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Single Unprovoked Seizure: Wait Time to Full Medical Assessment, Does it Matter?

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Abstract

Introduction
Single unprovoked seizures occur in about 4% of the population and they have significant psychosocial consequences for the patients and their families. Little information is available on the timeliness and safety of assessment of first unprovoked seizures. In this study, we review the timeliness of the referral and evaluation of patients with first unprovoked seizure in a Canadian neurological provincial referral center.

Method
Retrospective analysis of 51 patients over a 3.5 year period was performed and data were collected on patient demographics, date of event and time to evaluation by the epileptologist, evaluations completed, treatments initiated, and patient outcomes.

Results
We found that most patients were seen by the epileptologist within 6 months, there was only a 9% discrepancy in final diagnoses between the epileptologist and the referring physician, and there were no fatalities or serious complications in the patients we studied. However, a few patients waited very long periods before imaging and evaluation by the epileptologist, and restrictions on driving privileges were recommended in only 3% of the patients.

Conclusions
We conclude that the referral process for a first unprovoked seizure is timely. Primary care providers need further education with regards to the consequences of seizures and some areas of the referral region need better access to imaging and epileptologists.

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Background

A first unprovoked seizure is a sudden and unexpected life-event, occurring in 4% of the general population.[1] A prospective study from Iceland showed a mean annual incidence of 56.8 per 100,000 person-years for a first unprovoked seizure. Of these, 23.5 per 100,000 person-years had a single unprovoked seizure compared with 33.3 per 100,000 person-years who later developed epilepsy.[2] The numbers are considered representative for most developed countries. In another study,[3] the overall incidence of unprovoked seizures in both children and adults in Sweden was 60 per 100,000.

The overall risk of seizure recurrence following a single unprovoked seizure ranges from 27% to 71% .[4] The average risk of recurrence in a meta-analysis was found to be 40% in prospective studies and 52% in retrospective studies. The risk of recurrence is highest within the first weeks of the first seizure and decreases with time, with about 80% of recurrences occurring within two years of the initial seizure.[5]

Some studies have also shown that people with seizures/epilepsy are at high risk of premature mortality, with the risk being highest at onset of seizures.[6] Therefore, appropriate and timely assessment and investigation of these patients is essential in establishing the etiologies, ruling out treatable conditions, and providing appropriate management especially in those at high risk of recurrence.

For the above reasons, there is an urgent need to properly assess and manage patients after a single unprovoked seizure with the goals of establishing the clinical diagnosis; determining if the patient has epilepsy by ruling out possible underlying etiologies; and determining the risk of recurrence, prognosis, and the need for antiepileptic medication for patients at moderate or high risk of recurrence. Few studies have focused on the consequences of a prolonged waiting time after a patient has a single unprovoked seizure. In many countries, the establishment of single seizure clinics is a very well recognized strategy to improve the early diagnosis and treatment of patients with single unprovoked seizures. In Canada, not many provinces have single seizure clinics and the majority of patients are seen by general practitioners or emergency doctors and then referred to neurologists. This delay can have direct consequences on the patient such as injuries, death, or other potential negative outcomes, in addition to the stress and anxiety that patients can suffer without a proper diagnosis.

The main objective of this study was to investigate the wait time to completion of medical assessment of single unprovoked seizure patients referred to a local epilepsy clinic. Another goal was to evaluate the safety of the referral and assessment process. These would help determine if wait times for medical assessment and investigations have any impact on the outcomes of first unprovoked seizures.

Materials and Methods

A retrospective chart review from an epilepsy clinic run by a single epileptologist was performed over a period of 3.5 years (2007 – 2010). This is the only available epilepsy clinic in the Canadian province of Saskatchewan (population of one million), and ascertains patients with all kinds of seizure disorders. The clinic is located at the University hospital, which is the only hospital in the province with a certified electroencephalography laboratory to investigate patients. Data were collected on all patients referred to the epilepsy clinic because of single unprovoked seizures. Initially 70 cases were identified

