Guidelines on autopsy practice:
Deaths in patients with epilepsy including sudden deaths

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In accordance with the College’s pre-publication policy, this document was on the Royal College of Pathologists’ website for consultation from 6 February to 6 March 2019. Responses and authors’ comments are available to view on request.

This document is part of the ‘Guidelines on autopsy practice’ series.

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## Contents

Foreword .......................................................................................................................... 3

1 Introduction .................................................................................................................... 4

2 The role of the autopsy ................................................................................................. 5

3 Pathology encountered at autopsy ............................................................................... 5

4 Specific health and safety aspects ............................................................................... 5

5 Clinical information relevant to the autopsy ............................................................... 6

6 The autopsy procedure ............................................................................................... 7

7 Specific organ systems to be considered .................................................................... 7

8 Organ retention ........................................................................................................... 9

9 Histological examination ............................................................................................. 10

10 Toxicology .................................................................................................................. 11

11 Other relevant samples .............................................................................................. 12

12 Imaging ....................................................................................................................... 12

13 Clinicopathological summary ................................................................................... 12

14 Examples of cause of death opinions/statements ..................................................... 12

15 Criteria for audit ......................................................................................................... 14

16 References ................................................................................................................ 16

Appendix A   Summary table – Explanation of grades of evidence ................................. 18

Appendix B   Systematic review of evidence .................................................................. 19

Appendix C   AGREE II compliance monitoring sheet .................................................. 21

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NICE has accredited the process used by the Royal College of Pathologists to produce its autopsy guidelines. Accreditation is valid for 5 years from 25 July 2017. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.
Foreword

The autopsy guidelines published by the Royal College of Pathologists (RCPath) are benchtop guidelines for pathologists to deal with non-forensic consent and coroner’s post-mortem examinations in a consistent manner and to a high standard.

The guidelines are systematically developed statements to assist the decisions of practitioners and are based on the best available evidence at the time the document was prepared. Given that much autopsy work is single observer and one-time only in reality, it has to be recognised that there is no reviewable standard that is mandated beyond that of the FRCPath Part 2 exam or the Certificate of Higher Autopsy Training (CHAT). Nevertheless, much of this can be reviewed against ante-mortem imaging and other data. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the coroner and the deceased’s family.

There is a general requirement from the General Medical Council (GMC) to have continuing professional development in all practice areas and this will naturally encompass autopsy practice. Those wishing to develop expertise/specialise in pathology are encouraged to seek appropriate educational opportunities and participate in the relevant external quality assurance scheme.

The guidelines themselves constitute the tools for implementation and dissemination of good practice.

The following stakeholders were contacted to consult on this document: the Human Tissue Authority and its Histopathology Working Group, which includes representatives from the Association of Anatomical Pathology Technology, Institute of Biomedical Science, the Coroners’ Society of England and Wales, the Clinical Practice Committee of the British Neuropathological Society, the Home Office Forensic Science Regulation Unit and Forensic Pathology Unit, and the British Medical Association.

The information used to develop this document was derived from current medical literature and a previous version of this guideline. Much of the content of the document represents custom and practice and is based on the substantial clinical experience of the authors. All evidence included in this guideline has been graded using modified SIGN guidance (see Appendix A). The search strategy for reviewing the literature is outlined in Appendix B. The sections of this autopsy guideline that indicate compliance with each of the AGREE II standards are indicated in Appendix C.

No major organisational changes or cost implications have been identified that would hinder the implementation of the guidelines.

A formal revision cycle for all guidelines takes place on a five-year cycle. The College will ask the authors of the guideline to consider whether or not the guideline needs to be revised. A full consultation process will be undertaken if major revisions are required. If minor revisions or changes are required, an abridged consultation process will be undertaken whereby a short note of the proposed changes will be placed on the College website for two weeks for members’ attention. If members do not object to the changes, the changes will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

The guideline was reviewed by the Death Investigation Group, Neuropathology Specialty Advisory Committee, Lay Governance Group and Clinical Effectiveness department. It was placed on the College website for consultation with the membership from 6 February to 6 March 2019. All comments received from the membership were addressed by the authors to the satisfaction of the Clinical Lead for Guideline Review (Cellular Pathology).
The guideline was developed without external funding to the writing group. The College requires the authors of guidelines to provide a list of potential conflicts of interest; these are monitored by the Clinical Effectiveness department and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

Epilepsy is a common neurological condition. It may arise from many types of underlying brain pathology, from neurodevelopmental disorders in the young to tumours, stroke and neurodegenerative diseases in adults. Epilepsy can also be a manifestation of a genetic disorder (for example a channelopathy) or may be idiopathic, for which no brain lesion may be found.

