These guidelines have been withdrawn

MOH clinical practice guidelines are considered withdrawn five years after publication unless otherwise specified in individual guidelines. Users should keep in mind that evidence-based guidelines are only as current as the evidence that supports them and new evidence can supersede recommendations made in the guidelines.
# Levels of evidence and grades of recommendation

## Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.</td>
</tr>
<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.</td>
</tr>
<tr>
<td>1-</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>2++</td>
<td>High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.</td>
</tr>
<tr>
<td>2+</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal.</td>
</tr>
<tr>
<td>2-</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
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<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, case series</td>
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<td>Expert opinion</td>
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## Grades of recommendation

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<th>Grade</th>
<th>Recommendation</th>
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<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review of RCTs, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+</td>
</tr>
<tr>
<td>GPP (good practice points)</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
</tr>
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</table>
Epilepsy in Adults
Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
Foreword

Epilepsy is one of the more serious yet treatable neurological disorders, affecting over 50 millions people worldwide. An estimated 20 million new cases occur each year globally. If properly treated, about 70-80% people with epilepsy could lead normal lives. According to an estimate by the Singapore Epileptic Foundation, based on the prevalence of epilepsy in most developed countries, Singapore has more than 20,000 people with epilepsy.

The MOH Guidelines for the *Diagnosis and Management of Epilepsy in Adults* in Singapore were first drawn up by the National Committee on the Neuroscience in 1999. Since then, more facts about this important condition have emerged and it is timely to issue a new edition of these guidelines. Important changes in this new edition include an update on classification, diagnosis and management of epilepsy. Cost-effectiveness is an important factor which is also considered by the workgroup in making recommendations.

I hope that all medical practitioners will find this set of guidelines useful in the management of patents with epilepsy.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES
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3 Initial treatment
   1. When should treatment with anti-epileptic drug(s) be initiated?
   2. What initial anti-epileptic drug should be chosen? What are the considerations pertaining to women, children and the elderly?
   3. What practical advice can be given to individuals with epilepsy and their carers?
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      (b) First-aid
      (c) Home and workplace safety
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4 Emergency treatment for seizure/prolonged seizure at the primary care setting
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Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

Diagnosis

**GPP** The following paroxysmal events may be mistaken for seizures and a primary physician should be aware of them so that he could consult the appropriate specialist, if necessary.

Patient presents with loss of awareness:
- Transient cardiac arrhythmia
- Transient ischaemic attacks
- Hypoglycemia
- Panic attacks

Patient presents with abnormal movement:
- Movement disorders in sleep and wake.
- Tremor or paroxysmal choreoathetosis or dystonia.
- Drop attacks and cataplexy.

(Gr 14)

**GPP** Individuals requiring an Electroencephalogram (EEG) should have the test performed soon after the attack. The earlier the EEG is performed, the more likely a helpful result will emerge from the EEG.

**D** EEG should be performed to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin.

**D** An EEG should not be performed in the case of probable syncope because of the possibility of a false positive result.

**D** EEG should not be used in isolation to make a diagnosis of epilepsy because it can be falsely positive.
Repeated EEG may be helpful when the diagnosis of epilepsy is unclear. When a standard EEG has not contributed to diagnosis or classification, a sleep EEG should be performed (pg 15).

Grade D, Level 3

Long-term video or ambulatory EEG may be used in the assessment of individuals who present diagnostic difficulties after clinical assessment and standard EEG (pg 15).

Grade C, Level 2+

Photic stimulation and hyperventilation should be a part of standard EEG assessment (pg 15).

Grade D, Level 3

Electrocardiogram (ECG) should be performed in the assessment of all patients with altered consciousness, particularly in the older age group when cardiac arrhythmias can simulate epilepsy (pg 15).

Grade D, Level 3

Routine blood studies are indicated to identify common metabolic causes of seizure such as abnormalities in electrolytes, glucose, calcium, magnesium, hepatic and renal diseases. Screening for toxins is sometimes done. Lumbar puncture is necessary when meningitis or encephalitis is suspected (pg 15).

GPP

Magnetic resonance imaging (MRI) is the imaging of choice in patients with epilepsy and is particularly useful in those:

- who have suggestions of a focal seizure onset from history, examination or EEG.
- in whom seizures continue in spite of first line medication.

(pg 16)

Grade D, Level 4

Computed tomography (CT) scan has a role in the urgent assessment of seizures or when MRI is contraindicated (pg 16).

Grade D, Level 4

Brain imaging is not routinely required when there is a confident diagnosis of idiopathic generalised epilepsy and if there is rapid and complete response to the first line antiepileptic drugs (pg 16).

Grade D, Level 4
**Initial Treatment**

D Before making the decision to start antiepileptic drugs after a first unprovoked seizure, it is important to verify that the patient has had only one unprovoked seizure, and to confirm that there is no prior history of absence or myoclonic seizures, or partial seizures (pg 17).

*Grade D, Level 4*

D The decision to start antiepileptic drugs after a first unprovoked seizure is based on the risk of seizure recurrence. Early treatment with antiepileptic drugs after a first seizure approximately halves the recurrence risk but does not alter the long-term prognosis of the epilepsy. The decision to treat is made on individually tailored basis (pg 17).

*Grade D, Level 4*

D The overall risk of a second seizure occurring after a first unprovoked seizure ranges between 27-52%. However, this is an overall estimate and the recurrence risk of another seizure after a first unprovoked seizure increases to over 80% in the presence of (1) epileptiform abnormalities on the EEG, (2) a neurological deficit, and (3) a structural abnormality in the brain. Antiepileptic drugs therefore should be offered to the patient in these 3 circumstances (pg 17).

*Grade D, Level 4*

D Antiepileptic drugs should also be considered if the patient or his/her carers consider the risk of a recurrent seizure unacceptable (pg 17).

*Grade D, Level 4*

D Starting antiepileptic drug treatment is often not a straightforward decision, and the decision should be made jointly with the patient (or his/her caregiver) after explaining the risks and benefits and after assessing his/her preferences. In other words, the decision should be individualized (pg 17).

*Grade D, Level 4*

B The risk of seizure recurrence after 2 unprovoked seizures is 73%. Antiepileptic drugs therefore should be offered to the patient after explaining the risks and benefits and after assessing his/her preferences (pg 18).

*Grade B, Level 2**
Antiepileptic drug treatment strategy should be individualised according to the seizure type, epilepsy syndrome, co-medication, co-morbidity and the individual's lifestyle and preferences (and/or those of their family and/or carers as appropriate) (pg 18).

Grade A, Level 1++

Patients should be commenced on monotherapy initially. Should the patient develop an adverse reaction to the initial drug or if the initial monotherapy is unsuccessful, monotherapy using another drug should be tried (pg 18).

Grade A, Level 1++

All antiepileptic drugs licensed for monotherapy have similar efficacy in newly diagnosed epilepsy. For this reason, the medicine the prescribing physicians are most familiar with can be used (pg 18).

Grade A, Level 1++

Carbamazepine, phenytoin and sodium valproate can be considered first line treatments for newly diagnosed partial and generalized tonic-clonic seizures (pg 18).

Grade A, Level 1+

Sodium valproate, lamotrigine and clonazepam may be prescribed for absence and myoclonic seizures (pg 18).

