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

Dataset for lung cancer histopathology reports

September 2016

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Unique document number	G048
Document name	Dataset for lung cancer histopathology reports
Version number	5
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Date active	September 2016
Date for review	September 2019
Comments	This document supersedes the 2014 document *Dataset for lung cancer histopathology reports (3rd edition).* In accordance with the College's pre-publications policy, this document was on the College website for consultation 1–29 June 2016. Seventeen items of feedback were received and the dataset was amended as necessary. Please email publications@rcpath.org if you wish to see the responses. **Dr Lorna Williamson** **Director of Publishing and Engagement**

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Registered charity in England and Wales, no. 261035

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First published: 2016

INVESTORS IN PEOPLE

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NICE has accredited the process used by The Royal College of Pathologists to produce its Cancer Datasets and Tissue Pathways guidance. Accreditation is valid for 5 years from July 2012. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

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Foreword

The cancer datasets published by The Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

Each dataset contains core data items that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 90% of reports on cancer resections should record a full set of core data items. Other, non-core, data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The document was circulated to the following stakeholder groups:

- British Thoracic Oncology Group
- British Thoracic Society
- Society for Cardiothoracic Surgery in Great Britain and Ireland.

The evidence has been evaluated according to the modified SIGN guidance and the level of evidence for the recommendations has been summarised according to College guidance (see Appendix H).

No major organisational changes have been identified that would hinder the implementation of the dataset.

A formal revision cycle for all cancer datasets takes place on a three-yearly basis. However, each year, the College will ask the author of the dataset, in conjunction with the relevant subspecialty advisor to the College, to consider whether or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken whereby a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Working Group on Cancer Services and was on the College website for consultation with the membership 1–29 June 2016. All comments received from the Working Group and membership were addressed by the authors to the satisfaction of the Chair of the Working Group and the Director of Publishing and Engagement.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Director of Clinical Effectiveness and are available on request. The authors have declared that they have

previously received payment for advisory and educational work for commercial organisations involved in molecular testing and treatment of lung cancer. They give their assurances that these conflicts of interest have not influenced the content of this dataset.

1 Introduction

This document is an update to version 4.1, published in 2014. Full and accurate provision of pathology data in both biopsy and resection specimens is of vital importance in:[1–6]

a) deciding on the most appropriate treatment for particular patients, including the need for and choice of adjuvant therapy, as well as the suitability for targeted therapies in both clinical and trial settings

b) providing prognostic information to clinicians and patients

c) providing more reliable staging than can be achieved with clinical data alone

d) monitoring the clinical effectiveness of therapeutic trials

e) providing accurate data for cancer registration

f) enabling audit of clinical and radiological investigation (decisions about the feasibility of surgical resection are made following clinical and radiological staging procedures and correlation of these results with information obtained from resection specimens allows monitoring of the accuracy of staging procedures and the appropriateness of surgical intervention)

g) evaluating newer surgical techniques (newer, less invasive surgical techniques such as video-assisted thoracoscopic surgery [VATS] have been introduced, and the evaluation of the efficacy and appropriateness of these techniques requires analysis of the pathological data)

h) collecting accurate data for cancer registration and epidemiology (there is evidence of changing patterns of disease in lung cancer – for example, a progressive increase in the proportion of adenocarcinomas – which does not entirely reflect changes in smoking habit, and information on tumour type forms part of the epidemiological dataset).

The purpose of this document is to define the core data that should be determined for all resected cases of lung cancer. These are guidelines and not rigid rules and are intended to help a given pathologist provide the information necessary to local clinicians for effective management of their patients. Consistency in reporting and staging is improved by the use of standard terminology – for example, for bronchopulmonary segments and lymph node stations – and the use of a standard proforma or checklist. A form is intended to supplement and not replace the usual ‘in-house’ text report. The use of diagrams to show the extent of local invasion and involvement of lymph node stations can be advantageous. It is also important to realise that staging at the time of resection is only partly informed by pathological assessment of the specimen and that clinical details will be required with respect to some parameters, for instance proximity of tumour to the carina (pT2 versus pT3) in central lesions.