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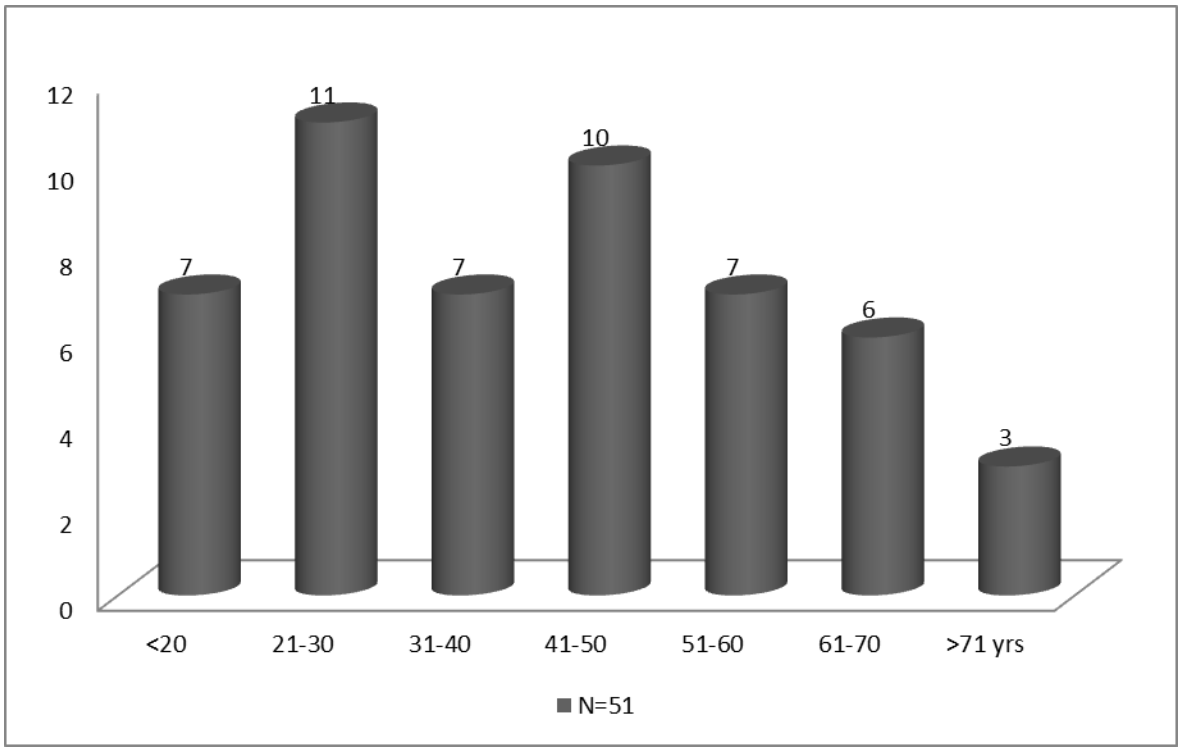

Figure 1: Age Distribution Chart

for the said period. 51 of the reviewed charts fulfilled the criteria for a single unprovoked seizure. 19 were excluded from the study; some had presented with a status epilepticus and in others, a review of history and hospital records revealed that they had a prior history of seizures or a known seizure disorder. Patients with provoked seizures (known cause of seizure, for example metabolic or electrolyte disorders) were also excluded. Information collected on driving was based on review of hospital charts and ambulatory care notes written by primary care physicians and the patient's account on whether or not counseling regarding driving (including any driving restrictions) had been provided. Given the retrospective nature of this study, the motor vehicle licensing department could not be contacted without informed consent for verification.

Data gathered included: Age of patient, date of single seizure/spell, date of initial assessment, the initial assessment and impression, specialty of physician performing initial assessment, date of referral to the epileptologist, date seen by epileptologist and wait times for imaging, computed tomography (CT) and magnetic resonance imaging (MRI) of the brain and electroencephalogram (EEG) from time of event. Median and mean wait times were determined and the final diagnosis by the epileptologist was compared to the initial impression of the referring physician. Seizure recurrence during the wait times or during the assessment period was considered a major adverse event and associated injuries were classified as minor if they resulted in no substantial bodily harm (bruising, etc.) requiring no medical attention or treatment and as major if bodily harm (fractures, etc.) was obvious requiring medical attention. Apart

