

Guidelines on autopsy practice

Fetal autopsy following antepartum or intrapartum death of non-malformed fetuses

DRAFT February 2024

Series authors:	Dr Esther Youd, Clinical Lead for Autopsy Guidelines Dr Ben Swift, Forensic Pathology Services, Oxon
Specialist authors:	Dr Tamas Marton, Birmingham Women's and Children's Hospital NHS Foundation Trust
	Dr Beata Hargitai, Birmingham Women's and Children's Hospital NHS Foundation Trust
	Dr Flora Jessop, Cambridge University Hospitals NHS Foundation Trust
	Dr J Ciaran Hutchinson, Great Ormond Street Hospital NHS Foundation Trust
	Professor Christoph Lees, Imperial College Healthcare NHS Trust Dr Tracey Johnston, Birmingham Women's and Children's Hospital NHS Foundation Trust

Unique document number	G160
Document name	Guidelines on autopsy practice: Fetal autopsy following antepartum or intrapartum death of non-malformed fetuses
Version number	2
Produced by	The specialist content of this guideline has been produced by: Dr Tamas Marton MD, FRCPath, PhD, Consultant Perinatal Pathologist, Birmingham Women's and Children's Hospital Foundation Trust and Department of Obstetrics and Gynaecology, Semmelweis University, Faculty of Medicine, and Department of Pathology, Forensic and Insurance Medicine, Semmelweis University, Budapest, Hungary Dr Beata Hargitai, MD, Affiliate Member of RCPath, PhD, Consultant Perinatal Pathologist, Birmingham Women's and



1 V2

Draft

	Children's Hospital Foundation Trust and Department of Obstetrics and Gynaecology, Semmelweis University, Faculty of Medicine and Department of Pathology, Forensic and Insurance Medicine, Semmelweis University, Budapest, Hungary Dr Flora Jessop, Cambridge University Hospitals NHS Foundation Trust Dr Ciaran Hutchinson, Great Ormond Street Hospital NHS Foundation Trust Professor Christoph Lees Imperial College Healthcare NHS Trust Dr Tracey Johnston MD FRCOG, Birmingham Women's and
Date active	Children's Hospital NHS Foundation Trust. February 2024 (to be implemented within 3 months)
Date for full review	February 2029
Comments	This document will replace the 1st edition of the <i>Guidelines on</i> autopsy practice: Third trimester antepartum and intrapartum
	stillbirth, published in June 2017.
	<i>stillbirth</i> , published in June 2017. In accordance with the College's pre-publications policy, this document will be on the Royal College of Pathologists' website for consultation from 28 February to 27 March 2024. Responses and authors' comments will be available to view on

The Royal College of Pathologists 6 Alie Street, London E1 8QT Tel: 020 7451 6700 Fax: 020 7451 6701 Web: <u>www.rcpath.org</u>

Registered charity in England and Wales, no. 261035 © 2024, the Royal College of Pathologists

This work is copyright. You may download, display, print and reproduce this document for your personal, non-commercial use. Requests and inquiries concerning reproduction and rights should be addressed to The Royal College of Pathologists at the above address. First published: 2024.

Contents

Fore	word		4
1	Introductio	on	6
2	The role of	of the autopsy	9
3	Consent.		9
4	Clinical in	formation relevant to the autopsy	.10
5	The autop	osy procedure	.11
6	Specific h	ealth and safety aspects	.14
7		autopsy – limited by parental consent or by a stepwise post-mortem	. 14
8	Full conventional post mortem16		
9	Autopsy report16		
10	Clinicopathological summary17		
11	Coding		.18
12	Criteria fo	or audit	.19
13	Reference	es	.21
Арре	endix A	Exemplar autopsy request form	.24
Арре	endix B	Autopsy-related SNOMED CT codes	.28
Арре	endix C	Summary table – Explanation of grades of evidence	.30
Appe	endix D	AGREE II guideline monitoring sheet	.31



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

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

Foreword

The autopsy guidelines published by the Royal College of Pathologists (RCPath) are guidelines that enable pathologists to deal with non-forensic consent, coroner's and procurator fiscal post-mortem examinations in a consistent manner and to a high standard. They are intended primarily for the profession; some technical content may be distressing 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 cannot realistically be repeated, it has to be recognised that there is no reviewable standard that is mandated beyond that of the FRCPath Part 2 examination. Practitioners should note that post-mortem findings can, in many cases, be reviewed against ante-mortem imaging and other data. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The medico-legal risk of departing from the guidelines should be assessed by the autopsy pathologist.

At the time of drafting these guidelines, there was some uncertainty around workflow and the optimisation of patient pathways, despite great efforts by regional units to maintain service provision. Relevant additional material, including a parent pathway, is being drafted by NHS England, which aims to optimise the pathway and experience for parents at what is a very difficult time. Timely communication with parents via appropriate channels is critical to providing status updates regarding the examination and its findings, and providing answers for families experiencing great distress. Reference to these materials should be made, where required.

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 assurance (EQA) scheme.

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

The following stakeholders will be contacted to consult on this document:

• British and Irish Paediatric Pathology Association (BRIPPA)

- Stillbirth and Neonatal Death Charity (SANDs)
- The Royal College of Obstetrics and Gynaecologists (RCOG)
- Human Tissue Authority (HTA)
- The Coroners' Society of England and Wales
- Crown Office and Procurator Fiscal Service (COPFS) Scotland
- Coroner's Service for Northern Ireland
- The Home Office Forensic Science Regulation Unit and Forensic Pathology Unit and the British Medical Association.

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

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

A formal revision cycle for all guidelines takes place on a 5-yearly cycle. The College will ask the authors of the guideline to consider whether 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 changes will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

The guideline has been reviewed by the Professional Guidelines team, Death Investigation Committee, Forensic Pathology Specialty Advisory Committee and Lay Advisory Group. It will be placed on the College website for consultation with the membership from 28 February to 27 March 2024. All comments received from the membership will 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

5

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 1 Introduction

2 This guideline is a review of G160 Guidelines on autopsy practice: Third trimester
3 antepartum and intrapartum stillbirth.