Epilepsy may be unrelated to the cause of death but in many cases it is directly relevant, for example an accident during a seizure or sudden unexpected death in epilepsy (SUDEP). SUDEP is the most common cause of premature death in adults with epilepsy and is more common in patients with poorly controlled generalised convulsive seizures. Other recognised risk factors include early onset of epilepsy, long disease duration, poor compliance with medication, recent change in treatment and alcohol misuse. SUDEP are often unwitnessed, nocturnal deaths and, by definition, no cause of death can be ascertained at post mortem. The mechanisms are unknown but current evidence, including from witnessed SUDEP deaths on monitoring units, favour a centrally mediated depression of cardiac and respiratory regulation.

Common challenges when facing a post-mortem examination on a person with epilepsy or death associated with a seizure include:

• full clinical information may not be available at the time of autopsy regarding the epilepsy history and/or its underlying cause
• many deaths in epilepsy are unwitnessed and there may be a prolonged post-mortem interval, particularly if they live alone
• brain retention protocols and coronial practice varies widely regarding epilepsy-related deaths
• death can be associated with a seizure without epilepsy (e.g. seizures provoked by alcohol, febrile seizures, etc.)
• death can be due to the disease causing epilepsy (e.g. malignant brain tumour, stroke)
• in SUDEP, the brain can show neuropathology and is not always normal, but this does not account for the sudden death
• in sudden deaths, attributing the relative contributions of comorbidities identified (e.g. mild coronary artery disease) and epilepsy can be problematic
• SUDEP can still go unrecognised with ‘unascertained’ or other terms used in their categorisation
• a seizure does not have to occur (or be witnessed) for SUDEP categorisation in a patient with sudden death, epilepsy and a negative post mortem.

1.1 Target users and health benefits of these guidelines

The target primary users of these guidelines are general pathologists, trainees and neuropathologists performing consented and coronial post mortems in persons with epilepsy. The recommendations will also be of value to the coroner’s office in dealing with epilepsy-related deaths and to epilepsy healthcare professionals.
2 The role of the autopsy

- To establish whether epilepsy has caused or contributed to:
  - death as a result of status epilepticus
  - death as a result of trauma sustained during a seizure
  - death as a result of drowning during a seizure
  - death as a result of airway obstruction during a seizure
  - death as a result of aspiration during a seizure
  - death as a result of epilepsy treatment (e.g. anticonvulsant drug interaction, overdose or surgical treatments)
  - death as result of epilepsy-related suicide
  - SUDEP (see definitions in section 14).
- To exclude causes of death that might mimic SUDEP, e.g. sudden cardiac death.
- To exclude death from drugs or poisoning.
- To identify or confirm the cause of the epilepsy if present, e.g. neuropathological lesion (brain tumour, cortical dysplasia, old contusion).
- To provide accurate data for the inquiries and audits into the incidence of and remedial factors around epilepsy-associated deaths.

[Level of evidence D – evidence from case series.]

3 Pathology encountered at autopsy

- External evidence of a seizure, e.g. incontinence, tongue biting.
- Evidence of traumatic injury sustained during a seizure, e.g. head injury, bruises, burns, etc.
- Brain swelling, focal brain abnormalities, e.g. tumours, cortical dysplasias, contusions, etc.
- Cardiac abnormalities that might be associated with sudden death (coronary artery disease, myocardial infarction, cardiomegaly, cardiomyopathy, myocarditis, etc.)
- Pulmonary oedema, aspirated gastric contents.

