## **FULL-LENGTH ORIGINAL RESEARCH**

# A comparison of waiting times for assessment and epilepsy surgery between a Canadian and a Mexican referral center

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> Epilepsia Open, 2(4):453-458, 2017 doi: 10.1002/epi4.12082



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## SUMMARY

Objective: To provide a comprehensive transnational overview of wait times for epilepsy surgery in Canada and Mexico.

Methods: We reviewed all cases referred for epilepsy surgery between 2007 and 2015 at the Saskatchewan Epilepsy Program Royal University Hospital (SEP) (n = 70; Saskatoon, Canada) and the National Institute of Neurology and Neurosurgery (NINN) (n = 76; Mexico City, Mexico) and compared wait times, calculated as the time from diagnosis of epilepsy on assessment at an epilepsy center to epilepsy surgery.

Results: Mean wait times were similar across centers. Mean patient age was 37.4  $\pm$  9 years (NINN) and 36.7  $\pm$  13.2 years (SEP). The mean time from epilepsy diagnosis to referral was 18.9 (NINN) and 16.9 years (SEP), p = 0.30; first consult with the epileptologist, 19.7 (NINN) and 17.4 years (p = 0.23); neuropsychology consult, 21.4 (NINN) and 17.9 years (SEP); video electroencephalogram (video-EEG) telemetry, 21.1 (NINN) and 18.6 months (SEP); initial neurosurgical consult, 21.9 (NINN) and 19.1 years (SEP) (p = 0.35); and epilepsy surgery, 19.7 (NINN) and 19.6 years (SEP) (p = 0.29).

Significance: This is the first study to compare wait times between Canada and Mexico. Despite disparity in their health delivery systems and financial resources, surgical wait times appeared to be protracted in both nations, confirming that delayed treatment is a universal problem that requires collaborative scrutiny.

**KEY WORDS**: Wait times, Epilepsy surgery, Drug resistant epilepsy.

Epilepsy is a chronic neurological condition characterized by recurrent unprovoked seizures with serious effects on neurobiological, cognitive, psychological, and social functioning.<sup>1</sup> Epilepsy affects 1% of the population, and it is one of the most common neurological diseases.<sup>1</sup> Despite its prevalence, epilepsy is poorly understood by the public, healthcare practitioners, and even patients and their families. Approximately 30% of people with epilepsy (PWE) are drug-resistant and have seizures despite treatment with antiepileptic drugs (AEDs).<sup>2,3</sup> In appropriately selected patients, epilepsy surgery (ES) is potentially curative and has been shown to durably improve quality of life (OOL) and mortality.<sup>4</sup> The safety and efficacy of ES has been established in two randomized controlled clinical trials (RCCTs).<sup>5,6</sup>

Accepted September 9, 2017.

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## **KEY POINTS**

- Prolonged wait times for epilepsy surgery remain a significant problem in both Canada and Mexico
- We suggest that the focus of management and treatment of patients with epilepsy should be shifted toward early referral to comprehensive epilepsy centers
- The current situation of wait times spanning 20 years is probably not acceptable and potentially exposes patients to increased mortality and morbidity

Current recommendations are that patients with drugresistant epilepsy (DRE) have to be referred to an epilepsy center for surgical consideration in a timely manner.<sup>5</sup> Yet, ES remains one of the most underused medical interventions.<sup>7</sup> A population-based study performed in Ontario using the provincial databases showed that <2% of patients with DRE have the benefit of epilepsy surgery, suggesting a potential lack of referral of patients to epilepsy centers.<sup>8,9</sup> Equally concerning is the significant problem of wait times for assessment.<sup>10</sup> The average delay from onset of seizures to surgery is 20 years for adults and 10 years for children.<sup>11</sup>

There is a pressing need to provide updated wait times for epilepsy surgery to inform healthcare policy discussion. To the best of our knowledge, this is the first study to directly compare wait times between epilepsy centers in Canada and Mexico. We believe that the comparison of wait times between high- versus lower-middle-income countries is valid and relevant because most previous reports have been done in high-income countries.