4 The most important change to the previous perinatal autopsy guidelines is that previous

- 5 guidelines titled G160 Guidelines on autopsy practice: Third trimester antepartum and
- 6 intrapartum stillbirth and G161 Guidelines on autopsy practice: Fetal autopsy (2nd
- 7 trimester fetal loss and termination of pregnancy for congenital anomaly) were based on
- 8 gestational age and addressed the autopsy of both malformed and non-malformed
- 9 fetuses, including termination of pregnancy for developmental abnormality. During the

10 review of the fetal autopsy series, 3 guidelines were developed to cover perinatal post

- 11 mortems. The new guideline addresses the malformed fetuses of any gestational age with
- 12 particular focus on the new diagnostic modalities.
- The following are the new post-mortem guidelines published in the fetal perinatal autopsyseries:
- G160 Guidelines on autopsy practice: Fetal autopsy following antepartum or
 intrapartum death of non-malformed fetuses
- G161 Guidelines on autopsy practice: Fetal autopsy of 2nd trimester fetal loss
 (excluding termination of pregnancy for congenital anomaly)
- G193 Guidelines on autopsy practice: Fetal autopsy after termination of pregnancy for
 congenital anomaly.
- 21

Post-mortem examination of a baby following an antepartum fetal death may provide a cause of death or at the least provide a partial explanation of the loss and information relevant to the management of subsequent pregnancies.¹ While uncertainty remains about the depth of evidence relating to best practice, autopsy is the single most useful investigation and provides information that is likely to change or significantly add to existing clinical information that will be used to counsel families.^{2–4} The autopsy is also a valuable audit of clinical care and may facilitate learning from adverse events.

The voice of bereaved parents has been central to producing these guidelines. Many
bereaved parents want to access a post-mortem examination for their baby, seeking the

6

Draft

1 possibility of answers, even if only to rule out some underlying conditions rather than elicit 2 specific positive findings. Bereaved parents have told us that the post mortem can be an 3 important part of their path through their grief. The post-mortem report can support difficult 4 decisions about another pregnancy. It is, of course, extremely common for parents to feel 5 protective and strongly connected to their baby – the acute sensitivities and emotional 6 context make perinatal post mortem unlike any other investigative procedure. The report 7 authors have held the narrative of parents' vulnerabilities and wishes at the heart of the 8 discussions involved in producing these guidelines.

9 This guideline has been created to assist the perinatal pathologist undertaking autopsies in 10 cases of antepartum intrauterine death (stillbirth) of babies after a normal anomaly scan 11 (i.e. ≥20 weeks gestation) and in the third trimester. It provides practical technical advice 12 on performing the autopsy, guidance on the use of additional investigations and minimum 13 standards for the content of the autopsy report. It is intended as a guide to reasonable 14 practice, rather than a policy statement. Where possible, references are provided. If 15 followed, the output from the autopsy should be sufficient to provide useful feedback to the 16 family, to the clinicians involved in the case and for local and national audit.

17 This is predominantly a scenario-based guideline. We support, where appropriate, a

18 flexible approach to the extent and nature of the post-mortem investigation (see section 7).

19 We acknowledge that the aetiology of pregnancy loss is variable and that the perinatal

20 pathologist should maintain an open mind as to the most appropriate investigations as the21 autopsy proceeds.

22 This guideline applies to autopsies which are carried out after fetal loss following a normal 23 second trimester anomaly scan.⁵ This statement needs to be treated with a degree of 24 caution: it is always the pathologist's discretion to determine the extent of examination that 25 is required in the given case, within the remit of consent provided. Where possible, strong parental preferences (as documented on the consent form or in the referral 26 27 documentation) should be taking into consideration by the responsible consultant. The 28 second trimester anomaly scan screens specifically for 11 specific structural anomalies 29 and markers for an uploidy, but others may be identified. Not all women undergo an 30 anomaly scan and not all anomalies will be detected (recognised false-negative rates, 31 some are not identifiable in the mid-trimester). Pathologists need to have a low threshold 32 in these cases for converting to full post mortem if there is any suspicion of anomaly;

33 women should be counselled that only around 2/3 of anomalies are detected antenatally.

Cases of entirely unanticipated major anatomical abnormality at delivery (either due to a false-negative second trimester anomaly scan (1/3 of anomalies are not detected or patient not engaging with healthcare services) are now rare;⁶ providing guidance in the approach to confirming of normal anatomy is not the main scope of this document, as the approach to the autopsy of malformed fetuses is covered elsewhere.⁷ If indicated, the perinatal pathologist should, of course, undertake a review of fetal anatomy and comment appropriately.

8 Many pathologists have adopted approaches based on their own experience, evidence 9 and resources, which may differ from these guidelines but achieve similar outcomes. This 10 document does not aim to change such approaches, as long as the outcome of the 11 autopsy is not put at risk. This is particularly relevant for centres with pre-existing capacity 12 or plans to develop access to alternative, image-based resources to post-mortem 13 examination. There is an accumulating body of evidence that an image based approach 14 can complement or replace dissection based post-mortem examination.^{8–13}

15 The use of such approaches should be at the discretion of the examining pathologist.

16 Currently, however, most UK-based perinatal pathologists are trained in a traditional,

17 dissection-based approach to fetal autopsy, only have access to conventional-autopsy-

18 based EQA programmes and lack local resources to expand their practice into alternative

19 methods. For these reasons, providing more detailed guidance to perinatal pathologists in

- 20 delivering a predominantly image-based service is not possible at the time of issuing these21 guidelines.
- 22 Finally, this document is not intended as a replacement for standard textbooks but
- 23 highlights the principles of undertaking and reporting perinatal autopsies. For detailed
- 24 guidance on undertaking the autopsy in specific circumstances, the reader is referred to
- 25 the reference section below.

26 In England, Wales and Northern Ireland, autopsy facilities and procedures must be

27 covered by appropriate licences (issued by the Human Tissue Authority) and consent

28 procedures must be compliant with the relevant Human Tissue Authority's Code of

- 29 Practice.¹⁴ Separate legislation that applies in Scotland does not impose a system of
- 30 licensing.¹⁵

31 **1.1 Target users of this guideline**

- 32 The target primary users of this guideline are UK consultant and trainee
- 33 perinatal/paediatric pathologists and general histopathologists with an interest in perinatal

PGD 280224

8

V2

Draft

- 1 pathology. The recommendations will also be of value to pathologists working outside the
- 2 UK, obstetricians, neonatal paediatricians, anatomical pathology technologists (APTs) and
- 3 bereavement midwives.

