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

Guidelines on autopsy practice: Aviation-related fatalities

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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 post-mortem examinations in a consistent manner and to a high standard. They may contain some distressing information and as such are not intended for the lay audience. 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/or other data. These guidelines have 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 these guidelines 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 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 stakeholders consulted for this document were the Air Accidents Investigation Branch (AAIB), the Civil Aviation Authority and 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 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. 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 sections of this guideline that indicate compliance with each of the AGREE II standards are outlined 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 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, 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 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 Clinical Effectiveness department, Death Investigation Group and Lay Governance Group. This document was placed on the College website for consultation with the membership from 22 June 2018 to 20 July 2018. All comments received from the membership were addressed by the author to the satisfaction of the Clinical Director of Clinical Effectiveness.

These guidelines were 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

Previously the Royal Air Force (RAF) possessed expert aviation pathologists who could be called upon following aviation-related fatalities either to carry out autopsies, or to provide advice or subsequent specialist review. While the RAF Centre of Aviation Medicine may still be able to offer some specialist advice, there are no longer any active RAF aviation pathologists. Therefore, it has become much more likely that such cases will be examined by pathologists who may not have particular experience of aviation pathology. A pathologist who does not specialise in aviation fatalities is not expected to encounter such cases frequently, and so specific guidelines are justified to assist where there is unfamiliarity and ensure reproducible standards between different practitioners. This document is intended to provide an approach that will yield sufficient information to answer the types of investigative questions commonly encountered in such cases. It is not intended to replace more comprehensive texts that already exist on the specialist subject of aviation pathology.[1–6]

The specific topic of mass fatality incidents is beyond the scope of this document, which is intended to inform practitioners undertaking occasional cases during routine autopsy workload rather than large-scale investigations. (A separate guideline detailing the response to mass disasters is currently in preparation.) Depending on the nature of the incident, there is the potential for a level of investigative scrutiny at a later date that may not be immediately apparent at the time of autopsy. For this reason, these examinations should be conducted to a level of detail that may seem excessive for a 'routine' case. If a pathologist feels that they do not have the available time or resources to achieve a sufficiently high standard, then it is safer not to commence the examination, rather than risk becoming involved with a case in which inadequate documentation or sampling might result in difficulty at a later date. The likelihood of such cases occurring within a pathologist's routine practice may be greater if working in close proximity to an aerodrome, but it should be remembered that aircraft can crash anywhere, and thus autopsy pathologists working in any geographical location could be called upon to undertake this type of work.

1.1 Target users of these guidelines

The target primary users of these guidelines are pathologists who currently conduct autopsies, and who may wish to seek specific information about aviation-related pathology before commencing a case that is not normally encountered in their routine workload. The recommendations will also be of value to trainee pathologists looking to acquire knowledge in preparation for examinations. In addition, any individuals tasked with investigating a fatal aircraft crash (e.g. coroners, police officers or air accident investigators) may seek to determine the information needed prior to, or to be expected following, pathological examination.

2 The role of the autopsy

The purpose of conducting a post-mortem examination following an aviation fatality is to:

- determine the cause of death
- detect any underlying natural disease or intoxication in flight crew
- analyse patterns of injury
- assess the effectiveness of safety equipment
- assess the efficacy of aircraft crashworthiness.

While it may be felt that some of these roles extend beyond the remit of the autopsy pathologist, detailed documentation of findings and appropriate sampling will allow all aspects of the case to be investigated subsequently by other individuals if necessary.

[Level of evidence – GPP.]

3 Pathology encountered at autopsy

Consequences of rapid deceleration, direct blunt force trauma, penetrative injuries and burns are commonly encountered, and there will be some overlap with the types of injuries more commonly seen in cases of road traffic or other transportation-related fatality. For a more detailed discussion, please refer to section 13.

[Level of evidence – GPP.]

4 Specific health and safety aspects

The nature of air crash fatalities means that bodies are often severely traumatised. This can result in the production of sharp fragments of bone that can remain hidden deep within body cavities. Bone fragments may come to lie in unexpected positions and foreign bodies such as jagged metal or broken glass may also represent a hazard. In incidents where ejection seats or other pyrotechnic safety devices have been involved, this equipment should have been rendered safe by appropriate personnel prior to the autopsy. However, caution should still be exercised when removing any clothing or other item that has the potential to cause injury. The possibility of chemical or other contamination should be considered, depending on the aircraft, cargo and crash site involved. Post-crash fires involving aircraft constructed using glass-reinforced plastic or carbon fibre components are likely to result in these materials being present on the occupants' bodies, therefore respiratory protection may be indicated during mortuary operations.