4 Specific health and safety aspects

No specific precautions beyond standard protocols are generally required in epilepsy post mortem. Local guidelines for the mortuary should be followed in each case to assess the risk based on available clinical information from the coroner or hospital records. Personal protective equipment should be used as appropriate to minimise risks, for example in epilepsy patients with coincidental HIV, hepatitis B and post mortem in suspected prion disease carried out according to local protocols, etc. Some patients with epilepsy may have internal devices (e.g. vagal nerve stimulators) or pacemakers in situ (e.g. history of seizure-related arrhythmias/asystole).
5 Clinical information relevant to the autopsy

Before commencing the examination, information from the coroner’s officer or from the hospital records should be obtained as listed below. Additional information may be obtained from GP records, and the family, through the coroner’s office, are often a key source of information. The autopsy report should contain a summation of all clinical information available to the pathologists at the time of issue of the final report. A separate neuropathology report from a specialist centre can be integrated into the main report.

5.1 Circumstances of death

- Deaths in community:
  - witnessed deaths: if death occurred during seizure, or the recovery (post-ictal) phase or no seizure/convulsive movements were noted, duration of seizure (status epilepticus >30 minutes), any resuscitation attempts made and survival time
  - unwitnessed deaths: any photographs taken at scene, evidence of incontinence/vomiting, position of body (supine versus prone), evidence for suffocation/airways obstruction or compromise (e.g. pillow covering face or abnormal position of neck), circumstances that might have caused injury, deaths in bath/water (e.g. if head was submerged), if death occurred during night/sleep
  - number of tablets in bottles and dates of prescribing/doses, eye-witness accounts
  - when the person was last seen alive and their state of health.

- Deaths in hospital/care:
  - details of recent seizure control, witness reports, any monitoring around the time or during death (electroencephalogram [EEG], cardiac, video, etc.), changes in medications or recent procedures.

5.2 Epilepsy history

- Details of age of onset, type and frequency of seizures.
- Details of any recent change in seizure frequency or severity.
- Details of anti-epileptic drugs (AEDs), compliance and any recent changes to treatment (drug, dose, etc.), a history of non-drug treatments (e.g. vagal nerve stimulation, epilepsy surgery), and a full drug history for other comorbidities should be taken.
- Cause of epilepsy (if known) and any information from hospital investigations (e.g. magnetic resonance imaging [MRI] and EEG findings).
- Any history of previous episodes of collapse (e.g. seizure-related asystole, near miss SUDEP), status epilepticus or traumatic events associated with seizures.

5.3 Other relevant history

- Cardiac disease, abnormal electrocardiograms, syncopal attacks, family history of sudden cardiac death.
- History of previous traumatic brain injury or neurosurgery. In cases of post-traumatic epilepsy consequent of a previous criminal act, full discussion of the case with the coroner and any legal implications is advisable prior to the autopsy.
• Alcoholism, psychiatric illness, learning difficulties, etc.

[Level of evidence D – evidence from case series.]

6 The autopsy procedure

6.1 External examination

• Identification of body and any decomposition (if unwitnessed death in community).
• Distribution of hypostasis in relation to information of position of body when found.
• Signs of resuscitation (e.g. cannulas).
• Documentation of external injuries/burns (old or recent) that may have been sustained during seizures and/or any surgical scars (including cranium).
• Evidence of tongue biting (tip or lateral sides of tongue, fresh or old scars) or any blood-tinged foam around mouth.
• External evidence of disorders such as neurofibromatosis, Sturge-Weber syndrome or tuberous sclerosis often associated with epilepsy.

[Level of evidence D – evidence from case series.]

7 Specific organ systems to be considered

In suspected epilepsy-related deaths, a full post-mortem examination, including neuropathology, organ histology and toxicology, is required. All organs that have not been previously harvested should be weighed and examined. In the post mortem, particular attention should be given to the following systems.

7.1 Cardiovascular system

• Structural cause for sudden cardiac death including:
  – ischaemic heart disease/coronary artery disease
  – myocardial hypertrophy, cardiomyopathy, cardiomegaly
  – valve disease (refer to Guidelines on autopsy practice: Sudden death with likely cardiac pathology).7

Notes:

1. Although an increased incidence of mild cardiac hypertrophy and fibrosis has been reported in epilepsy/SUDEP series,8–11 there is conflicting evidence for this.12,13 Careful consideration is required for attributing minor cardiac pathologies as the underlying cause of death (see section 14).

