GUIDELINE FOR THE MANAGEMENT OF FIRST SEIZURE IN THE EMERGENCY DEPARTMENT

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For The College of Emergency Medicine

CONTENTS

1. Executive summary

- The Guidelines in Emergency Medicine Network (GEMNet) has been created to promote best medical practice in a range of conditions presenting to Emergency Departments (EDs) in the UK.
- This guideline presents a summary of the best available evidence to guide the management of adult patients who present to the ED following first seizure.
- The document has been developed following discussion amongst Emergency Physicians to decide which topics would benefit from the development of clinical guidelines.
- The document is intended as a guideline for use in the ED by Emergency Physicians and is based on a review of the best existing evidence for the diagnostic tools and treatments used in this setting.
- The document is summarised as a Clinical Decision Support Guideline that has been presented as an easy to follow algorithm
- The intention is for each guideline to be updated and reviewed as further evidence becomes available. The formal revision date has been set at 5 years from publication though the guideline is subject to continuous informal review.

2. Introduction

2.1 Responsibility for development

This document has been developed in response to a perceived need to improve clinical effectiveness for care in this field. The intention is to distil this information into practical advice for clinicians working in the department. The information is presented in the form of Clinical Decision Support Guidelines, available on shop floor in the form of a Clinical Decision Support Manual and on individual A4 sized forms.

Departmental Consultants have considered clinical conditions that may benefit from evidence based guidelines and following discussion with other clinical staff have compiled a list of topics that included the management of first seizure in adults.

2.2 Funding

Funding for the development for this guideline has been received from the College of Emergency Medicine.

2.3 The Guideline Working Group

A Guideline Working Group met to discuss this condition and decide on the clinical questions, consider the evidence available and develop the recommendations. The group process ensured that the working group had access to the relevant information and the required resources in order to develop in a constructive manner.

The guideline has been developed in accordance with the principles described by the National Institute for Health and Clinical Excellence guideline development methods.[1]

3. Topic Introduction

Seizures are a common occurrence. Prospective, population based studies show up to an 8-10% lifetime risk of one seizure, and a 3% chance of epilepsy.[2;3] People with epilepsy have a risk of premature death that is 2–3 times higher than in the general population.[4]

Seizures may be divided into those which are unprovoked, and those "provoked" by an acute brain insult (also known as acute symptomatic seizures) or pre-existing brain abnormality (known as remote symptomatic seizures). Provoking factors include electrolyte disturbance and hypoglycaemia as well as head injury, alcohol excess or withdrawal, stroke and intracerebral neoplasm.[3] Population based studies indicate that 25-30% of first seizures are provoked.[3;5] Each type of acute symptomatic seizure has age, gender and time period patterns that reflect the occurrence of the underlying cause. For example, among young adults aged 15-34 years, drug and alcohol abuse and withdrawal, and head trauma are the predominant causes, but cerebrovascular disease accounts for about half of all acute symptomatic seizures in people aged over 65 years.[3]
If a first seizure is unprovoked, around a third to a half will recur, leading to a diagnosis of epilepsy (a tendency for recurrent seizures).[6;7] After a second unprovoked seizure 70-80% will recur, justifying the diagnosis.[8]

Seizures are a frequent reason for attendance to the emergency department (ED), accounting for around 1.2% of attendances.[9] Around a quarter of these are due to first seizure.[9] Some studies have shown that at least half of first seizure patients presenting to a first fit clinic are referred from an ED as opposed to other primary care facilities.[10;11]

Various authors have suggested management strategies for patients presenting to the ED, but no nationally agreed protocol exists. This aim of this guideline is to summarise the evidence supporting the various management options that have been advocated in the management of first seizure within the ED. It is hoped that this will help to optimise and standardise the standard of care that may be delivered to this patient group.

4. Scope

This guideline encompasses adult patients (≥16 years of age) presenting to the ED with suspected first seizure. The key aspects included are appropriate investigations, use of antiepileptics, disposition of the patient from the ED, fitness for discharge, follow-up and advice to be given on discharge. The recommendations can be followed using resources available in any UK ED. Disposition may vary dependent on local resources but the guideline may be adapted as appropriate.

The guideline addresses convulsive seizures only, as other seizure types such as absence or complex partial seizures typically occur several times before the person or family seek medical help and are often not dealt with primarily in the ED. As it is usually not initially known following first seizure whether the episode was provoked or not, the guidelines will cover both acute symptomatic seizures, and those provoked by various brain insults (as outlined above) in all adult patients aged 16 years or over. However, the guideline will not address the emergency management of the fitting patient, for which there are already guidelines in place,[12-14] and will not address seizures in children or seizures due to head injury or eclampsia.

5. METHODOLOGY

Medline, EMBASE, CINAHL, and the Cochrane library were searched under the headings "first seizure," "initial seizure" and "new seizure." using the following strategy: [(seizure$ OR convulsion$ OR epileps$).ti. AND (first OR new OR first-ever OR new onset OR emergency OR new-onset OR initial).ti.] The references generated were sifted for relevance based on their title and abstract; and other references were followed-up from the papers identified. The internet was searched using the Google search engine.

Only papers looking at an unselected population of adult patients (aged ≥ 16 years) presenting with first generalised seizure (or a population including majority of adults and/or a subset presenting with first generalised seizure) were included.

Findings and recommendations were grouped under the subheadings of laboratory investigations and bedside tests, neuroimaging, EEG, need for admission, advice to be given to patients, treatment with AEDs and requirements for follow-up.

Having gathered and collated the evidence for each clinical question, a series of guideline recommendations were developed, which were used to create an evidence-based flowchart.

5.1 Levels of evidence and grading of recommendations

Studies included in this guideline were graded for level of evidence according to previously accepted definitions[15]. In summary, level 1 evidence comes from well-designed randomised controlled trials (RCTs), level 2 evidence from large cohort studies or poorly designed RCTs, level 3 evidence from small cohort studies or case-control studies and level 4 evidence from experimental studies, case series or case studies. The suffix 'a' implies that evidence at this level is from systematic review or meta-analysis, whereas the suffix 'b' implies that the evidence is from original research.