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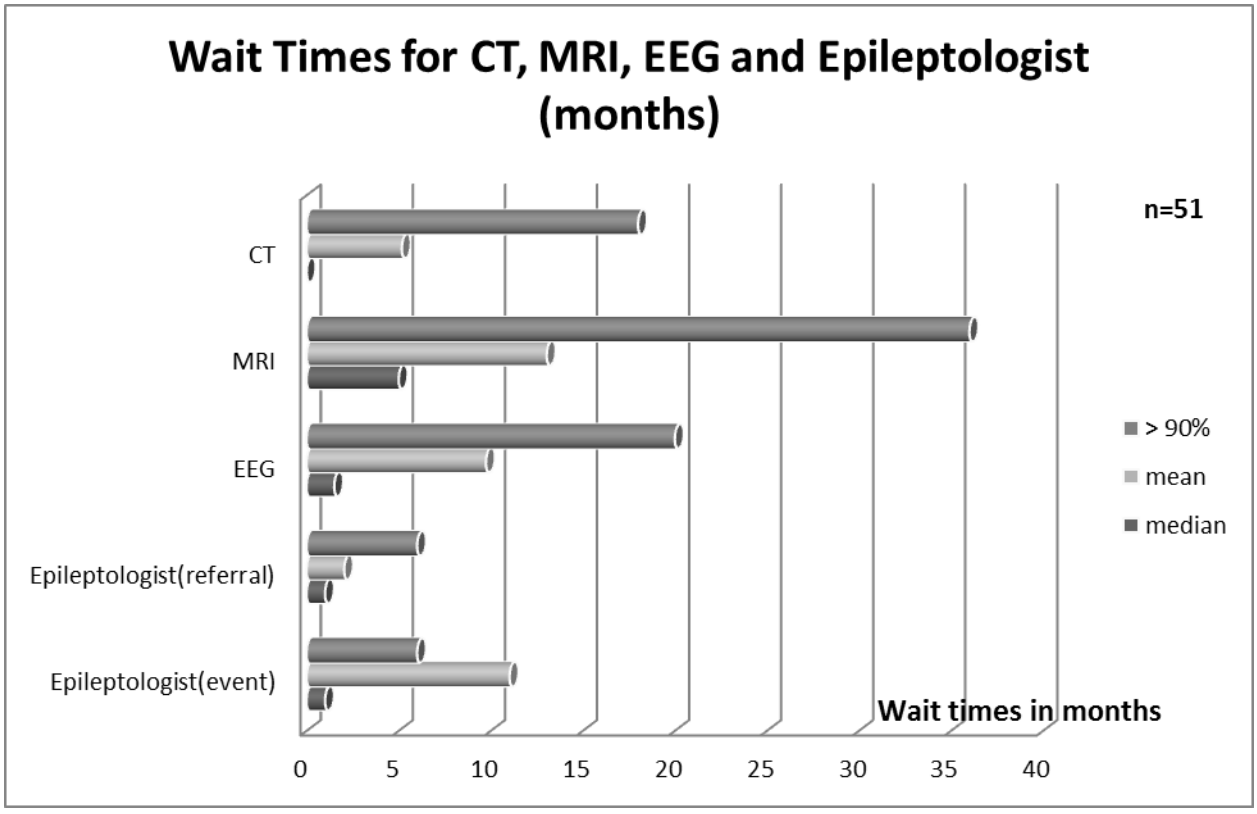

Figure 2: Wait times for investigations and epileptologist (initial event versus referral)

from the above, other safety variables included abnormal EEG and abnormal MRI findings considered predictive of a higher risk of seizure recurrence. Microsoft Excel and SPSS software were used to analyze collected data. For the diagnosis of epilepsy, we used the new definition by the International League Against Epilepsy (ILAE),[7] which requires the occurrence of at least one seizure. All the cases were investigated with EEG, CT, and/or MRI. This study represents a pilot study trying to obtain evidence for the establishment of single seizure clinics in Canada and other countries.

Results

Fifty-one patients were included. Median age at single seizure was 41 years (range 16–81). The sex distribution was 51.9% (28) male and 48.1% (23) female. Figure 1 shows the distribution of events across the different age groups.

The description of the spell was consistent with seizure in 90.7% (48), syncope in 3.9% (2), and migraine variant in 1.9% (1) of cases. The three seizure types described were generalized tonic-clonic seizures (grand mal) in 93.8% (45), complex partial seizures in 4.2% (2), and tonic seizures in 2.1% (1) of presumed seizures.