2. Channelopathies and genes causing long QT syndrome may be relevant to both sudden arrhythmic death syndrome (SADS with no gross cardiac pathology) and as a cause of the epilepsy. Consider genetic testing in suspected cases and hereditary implications (see section 11).
7.2 Respiratory system

- Check airways and larynx for any obstruction or foreign bodies (exclude choking during seizure).
- Evidence of aspiration (gastric contents may be displaced in main airways [trachea and bronchi] in SUDEP; presence in distal airways may represent true aspiration).\(^{14}\)
- Pulmonary oedema, congestion and haemorrhage have been consistently reported in SUDEP series to varying degrees\(^ {15}\) and is regarded as a non-specific finding.\(^ {14}\)
- For bodies found in water (bath, swimming pool), any evidence of drowning including over-distended lungs and emphysema aquosum (refer also to *Guidelines on autopsy practice: Autopsy for bodies recovered from water*).\(^ {16}\)

7.3 Central nervous system

7.3.1 Assessments prior to brain slicing

- The scalp should be examined for any bruises or other injury.
- The skull should be examined for any fractures.
- The dura should be examined for any evidence of acute or old haemorrhage.
- The dural venous sinuses should be opened.
- Meninges should be assessed for evidence of meningeal infiltration (excess cloudiness).
- The circle of Willis should be examined for vascular disease.
- Brain swelling and any herniation (uncal, tonsillar, subfalcine or at old surgical site) should be evaluated. Mild degrees of brain swelling (effacement of gyri but without herniation) can occur in SUDEP.\(^ {15,17}\)
- The surface of the brain should be examined for evidence of old contusions, previous surgery, arteriovenous malformation, tumours, etc.

7.3.2 Brain slicing (fixed or unfixed)

The aims of macroscopic brain examination are to:

- identify the structural cause of epilepsy
  - common lesions identified in SUDEP and epilepsy autopsy series include hippocampal sclerosis, cortical malformations (e.g. cortical dysplasia), vascular malformations/cavernomas, primary brain tumours, old contusions, etc.\(^ {17,18}\)
  - there is no evidence that any single neuropathology is more often associated with SUDEP.\(^ {15}\)
- identify the effects of previous/recent seizures
  - acute neuronal injury/eosinophilic neurones (can be limited to hippocampus or extensive if patient resuscitated for short period)
  - cerebellar atrophy, thalamic atrophy
  - cortical atrophy/scarring from seizures (status epilepticus, mitochondrial disease, epileptic encephalopathies, autoimmune encephalitides)
  - evidence of neurosurgery
- identify any unsuspected (unrelated) cause of death
  - colloid cysts in third ventricle/hydrocephalus
  - acute stroke/brain swelling
- acute (infective) meningo-encephalitis.

The brainstem and cerebellum should be removed by an axial slice through the midbrain. The cerebellum should be removed from the brainstem by cutting through the three pairs of cerebellar peduncles. The brainstem is then sliced in the axial plane at 5 mm thick blocks. The cerebellum is sectioned through the sagittal midline to inspect the vermis and the hemispheres through the dentate nucleus/superior peduncle.

The cerebral hemispheres should be sliced in the coronal plane at approximately 1 cm intervals (see Figure 1).

The following key elements are assessed on coronal slices:
- greenhall line to assess for diencephalic descent/brain swelling
- ventricles for symmetry, dilatation or compression
- cortical ribbon (any lesions and acute/chronic infarct – attention to watershed regions)
- symmetry of hemispheres and hippocampus/amygdala
- regions of relative atrophy, e.g. cerebellum or thalamus (hindbrain weight should represent 12–15% of total).

[Level of evidence – GPP.]

8 Organ retention

It is not possible or necessary for specialist neuropathologists to perform all of the authorised autopsies on patients with epilepsy, but it is best practice for a specialist to be involved in the interpretation of the neuropathology/histology. Organ retention must abide within the limits of the consent from the relatives or following discussion with the coroner. The coroner can provide families with details of the support organisation SUDEP Action (www.sudep.org).