1.1 Changes since the previous edition

1.1.1 Tumour classification

The 4th edition of the World Health Organization’s classification of lung tumours was published in 2015.[7] This edition should now be used for tumour classification, along with the updated SNOMED codes (Appendix C).

1.1.2 Molecular testing

The number of molecular tests that a pathologist may be asked to manage is ever increasing. These tests relate to targeted therapies that are approved for clinical use, with additional tests on the horizon in relation to immunomodulatory therapy (e.g. PD-L1).[8] Most of these are currently considered as non-core items apart from testing for epidermal growth factor receptor (EGFR) mutations. At the present time, international evidence-based guidelines on what types of tests should be considered on a routine basis remain unchanged since the previous edition,[9] but this is a rapidly developing field. The international guidelines are currently being updated and this dataset will no doubt need further amendment in less than three years. Meanwhile, pathologists are increasingly being asked to manage samples with these tests in mind. As such, the authors consider that the dataset should cover these eventualities. The section on small biopsies (Section 6) has therefore been expanded to provide guidance on handling of these specimens.

The authors emphasise that this document is for guidance only. Local pressures and policies may need to be followed preferentially, as many of the steps herein are not considered 'core', due to lack of evidence for the clinical utility of some tests. There is also considerable variation in practice within the NHS but it is hoped that this advice and guidance will help decrease this variation. Furthermore, phase 2 of Cancer Research UK's Stratified Medicine Programme is well underway in relation to the usage of next-generation sequencing to identify a panel of molecular abnormalities. This renders the optimum processing and preservation of small diagnostic specimens by all laboratories handling such material of crucial importance.

1.1.3 Staging

The document remains largely unchanged in relation to staging. The guidance and reporting form in the following pages are based on the WHO classification of lung tumours,[7] and incorporates the update on adenocarcinoma classification from the International Association for the Study of Lung Cancer (IASLC)[2] and the 2009 revision of TNM 7, International Staging Systems for Lung Cancer,[1] and follows consultations with pulmonary pathologists and clinicians involved in the treatment and management of lung cancer. The staging system is a valid and reproducible instrument. However, the 8th edition of TNM is expected in the near future. Readers are advised to review upcoming publications in the *Journal of Thoracic Oncology* that will likely inform the 8th TNM staging system.[10–18]

1.1.4 ICCR lung cancer dataset

With the publication of the International Collaboration on Cancer Reporting (ICCR) *Lung Cancer Dataset*, core items (Section 5) have been adapted to be consistent with this initiative.[19]

1.2 Target users and health benefits of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of information technology products to laboratories. The secondary users are surgeons and oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and multidisciplinary team (MDT) working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. Collection of standardised cancer-specific data also provides information for healthcare providers and epidemiologists, and facilitates international benchmarking and research.

2 Clinical information required on the specimen request form

Name, date of birth, hospital, hospital number, NHS or CHI number, procedure, specimen type, date of procedure and surgeon/physician should be provided. In addition, the proximity of tumour to the carina should be stated (for pneumonectomies only), together with details of any previous biopsy or cytology, any previous malignancy and any previous treatment, such as neoadjuvant chemotherapy and/or radiotherapy.

3 Preparation of specimens before dissection of resection specimens

Ideally, specimens should be received fresh in the pathology laboratory to allow tumour banking, if feasible, and also to have lung inflation undertaken by laboratory staff. Resected lung tissue should be distended with formalin before description and examination. This can be performed through the supplying bronchus using a reservoir attached to flexible tubing and nozzle or by using a large-volume syringe with a wide nozzle ('bladder syringe'). Segmentectomy specimens with stapled margins may be inflated through the pleural surface using a needle and syringe. The specimen is distended until the pleural surface is smooth and it is then placed in a large volume of formalin and allowed to fix for approximately 24 hours. Inflation must be carried out before or shortly after the specimen has been placed in formalin, otherwise fixation of the outer lung may prevent expansion.

