These Guidelines are a Product of Critical Care Services Ontario (CCSO)

Provincial Guidelines for the Management of Epilepsy in Adults and Children is the result of a collaborative effort between CCSO, the Epilepsy Implementation Task Force (EITF), and Provincial Neurosurgery Ontario (PNO). The EITF was established in June 2013 to develop and implement a provincial framework to maximize value from the system of epilepsy care in Ontario. To support the flow of patients towards appropriate treatment for epilepsy, this document contains a set of guidelines to help with the diagnosis, treatment and referral practices from the moment of a patient’s first seizure. The EITF works in collaboration with PNO to support equitable and timely access to neurosurgical care, including epilepsy surgery, and to help maintain the province’s neurosurgical capacity.
How to Use This Document

The Guidelines included in this document have been developed by a sub-group of the Epilepsy Implementation Task Force for any health care provider engaged in the care of patients with epilepsy before referral to surgery. The guidelines are based on current processes and represent expectations for the highest standards of epilepsy care.

This document provides recommendations only.

For information about these Guidelines, please contact:
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Phone: 416-340-4800 x 5577
Email: ccsadmin@uhn.ca
Website: www.criticalcareontario.ca

CCSO is funded by the Government of Ontario.
Version Control

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<tr>
<td>Version 1.0</td>
<td>Created January 2015</td>
</tr>
<tr>
<td>Recommended next review</td>
<td>November 2016</td>
</tr>
<tr>
<td>Approved By</td>
<td>The Epilepsy Implementation Task Force (EITF) and Provincial Neurosurgery Ontario (PNO)</td>
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Disclaimer: The contents of these Guidelines may change over time. Clinicians and hospital administrators should use sound judgment for individual patient encounters. Critical Care Services Ontario, the Epilepsy Implementation Task Force and Provincial Neurosurgery Ontario strongly recommend evidence-based practices.
Acknowledgements

We would like to thank the following individuals for their contribution to the development of this document:

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<td>Parent Representative</td>
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Please see Appendix 1 for a list of the EITF membership.
Abbreviations

AED  Antiepileptic Drug (also known as Antiseizure or Anticovulsant drug)
CPSO  College of Physicians and Surgeons of Ontario
CPO  College of Psychologists of Ontario
CSF  Cerebral Spinal Fluid
CT  Computed Tomography
ECG  Electrocardiography
ED  Emergency Department
EEG  Electroencephalography
EMU  Epilepsy Monitoring Unit
EITF  Epilepsy Implementation Task Force
FHP  First Healthcare Provider
FP  Family Physician
GP  General Practitioner
ILAE  International League Against Epilepsy
LP  Lumbar Puncture
MRI  Magnetic Resonance Imaging
NP  Nurse Practitioner
OC  Oral Contraception
OCSWSSW  Ontario College of Social Workers and Social Service Workers
PNO  Provincial Neurosurgery Ontario
TDM  Therapeutic Drug Monitoring
WWE  Women with Epilepsy
**Definitions**

<table>
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<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Adolescent</td>
<td>A person 13 to 17 years of age.</td>
</tr>
<tr>
<td>Adolescent Medicine Specialist</td>
<td>Paediatrician practising adolescent medicine.</td>
</tr>
<tr>
<td>Child</td>
<td>A person less than 18 years of age.</td>
</tr>
<tr>
<td>Community Epilepsy Agencies</td>
<td>Community Epilepsy Agencies provide a range of support services to persons with epilepsy and their families. These services include epilepsy information, seizure first aid training, support groups, social opportunities, employment counseling and school advocacy.</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td>Co-morbidity refers to the co-occurrence of two conditions with a greater frequency than found in the general population. This does not infer a causal relationship. Co-morbid conditions are common in people with epilepsy. They are found across the lifespan and have important implications for treatment and quality of life.</td>
</tr>
<tr>
<td>Epileptologist</td>
<td>Qualifications and Training: 1. Clinical fellowship training in epilepsy and video-EEG for at least 12 months in a specialized center in Canada, US or abroad; 2. Recognized as a neurologist by the College of Physicians and Surgeons of Ontario (CPSO); and 3. Certification for EEG reporting (EEG examination by the Canadian Society of Clinical Neurophysiologists or APBN exam in Epilepsy) is mandatory. Neurologists who have/had been reporting Video EEG recordings without supervision in any jurisdiction in Canada or the United States of America anytime in or before 2013 are exempt from EEG/Epilepsy examination.</td>
</tr>
<tr>
<td>Epileptic Seizure</td>
<td>An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive and or synchronous neuronal activity in the brain (Fisher et al, 2005).</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>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 (Fisher et al, 2005). In most situations, occurrence of two epileptic seizures is evidence of enduring predisposition to generate epileptic seizures.</td>
</tr>
<tr>
<td>Family Physician</td>
<td>A physician recognized by the CPSO as a family physician.</td>
</tr>
<tr>
<td>General Practitioner</td>
<td>A physician licensed by the CPSO for general practice.</td>
</tr>
<tr>
<td>Internist</td>
<td>A physician recognized by the CPSO as a specialist in internal medicine.</td>
</tr>
<tr>
<td>Medically-Refractory Epilepsy</td>
<td>Failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drugs (whether as monotherapy or in combination) to achieve sustained seizure-freedom (Kwan, 2010 from International League Against Epilepsy).</td>
</tr>
<tr>
<td>Neurologist</td>
<td>A physician recognized by the CPSO as a specialist in Neurology.</td>
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<tr>
<td>Neuropsychologist</td>
<td>A psychologist registered with the College of Psychologists of Ontario (CPO) for the practice of clinical neuropsychology.</td>
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<tr>
<td><strong>Nurse Practitioner</strong></td>
<td>A nurse registered with the College of nurses of Ontario in the extended class.</td>
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<tr>
<td><strong>Pediatrician</strong></td>
<td>A physician recognized by the CPSO as a specialist in Pediatrics.</td>
</tr>
<tr>
<td><strong>Psychiatrist</strong></td>
<td>A physician recognized by the CPSO as a specialist in Psychiatry.</td>
</tr>
<tr>
<td><strong>Psychologist</strong></td>
<td>A healthcare provider registered with the College of Psychologists of Ontario (CPO) for the practice of clinical psychology.</td>
</tr>
<tr>
<td><strong>Social Worker</strong></td>
<td>A healthcare provider registered as a social worker with the Ontario College of Social Workers and Social Service Workers (OCSWSSW).</td>
</tr>
<tr>
<td><strong>Senior</strong></td>
<td>A person 65 years of age or older.</td>
</tr>
<tr>
<td><strong>Specialists</strong></td>
<td>Internists, pediatricians, and neurologists.</td>
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I. Introduction

Epilepsy affects around 95,000 Ontarians, of whom approximately 80,000 are adults and over 15,000 are children under the age of 18 (Institute for Clinical and Evaluative Sciences [ICES] & Ontario Brain Institute [OBI], in press). While most individuals with epilepsy can be treated effectively by a primary care physician or general neurologist, an estimated 30% of those diagnosed have medically refractory epilepsy, experiencing seizures that do not respond to treatment with two or more appropriate antiepileptic drugs (Kwan & Brodie, 2000). These numbers are not static. Each year it is estimated that 6,500 Ontarians will develop epilepsy, and 1,950 of them will have medically refractory epilepsy (Tellez-Zenteno, Pondal-Sordo, Matijevic, & Wiebe, 2004; Wiebe, Bellhouse, Fallahay, & Eliaziy, 1999).

Epilepsy surgery has shown positive outcomes for epilepsy sufferers; there is approximately an 80% chance that an individual will be seizure-free after surgery, resulting in far better outcomes with respect to seizure freedom, improved quality of life, and reduction of psychosocial comorbidities that accompany medically refractory epilepsy than continued medical treatment (Bowen, Snead, Chandra, Blackhouse, & Goeree, 2012). However, not all individuals with epilepsy are candidates for surgery – approximately one third of those suffering from medically refractory epilepsy will not be considered candidates. Despite its effectiveness, surgical treatment is underutilized in Ontario, with only a fraction of the population who may be eligible for surgery assessed every year. A 2012 report by the Expert Panel on a Provincial Strategy for Epilepsy Care (Health Quality Ontario [HQO], 2012) identified that long wait lists at the province’s Epilepsy Monitoring Units (EMUs) and low referral rates contributed to the underutilization of surgical treatment. The Panel also noted that awareness of surgical treatment options was low and patients were not diagnosed, treated and referred appropriately. A 2011 estimate determined that less than 2% of potential surgical candidates accessed surgical treatment (HQO, 2011).