Wait times for investigations and the epileptologist are shown in Figure 2. Median wait times to see the epileptologist were one month from either time of single seizure or time of referral. 54.9% of patients were seen

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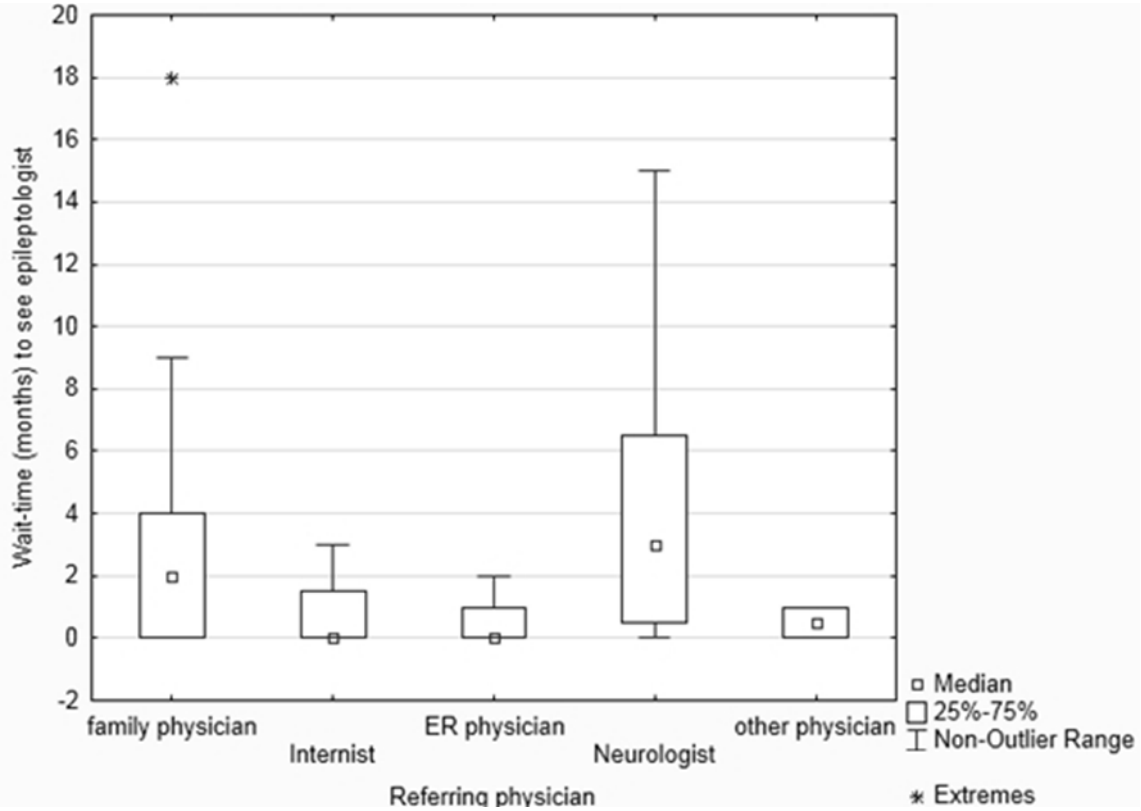

Figure 3: Wait times to see epileptologist based on referring physician

within 2 months and 98.5% were seen within 6 months of initial event by the epileptologist.

The median wait time for EEG was 1.5 months (0 – 14.5); 59.6% of the EEGs were performed within 2 months and 75% within 7 months from the initial event. Mean wait time for head CT scan was 5 months (0 – 22); 55% of these were performed within 48 hours of the event. Median waiting time for brain MR-imaging was 5 (0 - 36) months; 59.3% of MRIs were completed within 6 months of event.

The initial assessment was performed in 42.6% by an ER physician, 25.9% by a family physician, 7.4% by an internist, and 14.8% by a general neurologist. In 3.7% of cases the specialty of the initial assessing physician was unknown.

Figure 3 shows the median wait times to see the epileptologist as a function of the referring physician. Patients referred by either an emergency physician or an internist had the shortest median wait times, while those referred by another neurologist had the longest wait times.