The recommendations that have been made were graded according to the level of evidence upon which they were based:

Grade A: Based upon multiple level 1a or 1b papers.
Grade B: Based upon individual level 1a or 1b papers or multiple level 2a or 2b papers.
Grade C: Based upon individual level 2a or 2b papers or multiple level 3a or 3b papers.
Grade D: Based upon individual level 3a or 3b papers or level 4 papers.
Grade E: Based on consensus guidelines or studies of expert opinion.

6. Summary of Recommendations

6.1 Investigations

6.1.1a Laboratory investigations and bedside tests

Determine a Serum glucose and sodium level should be determined on patients with a first-time seizure with no co-morbidities who have returned to their baseline.

A breath alcohol test should be performed if available.

A pregnancy test should be obtained if a woman is of childbearing age.

An ECG should be done on all patients.

Other laboratory investigations, toxicology screening, bedside tests, chest x-ray and lumbar puncture should only be done if clinically indicated.

6.1.2 Neuroimaging

Neuroimaging should be performed immediately whenever an intracranial lesion is suspected; and specifically in patients with new focal deficit or persistent altered mental state, fever, persistent headache, focal or partial onset before generalization, or a history of acute head trauma, malignancy, immunocompromise, HIV infection, alcoholism, anticoagulation or bleeding diathesis.

Deferred early outpatient neuroimaging may be used when reliable follow-up is available. Otherwise, neuroimaging in the ED should be performed on all patients.

MRI (Magnetic resonance imaging) is preferable to CT (computed tomography), if readily available within an acceptable time period, in a patient who has fully recovered. CT should be used if MRI is not readily available or in an individual who has not fully recovered. In acutely ill patients, CT is the modality of choice.

6.1.3c Electroencephalography (EEG)

EEG should not be routinely performed in the ED or requested by the emergency physician.

6.2 Need For Admission

Patients who have fully recovered, have no neurological deficit, and have normal initial investigations can be discharged from the ED.

Admission should be considered in all patients with alcoholism, poor social circumstances or those without a responsible adult to stay with.

6.3 Treatment

AEDs (antiepileptic drugs) should not routinely be prescribed in the ED.

If AEDs are to be prescribed, this should only be after consultation with an epilepsy specialist.

6.4 Advice

Patients should be given verbal and written advice about driving and lifestyle changes prior to being discharged from the ED.

Advice given to patients should be documented in the medical notes.

6.5 Follow-up

All patients should be followed-up by an epilepsy specialist urgently, ideally within 2 weeks.

Robust pathways should be established to ensure specialist follow-up of all patients. Current evidence supports direct referral from the ED.

7. Findings & Recommendations

Evidence used to establish the recommendations for this guideline are summarised below.

7.1 Investigations

7.1.1 Laboratory investigations and bedside tests

Haematological and biochemical investigations are often abnormal following first seizure, but this may not be reflected in the provision of any useful information as regards seizure aetiology. Glucose abnormalities, metabolic derangements related to alcohol, and hyponatraemia are the most frequently identified abnormalities[9] Some of these abnormalities may be due to the fit itself. For example, around a third of patients may have an increased white cell count and/or hyperglycaemia, related to an acute stress response.[10] Although metabolic disturbances can provoke seizures, abnormalities sufficient to cause seizures will generally not be associated with normal mental function.[16;17] Furthermore, most of these abnormalities can be predicted on the basis of clinical findings. For example, hypoglycaemia may be predicted in a known diabetic, and a more focused approach to investigation may be appropriate. It is indubitable that patients with certain abnormal clinical findings, such as altered mental status, require more extensive evaluation. The controversial question is which laboratory tests are indicated in an otherwise healthy patient who presents to the ED after having a first seizure and is alert, orientated, and has no abnormal clinical findings.

590 papers were identified with Medline using the search strategy previously described, of which 12 were directly relevant to the three-part review question. No further relevant papers were identified using other search strategies. A further 2 relevant studies were found from the grey literature. Of these 14 papers, 12 were found to fulfill the inclusion criteria.

All studies were small, with the largest only having 408 patients. There were 6 prospective observational studies,[10;18-22] and 6 retrospective observational studies,[23-28]

Data from the 6 prospective studies revealed 4 cases of unexpected metabolic derangement causing seizure in a total of over 1000 patients, of which 805 were patients with first seizure. In 3 cases these were derangements of serum glucose (2 hypoglycaemia, 1 hyperglycaemia) and there was one case of hyponatraemia.

Eisner *et al*, in a prospective study of 163 patients including 24 patients with first seizure, found 3 cases of seizure due to metabolic derangement.[18] All three were serum glucose abnormalities, of which, only one case (of hyperglycaemia) was unexpected. In the one unexpected case of hyperglycaemia in patient with first seizure, a provisional diagnosis of cerebrovascular accident was made before laboratory test results were available. Disposition was unchanged.

In a similar prospective study of 136 patients with first seizure, Turnbull *et al* found 11 patients with significant laboratory abnormalities.[19] Of these, only two cases of hypoglycaemia were not suspected on the basis of the history and physical examination. Sempere *et al* found one case of unsuspected hyponatraemia in a 17 year old female patient with psychogenic water ingestion in a cohort of 98 patients that was prospectively studied.[20] Breen *et al* found that 40% of patients with seizure were hyperglycaemic, but in none of these cases was hyperglycaemia thought to be the cause of the seizure.[10] Rather, it was felt that hyperglycaemia was a stress response due to the seizure.