## **Methods**

#### **Basic study design**

This is a retrospective comparative study performed at two epilepsy centers in Canada and Mexico. The aim of the current study was to compare the waiting times at two epilepsy programs that provide epilepsy surgery and other specialized treatments.

#### **Participant centers**

#### Saskatchewan Epilepsy Program

The province of Saskatchewan in Canada has developed a comprehensive provincial epilepsy program, active since 2007. The program serves as an active referral system for patients with DRE throughout the province (catchment population of 1.2 million).<sup>3</sup> Clinical services for patients include: (1) the ability to implant vagal nerve stimulators for selected cases with intractable epilepsy; (2) a single seizure clinic; (3) the ability to implant depth (intracranial) electrodes for complex cases; (4) the use of the Wada test for diagnostic purposes; (5) two beds for video electroencephalogram (video-EEG) telemetry investigations (i.e., surgical work-up); (6) an active program to perform portable electroencephalograms (EEGs); (7) electrocorticography and brain stimulation for selected cases; and (8) 3T MRI, functional MRI (fMRI), and PET scan. There is an active list of 1,000 patients with epilepsy who have been referred, and more than 300 patients have been investigated for potential epilepsy surgery since 2007, with approximately 30% of those patients receiving surgery. The program maintains a comprehensive database of all patient records.<sup>3</sup>

#### NINN epilepsy clinic

The National Institute of Neurology and Neurosurgery (NINN) operates as a national active referral center in Mexico City, where the epilepsy clinic attends patients with DRE. In a study published in 2012, DRE accounted for 56% of patients who attended the clinic.<sup>12</sup> Preoperative work-up at the NINN includes the following: clinical history, neurological examination, interictal EEG, video-EEG, highresolution 1.5 and/or 3T MRI, neuropsychological testing, and neuropsychiatry evaluation. The program offers the following services for patients: (1) the ability to implant vagal nerve stimulators for selected cases with DRE; (2) the implantation of grids; (3) the use of the Wada test for diagnostic purposes; (4) two beds for video-EEG investigations (i.e., surgical work-up); (5) fMRI and PET scan; and (6) electrocorticography for selected cases. The program has a comprehensive database of all patients. NINN has epilepsy sessions in which most of the surgical cases are discussed; however, not all patients with DRE or lesional epilepsies are presented in those sessions. Some patients with lesional or structural-metabolic epilepsy go directly to surgery and are not considered in this sessions.

#### Waiting times

For this study, we included all patients who were referred for ES work-up between 2007 and 2015. We collected the following wait times data (expressed in months): (1) waiting period from the onset of seizures to the time that patients are assessed by the epileptologist, neuropsychologist, and neurosurgeon; (2) waiting period from the onset of seizures to the video-EEG telemetry and epilepsy surgery; (3) waiting period from the time of referral of patients from the family doctor/neurologist/general practitioner to the assessment by the epileptologist, neuropsychologist, and neurosurgeon; (4) waiting period from the time of referral of patients from the doctor/neurologist/general practitioner to the video-EEG telemetry and epilepsy surgery; (5) waiting period from the time of referral of patients from the epileptologist to the assessment with the neuropsychologist and neurosurgeon; and (6) waiting period from the time of referral of patients from the epileptologist to the video-EEG telemetry and epilepsy surgery.

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#### **Patient demographics**

We also gathered the following information from patient records: a detailed history of their epilepsy, history of previous treatments, physical exam findings, comorbidities, AEDs use, criteria of DRE, imaging findings, and other clinical variables.

## Statistical analysis

Descriptive statistics (mean, frequencies, and proportions) were used to characterize demographic and clinical variables. For categorical and continuous variables, comparisons were made using Person's chi-square test ( $\chi^2$ ) and Student's *t* test, respectively. Statistical analyses were carried out using IBM SPSS software (version 20, IBM Corporation, Amonk, NY) and Epidat 3.1.