The diagnosis of seizure disorder by the epileptologist differed only by 9% from the original assessment performed by the referring physician, representing a high degree of convergence (91%). Of all 51 cases reviewed, 4 diagnoses were altered after assessment by the epileptologist. Two cases previously considered possible syncopes

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Table 1: Reasons for initiating AEDs after 1st unprovoked seizure

Reason	# of cases
EEG abnormalities	10
MRI abnormalities	2
CT abnormalities	5
Seizure recurrence	9
Other reasons*	13

*Other reasons (n=13):

- job as fireman (1)
- desire to resume driving (2)
- two generalized tonic-clonic seizures in 24 hours (2)
- developmental delay (1)
- violent seizure (1)
- history of head injury - not seizure related (1)
- unknown (5)

were diagnosed with primary generalized epilepsy. One diagnosis of possible migraine was changed to primary generalized epilepsy, and one diagnosis of seizure disorder was inconclusive (possible migraine variant). The latter was not excluded from the study.

Anti-epileptic medication was initiated in 20.4% of patients prior to referral. Most frequently used antiepileptic drugs (AEDs) were phenytoin (33%) and lamotrigine (27.8%). The decision to treat was attributed to: concerns for seizure recurrence in 16.7%, EEG abnormalities in 18.5%, abnormal imaging findings in 13%, and other reasons in 51.8%. The reasons for starting AEDs are shown on table 1.

A positive family history of seizures was reported in 22.2% (12 patients), childhood seizures and/or febrile seizures in 9.3% (n = 5), history of head trauma and/or central nervous system (CNS) infections in 14.8 % (n = 8). Alcohol and illicit drugs were considered possible triggers in 7.4% and 3.7% of cases, respectively.

Seizure recurrence was noted in 25.5% (13 of 51) after a follow-up of at least 12 months. 46.2% of these patients showed imaging abnormalities while 38.5% had abnormal EEG findings. 29% of patients started on AEDs had both abnormal EEG and imaging findings, 29% had abnormal EEG only, and 19.5% had abnormal imaging only. Seizure recurrence was 28.2% (11 of 39) in patients with normal CT head and 16.7% (2 of 12) in patients with structurally abnormal CT head. Normal and abnormal EEGs were associated with recurrence rates of 26.7% and 23.8%, respectively. The EEGs of two patients with focal slowing were considered abnormal, although no other epileptiform features were observed. Abnormal MR-imaging was associated with a recurrence rate of 25% (4 of 16), and in those with both abnormal MR-imaging and EEG, the recurrence rate was only 10% (1 of 10). Table 2 shows the different EEG patterns (patients who had more than one EEG are also included). Figure 4 shows the distribution of seizure recurrence across the different age sub-groups.

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Table 2: EEG findings and distribution of documented abnormalities

EEG findings			Frequency
1	Spikes	Generalized spike and wave	11
		Right temporal spikes	1
		Right frontal spikes	2
		Bilateral temporal spikes	2
2	Slowing	Left TIRDA	1
		Right frontal slowing	1
		Left temporal slowing	1
		Generalized slowing	2
3	Other patterns	Breach rhythm	2
		Triphasic waves	1
4	Normal		29