4 2 The role of the autopsy

- 5 The role of the autopsy in stillbirth is:
- to establish the cause and/or the mechanism of fetal death
- 7 to identify concomitant diseases, fetal, maternal and placental conditions, particularly
- 8 those with implications for subsequent pregnancies (e.g. fetal growth restriction,
- 9 malformation, maternal diabetes)
- to identify evidence of genetic disease and allow determination of the likely recurrence
 risk.
- 12
- 13 The post-mortem report should:
- 14 support pathology input into local perinatal mortality review meetings
- provide information for audit purposes (e.g. antenatal diagnosis, pregnancy and
- 16 intrapartum care).

17 3 Consent

- Consent must always be obtained for the hospital post-mortem examination of a baby,whether born alive or dead, and at any gestation.
- 20 Consent is also required for all genetic testing, including of placental samples. Local
- 21 protocols should be established between clinical genetics and histopathology departments.
- 22 This will help to ensure that appropriate consent is in place prior to the release of tissue for
- 23 any genomic investigation.
- 24 The only time when parental consent/authorisation for a post-mortem examination on a
- 25 baby is not required is when a coroner or procurator fiscal orders a post-mortem
- 26 examination; this is unlikely to be relevant in the clinical context of these guidelines.
- 27 Regardless of the gestation, perinatal post-mortem examination may only be performed if
- informed consent has been given by the mother, unless there are exceptional

- 1 circumstances, e.g. if she is too ill to consent. Wherever possible, in this situation, the
- 2 partner's consent/authorisation should also be sought.
- 3 The consent process should be compliant with the requirements of the HTA's Code of
- 4 Practice: Code A: Guiding Principles and the Fundamental Principle of Consent.¹⁴ In
- 5 Scotland, the Human Tissue (Scotland) Act 2006 is in force and the consent process
- 6 should follow the legislation.¹⁵
- 7 The autopsy consent form should be compliant with the model 'Consent form for perinatal
- 8 post mortem' developed by SANDs in conjunction with the HTA.¹⁶ The pathologist
- 9 performing the autopsy must see the completed consent form, either as a physical copy or
- 10 electronically, before commencing the autopsy. Any limitations on the scope of the autopsy
- 11 must be complied with.
- Any concerns regarding the validity of the consent should be resolved before commencingthe autopsy.
- 14 The consent form indicates the maximal extent of the post-mortem examination that
- 15 should be performed. For some patients, if the responsible consultant considers that a
- 16 more limited examination can adequately answer the questions raised, the examination
- 17 may not include some of the components, in keeping with the latest NHS guidance.¹⁷ This
- 18 depends on the specific features and history for each patient and is at the discretion of the
- 19 consultant pathologist responsible for the examination.
- 20 Change to the depth of the post-mortem investigation should be communicated to the
- 21 family. The communication must be documented appropriately, including concerns of the
- 22 family. The best practice for this is to communicate through the bereavement services, but
- 23 individual local practices may vary. Please see the Parent Pathway, which is under
- 24 development by NHS England.
- 25 [Level of evidence GPP in line with statutory obligations.]

26 4 Clinical information relevant to the autopsy

- 27 The relevant clinical information (best obtained using structured request form, see28 Appendix A) includes:
- 29 patient identification details
- 30 maternal age/date of birth

- 1 maternal height, weight and BMI
- 2 relevant medical and family history, including consanguinity
- obstetric history, previous pregnancies/deliveries, including previous fetal and neonatal
- 4 losses (if post-mortem examination had been carried out), malformation and growth
- 5 restriction and other complications
- 6 history of current pregnancy, including:
- 7 estimated delivery date (gestation by date and by scan)
- 8 antenatal infection screen, including cytomegalovirus, toxoplasma, HIV
- 9 abnormal findings from ultrasound or other antenatal investigations (a copy of the
 10 ultrasound report is highly desirable, mandatory with antenatally diagnosed
 11 structural abnormalities)
- first trimester screening, result of non-invasive and invasive tests, chorionic villous
 sample (CVS) and amniocentesis
- if screening returned a high-risk result but further invasive testing was declined,
 this should be stated, as this may inform the direction of additional post-natal
 testing
- any clinical concerns regarding fetal growth/fetal monitoring including Doppler
 investigations of the maternal and fetal circulations
- 19 the presence of complications, such as pregnancy-induced
 20 hypertension/preeclamptic toxaemia/diabetes/antenatal bleeding/maternal pyrexia
- events leading up to intrauterine death and/or delivery (membrane rupture,
 reduced fetal movements, fetal distress, last evidence of fetal heartbeat)
- 23 delivery: mode, complications and use of instrumentation.

24 25

5 [Level of evidence – B.]

26 **5 The autopsy procedure**

- Whole body X-ray for gestational age assessment, malformation, etc. Recommended
 in all cases; mandatory for suspected skeletal dysplasia and multiplex developmental
 abnormalities. If available, this may be complemented by other imaging modalities,
- 30 e.g. CT, MRI.