There was no evidence from the 6 prospective studies to support more in-depth routine laboratory testing such as measurement of haematological parameters, serum calcium or magnesium levels in otherwise healthy individuals. Of note, however, Turnbull *et al* did find 2 patients with hypocalcaemia in 136 patients with new-onset seizure who were prospectively studied; one with cancer, and one with renal failure.[19]

Tardy *et al*, in a retrospective review of 247 patients with new onset seizures, found 4 cases of hyponatraemia, only one of which was not suspected on the basis of history and physical examination.[26] They also found one case of unsuspected hypoglycaemia and one case of unsuspected hypocalcaemia. Powers found only one case of first seizure attributed to metabolic abnormality, a case of hypoglycaemia identified previously from clinical findings.[23] Henneman *et al* found seizure due to hyponatraemia in 7 of 333 patients, and seizure due to "other metabolic" aetiology not further defined in 9 of 333 patients.[27] One third of patients with normal examination had abnormal laboratory investigations. Morrison *et al* found that laboratory tests gave no useful information in terms of aetiology of seizure.[25] Edmondstone found that 4 of 56 patients presenting with seizure were hyponatraemic.[28] Three of these cases were in alcoholics, and one was in a patient with dehydration. All abnormalities were suspected clinically. Rosenthal *et al*, in a retrospective observational study, found that abnormal electrolyte and urea results were essential to diagnosis in 2 of 86 cases and glucose result was essential in one case.[24]

There is debate as to whether blood tests are of any value initially, with different authors offering different opinions. Current guidelines from the National Institute for Clinical Excellence (NICE) advocate that the clinician consider appropriate blood tests (for example, plasma electrolytes, glucose, calcium) to identify potential causes or significant co-morbidity.[12] Scottish Intercollegiate Guidelines Network (SIGN) guidelines give no advice regarding blood tests in the workup of first fit[14]. The American College of Emergency Physicians' (ACEP) guidelines advise determining only a serum glucose and sodium level on patients with a first-time seizure with no co-morbidities who have returned to their baseline.[13]

The literature has multiple limitations. There is a scarcity of available evidence - all 12 studies were non-experimental observational studies and several of the papers included were of low quality. The evidence found is not conclusive regarding appropriate and necessary investigations - results were sometimes conflicting, and there was no consensus between authors. Despite the above-mentioned limitations, evaluation of the available evidence suggests that there is little justification for extensive routine laboratory testing. The circumstances of a first seizure should direct management. Laboratory tests should be ordered based on individual clinical circumstances that include suggestive historical or clinical findings such as vomiting or diarrhoea, or failure to return to baseline alertness. It would seem prudent to assess serum glucose and sodiuma in all patients, as hyperglycaemia, hypoglycaemia and hyponatraemia are the commonest metabolic derangements found, and derangements are not always predictable. A "BM Stix" measurement may be adequate, but this requires further research. There is little evidence to support any other routine laboratory investigations.

Identification of pregnancy in a patient with a first time seizure is important because it may affect testing, disposition, and initiation of antiepileptic drug therapy, although there is no further evidence to support this.[29]

A drug of abuse screen is a consideration in patients with a first-time seizure. However, there are no prospective studies that demonstrate a benefit of routine use.[30-32] One prospective study from the United States found that, of 248 patients presenting with

seizure tested for stimulant drug use (cocaine and amphetamines), 5.6% tested positive for cocaine, but none tested positive for amphetamine.[33] Positive test results were more common in patients where there was a history or suspicion of cocaine or amphetamine abuse. They concluded that routine screening for stimulant drugs would yield few cases of drug use in which there was neither a history nor suspicion of drug abuse. Dhuna *et al*, in a retrospective review, reported that 69 of 90 admitted patients with cocaine-related seizures had no prior seizure history.[30] Pesola and Westfal reported 4 cases of cocaine-related seizures in 120 patients studied, although not all patients received the same tests nor was a direct correlation demonstrated.[32] Alcoholism is an independent risk factor for first generalised tonic-clonic seizure,[34] and has been implicated in up to one third of seizures.[25;26;28] Breen *et al* found breath alcohol detectable in 14 of 39 patients tested (36%, range 10–80mg%), and McFadyen found three of four blood alcohol levels elevated, but how the patients tested were selected was not commented upon in either study[10;22] It would seem prudent to measure breath alcohol level in the ED as this may give a clue as to aetiology.[35]

An electrocardiogram (ECG) is a cheap and non-invasive test which can detect causes of collapse other than seizure, such as cardiac arrhythmia or Wolff-Parkinson-White syndrome. Long-QT syndrome, which can present as a seizure, may also be detected.[35;36] McFadyen found 4 of 112 patients had a borderline or prolonged QT interval on ECG.[22] Breen *et al* found six of 136 patients (4%) with a recorded abnormality on ECG (two T wave inversion, two right bundle branch block, one left ventricular hypertrophy, and one first degree heart block).[10] SIGN guidelines recommend that ECG should be performed in the assessment of all patients with altered consciousness, particularly those in older age-groups, when disorders of cardiac rhythm may simulate epilepsy.[14] NICE suggest that a 12-lead ECG should be performed in adults with suspected epilepsy as a good practice point.[12]

There are no studies that support performing a chest x-ray as part of the diagnostic work-up of uncomplicated first fit patients.[25]

There are no prospective studies that support performing a lumbar puncture as part of the diagnostic evaluation in the ED on patients who are alert, oriented, afebrile, and not immunocompromised. There are no adult studies, but in one retrospective paediatric case series of 503 cases of meningitis in children aged 2 months to 15 years, there was no case of occult bacterial meningitis manifesting solely as a simple seizure.[37] Sempere *et al* reported that 5 of 9 patients with a first seizure who had a fever had a central nervous system infection.[20] However, the population in this study was from an inner city hospital with a high prevalence of HIV (Human immunodeficiency virus) infection (8% of the patients in the study were HIV positive).

Recommendation
Serum glucose and sodium level should be determined on patients with a first-time seizure with no co-morbidities who have returned to their baseline **(Grade C)**.
A breath alcohol test should be performed if available **(Grade D)**.
A pregnancy test should be obtained if a woman is of childbearing age **(Grade D)**.
An ECG should be done on all patients **(Grade D)**.
Other laboratory investigations, toxicology screening, bedside tests, chest x-ray and lumbar puncture should only be done if clinically indicated **(Grade C)**.