EEG report missing in one case

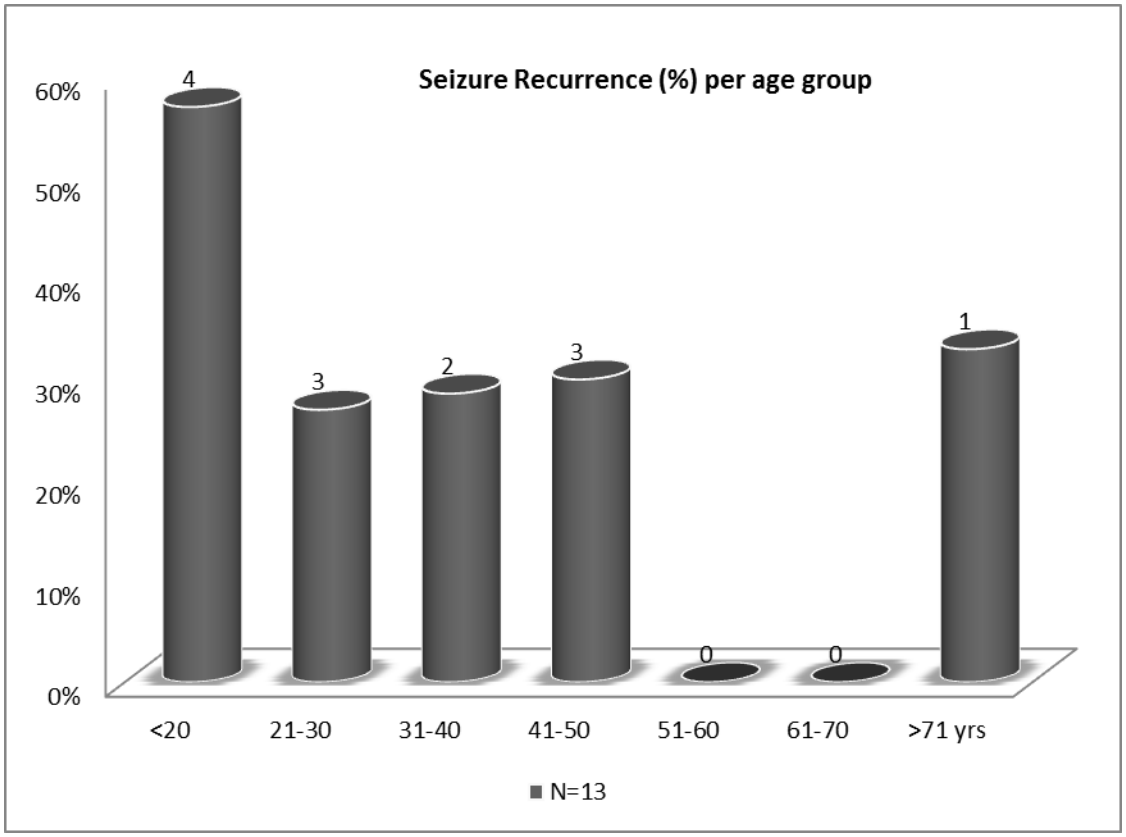

Figure 4: Seizure recurrence rates in different age groups

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Seizure recurrence rates were: 40% (2 of 5) in patients with a past history of febrile or childhood seizures, 25% (2 of 8) in those with a prior history of CNS infection or head trauma, and 41.7% (5 of 12) in those with a positive family history of seizure disorder. The rate was 20.5% (8 of 39) in patients with a negative family history of seizure disorder. Seizures recurred in 50% (2 of 4) if the initial event was related to illicit drug use or alcohol intoxication.

During the waiting period, minor injuries (bruising) were reported in two patients; there were no reported mortalities. Formal documentation on counselling about driving restrictions and reporting of patients following seizure or seizure-like events by primary care physicians to the driver's licensing authority as mandated by provincial legislation in the province of Saskatchewan could only be found in 3% of cases.

Discussion

We found that 98.5% of patients in the district were seen by the epileptologist within 6 months and that during the waiting period there were no case fatalities, and only 2 cases of minor seizure-related injuries (due to seizure recurrence). These findings suggest that patient referral and assessment is being done in a safe and relatively timely fashion given the otherwise long wait times for neurologists in the province. We consider the wait time from time of event to time the patient was seen by the specialist to be excessively long, not albeit comparable to the data from the National Clinical Audit of epilepsy-related death from the UK,[8] where only 69% of referrals were completed within 1 week and 15% of individuals had to wait more than 6 months for specialist appointments. The delay in the referral process is reflected in our study and some cases with extremely long wait times from time of event could be attributed to lack of knowledge about the referral process by primary care physicians or an attempt to manage by same. The establishment of a first seizure clinic with clear referral guidelines would reduce this unnecessary delay and make the process more efficient and safer. The National Clinical Audit of epilepsy-related death by the National Institute for Clinical Excellence (NICE) in the United Kingdom[8] showed that wait times for specialist appointment after first seizures were long, with 15% of patients waiting more than 6 months. Based on this audit, they recommended an urgent follow-up by an epilepsy specialist ideally within 2 weeks for all patients with first seizure. Wait times longer than 2 weeks are therefore considered long based on the NICE recommendations.

Seizure recurrence was highest in the age group younger than 20 years and also slightly higher in those older than 70 years.[10] This finding is similar to that reported in the UK National General Practice Study of Epilepsy, with highest recurrence in patients under the age of 16 and those older than 59 years.[11] Early seizure frequency, etiology of seizures, and an abnormal EEG are known to be predictive factors for seizure recurrence[12] and long term outcomes as observed in the MESS trial[13] and a long term follow-up study[14]; recurrence in our study was altered by the early use of AEDs in patients with abnormal EEGs and/or abnormal MRIs. The high rate of neuroimaging and EEG abnormalities in this study most likely reflects the highly selective nature of the group; considered high risk for seizure recurrence or likely focal seizure in origin, as not all patients with first unprovoked seizures are referred to the epileptologist in the province of Saskatchewan.

