with EEG examinations being ordered by the neurologist at the time of the visit, hence explaining the peak of examinations in week five (22.2%, Figure 8) in 2017, and not by the ER physician. If that is the case, it suggests that fewer unnecessary investigations are done as the neurologist orders EEG upon necessity as opposed to EEGs being ordered routinely from the ER. The time from suspected seizure to EEG did not differ significantly in this study. To examine this suggestion further studies are necessary.

There was no significant difference in amount of EEGs between the two years but in absolute numbers there was a decrease with 17.6 percentages from 2016 to 2017 (from 75.9% to 58.3%, Figure 11). The reduction could further imply a decrease in unnecessary EEGs, especially considering the proportion of patients with the final diagnosis of epileptic seizure increased in absolute numbers from 48.3% to 58.3% (Figure 2). EEG examinations are unnecessary when done on syncope patients. There was no significant difference found when comparing this group between the years, probably largely due to the fact that there were very few cases in each group (Figure 12).

Speculations that the non-significant results imply that more patients who actually have had an epileptic seizure are referred to the first seizure clinic and fewer unnecessary examinations are done are discussed but would need further studies to prove. A study over longer periods of time would increase the study population and hopefully give more significant results.

#### **6.4 Other aspects to study**

One interesting aspect to explore is if this change of how suspected seizures are managed at SU has had any economical benefits. First seizure clinics are thought to enable the decrease of unnecessary examinations (8) and the result of this study could point in that direction. It has been shown in a study that patients who has experienced a single seizure has a significantly higher rate of visits to health providers compared to patients with well-controlled epilepsy (3). The authors of that study suggest that the increase in utilization of health care could signify a need for a more efficient process to evaluation and treatment. A first seizure clinics purpose is just that, to make the process more efficient. There are several ways in which a first seizure clinic can decrease the coasts, analysing if that is true and in that case, by how much would be interesting.

Another interesting aspect to examine is if the first seizure clinic improves the patients' psychiatric well-being. As earlier mentioned, prevalence of depression is higher amongst people with an unprovoked first seizure and the prevalence increases with time in patients with undiagnosed epilepsy (20). It has been shown that 39% of patients diagnosed with a seizure at a first seizure clinic has a history of earlier seizures (23), and may therefore fulfil the criteria for epilepsy. Do these patients who fulfil the diagnosis of epilepsy experience less depression if they quickly see a neurologist and receive their diagnosis?

Finally it would be interesting to investigate how patients with other neurological issues than epileptic seizures are affected by the new routine and the first seizure clinic. When seizure

patients are prioritized others inevitably have to stand back. Who are these patients, how much is their wait-time increased and how are they affected by the longer wait-time?

## **6.5 Methodological considerations**

Examining medical charts over a longer period of time would have generated a bigger study population, giving more power to the study. The time periods (January thru May 2016 and 2017) were chosen in order to give an appropriate amount of data suitable for a degree project in medicine.

Examination of the same five months two different years has the advantage of making the periods alike. Any holidays causing the neurologists office to be closed would not differ between the periods. There were six months from the change of routine to the start of the second time period examined. After the introduction of the new routine, physicians in the ER may pay more attention to symptoms compatible with a seizure, resulting in more referrals. A heightened awareness of seizures might have affected the results.

One weakness of the study is that the periods examined may have been too close in time. In 2017 there were two patients (5.6%) who waited 53 weeks or more for their neurologist visit after the suspected seizure (Figure 4). Since the day of the seizure and not the day of the ER visit was recorded in the CRF it is impossible to know if the patients waited for a long time before seeking medical attention or if their ER visit was in fact 53 weeks or more before their neurologist visit. If the latter is the case, they should have been excluded as their ER visit was before the change of the routine for managing seizures. This problem had been avoided if the day of the ER visit was used as start of latency time instead of day of suspected seizure.

Patient's delay is a factor that generally would have been avoided if the day of ER visit had been used as latency time start.

Another weakness is that patients were seen by different physicians the two years examined and assessments may therefore differ. In 2017 patients were seen by physicians assigned to the first seizure clinic, who had greater experience of seizure patients than the physicians in 2016 may have had. This can be hypothesized to be the cause of the non-significant decrease of patients diagnosed as “others” seen from 2016 to 2017. The physicians in 2017 may have been more confident in their diagnoses due to greater experience.