Grade A, Level 1++

Newer antiepileptic medications (gabapentin, lamotrigine, topiramate, levetiracetam, tiagabine, zonisamide, oxcarbazepine) are recommended as add-on medications for the treatment of individuals who have suboptimal treatment response to the older medications (phenytoin, carbamazepine, sodium valproate, phenobarbitone, clonazepam, clobazam) or as monotherapy (lamotrigine, topiramate) in individuals whom the older medications are unsuitable (adverse drug reactions, intolerable side effects, multiple drug interactions to concomitant medications) (pg 19).

Grade A, Level 1++

For women of childbearing age or who are pregnant, the appropriate antiepileptic monotherapy at the lowest dose to control seizures is recommended (pg 19).

Grade C, Level 2++
A Folate supplementation is recommended for women of childbearing age on antiepileptic treatment to prevent neural tube defects. Folic acid, 5 mg per day, should be given in these women from pre-conception till the first trimester of pregnancy (pg 19).

Grade A, Level 1**

GPP Seizure precautions - people with epilepsy and their carers should be educated that the following are associated with increased risk for breakthrough seizures:

a) Non-compliance to antiepileptic medication or drug interactions with antiepileptic medications lowering blood levels of antiepileptic drugs.
b) Alcohol abuse.
c) Sleep deprivation.
d) Concurrent illness.

(pg 19)

GPP Seizure first-aid:

a) Place the seizing individual in recovery position or on his/her side.
b) Remove surrounding objects that may harm the individual.
c) Do not place any object in the individual's mouth.
d) Call for an ambulance in the event of injury during seizure, prolonged seizure (>5 minutes), or seizure clustering without return to individual's baseline state.

(pg 19)

GPP Home and workplace safety:

a) Minimise exposure to open fires and sharp instruments. Microwave ovens, blenders are options to consider.
b) Refrain from soaking in baths over extended periods of time or locking toilet doors; showers should be preferred over baths..
c) Operation of heavy machinery is discouraged.

(pg 20)

Grade D, Level 4

D Antiepileptic drugs are not a contraindication for women to breastfeed. All breastfeeding mothers on antiepileptic drugs should be encouraged to breastfeed and receive support from relevant healthcare personnel (pg 20).

Grade D, Level 4
Women with epilepsy should be referred to specialist care for pre-conception counseling as indicated (pg 20).

**D Immediate management of seizure**

- Remove hazards from the immediate surroundings.
- Protect the patient from falling unsupported to the ground or striking objects.
- Position the patient on their side, with the head supported in a neutral in-line position.
  - Protect the head and other parts of the body from striking objects but do not restrain the patient.
- Establish Airway, Breathing and Circulation (ABC) and administer high concentration oxygen.
- Observe and record the pattern of the seizure(s).
- Note and record the duration of the seizure(s).
- Do not force anything, including your fingers, into the person's mouth. This may cause injuries such as chipped teeth or a fractured jaw. You could also get bitten.

( pg 21)

**Grade D, Level 4**

If the clinical scenario is suggestive of hypoglycaemia, capillary blood glucose level should be checked. With confirmed hypoglycaemia, the patient should be treated with 50 ml of Dextrose 50%. In the setting of malnutrition or suspected ethanol abuse, 100 mg thiamine may also be given as an intravenous push (pg 21).

**D When convulsive seizures continue beyond 5 minutes, pharmacotherapy to abort the seizure is recommended (pg 22).**

**Grade D, Level 4**

Intravenous diazepam and lorazepam are effective first line treatments for prolonged seizures in the community (pg 22).

**Grade A, Level 1**

Initially a dose of 5-10 mg diazepam is given either intravenously or rectally. If there is no response, the same dose can be repeated after 10 minutes. Respiratory or circulatory effects should be monitored for and usually come into effect with doses greater than 20 mg (pg 22).

**Grade D, Level 4**
Emergency medical services (EMS) should be activated if:

- Seizures continue beyond 5 minutes.
- Cardio-respiratory complications from treatment develop and there are no adequate conditions for monitoring the patient's condition.
- There is suspected fracture or central nervous system injury from the seizure.

Follow-on Treatment and Management

Antiepileptic drug levels may help clinical management under the following clinical indications: (1) assessment of compliance to drug treatment for patients with refractory epilepsy (2) assessment of symptoms due to possible antiepileptic drug toxicity (3) titration of phenytoin dose. Routine checking of antiepileptic drug levels without a clear clinical indication is not required, and is not cost-effective.

Depending on clinical suspicion of other differential diagnoses, blood tests such as blood glucose, urea, electrolytes, liver function tests and serum calcium may be indicated.

Before commencing multiple antiepileptic drug therapy, monotherapy involving two of the standard drugs (phenytoin, carbamazepine, sodium valproate) should have been tried. When two of these antiepileptic drugs have failed as monotherapy, the chance of seizure-freedom with further monotherapy is very low.

If acceptable seizure control is not achieved with monotherapy using phenytoin, sodium valproate or carbamazepine: add sodium valproate to carbamazepine or phenytoin, add carbamazepine or phenytoin to sodium valproate.

A systematic review has confirmed the efficacy and tolerability of the newer antiepileptics vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine, oxcarbazepine and levetiracetam. All may be used as adjunctive therapy for patients with drug-resistant, focal epilepsy.
Although newer antiepileptic drugs (gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate) have been shown to be effective, there is little good quality evidence from clinical trials supporting their superiority as adjunctive therapy over older drugs (pg 24).

Grade A, Level 1

If trials of combination therapy do not confer benefit, treatment should revert to the regimen (monotherapy or combination therapy) that has proven most acceptable to the individual, in terms of providing the best balance between effectiveness in reducing seizure frequency and tolerability of side effects (pg 24).

Grade D, Level 3

Changing the formulation or brand of antiepileptic drugs is not recommended because different preparations may vary in bioavailability or have different pharmacokinetic profiles and, thus, increased potential for reduced effect or excessive side effects (pg 24).

Grade D, Level 3

Lamotrigine, topiramate, levetiracetam and sodium valproate have a wide spectrum of activity for most types of generalised seizures. Although there is no published evidence of an "add-on" effect of these drugs in generalised epilepsies, this is supported by circumstantial evidence. Any one of these drugs can be added to a standard antiepileptic drug (phenytoin, carbamazepine, sodium valproate) (pg 25).

Grade D, Level 4

Addition of a third antiepileptic may be worth trying if an encouraging but sub-optimal effect is obtained with a particular combination of two drugs (pg 25).

Grade D, Level 4

All individuals with a first-onset suspected seizure should be evaluated by a specialist who has experience in epilepsy. This is to ensure accurate and early diagnosis, and initiation of appropriate therapy. Subsequent follow-up can be carried out by a general practitioner (pg 25).

GPP

Withdrawal of antiepileptic drugs can be explored at the end of at least a two-year seizure-free period, after a discussion on the potential risks and benefits (pg 25).

Grade A, Level 1
A The decision to withdraw treatment should be individualised, taking into account lifestyle issues and a clear plan agreed upon should the seizures recur (pg 26).

*Grade A, Level 1*+

D A repeat EEG prior to initiation of drug withdrawal is not routinely required (pg 26).

*Grade D, Level 4*

D Withdrawal of treatment should be a gradual process. There is no clear evidence for the length of the withdrawal period although most specialists would advocate a period of few months. Patients on polytherapy should have only one drug withdrawn at a time (pg 26).