- Photography is mandatory in all cases, particularly important to document external and
 internal abnormalities. Digital photography and secure storage are the standards in
 line with local information governance standards are required.
- Routine morphometry (mandatory: body weight, crown-heel length, foot length.
 Consider: crown-rump length, occipito-frontal circumference, inner and outer canthal
 measurements). Abdominal circumference has not been validated as a post-mortem
 measurement.
- Detailed external examination, including nutritional status/soft tissue and muscle bulk,
 maceration, local/generalised oedema, pallor, meconium staining, dysmorphic
 features, evidence of trauma (intrapartum death) and other iatrogenic lesions,
 assessment of patency of orifices (including choanae) and palatal fusion, limbs
 (positional abnormalities, skin webs), hands and feet, and genitalia. Recording of
 negative findings is not required unless clinically requested or relevant.
- 14 Cases being submitted for MRI/ultrasound/micro-CT examination should be examined 15 by a pathologist and then transferred to appropriate imaging facilities before returning 16 for further assessment, ideally with any available interim imaging reports. At this time, follow up with dissection-based autopsy (in line with parental consent) is appropriate, 17 18 but may be omitted at the discretion of the examining pathologist in line with their 19 experience and expertise in these modalities. In practice, if the findings are discordant 20 with the antenatal information, follow up dissection is recommended, where consent permits.¹¹ 21
- Incisions on the body should be placed with due regard to the requirement for
 reconstruction. Standard incisions include typically T- or Y-shaped; an inverted Y shaped incision of the lower abdominal wall can be considered for assessment of the
 internal lower abdominal wall.
- Detailed systematic examination of other internal organs, including:
- 27 umbilical arteries and vein, ductus venosus
- in-situ examination of the heart and great vessels with sequential segmental
 analysis of malformations
- in-situ examination of thoracic and abdominal organs; consider removing in
 continuity to assess abnormal structures crossing diaphragm

- 1 weights of internal organs (minimum: brain, heart, lungs, liver, kidneys, thymus,
- adrenals, spleen) and calculate organ to organ weight ratios (brain to liver, brain to
 thymus, lung to body weight, body weight to placenta weight).
- Apply special dissection techniques, where appropriate.
- 5

6 [Level of evidence – GPP.]

7 5.1 Central nervous system examination

8 The extent of the neuropathological examination should be determined by the responsible 9 pathologist in the clinical context of the case. Thorough examination and sampling of the 10 brain is strongly advised in cases where timing/severity of hypoxia may be of importance 11 to the investigation (e.g. peri-partum stillbirth). Examination of the brain may also assist 12 with the detection of infection and complex developmental abnormalities of the brain. If 13 these factors are suspected clinically, a full examination is recommended.

- 14 If there are concerns about possible neuromuscular problems, such as arthrogryposis
- 15 (some may not be picked up on antenatal screening), full examination of the central
- 16 nervous system (CNS) is recommended. Similarly, if head biometry is abnormal (large,
- 17 small, abnormal shape), full examination is advised.
- The diagnostic yield of brain examination in the context of a non-dysmorphic, normally grown fetus with a normal mid-trimester scan is low;^{18,19} in this situation, in the absence of a clinical, radiological or pathological indication for invasive examination, full CNS examination may be omitted at the discretion of the consultant responsible for the post
- 22 mortem.

23 **5.2** Approaches to brain examination

- Median posterior or transverse scalp incision.
- Skull incisions to allow assessment of falx and venous sinuses.
- Observation of gyral pattern to assist gestational assessment.
- Consider removal under water (or direct in formalin) and perhaps in dura especially
 with marked autolysis: will permit weighing and assessment of gyral pattern.
- Consider, following external and macroscopic assessment, whether histological
 examination is indicated
- Consider specialist neuropathologist review.

1 2 [Level of evidence – GPP.]

3 5.3 Placental examination

- 4 Placental examination is an integral part of the perinatal post-mortem examination.
- 5 Submission to pathology with the baby is mandatory; non-conformances should be
- 6 monitored in line with local policies. Guidance for detailed examination of the placenta is
- 7 given in the tissue pathway for examination of the placenta.²⁰
- 8 [Level of evidence B.]

9 6 Specific health and safety aspects

- The pathologist should be informed as part of the referral if there is a potential biohazardrisk.
- 12 Autopsy practice using universal precautions will significantly protect against accidental
- 13 transmission of infection, including HIV, SARS CoV-2 and other blood-borne viruses.

7 Focused autopsy – limited by parental consent or by

15 a stepwise post-mortem examination

- 16 Where consent for a full autopsy is not given, a focused examination may be of value
- 17 within the limitations of the investigation. Forms of limited examination may include:
- 18 autopsy limited to 1 or more body cavities or head
- external examination of the body with X-ray, photography and genetics (if indicated)
- placental examination only (with genetic testing if indicated)^{20–23}
- minimally invasive autopsy: external examination and imaging (CT, MRI, ultrasound
 examination if available) alone or with targeted biopsies of specific organs.^{24,25}
- 23
- 24 [Level of evidence B.]
- 25 In some clinicopathological settings, the pathologist may elect to undertake the autopsy
- 26 procedure in a stepwise manner, which may include digital photographs, digital plain film
- 27 radiology,²⁶ external examination, tissue sampling for genetic investigation,²⁷ placental
- 28 macroscopic/histological examination and calculation of the fetal weight:placental weight

- ratio.²⁸ Full internal dissection in these circumstances may not be indicated. Possible
 scenarios include:
- antepartum death of non-dysmorphic, normally grown fetus with normal second
 trimester anomaly scan and unequivocal clinical evidence of significant ascending
 intrauterine infection²⁹
- antepartum death of non-dysmorphic fetus with normal second trimester anomaly scan
 and clinical diagnosis of severe fetal growth restriction (where the post-mortem
- 8 findings are consistent with the clinical history)
- antepartum death of non-dysmorphic, normally grown fetus with normal second
 trimester anomaly scan and with history of clinically recognised, acute, critical
 placental complications: acute abruption, ruptured vasa previa, acute umbilical cord
 prolapse or rupture, tight true knot, etc.
- antepartum death of non-dysmorphic, normally grown fetus with normal second
 trimester anomaly scan and clinical evidence of critical maternal illness (such as
 sepsis, diabetic ketoacidosis, trauma, cardiac arrest, etc.).
- 16

17 Circumstances in which the pathologist should consider a more extensive, i.e.

18 conventional, autopsy include:

- antepartum death of non-dysmorphic, normally grown fetus with normal second
 trimester anomaly scan and no significant clinical events during pregnancy
- organ weight ratios may be contributory to understanding the trajectory of intrauterine
 fetal growth³⁰
- extensive histological sampling of normally formed organs is unlikely to provide
 significant additional information.¹⁷ Histological examination of lungs, thymus and brain
- 25 may be contributory in understanding the mechanism of death.
- intrapartum death of non-dysmorphic, normally grown fetus with normal second
 trimester anomaly scan
- microbiological investigations are recommended
- histological examination of lungs, adrenals and thymus is required
- histological examination of other fetal tissues should be considered
- neuropathological examination of fetal brain is required.