4 Specimen handling and block selection for resection specimens

The report must state whether the specimen is from the left or right lung. The type of operative procedure (VATS, VATS proceeding to open, or open) and the type of specimen should be recorded. The distinction between an intra-pericardial and extra-pericardial plane of vascular resection in pneumonectomy specimens is important as it highlights the need to examine the pericardial tissue with regard to pT3 versus pT4 tumours. These data, along with the limits of the mediastinal pleura, are sometimes better identified by discussing the case with the surgeon.

If circumstances permit and appropriate ethical consent is in place, fresh tissue may be taken for research biobanks, as long as this does not compromise the pathology report. Consideration should also be given to sending small samples from masses resected without diagnosis to microbiology, in case the diagnosis proves to be an infection.

Care should be taken to identify all structures involved by central and perihilar tumours. An en-bloc resection may include portions of mediastinal pleura, pericardium, great vessels or atrial wall and all of these need thorough sampling.

The bronchial and vascular margins, which include the cut ends of the tied vessels and adjacent soft tissues, must be sampled before the lung is sectioned. In wedge resections, the nearest parenchymal margin should be sampled, and the limitations of stapled and cauterised edges, if present, should be commented upon. If tumour is close to a stapled margin, tissue can be scraped from the stapled margin. The location of the tumour is identified by palpation and the tumour is either sectioned along the major airways or multiple transverse cuts or sagittal sections are made to transect and expose the tumour according to the preference of the examining pathologist. Blocks are taken to include the tumour. The whole of the tumour should be processed if it is <2 cm, or <3 cm if it is suspected of being an adenocarcinoma *in situ*. At least three blocks should be taken for larger neoplasms, ideally one per cm of maximum diameter. Blocks should include the closest area of visceral pleura, intrapulmonary and hilar (pN1) lymph nodes, extrapulmonary/mediastinal (pN2/3) lymph nodes, and background lung tissue (a minimum of one block but ideally three are recommended). Any other nodules should be sampled. The vascular/mediastinal planes of resection and any chest wall resection

margins should be marked by a suitable method, when appropriate, and sampled for histology. Mediastinal and chest wall margins should be sampled as appropriate.

All lymph nodes should be cut into slices of 2–3 mm thickness, blocked, processed in their entirety and examined histologically. If, however, the node appears to be macroscopically involved, only one slice needs to be submitted.

All the tissue from bronchoscopic and needle biopsies should be fixed in formalin and routinely processed according to the College's tissue pathway recommendations.

5 Core data items for resection specimens (see Appendix D)

5.1 Clinical

Name, date of birth, hospital, hospital number, NHS/CHI number, specimen type, procedure, date of procedure and surgeon/physician should be supplied. Proximity of tumour to carina should be stated. Any additional attached anatomic structures should also be documented.

5.2 Pathological

5.2.1 Location of tumour

The location of the tumour should be recorded. Proximal tumours in the main bronchus may require bronchoscopic data to distinguish between pT2 and pT3 tumours and this should have been provided on the request form for pneumonectomies. If the tumour involves more than one lobe, record all lobes that are involved. The terms 'central', 'endobronchial' or 'hilar' may be used as appropriate to describe tumours located solely either within the airways or not within a specific lobe at the hilum.

5.2.2 Size of tumour and distance of tumour from bronchial margin

For staging purposes, the maximum diameter of tumour should be measured to the nearest millimetre. The distance from the tumour to the bronchial resection margin will assist surgical audit. If the specimen is a completion lobectomy following wedge resection, then the distance from the nearest point of the stapled margin to the specimen resection margin should be given.

5.2.3 Atelectasis

Atelectasis/obstructive pneumonia is a common finding distal to tumours and although more of a radiological parameter and difficult to assess macroscopically, it should be described in the free-text report. However, if the changes extend to the hilum (with tumours involving the proximal lobar bronchi) or the whole lung (with tumours obstructing the main bronchus), this should be recorded, as it may 'upstage' small central tumours. For example, atelectasis/obstructive pneumonia involving the whole lung would put the tumour into the pT3 category.