*Grade D, Level 4*

D Patients on benzodiazepines or barbiturates should have these medications reduced over a longer time-course (up to 6 months or longer) (pg 26).

*Grade D, Level 4*

A Vagus nerve stimulation is indicated for adjunctive therapy and has been shown to reduce frequency of seizures in adults refractory to antiepileptic medication who are not suitable for epilepsy surgery. This includes adults whose epileptic disorder is dominated by partial seizures (with or without secondary generalisation) or generalised seizures (pg 26).

*Grade A, Level 1*+

A Complementary treatment such as acupuncture, chiropractic, herbal medicine, homeopathy, osteopathy and yoga should not be advised to the epileptic patient (pg 27).

*Grade A, Level 1*+

D Patients should be asked if they are using any complementary medicines and warned about the possibility of adverse effects. Problems may arise with the use of some herbal medicines because of interaction with prescribed medication. The potential reduction of the plasma concentrations of carbamazepine and phenytoin should be noted if St John's Wort is used concomitantly. Caution is also advised in the use of evening primrose oil but the evidence for this is less robust (pg 27).

*Grade D, Level 4*
Some aromatherapy preparations (e.g. hyssop, rosemary, sweet fennel, sage and wormwood) may have an alerting effect on the brain and so may exacerbate seizures (pg 27).

**Grade D, Level 4**

The ketogenic diet is not recommended for adults with epilepsy. There is no evidence of a worthwhile therapeutic effect. In addition, compared to children, in adults, it is difficult for dietary measures to result in great enough ketogenicity (pg 27).

**Grade D, Level 4**

There is evidence that control of precipitating factors (emotional stress, sleep deprivation) may help better control seizures. This can only be recommended in addition to pharmacological treatments (pg 27).

**Grade C, Level 2**
1 Guideline development and objectives

1.1 Guideline development

This second set of clinical practice guidelines on adult epilepsy differs from the first guidelines published in 1999 in that it is tailored towards the busy general physician in need of a quick "easy-to-read" reference.

The format of the guidelines is designed to be as user friendly as possible and therefore presented in the format of "frequently asked questions" concerning seizures in the adult. The guidelines are not meant to be comprehensive but rather enable the physician to make evidence based decisions on frequently encountered questions.

The recommendations include and are often similar to those of other guidelines on adult epilepsy: The Scottish Intercollegiate Guidelines Network (SIGN) guidelines on Diagnosis and management of epilepsy in adults,1 NICE guidelines on diagnosis and management of epilepsy in adults and children in primary and secondary care,2 Epilepsy Frequently Asked Questions. The present revision was undertaken by a group of neurologists from both public and private institutions as well as a family physician.

1.2 Objectives

The main aim of these guidelines is to help general practitioners address frequently encountered and important issues on epilepsy in adults on the topics of diagnosis, treatment and other aspects of management.

1.3 Target group

These guidelines are mainly developed for primary care clinicians involved in the care of epilepsy in adults.
1.4 What's new in the revised guidelines

The following is a list of major revisions or additions to the guidelines:

- The detailed specifications of the international classification have not been alluded to in these practical guidelines, but the division of epileptic seizures into generalized and partial seizures has been retained because of its practical importance.

- Chapter 2 on diagnosis of epilepsy has been updated and the section on referral of patients for evaluation of first seizure has been added.

- Chapter 3 on initial treatment has been extensively revised to include emergency treatment at primary care setting. The section also discussed practical advice that should be given to the epileptic individuals and their care givers.

- Chapter 4 updates information on treatment and management and reviewed evidence on alternative treatment available, besides drugs, for epilepsy.

- Chapter 5 addresses cost-effective issues in epilepsy.

- Chapter 6 provides an update on clinical quality indicators.

1.5 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 4 years after publication, or if new evidence appears that requires substantive changes to the recommendations.
2 Diagnosis

2.1 What in the history of spells points to epileptic seizures or their differential?

A thorough history from the patient or a witness is essential as often the diagnosis of a seizure is based solely on clinical grounds. A videotape record on a hand held recorder can be valuable. The history of symptoms before, during and after the episode is needed to differentiate seizures from other paroxysmal events. The clinical phenomena of loss of consciousness, generalised convulsion, transient focal motor or sensory attacks, psychic experiences, aggressive outbursts, episodic motor phenomena in sleep and prolonged confusional states can be epileptic or non-epileptic in nature.

**Characteristic features of epileptic seizures** include aura, cyanosis, unconsciousness and motor manifestations (the classical sequence being generalised stiffness of body and limbs followed by jerking of limbs, tongue biting, urinary incontinence, post-ictal confusion, muscle soreness and headaches).

**Syncope** is the commonest mimic when loss of awareness presents. Often, it is provoked by pain, arising from a squatting position or prolonged standing. Typical is a stereotyped transition from consciousness to brief unconsciousness that includes sweating, nausea and blacking out of vision. Differentiation from epileptic seizure is easy except if a brief (1-10s) convulsive motor activity occurs which frequently occurs when the patient cannot lie down as occurs in a dental chair.

**Psychogenic seizures** can be hard to diagnose and should only be suspected in prolonged attacks with "odd" behaviors like pelvic thrusting. Usually the distinction is difficult and should be left to an experienced epileptologist.

Meticulous history can differentiate **microsleep** from the brief loss of consciousness in epileptic attacks.
The following paroxysmal events may be mistaken for seizures and a primary physician should be aware of them so that he could consult the appropriate specialist, if necessary.

Patient presents with loss of awareness:
- Transient cardiac arrhythmia
- Transient ischaemic attacks
- Hypoglycemia
- Panic attacks

Patient presents with abnormal movement:
- Movement disorders in sleep and wake.
- Tremor or paroxysmal choreoathetosis or dystonia.
- Drop attacks and cataplexy.

For understanding an event thought to be an epileptic seizure, a simple classification into focal epilepsy and generalised epilepsy should be attempted.3,4

2.2 What is a provoked seizure?

These are seizures with an obvious and immediate preceding cause. Most commonly these are stroke, trauma, infection, effects of alcohol and sleep withdrawal.

2.3 What investigations are used in the evaluation of a first unprovoked seizure?

Once a general practitioner (GP) makes the initial diagnosis clinically, the investigation (and initiation of treatment) is best left to the specialist. However as the GP is involved in the long-term management, the following guidelines on investigations are meant as an overview of commonly used investigations.

2.3.1 The role of electroencephalogram (EEG) in seizure

Electroencephalogram (EEG) is often useful in the diagnosis, classification and prognostication of epilepsy but has its limitations.5-7
Individuals requiring an EEG should have the test performed soon after the attack. The earlier the EEG is performed, the more likely a helpful result will emerge from the EEG. Grade D, Level 3

EEG should be performed to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin. Grade D, Level 3

An EEG should not be performed in the case of probable syncope because of the possibility of a false positive result. Grade D, Level 3

EEG should not be used in isolation to make a diagnosis of epilepsy because it can be falsely positive. Grade D, Level 3

Repeated EEG may be helpful when the diagnosis of epilepsy is unclear. When a standard EEG has not contributed to diagnosis or classification, a sleep EEG should be performed. Grade D, Level 3

Long-term video or ambulatory EEG may be used in the assessment of individuals who present diagnostic difficulties after clinical assessment and standard EEG. Grade C, Level 2+

Photic stimulation and hyperventilation should be a part of standard EEG assessment. Grade D, Level 3

Electrocardiogram (ECG) should be performed in the assessment of all patients with altered consciousness, particularly in the older age group when cardiac arrhythmias can simulate epilepsy. Grade D, Level 3

Routine blood studies are indicated to identify common metabolic causes of seizure such as abnormalities in electrolytes, glucose, calcium, magnesium, hepatic and renal diseases. Screening for toxins is sometimes done. Lumbar puncture is necessary when meningitis or encephalitis is suspected. GPP
**Brain Imaging:** This is used to identify structural abnormalities that cause certain epilepsies.