8.1 Brain retention protocol scenarios

i. Recommended practice: a case should be made for whole brain retention with fixation for 2–3 weeks and referral to a neuropathologist (particularly in cases where there is consent for research donation).

ii. The next best practice is to fix the brain for a short interval, slice (either locally or at regional neuropathology referral centre), document the gross appearances of the brain (ideally with photography), sample for histopathology and reunite the organ with the body.

iii. A further option is to fix a single coronal slice 1–2 cm thick at the hippocampus level (see Figure 1) and a section of brainstem and cerebellum (amounting to ~5–10% of brain weight), returning the rest of the brain to the body. The fixed tissue samples can be examined by a neuropathologist.\(^1\)

iv. Histological sampling is done at the time of autopsy with no organ retention.

In making the case for whole brain retention to the coroner, the importance of optimal examination in epilepsy-related deaths must be emphasised. UK-wide audits have shown that adhering to protocol (i) increased detection of relevant underlying neuropathology.\(^1\)
8.2 Heart retention

If sudden cardiac death is suspected, such as SADS or conduction defect, retention of the heart and referral to specialist centre should be considered.

[Level of evidence – D.]

9 Histological examination

Tissue sampling must be taken within the limits of consent from the next of kin or agreement with the coroner. Recommend sampling protocols include any grossly abnormal areas and:

1. vascular watershed region/frontal watershed regions (F1/2): acute hypoxic/ischaemic damage/meningitis/encephalitis/chronic neuronal loss (from previous seizures or episodes of status epilepticus, e.g. laminar atrophy)
2. insular cortex/basal ganglia: acute neuronal injury, hypoxic/ischaemic damage/meningitis/encephalitis
3. amygdala: acute neuronal injury, hypoxic/ischaemic damage/limbic encephalitis/chronic astrocytosis
4. hippocampus: acute neuronal injury (CA1), hypoxic changes/limbic encephalitis/hippocampal gliosis/sclerosis/malformation/neurodegenerative disease
5. thalamus: acute neuronal injury/chronic regional gliosis
6. temporal cortex (T1/2): meningitis/encephalitis/gliosis/global hypoxic changes/chronic atrophy/traumatic brain injury/neurodegenerative pathology
7. cerebellum: acute or chronic atrophy/inflammation
8. medulla: inflammatory disease.

Figure 1: Lines indicate approximate coronal levels for block sampling, following hindbrain removal. (This is also the level for ‘slice fixation’ protocol (iii), section 8.) The samples 1–6 are shown on one hemisphere to illustrate anatomy, but paired samples from left and right hemisphere for blocks 3–5 are recommended as good practice.

Tissue sampling may also be guided by clinical information of seizure localisation from EEG or MRI investigations during life. Samples from both left and right hemispheres should be taken where possible as epilepsy can lateralise (particularly in the hippocampus as sclerosis can be unilateral). All blocks should be stained with haematoxylin and eosin stain. Myelin stains are useful for neuroanatomical assessment. Gliosis can be demonstrated with glial fibrillary acidic protein and neuronal loss with Cresyl violet or neuronal markers. Seizure-specific patterns of reorganisation (e.g. hippocampal mossy fibre pathway) can be carried out in specialist centres.
9.1 Organ blocks for histology

- Heart: if there is no identified lesion, multiple blocks should be taken across the right ventricle and left ventricle/septum with histological examination for fibrosis, myocarditis, etc. (refer to Guidelines on autopsy practice: Sudden death with likely cardiac pathology).7
- Lung: to confirm any suspected pneumonia or aspiration. The presence of acute inflammatory response does not necessarily indicate aspiration prior to death.
- Other samples from organs based on post-mortem findings as determined by the pathologist as relevant to the investigation and cause of death.

[Level of evidence D – this is the conclusion from large published post-mortem studies in epilepsy deaths as well as clinical SUDEP studies].

10 Toxicology

This is carried out to evaluate:

- blood levels of AEDs and compliance:20
  - to confirm prescribed AEDs were being taken at the correct dosage
  - to establish whether the patient had stopped taking the prescribed AEDs (this is common in pregnancy-associated fatal epilepsy, e.g. for fear of damaging the foetus)
  - to establish whether there was an accidental or intentional overdose
- other medications or non-prescribed drugs
- alcohol levels.21

The occurrence of epilepsy and acute symptomatic seizures with alcohol, drugs of abuse and withdrawal is recognised.14 Alcohol intoxication can also trigger seizures in patients with an epilepsy diagnosis. Death due to seizure in acute intoxication (without epilepsy diagnosis) is not SUDEP but does not preclude the seizure as a contributor to death.