1 2 [Level of evidence – B.]

3 8 Full conventional post mortem

- Short-term retention of organs to allow fixation does not require specific consent,
 provided they are reunited with the body before release for burial/cremation.
- Organ and tissue retention should be dealt with in line with the parental consent form.
- 7 The diagnostic yield for histology taken from macroscopically normal organs is low.^{17,18} • 8 The extent of the examination is at the discretion of the pathologist and should be 9 interpreted in the clinical context of the case. For some patients, if the responsible 10 consultant considers that a more limited examination can adequately answer the 11 questions raised, the examination may not include some of the components, in 12 keeping with the latest NHS guidance.¹⁷ This depends on the specific features and history for each patient and is at the discretion of the consultant pathologist 13 14 responsible for the examination.
- A record of the samples taken should be kept and tissue blocks and slides should be traceable within the laboratory, in line with the requirements of the HTA and the UK
 Accreditation Service (ISO 15189).
- Microbiology: consider bacteriology and virology as clinically indicated.
- Genetic sample: diagnostic yield of microarray, karyotype and quantitative fluorescent
 PCR (QF-PCR) is low in the context of a morphologically normal fetus. With regard to
 further genetic testing, the current Genomic Laboratory Hub (GLH) guideline should be
 followed by the fetal medicine multidisciplinary team (MDT) collaborating with the
 pathologist. (Wales: All Wales Genomics Laboratory; Scotland: Scottish Strategic
 Network for Genomic Medicine laboratories; Northern Ireland: Northern Ireland
 Genomics Medicine Centre.)
- 26

27 [Level of evidence B and C – in line with statutory obligations.]

28 9 Autopsy report

Units may choose, if resources allow, to issue a provisional report giving details of the
macroscopic findings shortly after the examination of the body, followed by a final report

16

- 1 when all histology and other tests have been completed. Alternatively, only a single, final
- 2 report may be produced.
- 3 The report should include the following sections:
- 4 demographic and identification data
- 5 details of autopsy consent and limitations
- 6 body weight and centile (crude or customised)
- 7 body measurements
- 8 list of main findings
- 9 clinicopathological summary (final report)
- 10 summary of clinical history
- systematic description of external and internal findings and placental examination
- 12 organ weights with relevant reference values and ratios
- details of ancillary tests taken (and results in final report)
- 14 histology (final report)
- 15 list of histology tissue blocks (final report).
- 16
- 17 [Level of evidence GPP.]

18 10 Clinicopathological summary

- 19 The summary should include:
- an assessment of gestational age at death
- in antepartum stillbirth, the degree of maceration and likely timing of death
- explicit statements regarding the presence/absence of fetal growth abnomality whether
 restriction or excessive growth, relating to standard reference charts
- evidence of malformation, infection and (where appropriate) trauma (negative findings
 are helpful and may be crucial)
- a discussion of the likely mechanism of death

- concordance or discordance of findings with the clinical history and prenatal testing (if
 appropriate)
- identification of those cases with an increased risk of recurrence (including growth
 restriction, maternal diabetes, genetic disease) and requirement/possibility of
- 5 additional testing
- reference to previous losses/terminations of pregnancy, their outcome and relevance
 to the current pregnancy loss
- results of MDTs, such as the clinical genetics MDT and its outcome, including
 molecular genetic diagnosis. In these cases, an addendum report or reports would be
 appropriate.
- 11

12 [Level of evidence – GPP.]

13 **11 Coding**

- 14 The autopsy procedure and principal findings should be coded according to the SNOMED
- 15 CT system using appropriate body structure, finding, disorder and morphologic
- 16 abnormality codes for SNOMED CT or appropriate T (topographic) and M (morphologic)
- 17 for older versions of SNOMED (local protocols should be followed).
- 18 SNOMED notably ceased to be licensed by the International Health Terminology
- 19 Standards Development Organisation from 26 April 2017; the authors recognise that NHS
- 20 England aspires to fully transition to SNOMED CT.
- 21 The requirement to enable SNOMED CT content in secondary care systems is yet to be
- fully achieved, although it is known that many providers have SNOMED CT enabled EPR
- 23 systems in place. SNOMED CT is used in many different healthcare settings
- 24 internationally and is an NHS-approved fundamental standard (SCCI0034). SNOMED CT
- 25 gives clinical IT systems a single shared language, making the exchange of information
- 26 between systems easier, safer and more accurate. It contains all the clinical terms needed
- 27 for the whole NHS, from procedures and symptoms through to clinical measurements,
- 28 diagnoses, medications and pathological findings.
- 29 The NHS Digital SNOMED CT UK browser can be accessed for free.
- 30 A non-exhaustive list of autopsy-related SNOMED CT codes is provided in Appendix B.

1 12 Criteria for audit

- 2 The following standards are suggested criteria that might be used in periodic reviews to
 3 ensure a post-mortem examination reports meet national standards.
- 4 Supporting documentation:
- standards: supporting documentation was submitted with the body in 95% of cases
- 6 [pre-analytical]. (NB: it is recommended that an autopsy should not be commenced in
- 7 the absence of clinical information.)
- standards: 95% of submitted information is satisfactory, good or excellent [pre analytical]
- standards: a correctly completed autopsy consent form, meeting national requirements
- 11 is submitted with 95% of cases [pre-analytical]. (NB: an autopsy must not be
- 12 commenced unless the pathologist has seen a physical copy of the consent form and
- 13 it is correctly completed.)
- 14
- 15 Autopsy report:
- standards: 100% of autopsy reports must include all of the sections detailed in section
- 17 15, within the limits of parental consent and extent of the examination determined by18 the responsible consultant (above) [analytical]
- standards: in 100% of autopsy reports, the information documented is satisfactory,
 good or excellent [analytical]
- standards: in 100% of autopsy reports, the clinicopathological summary is clear and
 concise and, when appropriate, contains the information detailed above [analytical]
- standards: 80% of autopsy reports are completed within the turnaround times agreed
 with local clinical teams, excluding cases where turnaround time is compromised by
 testing outside of the control of the responsible consultant (e.g. genetic array,
 neuropathological examination) [post-analytical]
- standards: 100% of autopsy reports are communicated to referring centres using
 secure email (e.g. nhs.net email) or encrypted email [post-analytical]
- standards: 100% of autopsy cases are coded appropriately according to local
 guidelines [post-analytical].
- 31

For reference, the NHS specifications (from the 2013/2014 standard contract for perinatal
 pathology)³¹ are as follows:

- 3 60% of final reports for routine post-mortem examination will be issued to referrers
- 4 within 42 days of examination and 90% should be issued within 56 days. This will
- 5 exclude those cases in which there may be a specialist referral opinion required (e.g.
- 6 neuropathology) or very complex metabolic or genetic testing required.