**D** Magnetic resonance imaging (MRI) is the imaging of choice in patients with epilepsy\(^1\),\(^2\) and is particularly useful in those:
- who have suggestions of a focal seizure onset from history, examination or EEG.
- in whom seizures continue in spite of first line medication.

*Grade D, Level 4*

**D** Computed tomography (CT) scan has a role in the urgent assessment of seizures or when MRI is contraindicated.\(^1\)

*Grade D, Level 4*

**D** Brain imaging is not routinely required when there is a confident diagnosis of idiopathic generalised epilepsy and if there is rapid and complete response to the first line antiepileptic drugs.\(^1\)

*Grade D, Level 4*

### 2.4 **Who and when to refer for evaluation of first seizure?**

On diagnosing a first seizure clinically, the general practitioners should refer the patient to the best available specialist epilepsy services within reasonable traveling distance (A&E or specialist clinics in Singapore) for initial evaluation. The general practitioner arranges for regular review of patients as clinically appropriate.

Referral to specialist services is necessary in a first unprovoked seizure or when there is uncertainty of the diagnosis of a spell.
3 Initial Treatment

3.1. When should treatment with antiepileptic drugs be initiated?

3.1.1 Should antiepileptic drug treatment be started after a first unprovoked seizure?

Before making the decision to start antiepileptic drugs after a first unprovoked seizure, it is important to verify that the patient has had only one unprovoked seizure, and to confirm that there is no prior history of absence or myoclonic seizures, or partial seizures.1

Grade D, Level 4

The decision to start antiepileptic drugs after a first unprovoked seizure is based on the risk of seizure recurrence. Early treatment with antiepileptic drugs after a first seizure approximately halves the recurrence risk but does not alter the long-term prognosis of the epilepsy. The decision to treat is made on individually tailored basis.1,13

Grade D, Level 4

The overall risk of a second seizure occurring after a first unprovoked seizure ranges between 27-52%.13 However, this is an overall estimate and the recurrence risk of another seizure after a first unprovoked seizure increases to over 80% in the presence of (1) epileptiform abnormalities on the EEG, (2) a neurological deficit, and (3) a structural abnormality in the brain. Antiepileptic drugs therefore should be offered to the patient in these 3 circumstances.1,13

Grade D, Level 4

Antiepileptic drugs should also be considered if the patient or his/her carers consider the risk of a recurrent seizure unacceptable.1,2

Grade D, Level 4

Starting antiepileptic drug treatment is often not a straightforward decision, and the decision should be made jointly with the patient (or his/her caregiver) after explaining the risks and benefits and after
assessing his/her preferences. In other words, the decision should be individualised.¹

Grade D, Level 4

3.1.2 Should antiepileptic drug treatment be started after two unprovoked seizures?

B The risk of seizure recurrence after 2 unprovoked seizures is 73%. Antiepileptic drugs therefore should be offered to the patient after explaining the risks and benefits and after assessing his/her preferences.²,¹⁴

Grade B, Level 2++

3.2 Which antiepileptic drug should be chosen initially?

A Antiepileptic drug treatment strategy should be individualised according to the seizure type, epilepsy syndrome, co-medication, co-morbidity and the individual’s lifestyle and preferences (and/or those of their family and/or carers as appropriate).¹⁵-²⁰

Grade A, Level 1++

A Patients should be commenced on monotherapy initially. Should the patient develop an adverse reaction to the initial drug or if the initial monotherapy is unsuccessful, monotherapy using another drug should be tried.¹⁵-²⁰

Grade A, Level 1++

A All antiepileptic drugs licensed for monotherapy have similar efficacy in newly diagnosed epilepsy. For this reason, the medicine the prescribing physicians are most familiar with can be used.²¹-²³

Grade A, Level 1++

A Carbamazepine, phenytoin and sodium valproate can be considered first line treatments for newly diagnosed partial and generalized tonic-clonic seizures.²⁴-²⁷

Grade A, Level 1+

A Sodium valproate, lamotrigine and clonazepam may be prescribed for absence and myoclonic seizures.²⁸-³³

Grade A, Level 1++
Newer antiepileptic medications (gabapentin, lamotrigine, topiramate, levetiracetam, tiagabine, zonisamide, oxcarbazepine) are recommended as add-on medications for the treatment of individuals who have suboptimal treatment response to the older medications (phenytoin, carbamazepine, sodium valproate, phenobarbitone, clonazepam, clobazam) or as monotherapy (lamotrigine, topiramate) in individuals whom the older medications are unsuitable (adverse drug reactions, intolerable side effects, multiple drug interactions to concomitant medications).\textsuperscript{15-20,34-41}

Grade A, Level 1++

For women of childbearing age or who are pregnant, the appropriate antiepileptic monotherapy at the lowest dose to control seizures is recommended.\textsuperscript{42}

Grade C, Level 2++

Folate supplementation is recommended for women of childbearing age on antiepileptic treatment to prevent neural tube defects. Folic acid, 5 mg per day, should be given in these women from pre-conception till the first trimester of pregnancy.\textsuperscript{43-47}

Grade A, Level 1++

### 3.3 What practical advice can be given to individuals with epilepsy and their carers?

1. **GPP** Seizure precautions - people with epilepsy and their carers should be educated that the following are associated with increased risk for breakthrough seizures:
   
   a) Non-compliance to antiepileptic medication or drug interactions with antiepileptic medications lowering blood levels of antiepileptic drugs.
   b) Alcohol abuse.
   c) Sleep deprivation.
   d) Concurrent illness.

2. **GPP** Seizure first-aid:
   
   a) Place the seizing individual in recovery position or on his/her side.
   b) Remove surrounding objects that may harm the individual.
c) Do not place any object in the individual's mouth.
d) Call for an ambulance in the event of injury during seizure, prolonged seizure (>5 minutes), or seizure clustering without return to individual's baseline state.

GPP

3. **Home and workplace safety**

   a) Minimize exposure to open fires and sharp instruments. Microwave ovens, blenders are options to consider.
   b) Refrain from soaking in baths over extended periods of time or locking toilet doors; showers should be preferred over baths.
   c) Operation of heavy machinery is discouraged.

   **Grade D, Level 4**

4. The Road Traffic Act [Cap 276;37(1)] may prohibit individuals with epilepsy from driving in Singapore.

   “—(1) On an application for the grant of a driving licence, the applicant shall make a declaration in the prescribed form as to whether or not he is suffering from any such disease or physical disability as may be specified in the form or any other disease or physical disability which would be likely to cause the driving by him of a motor vehicle, being a motor vehicle of such a class or description as he would be authorised by the licence to drive, to be a source of danger to the public.
   (2) If from the declaration it appears that the applicant is suffering from any such disease or disability as specified in subsection (1), the Deputy Commissioner of Police shall refuse to grant the driving licence.”