[Level of evidence B – Tumour location and atelectasis form part of established staging criteria.]

5.2.4 Histological type

Histological type is recorded according to the 2015 WHO classification of tumours.[7]

Squamous cell carcinoma requires the presence of at least one of the following: keratin, keratin pearls or intercellular bridges. For non-keratinising squamous cell carcinomas, confirmatory immunohistochemistry is recommended to ensure that a solid pattern adenocarcinoma is not missed.

For adenocarcinomas, if non-mucinous, then the histological patterns should be documented at 5% increments up to 100%. The current recognised patterns are lepidic (previously bronchioloalveolar pattern), acinar (gland formation), papillary, micropapillary (papillaroid structures without stromal cores) and solid. For a solid pattern, the tumour cells must either (a) have intracellular mucin-containing vacuoles in more than five cells in two consecutive high-power fields of an otherwise undifferentiated carcinoma, or (b) show immuno-histochemical evidence of adenocarcinomatous differentiation, or both.

Adenocarcinoma *in situ* (AIS) is diagnosed only in resected localised lesions of 30 mm or less, with a purely lepidic pattern.

Minimally invasive adenocarcinoma (MIA) is diagnosed only in resected localised lesions of 30 mm or less, with an invasive area measuring no more than 5 mm, with a lack of necrosis, lymphatic invasion, pleural invasion or spread through air spaces (STAS).

Invasive mucinous adenocarcinoma (formerly 'mucinous bronchiolo-alveolar carcinoma', BAC) has a distinctive histological appearance with tumour cells having a goblet or columnar cell morphology with abundant intracytoplasmic mucin. These tumours differ from *in situ* or minimally invasive mucinous adenocarcinoma by one or more of the following criteria:

- size >3 cm
- extent of invasion >0.5 cm
- multiple nodules
- lack of a circumscribed border with typically multifocal spread into adjacent lung parenchyma.

If there is at least 10% of each component, it should be classified as 'mixed mucinous and non-mucinous adenocarcinoma'.

Invasive mucinous adenocarcinomas need to be distinguished from adenocarcinomas that produce mucin but lack the characteristic goblet cell or columnar cell morphology of such tumours. Mucinous adenocarcinomas should also have their architectural patterns documented in similar fashion to non-mucinous variants.

Large cell carcinomas are composed of large undifferentiated epithelial cells that lack the nuclear morphology of small cell carcinoma and show no morphological or immunohistochemical evidence of squamous or glandular differentiation. Morphologically undifferentiated non-small cell carcinoma (NSCCs) that stain for TTF-1 should be classified as solid pattern adenocarcinomas and those that stain for P40 and/or CK5/6 and/or p63 should be classified as non-keratinising squamous cell carcinomas.

Neuroendocrine tumours are classified using the same criteria as the 2004 WHO classification, although they are grouped together in the 2015 WHO classification.[7] This group comprises carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma and small cell lung carcinoma. For carcinoid tumours, an absence of necrosis and a mitotic rate of less than 2 mitoses per 2 mm^2 indicate classification as typical carcinoid. If there is either necrosis or a mitotic rate of between 2 and 10 mitoses per 2 mm^2, or both, then classification is atypical carcinoid. Non-small cell lung carcinomas with more than 10 mitoses per 2 mm^2, neuroendocrine morphology and neuroendocrine immunophenotype should be classified as large cell neuroendocrine carcinoma. Small cell carcinoma comprises small cells with scanty cytoplasm, poorly defined cell borders, finely dispersed granular chromatin and absent or inconspicuous nucleoli. Necrosis is typically extensive and mitotic count is high, with most tumours expressing neuroendocrine markers.

A significant proportion of carcinomas show more than one histological type and these should be listed after 'combined tumour' – noting that to designate a tumour as 'combined' requires each component to be at least 10% of the total tumour volume.[14] All other tumours, except small cell carcinoma, should be listed as 'other primary tumour'.

[Level of evidence B – Histopathological type is important for cancer registration and prognosis.]