[Level of evidence – GPP.]

5 Information relevant to the autopsy

As much background information as possible should be obtained prior to commencement to plan a thorough examination and avoid potential loss of sampling opportunities. Varying levels of detail may already have been provided by the instructing authority (e.g. HM Coroner's Office), but additional information may be available from other sources such as police and/or personnel of the AAIB. This information will provide some indication of the type of incident being dealt with. Knowing in advance whether the incident involved military, commercial or private aircraft, and distinctions such as rotary (helicopter) or fixed-wing, glider or powered aircraft etc. will be of benefit when considering the types of injuries likely to be encountered. The occurrence of a post-crash fire will also affect the conduct of the autopsy, and so advance notification of this eventuality should be sought. An understanding of scene factors may be crucial, since mechanisms of death such as positional/crush asphyxia may be overlooked entirely if the examination is restricted solely to the mortuary findings. Discussion with the AAIB investigator assigned to the incident will assist in establishing initial circumstances and whether any specific factors need to be explored (e.g. potential for medical incapacitation or likelihood of carbon monoxide fumes having entered the cockpit).

Pilots, depending on the type of licence held, are normally required to undergo regular aviation medical examinations, and the records of these examinations should be made available. In addition to indicators of natural disease, other information may be contained within these records that is of relevance to the investigation (e.g. a pilot may have been required to wear spectacles while flying, therefore any evidence of spectacle wear should be documented). It should be remembered that the aeromedical examiner (AME) who carried out a pilot's medical examination may not have had access to general practitioner's or

hospital notes. These should be obtained via the HM Coroner's Office as they could include vital information that was not known to the AME. The possibility that pilots, out of reluctance to lose flight medical classification, may have withheld information during these examinations should not be overlooked.

It must be remembered that aviation-related fatalities can and do occur abroad, and repatriated bodies may arrive following varying levels of prior examination and/or embalming. As far as possible these cases should be dealt with in a similar manner in order that important findings are not overlooked.

It is worth noting that fatalities resulting from sporting and recreational activities such as hang gliding and paragliding may not attract the attention of the AAIB or police, but similar principles apply in such cases and the information laid out in this document will still be of benefit. Specialist technical advice can be sought in advance from the British Hang Gliding and Paragliding Association (BHPA), and liaison with this organisation's technical investigation division is encouraged.

[Level of evidence – GPP.]

6 The autopsy procedure

Every effort should be made to document the presence of injuries in a detailed manner. While this may not seem necessary to establish the cause of death, key information about circumstances and contributory factors can be lost if sufficient detail is not recorded during the examination. It may not be known in the initial stages of an investigation how much interpretation of injury patterns will ultimately be necessary, and information of vital importance cannot be retrieved after the body has been released. Once the information has been recorded it will be available for future specialist appraisal if necessary, even if the significance of both positive and negative findings is not immediately appreciated at the time of the autopsy. A severely traumatised and/or burned body may present a daunting prospect to those unaccustomed to dealing with such cases, but a systematic approach will allow the necessary information to be recorded for subsequent analysis.

6.1 Clothing

It is standard practice to include the body weight in an autopsy report, but it is worth also documenting a clothed weight. Investigators may wish to conduct centre of gravity calculations for certain aircraft types, and their accuracy will be improved by recording this information prior to removing clothing and equipment. This will vary with the type of aircraft, and could include specialist aviation garments or simply reflect everyday items of clothing. Particular attention should be paid to any safety equipment, such as helmets, parachutes, harnesses, etc. that may remain with the body. Evidence of damage to or failure of these items will be of benefit to the subsequent investigation, and so-called 'witness marks' may help with reconstruction of events at a later date. Whether a sleeve or strap was torn during the impact sequence or cut by emergency medical personnel attempting resuscitation at the scene is a distinction worth making to inform the wider investigation. While it is certainly not within the remit of the autopsy pathologist to attempt to interpret all of this information, accurate documentation of any visible damage during the removal of clothing and equipment should still be carried out to ensure a detailed, high-quality report. The soles of shoes/flying boots may bear rudder pedal imprints or other damage, and such detail could easily be missed if a methodical approach is not adopted. As noted previously, spectacle use may have been a requirement of a pilot's flying status, so the presence or absence of glasses (or contact lenses), even if carried within a pocket, should be described. The effectiveness or otherwise of fireproof or flame-retardant materials should be considered, and in the event that hyperthermia is thought to have contributed to diminished aircrew performance, the

presence of survival clothing such as the dry suits worn during flights over water should be considered to be of potential relevance.