The Panel recommended action to improve epilepsy care infrastructure and surgical referral in the Province (HQO, 2012). As a result, the Ministry of Health and Long-Term Care (MOHLTC) made an investment of 21 new Epilepsy Monitoring Unit (EMU) beds in Ontario, bringing the total number of EMU beds to 39 (26 adult and 13 paediatric). The Ministry also resourced additional epilepsy surgery and vagal nerve stimulator capacity through the Provincial Neurosurgery Strategy and established the Epilepsy Implementation Task Force (EITF) to oversee epilepsy system improvements.

Epilepsy Implementation Task Force

The Epilepsy Implementation Task Force (EITF) was formed in June 2013 to develop and implement a provincial approach to an integrated system for epilepsy care in Ontario. Supported by CCSO, this committee is co-chaired by Dr. Carter Snead, Paediatric Neurologist at the Hospital for Sick Children, and Brenda Flaherty, Executive VP and Chief Operating Officer at Hamilton Health Sciences.
The EITF brings together senior clinical and administrative leaders from the epilepsy community to:

- Improve access along the full continuum of care by coordinating resources and wait lists;
- Establish standardized diagnostic and surgical protocols across hospitals with comprehensive epilepsy programs; and
- Develop supports for primary care providers.

The EITF is a subgroup of Provincial Neurosurgery Ontario (PNO), a committee working to develop a comprehensive provincial neurosurgical system. The EITF works in collaboration with PNO to support equitable and timely access to neurosurgical care, including epilepsy surgery, and to help maintain the province’s neurosurgical capacity. This work is supported by the Ministry through Critical Care Services Ontario (www.criticalcareontario.ca). For a list of EITF membership, please see Appendix 1.

The creation of the EITF stemmed from the expert panel report to Health Quality Ontario assessing the challenges to access in epilepsy care in Ontario (HQO, 2012). The report notes that the community of healthcare providers treating epilepsy needs support with a standardized approach to diagnosis and treatment (such as antiepileptic drugs (AED), Electroencephalography (EEG) or neuroimaging), and process for referral to a neurologist or for surgery (if the seizures are determined to be medically refractory). This document is the outcome of the recommendation to provide province-wide guidelines for first-contact healthcare providers (such as primary care and emergency department physicians) to standardize the diagnosis, treatment and referrals of patients with epilepsy in the province.

**Epilepsy Care in Ontario**

In order to maximize value and ensure that patients are receiving timely, high quality care, it is crucial to clarify system capacity and referral paths. This will help set clear expectations for planning, coordination and performance for all hospitals with specialty epilepsy care programs.

The EITF has developed a definition of a Comprehensive Epilepsy Program (CEP) and established a planning and integration framework for epilepsy care in Ontario:

A CEP is an integrated care model for the management of individuals with epilepsy within a multidisciplinary team. A CEP covers various aspects of care including medical, psychosocial, and nutritional management, appropriate neurodiagnostic investigations, a mandatory EMU, capability for presurgical diagnostic evaluation, and established links to Community Epilepsy Agencies.

Hospitals with CEPs are divided into two categories based on the level of services they provide:

1. A District Epilepsy Centre (DEC) houses a comprehensive epilepsy program that provides all appropriate epilepsy related clinical services except epilepsy surgery. A DEC should provide basic investigations necessary to determine candidacy for epilepsy surgery including assessment by an Epileptologist, and full EMU service including neuropsychological evaluations.
The following hospitals are classified as District Epilepsy Centres:

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<thead>
<tr>
<th>Hospital</th>
<th>Adult Beds</th>
<th>Paediatric Beds</th>
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<tbody>
<tr>
<td>Health Sciences North (operational 2015)</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Hamilton Health Sciences</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>The Ottawa Hospital</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Children’s Hospital of Eastern Ontario</td>
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</table>

2. A Regional Epilepsy Surgery Centre of Excellence (RESC) is a facility with a comprehensive epilepsy program that provides all the services available in a DEC, and in addition, epilepsy surgery including facility for intracranial monitoring. An RESC is also a DEC for its catchment area.

The following hospitals are classified as Regional Epilepsy Surgery Centres of Excellence:

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<tr>
<th>Hospital</th>
<th>Adult Beds</th>
<th>Paediatric Beds</th>
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<tr>
<td>London Health Sciences Centre</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Hospital for Sick Children (SickKids)</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>University Health Network (Toronto Western Hospital)</td>
<td>10</td>
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Map of Ontario’s Epilepsy Centres

About this Document

The EITF has developed this document in an effort to provide guidelines for evidence-based practice for all healthcare providers in Ontario who provide primary point of care for patients with epilepsy. This
document includes guidance in the initiation of diagnostic evaluation and treatment of adults and children across the province who present with an initial diagnosis of epilepsy. These guidelines are also intended for all specialists involved in the care of patients with new onset and/or established epilepsy.

**Target Audience**

The intended target audience of these guidelines includes, but is not limited to, family physicians (FP), nurse practitioners (NP), pediatricians, internists, emergency physicians, community epilepsy agencies and neurologists. The guidelines should be shared with anyone involved in the care of patients with epilepsy.

**The EITF Guidelines Series**

The Epilepsy Implementation Task Force is developing a series of guidelines intended to support primary care providers, community neurologists, and District and Regional Epilepsy Centres. These guidelines aim to increase the awareness of, and referrals to, appropriate diagnostic assessment and surgical care of patients in Ontario.

**For Primary Care Providers:**

1. *Provincial Guidelines for the Management of Epilepsy in Adults and Children (January 2015)*
   
   To support the flow of patients towards appropriate treatment for epilepsy, this document contains a set of guidelines to help with the diagnosis, treatment and referral practices from the moment of a patient’s first seizure.

2. *Provincial Guidelines for Epilepsy Surgery Referrals in Ontario (forthcoming)*
   
   This document provides an approach to referral of medically-refractory epilepsy patients by defining evidence-based indications to epilepsy surgery in all age groups, with careful consideration given to age-specific issues ranging from infants to the elderly.

3. *Provincial Guidelines for the Management of Medically Refractory Epilepsy in Adults and Children Who are not candidates for Epilepsy Surgery (forthcoming)*
   
   This guideline will provide an approach to the management of the patient with medically intractable epilepsy in whom surgical treatment is not an option. It will include the use of antiepileptic medications and non-antiepileptic therapy such as dietary management and neurostimulation.

4. *Provincial Guidelines for Transitional Care of Paediatric Epilepsy Programs to Adult (forthcoming)*
   
   To ensure uninterrupted quality medical care for adolescent patients with chronic disorders, this document provides guidelines for paediatric and adult practitioners to assist in the seamless transition of epilepsy care for adolescents who are departing the paediatric system and entering the adult health care network.

**For Providers and Administrators in District and Regional Epilepsy Centres:**

5. *Provincial Epilepsy Monitoring Unit (EMU) Guidelines for Ontario (January 2014)*
   
   This document outlines protocols and provides guidelines for EMUs for diagnostic evaluation for epilepsy. It can be used as a guide for neurosurgical centres with EMU beds.

6. *Provincial Guidelines for Regional Epilepsy Surgical Centres of Excellence (forthcoming)*
   
   This document presents best practice guidelines and sets out accountabilities for hospitals and their collaborative interdisciplinary teams that provide care for patients at Regional Epilepsy Surgical Centres of Excellence.
II. Diagnosis of Epilepsy

Epileptic Seizure: An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive and/or synchronous neuronal activity in the brain (Fisher et al., 2005).

Epilepsy: 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 (Fisher et al., 2005). In most situations, occurrence of two epileptic seizures is an indication of enduring predisposition to generate epileptic seizures.

Epileptic seizures and epilepsy in patients are best classified using a multi-axial diagnostic scheme (when possible) (National Institute for Health and Clinical Excellence [NICE], 2012). Axes that should be considered are:

- Seizure type;
- Description of seizure (ictal phenomenology);
- Syndrome; and
- Etiology

Classification of Epileptic Seizures

1. Generalized seizures: Generalized epileptic seizures are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed networks. Such bilateral networks do not necessarily include the entire cortex. Generalized seizures can be asymmetric. They can be classified in the following ways (Berg et al., 2010):

- Tonic–clonic (in any combination)
- Absence
  - Typical
  - Atypical
  - Absence with special features
    - Myoclonic absence
    - Eyelid myoclonia
- Myoclonic
  - Myoclonic
  - Myoclonic atonic
  - Myoclonic tonic
- Clonic
- Tonic
- Atonic

2. Focal seizures: Focal epileptic seizures are conceptualized as originating within networks limited to one hemisphere. Recognition of impairment of consciousness/awareness or other dyscognitive features, localization, and progression of ictal events can be of primary importance in the evaluation of individual patients and for specific purposes (e.g., differential diagnosis of non-epileptic events from epileptic seizures, randomized AED trials, and surgery).
There are descriptors of focal seizures:

- Without impairment of consciousness or awareness (concept of a simple partial seizure):
  - With observable motor or autonomic components (“Focal motor” and “autonomic” are terms that may adequately convey this concept depending on the seizure manifestations). Involving subjective sensory or psychic phenomena only (this corresponds to the concept of an aura) (Berg et al., 2010).