7.1.2 Neuroimaging

The timing and indications for neuroimaging in patients with a first seizure are controversial. Many studies have shown that neuroimaging is helpful in making or excluding specific diagnoses, quantifying risk of seizure recurrence and guiding management.[21;24-26;38-41] There is agreement in the literature that emergency neuroimaging should be carried out in those with focal seizures or focal neurological deficit post-seizure. However, there is a lack of consensus as to whether neuroimaging should be performed as part of the work-up for an uncomplicated first seizure, with full recovery. The decisions that have to be made in the ED are whether the patient needs an emergency scan or whether this can wait to be performed as an out-patient if required, and what modality of neuroimaging should be carried out - computed tomography (CT) scanning or magnetic resonance imaging (MRI).

12 to 41% of patients with a first seizure have abnormal head CT scan results.[11;20;21;26;27;39;41] This figure rises to 59-82% if there are focal abnormalities on examination.[20;26;27;39] Even if there are no focal neurological signs on examination, abnormalities are still found on 6–22% of CT scans.[26;27;39;41] These rates suggest that neuroimaging should be performed in all patients presenting with a first seizure, if identifying CT abnormalities in patients with normal neurological examinations affects outcome. However, there is an absence of studies demonstrating an outcome benefit from ED imaging.[38]

In a prospective study, Eisner *et al* found that CT scans are high yield tests in the evaluation of first seizures in an unselected group of emergency patients, with a 37% incidence of significant abnormalities, and, even more significantly, CT resulted in a change of diagnosis in 44% of patients and a change in disposition in 26% of patients in whom it was used.[18] Mower *et al* found that using a clinical decision rule failed to reliably identify first seizure patients who have important lesions on CT.[42] Their decision rule, using age 65 years or over, focal neurological findings, altered mentation, high risk or known HIV infection, history of cysticercosis, and Hispanic ethnicity, had a sensitivity of just 90% in detecting individuals with emergent tomographic findings. They recommended liberal use of imaging in evaluating patients with first seizures.

Greenberg *et al*, in a systematic review forming the basis of an American multidisciplinary clinical policy on neuroimaging of emergency patients with seizure, reviewed 49 articles for data on the role of neuroimaging in the evaluation of seizure patients.[38;43] Patients with focal neurological examination findings were found to have a much higher likelihood of abnormal CT (41%) than patients with a normal examination (13%), but the type of lesions found could not be extracted from the papers. There was a small increase in the likelihood of finding an abnormality with partial-onset seizures when compared with generalised seizures. However, there was a greater percentage of tumour and stroke in the partial-onset seizure subgroup. Altered mental status was also associated with a higher rate of CT abnormalities. Lesions found in the first seizure subgroups were represented by stroke, neoplasm and cerebral atrophy in descending order of frequency. The combination of infection, subdural haematoma, and intracerebral haematoma made up about 1% of the first seizure patients. In contrast, the studies on alcohol-related and head injury-related seizures demonstrated a disproportionate number of patients with intracranial bleeding. The authors comment that clinical studies have shown a higher frequency of 'life-threatening lesions' in patients with new focal deficits, persistent altered mental status (with or without intoxication), fever, recent trauma, persistent headache, history of cancer, history of anticoagulation, or suspicion of AIDS (acquired immune deficiency syndrome), but give no data to support this.

Patients presenting with alcohol withdrawal seizures were evaluated by CT in two studies. The first, by Feussner *et al*, found 51% had abnormal CTs, with most, 34.4%, being diffuse atrophy.[44] Of the focal lesions found, 11 were old strokes and another 11 were considered potentially reversible (7 subdural haematomas, 2 hygromas, 2 intracranial haemorrhages) of which 6 went to surgery. Thirty percent of patients with focal deficits had abnormal CTs, whereas only 6% without such deficits did. Only one seizure patient without focal deficits was treated surgically. Interestingly, a cohort of alcoholics without seizures yielded similar CT results. Earnest *et al*, in a study of 259 patients with first seizure suspected to be due to alcohol withdrawal, found 58% of patients had abnormal CT scan results, of which 16 (6%) had a clinically significant lesion.[45] These included eight patients with subdural haematomas or hygromas, two arteriovenous malformations, two cysticercosis, and one each of aneurysm, possible tumour, skull fracture, and probable cerebral infarction. Of the 16 patients with significantly abnormal CT scan results, 7 were alert, had a normal neurological examination, and no signs of head trauma. In this study, history or signs of minor head trauma, headache, level of consciousness, and focal neurological signs did not significantly correlate with CT abnormalities.

Pesola and Westfal reported that 6 of 26 HIV-positive patients had an acute lesion found on CT scan, 2 of which were not suspected on physical examination.[32]

Patients over 40 years old have a conspicuous increase in the likelihood of having an abnormal CT, the frequency of abnormal scans nearing 60% in the over 50s.[38] This increased yield from scanning is most often related to cerebrovascular events and tumours,[20;39;41] with an increase in tumour prevalence beginning at age 40, and stroke in the over 60 year age group.[38] Because of this, some physicians operate an age-dependent policy with regard to neuroimaging.[28;38;46]

The American College of Emergency Physicians advocate neuroimaging in the ED as part of the routine evaluation of first seizures.[13] However, they suggest that deferred outpatient neuroimaging may be used instead when reliable follow-up is available. SIGN guidelines recommend brain imaging in all cases where a confident diagnosis of an idiopathic generalised epilepsy syndrome cannot be made.[14] Timing of neuroimaging is not discussed. NICE offer similar advice to SIGN, but state that neuroimaging should take place within 4 weeks.[12] Similarly, the International League Against Epilepsy (ILAE) recommends that neuroimaging be performed in all those without a diagnosis of idiopathic epilepsy.[47]

