The Royal College of Pathologists
Pathology: the science behind the cure

Guidelines on autopsy practice

Autopsy when drugs or poisoning may be involved

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Foreword

The autopsy guidelines published by the Royal College of Pathologists (RCPath) are guidelines which enable pathologists to deal with non-forensic consent and coroner's and procurator fiscal's post-mortems 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 1-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. These guidelines have been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a case in a way that maximises benefit to the pathologist, coroner/procurator fiscal and the deceased's family.

There is a general requirement from the General Medical Council (GMC) to have continuing professional development (CPD) 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 assessment (EQA) 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
- Crown Office and Procurator Fiscal Service
- Northern Ireland Coroner's Service
- the Home Office Forensic Science Regulation Unit and Forensic Pathology Unit
- the British Medical Association.

The information used to develop this document was derived from current medical literature and a previous version of the guideline. Much of the content of the document represents

custom and practice and is based on collective substantial clinical experience amongst the consultant authors. All evidence included in these guidelines has been graded using modified SIGN guidance (see Appendix A). The sections of this document that indicate compliance with each of the AGREE II standards are indicated in Appendix B.

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

A formal revision cycle for all guidelines takes place on a 5-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, a short note of the proposed changes will be placed on the College website for 2 weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

These guidelines have been reviewed by the Professional Guidelines team, Death Investigation Committee, Toxicology Special Advisory Committee and Lay Advisory Group. This document was placed on the College website for consultation with the membership from 24 June to 22 July 2024. All comments received from the membership were be addressed by the author to the satisfaction of the Clinical Lead for Guideline Review.

This 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 Professional Guidelines team and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

This document was created to address the needs of the non-forensic autopsy pathologist dealing with deaths in which drugs, poisons or toxins may be involved but that have nonetheless been deemed non-suspicious. Consequently, these deaths do not require a special (forensic) post-mortem on behalf of the coroner or procurator fiscal (and, where appropriate, also by the police and any other relevant investigating authorities).

Drug and poisoning deaths pose unique challenges for the following reasons:

- the initial suspicion for a drug in the first place is largely dependent on the circumstances provided to the pathologist
- the focus of the autopsy is both to exclude a morphological cause of death and investigate pathological consequences of drugs and toxins
- one of the most important purposes of the autopsy is to obtain samples for further investigation
- there may be limited natural disease present, but significant toxin-related disease, particularly in younger people
- the toxicology findings may not be reported for several weeks after the body itself has been interred or cremated
- the laboratory findings may be non-contributory
- the drugs and toxins may have been administered by a third party. In such cases, the post-mortem should be performed as a forensic post-mortem by a forensic pathologist. It must be noted that information available at the time of post-mortem may subsequently change – and then a third party might be implicated – thus the importance of an accurate, detailed internal and external examination is highlighted.

As such, all potential drug deaths should be carried out with high suspicion. The pathologist should be prepared to decline to commence the post-mortem and seek further advice when necessary.

Although experience will be gained of common drug deaths, each post-mortem service should be served by a toxicology laboratory that can offer advice and support when it is needed.

1.1 Target users of these guidelines

The target primary users of these guidelines are pathologists performing coronial or procurator fiscal post-mortems. If there is any question of a toxicological involvement in the death the case must be referred to the coroner or procurator fiscal who will decide whether an autopsy is required. The recommendations will also be of value to trainees, particularly those approaching the Certificate of Higher Autopsy Training examination. These guidelines are not aimed at and do not claim to cover the investigation of deaths that are deemed suspicious by the relevant investigating parties. Such cases should be

conducted as a special (forensic) post-mortem by a suitably trained forensic pathologist working to guidelines developed for such suspicious scenarios.

[Level of evidence – Good practice point (GPP).]

2 Role of the autopsy

The role of the autopsy is to determine various aspects related to the deaths, including:

- to establish whether death is related to a drug or toxin or another process (e.g. positional asphyxia/pneumonia, or a combination of both)
- to establish the pathological consequences of drug or toxin use or misuse
- to establish if any traumatic injuries were a consequence of previous drug use
- to establish if there was any natural disease that might have increased susceptibility to the effects of a drug or toxin
- to obtain appropriate samples for toxicological analysis.

[Level of evidence D – The evidence has been taken from reviews of various texts/case reports and other presented cases in medical and legal settings.]

3 Information required prior to autopsy

Before undertaking a post-mortem examination, the pathologist should be briefed by the coroner's officer or procurator fiscal, or other parties involved in the investigation. Every examination must be approached with an open mind. However, the initial approach to the examination will rely heavily on any information provided. It is therefore important that the final report contains pertinent details of the history of the case and the source of the information.

The importance of a thorough history cannot be overemphasised. The following information aids any post-mortem examination and, when available, should be provided to the pathologist by the coroner's officer or procurator fiscal or be sought in the available medical records before the post-mortem commences.

3.1 Scene of death

This should include:

- full details of the scene of death (indoors/outdoors, temperature, exposure)

- how the body was discovered
- security of the scene
- place, posture and clothing of the body
- presence/absence of needles, syringes, burnt tin foil, white powder/residue, crack pipes, new psychoactive substance packaging, empty packets, illicit drugs, drug paraphernalia, medicine containers and pills including details of whether medications at the scene were prescribed to the deceased or to someone else
- provisional description of the body, including injuries (if any)
- identity of the person discovering the dead person.

3.2 Circumstances of death

This should include:

- witness statements (coroner's officer or procurator fiscal, police)
- previous medical history (coroner's officer or procurator fiscal, ambulance notes, general practitioner [GP], hospital clinical notes)
- medical therapy regimen – current and prior (GP, hospital clinical notes, pharmacist, addiction services)
- previous surgical operations and other interventions (GP, hospital clinical notes, family members)
- alcohol usage
- illicit drug use and non-controlled substances, potentially including the use of 'vapes' (coroner's officer or procurator fiscal, police, relatives and friends)
- previous imprisonment and date of latest release from prison (GP, coroner's officer, police)
- if there are multiple deaths. The circumstances found at the scene should direct the pathologist on which examinations are appropriate; this may differ between the bodies, e.g. one death may be drug related, the other traumatic. The possibility of 'murder-suicide' should always be considered in such cases, as should whether carbon monoxide testing is relevant.