The following samples are recommended:

- 10 ml peripheral blood (femoral or iliac) and 20 ml urine
- gastric contents, which should be inspected for any undigested tablets that can be separated off
- hair for AED analysis to assess long-term compliance if indicated, e.g. allegations of medical negligence or of possible inappropriate drug administration.

For other samples (e.g. vitreous), refer to Guidelines on autopsy practice: Autopsy when drugs or poisoning may be involved.22

[Level of evidence D – published studies.]
11 Other relevant samples

11.1 Microbiology

If encephalitis is suspected, a cerebrospinal fluid sample and fresh tissue should be retained for microbiological/viral studies.

11.2 Molecular genetics

If a potentially inheritable/genetic cause of epilepsy (e.g. a channelopathy causing both arrhythmia and seizures) is suspected, fresh blood and/or a 2 cm cube of fresh spleen for freezing should be reserved. Genetic testing may also be considered to identify epilepsy conditions and mutations associated with SUDEP. The authority/consent for this retention must be ensured by the pathologist conducting the post mortem.

11.3 Metabolic

If the possibility of metabolic brain disorders/mitochondrial disease is considered, appropriate samples (guided by clinicians and chemical pathologists) should be reserved.

[Level of evidence D – published studies.]

12 Imaging

Imaging-based post-mortem examination should never be undertaken without an expert external examination of the body having first been performed by an appropriately trained and experienced individual. The role of post-mortem imaging is increasingly used in cases of sudden death but no specific protocols currently exist for suspected epilepsy-related and sudden deaths and there is currently no evidence for its primary role in these investigations. Structural lesions may be identified in the brain pertaining to epilepsy (and should be correlated with any neuroimaging during life). If cause of death is not ascertained, post-mortem examination, including brain removal/neuropathology and toxicology, is advised.

13 Clinicopathological summary

- Documentation of all morbid anatomical, histological and toxicological findings.
- Description of if and how epilepsy has caused or contributed to death.
- The aetiology of the epilepsy, if ascertained.

14 Examples of cause of death opinions/statements

14.1 Definitions and notes

1. **SUDEP**: ‘Sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning deaths in patients with epilepsy, with or without evidence for a seizure, and excluding documented status epilepticus, where necropsy examination does not reveal a toxicological or anatomical cause of death.’
   a. Neuropathological abnormalities may be identified but do not account for the sudden death.
b. A seizure does not have to occur/be witnessed for a SUDEP diagnosis in an epilepsy patient with unexplained sudden death.\(^{30}\)

2. **Possible SUDEP**: Where a competing cause of death is identified at post mortem (e.g. non-significant coronary atheroma [50–75\% occlusion], cardiac hypertrophy, dead in bath but no drowning), the term ‘possible SUDEP’ can be used. SUDEP also includes cases with short survival following resuscitation but with no recovery following a seizure-related cardiac arrest.

3. For neuropathologists examining the brain only in epilepsy deaths (and not conducting the full post mortem) where no neuropathological cause of death is identified, an example of wording that can be used on their report is ‘neuropathology findings in keeping with SUDEP in the context of a negative full post mortem with toxicology’.

4. **Status epilepticus** requires witnessed evidence of unremitting seizure activity for >30 minutes or electro-clinical (EEG) evidence of prolonged seizure activity.

14.2 The following scenarios fulfil criteria for SUDEP

1. Epilepsy patient; no other relevant pre-existing conditions; found dead; negative post-mortem examination.
2. Epilepsy patient; witnessed sudden death in sleep or during activity including exercise, no seizure; negative post-mortem examination.
3. Epilepsy patient; no other relevant pre-existing conditions; witnessed seizure, post-ictal coma, no evidence or history of terminal status epilepticus; negative post-mortem examination.
4. Epilepsy patient found dead face down in bed or on floor; negative post-mortem examination.
5. Sudden death in conjunction with first seizure; post mortem shows brain tumour without significant mass effect, otherwise negative post mortem. (The enduring predisposition for seizures when a tumour is identified meets criteria for epilepsy despite death coinciding with first seizure.)