- With impairment of consciousness or awareness:
  - Roughly corresponds to the concept of complex partial seizure. “Dyscognitive” is a term that has been proposed for this concept.
  - Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components). This corresponds to the term “secondarily generalized seizure” (Berg et al., 2010).

3. **Unknown (i.e. epileptic spasms):** A seizure that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis. Please note, this is not considered a classification category.

**Electroclinical syndrome:** A group of clinical entities that are reliably identified by a cluster of electroclinical characteristics (i.e. age, seizure types, EEG characteristics). Patients whose epilepsy does not fit the criteria for a specific electroclinical syndrome can be described with respect to a variety of clinically relevant factors, such as known etiology and seizure types (Berg et al., 2010.) For more information please see Appendix 2: Examples of Electroclinical syndrome arranged by age at onset.

**Types of Epilepsy Depending on Underlying Etiology**

1. **Genetic:** The concept of genetic epilepsy is that the epilepsy is, as best as understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder. Examples include SCNIA mutation and Dravet syndrome.

2. **Structural/metabolic:** Conceptually, there is a distinct other structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy in appropriately designed studies. Examples include stroke, trauma, and infection.

3. **Unknown cause:** Unknown is meant to be viewed neutrally and to designate that the nature of the underlying cause is as yet unknown; it may have a fundamental genetic defect at its core or it may be the consequence of a separate as yet unrecognized disorder.

4. **Other:** Etiological categories like ‘infections’ and ‘autoimmune’ are currently being proposed (Berg et al., 2010).

**Epilepsy constellations:** There are a number of entities that are not exactly electroclinical syndromes in the same sense but represent clinically distinctive constellations on the basis of specific lesions or other causes. These are diagnostically meaningful forms of epilepsy and may have implications for clinical treatment, particularly surgery. Examples include Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS), Rasmussen syndrome, Gelastic seizures with hypothalamic hamartoma, and Hemiconvulsion–hemiplegia–epilepsy.
III. Initial Evaluation

After their first unprovoked epileptic seizure, patients are typically evaluated by ED physicians or in a clinic setting by a nurse practitioner, family physician, internist, pediatrician or neurologist. These first healthcare providers (FHP) are responsible for the initial and/or continued management of patients.

Identification of coexisting conditions or disorders causing seizures requiring emergency department (ED) diagnosis and treatment is beyond the scope of this document. Similarly, recommendations on the management of acute prolonged seizure are beyond the scope of this document. Each hospital should have a guideline in place for the management of patients who present with acute prolonged seizures, and require inpatient treatment and evaluation.

Although patients present in diverse situations, the FHP should provide as accurate a diagnosis as possible and appropriate information regarding their condition. A strategy in partnership with the patient, utilizing all currently available treatment options with the goal of abolishing seizures may not be possible at the first contact visit. Patients should be educated about their condition and encouraged to address factors under their control.

Clinical Diagnosis of Epileptic Seizures

The diagnosis of epilepsy should not be based on the presence or absence of single features. The clinical decision as to whether an epileptic seizure has occurred should be based on the combination of the description of the event, associated symptoms and ancillary information. A detailed history should be taken from the child, young person or adult and an eyewitness to the clinical event, where possible, to determine whether or not an epileptic seizure is likely to have occurred (see Appendix 3). A careful history and neurologic examination may allow a diagnosis without extensive further evaluation.

It may not be possible to make a definite diagnosis of epilepsy initially. If the diagnosis cannot be clearly established, referral to an appropriate specialist should be considered.

Misdiagnosis of epilepsy has several implications (Ferrie, 2006) including:
- Misuse of available resources for epilepsy treatment
- Restrictions on activities are commonly applied and educational expectations and employment prospects may be lowered
- Patients who are misdiagnosed are treated with AEDs that have adverse effects
- Treatable serious conditions are overlooked
- Benign conditions, for which treatment is reassurance, are neglected
- Concerns regarding the standard of care may be raised

Episodic disorders including but not limited to: syncope, migraine, drug reaction or intoxication, and mental disorders such as psychogenic seizures may be confounders at first contact (Zaidi, Clough, Cooper, Scheepers, & Fitzpatrick, 2000). When psychogenic seizure is suspected, suitable referral should be made to psychological or psychiatric services for further investigation and treatment.
Examination: A clinical examination that includes a neurologic examination is essential, since an abnormal examination after a first seizure also predicts recurrence (Berg, 2008). This should address their cardiac, neurological and mental status, and should include a developmental assessment where appropriate.

Reporting: While confidentiality is to be maintained, there is a duty of mandatory reporting in Canada and Ontario imposed on the FHP. These are primarily, but not exclusively, limited to notification of the Ministry of Transportation. This is more extensively covered under: http://www.cpso.on.ca/uploadedFiles/policies/policies/policyitems/mandatoryreporting.pdf

Guideline on Initial Laboratory Tests After First Afebrile Seizures or New Onset Epilepsy

Adults: A drug screen is a consideration in patients with a first-time seizure. However, there are no prospective studies that demonstrate a benefit of routine use. Individual consideration should be given to the circumstances (College of Emergency Medicine [CEM], 2009). The ED presentation may require knowledge of pregnancy status to enable informed treatment decisions.

Children: Laboratory tests should be ordered based on individual clinical circumstances that include suggestive historic or clinical findings such as vomiting, diarrhea, dehydration, or failure to return to baseline alertness. Toxicology screening should be considered across the entire paediatric age range if there is any question of drug exposure or substance abuse (Hirtz et al., 2000).

Guideline on Lumbar Puncture in Children

In the very young child (<6 months), in the child of any age with persistent (cause unknown) alteration of mental status or failure to return to baseline, or in any child with meningeal signs, lumbar puncture (LP) should be performed. If increased intracranial pressure is suspected, the LP should be preceded by an imaging study of the head (Hirtz et al., 2000).

Guideline on Neuroimaging in Adult and Pediatric Patients After First Afebrile Seizure or New Onset Epilepsy

Brain imaging should be considered as part of the neurodiagnostic evaluation of adults presenting with an apparent unprovoked first seizure (Krumholz et al., 2007).

Magnetic Resonance Imaging

Where ever possible, Magnetic Resonance Imaging (MRI) is the preferred neuroimaging method in adults and children presenting with first afebrile seizure - although MRIs may not be readily available for urgent neuroimaging in some situations.

Non-urgent imaging studies with MRI should be seriously considered in any child with a significant cognitive or motor impairment of unknown etiology, unexplained abnormalities on neurologic examination, a seizure of focal onset with or without secondary generalization, an EEG that does not represent a benign focal epilepsy of childhood or primary generalized epilepsy, or in children under 2 year of age (Hirtz et al., 2000;
Gaillard et al., 2009). MRI has far better resolution for developmental anomalies of the brain that lead to epilepsy in children (e.g. focal cortical dysplasia) than a computed tomography (CT) scan.

Computed Tomography Scan
Given the potential for intracranial bleeds, strokes, and brain tumors to present with seizures in adults, an emergent CT scan may be considered in adults with first seizure. The clinical and historical features of an abnormal neurologic examination or a focal seizure onset are probably predictive of an abnormal CT study for patients presenting with seizures in the emergency department.

An emergency CT should be considered in children presenting with first afebrile seizure in the emergency department who have:

- an abnormal neurologic examination;
- predisposing history (age less than 6 months, closed head injury, recent cerebral spinal fluid (CSF) shunt revision, malignancy, or neurocutaneous disorder); or
- focal seizure onset (Harden et al., 2007).

The evidence is inadequate to support or refute the usefulness of emergency CT in persons with chronic seizures. There is no recommendation regarding an emergency CT in persons with chronic seizures (Harden et al., 2007).