5.2.5 Local invasion

Visceral pleural invasion (VPI) is recognised by a breach of the superficial (outer) elastic layer of the pleura and increases the T stage of some tumours. Involvement of the visceral pleura without breach of the superficial layer should not be classified as VPI, since it appears to make no prognostic difference.[20] However, extension of tumour to the visceral pleural surface may have prognostic significance and the 7th TNM recommends that pleural involvement be divided into:

- PL0 – no pleural involvement
- PL1 – breaching of the outer layer of the visceral pleura but no infiltration of tumour cells to the pleural surface
- PL2 – breaching of the outer layer of the visceral pleura and infiltration of tumour cells to the pleural surface
- PL3 – involvement of the parietal pleura.[1,21]

In some instances, a peripheral tumour can pucker and draw in the pleura without invading, which can make the identification of pleural invasion extremely difficult. The area should be extensively blocked. An elastic tissue stain is recommended in the recognition of invasion, but sometimes the duplication and fusion of the internal and external elastic laminae provides difficulties in discernment from the underlying fibroelastotic lung.

Invasion of pericardium, heart, diaphragm, chest wall and great vessels should be recorded if present.

[Level of evidence B – Local invasion forms part of established staging criteria.]

5.2.6 Separate tumour nodules: satellite nodules (intrapulmonary metastases) versus synchronous primary tumours

The 8th TNM has proposed refinements to the staging and handling of separate tumour nodules,[14–17] and both macroscopic and microscopic features of all of these should be recorded.

If nodules are viewed as satellite nodules (intrapulmonary metastases) from a single primary lung tumour, then these should be classified as pT3 if in the same lobe, pT4 if in a different ipsilateral lobe and pM1a if in the contralateral lung. Comprehensive histological assessment has proved to be as accurate as molecular analysis in distinguishing satellite metastatic nodules from synchronous independent primary lesions.[22]

If nodules are viewed as separate primaries, then the highest-stage lesion should be recorded with either multiplicity or the number of lesions provided in parentheses, for example T2b(m) or T2b(3).

Of note, the definition of a satellite lesion in terms of size and distance from the primary is not well defined and distinction from a synchronous primary tumour usually relies on the subjective opinion of the pathologist after assessment of both lesions, as well as multidisciplinary review of other modalities, such as imaging.

[Level of evidence B – Satellite nodules form part of established staging criteria.]

5.2.7 Resections following therapy

Increasingly, cases are resected following neoadjuvant therapy. These should be staged as for other tumours, with the pTNM categorisation being based on areas of viability and prefixed with the letter ‘y’, for example ypT2aN1. An estimation of whether more or less than 10% residual viable tumour is present in the resection specimen should be reported. Complete response would be classified as ypT0.

5.2.8 Lymph node spread

Lymph nodes sent separately from the main specimen should be identified by their lymph node station number or name.[1] pN1 nodes are defined as involved ipsilateral hilar/peribronchial or intrapulmonary nodes, pN2 as involved ipsilateral mediastinal or subcarinal nodes, and pN3 as involved contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular nodes. In a pneumonectomy specimen, lymph nodes around the main bronchus which are outside the hilar pleural envelope are categorised as pN2 nodes (tracheobronchial or subaortic nodes). It is not a core data item to count the number of lymph nodes involved, only whether metastasis is present or not in a lymph node station. Nodes involved by direct spread of the primary tumour are regarded as positive. Lymph nodes in which there are isolated tumour cells, defined as single cells or small clusters less than 0.2 mm, should be classified as pN0 but documented as pN0(i+), or pN0(mol+) if non-morphological techniques are used.

5.2.9 Margins

Before assigning a pT value to central tumours, information will need to be obtained from the surgeon. However, the most important determinants of prognosis appear to be completeness of surgical resection (bronchial, mediastinal, vascular, chest wall) and nodal status.[23] Distance of tumour from the nearest margin should be documented (see also Section 5.2.2). Complete resection should be classified as R0, microscopic incomplete resection as R1 and macroscopic incomplete resection as R2. Increasingly, VATS lobectomies are being undertaken with the hilar margin stapled closed. In this instance, the nearest block to the margin should be sampled, with a statement being made that this is not the true margin if there is tumour identified at this point. Completeness of resection should then be decided through discussion with the surgeon, if material cannot be retrieved from the staple line.