5. **Special issues of women and epilepsy**

   a) Most women with epilepsy will have healthy pregnancies though the risk for complications during pregnancy and labour is higher.

   b) **Antiepileptic drugs are not a contraindication for women to breastfeed. All breastfeeding mothers on antiepileptic drugs should be encouraged to breastfeed and receive support from relevant healthcare personnel.**

   **Grade D, Level 4**

   c) **Women with epilepsy should be referred to specialist care for pre-conception counseling as indicated.**

   **GPP**
3.4 Emergency treatment for seizure/prolonged seizure at the primary care setting

3.4.1 Introduction

By the time the doctor gets to see the patient, most seizures have spontaneously aborted as they usually do not last beyond 2-3 minutes. If seizures last 5 or more minutes or recur more than 3 times an hour, they require emergency treatment as these are associated with increased morbidity and mortality if not treated promptly.\(^{51-56}\)

3.4.2 Immediate management of seizure\(^ {57}\)

- Remove hazards from the immediate surroundings.
- Protect the patient from falling unsupported to the ground or striking objects.
- Position the patient on their side, with the head supported in a neutral in-line position.
  - Protect the head and other parts of the body from striking objects but do not restrain the patient.
- Establish Airway, Breathing and Circulation (ABC) and administer high concentration oxygen.
- Observe and record the pattern of the seizure(s).
- Note and record the duration of the seizure(s).
- Do not force anything, including your fingers, into the person's mouth. This may cause injuries such as chipped teeth or a fractured jaw. You could also get bitten.

\[\text{Grade D, Level 4}\]

If the clinical scenario is suggestive of hypoglycaemia, capillary blood glucose level should be checked. With confirmed hypoglycaemia, the patient should be treated with 50 ml of Dextrose 50%. In the setting of malnutrition or suspected ethanol abuse, 100 mg thiamine may also be given as an intravenous push.

\[\text{GPP}\]

3.4.3 Treatment of seizures

If seizures last 5 or more minutes or recur more than 3 times an hour, they require emergency pharmacotherapy because of increased morbidity and mortality. Benzodiazepines are safe and effective when
used for prolonged seizures in the community. While there are advantages in using intravenous lorazepam over diazepam, such as faster onset of action, extended duration of action and possibly less cardio-respiratory depression, lorazepam is not widely available in general practice in Singapore. Efficacy per se comparison however did not reveal significant differences between intravenous lorazepam and diazepam. Rectal diazepam is as effective as intravenous diazepam and may be administered (either as rectal solution e.g. Stesolid or intravenous solution) if intravenous access is delayed.60,61 Buccal midazolam is an effective alternative although it should be noted that such use is still unlicensed.62-64

\[D\] When convulsive seizures continue beyond 5 minutes, pharmacotherapy to abort the seizure is recommended.65

\[Grade D, Level 4\]

\[A\] Intravenous diazepam and lorazepam are effective first line treatments for prolonged seizures in the community.

\[Grade A, Level 1\]

\[D\] Initially a dose of 5-10 mg diazepam is given either intravenously or rectally. If there is no response, the same dose can be repeated after 10 minutes. Respiratory or circulatory effects should be monitored for and usually come into effect with doses greater than 20 mg.65

\[Grade D, Level 4\]

\[GPP\] Emergency medical services (EMS) should be activated if:
- Seizures continue beyond 5 minutes.
- Cardio-respiratory complications from treatment develop and there are no adequate conditions for monitoring the patient's condition.
- There is suspected fracture or central nervous system injury from the seizure.

\[GPP\]
4 Follow-on Treatment and Management

4.1 When are antiepileptic drug levels tested?

Physicians should be aware that the published "therapeutic range" exists only as a guide. Patients may have good seizure control below this range, while others tolerate levels above the range.

**D** Antiepileptic drug levels may help clinical management under the following clinical indications: (1) assessment of compliance to drug treatment for patients with refractory epilepsy (2) assessment of symptoms due to possible antiepileptic drug toxicity (3) titration of phenytoin dose.1,2 Routine checking of antiepileptic drug levels without a clear clinical indication is not required, and is not cost-effective.1,2

Grade D, Level 4

4.2 When are ancillary blood tests (FBC, U/E, LFT) indicated?

**GPP** Depending on clinical suspicion of other differential diagnoses, blood tests such as blood glucose, urea, electrolytes, liver function tests and serum calcium may be indicated.

**GPP**

4.3 What are possible drug combinations and how should these be initiated?

Single drug therapy is able to provide optimal seizure control in about 80% of all patients with epilepsy.66

**B** Before commencing multiple antiepileptic drug therapy, monotherapy involving two of the standard drugs (phenytoin, carbamazepine, sodium valproate) should have been tried. When two of these antiepileptic drugs have failed as monotherapy, the chance of seizure-freedom with further monotherapy is very low.67

Grade B, Level 1+
4.3.1 Focal epilepsies

**B** If acceptable seizure control is not achieved with monotherapy using phenytoin, sodium valproate or carbamazepine: add sodium valproate to carbamazepine or phenytoin, add phenytoin or carbamazepine to sodium valproate.  

Grade B, Level 1++

**A** Systematic review have confirmed the efficacy and tolerability of the newer antiepileptics vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine, oxcarbazepine and levetiracetam. All may be used as **adjunctive** therapy for patients with drug-resistant, focal epilepsy.  

Grade A, Level 1++

The development of concentric visual field defects with vigabatrin has substantially limited its clinical use.

**A** Although newer antiepileptic drugs (gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate) have been shown to be effective, there is little good quality evidence from clinical trials supporting their superiority as adjunctive therapy over older drugs.

Grade A, Level 1+

The main disadvantage of using newer antiepileptic drugs is cost, which can be up to 100 times more expensive than when using standard drugs.

**D** If trials of combination therapy do not confer benefit, treatment should revert to the regimen (monotherapy or combination therapy) that has proven most acceptable to the individual, in terms of providing the best balance between effectiveness in reducing seizure frequency and tolerability of side effects.

Grade D, Level 3

**D** Changing the formulation or brand of antiepileptic drugs is not recommended because different preparations may vary in bioavailability or have different pharmacokinetic profiles and, thus, increased potential for reduced effect or excessive side effects.

Grade D, Level 3
4.3.2 Generalised epilepsy

**D** Lamotrigine, topiramate, levetiracetam and sodium valproate have a wide spectrum of activity for most types of generalised seizures. Although there is no published evidence of an "add-on" effect of these drugs in generalised epilepsies, this is supported by circumstantial evidence. Any one of these drugs can be added to a standard antiepileptic drug (phenytoin, carbamazepine, sodium valproate). 

*Grade D, Level 4*

**D** Addition of a third antiepileptic may be worth trying if an encouraging but sub-optimal effect is obtained with a particular combination of two drugs.

*Grade D, Level 4*

4.4 When should I refer for further evaluation?

**GPP** All individuals with a first-onset suspected seizure should be evaluated by a specialist who has experience in epilepsy. This is to ensure accurate and early diagnosis, and initiation of appropriate therapy. Subsequent follow-up can be carried out by a general practitioner.