Electroencephalography
1. Considered as part of the neurodiagnostic evaluation of the adult with an apparent unprovoked first seizure because it has a substantial yield and has value in determining the risk for seizure recurrence (Krumholz, 2007).
2. Recommended as part of the neurodiagnostic evaluation of the child with an apparent first unprovoked seizure (Hirtz et al., 2000).
3. There is no evidence that the EEG must be done before discharge from the emergency department; the study may be arranged on an elective outpatient basis, unless there is a concern for non-convulsive status epilepticus.
4. Epileptiform abnormalities on the EEG may be useful in confirming that the event was a seizure; however, an EEG abnormality by itself is not sufficient to make a diagnosis that an epileptic seizure occurred, nor can its absence rule out a seizure (Vining & Freeman, 1986; Holmes, 1988).
5. An EEG is necessary to determine the epilepsy syndrome and the diagnosis of an epilepsy syndrome may be helpful in determining the need for imaging studies and specific AED treatment.
7. An EEG done within 24 hours of the seizure is most likely to show abnormalities, physicians should be aware that some abnormalities such as postictal slowing that can be seen on an EEG done within 24 to 48 hours of a seizure may be transient and must be interpreted with caution (Hirtz et al., 2000).
8. Repeated standard EEGs should not be used in preference to sleep or sleep-deprived EEGs. When a standard EEG has not contributed to diagnosis or classification, a sleep EEG should be performed,
if clinically indicated. In children and young people, a sleep EEG is best achieved through sleep deprivation or the use of melatonin (NICE, 2012).

9. EEGs should be performed in accordance with the guidelines endorsed by the Canadian Society of Clinical Neurophysiologists (CSCN). The current guideline published in 2002 (Minimal Standards for Electroencephalography in Canada, 2002) will be used until the CSCN publishes new guidelines.

Guideline for Other Tests

Seizure-like attacks with a cardiovascular cause may be misdiagnosed as epilepsy. A 12-lead electrocardiography (ECG) should be performed in adults with suspected epilepsy. In children and young people, a 12-lead ECG should be considered in cases of diagnostic uncertainty (Stokes, Shaw, Juarez-Garcia, Camosso-Stefinovic, & Baker, 2004; MacCormick et al., 2009).
IV. Drug Treatment: Guideline on Drug Initiation and Monitoring

Initiation of Antiepileptic Drugs (AED) for the Treatment of Seizures in Epilepsy

Treatment with AED in patients with epilepsy aims to provide the best quality of life with no seizures and fewest adverse effects from treatment (Glauser et al., 2006). Decision to initiate AED in patients with newly diagnosed epilepsy (including patients not currently on AED) should be based on the discussion between the physician and the patient (or legal guardian/caregiver). This discussion should include the following:

- Risk of seizure recurrence
- Type of seizures
- Type of epilepsy and the natural course of epilepsy
- AED options
- Potential side effects of AED(s)
- Cost of treatment
- Potential duration of treatment
- Negative effects of seizures
- Goals of treatment (including optimal seizure control target)

Choice of AED depends on multiple factors, including (Glauser et al. 2006; Donner & Snead, 2006):

- Patient specific variables: age, gender, co-medications, co-morbidities, affordability/insurance status, and ability to swallow pills/tablets
- AED specific variables: seizure or epilepsy syndrome, adverse effects, ease and speed of drug initiation, teratogenicity, interactions, pharmacokinetics, and availability

General Principles of AED Treatment (NICE, 2012):

1. It is recommended that children, young people and adults should be treated with a single AED (monotherapy) whenever possible.

2. If the initial treatment is unsuccessful, then monotherapy using another drug or add-on treatment with a second drug can be tried. Caution is needed during the changeover period. If an AED has failed because of adverse effects or continued seizures, a second drug should be started (which may be an alternative first-line or second-line drug) and built up to an adequate or maximum tolerated dose and then the first drug may be tapered off slowly.

3. If the second drug is unhelpful, either the first or second drug may be tapered, depending on relative efficacy, side effects and how well the drugs are tolerated before starting another drug. Some patients are required to be on more than 2 AEDs.

4. It is recommended that combination therapy (adjunctive or ‘add-on’ therapy) should only be considered when attempts at monotherapy with the tolerated dose of AED have not resulted in seizure freedom. If trials of combination therapy do not bring about worthwhile benefits, treatment should revert to the regimen (monotherapy or combination therapy) that has proved most acceptable to the child, young person or adult, in terms of providing the best balance between effectiveness in reducing seizure frequency and tolerability of side effects.

5. AED interactions and comorbidities should be taken into consideration when choosing combination therapy.

6. If there is no improvement after two adequate trials of AEDs, the patient should be referred for epilepsy surgery evaluation.
Options for AEDs (NICE, 2012; Glauser et al., 2006; Glauser et al., 2013)
These are some of the examples. The list is not exhaustive. Some of the drugs can be used only for ‘off label’ purposes in Ontario. There are useful websites/resources that provide information on common AEDs. One example of such a resource is the National Centre for Biotechnology Information: http://www.ncbi.nlm.nih.gov/books/NBK2597/#ch14.s1.

1. **Adults with focal seizures**: Carbamazepine, Phenytoin, Topiramate, Oxcarbazepine, Levetiracetam, Lamotrigine and Valproic Acid. Other options include Phenobarbital and Primidone. In elderly adults Gabapentin, Lamotrigine and Clobazam may be considered.

2. **Adults with generalised convulsive seizures**: Valproic Acid, Levetiracetam, Topiramate, Lamotrigine, Phenobarbital, Carbamazepine and Oxcarbazepine. Carbamazapine, Phenytoin and Oxcarbazepine should be used carefully in epilepsy syndromes in which myoclonic or absence seizure can occur, as they may worsen them. Lamotrigine may exacerbate myoclonus.

3. **Children with focal seizures**: Oxcarbazepine, Carbamazepine, Valproic Acid, Topiramate, Clobazam, and Phenobarbital.

4. **Children with generalised tonic clonic seizures**: Valproic Acid, Topiramate, Clobazam, Carbamazepine, Lamotrigine, Levetiracetam and Phenobarbital. Carbamazepine and Phenytoin may precipitate or aggravate generalised tonic clonic seizures.

5. **Children with absence seizures**: Ethosuximide, Valproic Acid and possibly Lamotrigine

6. **Benign Epilepsy of childhood with centrotemporal spikes**: Valproic Acid and Carbamazepine. Other options include Oxcarbazepine and Levetiracetam.

7. **Juvenile Myoclonic Epilepsy**: Valproic Acid, Levetiracetam, and Topiramate.

8. **Infantile spasm**: Vigabatrin, Steroids (Oral prednisolone/injection ACTH).

**AEDs to be avoided or used with caution**:

1. **Absence seizures**: Carbamazepine, Oxcarbazepine, Phenytoin, and Gabapentin (avoided) (Guerrini, Belmonte, & Genton, 1998).


3. **Children less than 1 year of age**: Valproic acid (avoided) (Hirsch & Genton, 2003).

4. **Children 1-2 years**: Valproic acid (use with caution due to hepatotoxicity). This risk is high in combination with phenobarbital. (Nanau & Neuman, 2013; Dreifuss et al., 1987; Gayatri & Livingston, 2006).

5. **Women of child bearing age group**: Valproic acid (avoided due to teratogenicity) (Chaves & Sander, 2005)

6. Severe allergic reactions including Stevens Johnson Syndrome and toxic epidermalnecrolysis are possible with the use of Carbamazepine in certain ethnicities like Asians, especially Han Chinese (Grover & Kukreti, 2014; Jentink et al., 2010).
Therapeutic Drug Monitoring

Physicians may consider Therapeutic Drug Monitoring (TDM) in the following situations (Patsalos et al., 2008):

Please note: Decision to do TDM in a particular patient depends ultimately on the clinical judgement of the treating physician.

1. Once the desired clinical response has been achieved, to establish the “individual therapeutic range.”
2. To assist the clinician in determining the magnitude of a dose increase, particularly with AEDs showing dose-dependent pharmacokinetics (most notably, Phenytoin).
3. When there are uncertainties in the differential diagnosis of signs or symptoms suggestive of concentration-related AED toxicity, or when toxicity is difficult to assess clinically (for example, in young children or in patients with mental disability).
4. When seizures persist despite an apparently adequate dosage.
5. When an alteration in pharmacokinetics (and, consequently, dose requirements) is suspected, due to age-related factors, pregnancy, associated disease, or drug-drug interactions.
6. To assess potential changes in steady state AED concentration when a change in drug formulation is made, including switches involving generic formulations.
7. Whenever there is an unexpected change in clinical response.
8. When poor compliance by the patient is suspected.