[Level of evidence B – The above staging criteria are known to provide important prognostic data that govern post-surgical management.]

5.2.10 Ancillary data

EGFR mutation status and anaplastic lymphoma kinase (ALK) translocation status should be recorded if testing is undertaken. At present, other molecular data are not considered as core items but should be documented within the pathology report.

Lymphovascular invasion has been demonstrated to be an independent prognostic factor and should also be documented.[24,25]

[Level of *evidence A – The presence of certain EGFR mutations has been consistently shown to be associated with response to targeted therapy.]*

6 Handling and reporting of non-resection specimens (e.g. biopsies and cytology)

6.1 Handling of biopsies

Handling of small biopsies is becoming increasingly important as requirements for molecular testing increase (Figure 1).

In the pre-examination phase, specimens should not be allowed to dry out before fixation and should be fixed for an appropriate period (around 24 hours). Consideration should be given to blocking tissue cores in more than one block, especially in cases where it is known that molecular testing is likely. MDT discussions prior to biopsy should increasingly have a role to play in the planning of tissue usage, especially as there is often now a need for re-biopsy in patients who develop resistance to targeted therapies. In these cases, the diagnosis is already known and often all that is required is confirmation that malignancy is present before specific molecular tests (e.g. T790M mutation) are requested in this setting.

In the examination phase, pathologists need to be thinking constantly about the preservation of tissue for these tests and balance this against the need for other ancillary investigations used in diagnosis. In particular, overuse of immunohistochemistry and excessive levelling should be avoided.

In the post-examination phase, data from the 2012 audit undertaken by the Health Quality Improvement Project indicate that practice is split between those who routinely test for EGFR mutations and those who order tests only after MDT discussion or a request from an oncologist.[26] Individual practice is likely best dictated by local pressures, in that centres where MDT decisions cannot be reached in a timely fashion should routinely test and accept some wastage, while the remainder should ensure that no tests are delayed inappropriately for patients potentially suitable for targeted therapy. The sequence and extent of testing should also be discussed with oncologists, so as to minimise tissue wastage.