- known or suspected blood-borne virus status, e.g. HIV, hepatitis B (HBC), hepatitis C (HCV) (GP, clinical notes)
- family history (relatives, GP)
- electrocardiogram (ECG), cardiac enzyme results and other pathological data (GP, clinical notes)
- serum lipid profiles and other biochemical tests (GP, clinical notes, internal laboratory results).

[Level of evidence – D]

3.3 Possible sources of this information

Pertinent information (and samples for further analysis) may be available from a variety of sources and this list is not exhaustive. However, common sources of this material are listed below.

3.3.1 Death in the community

- Coroner's officer's report/Police Death Report.
- Pre-hospital clinician notes (known as patient report forms, PRFs); these come in electronic and different paper versions.
- GP clinical notes (including past investigations and prescription records).

3.3.2 Death in hospital

- Admission bloods/samples obtained in hospital pre-mortem if admission bloods are no longer available (always preferable to post-mortem).
- Urine sample if catheter in situ/urine samples obtained in hospital pre-mortem if available (may require pre-arrangement with ward).
- Laboratory investigations (arterial blood gas, ECG, imaging, etc).
- Clinical notes (including nursing, prescription charts and paramedic notes).
- Coroner's officer's report/Police Death Report.

3.4 Information to be included in the 'History' section of the pathologist's report

The pathologist may be provided with varying levels of history and information relating to the circumstances of death in a particular case. It is advisable for the pathologist to include sufficient information to ensure that their own report is adequate as a standalone document. This is so the reader is aware of the context in which the examination was performed and to aid recall at inquest.

4 Health and safety precautions

Mortuaries will have their own local guidelines for dealing with potentially hazardous or infectious cases, and the approach taken in suspected drug deaths will vary in line with these. In all cases, the pathologist conducting the post-mortem should assess the risks posed by the case and ensure the post-mortem is conducted in such a way as to minimise any risk to the pathologist themselves and to all other parties involved. Risk assessment is crucial, and use of personal protective equipment is mandatory. Adequate mortuary ventilation is also required and use of downflow mortuary tables is recommended for high-risk cases.

It should be remembered that intravenous drug users (IVDUs) and homeless populations are at an increased risk of hepatitis, HIV and tuberculosis, as well as opportunistic infections if their immune system is compromised.

4.1 Chemicals

Many industrial activities involve the use of toxic chemicals. Companies involved in such work should have full assessments regarding the Control of Substances Hazardous to Health (COSHH) for any chemicals they use, but this may not always be the case. In addition, a variety of chemicals can be purchased and used for various purposes including suicide. These agents may be colourless and odourless. A high level of suspicion is needed to detect them before mortuary staff or others are exposed to lethal levels.

In particular, if there is a history of cyanide ingestion or exposure to hydrogen sulphide, extreme caution is required. If cyanide is ingested prior to death, it can be converted to the poisonous gas hydrogen cyanide in the stomach, which may be fatal if inhaled; therefore caution should be exercised when performing dissection. There is also a potential risk to the toxicologists performing analyses if cyanide is inadvertently released and inhaled from the headspace gas. Although cyanide is said to have a bitter almond smell, not everyone can smell it.[1]

Hydrogen sulphide can have similar effects to hydrogen cyanide if it is inhaled or its salts are ingested in high amounts. Trace amounts of hydrogen sulphide in the ambient atmosphere have a characteristic foul odour of rotten eggs.

In cases involving toxic chemicals, the possibility of environmental contamination should also be considered.

It may be that the lead pathologist will be asked to provide safety advice in such cases. This should only be provided if that pathologist is competent to provide such information. Otherwise, resources such as the National Poisons Information Service (NPIS)[2] or the Centers for Disease Control and Prevention (CDC) website[3] may provide useful information.

However, if there is any doubt that the post-mortem can be conducted and the body disposed of in a suitable way, the post-mortem should not be conducted, and the case should be referred to an appropriately equipped mortuary with the correct expertise to deal with such a case.

[Level of evidence – GPP.]

5 Imaging

5.1 Post-mortem imaging

Imaging to determine the possibility of body packing, for the documentation of trauma, or for other reasons peculiar to any particular case may be indicated in suspected drug-related deaths. If such imaging studies are felt necessary, access to local service provision should be sought prior to the commencement of the autopsy.

In addition, the role of post-mortem CT (PMCT) is expanding as experience and expertise in this field develops. There is clear evidence[4-6] to support the use of PMCT in suspected drug-related deaths. In addition, in deaths in which there has been exposure to poisonous or highly toxic substances that pose too great a risk to those performing or assisting in a full invasive post-mortem examination, and where the circumstances are apparent (e.g. suicide act with documentation at the scene indicating intent and chemicals present), then PMCT plus toxicology may be sufficient for the purpose of identifying the cause of death. These cases may require input from those trained in chemical, biological, radiological and nuclear (CBRN) techniques. The use of PMCT and minimally invasive

techniques could also be considered in high-risk cases where there is a risk of infection such as HIV and hepatitis C.[4]

If the history, scene examination, external examination, laboratory results and PMCT images together support a diagnosis of drug-related death, then such a cause of death may be provided without the need for a full invasive post-mortem. In these cases percutaneous toxicology samples, minimally invasive toxicology samples or a limited post-mortem may be appropriate; however, this is at the discretion of the coroner, procurator fiscal, pathologist or other investigating authority.

Caution should be exercised when considering an external examination with percutaneous toxicology sampling and minimally invasive or limited post-mortem in such cases, and the limitations of not carrying out a full post-mortem should be considered in the event the toxicology results are subsequently negative or reveal only borderline toxicity. Given that toxicology results will not be available at the time of post-mortem examination, a full post-mortem is recommended if the cause of death is initially unascertained.