Other Blood Tests

There is no evidence to recommend routine blood tests (blood counts and liver enzymes) either before or during AED treatment. In special circumstances depending on the clinical situations, blood tests may be considered (NICE, 2012; Camfield & Camfield, 2006).

Examples of blood tests include:

- Before surgery – (e.g. clotting studies in those on sodium valproate).
- Full blood count, electrolytes, liver enzymes, Vitamin D levels, and other tests of bone metabolism (for example, serum calcium and alkaline phosphatase) every 2–5 years for adults taking enzyme-inducing drugs (e.g. Phenytoin, Phenobarbital, Carbamazepine).
- Asymptomatic minor abnormalities in test results are not necessarily an indication for changes in medication.
- Liver function tests when there is concern of liver injury, particularly in the presence of comorbidities or other therapies that may affect liver health.

Clinical Follow-up of Patients on AED(s)

At each visit, clinician should enquire about the side effects of AED(s).
Discontinuation of AED(s)

There is no strong evidence in the literature to support a specific protocol for AED withdrawal. Hence the physician may use his/her clinical judgement in deciding on AED discontinuation on individual patients. The following suggestions may be helpful in making that decision (Beghi et al., 2013).

1. The decision to continue or withdraw medication should be taken by the patient, their family and/or caregivers as appropriate, and the specialist after a full discussion of the risks and benefits of withdrawal. At the end of the discussion, the patient and their caregivers should understand their risk of seizure recurrence on and off treatment. This discussion should take into account details of the patient's epilepsy syndrome, prognosis and lifestyle.

2. Withdrawal of AEDs must be managed by, or be under the guidance of, a pediatrician, internist or neurologist.

3. Antiepileptic treatment might be discontinued after a minimum period of 1-2 years of seizure freedom; shorter seizure-free period should be discouraged because of a higher risk of relapse.

4. A patient with an abnormal EEG (with or without epileptiform discharges) at the time of treatment discontinuation should be informed of an increased risk of relapse but should not be encouraged to continue treatment if the abnormal EEG is the only negative prognostic predictor. This recommendation should also apply to the presence of EEG epileptiform discharges or specific EEG patterns. Decision to stop treatment should take into consideration the social and personal complications of seizure recurrence.

5. A patient with a documented etiology for his/her seizures should be informed of an increased risk of relapse but should not be encouraged to continue treatment if this is the only negative prognostic predictor.

6. Epilepsy syndrome and its natural history should be always included in the decision process at the time of treatment discontinuation.

7. When AED treatment is being discontinued in a patient who has been seizure free, it should be carried out slowly and one drug should be withdrawn at a time. Particular care should be taken when withdrawing benzodiazepines and barbiturates (may take up to 6 months or longer) because of the possibility of drug-related withdrawal symptoms and/or seizure recurrence.

8. There should be a failsafe plan agreed with patients and their caregivers as appropriate, whereby if seizures recur, the last dose reduction is reversed and medical advice is sought.
V. Patient Education and Counseling

Patient Education

Once a diagnosis of epilepsy is made, patients and their families will have questions concerning this diagnosis and how it will affect their lives. The lack of knowledge increases the level of felt stigma and negative attitudes about the condition (Austin, Carr, & Hermann, 2006). It is the responsibility of the health care provider to ensure that patients and their families are provided with clear, accurate and timely information about their condition and how they can access needed resources as this affects long-term adjustment to the condition (Institute of Medicine [IOM], 2012). Education and counseling needs will vary across the lifespan.

Children and adolescents:
- Managing seizures at school, common learning problems, safety, participation in extracurricular activities
- Dealing with fears (e.g.: future, death, mental health conditions, stigma)
- School and vocational planning
- Establishing healthy habits, drugs, and alcohol
- Transition to adulthood (e.g.: independence, driving, sexuality)
- Impact on family dynamics

Adults:
- Career and vocational concerns
- Discussions with employers
- Driving regulations and transportation concerns
- Sexual and gender-specific topics, such as reproductive health and family planning, hormonal changes and seizure frequency, effects of seizure medications on pregnancy
- Drug-alcohol interactions
- Impact on relationships and family dynamics
- Independent living

Seniors:
- Medication side effects, adverse interactions, and adherence
- Drug-alcohol interactions
- Independent living
- Safety and injury risks
Epilepsy Education Check List

This checklist can be used by both patients and healthcare professionals to ensure that patients and their families have the information they need. Ideally, this information can be shared in a timely manner. The information checklist may be revisited if new concerns develop (IOM, 2012). Healthcare providers may discuss the topics listed below based on their clinical judgement.

**General epilepsy information**
- Definition, seizure types, syndromes, potential causes
- Explanation of investigative procedures
- Prognosis
- Treatment options
- Seizure diary

**Medications**
- Choice of drug
- Side effects
- Compliance
- Drug interactions
- Missed and sudden cessation of medications
- Medication subsidies/drug plans
- Rescue medications

**First Aid**
- General first aid information
- When a seizure is a medical emergency

**Lifestyle**
- Diet
- Exercise
- Sleep
- Alcohol, substance abuse
- Driving regulations
- Employment
- School

**Safety and Risk factors**
- Injury prevention at home and in community
- Sudden Unexpected Death in Epilepsy (SUDEP)
- Medic Alert jewellery

**Possible psychosocial consequences**
- Perceived stigma
- Memory loss
- Depression
- Anxiety
- Sexual difficulties
- Low self-esteem

**Women and Epilepsy Issues**
- Contraception
- Preconception
- Pregnancy and breastfeeding
- Pregnancy registry
- Menopause

**Community Supports**
- Discussion about Community Epilepsy Agency
- Call 1-866-Epilepsy or find list of local agencies at www.epilepsyontario.org
Role of Social Worker

Following discussion with the patient/family, referral to a social worker (where one is available) may be appropriate. The social worker can provide counseling and assist the patient/family with navigating community resources.

Role of Social Worker and Community Epilepsy Agency

Epilepsy is not just a seizure disorder but one that is known to be associated with major psychosocial challenges (Jacob, Baker, Steen, Potts, & Chadwick, 1996). Caregivers and patients report high satisfaction with having someone on the care team that is more accessible and who has the capacity to advocate on their behalf (Scottish Intercollegiate Guidelines Network [SIGN], 2003).

A Community Epilepsy Agency can:
- Provide epilepsy education and first aid training to family, friends, employers and other relevant groups.
- Provide counseling for anxiety/depression, stress management, problem-solving; self-esteem etc.
- Facilitate connection to peer supports and support groups based on needs identified.
- Advocate for patients and their families at schools, workplaces and other community agencies where they are experiencing stigma and discrimination relating to epilepsy.
- Assist patients with accessing and navigating community resources (apply for disability, respite, Trillium Drug Program etc.).

Where there is no local agency, Epilepsy Ontario can provide this support. Contact information of the Community Epilepsy Agencies in Ontario is listed in Appendix 4.
VI. Guideline for Management of Women with Epilepsy with Special Focus on Pregnancy

A management plan for women with epilepsy (WWE) should address issues related to pregnancy, contraception, and menopause. The following information outlines the basic principle of epilepsy management in WWE.

Oral Contraception

In the general population, failure rate of oral contraception (OC) is between <1 to 7 %. There is evidence of increase failure rate in WWE taking enzyme inducing AEDs (such as Phenytoin, Carbamazepine, Phenobarbital), as well as Topiramate (at higher doses than 200mg/day), and Oxcarbazepine. This has been studied particularly well with Carbamazepine (Davis, Westoff, & Stanczyk, 2011). Studies indicate that OC may reduce levels of Lamotrigine. Intrauterine devices do not appear to interact with AEDs.

**Recommendations**

1. Avoid the use of enzyme inducing AEDs, if possible (e.g. Phenytoin, Phenobarbital, Carbamazepine) in WWE using OC, transdermal patch and levonorgestrel implants

Pregnancy

During pregnancy there are risks associated with treatment as well as seizure recurrence. These risks involve the mother (patient) as well as the embryo/fetus.