4.5 When and how can I stop drug treatment?

In patients treated for epilepsy, certain indicators may predict better outcome in terms of remission from seizures. These include absence of brain damage, absence of generalized epileptiform activity on EEG and absence of generalized tonic-clonic seizures. With treatment, up to 70% of patients can achieve a 5-year remission up to 9 years from the time of diagnosis, the strongest prognostic indicator being the frequency of seizures in the first 6 months after initial presentation. The risk relapse after withdrawal of antiepileptic medication is approximately 25% at 1 year and 29% at 2 years. A higher risk of relapse is present in those with a history of myoclonus, up to 70%.

**A** Withdrawal of antiepileptic drugs can be explored at the end of at least a two-year seizure-free period, after a discussion on the potential risks and benefits.

*Grade A, Level 1*
The decision to withdraw treatment should be individualised, taking into account lifestyle issues and a clear plan agreed upon should the seizures recur.  

**Grade A, Level 1**

In these patients, those with a higher risk of seizure recurrence include:

i) Those who had seizures after initiation of treatment.
ii) Those requiring multiple antiepileptic therapy.
iii) A shorter seizure-free duration.
iv) A history of myoclonus.

**Grade D, Level 4**

A repeat EEG prior to initiation of drug withdrawal is not routinely required.  

Withdrawal of treatment should be a gradual process. There is no clear evidence for the length of the withdrawal period although most specialists would advocate a period of few months. Patients on polytherapy should have only one drug withdrawn at a time.  

**Grade D, Level 4**

Patients on benzodiazepines or barbiturates should have these medications reduced over a longer time-course (up to 6 months or longer).  

**Grade D, Level 4**

### 4.6 Besides drugs, what alternative treatments are there for epilepsy?

#### 4.6.1 Vagus nerve stimulation

Vagus nerve stimulation is indicated for adjunctive therapy and has been shown to reduce frequency of seizures in adults refractory to antiepileptic medication who are not suitable for epilepsy surgery. This includes adults whose epileptic disorder is dominated by partial seizures (with or without secondary generalisation) or generalised seizures.  

**Grade A, Level 1**
4.6.2 Complementary therapy for epilepsy

A Complementary treatment such as acupuncture, chiropractic, herbal medicine, homeopathy, osteopathy and yoga should not be advised to the epileptic patient.\textsuperscript{83,84}  

\textit{Grade A, Level 1+}

Complementary therapy is increasingly popular and is often used in addition to conventional medication. There is no evidence that treatments such as acupuncture, chiropractic, herbal medicine, homeopathy, osteopathy or yoga improve seizure control.

D Patients should be asked if they are using any complementary medicines and warned about the possibility of adverse effects. Problems may arise with the use of some herbal medicines because of interaction with prescribed medication. The potential reduction of the plasma concentrations of carbamazepine and phenytoin should be noted if St John's Wort is used concomitantly. Caution is also advised in the use of evening primrose oil but the evidence for this is less robust.\textsuperscript{85}

\textit{Grade D, Level 4}

D Some aromatherapy preparations (e.g. hyssop, rosemary, sweet fennel, sage and wormwood) may have an alerting effect on the brain and so may exacerbate seizures.\textsuperscript{1}

\textit{Grade D, Level 4}

4.6.3 Diet

D The ketogenic diet is not recommended for adults with epilepsy. There is no evidence of a worthwhile therapeutic effect. In addition, compared to children, in adults, it is difficult for dietary measures to result in great enough ketogenicity.\textsuperscript{2}

\textit{Grade D, Level 4}

4.6.4 Control of seizure precipitating factors

C There is evidence that control of precipitating factors (emotional stress, sleep deprivation) may help better control seizures. This can only be recommended in addition to pharmacological treatments.\textsuperscript{86}

\textit{Grade C, Level 2+}
5 Cost-effectiveness

As stated under 3.2, all antiepileptic drugs licensed for monotherapy have similar efficacy in newly diagnosed epilepsy. Carbamazepine, phenytoin and sodium valproate can be considered first line treatments for newly diagnosed partial and generalized tonic-clonic seizures. These three medicines are particularly cost-effective.\textsuperscript{71}
The desired clinical outcome for epilepsy in the adult is seizure control at a level which enables the patient being able to live a normal as possible private and public life. In general this will mean that treatment will aim to reduce the number and severity of seizures whilst causing as few side effects as possible.

Audit should look at:

- Proportion of patients who are compliant with the medication (if using monotherapy with phenytoin, tegretol or sodium valproate, 70% should be compliant). (Page 19, 3.3)

- Proportion of patients who change or stop medication because of side effects (Less than 10 % change medications because of side effects). (Page 18, 3.2)
References


34. Review: 6 newer drugs reduce seizures with no detectable differences among them. ACP Journal Club 1997 May-Jun;v126:72.


Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to "judge" your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose the most appropriate answer.

1. Besides drugs, what effective alternative treatments are there for epilepsy?
   A) Accupuncture
   B) Yoga methods
   C) Diet
   D) Vagus nerve stimulation

2. Regarding antiepileptic drug levels, which of the following statements is false:
   A) Drug levels should be checked when non-compliance is suspected.
   B) Drug levels should be checked when the patient has symptoms of drug toxicity.
   C) Checking phenytoin levels should be considered when titrating doses, especially on high doses.
   D) Routine drug levels at every clinic visit is a useful, cost-effective way to assess compliance.

3. Which is the most likely indicator of a seizure recurrence after medication withdrawal?
   A) Patient was on a high dose of a single antiepileptic agent.
   B) Patient was seizure-free but had poor compliance with treatment.
   C) Patient was on multiple antiepileptic drugs.
   D) There was a long period of seizure freedom whilst on treatment.
4. A middle aged man who had fallen on the road side was noted to be jerking in all four limbs and unconscious for more than 5 minutes. He was brought to your clinic by a passerby. The following measures may be appropriate except:

A) Intravenous lorazepam
B) Oral diazepam
C) Activate emergency medical services
D) Check capillary glucose level
E) Give intranasal oxygen

5. The following are known to be effective for myoclonic seizures except:

A) Carbamazepine
B) Valproate
C) Lamotrigine
D) Clonazepam

6. A patient consults his GP. The family says he passed out at a parade, and some twiches were noted in all limbs. He has had similar attacks since 15 years of age.

A) The diagnosis is epilepsy.
B) Send the patient for an EEG.
C) Gather detailed history from the patient and a witness, if available.
D) Start antiepileptic medication.
Answers

1. D (pg 26)
2. D (pg 23)
3. C (pg 26)
4. B (pg 22)
5. A (pg 18)
6. C (pg 13)
# Workgroup members

The members of the workgroup, who were appointed in their personal professional capacity, are:

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Acknowledgement:

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Executive summary of recommendations
Details of recommendations can be found in the main text at the pages indicated.

Diagnosis

**GPP** The following paroxysmal events may be mistaken for seizures and a primary physician should be aware of them so that he could consult the appropriate specialist, if necessary.

Patient presents with loss of awareness:
- Transient cardiac arrhythmia
- Transient ischaemic attacks
- Hypoglycemia
- Panic attacks

Patient presents with abnormal movement:
- Movement disorders in sleep and wake.
- Tremor or paroxysmal choreoathetosis or dystonia.
- Drop attacks and cataplexy.

**(pg 14)**

**D** Individuals requiring an electroencephalogram (EEG) should have the test performed soon after the attack. The earlier the EEG is performed, the more likely a helpful result will emerge from the EEG (pg 15).