## RESULTS

#### General characteristics of sample

Seventy-two patients were recruited at the SEP and 76 at the NINN. Patients' mean age at the SEP was 36.7 + 13.2 years versus 37.4 + 9.0 years at the NINN. Years of evolution with epilepsy in patients at the SEP were 20.2 + 13.6 versus  $27.38 \pm 10$  at the NINN. The most common MRI findings at the SEP were mesial temporal sclerosis (MTS) in 35 patients (48.6%), normal MRI in 20 patients (28%), and encephalomalacia in 7 patients (10%). At the NINN, the most common MRI findings were MTS in 59 patients (78.9%), cortical dysplasia in 6 (7.9%), and stroke in 4 patients (5.3%). MRI findings are displayed in Table 1.

#### Type of procedures, syndromes, and etiology

Fifty-four patients (75%) had a standard temporal lobectomy at the SEP, and 46 (60.5%) at the NINN. The second most common type of procedure at the NINN was a selective hippocampectomy in 19 cases (25%); at the SEP it was extratemporal resections in 6 patients (8%). Overall, the analysis showed that the differences between procedures were statistically significant between centers (see Table 1). Fifty-seven patients (79.2%) had structural-metabolic epilepsy, 14 (19.4%) had unknown epilepsy, and 1 (1.4%) had genetic epilepsy syndromes at the SEP. At the NINN, 73 (96.1%) patients had structural-metabolic epilepsy, 3 (3.9%) had unknown epilepsy, and no patient had genetic epilepsy. The difference between centers was statistically significant (p = 0.006). A detailed description is provided in Table 1.

## Seizure outcomes

Fifty patients (69%) were rendered Engel class I after ES at the SEP, and 54 (71.1%) at the NINN. Twelve patients (16%) had Engel class II at the SEP, and 6 (7.9%) at the NINN. Engel classes III and IV were similar in both groups, and they are displayed in Table 1.

Table 1. General characteristics of epilepsy surgical patients in both centers (n = 148)					
	Saskatoon,	Mexico	-		
	Canada	City, México			
	n = 72	n = 76	Р		
Age ( $\pm$ SD)	36.7 (± 13.2)	37.4 (± 9.03)	0.70		
Sex (%)					
Male	38 (53%)	34 (49%)	0.41		
Female	34 (47%)	42 (51%)			
Years of evolution	20.2 ( $\pm$ 13.6)	$\textbf{27.38} \pm \textbf{10}$	0.0004		
of epilepsy mean ( $\pm$ SD)					
Epileptic syndromes (%)	F7 (00%)	72 (0(0())	0.007		
Structural-metabolic	57 (80%)	73 (96%)	0.006		
Unknown Genetic	14 (19%)	3 (4%)			
VEEG localization	l (1%)	0 (0%)			
Right	31 (43%)	37 (49%)	0.0007		
Left	37 (51%)	22 (29%)	0.0007		
No clear localization	0	11 (14%)			
Multifocal	2 (3%)	6 (8%)			
Generalized	2 (3%)	0			
MRI findings	( )				
MTS	35 (48%)	59 (78%)	<0.001		
Cortical dysplasia	3 (4%)	6 (8%)			
Stroke	2 (3%)	4 (5%)			
Cyst	0	2 (3%)			
Cerebral neoplasm	4 (6%)	0 (0%)			
AVM	l (1%)	0 (0%)			
Normal	20 (28%)	0 (0%)			
Encephalomalacia	7 (10%)	1 (1%)			
Others	0	2 (3%)			
Not done	0	I (I%)			
Seizures per month (group) I to 3	27 (51%)	14 (10%)	0.0001		
4 to 6	37 (51%) 11 (15%)	4 ( 8%)  5 (20%)	0.0001		
7 or more	24 (33%)	47 (62%)			
Number of AEDs (group)	21(3370)	17 (02/0)			
0	0	2 (3%)	0.06		
1	8(11%)	3 (4%)			
2	33 (46%)	31 (41%)			
3	25 (35%)	28 (37%)			
4 or more	6 (8%)	12 (15%)			
Type of epilepsy surgery					
Standard temporal lobectomy	54 (75%)	46 (61%)	0.0004		
Selective hippocampectomy	3 (4%)	19 (25%)			
Extratemporal resection	6 (8%)	0 (0%)			
Lesionectomy	2 (3%)	5 (6%)			
Callosotomy	3 (4%)	6 (8%)			
Frontotemporal resection VNS	3 (4%)	0 0			
Engel classification	I (I%)	U			
at last follow-up Engel					
	50 (69%)	54 (71%)	0.06		
1	12 (17%)	6 (8%)	2.00		
	5 (7%)	6 (8%)			
IV	5 (7%)	10 (13%)			
Data are presented % = percer	ntage; AED, antiep	oileptic drugs; AV	M, arteri-		