6.2 External examination

Documentation of all injuries should essentially be to a forensic level of detail, as it may not be immediately apparent which specific injuries may prove crucial during the subsequent investigation. The locations, appearance and dimensions of all bruises, abrasions, lacerations and incised wounds should be documented. Particular attention should be paid to patterned marks that may provide evidence of contact with a specific item or surface. Marks resulting from harnesses, straps, etc. are of prime importance as they will provide some evidence of correct or improper use. Amputations and areas of burning should also be documented in as much detail as possible. It is worth noting that skin that has been in contact with aviation fuel for a period of time can develop artefactual erythema and epidermal slippage, mimicking burns. The back of the body should be described in as much detail as the front.

Body diagrams may be useful, but photography of injuries is strongly advised as this will provide a greatly superior resource for subsequent investigation. Right-angled measurement scales are readily available to assist with photographic documentation, but in the absence of such a specific photographic aid, a ruler can be used to include a dimensional reference within injury photographs that will assist subsequent correlation with aircraft components and structures. Depending upon local arrangements, hospital medical photography or illustration department personnel may be willing to attend the mortuary and conduct high-quality injury photography. As with all photographic injury documentation, a wide view to allow orientation should be followed by close-up views, both with and without a measurement scale. These images should be taken perpendicular to the skin's surface to avoid distortion, although it is appreciated that complex injuries or those involving large areas of the body may be difficult to record in the standard fashion described previously.

6.3 Internal examination

Practice varies with geographical location, and in some jurisdictions the legal authority to carry out an invasive internal examination may not have been granted. Provided that authority has been given for an invasive autopsy, this should proceed as for a standard examination. Some elements of the standard examination may not be possible (e.g. the brain cannot be examined if it is not present owing to traumatic disintegration of the head or complete incineration) and such occurrences should be documented for the avoidance of doubt at a later stage. A detailed inventory of all skeletal trauma should be made, as this will allow subsequent correlation with forces occurring during the crash sequence. The presence (and absence) of traumatic injuries and natural disease processes within the various organ systems and soft tissues of the body should be detailed as thoroughly as possible, and if this is not possible owing to severe destruction (or complete absence) of a particular structure then this fact should also be recorded. If ante-mortem medical records are available, the known medical history can be correlated with the pathological findings. Interpretation should be cautious in the context of trauma (e.g. a traumatic coronary artery lesion may simulate, or mask, genuine pathology).

[Level of evidence – GPP.]

7 Specific organ systems to be considered

All organ systems should be considered in every case, with particular attention being paid where incident circumstances or background medical history suggest potential medical incapacitation.

[Level of evidence – GPP.]

8 Organ retention

As for section 7, referral to an organ-specific specialist pathologist may be indicated based upon the circumstances of the incident or background medical history.

[Level of evidence – GPP.]

9 Histological examination

The legal framework surrounding authority to retain human tissue will vary depending on geographical location, and local practices will vary within each region. It may be that no authority is granted for histological sampling in cases where an obvious traumatic cause of death has been established. Similarly, under certain circumstances in some jurisdictions no authority will be granted for an invasive examination to be undertaken at all. In many cases histological examination will not significantly affect the ultimate conclusions of the examination. However, if medical incapacitation is thought by the investigators to have been a potential factor then as thorough a search as possible should be made to identify any evidence of this. For example, coronary artery histology may be necessary to determine the difference between genuine pathology and traumatic artefact. Correlation with ante-mortem medical records will be of benefit, and in specific instances it may be desirable to retain the heart or brain in order that formal specialist opinion can be obtained. Pilots certified as being medically fit to fly may still show evidence of occult natural disease, and its relevance in the cause of death and wider circumstances must be taken into consideration.

[Level of evidence – GPP.]

10 Toxicology

Several considerations are worthy of particular note in relation to aviation. Sampling can be hampered by severe disruption of bodies, especially following high-energy impact sequences. If the crash scene is in a remote location, or extrication of bodies is complex, disrupted bodies may be exposed to ambient conditions for a prolonged period with resultant exacerbation of artefacts such as post-mortem redistribution and putrefactive ethanol production. These factors must be borne in mind when interpreting any toxicological results obtained.