In a multidisciplinary collaboration between emergency medicine, neurology, and neuroradiology, an evidence-based clinical policy on neuroimaging of patients with seizures (including first seizures) was published in 1996.[48] They recommended that a head CT scan be performed in the ED in patients with first seizure whenever an acute intracranial process was suspected. Patients with a history of acute head trauma, malignancy, immunocompromise, or anticoagulation, or patients with a fever, persistent headache, a new focal neurological deficit on examination, or focal onset before generalisation, or patients older than 40 years, were specifically noted to be at greater risk of life-threatening lesions. This multidisciplinary guideline allowed for a deferred neuroimaging study as an outpatient in those patients with a first seizure who were alert and had returned to baseline, if there was no obvious cause identified. This recommendation was based on the absence of studies demonstrating an outcome benefit from ED imaging. Unfortunately, concerns regarding timely follow-up and social issues must be considered when deciding on the timing of required tests. Similarly, guidelines by Dunn *et al* advocate neuroimaging in all those with focal neurological deficit, persistent altered mental state, fever, persistent headache, recent head trauma, a history of cancer or HIV infection, focal onset before generalisation, anticoagulation or bleeding diathesis, past history of stroke or transient ischaemic attack (TIA), or in patients in whom follow-up cannot be guaranteed.[35] No evidence

could be found supporting the need for emergent neuroimaging in patients with a history of stroke or TIA. Indeed, the American multidisciplinary practice parameter suggests that prior history of stroke with no change in neurological findings militates against the need for neuroimaging.[49] Bladin *et al*, in a large prospective trial of seizures post-stroke, found no association between haemorrhagic transformation and risk of seizures.[50]

The type of imaging has also been addressed. CT scanning has important limitations, including limited sensitivity to detect small or low-grade tumours, recent cerebral infarcts, early inflammatory lesions (e.g. encephalitis) or other subtle pathologies such as mesial temporal sclerosis, cortical dysplasia and vascular malformations.[11;14;16;47;51] MRI is very sensitive to such lesions. Several case series comparing MRI with CT in the same patient indicate that the former may pick up a number of additional significant abnormalities.[11;51] King *et al* found that CT scanning detected only 12 of the 28 brain lesions that were detected by MRI; 7 of the missed lesions were brain tumours, including four astrocytomas.[11] Other authors have argued that the additional yield from MRI may not affect management in the ED.[20;52] Sempere *et al* found that MRI revealed additional lesions in 22% of cases with normal CT, but did not change management in any of them.[20] Chadwick and Smith comment that tumours that are not obvious on CT scan are likely to be low grade gliomas.[52] Most tumours presenting with seizures run a very benign course and may not benefit from early tumour treatment.[52;53] In addition, CT has a number of advantages over MRI. These include lower cost, faster scan speed and ease of access. In the acutely ill patient, CT is widely recommended as the modality of choice because of its ability to accurately detect haemorrhage and major structural changes, and the ease of access.[47;54;55] The average wait for non-emergency patients for MRI and CT scans in 2006 were seven and a half and two and a half weeks respectively, with some patients having to wait over 6 months for MRI.[56] For these reasons, Chadwick and Smith, in 1998, concluded that plausible arguments may be made for obtaining routine early CT scanning and reserving MRI for patients with epilepsy whose seizures are not controlled by antiepileptic drugs.[52]

The SIGN and NICE guidelines recommend MRI over CT where resources permit.[12;14] However, both institutes suggest that in an acute situation, CT may be used instead of MRI for emergent imaging. ACEP guidelines discuss only the indications for CT scanning in the ED, and do not compare CT with MRI.[13] The ILAE guidelines for neuroimaging studies suggest that a CT may be used if an MRI is not available although MRI is the imaging procedure of choice in patients with suspected focal epilepsy.[47]

Recommendation

Neuroimaging should be performed immediately whenever an intracranial lesion is suspected; and specifically in patients with new focal deficit or persistent altered mental state, fever, persistent headache, focal or partial onset before generalization, or a history of acute head trauma, malignancy, immunocompromise, HIV infection, alcoholism, anticoagulation or bleeding diathesis **(Grade B)**.

Deferred early outpatient neuroimaging may be used when reliable follow-up is available. Otherwise, neuroimaging in the ED should be performed on all patients **(Grade B)**.

MRI (Magnetic resonance imaging) is preferable to CT (computed tomography), if readily available within an acceptable time period, in a patient who has fully recovered. CT should be used if MRI is not readily available or in an individual who has not fully recovered. In acutely ill patients, CT is the modality of choice **(Grade B)**.

7.1.3 Electroencephalography

EEG following first seizure is perhaps even more contentious than CT scanning. If a first seizure is unprovoked, large case series support the value of EEG to identify the cause.[6;11;21;57;58] EEG, however, should not be used to differentiate between seizures and other syncopal episodes—the diagnosis can only be made from the history.[59] In a patient in whom the clinical history suggests an epileptic seizure but is not conclusive, the prevalence of epilepsy will be high, the finding of epileptiform abnormalities is specific, and the diagnostic value of the test is good. In a patient in whom the history is typical of some other disorder, such as syncope, the prevalence of epilepsy will be low, and any epileptiform abnormalities are more likely to be incidental. The test should not be performed in this circumstance.[14] Furthermore, a normal EEG does not disprove the diagnosis of epilepsy.

The value of EEG is to point to focal lesions (especially localised slow waves), predict recurrence, and indicate a specific epilepsy syndrome (spike pattern).[11;57-59] When performed within 24-48 hours of a first seizure EEG shows substantial abnormalities in about 70% of cases.[11;60] The yield may be lower with longer delays after the seizure.[11] When standard EEG is negative, systematic case series have shown that sleep deprived EEG will detect epileptiform (spike) discharges in an additional 13-31% of cases.[11;60]

However, as most physicians would not start anticonvulsant treatment following a single seizure (except in special circumstances) and neuroimaging is being performed and will pick up focal lesions, this casts some doubt over the value of the EEG in the work-up of first seizure. In addition, EEG has a 0.5–4% false positive rate and a relatively low sensitivity.[14;61] Incidental epileptiform abnormalities are found in 0.5% of healthy young adults, but are more likely in people with learning disability and psychiatric disorders, patients with previous neurological insult (e.g. head injury, meningitis, stroke, cerebral palsy) and patients who have undergone neurosurgery.[14;61]

Despite differing recommendations, there is little evidence to suggest that the EEG must be done before discharge from the emergency department.[62] A multicentre survey of management of patients with seizures revealed that EEG was uncommonly performed in the ED.[9] The American College of Emergency Physicians advises that the widespread practice of neurological consultation before obtaining an EEG seems reasonable given that EEG interpretation is a specialised province within the specialty of neurology.[13] The SIGN guidelines recommend that EEG is not routinely indicated, but should be performed in young patients presenting with a generalised seizure to aid classification, and in cases where there is clinical doubt about classification.[14] NICE guidelines include EEG to help determine seizure type, but do not recommend EEG routinely.[12] Neither SIGN nor NICE guidelines give recommendations on EEG in the Emergency Department.