Data are presented % = percentage; AED, antiepileptic drugs; AVM, arteriovenous malformation; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis; SD, standard deviation; VEED, video electroencephalography; VNS, vagus nerve estimulation.

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#### Assessment wait times

Patients at the SEP waited 16.9 years and patients at the NINN 18.9 years from the time of diagnosis of epilepsy to the referral to the epilepsy center. (See Table 2) Patients at the SEP waited 17.9 years and patients at the NINN 21.4 years from the time of diagnosis to the consult with neuropsychology. Patients at the SEP waited 18.6 years and patients at the NINN 21.1 years from the time of diagnosis to the video-EEG. Finally, patients at the SEP waited 19.6 years and patients at the NINN 19.7 years from the time of diagnosis to epilepsy surgery. None of the wait times were statistically significant between the centers.

Regarding waiting times from the first consult of epilepsy program to main investigations and epilepsy surgery (in months), patients at the SEP waited 11.1 months and patients at the NINN 23.5 months from the first epilepsy consult to the consult with neuropsychology. Patients at the SEP waited 15.1 months and patients at the NINN 27.4 months from first epilepsy consult to the video-EEG; no statistically significant differences were seen between the centers. Finally, patients at the SEP waited 25.7 months and patients at the NINN 42.19 months from the diagnosis to epilepsy surgery (p = 0.004); this was statistically significant. See Table 3 for details.

## DISCUSSION

This is the first study comparing wait times for assessment for ES in two epilepsy centers from two different countries. It is striking that despite different healthcare delivery systems and disparate economic and social factors, excessive wait times are a major issue in both Canada and Mexico. Thus, this study demonstrates that the issue of wait times is not only pertinent to developed countries,<sup>13</sup> as has been previously documented, but is a crucial factor that must be addressed by all healthcare systems, including those of developing nations. It is concerning that patients in the province of Saskatchewan in Canada wait 16.9 years to be referred to an epilepsy center, and this time is comparable to the time that patients wait in Mexico to be seen at the NINN (18.9 years). Specifically, the time that patients waited to be operated on in the SEP was 19.6 years compared with 19.7 years at the NINN. This investigation supports the notion that access to care and delayed referral to an epilepsy center is a universal problem.