**Antiepileptic Drugs (AED) during pregnancy (Harden et al., 2009):**

- Exposure to valproate or valproic acid is associated with midline birth defects including spina bifida (6-10%), autism-spectrum disorder, as well as lower verbal IQ in children of mothers exposed during pregnancy.
- There is increased risk of birth defects with polytherapy with AED (when compared with monotherapy).
- There appears to be an associated risk of facial clefts with Topiramate (Hunt et al., 2008; Margulis et al., 2012).
- According to the latest review of the North American Pregnancy Registry, the safest medications appear to be Lamotrigine and Levetiracetam (Margulis et al., 2012) but this may change in the future depending on the findings from different national pregnancy registries.
- Preconceptional folate decreases the risk of midline birth defects and low IQs in the offspring of WWE.
- There is insufficient evidence to determine if the risk of neonatal hemorrhagic complications in the newborns of WWE taking AED are substantially increased (Harden et al., 2009).
- AED levels may decline during pregnancy due to changes in the volume of distribution. This is particularly seen with Lamotrigine and Phenytoin.
Seizure Recurrence

- WWE whose seizures are well controlled are likely to remain seizure-free during pregnancy (84-92%)
- There is some evidence of increased risk of premature contractions and premature labor and delivery in WWE who smoke.
- There is not strong evidence of an increased risk of caesarean delivery in WWE taking AEDs (Harden et al., 2009).

Recommendations
1. Treating physician should aim for seizure freedom prior to pregnancy
2. Simplify regimen to monotherapy at the lowest dose, if possible
3. Use of Folic Acid 1-5 mg/day is highly recommended, starting pre-conceptionally
4. Determine AED levels during each trimester of pregnancy. If possible, obtain two serum concentration levels before pregnancy when the seizures are well controlled. This can be used as a reference range during pregnancy. More frequent monitoring is suggested if the patient has difficult to control seizures or is sensitive to change in dose/concentrations, and with Lamotrigine or Oxcarbazepine (Patsalos et al., 2008)
5. Monitor closely for obstetrical complications
6. Encourage smoking cessation in WWE
7. Use of Vitamin K prior to delivery is not routinely indicated
8. Breastfeeding is not contraindicated

Menopause

There is evidence that the use of enzyme inducing AEDs increase the rate of fractures (Brodie et al., 2013).

Recommendations
1. If possible, avoid enzyme inducing AEDs in persons with epilepsy at risk of osteoporosis
2. Daily use of Vitamin D and Calcium supplements
3. Screening for osteoporosis should be done in those taking enzyme inducing AEDs on a regular basis
VII. Guideline on Referring Patients

From the Emergency Department

- Patients with new onset epileptic seizure(s) should be advised to follow up with their General Practitioner (GP) or Family Physician (FP). If the patient has no GP/FP, referral to a pediatrician/internist (depending on the age of the patient) or neurologist should be made.
- Availability, geographic proximity, and wait time should be considered when choosing the appropriate specialist. Some hospitals have first seizure clinics run by neurologists.
- ED physicians should facilitate an outpatient EEG requisition if a follow up plan has been arranged with the appropriate specialist.
- Patients with an established diagnosis of epilepsy may present to the ED after recurrence of seizures. These patients should be advised to follow up with their GP/FP or specialist.

From General Practitioner/Family Physician

- After the first unprovoked epileptic seizure, patients should be referred for an EEG, and if necessary MRI brain. Patients with abnormalities in the MRI should be referred to a specialist. Availability, geographic proximity, and wait time should be considered when choosing the appropriate specialist.
- Once the diagnosis of epilepsy is established, AED treatment may be initiated by the GP/FP if the physician is comfortable in initiating AED treatment. Otherwise, patient should be referred to a specialist.
- All patients who fail to respond to adequate trial of the first AED should be referred to a neurologist. If the first AED is withdrawn due to side effects, it may not necessarily be concluded that the threshold for adequate trial with the first AED was reached.

From Pediatricians/Internist

- Appropriate investigations (e.g. EEG and if needed MRI) should be arranged before referring the patient to a neurologist.
- All patients who fail to respond to adequate trial of the first AED should be referred to a neurologist. If the first AED is withdrawn due to side effects, it may not necessarily be concluded that the threshold for adequate trial with the first AED was reached.

Referring Patients to Epileptologists

Currently in Ontario there is a delay from time of diagnosis to time of surgery in those who have surgically remediable epilepsy. The longer the medically-refractory epilepsy goes on, the worse the psychosocial and cognitive outcomes are. Therefore, any patient, adult or child, with medically refractory focal seizures is a surgical candidate until proven otherwise. This is especially true for those with lesional medically refractory focal seizures. All patients in Ontario with medically refractory focal seizures should be referred to an epileptologist in a District Epilepsy Centre in order to assess surgical candidacy, sooner rather than later.

More specific indications for referral to an epileptologist are mentioned below:

Adult patients
- All patients with medically refractory epilepsy
• Patients requiring prolonged Video EEG Monitoring in the EMU.
• Epileptologists are available usually only in tertiary care teaching hospitals. If geographical proximity is not an issue, epilepsy in women during pregnancy is ideally managed by an epileptologist. If this is not practical, attempt should be made to obtain one-time clinic consultation or telephone consultation (with on-going communication) with the epileptologist.
• Patients with epilepsy can be referred to an epileptologist by a physician based on his/her clinical judgment, even if the epilepsy is not medically refractory.

Pediatric Patients
• All patients who are potential surgical candidates
• All patients who require diet therapy for epilepsy
• If geographical proximity is not an issue, all patients with medically refractory epilepsy should be evaluated by an epileptologist at least once to ensure diagnostic accuracy, appropriate work up, correct medications, and to determine surgical candidacy. If this is not practical, attempt should be made to obtain telephone consultation (with on-going communication) with the epileptologist.
• Patients with epilepsy can be referred to an epileptologist by a physician based on his/her clinical judgment, even if the epilepsy is not medically refractory.

Model for Co-management

Co-management of patients by GP/FP and the neurologists: Patients who do not need to be followed by the neurologists after the initial consultation are followed by the GP/FP for implementing the neurologist’s recommendations, prescription renewal and follow up assessment as outlined in the ‘guideline on follow up’. GP/FP may request re-assessment by the neurologist, if needed.

Co-management of patients by pediatrician/internist and the neurologists: Patients who do not need to be followed by the neurologists after the initial consultation are followed by the internist/pediatrician for implementing the neurologist’s recommendations, prescription renewal and follow up assessment as outlined in the ‘guidelines on follow up’ below. Pediatrician/internist may request re-assessment by the neurologist, if needed.

Co-management by Nurse Practitioners: In a primary care setting, NPs play a vital role in co-managing patients with epilepsy. It is recommended that NPs initiate the first AED only in consultation with the GP/FP. EEG and MRI brain are requested by the GP/FP as outlined in this document. After the initial specialist consultation, those who do not need to be followed by the specialist on a regular basis may be followed by the NPs for implementing the specialist’s recommendations, prescription renewal within the scope of practice and follow up assessment as outlined in the ‘guideline on follow up’ below.

In a hospital setting where NP is part of a healthcare team that includes specialist, a co-management model with the specialist should be developed where the role of NP is clearly outlined. All AED management should be performed under the supervision of the specialist.
VIII. Guidelines on Follow-up

Patients Without Prolonged Seizure Free Period

During follow up, enquiry should be made regarding new seizure types, efficacy and side effects of AEDs, and in children, impact on growth and development. Based on new clinical information including results of investigation(s), diagnosis and management plan may have to be changed.

In the first year of life, infants should be seen every 3 months for assessment of their growth and development for the following reasons:
  • To assess the neurodevelopmental progress
  • To adjust their medication dose for growth, if required

Age 1 year to 12 years, toddlers and children should be reviewed every 3-6 months for the following reasons:
  • To assess the developmental progress
  • To discuss the school performance
  • To discuss risks of seizures while engaged in water sports, bathing etc.

Age 13-17 teens can be reviewed every 6-12 months:
  • To readjust medication need at the onset of puberty, if required
  • To discuss the effect of alcohol on epilepsy threshold
  • To discuss pregnancy planning need in teenage girls with epilepsy
  • To discuss driving laws as applicable to epilepsy
  • To discuss transition to adult care

Adults with epilepsy can be reviewed every 3-6 months:
  • To adjust medication for side effects/ poor seizure control
  • To assess social adjustment and offer counseling in patients experiencing difficulty/discrimination
  • To review seizure control during pregnancy

At all ages, patients with breakthrough seizures should have access to epilepsy care and communication with their treating physician/NP for advice on seizure management and assessment of medication compliance.

Patients After Prolonged Seizure Free Interval

In general, patients who have been seizure free for one-two years or more should be reassessed for the need for continuation or discontinuation of AED.
IX. Guidelines on Co-morbidities

Co-morbidity refers to the co-occurrence of two conditions with a greater frequency than found in the general population. This does not infer a causal relationship.