Access to appropriate imaging facilities and expertise to make such a diagnosis varies around the country, but when available their use should be supported in appropriate circumstances assessed on a case-by-case basis following the criteria used for other prospective PMCT cases.

5.2 Photography

It is highly desirable to have facilities available to photograph any findings of particular interest.

[Level of evidence – GPP.]

6 External examination

6.1 Clothing

Ideally, clothing should be left in situ. However, this is often not the case in practice, particularly if the deceased has been admitted to hospital prior to death. Any clothing should be documented and a note made of any drug paraphernalia in the pockets or on the person. Be careful when checking the pockets as needles may be present.

6.2 External examination

Once items of clothing are removed, a thorough external examination is required to look for signs of recent and chronic misuse of drugs.

Recent signs include needle puncture marks, powder and frothy blood-tinged fluid from the mouth or nose, faecal or urinary soiling, petechiae (ears, mouth, chin and forehead), vomitus, recent bruising and injury. Make sure there is no foreign body within the mouth and no injury to the back.

Chronic signs of drug use include perforated nasal septum, thrombophlebitis, round 'skin popping' scars from subcutaneous injection, self-harm marks, leg ulcers, injection sinuses in the groin creases, recent bruising or injury.

The features listed in sections 6.2.1–6.2.5, while non-specific, are associated with drug and chronic alcohol abuse, and these should be specifically checked for.

6.2.1 General

- Identification – it is especially important to note in cases of decomposition/trauma how identification was made and the chain of identification to the point of autopsy.
- Malnourished, unkempt.
- Recent injury.
- Needle puncture marks.
- Chronic injection sinuses in the groin creases.
- Evidence of previous/current self-harm.
- Examination of mouth, anus, vagina and under foreskin for evidence of body packing.
- Signs of resuscitation (cannulas, Lund University Cardiopulmonary Assist System [LUCAS] mark, intraosseous devices, ECG stickers) – may explain the presence of needle puncture marks.
- Skin abscess.
- Skin popping scars.
- Track hyperpigmentation.
- Scars.
- Skin discoloration – for example, bright red hypostasis is associated with carbon monoxide poisoning, red discolouration over large joints with hypothermia, grey/blue

discolouration along the track of blood vessels with intravenous drug use, generalised grey/blue discolouration seen in methaemoglobin with sodium nitrite poisoning or accidental ingestion of amyl nitrites (‘poppers’).

- An abnormal pattern of hypostasis (particularly head or torso dependent) should prompt contemplation of so-called postural/positional asphyxiation while intoxicated and/or incapacitated, as the physical signs are not specific and this potential mode of dying is easily overlooked without an index of suspicion. Scene photos and witness statements should also be reviewed if available.
- Always check the back for any of the above.

6.2.2 Chest/abdomen

- Spider naevi (superior vena cava distribution).
- Gynaecomastia.
- Abdominal distension (ascites).
- Bruising.
- Caput medusae.
- Haemorrhoids.
- Testicular atrophy.

6.2.3 Face

- Jaundice (sclera and skin).
- Nasal septum perforation (cocaine).
- Necrosis of the nasal tip (endocarditis).
- Thermal burn tip of nose and facial hair singeing due to lighter flames.
- Blood-tinged froth around mouth/nose (pulmonary oedema).
- Abnormal coating on the tongue.
- Foreign body in the mouth or nose.
- Damage to teeth and gums.
- To note: unlike in life, pupil size is rarely of value after death owing to rigor mortis of intrinsic eye muscles.

6.2.4 Limbs

- Peripheral oedema.
- Erythema over joints (hypothermia).

6.2.5 Hands

- Clubbing, tar staining, splinter haemorrhages (infective endocarditis).
- Dupuytren's contracture.
- Palmar erythema.
- Finger tip burns due to use of 'crack pipe' and callus on the thumb from repeated use of a lighter in crack cocaine abuse.

[Level of evidence – GPP.]

7 Internal examination

Complete evisceration and examination of the organ systems should be conducted in cases where PMCT in combination with toxicology samples and external examination alone are unlikely to ascertain a cause of death. This should also be done if the case history, scene examination or external examination merit an invasive post-mortem and if PMCTI is not available. The internal findings listed in sections 7.1–7.6 are non-specific but can be associated with drug use.

7.1 Cardiovascular system

- Accelerated atherosclerosis (stimulant misuse).
- Aortic dissection (stimulant misuse).
- Left ventricular hypertrophy (stimulant misuse).
- Petechial haemorrhages on the surface of the heart (methylenedioxymethamphetamine [MDMA]).
- Dilated cardiomyopathy (ethanol).
- Infective endocarditis (uncommon; more likely right sided).

7.2 Gastrointestinal system

Evert the oesophagus to look for pills or signs of lacerations from violent retching (Mallory-Weiss tears). Varices are difficult to demonstrate post-mortem owing to the collapse of venous circulation and lack of active bleeding. Chronic haemorrhagic gastritis is a well-known consequence of ethanol abuse.

It is unlikely that the ingestion of medications will cause marked gastric changes as these drugs are often designed to minimise such effects. By contrast, ingestion of caustic chemicals such as acids/alkalis will often result in marked necrosis and inflammation of mucosa. Acute gastroduodenal perforation can be associated with cocaine use.

The pancreas may show signs of acute haemorrhagic pancreatitis (a potential cause of death) or chronic pancreatitis, often owing to chronic ethanol abuse. In practice this is often difficult to assess owing to haemorrhagic autolytic changes, and histology is recommended if there is doubt.

The liver may be obviously steatotic or cirrhotic in cases of chronic hepatitis or alcoholic liver disease. It may show drug/toxin-induced hepatitis or acute hepatic necrosis in correlation with toxicological findings. It is not possible to rule out more uncommon causes of liver disease macroscopically, and histology should be taken where possible to rule out more unusual diseases such as hereditary haemochromatosis, particularly in at-risk populations.