*Grade D, Level 3*
D EEG should be performed to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin (pg 15).

Grade D, Level 3

D An EEG should not be performed in the case of probable syncope because of the possibility of a false positive result (pg 15).

Grade D, Level 3

D EEG should not be used in isolation to make a diagnosis of epilepsy because it can be falsely positive (pg 15).

Grade D, Level 3

D Repeated EEG may be helpful when the diagnosis of epilepsy is unclear. When a standard EEG has not contributed to diagnosis or classification, a sleep EEG should be performed (pg 15).

Grade D, Level 3

C Long-term video or ambulatory EEG may be used in the assessment of individuals who present diagnostic difficulties after clinical assessment and standard EEG (pg 15).

Grade C, Level 2*

D Photic stimulation and hyperventilation should be a part of standard EEG assessment (pg 15).

Grade D, Level 3

D Electrocardiogram (ECG) should be performed in the assessment of all patients with altered consciousness, particularly in the older age group when cardiac arrhythmia can simulate epilepsy (pg 15).

Grade D, Level 3

GPP Routine blood studies are indicated to identify common metabolic causes of seizure such as abnormalities in electrolytes, glucose, calcium, magnesium, hepatic and renal diseases. Screening for toxins is sometimes done. Lumbar puncture is necessary when meningitis or encephalitis is suspected (pg 15).

GPP
Magnetic resonance imaging (MRI) is the imaging of choice in patients with epilepsy and is particularly useful in those:
• who have suggestions of a focal seizure onset from history, examination or EEG.
• in whom seizures continue in spite of first line medication.

Grade D, Level 4

Computed tomography (CT) scan has a role in the urgent assessment of seizures or when MRI is contraindicated.

Grade D, Level 4

Brain imaging is not routinely required when there is a confident diagnosis of idiopathic generalised epilepsy and if there is rapid and complete response to the first line antiepileptic drugs.

Grade D, Level 4

**Initial Treatment**

Before making the decision to start antiepileptic drugs after a first unprovoked seizure, it is important to verify that the patient has had only one unprovoked seizure, and to confirm that there is no prior history of absence or myoclonic seizures, or partial seizures.

Grade D, Level 4

The decision to start antiepileptic drugs after a first unprovoked seizure is based on the risk of seizure recurrence. Early treatment with antiepileptic drugs after a first seizure approximately halves the recurrence risk but does not alter the long-term prognosis of the epilepsy. The decision to treat is made on individually tailored basis.

Grade D, Level 4

The overall risk of a second seizure occurring after a first unprovoked seizure ranges between 27-52%. However, this is an overall estimate and the recurrence risk of another seizure after a first unprovoked seizure increases to over 80% in the presence of (1) epileptiform abnormalities on the EEG, (2) a neurological deficit, and (3) a structural abnormality in the brain. Antiepileptic drugs therefore should be offered to the patient in these 3 circumstances.

Grade D, Level 4
Antiepileptic drugs should also be considered if the patient or his/her carers consider the risk of a recurrent seizure unacceptable (pg 17).

Grade D, Level 4

Starting antiepileptic drug treatment is often not a straightforward decision, and the decision should be made jointly with the patient (or his/her caregiver) after explaining the risks and benefits and after assessing his/her preferences. In other words, the decision should be individualized (pg 17).

Grade D, Level 4

The risk of seizure recurrence after 2 unprovoked seizures is 73%. Antiepileptic drugs therefore should be offered to the patient after explaining the risks and benefits and after assessing his/her preferences (pg 18).

Grade B, Level 2**

Antiepileptic drug treatment strategy should be individualised according to the seizure type, epilepsy syndrome, co-medication, co-morbidity and the individual’s lifestyle and preferences (and/or those of their family and/or carers as appropriate) (pg 18).

Grade A, Level 1**

Patients should be commenced on monotherapy initially. Should the patient develop an adverse reaction to the initial drug or if the initial monotherapy is unsuccessful, monotherapy using another drug should be tried (pg 18).

Grade A, Level 1**

All antiepileptic drugs licensed for monotherapy have similar efficacy in newly diagnosed epilepsy. For this reason, the medicine the prescribing physicians are most familiar with can be used (pg 18).

Grade A, Level 1**

Carbamazepine, phenytoin and sodium valproate can be considered first line treatments for newly diagnosed partial and generalized tonic-clonic seizures (pg 18).

Grade A, Level 1*

Sodium valproate, lamotrigine and clonazepam may be prescribed for absence and myoclonic seizures (pg 18).

Grade A, Level 1**
Newer antiepileptic medications (gabapentin, lamotrigine, topiramate, levetiracetam, tiagabine, zonisamide, oxcarbazepine) are recommended as add-on medications for the treatment of individuals who have suboptimal treatment response to the older medications (phenytoin, carbamazepine, sodium valproate, phenobarbitone, clonazepam, clobazam) or as monotherapy (lamotrigine, topiramate) in individuals whom the older medications are unsuitable (adverse drug reactions, intolerable side effects, multiple drug interactions to concomitant medications) (pg 19).

**Grade A, Level 1**

For women of childbearing age or who are pregnant, the appropriate monotherapy antiepileptic at the lowest dose to control seizures is recommended (pg 19).

**Grade C, Level 2**

Folate supplementation is recommended for women of childbearing age on antiepileptic treatment to prevent neural tube defects. Folic acid, 5 mg per day, should be given in these women from pre-conception till the first trimester of pregnancy (pg 19).

**Grade A, Level 1**

**GPP** Seizure precautions - people with epilepsy and their carers should be educated that the following are associated with increased risk for breakthrough seizures:

a) Non-compliance to antiepileptic medication or drug interactions with antiepileptic medications lowering blood levels of antiepileptic drugs.
b) Alcohol abuse.
c) Sleep deprivation.
d) Concurrent illness.

(pg 19)

**GPP** Seizure first-aid:

a) Place the seizing individual in recovery position or on his/her side.
b) Remove surrounding objects that may harm the individual.
c) Do not place any object in the individual’s mouth.
d) Call for an ambulance in the event of injury during seizure, prolonged seizure (>5 minutes), seizure clustering without return to individual’s baseline state.

(pg 19)
Home and workplace safety:

a) Minimise exposure to open fires and sharp instruments. Microwave ovens, blenders are options to consider.
b) Refrain from soaking in baths over extended periods of time or locking toilet doors; showers should be preferred over baths.
c) Operation of heavy machinery is discouraged.

Grade D, Level 4

Antiepileptic drugs are not a contraindication for women to breastfeed. All breastfeeding mothers on antiepileptic drugs should be encouraged to breastfeed and receive support from relevant healthcare personnel (pg 20).

Grade D, Level 4

Women with epilepsy should be referred to specialist care for pre-conception counselling as indicated (pg 20).

GPP

Immediate management of seizure

- Remove hazards from the immediate surroundings.
- Protect the patient from falling unsupported to the ground or striking objects.
- Position the patient on their side, with the head supported in a neutral in-line position.
  - Protect the head and other parts of the body from striking objects but do not restrain the patient.
- Establish Airway, Breathing and Circulation (ABC) and administer high concentration oxygen.
- Observe and record the pattern of the seizure(s).
- Note and record the duration of the seizure(s).
- Do not force anything, including your fingers, into the person's mouth. This may cause injuries such as chipped teeth or a fractured jaw. You could also get bitten.