7 These are mandatory contractual requirements of units commissioned to provide perinatal 8 pathology services and are important measures of service quality and outcomes. The 9 authors recognise that paediatric and perinatal pathology services have ongoing staffing 10 and associated operational challenges and where services are shorthanded or otherwise 11 under provisioned, or are providing mutual aid to other units, specific audit targets will be 12 agreed between commissioners and clinical teams, but with the view that all units should 13 be working towards the standards set out in the service specification. 14 The authors recognise that many units are inadequately staffed with either pathologists or 15 APTs. Failure to achieve targets is unlikely to reflect the performance of individual 16 pathologists but may indicate the need for a managerial review of local systems in place to

17 ensure timely reports, and measures such as mutual aid should be considered. Where

18 services are shorthanded or otherwise under provisioned, temporary audit targets should

- 19 be agreed with clinical teams and outsourcing of reporting or other measures should be
- 20 considered.

V2

13 References

- Wojcieszek AM, Shepherd E, Middleton P, Gardener G, Ellwood DA, Cochrane Pregnancy and Childbirth Group *et al.* Interventions for investigating and identifying the causes of stillbirth. *Cochrane Database Syst Rev* 2018;30:4.
- Tsakiridis I, Giouleka S, Mamopoulos A, Athanasiadis A, Dagklis T. Investigation and management of stillbirth: a descriptive review of major guidelines. *J Perinat Med* 2022;21;796–813.
- Lou SK, Keating S, Kolomietz E, Shannon P. Diagnostic utility of pathological investigations in late gestation stillbirth: A cohort study. *Pediatr Dev Pathol* 2020;23:96–106.
- Miller ES, Minturn L, Linn R, Weese-Mayer DE, Ernst LM. Stillbirth evaluation: A stepwise assessment of placental pathology and autopsy. *Am J Obstet Gynecol* 2016;214:115–116.
- 5. NHS England. *Fetal Anomaly Screening Programme Handbook.* Available at: www.gov.uk/government/publications/fetal-anomaly-screening-programme-handbook
- NHS England. NCARDRS Congenital Anomaly Official Statistics Report, 2020. Available at: <u>https://digital.nhs.uk/data-and-information/publications/statistical/ncardrs-congenital-anomaly-statistics-annual-data/ncardrs-congenital-anomaly-statistics-report-2020</u>
- The Royal College of Pathologists. Guidelines on autopsy practice: fetal autopsy after termination of pregnancy or fetal loss associated with congenital anomaly. (2024) (In Press).
- Kang X, Carlin A, Cannie MM, Sanchez TC, Jani JC. Fetal postmortem imaging: An overview of current techniques and future perspectives. *Am J Obstet Gynecol* 2020;4:493–515.
- 9. Shruthi M, Gupta N, Jana M, Mridha AR, Kumar A, Agarwal R *et al.* Conventional *vs* virtual autopsy with postmortem MRI in phenotypic characterization of stillbirths and fetal malformations. *Ultrasound Obstet Gynecol* 2018;51:236–245.
- 10. Arthurs OJ, Bevan C, Sebire NJ. Less invasive investigation of perinatal death. *BMJ* 2015;8:h3598.

21

- Hyde G, Rummery R, Whitby EH, Bloor J, Raghavan A, Cohen MC. Benefits and limitations of the minimally invasive postmortem: A review of an innovative service development. *Pediatr Dev Pathol* 2020;6:431–437
- Shelmerdine SC, Arthurs OJ, Gilpin I, Norman W, Jones R, Taylor AM *et al.* Is traditional perinatal autopsy needed after detailed fetal ultrasound and post-mortem MRI? *Prenat Diagn* 2019;9:818–829.
- Cohen MC, Paley MN, Griffiths PD, Whitby EH. Less invasive autopsy: benefits and limitations of the use of magnetic resonance imaging in the perinatal postmortem. *Pediatr Dev Pathol* 2008;1–9.
- 14. Human Tissue Authority. Codes of Practice. Accessed at: <u>www.hta.gov.uk/codes</u>
- 15. Acts of Scottish Parliament. *Human Tissue (Scotland) Act 2006*. Available at: https://www.legislation.gov.uk/asp/2006/4/contents
- 16. Human Tissue Authority. *The Sands Perinatal Post Mortem Consent Package*. Available at: <u>www.hta.gov.uk/guidance-professionals/regulated-sectors/post-mortem-model-consent-forms/sands</u>
- 17. NHS England. Interim Clinical Commissioning Urgent Policy Statement: Perinatal Post-Mortem Investigation of Fetal and Neonatal Deaths (England, Scotland and Wales). Available at: <u>www.england.nhs.uk/publication/perinatal-post-mortem-</u> <u>investigation-of-fetal-and-neonatal-deaths-england-scotland-and-wales/</u>
- Man J, Hutchinson JC, Ashworth M, Judge-Kronis L, Levine S, Sebire NJ. Stillbirth and intrauterine fetal death: role of routine histological organ sampling to determine cause of death. *Ultrasound Obstet Gynecol* 2016;48:596–601.
- Lewis C, Hutchinson JC, Riddington M, Hill M, Arthurs OJ, Fisher J *et al.* Minimally invasive autopsy for fetuses and children based on a combination of post-mortem MRI and endoscopic examination: a feasibility study. *Health Technol Assess* 2019;46:1– 104.
- 20. The Royal College of Pathologists. *Tissue pathway for histopathological examination of the placenta*. Available at: www.rcpath.org/profession/guidelines/cancer-datasets-and-tissue-pathways.html
- 21. Heazell AEP, Martindale EA. Can post-mortem examination of the placenta help determine the cause of stillbirth? *J Obstet Gynaecol* 2009;29:225–228.