Relevance to Epilepsy:
Co-morbid conditions are common in people with epilepsy, and their presence has important implications for diagnosis, treatment, medical costs and quality of life. Co-morbid conditions in epilepsy are found across the lifespan, and include medical, psychiatric and cognitive conditions alone or in combination. Co-morbid conditions with significantly higher rates in patients with epilepsy than the general population:

Medical
- Musculoskeletal system disorders
- Gastrointestinal and digestive disorders
- Respiratory system disorders
- Chronic pain disorders
- Cerebrovascular accidents
- Migraine
- Neoplasia
- Arthritis/rheumatism
- Obesity
- Diabetes
- Infections
- Fractures
- Allergies
- Alcoholism
- Drug abuse

Psychiatric
- Depression
- Anxiety
- Autism spectrum disorders
- Interictal dysphoric disorder
- Interictal behavior syndrome
- Psychosis of epilepsy

Cognitive
- Attention-deficit hyperactivity disorder
- Learning disability
- Intellectual Development Disorder
- Alzheimer’s disease/dementia

Anxiety: The prevalence of various forms of anxiety is very high among persons with epilepsy, ranging from 19-60% (Jones et al., 2005). Panic disorder, generalized anxiety disorder, phobias and obsessive compulsive disorders are all increased in persons with epilepsy (Beyenburg et al., 2005). Focal epilepsies, associated with the temporal lobe have a stronger association than other seizure types. The effects of anxiety on quality of life are substantial and separate from the effects of depression (Cramer, Brandenburg, & Xu, 2005).

Patients with epilepsy should be screened for symptoms of anxiety. The diagnosis and management of anxiety disorders should be incorporated into the patient’s treatment plan. Patients should be referred to neuropsychiatry/psychiatry or a clinical psychologist, as appropriate.

Depression: Depression is increased in people with epilepsy, with a lifetime prevalence of about 30% (Tellez-Zenteno, Patten, Jette, Williams, & Wiebe, 2007). Despite the frequency and significance of depression in persons with epilepsy, it remains underdiagnosed and undertreated (Barry, Ettinger, & Friel, 2008).
Screening for depression using the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), Patient Health Questionnaire (PHQ-2), or equivalent tool should ideally be undertaken for all patients (adults and adolescents aged 13-17 years) with epilepsy by their primary care physicians or specialists. This screening should be conducted soon after the diagnosis, and thereafter on an annual basis (Kerr et al, 2011). Use of antidepressant drugs is safe in patients with epilepsy when used at therapeutic doses. Anti-depressant drugs of the SSRI or SNRI families are the first line of therapy in depressive disorders (Kanner, 2013). Non-pharmacological approaches such as cognitive behavioural therapy may also be appropriate (Dobson, 1989). Patients who are depressed should be treated or referred appropriately for treatment.

Please see Appendix 5 for a list and description of some of the co-morbidities associated with epilepsy other than anxiety and depression.
References


Provincial Guidelines for the Management of Epilepsy in Adults and Children


## Appendix 1: Epilepsy Implementation Task Force Membership

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<td>Dr. Carter Snead (Co-Chair)</td>
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<td>The Hospital for Sick Children</td>
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<tr>
<td>Brenda Flaherty (Co-Chair)</td>
<td>Executive Vice President &amp; Chief Operating Officer</td>
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<td>Dr. Jorge Burneo</td>
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<td>London Health Sciences Centre</td>
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<td>Vice President Clinical Programs/CNO</td>
<td>Health Sciences North</td>
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<tr>
<td>Janet Newton</td>
<td>Clinical Director</td>
<td>University Health Network</td>
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<tr>
<td>Kirk Nylen</td>
<td>Director, Outreach</td>
<td>Ontario Brain Institute</td>
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<tr>
<td>Dr. Rajesh RamachandranNair</td>
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<td>McMaster Children’s Hospital / HHS</td>
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<tr>
<td>Mary Secco</td>
<td>Director of Strategic Initiatives</td>
<td>The Epilepsy Support Centre, London</td>
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<tr>
<td>Dr. Laurene Sellers</td>
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<td>Dr. Michelle Shapiro</td>
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<td>Rosie Smith</td>
<td>Director of Adult Services</td>
<td>Epilepsy Toronto</td>
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<td>Mike Tierney</td>
<td>VP Clinical Programs</td>
<td>The Ottawa Hospital</td>
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<tr>
<td>Dr. Taufik Valiante</td>
<td>Adult Neurosurgeon</td>
<td>University Health Network</td>
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<tr>
<td>Dr. Sharon Whiting</td>
<td>Paediatric Neurologist</td>
<td>Children’s Hospital of Eastern Ontario</td>
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</table>
Appendix 2: Examples of Electroclinical Syndrome Arranged by Age at Onset

Neonatal period
- Benign familial neonatal epilepsy (BFNE)
- Early myoclonic encephalopathy (EME)
- Ohtahara syndrome

Infancy
- Epilepsy of infancy with migrating focal seizures
- West syndrome
- Myoclonic epilepsy in infancy (MEI)
- Benign infantile epilepsy
- Benign familial infantile epilepsy
- Dravet syndrome
- Myoclonic encephalopathy in nonprogressive disorders

Childhood
- Febrile seizures plus (FS+) (can start in infancy)
- Panayiotopoulos syndrome
- Epilepsy with myoclonic atonic (previously astatic) seizures
- Benign epilepsy with centrotemporal spikes (BECTS)
- Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
- Late onset childhood occipital epilepsy (Gastaut type)
- Epilepsy with myoclonic absences
- Lennox-Gastaut syndrome
- Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)
- Landau-Kleffner syndrome (LKS)
- Childhood absence epilepsy (CAE)

Adolescence – Adult
- Juvenile absence epilepsy (JAE)
- Juvenile myoclonic epilepsy (JME)
- Epilepsy with generalized tonic–clonic seizures alone
- Progressive myoclonus epilepsies (PME)
- Autosomal dominant epilepsy with auditory features (ADEAF)
- Other familial temporal lobe epilepsies

Less specific age relationship
- Familial focal epilepsy with variable foci (childhood to adult)
- Reflex epilepsies

(Berg et al, 2010)
Appendix 3: Outline for Seizure Assessment

Features of a seizure (Hirtz et al, 2000; Krumholz et al, 2007)

Associated factors
- Age
- Family history
- Developmental status
- Behavior
- Health at seizure onset
- Precipitating events other than illness—trauma, toxins

First Nonfebrile Seizure
- Health at seizure onset—febrile, ill, exposed to illness, complaints of not feeling well, sleep deprived
- Symptoms during seizure (ictal)
- Aura: Subjective sensations
- Behavior: Mood or behavioral changes before the seizure
- Preictal symptoms: Described by patient or witnessed
- Vocal: Cry or gasp, slurring of words, garbled speech
- Motor: Head or eye turning, eye deviation, posturing, jerking (rhythmic), stiffening, automatisms (purposeless repetitive movements such as picking at clothing, lip smacking); generalized or focal movements
- Respiration: Change in breathing pattern, cessation of breathing, cyanosis
- Autonomic: Pupillary dilatation, drooling, change in respiratory or heart rate, incontinence, pallor, vomiting
- Loss of consciousness or inability to understand or speak
- Duration of seizure

Symptoms following seizure (postictal)
- Amnesia for events
- Confusion
- Lethargy
- Sleepiness
- Headaches and muscle aches
- Transient focal weakness (Todd’s paresis)
- Nausea or vomiting
## Appendix 4: Ontario Epilepsy Community Agencies

1-866-EPILEPSY (1-866-374-5377)