Recommendation
EEG should not be routinely performed in the ED or requested by the emergency physician.
The decision as to whether it might be helpful should be made in a first seizure clinic or by an epilepsy specialist **(Grade C)**.

7.2 Need For Admission

The question to be answered is which patients who have returned to normal baseline following first seizure need to be admitted to hospital? There is a dearth of evidence on the need for admission following first seizure. There are no studies that have looked early morbidity or mortality of first seizure patients discharged from the ED. There are no prospective studies and only one retrospective study that looked at the seizure recurrence in the first 24 hours of admitted patients.[26]

The chance of a patient having a recurrent event after one unprovoked seizure varies depending on the patient's age, the seizure's underlying aetiology, combined with neuroimaging and EEG findings.[6;6;63-65] The overall risk of seizure recurrence after a first unprovoked seizure is around 50%.[2;21;66] However, when no aetiology is identified and the EEG findings are normal, the recurrence rate is 14% at one year and 24% at 2 years.[64] Patients who have structural lesions on CT scan, or patients with focal seizures with secondary generalisation, have a risk of recurrence of up to 65% at 2 years.[6]

There is only one study that specifically investigated the incidence of seizure recurrence within 24 hours of ED presentation.[26] Tardy *et al* performed a retrospective review of all adult patients seen over a 2 year period who were admitted to the hospital with a first seizure. The authors reported a 19% seizure recurrence rate within 24 hours of presentation, decreasing to 12% if those patients with alcohol-related events or focal lesions on CT scan were excluded. A quarter of alcoholic patients had early recurrent seizures. This risk of early recurrent seizures in Tardy's study was higher than reported in other studies.[63-65]

In a retrospective review, Henneman *et al* reported that 136 (46%) of 294 patients seen in the ED with a first seizure required admission and 48 (15%) of the 294 patients had a recurrent seizure whilst in the ED.[27] However, clinical data on these patients were not provided. Krumholz *et al* reported that 63 of 200 seizure patients seen in an ED required hospitalisation; however, this retrospective study failed to provide a complete data set or outcome measures on the patients.[67] Breen *et al* reported a 19% admission rate using a clinical algorithm where only those patients with a normal neurological examination, normal investigations, a responsible adult to stay with, and those patients who were likely to attend out-patient investigations and follow-up were discharged.[10]

Various criteria to determine the need for admission in adults presenting with a first seizure have been used in retrospective studies, often including a barrage of tests.[24;27] Unfortunately, those patients requiring admission are not well described, and it is difficult to assess from the data provided whether need for admission could have been predicted from clinical findings alone. One study advised admission for all patients quoting a high early seizure recurrence rate and the difficulty of predicting early recurrence.[26] However, this may not be applicable in those with unprovoked seizures who have returned to baseline. Several studies have agreed admission is probably only necessary if the patient does not return to baseline or is at high risk of further seizures (e.g. alcohol withdrawal) or cannot be supervised by a responsible adult.[16;25;68;69] Despite this, first seizure patients in the UK are often referred to the inpatient medical team,[25] which is unnecessary and undesirable.[35]

The American College of Emergency Physicians recommend that patients with a normal neurological examination can be discharged from the ED with outpatient follow-up.[13] To this, the following provisos can sensibly be added: normal investigations, there being a responsible adult to stay with, patients who are likely to attend out-patient investigations and follow-up.[35] Neither the SIGN nor NICE guidelines offer any advice on which patients to admit.[12;14]

Recommendation
Patients who have fully recovered, have no neurological deficit, and have normal initial investigations can be discharged from the ED **(Grade D)**.
Admission should be considered in all patients with alcoholism, poor social circumstances or those without a responsible adult to stay with **(Grade D)**.

7.3 Treatment

The emergency physician must also decide whether or not to initiate antiepileptic drug (AED) therapy in the ED. The decision to initiate antiepileptic AEDs in the emergency department must be based on the predicted risk for seizure recurrence. However, as outlined in the previous section, recurrence risk is based on the underlying cause of the seizure. Determining this often requires the results of a neuroimaging study and an EEG, information that is rarely available before ED discharge. In addition, risk of recurrence must be balanced against the consequences of a second seizure to the patient, and the risk of AED toxicity.[65]

Four randomised controlled trials (RCTs) were found addressing the question of commencing AEDs after a single seizure.[66;70-72] Three RCTs found that treatment following a single seizure with antiepileptic drugs reduced seizure recurrence at 1–3 years compared with no treatment or placebo. However, there was no evidence that treatment alters long term prognosis. One RCT in people with one or more seizures found that immediate treatment with antiepileptic drugs increased the time to first and second subsequent seizure, and reduced the time to achieve 2 year remission of seizures compared with no treatment.