- 22. Graham N, Heazell AEP. When the fetus goes still and the birth is tragic. *Obstet Gynecol Clin North Am* 2020;47:183–196.
- 23. Odendaal H, Pattinson R, Schubert P, Mason D, Brink L, Gebhardt S *et al.* The key role of examining the placenta in establishing a probable cause for stillbirth. *Placenta* 2022;129:77–83.
- Hutchinson JC, Shelmerdine SC, Lewis C, Parmenter J, Simcock IC, Ward L *et al.* Minimally invasive perinatal and pediatric autopsy with laparoscopically assisted tissue sampling: feasibility and experience of the MinImAL procedure. *Ultrasound Obstet Gynecol* 2019;54:661–669.
- Shelmerdine SC, Hutchinson JC, Ward L, Sekar T, Ashworth MT, Levine S *et al.* Feasibility of INTACT (INcisionless TArgeted Core Tissue) biopsy procedure for perinatal autopsy. *Ultrasound Obstet Gynecol* 2020;55:667–675.
- 26. Arthurs OJ, Van Rijn RR, Sebire NJ. Current status of paediatric post-mortem imaging: an ESPR questionnaire-based survey. *Pediatr Radiol* 2014;44:244–251.
- 27. Stanley KE, Giordano J, Thorsten V, Buchovecky C, Thomas A, Ganapathi M *et al.* Causal Genetic Variants in Stillbirth. *N Engl J Med* 2020;17:1107–1116.
- 28. Kraus F, Redline R, Gersell D, Nelson D, Dicke J. *Placental Pathology (1st edition)*. Mishawaka, USA: American Registry of Pathology, 2005.
- 29. Goldenberg RL, McClure EM, Saleem S, Reddy UM. Infection-related stillbirths. *The Lancet* 2010;24:1482–1490.
- 30. Stephens AS, Bentley JP, Taylor LK, Arbuckle SM. Diagnosis of fetal growth restriction in perinatal deaths using brain to liver weight ratios. *Pathology* 2015;47:51–57.
- 31. NHS England. 2013/14 NHS Standard Contract for Perinatal Pathology. Available at: www.england.nhs.uk/wp-content/uploads/2013/06/e12-perinatal-path.pdf

23

Appendix A Exemplar autopsy request form

CLINICAL INFORMATION FOR FETAL / PERINATAL POST MORTEM

Mother (sticker if available)
Family Name: First Name: D.o.B.: / / Reg No
•

Fetus/ Infant (sticker if available)

Family Name:..... First Name:..... D.o.B.: / / D.o.D: / / Reg No....

Please carefully complete this form. Any missing information could potentially delay or alter the findings.

Parts 1, 2 and 3 ALL require completion for EVERY referral made.

REFERRING HOSPITAL: HOSPITAL OF BIRTH (if different): (Please include history/ notes from previous ho CONSULTANT OBSTETRICIAN: CONSULTANT PAEDIATRICIAN:	
Part 1. MOTHER'S DETAILS	
(ALL fields for this section are MANDATORY for	or ALL requests please)
Ethnic origin: Father's ethnic origin	gin (if known)
Consanguinity between parents? Y/N Blo	od group:

Maternal height:	cm	Booking weight:	kg	BMI:
------------------	----	-----------------	----	------

Obstetric History:

PREVIOUS PREGNANCIES

	Date	Gestation	Delivery	Sex	Outcome
1.					
2.					
3.					
4.					
5.					
6.					
7.					

Were there any complications with any previous pregnancies (this current pregnancy excluded)?* Yes / No / Not known – if yes, specify

*Further space for writing is provided on p4 of this form.

This form consists of 4 pages. All require your attention.

Please carefully complete this form. Any missing information could potentially delay or alter the findings.

Part 2. CURRENT PREGNANCY DETAILS (ALL fields for this section are MANDATORY for ALL requests please)			
Booked/Unbooked LMP :	EDD:		
Gestation: by dates:/40 by s	scan:/40 weeks		

Is there any relevant past medical history? (If yes, what?) ______ Were there any abnormal screening results? (If yes, what?, fetal growth issues and uterine artery doppler results?) ______ Medications (if any): ______

USS findings (please send report if abnormal):

	Date	Indication	Gestation	Findings
		(e.g. dating / anomaly, etc.)		(please include report if abnormal)
1.				
2.				
3.				
4.				

Antenatal diagnostic procedures (please include results if available / known): (e.g. CVS sampling or other invasive techniques / fetal MRI)

Additional antenatal history:		
Was this a twin pregnancy?	Y/N	If so, MCDA/MCMA/DCDA?
Any history of reduced fetal movements?	Y/N	If so, how many episodes for how long?
Was there antenatal bleeding?	Y/N	If so, when and how much?
Was there hypertension?	Y/N	BP = mmHg
Was there pre-eclampsia?	Y/N	BP = mmHg
Was there anaemia?	Y/N	
Is there anything else of relevance regarding		
pathologist? Labour and delivery details are	detailed	t in the following section*.

*Further space for writing is provided on p4 of this form.

N.B. Would this PM examination be classed as an infection risk to relevant staff? Y/N

This form consists of 4 pages. All require your attention.

Please carefully complete this form. Any missing information could potentially delay or alter the findings.

Have you completely filled part 1 & 2? A	ny missing information car	alter the findings.			
 Was this a TOP? a) If TOP – Feticide Y/N Was this a miscarriage (i.e. pregnancy Was this an IUD > 24 weeks' gestation If so, when was the last documented evid Was this an intrapartum or neonatal de What was the presenting part? Vertex / E b) Rupture of membranes: date tic 1st stagehmin 2nd :hmin d) Abnormal fetal monitoring or suspected 	i (i.e. macerated stillbirth)? lence of fetal / infant viabili eath (i.e. fresh stillbirth / liv Breech / Other ime Augmentation ()? Y/N Y/N ty / fetal heart beat? e birth)? Y/N Syntocinon): Y/N			
e) DELIVERY: Spont. / Assisted (forceps Time f) Apgars: 1st min 5th min Did labour commence spontaneously/ did	10th min I it require induction?				
Date of induction, if applicable:		Date of delivery:			
Liquor: Normal / reduced volume / increas		Abnormal liquor colour?			
Was there antepartum haemorrhage?		Was there maternal pyrexia, concerns re: maternal infection?			
The infant or fetusMale ♂Female ♀IndeterminateBirth Weight (g):		s in the fetus / infant at time of			
*Further space is provided for writing on p	*Further space is provided for writing on p4 of this form.				
Part 4: For LIVEBORN infants ONLY (i.e.					