The above and similar scenarios should be recorded as:

1a) SUDEP
1b) Epilepsy
1c) Cause of epilepsy if known, e.g. oligodendroglioma

14.3 In the following scenarios, SUDEP is excluded

1. Death during documented status epilepticus (defined as unremitting seizure activity for >30 minutes) should be given as:
   1a) Status epilepticus
   1b) Antecedent cause if appropriate.
2. Evidence of significant aspiration during fatal seizure (minor degrees of aspiration allowed in SUDEP).
3. Evidence of fatal traumatic injury sustained during seizure.
4. Evidence of drowning during seizure.
5. Death during or following a provoked seizure (where there is not an epilepsy diagnosis), e.g. alcohol-withdrawal seizure, febrile seizure.
6. A clear alternative cause of death is found at post mortem.
Examples of non-SUDEP cause of death formulations in epilepsy include:

1a) Status epilepticus
1b) Primary generalised epilepsy

1a) Status epilepticus
1b) Oligodendroglioma (WHO grade II)

1a) Acute subdural haemorrhage with mass effect
1b) Traumatic head injury
1c) Generalised epileptic seizure

1a) Drowning
1b) Idiopathic generalised epilepsy

1a) Aspiration
1b) Drug overdose

2) Epilepsy

There is an epilepsy deaths register in the UK for SUDEP and other epilepsy-related deaths at www.epilepsydeathsregister.org.

15 Criteria for audit

The following standards are suggested criteria that might be used in periodic reviews to ensure a post-mortem report for coronial autopsies conducted at an institution complies with the national recommendations provided by the 2006 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) study (www.ncepod.org.uk/2006Report/Downloads/Coronial%20Autopsy%20Report%202006.pdf):

• supporting documentation:
  – standards: 95% of supporting documentation was available at the time of the autopsy
  – standards: 95% of autopsy reports documented are satisfactory, good or excellent.

• reporting internal examination:
  – standards: 100% of the autopsy reports must explain the description of internal appearance
  – standards: 100% of autopsy reports documented are satisfactory, good or excellent.

• reporting external examination:
  – standards: 100% of the autopsy reports must explain the description of external appearance
  – standards: 100% of autopsy reports documented are satisfactory, good or excellent.
A template for coronial autopsy audit can be found on the Royal College of Pathologists’ website (www.rcpath.org/profession/quality-improvement/conducting-a-clinical-audit/clinical-audit-templates.html).
References


## Appendix A  Summary table – Explanation of grades of evidence
(modified from Palmer K et al. BMJ 2008;337:1832)

<table>
<thead>
<tr>
<th>Grade (level) of evidence</th>
<th>Nature of evidence</th>
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| Grade A                   | At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target population  
or  
A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target population. |
| Grade B                   | A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population  
or  
Extrapolation evidence from studies described in A. |
| Grade C                   | A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population  
or  
Extrapolation evidence from studies described in B. |
| Grade D                   | Non-analytic studies such as case reports, case series or expert opinion  
or  
Extrapolation evidence from studies described in C. |
| Good practice point (GPP) | Recommended best practice based on the clinical experience of the authors of the writing group.                                                                                                                                 |

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Appendix B  Systematic review of evidence

Search strategy

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<thead>
<tr>
<th>Date (from – to)</th>
<th>Published literature from 1994 to 2018</th>
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<table>
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<tr>
<th>Literature sources</th>
<th>Search term(s)</th>
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<tbody>
<tr>
<td>PubMed</td>
<td>Epilepsy + Post mortem = 213</td>
</tr>
<tr>
<td>References cited within papers included in this synthesis and not captured in the PubMed search (e.g. papers pre-1994) were also sourced for further information.</td>
<td>'SUDEP' (2018 to 2008 – 10 years) = 671 articles</td>
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Inclusion and exclusion criteria