In many cases it will still be possible to obtain blood, urine and vitreous samples even in the context of severe traumatisation of the body. When these samples cannot be obtained, a sample of liver or skeletal muscle can be submitted for analysis. If there is apparent surface contamination and/or decomposition, a better-preserved sample may often be obtained from central or deeper portions of the tissue. While homogenates prepared from these samples in the laboratory may provide an indication of the presence or absence of substances, meaningful quantitation cannot be attempted.

As with all toxicology requests, the laboratory should be provided with all of the available relevant information so that processes can be prioritised and modified if necessary, and to enable meaningful interpretation of the generated results. Certain substances may not be included in routine screens, therefore if the possible presence of a specific drug is of potential significance, then this information must be explicitly conveyed to the analysing laboratory. Lists of prescription medication can be obtained from medical records, and over-the-counter medications may have been found at the scene or within the deceased's residence. In addition to medications, screens for illicit drugs and ethanol should be carried out in all cases. The current legal limit for flying an aircraft is a blood ethanol concentration of 20 mg/100 ml (considerably lower than for driving a motor vehicle).[7] Such a level can be artefactually produced by putrefactive change, but the presence of impurities (such as acetone, propanol

or butanol) can provide an indication of this possibility. Note that ethyl glucuronide is not formed after death, and so its presence provides an indication of genuine ante-mortem ethanol exposure. However, persistence in the body from previous consumption may give a false impression of blood ethanol elevation at the time of the death, thus all such interpretation must be done with caution.

When interpreting toxicological findings, it should be remembered that medications that may seem innocuous on the ground could have exaggerated effects at altitude or while operating in the high workload environment of an aircraft cockpit. If a pathologist is unsure of the relevance of a detected medication, advice can be sought from the UK Civil Aviation Authority Medical Department.

When determining the relevance of any post-crash fire in the causation of death, measurement of carboxyhaemoglobin (and other products of combustion such as cyanide) should be requested when it has been possible to obtain a sample of blood from the deceased. However, even in incidents where no fire has occurred, carbon monoxide contamination within the cockpit (from engine or heating systems) may have been a factor in the causation of the crash. It would therefore be prudent to establish carboxyhaemoglobin levels in all cases of powered flight, but especially in small, piston-engined aircraft. Inclusion of cyanide and any other available products of combustion will help distinguish between fumes resulting from fire and cockpit contamination from other sources.

Detected medications may provide clues as to underlying medical conditions, and these conditions may not have been disclosed previously to medical examiners. The potential must be considered not only for medical incapacitation, but also for side effects of medication. (A pilot may not need to be fully incapacitated for a crash to ensue; distraction alone at a critical moment may prove sufficient.) Medications, and the underlying medical conditions, could be the cause of a crash, could be significant contributory factors or could be merely a coincidence. It may not be possible to determine this significance with certainty, but cautious consideration should be given alongside the other pathological findings and overall circumstances of the incident. The possibility of suicide may need to be considered, and toxicological findings may provide an important indication to investigators.

[Level of evidence – GPP.]

11 Other relevant samples

None.

12 Imaging

Radiology plays a crucial role in the identification and documentation of post-mortem findings. Imaging is invaluable in demonstrating not just skeletal trauma, but also the presence or absence of foreign bodies. At the time of writing, post-mortem computed tomography (PMCT) scanning is already established as an investigative tool, and even if this is not routinely carried out at the facility where the autopsy is due to take place, aviation-related fatalities are exactly the types of cases that justify additional effort to ensure adequate recording of information. Any additional logistical burden necessary to acquire a scan will be offset by the rapidity and superiority of skeletal injury documentation. This also includes the ability to plan the examination thoroughly, limitation of extensive or complicated dissection and the identification of hazards prior to entering the mortuary. As an additional benefit, the information will be archived and available for specialist review at a future date if required.

The joint Royal College of Radiologists (RCR)/RCPath statement on standards for medico-legal post-mortem cross-sectional imaging in adults[8] is in the process of being updated, and

the most recent document should be consulted when arranging such imaging. PMCT is becoming an increasingly routine post-mortem investigative tool, and many of its benefits are particularly pertinent to aviation-related fatalities. It is appreciated that many autopsy practitioners will as yet not have had experience of this type of investigation. Readers are encouraged to explore local possibilities to facilitate scanning, and should be reassured that support and advice are available to assist if necessary.