The anus, rectum and vagina should be examined for evidence of ‘body stuffing’ and it should be noted that illicit drug packages may be inserted within containers such as the plastic toy receptacle within children's chocolate eggs. The intestines should be fully opened whenever ‘drug packing’ might reasonably be suspected (custodial deaths or recent travel from another country). Assess for any evidence of mucosal discolouration.

When removing the intestines, check for segments of infarcted bowel due to hypotension, cocaine-related mesenteric artery vasospasm or emboli, and intestinal obstruction due to ingested drug packages.

Other potential findings include:

- cirrhosis/fatty liver (ethanol)
- upper gastrointestinal haemorrhage from gastritis, gastric erosions, Mallory-Weiss tears

- intestinal ischaemia
- pancreatitis
- thrombosis of the splenic mesenteric artery (chronic cocaine).

Consequences of cirrhosis (and subsequent portal hypertension) include:

- splenomegaly
- oesophageal varices
- spontaneous bacterial peritonitis
- increased cancer risk associated with chronic alcohol abuse (hepatocellular, oesophageal, oral, pharyngeal).

7.3 Central nervous system

The head should be opened and examined in all cases to exclude trauma or occult bleeding and to demonstrate hypoxic change. This includes examination of the sinuses and dural stripping.

The brain may show cerebral oedema demonstrated by increased weight, flattening of gyri and filling of sulci. If oedema is extreme, herniation may occur.

Other potential findings include:

- abscess, meningitis, mycotic aneurysms, empyema (subdural or epidural)
- cerebellar atrophy
- bilateral symmetric necrosis of the globus pallidus (associated with heroin)
- subdural haemorrhage (trauma)
- subarachnoid haemorrhage (if pre-existing berry aneurysm/weakness) – exacerbated by stimulant drug use
- Wernicke-Korsakoff syndrome (thiamine deficiency in alcoholics; mammillary body atrophy and haemorrhage)
- central pontine demyelination (associated with rapid rehydration and hyponatraemia).

7.4 Musculoskeletal system

Intoxicated individuals are more prone to trauma and are at higher risk of assault. Possible findings include:

- fractures
- osteoporosis
- infectious spondylitis and sacroiliitis (IVDU)
- thrombophlebitis (IVDU)
- myositis ossificans in the brachialis muscle (IVDU).

7.5 Respiratory system

- Bullous disease and chronic obstructive pulmonary disease (COPD) (often premature) (cannabis, smoking heroin and crack cocaine).
- 'Crack lung' (diffuse alveolar damage and haemorrhagic alveolitis).
- Barotrauma.
- Pyogenic Pneumonia in IVDU

Removal of the tongue along with the other neck structures is important; look for signs of tongue biting (seizure activity), airway obstruction and gross congestion of the pharynx (anaphylaxis).

The lungs may show massive pulmonary oedema, characterised by increased weight (weigh pre-dissection). There is an increased tuberculosis risk in homeless populations (see section 4: Health and safety precautions), and pneumonia is associated with chronic alcohol abuse as well as periods of reduced consciousness and respiratory depression due to drug intoxication.

7.6 Genitourinary system

The bladder should be removed and examined in all cases; urinary retention is associated with psychoactive substances, such as MDMA or amphetamine, and incontinence associated with seizure activity.

The vagina and foreskin should be examined for evidence of 'body stuffing' and the concealment of illicit drugs.

Other potential findings include:

- bladder distension (MDMA)
- urinary incontinence (seizure activity)

- urinary retention (anti-cholinergic drugs)
- haemorrhagic cystitis (ketamine).

[Level of evidence – GPP.]

8 Sampling: toxicology

8.1 When to take toxicology specimens

Toxicology samples are best taken before any significant disruption of the body has occurred from the autopsy, even if it is later decided that toxicology testing is not required. In non- forensic settings, post-mortem toxicology is generally taken:

- where death is very likely to be due to a drug
- where no cause of death is found at autopsy
- death by suicide/misadventure with the possibility of impaired reasoning
- where it is necessary to exclude toxicology as a likely cause of death
- any case where there is incarceration/deprivation of liberty
- where poor compliance may have contributed to death (e.g. antiepileptic medication).

8.1.1 What samples should be taken?[7]

Close collaboration between the pathologist and toxicologist is necessary to ensure the right samples are taken and that these are correctly preserved and submitted. Practices may differ slightly between toxicology laboratories; thus, liaison should occur before an autopsy is undertaken, e.g. if starting work in a new mortuary/hospital.

The name of the individual who collected the samples must be recorded.

The site from which each sample is taken must be recorded.

Sampling has barely changed since the seminal guidelines of the 1990s[8] but most toxicology laboratories will accept the samples listed below.

Currently, although point- of- care testing capacity may be available in some clinical settings, such analysis is not considered to have been sufficiently validated in the autopsy setting to be recommended.

Blood

The ideal samples are ante-mortem blood samples. The coroner/procurator fiscal has the power to seize any of such samples. Caution may be required with ante-mortem samples as the contents of many ante-mortem sample containers can affect drug concentrations and interpretation. . Coroner's officers or procurator's fiscal/pathologists should be mindful of cases where ante-mortem blood samples are likely to be required. They should be seized quickly to avoid disposal (there may be regional variation in how long a clinical laboratory will hold a sample prior to disposal).

In most post-mortem cases, blood remains the single most important specimen to analyse. In the UK, cardiac samples tend not to be taken but are useful for screening if there is minimal peripheral blood. Interpretation of the quantification of drugs in cardiac blood is more prone to the effects of post-mortem redistribution than peripheral blood. In addition, the published data used to aid quantitative interpretation is generally based upon analysis of peripheral blood, rather than cardiac.

Toxicology laboratories are moving towards more sensitive analysers and so the volume of blood required is reducing, but at present at least 10 ml peripheral blood (femoral or iliac access) is suggested. The evidence for clamping prior to sampling is variable. Often such volume (10 ml) may not be available and so as much as practical this must be accepted. Sodium fluoride/potassium oxalate (preferably 2% weight/volume) should be used as a preservative unless there is suspicion of poisoning with fluoride, or a fluoride-producing compound exists.