Grade D, Level 4

If the clinical scenario is suggestive of hypoglycaemia, capillary blood glucose level should be checked. With confirmed hypoglycaemia, the patient should be treated with 50 ml of Dextrose 50%. In the setting of
malnutrition or suspected ethanol abuse, 100 mg thiamine may also be given as an intravenous push (pg 21).

**GPP**

**D** When convulsive seizures continue beyond 5 minutes, pharmacotherapy to abort the seizure is recommended (pg 22).

*Grade D, Level 4*

**A** Intravenous diazepam and lorazepam are effective first line treatments for prolonged seizures in the community (pg 22).

*Grade A, Level 1*+

**D** Initially a dose of 5-10 mg diazepam is given either intravenously or rectally. If there is no response, the same dose can be repeated after 10 minutes. Respiratory or circulatory effects should be monitored for and usually come into effect with doses greater than 20 mg (pg 22).

*Grade D, Level 4*

**GPP** Emergency medical services (EMS) should be activated if:
- Seizures continue beyond 5 minutes.
- Cardio-respiratory complications from treatment develop and there are no adequate conditions for monitoring the patient’s condition.
- There is suspected fracture or central nervous system injury from the seizure.

(pg 22)

**Follow-on Treatment and Management**

**D** Antiepileptic drug levels may help clinical management under the following clinical indications: (1) assessment of compliance to drug treatment for patients with refractory epilepsy (2) assessment of symptoms due to possible antiepileptic drug toxicity (3) titration of phenytoin dose. Routine checking of antiepileptic drug levels without a clear clinical indication is not required, and is not cost-effective (pg 23).

*Grade D, Level 4*

**GPP** Depending on clinical suspicion of other differential diagnoses, blood tests such as blood glucose, urea, electrolytes, liver function tests and serum calcium may be indicated (pg 23).

**GPP**
Before commencing multiple antiepileptic drug therapy, monotherapy involving two of the standard drugs (phenytoin, carbamazepine, sodium valproate) should have been tried. When two of these antiepileptic drugs have failed as monotherapy, the chance of seizure-freedom with further monotherapy is very low (pg 23).

Grade B, Level 1*

If acceptable seizure control is not achieved with monotherapy using phenytoin, sodium valproate or carbamazepine: add sodium valproate to carbamazepine or phenytoin, add carbamazepine or phenytoin to sodium valproate (pg 24).

Grade B, Level 1**

A Systematic review have confirmed the efficacy and tolerability of the newer antiepileptics vigabatrin, lamotrigine, gabapentin, topiramate, tiagabine, oxcarbazepine and levetiracetam. All may be used as **adjunctive** therapy for patients with drug-resistant, focal epilepsy (pg 24).

Grade A, Level 1**

Although newer antiepileptic drugs (gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate) have been shown to be effective, there is little good quality evidence from clinical trials supporting their superiority as **adjunctive** therapy over older drugs (pg 24).

Grade A, Level 1*

If trials of combination therapy do not confer benefit, treatment should revert to the regimen (monotherapy or combination therapy) that has proven most acceptable to the individual, in terms of providing the best balance between effectiveness in reducing seizure frequency and tolerability of side effects (pg 24).

Grade D, Level 3

Changing the formulation or brand of antiepileptic drugs is not recommended because different preparations may vary in bioavailability or have different pharmacokinetic profiles and, thus, increased potential for reduced effect or excessive side effects (pg 24).

Grade D, Level 3

Lamotrigine, topiramate, levetiracetam and sodium valproate have a wide spectrum of activity for most types of generalised seizures. Although there is no published evidence of an “add-on” effect of these drugs in generalised
epilepsies, this is supported by circumstantial evidence. Any one of these
drugs can be added to a standard antiepileptic drug (phenytoin,
carbamazepine, sodium valproate) (pg 25).

**Grade D, Level 4**

**D** Addition of a third antiepileptic may be worth trying if an encouraging but
sub-optimal effect is obtained with a particular combination of two drugs (pg
25).

**Grade D, Level 4**

**GPP** All individuals with a first-onset suspected seizure should be
evaluated by a specialist who has experience in epilepsy. This is to ensure
accurate and early diagnosis, and initiation of appropriate therapy.
Subsequent follow-up can be carried out by a general practitioner (pg 25).

**GPP**

**A** Withdrawal of antiepileptic drugs can be explored at the end of at least a
two-year seizure-free period, after a discussion on the potential risks and
benefits (pg 25).

**Grade A, Level 1**

**A** The decision to withdraw treatment should be individualised, taking into
account lifestyle issues and a clear plan agreed upon should the seizures
recur (pg 26).

**Grade A, Level 1**

**D** A repeat EEG prior to initiation of drug withdrawal is not routinely
required (pg 26).

**Grade D, Level 4**

**D** Withdrawal of treatment should be a gradual process. There is no clear
evidence for the length of the withdrawal period although most specialists
would advocate a period of few months. Patients on polytherapy should
have only one drug withdrawn at a time (pg 26).

**Grade D, Level 4**

**D** Patients on benzodiazepines or barbiturates should have these medications
reduced over a longer time-course (up to 6 months or longer) (pg 26).

**Grade D, Level 4**

**A** Vagus nerve stimulation is indicated for adjunctive therapy and has been
shown to reduce frequency of seizures in adults refractory to antiepileptic
medication who are not suitable for epilepsy surgery. This includes adults whose epileptic disorder is dominated by partial seizures (with or without secondary generalisation) or generalised seizures (pg 26).

Grade A, Level 1*

A Complementary treatment such as acupuncture, chiropractic, herbal medicine, homeopathy, osteopathy and yoga should not be advised to the epileptic patient (pg 27).

Grade A, Level 1*

D Patients should be asked if they are using any complementary medicines and warned about the possibility of adverse effects. Problems may arise with the use of some herbal medicines because of interaction with prescribed medication. The potential reduction of the plasma concentrations of carbamazepine and phenytoin should be noted if St John’s Wort is used concomitantly. Caution is also advised in the use of evening primrose oil but the evidence for this is less robust (pg 27).

Grade D, Level 4

D Some aromatherapy preparations (e.g. hyssop, rosemary, sweet fennel, sage and wormwood) may have an alerting effect on the brain and so may exacerbate seizures (pg 27).

Grade D, Level 4

D The ketogenic diet is not recommended for adults with epilepsy. There is no evidence of a worthwhile therapeutic effect. In addition, compared to children, in adults, it is difficult for dietary measures to result in great enough ketogenicity (pg 27).

Grade D, Level 4

C There is evidence that control of precipitating factors (emotional stress, sleep deprivation) may help better control seizures. This can only be recommended in addition to pharmacological treatments (pg 27).

Grade C, Level 2*
Levels of evidence and grades of recommendation

Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1**</td>
<td>High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.</td>
</tr>
<tr>
<td>1*</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.</td>
</tr>
<tr>
<td>1'</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>2**</td>
<td>High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
</tr>
<tr>
<td>2*</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>2'</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
</tr>
<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, case series</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion</td>
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</tbody>
</table>

Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review of RCTs, or RCT rated as 1** and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1*, directly applicable to the target population, and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2**, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1** or 1'</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2*, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2**</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2*</td>
</tr>
<tr>
<td>GPP</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
</tr>
<tr>
<td>(good practice points)</td>
<td></td>
</tr>
</tbody>
</table>

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