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<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>• Post-mortem findings in epilepsy</td>
<td>• Case studies</td>
</tr>
<tr>
<td>• Death certificates review</td>
<td>• Review papers</td>
</tr>
<tr>
<td>• Toxicology studies in epilepsy post mortems</td>
<td>• Epidemiology papers</td>
</tr>
<tr>
<td>• Post-mortem molecular studies in epilepsy or other non-histological investigations</td>
<td>• Experimental models</td>
</tr>
<tr>
<td>• Post-mortem audit or review</td>
<td></td>
</tr>
</tbody>
</table>
PRISMA flowchart

Records identified through database searching (n = 878 article)

Additional records identified through other sources (n = 9)

Records after duplicates removed (n = 887)

Records screened (n = 887)

Records excluded (n = 0)

Full-text articles assessed for eligibility (n = 31)

Full-text articles excluded (n = 856)

Studies included in synthesis (n = 31)
Appendix C  AGREE II guideline monitoring sheet

The autopsy guidelines of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this autopsy guideline that indicate compliance with each of the AGREE II standards are indicated in the table.

<table>
<thead>
<tr>
<th>AGREE standard</th>
<th>Section of guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scope and purpose</strong></td>
<td></td>
</tr>
<tr>
<td>1 The overall objective(s) of the guideline is (are) specifically described</td>
<td>Introduction</td>
</tr>
<tr>
<td>2 The health question(s) covered by the guideline is (are) specifically described</td>
<td>Introduction</td>
</tr>
<tr>
<td>3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described</td>
<td>Foreword</td>
</tr>
<tr>
<td><strong>Stakeholder involvement</strong></td>
<td></td>
</tr>
<tr>
<td>4 The guideline development group includes individuals from all the relevant professional groups</td>
<td>Foreword</td>
</tr>
<tr>
<td>5 The views and preferences of the target population (patients, public, etc.) have been sought</td>
<td>Foreword</td>
</tr>
<tr>
<td>6 The target users of the guideline are clearly defined</td>
<td>Introduction</td>
</tr>
<tr>
<td><strong>Rigour of development</strong></td>
<td></td>
</tr>
<tr>
<td>7 Systematic methods were used to search for evidence</td>
<td>Foreword</td>
</tr>
<tr>
<td>8 The criteria for selecting the evidence are clearly described</td>
<td>Foreword</td>
</tr>
<tr>
<td>9 The strengths and limitations of the body of evidence are clearly described</td>
<td>Foreword</td>
</tr>
<tr>
<td>10 The methods for formulating the recommendations are clearly described</td>
<td>Foreword</td>
</tr>
<tr>
<td>11 The health benefits, side effects and risks have been considered in formulating the recommendations</td>
<td>Foreword and Introduction</td>
</tr>
<tr>
<td>12 There is an explicit link between the recommendations and the supporting evidence</td>
<td>2–14</td>
</tr>
<tr>
<td>13 The guideline has been externally reviewed by experts prior to its publication</td>
<td>Foreword</td>
</tr>
<tr>
<td>14 A procedure for updating the guideline is provided</td>
<td>Foreword</td>
</tr>
<tr>
<td><strong>Clarity of presentation</strong></td>
<td></td>
</tr>
<tr>
<td>15 The recommendations are specific and unambiguous</td>
<td>2–14</td>
</tr>
<tr>
<td>16 The different options for management of the condition or health issue are clearly presented</td>
<td>2–14</td>
</tr>
<tr>
<td>17 Key recommendations are easily identifiable</td>
<td>2–14</td>
</tr>
<tr>
<td><strong>Applicability</strong></td>
<td></td>
</tr>
<tr>
<td>18 The guideline describes facilitators and barriers to its application</td>
<td>Foreword</td>
</tr>
<tr>
<td>19 The guideline provides advice and/or tools on how the recommendations can be put into practice</td>
<td>2–14</td>
</tr>
<tr>
<td>20 The potential resource implications of applying the recommendations have been considered</td>
<td>Foreword</td>
</tr>
<tr>
<td>21 The guideline presents monitoring and/or auditing criteria</td>
<td>15</td>
</tr>
<tr>
<td><strong>Editorial independence</strong></td>
<td></td>
</tr>
<tr>
<td>22 The views of the funding body have not influenced the content of the guideline</td>
<td>Foreword</td>
</tr>
<tr>
<td>23 Competing interests of guideline development group members have been recorded and addressed</td>
<td>Foreword</td>
</tr>
</tbody>
</table>