All samples must be collected in separate containers. For most specimens, disposable hard plastic or glass tubes are recommended.

Samples should be stored at a maximum temperature of 4ºC when analysed promptly after autopsy. Otherwise they should be stored at -20ºC. When liquid specimens are to be frozen, it is recommended to leave a small (10–20%) headspace in the specimen tubes.

Urine

If practical, at least 20 ml urine should be collected in post-mortem cases. If catheter urine is sent, this is acceptable but it should be recorded as such. The use of fluoride as a preservative is encouraged.

Analysis of the drug concentration in urine (or its presence or absence) may give some idea of timescale between drug ingestion and the time of death.

Urine should be collected into a clean universal container by creating a nick in the upper anterior fundus, or by aspiration with a 20 ml needle and syringe.

Vitreous humour

Samples should be collected routinely in appropriate cases. At present, vitreous humour is used primarily to quantitate ethanol, urea, electrolytes and beta-hydroxybutyrate. As toxicology analysers become more sensitive, there is a growing database for vitreous drug concentrations, but these are not yet routine tests.

Glucose analysis may be useful in the investigation of deaths related to diabetes mellitus and can be particularly helpful in the setting of hyperglycaemia and determining diabetic ketoacidosis (when there are raised glucose levels coupled with raised ketones, usually acetone and beta-hydroxybutyrate). It is well recognised that glucose levels fall in the post-mortem period due to post-mortem bacterial consumption, thus a low glucose level is less helpful in determining hypoglycaemia, as it may simply reflect post-mortem consumption. Suspected hypoglycaemia deaths due to insulin overdose rely more on the circumstances of death, evidence from the scene, evidence from any glucose monitoring devices, and an otherwise negative autopsy. Neuropathology should be considered in these cases as changes in the brain related to either hyperglycaemia or hypoglycaemia may be identified.

All vitreous humour from both eyes should be collected; however, it can be collected into a single container. Following removal, the shape of the eyes can be restored by injecting water. If this has occurred, it should be recorded in case of a second autopsy requiring repeat sampling.

Gastric contents

Oral ingestion remains a common route of exposure to drugs and poisons. However, the most important investigation is the observation of undigested pills and tablets.

There are only a few toxicology laboratories in the UK that will now routinely screen or quantify drugs in gastric content, the reasoning being that the drugs do not have a pharmacological effect if they are in the stomach.

Stomach content is heterogeneous. If only an aliquot of stomach content is collected, the total volume/weight should be recorded. Quantitative measurement and a knowledge of the volume enables the total amount of the drug of interest in the stomach to be calculated, but this may overestimate drug concentration if the aliquot contains drug debris.

One caveat is that if cardiac/central blood is being quantified, there is the possibility that drugs may redistribute from the gastric content into blood after death.

Other samples

- Bile – can be a useful for screening (but not quantitation) if no other samples are available.
- Liver (deep within right lobe) – can be useful for screening but quantitation is hampered by poor databases of reference values.
- Muscle – can be useful for screening but quantitation is hampered by poor databases of reference values. There is much debate around which muscle should be sampled, but the psoas muscle is normally used. The source of the sample should be recorded.
- Injection site (skin) – may be useful in determining the type of substance that has been injected, such as insulin or heroin. Again, it is rarely required but needs to be considered. Always send a control site sample for comparison.
  - To sample the injection site, excise a wide skin ellipse, down to subcutaneous tissue. Place the specimens in clean, labelled universal containers.
  - If the specimen is for histology, add neutral buffered formalin. When fixed, examine and serially slice; if a tract is not identified, submit the entire specimen for histological examination. Otherwise, do not fix the specimen; instead, send the specimen immediately to the laboratory.
- Lung tissue – approximately 2 cm cubed, sealed in either a glass airtight container or a universal container wrapped in parafilm.
- Bone marrow – may be analysed qualitatively where only skeletonised remains are recovered, however, few laboratories offer this analysis.
- Hair analysis – has no direct link to the cause of death. Hair grows at about 1 cm per month (on the posterior vertex), thus hair samples may be of limited value in determining whether drugs have been taken in the few days prior to death. It is rarely taken or required for most coroner's or procurator's fiscal investigations. However, examination of hair can be useful in the following situations:
  - to assess claim of a drug-facilitated sexual offence prior to death
  - to provide long-term information on drug compliance or abstinence

- to assess previous use in drug users with abstinence, loss of tolerance and relapse
- chronic heavy metal poisoning.

Hair samples should be collected before the body is opened to avoid contamination of the hair with body fluids. The sample should be cut from the posterior vertex region of the head, as close as possible to the scalp, since this is the region of least variation in growth rate. If not, the source of the sampling should be described.[9]

Specify which end of the hair bundle is the cut end by tying a piece of cotton or string around the hair at that end, then wrap in an inert covering such as aluminium foil.

8.2 Toxicology sampling in the non-invasive/minimally invasive post-mortem

Post-mortem blood samples can be obtained percutaneously from the femoral vein using a 10/20 ml syringe and a large bore needle (the femoral vein is approximately 1 cm medial to the femoral artery, which is located in the inguinal canal midway between the superior anterior iliac spine and pubic tubercule). If this fails, minimally invasive samples can be obtained by performing a transverse lower abdominal incision and directly accessing the common iliac vein. Venous subclavian or jugular samples can also be attempted percutaneously using a needle and syringe. If this is undertaken then the site of sampling should be clearly stated.

Urine can be obtained percutaneously by suprapubic puncture directly above the pubic symphysis with a syringe and long needle or catheterisation. If this fails, minimally invasive samples can be obtained by performing a transverse lower abdominal incision and aspiration of the bladder with a needle and syringe internally. It should be noted that urine may not always be present in every case.

Vitreous humour can be collected by aspiration using a 10 ml syringe and 19G needle at a 30–45° angle with reshaping of the eye following removal by injecting water. If this has occurred, it should be recorded in case of a second autopsy requiring repeat sampling.