Have you completely filled parts 1, 2 & 3?

RESUSCITATION procedures employed: NEONATAL PROBLEMS & PROCEDURES: Surfactant: Y/N

BRIEF SUMMARY OF LATER SYMPTOMS/TREATMENTS AND MAJOR INVESTIGATIONS (including CPAP / ventilation, IV therapy, fits, episodes of collapse, pneumonia, pneumothorax, bleeding problems, type of feeding, etc.)

*Further space for writing is provided on p4 of this form.

<u>Attention please:</u> If this was a complex course, please consider sending YOUR summary and interpretation of events. Sending photocopies of the notes or the complete set of notes may be acceptable, but not advisable for optimal practice.

SUSPECTED CAUSE(S) OF DEATH: DEATH REGISTERED AS (if applicable):

ANY OTHER RELEVANT INFORMATION/SPECIAL POINTS TO BE NOTED AT POST MORTEM: *Further space for writing is provided on p4 of this form

This form consists of 4 pages. All require your attention.

Please carefully complete this form. Any missing information could potentially delay or alter the findings.

Please do not hesitate to contact us should you have any queries regarding the completion of this form.

Person completing form: No	Contact number / bleep
(Please PRINT)	
Copy of report to be sent to:	
Consultant obstetrician: (Mr/ Ms/ Mrs/ Dr) (Please PRINT)	and/or
Consultant paediatrician: (Please PRINT)	
Thank you for carefully completing all relevant parts attention please. May we remind you that any missing information cou	
Notes for any further relevant information and short narra	tive of the clinical synopsis:
L BABIES AND PLACENTAS SHOULD BE SENT FRES	H IN LEAKPROOF, OPAQUE CONTAINERS UNLES
IERE IS AN INFECTIOUS HAZARD (in this case phone to formalin before tra	o discuss whether the specimen should be fixed in 10 ⁶
S ESSENTIAL TO SEND THE PLACENTA WIT	H A FETUS / INFANT.

This form consists of 4 pages. All require your attention.

PGD

280224

Appendix B Autopsy-related SNOMED CT codes

The following codes are suggested for centres with SNOMED CT capabilities. Local coding procedures should be followed where SNOMED CT has yet to be implemented. The suggested lists below are not exhaustive but highlight examples of codes that could be used. The <u>NHS Digital SNOMED CT UK browser</u> can be accessed for free.

General autopsy codes

29240004	Ι	Autopsy examination (procedure)
702692002		Coroner's autopsy (procedure)
5785009		Forensic autopsy (procedure)
430339001		Pediatric autopsy (procedure)
308375000	I	Report for Procurator Fiscal (record artifact)

Specimen codes

309502007		Fetus specimen (specimen)
725957005		Formalin-fixed placenta tissue specimen (specimen)

Post-mortem imaging

717193008		Cone beam computed tomography (procedure)
699581005	Ι	Post mortem magnetic resonance imaging (procedure)
713599004		Post mortem ultrasonography (procedure)

Fetal findings

85811006	Ι	Autolysis (morphologic abnormality)	
248200007	I.	Dysmorphic facies (finding)	
87309006		Death of unknown cause (event)	
22033007	I	Fetal growth retardation (disorder)	
289448000	Ι	Fetus normal (finding)	
198901003	Ι	Macerated fetus (disorder)	
85728002	Ι	Morphologic description only (finding)	
PGD	280224	28	

- 723745006 | Morphological description only, with differential diagnosis (finding)
- 41962002 | Oligohydramnios sequence (disorder)

Placental findings

4532008	Ι	Acute inflammation (morphologic abnormality)	
84499006	I	Chronic inflammation (morphologic abnormality)	
396343006	I	Funisitis (disorder)	
65396000	I	Histiocytic infiltrate (morphologic abnormality)	
125563001	I	Hyalinized fibrosis (morphologic abnormality)	
55641003	I	Infarct (morphologic abnormality)	
73728008	I	Maturation acceleration (morphologic abnormality)	
50353005	I	Maturation deceleration (morphologic abnormality)	
309162003	I	Normal histology findings (finding)	
415105001	Ι	Placental abruption (disorder)	
268585006	Ι	Placental infarct (disorder)	
237292005	I	Placental insufficiency (disorder)	
448485001	I	Specimen satisfactory for evaluation but limited by cellular degeneration (finding)	
27696007		True knot of umbilical cord (disorder)	
75798003	I	Twin dichorionic diamniotic placenta (disorder)	
83787007	I	Twin monochorionic diamniotic placenta (disorder)	
388604008	T	Villitis (disorder)	
1155707008	I	High histologic grade	
1155708003		Low histologic grade (qualifier value)	
1155705000	I	Histologic grade cannot be assessed (qualifier value)	

Appendix C 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 1 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 cancer type.
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 D AGREE II guideline 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 guideline that indicate compliance with each of the AGREE II standards are indicated in the table.

A	GREE standard	Section of guideline
Sc	cope and purpose	
1	The overall objective(s) of the guideline is (are) specifically described	Introduction
2	The health question(s) covered by the guideline is (are) specifically described	Introduction
3	The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, Introduction
St	akeholder 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	Introduction
Ri	gour 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	Throughout
13	The guideline has been externally reviewed by experts prior to its publication	Foreword
14	A procedure for updating the guideline is provided	Foreword
CI	arity of presentation	
15	The recommendations are specific and unambiguous	Throughout
16	The different options for management of the condition or health issue are clearly presented	Throughout
17	Key recommendations are easily identifiable	Throughout

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	All appendices
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	12
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