<table>
<thead>
<tr>
<th>Agency Name</th>
<th>Address</th>
<th>Phone</th>
<th>Fax</th>
<th>Email</th>
<th>Website</th>
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</thead>
<tbody>
<tr>
<td><strong>Chatham Kent Epilepsy Support Centre</strong></td>
<td>690 Hale Street, London, Ontario, N5W 1H4</td>
<td>(519) 365-5131</td>
<td>(519) 433-4079</td>
<td><a href="mailto:epilepsychatham@epilepsysupport.ca">epilepsychatham@epilepsysupport.ca</a></td>
<td><a href="http://www.epilepsysupport.ca">www.epilepsysupport.ca</a></td>
</tr>
<tr>
<td><strong>Epilepsy Durham Region</strong></td>
<td>310 Byron Street South, Unit 3, Whitby, Ontario L1N 4P8</td>
<td>(905) 430-3090</td>
<td>(905) 430-3080</td>
<td><a href="mailto:support@epilepsydurham.com">support@epilepsydurham.com</a></td>
<td><a href="http://www.epilepsydurham.com">www.epilepsydurham.com</a></td>
</tr>
<tr>
<td><strong>Epilepsy Halton Peel Hamilton</strong></td>
<td>2160 Dunwin Drive, Unit 4, Mississauga, L5S 5M8</td>
<td>(905) 450-1900</td>
<td></td>
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<tr>
<td><strong>Epilepsy &amp; Seizure Disorder Resource Centre of South Eastern Ontario</strong></td>
<td>100 Stuart Street, Kingston, Ontario K7L 2V6</td>
<td>(613) 542-6222</td>
<td>(613) 548-4162</td>
<td><a href="mailto:admin@epilepsyresource.org">admin@epilepsyresource.org</a></td>
<td><a href="http://www.epilepsyresource.org">www.epilepsyresource.org</a></td>
</tr>
<tr>
<td><strong>Sarnia Lambton Epilepsy Support Centre</strong></td>
<td>690 Hale Street, London, Ontario, N5W 1H4</td>
<td>(519) 330-0416</td>
<td></td>
<td><a href="mailto:epilepsysarnia@epilepsysupport.ca">epilepsysarnia@epilepsysupport.ca</a></td>
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<tr>
<td><strong>London &amp; Area Epilepsy Support Centre</strong></td>
<td>690 Hale Street, London, Ontario, N5W 1H4</td>
<td>(519) 433-4073</td>
<td></td>
<td><a href="mailto:support@epilepsysupport.ca">support@epilepsysupport.ca</a></td>
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<tr>
<td><strong>Epilepsy Niagara</strong></td>
<td>7555 Montrose Road, Niagara Falls, Ontario L2H 2E9</td>
<td>(289) 929-5811</td>
<td>(866) 293-6300</td>
<td><a href="mailto:info@epilepsyniagara.org">info@epilepsyniagara.org</a></td>
<td><a href="http://www.epilepsyniagara.org">www.epilepsyniagara.org</a></td>
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<tr>
<td><strong>Epilepsy Ontario</strong></td>
<td>3100 Steeles Avenue East, Suite 803, Markham, ON L3R 8T3</td>
<td>(905)-474-9696</td>
<td>(905)-474-3663</td>
<td><a href="mailto:info@epilepsyontario.org">info@epilepsyontario.org</a></td>
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<tr>
<td><strong>Epilepsy Ottawa-Carleton</strong></td>
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<td>(613) 594-9255</td>
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<td><a href="mailto:info@epilepsyottawa.ca">info@epilepsyottawa.ca</a></td>
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<td><strong>Epilepsy Peterborough</strong></td>
<td>Unit 4, Charlotte Mews, 203 Simcoe Street, Peterborough, Ontario</td>
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<td><strong>Epilepsy Simcoe County</strong></td>
<td><strong>Timmins Seizure &amp; Brain Injury Centre</strong></td>
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<td>72 Ross Street, Unit 10, Barrie Ontario L4N 1G3</td>
<td>733 Ross Ave. East, Timmins, Ontario P4N 8S8</td>
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<tr>
<td><strong>Tel:</strong> (705) 737-3132</td>
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<td><strong>Fax:</strong> (705) 737-5045</td>
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<th><strong>Epilepsy Waterloo Wellington</strong></th>
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Appendix 5: Description of Some of the Co-morbidities Associated with Epilepsy

**ADHD:** Attention-deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder with prevalence in the general population of 5-7%. The prevalence is increased to 20-30% in children with epilepsy. If co-morbid ADHD occurs independent of seizure effect, specific ADHD treatment should be initiated (Brown, Becker, Pollard, & Anderson, 2013).

**Alcohol:** Alcohol is often associated with seizures due to alcohol withdrawal. These are most often generalized tonic-clonic seizures occurring within 6-48 hours after cessation of alcohol use. These seizures are provoked and are therefore not considered to be part of a definition of epilepsy. These types of seizures should not be treated with long-term administration of anti-epileptic drugs. The EEGs in these patients are usually normal. It is important to note, however, that alcoholic patients may have confounding causes for seizures and epilepsy including head trauma, subdural hematoma, stroke, abscess, meningitis and metabolic derangements. In cases of structural causes for epilepsy in these patients, long-term administration of anti-epileptic drugs would be appropriate. Poor compliance, drug overuse, and drug-alcohol interactions may be issues. In all patients with alcoholism, the treatment of alcohol dependence is extremely important (Shapiro & Cole, 2011; Gilhus, Barnes, & Brainin, 2011).

**Autism Spectrum Disorder:** Epilepsy and autism are co-morbid phenomena and may be related to a common brain abnormality. Epilepsy occurs in 10-30% of individuals with autism, with a higher incidence in girls. EEG is not recommended routinely in children with autism (American Academy of Neurology and the Child Neurology Society, 2000).

**Intellectual Developmental Disorder/Intellectual Disability (ID):** Estimates of the prevalence of epilepsy among patients with an intellectual disability range from 14% to 44%, a significant excess compared with the general population (Bowley & Kerr, 2000). Risk of potential behavioral side effects should be considered when prescribing AED to patients with ID and epilepsy. Healthcare professionals and or community epilepsy agencies should play an active role to help the patient and caregiver obtain appropriate support and services within the educational system, work place and community.

**Migraine:** The prevalence of migraine in populations of individuals with epilepsy is estimated at 8–24%, approximately twice that in the normal population (Rogawski, 2012). Children with migraine may have an increased incidence of epilepsy. In many cases it may be beneficial to treat the two conditions with the same medications. There is extensive evidence from randomized controlled clinical trials that divalproex sodium (valproate) and topiramate are effective in preventing migraine attacks (Rogawski, 2012).

**Neoplasia:** Seizures and epilepsy are common in people with brain tumors. They are particularly common with slow-growing gliomas, meningiomas located in the convexity of the brain, and with metastatic brain tumors. These patients present a complex therapeutic profile and the choice of antiepileptic drugs is challenging because brain tumor-related epilepsy (BTRE) is often drug-resistant and has a strong impact on quality of life. In brain tumour patients, the presence of epilepsy is considered the most important risk factor for long-term disability. In BTRE, AEDs with fewer drug interactions and fewer side effects are preferred (Maschio, 2012).
Obesity: Obesity is a common co-morbidity for adults and children with epilepsy (Janousek, Barber, Goldman, & Klein, 2013; Daniels, Nick, Lui, Cassidy, Glauser, 2009). Since obesity has a number of concomitant health risks, it is suggested that all patients with epilepsy and obesity be appropriately referred for treatment/weight loss. This can be done through the patient's primary care physician. With regards to epilepsy, the choice of medication for a given patient may well be influenced by this co-morbidity as a number of anti-seizure medications including valproic acid, carbamazepine, gabapentin, and vigabatrin are known to be associated with weight gain. In addition, some medications including topiramate are associated with weight loss (Biton, 2006).

Osteoporosis/Fractures: Treatment with various antiepileptic drugs including phenytoin, carbamazepine, phenobarbital, and valproic acid have been implicated in decreased bone mineral density. While rates from 20-75% have been reported in cross-sectional studies (Pack, 2003; Petty, O’Brien, & Wark, 2007) precise prevalence rates are not known (Lado, Spiegel, Masur, Boro, & Haut, 2008). There is also an increased risk of fracture among patients with epilepsy, with twice the increased risk of pathological fracture compared to the general population. This is likely at least in part due to higher rates of decreased bone mineral density in these patients. Screening for osteopenia and osteoporosis is recommended for patients receiving treatment with antiepileptic drugs (Herman, 2009). The standard screening tool is the dual energy x-ray absorptiometry (DEXA) scan.

Stroke: Stroke is the most common cause of epilepsy in patients 65 years old and over, the group with the highest incidence of epilepsy overall (Wallace, Shorvon, & Tallis, 1998; Bergey, 2004). It can, however, be a cause of epilepsy in patients of all ages. In older patients, stroke should always be sought as a potential cause of new onset seizures/epilepsy. In patients of all ages with presumed structural causes of seizures/epilepsy, stroke should be sought as a potential cause. Epilepsy caused by stroke is more common in hemorrhagic stroke and venous sinus thrombosis. However, there is no strong evidence for the role for seizure prophylaxis with medication in these cases, when acute head trauma is not also incurred (Herman, 2011). When choosing a medication, tolerability, cost, and potential interactions with other drugs should be considered (Bergey, 2004; Bleck, 2012; Herman, 2011).