8.2.1 Scenarios for toxicology analysis

Ideal sampling for most therapeutic, illicit drugs and non-controlled substances include:

- ante-mortem samples (blood and urine)
- post-mortem femoral/iliac venous blood
- post-mortem urine
- vitreous (preferably fluoride oxalate preserved).

Carbon monoxide cases require:

- ante-mortem samples (blood)
- post-mortem femoral/iliac venous blood.

Volatile compounds are poorly detected in blood, so ideally the following should be sampled:

- lung tissue (approximately 2 cm cubed), sealed in either in a glass airtight container or a universal container wrapped in parafilm
- brain tissue (approximately 2 cm cubed), sealed in either a glass airtight container or a universal container wrapped in parafilm.

Heavy metals cases require:

- ante-mortem samples (blood and urine)
- post-mortem femoral/iliac venous blood.

Note that hair is often required to investigate chronicity. Insulin overdose cases should consider the following:

- insulin and glucose degrade rapidly post-mortem, which can cause issues with accurately measuring concentrations. The assay for insulin in the UK is only an immunoassay, and post-mortem work on insulin analysis is still minimal. Suspected hypoglycaemia deaths due to insulin overdose rely more on the circumstances of death, evidence from the scene, evidence from any glucose monitoring devices, and an otherwise negative autopsy. Neuropathology may also be helpful as changes in the brain may be corroborative of hypoglycaemia. If required, samples can be sent abroad.
- ideally, a fluoride oxalate vitreous sample will be obtained for glucose analysis.
- blood should be sampled from a peripheral vein as soon as possible, ideally before any dissection, and separated by centrifugation with the serum component frozen

immediately prior to analysis (haemolytic enzymes will destroy insulin rapidly). There is some work on vitreous insulin and C-peptide, but this is not yet routinely available.

Rare poisoning cases should consider the following:

- if unusual poisoning suspected it is worth contacting either your local toxicology laboratory or national poisoning information service for further advice. Indeed, it is worth contacting your local laboratory with any queries.

8.2.2 Summary

If requesting toxicology, always test for a panel. Again, it is vital to liaise with the local toxicologist to determine what compounds are analysed as standard and which require specific additional requests or will need to be sent away for analysis. It is advised that before requesting analyses, which may need to be sent away, the coroner/procurator fiscal is informed so they are aware of the cost implications.

A 'fatal' level of a drug may not be the causative agent (particularly in long-standing addicts) and may mask overdose from another unsuspected drug, particularly novel psychoactive substances.

If you encounter a suspected death involving drugs, illicit or otherwise, the following steps should be taken:

- take, as standard, blood, vitreous fluid and urine
- request drugs of abuse panel and ethanol levels (be familiar with the local panel)
- be prepared if investigation comes back negative; is there other supporting evidence?
- be prepared if an unsuspected drug is found; does this correlate with clinical history and post-mortem findings? If not, consider referring to the findings in the report but without ascribing particular significance to it.
- there is limited value in carrying out post-mortem toxicology if a patient has been in hospital more than 24 hours (barring drug error cases), but ante-mortem samples are valuable in this scenario. Analyses for metabolites (both active and inactive) may still be helpful in these cases.

[Level of evidence – D.]

8.3 Extent of toxicology screens

8.3.1 The role of the toxicologist and referral laboratory

Pathologists should be aware of:

- what specific drugs or metabolites are tested for in standard drugs of abuse panels
- whether the laboratory is ISO accredited (15189 + ILAC 19/9 or 17025 + ILAC 19/9)
- what happens when a requested drug is not on the panel
- cost of off-site referral, and the addition time or delay this can introduce
- specific samples required.
- sample disposal policy

8.3.2 What information to provide the toxicology laboratory

The investigation of a death involving suspected drugs, illicit or otherwise, is very much a cooperative effort between the pathologist and toxicologist. The information made available to the pathologist by the coroner's office/procurator fiscal (G5/Sudden Death Report/coroner's referral document) should also be made available to the toxicologist.

Toxicology involves not only the identification and quantification of drugs in the body but also the interpretation of results. The most qualified person to do this is usually the toxicologist. However, while the toxicologist can comment on whether levels of a drug are those required to cause significant harm or death, it is the pathologist's role to determine the cause of death based on all the information available, including toxicology results and all other investigations, in the context of the clinical setting and the circumstances of death. In coroner's cases, the formulation of a cause of death is only 'preliminary' as the coroner will finalise the cause of death at inquest.

The pathologist has the obligation to provide the best possible samples in the best conditions and with good information regarding the circumstances of the case.

For qualitative documentation of a particular substance at the time of death, at a minimum the post-mortem interval and site sampled should be given.

However, if the candidate drug is suspected to have directly caused or contributed to death, then quantitation is more likely to be required and the more information provided the more helpful the analysis is likely to be. With sufficient background information, it may be possible to arrive at an explanation as to why death occurred at a specific concentration of drug, even if levels are below the reference lethal range.

Information of relevance to interpretation of toxicological data:

- sex, age, body habitus, state of decomposition
- occupational history, if relevant (industrial, agricultural)
- medical history (particularly drugs of abuse and medications and timeframes)
- symptoms, if any (length, onset)
- estimated interval since drug taken (if suspected overdose)
- circumstantial evidence (empty bottles, packets, powder, note)
- main pathological findings at autopsy and impression
- post-mortem interval before samples were obtained, and date and time of sampling
- high-risk group (IVDU) or known notifiable disease
- name, contact address and telephone number of pathologist.

If there has been a delay in submitting or transporting the samples, it is useful to note the condition in which they have been stored (refrigeration, deep freeze).

8.3.3 Interpretation of results

The autopsy pathologist and toxicologist must view the results in light of the clinical, scene and post-mortem findings. This goes beyond the remit of this autopsy practice guideline. The toxicologist's opinion on the likely contribution to death should be provided in their report. However, it is the pathologist's responsibility to provide a medical cause of death when autopsy has been carried out.