The final weakness found in this study was that there might have been patients eligible for the study that were missed when identifying the study population. In the administrative system ELVIS patients are registered with a code. As seen in appendix 2, there were three patients who were excluded due to faulty registration, which confirms that the registration process can go wrong. There is a probability of patients with suspected seizures being registered with other codes by mistake or under the code for “other” and therefore were not identified in this study.

## **7 Conclusions and Implications**

The introduction of the first seizure clinic at the neurologist, SU has lead to shorter wait-times for patients from suspected epileptic seizure to neurologist visit ( $P = 0.004$ ). This is helpful in preventing future seizures. The risk of seizure recurrence is greatest early after the first seizure and with an early neurologist visit the patient can, if necessary, receive treatment and possibly avoid the next seizure. An early visit also minimizes the time patients spend unknowing of what their prognosis is and wanting an explanation to what it is they have experienced. Hopefully this study can promote the introduction of first seizure clinics elsewhere.

## 8 Populärvetenskaplig sammanfattning

### Införande av tidig neurologbedömning efter ett första epileptiskt anfall

Epilepsi är en vanlig neurologisk sjukdom som betyder att drabbade personer har en bestående risk för epileptiska anfall. Man behöver inte ha epilepsi för att få ett epileptiskt anfall, uppskattningsvis kommer 10 % av befolkningen att drabbas någon gång under sitt liv. Trots att epilepsi är vanligt och epileptiska anfall kan drabba vem som helst är sjukdomen förknippad med många fördomar.

Att drabbas av ett epileptiskt anfall är en obehaglig upplevelse med risk för fysiska skador och det är viktigt att den drabbade så snart som möjligt får träffa en neurolog, helst inom fyra veckor. Väntetiden till neurologbesöket är ofta en jobbig tid med oro och obesvarade frågor och dessutom är risken för nya anfall störst tidigt efter det första anfallet. Ett tidigt neurologbesök kan minska risken för nya anfall då information kan ges om prognos och, om nödvändigt, kan behandling påbörjas.

För att förkorta väntetiden infördes nya rutiner för handläggning av förstagångsanfall på akuten, Sahlgrenska universitetssjukhuset i juli 2016. Dessutom infördes speciella besökstider på neurologmottagningen, Sahlgrenska som reserverades för patienter med misstänkt förstagångsanfall. Utöver förkortade väntetider hoppades man dessutom på att det efter förändringen i större utsträckning skulle vara patienter som faktiskt drabbats av ett epileptiskt anfall som remitterades från akuten till neurologen och att de remitterade patienterna skulle genomgå färre onödiga undersökningar.

En journalgranskning av 65 patientjournaler från neurologbesök januari – maj 2016 och 2017 gjordes för att se om den nya rutinen och de särskilda mottagningstiderna fått önskad effekt. Informationen som hämtades från journalerna var patientens ålder, kön, datum för det misstänkta anfallet, datum för neurologbesök, datum för eventuella undersökningar som

gjordes och diagnosen som sattes efter neurologbesöket. Informationen analyserades med syftet att hitta eventuella statistiskt säkerställda skillnader mellan besöken 2016 och 2017. Resultatet av analysen visade att väntetiden från misstänkt anfall till neurologbesök var signifikant kortare 2017 än 2016. Om andelen patienter som drabbats av ett anfall ökade bland de remitterade eller om färre onödiga undersökningar gjordes kunde inte säkerställas. En kortare väntetid från anfall till besök är positivt för både patienten och sjukvården. Förhoppningsvis kan resultatet av denna studie leda till att fler sjukhus följer Sahlgrenskas exempel och inför liknande rutiner för handläggning av misstänkta förstagångsanfall.

## 9 Acknowledgements

I would like to extend a big thank you to my supervisor Johan Zelano who has guided me throughout this project with valuable critique and encouraging words. You have truly inspired me with your enthusiasm for research in the field of epilepsy.

## 10 References

1. World Health Organization. Epilepsy 2018 [Available from: <http://www.who.int/mediacentre/factsheets/fs999/en/>].
2. Angus-Leppan H. First seizures in adults. *BMJ (Clinical research ed)*. 2014;348:g2470.
3. Dworetzky BA, Hoch DB, Wagner AK, Salmanson E, Shanahan CW, Bromfield EB. The impact of a single seizure on health status and health care utilization. *Epilepsia*. 2000;41(2):170-6.
4. Rizvi S, Ladino LD, Hernandez-Ronquillo L, Téllez-Zenteno JF. Epidemiology of early stages of epilepsy: Risk of seizure recurrence after a first seizure. *Seizure*. 2017;49:46-53.
5. Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Epilepsy Currents*. 2015;15(3):144-52.
6. National Institute for Health and Care Excellence. Epilepsies: diagnosis and management (NICE clinical guideline 137) 2012 [Available from: <https://www.nice.org.uk/guidance/cg137>].
7. Socialstyrelsen. Nationella riktlinjer för vård vid epilepsi - Stöd för styrning och ledning - Remissversion. In: Socialstyrelsen, editor. 2018-3-9 ed. Stockholm 2018.