Musicco *et al*, for the First Seizure Trial Group, compared immediate treatment after a first unprovoked seizure versus no immediate treatment.[71] People were randomised within 7 days of their first generalized seizure. The authors found that there were half as many second seizures with immediate treatment compared with no immediate treatment at 2 years (24% with immediate treatment v 42% with no immediate treatment). However, no significant difference was found in the proportion of people achieving a 2 year remission in seizures. Gilad *et al* compared immediate treatment versus no treatment.[72] The RCT found that immediate treatment significantly reduced the risk of relapse over 3 years of follow up: 10/45 (22%) with immediate treatment versus 29/42 (71%) with no treatment. Another RCT by Chandra compared immediate treatment with sodium valproate versus placebo in adults presenting within 2 weeks after their first seizure.[70] It found that sodium valproate reduced the number of people experiencing a recurrent seizure over 12 months. Five of 113 (4.4%) patients treated with sodium valproate experienced a recurrent seizure as opposed to 63 of 115 (54.8%) patients treated with placebo. Marson *et al*, for the Medical Research Council MESS (Multicentre Study of Early Epilepsy and Single Seizure) Study Group, compared immediate versus deferred antiepileptic drug treatment in 1443 people with one (56%) or more (44%) previous unprovoked seizures.[66] They found that early use of AEDs reduced the likelihood of seizure recurrence by 20%. Also, immediate treatment increased time to first and second subsequent seizure and reduced the time to achieve 2 year remission of seizures. However, the authors also found that deferring treatment of first seizures did no increase the danger of a worsened illness, dismissing the concern that "seizures beget seizures." That is, long-term seizure control was just as good in patients with deferred treatment. At 5 years, about 75% were in remission (seizure free for between 3 and 5 years), with no significant difference between groups.

These studies shows that about half of the patients taking AEDs after a first seizure probably do so unnecessarily, but it is very difficult to identify those patients beforehand; although clinical findings, EEG and neuroimaging can help better stratify the risk.[6;63-65] Also, in these studies, early therapy had no effect on the long-term prognosis of epilepsy, and its advantage in the short term must be weighed against costs and potential adverse effects. The adverse effects of antiepileptic drugs are well known and include idiosyncratic reactions, teratogenesis, and cognitive effects. Interim analysis in the RCT by the First Seizure Trial Group found that 14/204 (7%) of participants discontinued antiepileptic drug treatment owing to adverse events.[65]

Many authors agree that anticonvulsant medication should only be prescribed to patients following their first generalised seizure when the risk of seizure recurrence is particularly high; although neuroimaging, EEG, occupation, and patient opinion may influence this decision.[12;14;25;27;28;35] Acute symptomatic seizures provoked by metabolic, alcohol withdrawal or drug-related causes should not be treated with antiepileptic drugs.[14;61]

Both NICE and SIGN guidelines advocate that AEDs should only be commenced after a first seizure on the advice of an epilepsy specialist, and then, only if an EEG shows unequivocal epileptic discharges, if the patient has a congenital neurological deficit, if the patient and physician consider the risk of recurrence to be unacceptable, if the patient has had previous myoclonic, absence, or partial seizures (SIGN only), or if brain imaging shows a structural abnormality (NICE only).[12;14] The American College of Emergency Physicians recommend that patients with a normal neurological examination, no co-morbidities, and no known structural brain disease do not need to be started on an antiepileptic drug in the ED.[13] Dunn *et al* recommend that AEDs should not routinely be prescribed in the ED, but only after consultation with a neurologist or other specialist with an interest in epilepsy.[35]

Recommendation
AEDs should not routinely be prescribed in the ED. If AEDs are to be prescribed, this should only be after consultation with an epilepsy specialist **(Grade B)**.

7.4 Advice

The Driver and Vehicle Licensing Agency (DVLA) states that following a first seizure a patient should have one year off driving with medical review before restarting.[73] There may be special consideration when the epileptic attack is associated with certain clearly identified non-recurring provoking factors. A doctor has a duty to advise patients of these facts and of the patient's duty to inform the DVLA. Doctors should record in the medical notes that this advice has been given, but audits of medical records show that in only 0.9–21% of cases was it documented that such advice had been given.[25;28;74]

Practitioners are also poor at giving patients information about the particular dangers of seizures and epilepsy, and changes in lifestyle/occupation that should be considered.[14;75] Surveys have reported that up to 90% of patients with epilepsy want more information from health care professionals and feel that they receive little advice about their epilepsy, such as advice about hazardous activities.[76] Patients should be given advice about avoiding potentially dangerous situations such as swimming alone or bathing a baby alone. Patients should also be told to inform their employer that they have had a seizure. NICE and SIGN guidelines recommend that this advice should be given in various formats.[12;14]

Recommendation
Patients should be given verbal and written advice about driving and lifestyle changes prior to being discharged from the ED. Advice given to patients should be documented in the medical notes **(Grade D)**.