We hypothesize that a major impediment to ES is a lack of awareness and uptake among healthcare providers, including neurologists, who may be unaware of the benefits of ES and thus reluctant to pursue this modality and arrange referrals.<sup>11</sup> Another problem is the lack of clarity surrounding the concept of DRE, which has recently been addressed by an updated definition released by the International League Against Epilepsy (ILAE) to encourage early referral to comprehensive epilepsy centers and to promote consideration of ES early in the treatment continuum.<sup>2</sup> The new definition of DRE is as the failure of adequate trials of two tolerated, appropriately chosen and used AEDs (whether as monotherapy or in combination) with the goal of achieving sustained seizure freedom.<sup>2</sup> A recent study confirms the validity and reliability of this new definition compared with others.<sup>3</sup>

In our practices, referring physicians perform trials with multiple AEDs after failure of two AEDs before referral to a comprehensive epilepsy center, thereby prolonging wait

	Saskatoon, Canada n = 72	Mexico City, México n = 81	Р
Time from the diagnosis of epilepsy to the referral to epilepsy center (months $\pm$ SD)	203.3 (± 164.83) 2–588 16.9 years	227.8 (± 123.24) 1–573 18.9 years	0.30
Time from the diagnosis of epilepsy to the first consult at the	209.2 (± 165.65)	237.0 (± 119.92)	0.23
epilepsy center (months $\pm$ SD) (intervals)	(4–590) 17.4 years	(3–581) 19.7 years	
Time from diagnosis to the consult of NPS (months $\pm$ SD)	215.5 (± 167.54) (5–592) 17.9 years	257.6 (± 117.40) 37–592 21.4 years	0.09
Time from diagnosis to the VEEG (months $\pm$ SD)	224.3 (± 168.16) (4–604) 18.6 years	254.1 (± 118.68) 28–587 21.1 years	0.24
Time from diagnosis to the first consult at neurosurgery (months $\pm$ SD)	229.2 (± 165.5) (7–606) 19.1 years	232.8 (± 141.37) 14–597 19.3 years	0.35
Time from diagnosis to the ES (months $\pm$ SD)	235.5(± 164.20) (11–611) 19.6 years	237.0 (± 119.92) 50–602 19.7 years	0.95

Table 3. Waiting times from the first consult of epilepsy program to main investigations and epilepsy surgery (inmonths) in both centers (n = 148)				
	Saskatoon, Canada n = 72	Mexico City, México n = 81	Р	
Time from first EP consult to consult of NPS (months $\pm$ SD)	.  (±   .60)  −58	23.5 (± 33.47) I-117	0.007	
Time from first EP consult to the VEEG (months $\pm$ SD)	I 5.I (± 32.25) I−59	27.4 (± 48.03) I−214	0.08	
Time from first EP consult the ES (months $\pm$ SD)	25.7 (± 33.3) 4–63	42.19 (± 39.56) 2–244	0.004	

times.<sup>14</sup> Additionally, some neurologists prematurely appear to disregard the possibility of ES in DRE in patients with nonlesional MRIs or multifocal or bilateral epileptiform activity identified on scalp EEG.<sup>15</sup> These different practice styles could potentially contribute to the lengthy wait times patients endure at these centers.

With the a priori expectation of Canada's rigorous physician training system, licensure requirements, and superior healthcare funding, we had initially hypothesized that Canadian wait times would be shorter than those in Mexico. Yet, the data indicate no significant difference in wait times, reiterating the need to identify barriers to access, collaboratively tackle protracted wait times, and streamline patient referrals to epilepsy centers.

Patient beliefs also factor in to delayed wait times, notably the incorrect perception that, as an invasive therapy, ES is inherently dangerous and complication prone.<sup>16</sup> A metaanalysis reported minor and major medical complications after resective procedures in 5.1% and 1.5% of patients. respectively. Perioperative mortality was uncommon after epilepsy surgery, occurring in only 0.4% of patients with temporal lobe epilepsy and 1.2% of those with extratemporal.<sup>17</sup> Another fear is that of cognitive decline, especially in dominant temporal resections. However, this potential negative must be counterbalanced with the prospect of improved neurocognitive functioning resulting from seizure remission post-ES. It is therefore vital that patients with DRE be afforded the opportunity to be assessed at a comprehensive epilepsy center where their concerns can be adequately addressed and the risks and benefits of any interventional procedures thoroughly analyzed.