The occurrence of single unprovoked seizures has psychosocial implications for pa-

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tients and families, and concerns about etiology and likelihood of recurrence often impact life-style areas such as driving restrictions and restrictions in work, family, and leisure activities.[15] Although in this study there was no reported mortality or major injuries from the event or subsequent recurrence, the professional, financial, and psychosocial impact cannot be underestimated and patients probably have to be assessed in well-organized single seizure clinics.

There was a substantial delay in obtaining even basic imaging (CT head) with only 50% scanned within 24 hours, most likely due to unavailability of scanners in some parts of the province. Retrospective, prospective, and randomized controlled studies in both adults and children have provided data showing that early seizure recurrence is reduced by early initiation of anticonvulsant treatment, but this intervention does not alter the prognosis for the development of epilepsy.[16] The risk of recurrence is increased with abnormal imaging, epileptiform changes on EEG, positive family history of epilepsy, and remote symptomatic seizures.[9] These factors might increase the likelihood of AED use after a single event, reflecting the reasons for the early initiation of AED in our patients. Although the American Academy of Neurology does not recommend treatment with AED for the prevention of the development of epilepsy following first unprovoked seizure (level B), the guidelines suggest considering the use of AEDs where the benefits of second seizure risk reduction outweigh the risk of pharmacologic and psychosocial side effects. Overall, AEDs were started in 74.1% of first unprovoked seizure (only 25% recurrence rate in this subgroup). About 20% of these cases were started on AEDs by the primary care physician; the overall use of AED is higher than would be expected, but this is not different from that reported by Hauser, et al.[4] A possible explanation would be that the cases referred to the epileptologist represent higher risk patients when compared to the general population of patients with single unprovoked seizures. This is further supported by the high incidence of EEG and imaging abnormalities in this study. A good number of those patients with abnormal imaging or EEG findings were started on AEDs. This is the most likely explanation for the lower rate of seizure recurrence in this group. Consequently, as previously reported in other studies, we consider abnormal EEG to be a good predictor of seizure recurrence, but it might have been masked in this study by the early use of AEDs. In our study, predominantly first generation antiepileptic drugs were used: phenytoin and lamotrigine.

The low rate of reported driving restrictions by the primary care physician shows lack of awareness and probably lack of knowledge about the implications of a single seizure. This aspect has to be improved in a province like Saskatchewan where a mandatory written report to Saskatchewan Government Insurance (SGI) is required after a seizure. A better education of family practitioners and ER physicians about the social, occupational, and health implications of a single unprovoked seizure is required in the future. Established single seizure clinics also can improve proper driving restrictions and avoid the possibility of accidents in patients.

There are some limitations: our study was a retrospective chart review that only captured patients referred to the epileptologist, and as such does not reflect the outcome of those patients referred to other neurologists or physicians in Saskatchewan. Moreover, the wait times were calculated from the date of initial event or referral until the date of assessment or date on which the test was performed, and we did not take into consideration if any previous appointments were missed by the patient. A potential limitation

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of our study could be the sample size, although the age of our cohort, the recurrence rate, and other outcomes are similar to other epidemiological studies with single unprovoked seizures performed in other countries.

Conclusions

We conclude that the regional referral process of patients with a single unprovoked seizure is timely. Although there were no case fatalities, due to the limitations of this study as mentioned above, safety issues need to be addressed in a prospective study. The wait times are longer than we had expected and the process is slower than recommended in most guidelines. This situation could be similar in other Canadian centers, where patients are not seen immediately and wait substantial time to get fully investigated. Education of primary care physicians is important to avoid unnecessary delays and mismanagement of patients. Further improvements are needed to increase access to investigations (especially EEG, CT, and MRI) with the ultimate goal of maximizing diagnostic yield and hence, the ability to stratify the patients for risk of seizure recurrence. We suggest the establishment of a first/single seizure clinic as well as clear referral guidelines as the best approach for these patients. To our knowledge this is the first study in the literature reporting wait times after single unprovoked seizures.

A larger study (preferably, a prospective study with direct recruitment of patients from the emergency departments) involving several referral centers is necessary to evaluate the timeliness and safety of referrals of first unprovoked seizures.

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