8. Rizvi S, Hernandez-Ronquillo L, Moien-Afshari F, Hunter G, Waterhouse K, Dash D, et al. Evaluating the single seizure clinic model: Findings from a Canadian Center. *Journal of the neurological sciences*. 2016;367:203-10.
9. Fisher RS, Van Emde Boas W, Blume W, Elger C, Genton P, Lee P, et al. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia*. 2005;46(4):470-2.
10. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE Official Report: A practical clinical definition of epilepsy. *Epilepsia*. 2014;55(4):475-82.
11. Falco-Walter JJ, Scheffer IE, Fisher RS. The new definition and classification of seizures and epilepsy. *Epilepsy Research*. 2018;139:73-9.
12. Stafstrom CE, Carmant L. Seizures and epilepsy: an overview for neuroscientists. *Cold Spring Harbor perspectives in medicine*. 2015;5(6).
13. Beghi E, Carpio A, Forsgren L, Hesdorffer DC, Malmgren K, Sander JW, et al. Recommendation for a definition of acute symptomatic seizure. *Epilepsia*. 2010;51(4):671-5.
14. Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of epilepsy in adults. 2015; (SIGN publication no. 143). Available from: <http://www.sign.ac.uk>.
15. Zelano J, Kumlien E. Akut handläggning av epilepsi. *Läkartidningen*. 2010;107(46):2891 - 05.
16. Shneker BF, Fountain NB, Orłowski JM. Epilepsy. *Disease-a-Month*. 2003;49(7):421-78.
17. King MA, Newton MR, Jackson GD, Fitt GJ, Mitchell LA, Silvapulle MJ, et al. Epileptology of the first-seizure presentation: A clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. *Lancet*. 1998;352(9133):1007-11.
18. Berg AT. Risk of recurrence after a first unprovoked seizure. *Epilepsia*. 2008;49(SUPPL. 1):13-8.
19. Neligan A, Bell GS, Johnson AL, Goodridge DM, Shorvon SD, Sander JW. The long-term risk of premature mortality in people with epilepsy. *Brain*. 2011;134:388 - 95.
20. Lane C, Crocker C, Legg K, Borden M, Pohlmann-Eden B. Anxiety and Depression in Adult First Seizure Presentations. *Canadian Journal of Neurological Sciences*. 2018;45(2):144-9.
21. de Boer HM, Mula M, Sander JW. The global burden and stigma of epilepsy. *Epilepsy and Behavior*. 2008;12(4):540-6.
22. McFadyen MB. First seizures, the epilepsies and other paroxysmal disorders prospective audit of a first seizure clinic. *Scottish Medical Journal*. 2004;49(4):126-30.
23. Jackson A, Teo L, Seneviratne U. Challenges in the first seizure clinic for adult patients with epilepsy. *Epileptic disorders : international epilepsy journal with videotape*. 2016;18(3):305-14.

# 11 Appendices

## 11.1 Appendix 1. Clinical report form

### Formulär kvalitetsprojekt Förstagångsanfall

Studienummer \_\_\_\_\_

Födelseår \_\_\_\_\_

Kön:  Man  Kvinna

Datum för första epileptiskt anfall \_\_\_\_\_

Datum för besök på neurologen \_\_\_\_\_

Utredning efter anfallet

Datortomografi datum för undersökning \_\_\_\_\_

datum för svar \_\_\_\_\_

Magnetkameraundersökning datum för undersökning \_\_\_\_\_

datum för svar \_\_\_\_\_

EEG datum för undersökning \_\_\_\_\_

datum för svar \_\_\_\_\_

Diagnos efter besöket (avseende just medvetandeförlusten)

Synkope

Första oprovocerat epileptiskt anfall

Provocerat epileptiskt anfall, utlöst av:  alkohol  tramadol  annat narkot.

annat \_\_\_\_\_

Annan (oklar medvetandeförlust eller liknande)

Epilepsi (fler anfall tidigare, tex)



11.2 Appendix 2. Flowchart showing exclusion process