Another driver of wait times could be geography. Previous studies have indicated that patients who live in close proximity to epilepsy centers are more likely to be seen than those in distant regions, but this is not well demonstrated.<sup>18</sup> The SEP is the only center in the province that assesses patients with complex epilepsy and offers surgery. This could be a barrier because many patients living in the north and south of the province may not be referred on time or at all. A similar situation exists for the NINN, being one of the few available epilepsy centers that offer epilepsy surgery in Mexico. It is possible that patients from different provinces, away from Mexico City, may experience longer wait times. These factors have to be explored in the future.

By shedding light on protracted wait times, we hope to initiate a discussion on finding approaches to resolve this issue. Presently, the burden of caring for their epilepsy often falls on patients, who must navigate a needlessly complex series of referrals to attain appropriate care. The predictable result is unacceptably long wait times for diagnosis, tests, and treatment of epilepsy and its comorbidities, as evidenced by this study. There is a need for an efficient multi-disciplinary pathway that offers patients with epilepsy care from the onset of their first seizure to more complex management options if necessary.<sup>19,20</sup> Although the nuts and bolts of this system may vary from region to region, contingent on expertise and resources, the inception of a time-conscious team-based care approach is a sensible consideration.

We suggest that the focus of management and treatment of patients with epilepsy should be shifted toward early referral to comprehensive epilepsy centers where DRE can be identified and treated earlier.<sup>19,20</sup> The current situation of wait times spanning 20 years is probably not acceptable and potentially exposes patients to increased morbidity and mortality. A potential explanation of why surgically treatable epilepsies may take 20 years or longer to be referred to surgery is the demonstration in some studies that DRE can be preceded by a quiescent period followed by further remissions and that an average patient can take 9 years to become intractable.<sup>21</sup>

The key strength of this investigation is its comparison of wait times across two nations. The analysis shows the differences between the centers as well as the common aspects shared by the two centers, such as number of operated patients during the period of study, patient age at surgery, common epilepsy syndromes, use of AEDs, predominance of temporal lobectomies, and seizure outcomes. A limitation of this study is the different structures of the epilepsy centers. The NINN is one of the largest epilepsy centers in Mexico, and the SEP is a provincial program in Canada, making a direct comparison difficult. We recognize that both centers probably do not represent the practices in both

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countries, and the results of this study may not be generalizable. In the future international efforts involving more centers should be made to corroborate our observations. Still, with these limitations, our results are similar to those of previously reported studies.

Patient characteristics may be another confounder, and the retrospective nature of this study could be a bias. Another limitation could be the period of time selected for this study. It is possible that waiting times could change according decade and may depend on the number of physicians and equipment available; therefore, a future study comparing different periods of time will be relevant. A potential subanalysis of wait times according to the type of procedure could also be useful; unfortunately, the sample size in this study is small, making the comparison not valid.

## CONCLUSIONS

Prolonged wait times for ES remain a significant problem in both Canada and Mexico, suggesting that collaborative efforts that address health system, physician, and patient factors that result in lengthy referral delays must be addressed.

## **ACKNOWLEDGMENTS**

To participants in the Epilepsy Sessions at NINN.

## DISCLOSURE OF CONFLICT OF INTEREST

Jose F. Tellez-Zenteno receives grants from the University of Saskatchewan, UCB Canada, and the Royal University Hospital Foundation, Saskatoon, Saskatchewan, through the Mudjadik Thyssen Mining Professorship in Neurosciences. Julio C. Moreno-Castellanos received support from UCB Mexico for the logistics of his Observership at University of Saskatchewan, Canada. Elisa Bribiesca-Contreras and Lizeth Zertuche-Ortuño were awarded a scholarship from Fundación Armstrong. Iris E. Martínez-Juárez, Verónica Martínez-Bustos, Laura E. Hernández-Vanegas, Lizbeth Hernandez Ronquillo, and Syed Rizvi have nothing to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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