Most post-mortem toxicology data relies on small case studies and individual reports in the literature. These are well summarised in the standard toxicology textbooks[10,11] and larger databases based on, for example, femoral blood samples.[12]

There are minimal pharmacokinetic data on illicit drugs, and individuals often do not know the doses they are taking. Although there is some pharmacokinetic analysis carried out before therapeutic drugs are allowed to be prescribed, there is a lot of variation that may be caused by:

- sex, age, body habitus
- genotype/genetic polymorphisms
- fast/slow metabolisers
- whether taken on a full or empty stomach

- natural disease
- other concurrent substance (may accentuate or inhibit effects)
- tolerance
- dose of drug
- purity of drug.

If the toxicological findings raise the index of suspicion that a death is due to an adverse reaction to a prescription medicine, whether in normal clinical use or in cases of deliberate or inadvertent overdose, this should be reported via the recognised Yellow Card Scheme.

8.3.4 Summary

- The results of toxicology should be interpreted in the context of the clinical history and circumstances.
- There is often considerable variation between reference tables.
- The biological effect of a particular concentration of a drug varies between individuals and is dependent on other factors such as tolerance. The LD50 is a research device used by pharmacologists and toxicologists to compare toxicity between drugs in animal models. It is inappropriate to use it in a clinical context where there are too many variables between individuals and unknowns.
- Attempts to back-calculate dosage from levels at post-mortem should not be made.
- The pathologist's role is to obtain samples and, with the help of the toxicologist and coroner's officer or procurator fiscal, evaluate all non-toxicological data to see if they can modify circumstances enough to allow an explanation of death. This may include assimilating all the information including the autopsy findings, histology findings, toxicology results, and other investigations, all in the context of the clinical history and circumstances of death.

[Level of evidence – D.]

9 Sampling: histology

Histology is of value in confirming, evaluating and sometimes revising the course of natural disease processes. Histology may help identify toxin-related disease, or natural disease

that may have increased the susceptibility of the deceased to the effects of a drug or toxin. It is important that any natural disease in the deceased is well documented so any possible role it played in the cause of death is known.

In England and Wales, the Coroners (Amendment) Rules 2005 require the pathologist to retain material which, in their opinion, has a bearing on the cause and circumstances of the death.[13]

Any sampling must be within the limits of consent in the case of a consented autopsy or within the limits of the relevant medico-legal legislation and guidelines if the case is of a medico-legal nature.

Examples of histology and possible findings in a drug death are listed in sections 9.1–9.6.

9.1 Lung (at least 1 piece per lobe)

- Confirmation of pneumonia versus pulmonary oedema (macroscopic inspection is unreliable).
- Aspiration pneumonia, inhalation of vomit, presence and effect of injected or inhaled material.
- Emphysematous changes (smoking; much more accelerated with cannabis, heroin and crack cocaine).
- Marked anthracosis (cannabis).
- Septic pulmonary abscesses.
- Tuberculosis (IVDU).
- Perivascular pulmonary talc granulomas (IVDU) and foreign body granulomas.
- Foreign body emboli (IVDU).
- Pulmonary necrotising angiitis (IVDU).
- Atelectasis, fibrosis (smoking, cannabis).[14]
- Crack lung – diffuse alveolar damage and haemorrhagic alveolitis.

9.2 Kidney (one piece per kidney)

- Calcium oxalate crystals (ethylene glycol poisoning)

- Subnuclear vacuolation of tubular epithelial cells (acidosis)
- Glomerulosclerosis, amyloid (IVDU).
- 'Cocaine' nephropathy (cocaine).
- Rhabdomyolysis.

9.3 Cerebrum and cerebellum (particularly hippocampus, cerebral cortex and dentate nucleus)

- Evaluation of hypoxic/ischaemic neuronal damage.
- Ring haemorrhages associated with hyperpyrexia.
- Calcium oxalate crystals (ethylene glycol poisoning)

9.4 Heart (as per *Guidelines on autopsy practice: Sudden death with likely cardiac pathology*)[15]

- Evidence of stimulant-related cardiomyopathy (cocaine, amphetamine-type stimulants).
- Left ventricle – interstitial and perivascular fibrosis, contraction band necrosis, ischaemic heart disease (cocaine).
- Right ventricle – hypertrophy secondary to cor pulmonale (IVDU).
- If conduction anomaly suspected, refer to *Guidelines on autopsy practice: Sudden death with likely cardiac pathology*[15] and consider referral of the heart to a cardiac pathologist.
- Aortic wall in cases of dissection to exclude inherited connective tissue disorders.

9.5 Liver (one piece, away from capsule)

- Assessment of fatty liver/cirrhosis and investigation of aetiology (especially in those of a younger age).
- Investigation of hepatitis (viral, alcohol, other).
- Talc granulomas (IVDU).
- Investigation of hyperpyrexia/heatstroke – sinusoidal dilatation, steatosis and individual hepatocyte necrosis.

- Hepatitis and fulminant liver failure (MDMA, paracetamol).

9.6 Additional histology samples according to case

- Skin injection sites; determining their presence and age is critical (IVDU).
- Quadriceps and psoas muscle, if rhabdomyolysis suspected.

In all cases, the histological sampling required must be guided by the clinical judgement of the pathologist conducting the case and the specific requirements of that case. In cases with medico-legal implications, tissue should be retained until the coroner or procurator fiscal completes their investigations.

[Level of evidence – GPP.]

10 Sampling: organ retention

While there is no specific role for organ retention in a death from suspected illicit drugs or new psychoactive substances (NPS), these deaths tend to occur in a younger population than the average post-mortem and may demonstrate limited natural pathology at autopsy. By the time a negative toxicology report has been received, the opportunity to identify subtler causes of death may be lost.

The pathologist should keep an open mind when reading the clinical history for conditions such as cardiac abnormalities or epilepsy, which may require referral for expert opinion.

Where appropriate, these organs should be sampled as per their respective guidelines if no other pathology is identified at post-mortem.

[Level of evidence – GPP.]

11 Clinicopathological correlation

It is advisable for the pathologist to include sufficient information to ensure that their own report is adequate as a standalone document.