[Level of evidence – GPP.]

13 Clinicopathological summary

The vast majority of fatalities arise as a result of rapid deceleration, blunt force impact, direct penetration injuries, the effects of fire or some combination of these categories. Head injuries are very common, and if no safety helmet was worn, then a pathologist may be asked to express an opinion as to whether the addition of a helmet may have influenced the outcome in a particular case. As mentioned previously, it may be necessary to correlate the pathological findings with scene factors, as the injuries identified may not account for death and an alternate explanation may need to be found. If an individual was not fatally injured as a result of trauma at impact, potential reasons for failure to escape (from fire, drowning, etc.) may need to be explored.

Several pathological deductions are likely to be of assistance to the overall investigation. Confirmation of the deceased having been alive at the time of impact is useful, but it may not always be possible to determine this fact with certainty. For example, significant accumulation of blood in association with injuries implies a period of post-injury survival with an active circulation (but the potential for simple gravitational leakage of blood into a body cavity should be excluded before drawing this conclusion). Any reasons for potential incapacitation or distraction (whether natural disease, drug-induced or due to inhalation of toxic fumes) should be considered in the commentary of the report. When there is burning of the body, differentiation between ante-mortem and post-mortem fire damage should be made (and qualified with the degree of certainty). An elevated carboxyhaemoglobin level and soot deposition within the lower airways provides good evidence of breathing within a fire environment. Rapid death due to burns, or anoxia due to intense fire within a confined space, may potentially account for a low carboxyhaemoglobin level, so interpretation should be carried out with care and on a case-by-case basis.

At all stages the interpretation of pathological findings should be cautious. So-called ‘control injuries’ (damage to the hands and feet caused by contact with flight controls) are often taken into consideration when discerning if an individual was actively attempting to manoeuvre the aircraft at the time of impact. Such injuries may arise spontaneously during the impact sequence and do not indicate with certainty that an individual was making a conscious effort to fly. Likewise, injuries are not guaranteed to occur, and so their absence does not exclude the possibility that an individual was actively operating the controls at the time of ground impact. Careful documentation of the presence and absence of such injuries will assist in the overall interpretation of the incident.

The AAIB investigator will be able to provide estimates of likely impact velocity and angle-based on-scene findings, and where possible, this information should be correlated with the observed injuries. Comments correlating injuries sustained to the suggested impact sequence will be helpful, and an assessment of the forces experienced by aircraft occupants in relation to human tolerances may assist with the determination of survivability. If the initial impact was survived, but death occurred later, additional detail such as the inevitability of certain injuries leading to death or any potential role that might have been played by delays in rescue or medical treatment should be considered.

[Level of evidence – GPP.]

14 Examples of cause of death opinions/statements

Aviation-related fatalities often exhibit numerous sharp force, blunt force and thermal injuries throughout the body, and it may seem convenient to record the medical cause of death simply as 'multiple injuries'. Such oversimplification is to be avoided, and a more informative prioritisation of the immediately fatal injuries provides a more useful report to both the medico-legal and accident investigations. For example, if death at the point of impact was solely the result of a catastrophic head injury then this can be stated explicitly, rather than diluting this important fact by grouping it together with all of the other lacerations and fractures around the body under a non-specific label.

[Level of evidence – GPP.]

15 Summary

In summary, the aim should be to carry out a complete post-mortem examination, including toxicological sampling. There should be a full and detailed description of the types of injuries, their location and their relation to the cause of death. Photographic documentation of these injuries is strongly encouraged. Natural disease processes should be documented and consideration given, where relevant, to the potential for medical incapacitation. Every effort should be made to arrange a PMCT scan prior to the examination, even if this is not something that is currently considered part of local autopsy practice, to preserve as much information as possible in an undisturbed state for any future detailed analysis that may become necessary. Even if an autopsy practitioner feels that they have no particular expertise in relation to aviation fatalities, documentation and sampling to the minimum standards described previously will ensure that all pertinent information available is preserved for subsequent specialist analysis.

[Level of evidence – GPP.]

16 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 NCEPOD study:[9]

- 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 Royal College of Pathologists' website (www.rcpath.org/profession/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 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.

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 these guidelines that indicate compliance with each of the AGREE II standards are indicated in the table below.

AGREE II 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	2–15
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	2–15
16 The different options for management of the condition or health issue are clearly presented	Foreword
17 Key recommendations are easily identifiable	2–15
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	Foreword
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	16
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