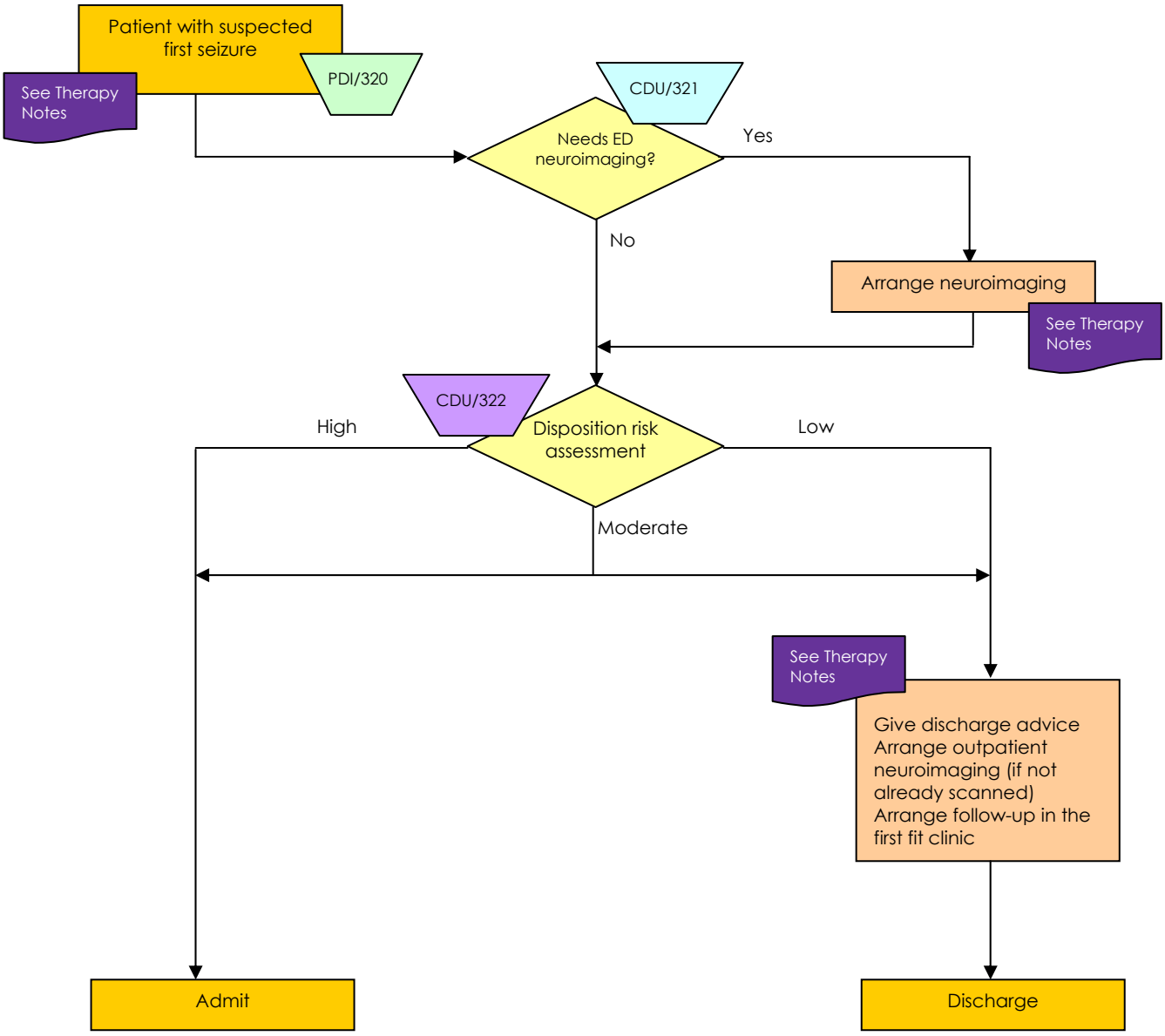
7.5 Follow-Up

NICE recommend that all people having a first seizure should be seen within 2 weeks by a "specialist in the management of the epilepsies to ensure precise and early diagnosis and initiation of therapy as appropriate to their needs."[12;14] The SIGN guidelines state that the diagnosis of epilepsy is most appropriately made in a dedicated first seizure clinic by an epilepsy specialist.[12;14]

The National Clinical Audit of Epilepsy-related Death found that waiting times for a specialist appointment after first seizure were long, with 15% (4/26) of individuals having to wait more than 6 months to be seen.[75] Also, for those with first seizure referred to secondary care by their General Practitioners (GPs), in 15% (4/26) it had taken between one and 6 months to be referred by their GP. The Clinical Standards Advisory Group (CSAG), in a report from 2000, also found that only 60% of patients with "newly developing epilepsy" were seen within 6 weeks of referral.[77] Bhatt *et al*, in a recent retrospective audit, found that 83% of patients with first fit discharged from ED with a letter to take to their general practitioners were lost to follow-up, but only 20% of those referred directly to the neurology clinic were lost.[78] Of the patients seen as out-patients by a neurologist, the median waiting time to clinic was 22 weeks. The currently proposed NICE target time to specialist review is clearly unrealistic without significant service reconfiguration.

Recommendation
All patients should be followed-up by an epilepsy specialist urgently, ideally within 2 weeks.
Robust pathways should be established to ensure specialist follow-up of all patients. Current evidence supports direct referral from the ED.
(Grade D).

8. EVIDENCE-BASED FLOWCHART



PDI/320: SUITABILITY FOR PROTOCOL DRIVEN INVESTIGATION (ALL YES)

16 years old or over	Yes
Suspected first seizure, convulsive	Yes
Not status epilepticus	Yes
Seizure not related to head injury or eclampsia	Yes

Order: T, P, R, BP, SpO_2
serum glucose and sodium
ECG
breath alcohol test
pregnancy test
Other investigations:
other bloods, CXR, LP, toxicology *only if clinically indicated*

CDU/321: NEED FOR NEUROIMAGING PRIOR TO DISCHARGE (ANY YES)

New focal deficit	Yes
Persistent altered mental status	Yes
Fever or persistent headache	Yes
Focal or partial onset seizure	Yes
History of cancer, HIV, immunosuppression, head injury, anticoagulation or bleeding diathesis, or alcoholism	Yes
Follow-up cannot be ensured	Yes

CDU/322: DISPOSITION RISK ASSESSMENT
(High if any HIGH, low if no HIGH and no MOD, otherwise moderate)

	Yes	No
Simple fit with full recovery		HIGH
No neurological deficit		HIGH
Normal initial investigations		HIGH
History of/suspected alcoholism	MOD	
Poor social circumstances	MOD	
No responsible adult to supervise	MOD	
Unlikely to return for follow-up	MOD	

THERAPY NOTES

Laboratory Investigations & Bedside Tests: Laboratory investigations other than those outlined in PDA/320, toxicology screening, bedside tests, chest x-ray and lumbar puncture should only be done if clinically indicated.

Choice of neuroimaging modality: MRI preferable to CT, if readily available within an acceptable time period, in a patient who has fully recovered. CT should be used if MRI is not readily available or in an individual who has not fully recovered. CT is the modality of choice if the patient is critically ill, requires monitoring or MRI is not available/contraindicated.

Treatment: AEDs should not routinely be prescribed in the ED. If AEDs are to be prescribed, this should only be after consultation with an epilepsy specialist

Discharge: Patients with a normal neurological examination and normal baseline investigations can be safely discharged from the ED with outpatient follow-up. Consider admitting those patients without a responsible adult to stay with, or patients who are unlikely to attend out-patient investigations and follow-up.

Advice: Give discharge advice (including first aid, driving, occupation and hazardous activities), document advice in notes and give advice leaflet. Advice given to patients should be documented in the medical notes.

Follow-up: Arrange follow-up in the first fit clinic, ideally within 2 weeks. Arrange outpatient neuroimaging if not already scanned or early follow-up cannot be ensured.

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