Non-forensic pathologists commonly encounter potential drug deaths in the following situations:

- where death is very likely to be due to a known drug (‘overdose’)

- where death is by suicide/misadventure with possibility of impaired reasoning by drugs
- in ‘negative’ autopsies
- where death is due to natural disease that has arisen as a result of drug use.

In potential overdose situations, it is important to consider whether the reported symptoms prior to death match the putative drug. Just because a drug or its metabolites have been identified does not mean the level is fatal or exclude the effects of another unsuspected drug.

In cases of suicide or misadventure, the cause of death may be obvious (e.g. hanging or drowning). However, intoxication may have played a role prior to death and, in these situations, may be listed under part 2 in the cause of death.

Natural diseases that arise from drug abuse are myriad and it is beyond the scope of this document to list them all. The effects may be the result of cumulative injury (alcohol cirrhosis) or a consequence of a transient effect of the drug (aortic dissection due to transient hypertension from cocaine).

It may not be possible to prove such findings resulted directly from drug use; however, it is acceptable to use past medical history and information available at the time of autopsy to make an informed interpretation provided the source of information is noted.

There may be a lag from the use of a drug to the eventual cause of death, and this raises the question of whether drug use should be listed as the cause of death if death resulted from, for example, the consequences of HIV contracted from needle sharing many years ago. There are social consequences to listing this in the death certificate. In many cases, the source may not be known. For this reason, it is advisable to list a drug as the cause of death only if it has a direct proven causality. It is acceptable to list prior drug use in part 2 of the certification. In all cases, care should be taken to minimise distress.

In situations where drug use has resulted directly in impaired consciousness with subsequent complications, e.g. aspiration pneumonia, the drug may still be considered a direct cause of death and should be included in part one of the death certificate. Toxicology may not be informative in these cases, but the history will be indicative.

[Level of evidence – D.]

11.1 Examples of causes of death

Direct toxic effects leading to death are difficult to demonstrate, require circumstantial information and toxicology, and do not require long-standing use. These include:

- transient hypertension (stimulants)
  - intracerebral haemorrhage
  - aortic dissection
  - acute cardiac necrosis
- arrhythmia
- cardiorespiratory depression (opiates, ethanol, antidepressants, benzodiazepines)
- biochemical imbalance (including hyponatraemia secondary to excess fluid intake due to MDMA).

Subacute direct toxic effects of a drug may be fatal. The inciting drug itself may not be detectable. These effects include:

- pulmonary oedema
- hypoxic encephalopathy
- aspiration of gastric contents and inhalational pneumonia.

Chronic indirect effects due to previous or current long-standing drug use include:

- natural disease arising due to drug use:
  - cirrhosis (alcohol)
  - cardiac fibrosis (amphetamine and cocaine abuse)
- infective endocarditis and mycotic aneurysm
- HCV, HBV and HIV infection
- pulmonary hypertension
- injection abscess
- secondary amyloidosis.

[Level of evidence – GPP.]

12 The negative autopsy

"The absence of injuries, evidence of poisoning, lethal infection or well-recognised natural disease is in itself significant negative evidence."[16]

Many deaths caused by suspected illicit drugs do not show significant pathology at the time of autopsy. This may be partially due to the younger age of these patients; the elderly are more likely to have existing natural disease that is significant to count as a cause of death 'on the balance of probabilities'.

As there is always the risk that toxicology may come back negative, it is advisable to take full histology and toxicology samples in cases where a likely cause of death is not identified at autopsy.

Negative autopsies are not a sign of failure on the part of the pathologist but rather confidence that any reasonable natural death has been routinely excluded. The documentation of absence of significant other findings is in itself an important negative finding. Of all deaths, 5% are unascertained.[17]

Death may be due to apnoea/central nervous system depression or biochemical imbalances. Alcohol may be associated with alcoholic cardiomyopathy/sudden death in association with alcohol misuse and other cardiac functional abnormalities. These are difficult to demonstrate on histology, and if toxicology is negative or not permitted the pathologist may be left with a conundrum.

The pathologist has the duty of candour; if significant natural disease is not identified, or is unlikely to be sufficient to cause death, it is best to be clear about this in the report rather than giving the impression of more certainty than is warranted. Attempts to ascribe more significance to minor findings simply because the toxicology has come back negative should be avoided.

It should be noted that under guidance by the GMC there is a duty of candour to release information about a person who has died in order for the death certificate to be completed 'honestly and fully', thus the presence of matters such as the role of drugs in the death must be fully disclosed if felt relevant. There is also a duty to assist the coroner or procurator fiscal in doing the same at inquest.

[Level of evidence – D.]

13 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 comply with the national recommendations provided by the 2006 National Confidential Enquiry into Patient Outcome and Death (known as NCEPOD) study:[18]

- clear rationale for taking toxicology:
  - standards: 95% of supporting documentation was available at the time of the autopsy
  - standards: 95% of autopsy reports documented are satisfactory, good or excellent
- 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 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 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 RCPath website: www.rcpath.org/profession/patient-safety-and-quality-improvement/conducting-a-clinical-audit/clinical-audit-templates.html.

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Appendix A Summary table – Explanation of grades of evidence

(Modified from Palmer K *et al. BMJ* 2008;337:1832)

Grade (level) of evidence	Nature of evidence
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 cancer type 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.

Appendix B AGREE II compliance monitoring sheet

The 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 below.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Foreword
2 The health question(s) covered by the guideline is (are) specifically described	Foreword, 1
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, 1
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	1
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	n/a
12 There is an explicit link between the recommendations and the supporting evidence	1–12
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	1–12
16 The different options for management of the condition or health issue are clearly presented	1–12
17 Key recommendations are easily identifiable	1–12
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword

19	The guideline provides advice and/or tools on how the recommendations can be put into practice	1–12
20	The potential resource implications of applying the recommendations have been considered	Foreword
21	The guideline presents monitoring and/or auditing criteria	13
Editorial independence		
22	The views of the funding body have not influenced the content of the guideline	Foreword
23	Competing interest of guideline development group members have been recorded and addressed	Foreword