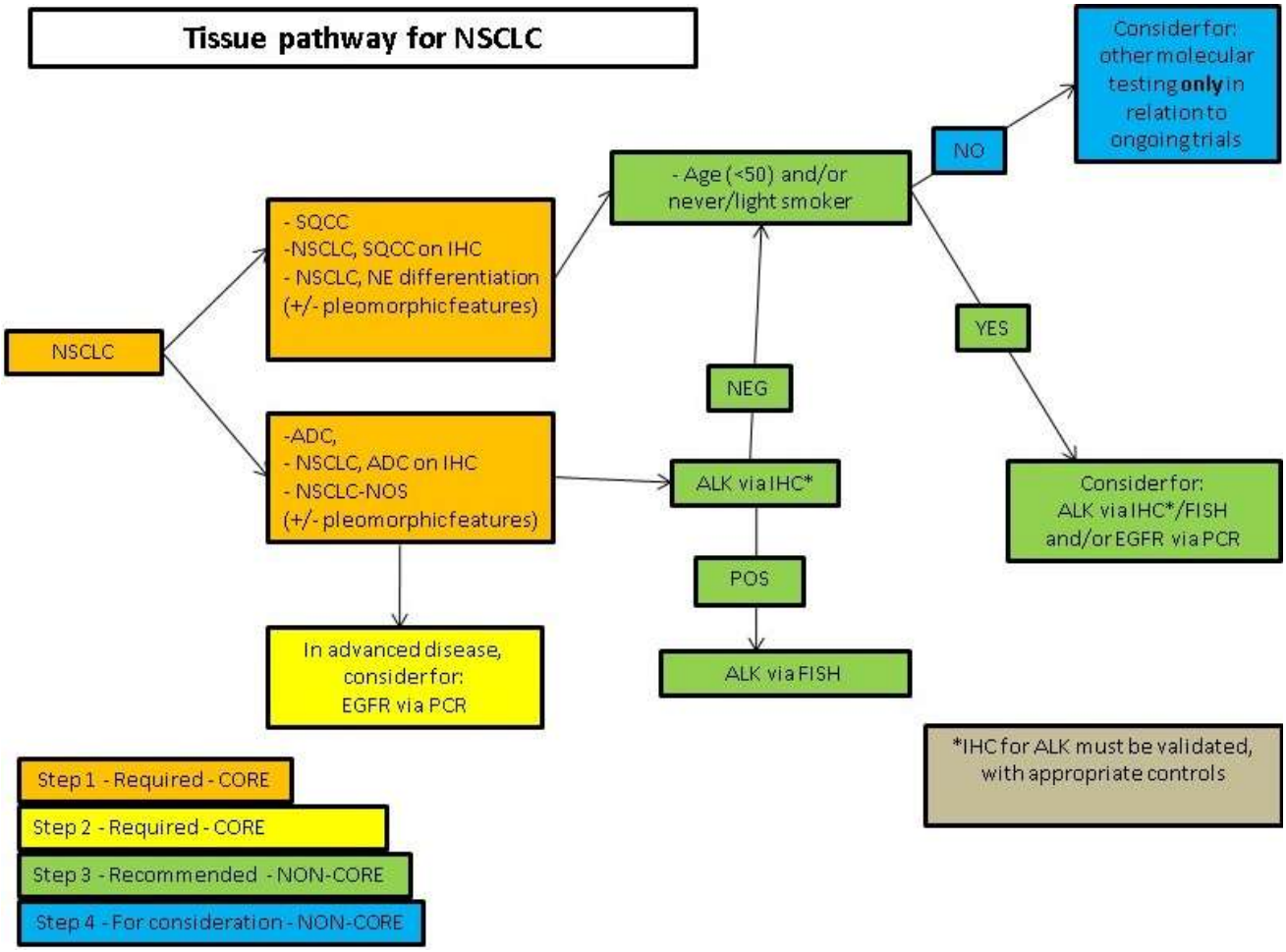

Figure 1: Suggested pathway for handling of non-small cell carcinoma specimens, highlighting core and non-core items (usage would be primarily for non-resection specimens, although may be considered for resections with advanced disease)

NSCLC – Non-small cell lung carcinoma
SQCC – Squamous cell carcinoma
NOS – Not otherwise specified
ALK – Anaplastic Lymphoma Kinase
PCR – Polymerase Chain Reaction
NEG – Negative; POS – Positive
ADC – Adenocarcinoma
IHC – Immunohistochemistry
NE –Neuroendocrine
EGFR – Epidermal Growth Factor Receptor
FISH – Fluorescence In-Situ Hybridisation

Step 1

*All points for Step 1 should ideally be undertaken on slides taken on **one** cutting from the block, although it is recognised that additional immunohistochemistry (IHC) may need to be undertaken if there is a question regarding the primary site.*

– Initial sectioning should go no further than 30% of the way into the sample, and unstained spares (for potential IHC) should be taken.

– If the biopsy is positive and shows morphological evidence of adenocarcinoma (ADC) or squamous cell carcinoma (SQCC), then IHC need not be undertaken (this should be 50–60% of cases), unless there is a question regarding the primary site.

– If the sample is a non-small cell lung cancer (NSCLC) and shows no morphological evidence of ADC or SQCC, then a panel of, at least one but no more than two, ADC-specific (e.g. TTF-1) and SQCC-specific (e.g. P40 or P63 and CK5/6) markers should be used on the unstained sections (thereby preserving tissue in the block). It is unnecessary and wasteful of tissue to perform 'confirmatory' immunochemistry when a classification of NSCLC into squamous or adenocarcinoma is possible on morphological grounds alone and such immunochemistry should not be ordered as a matter of routine before morphology has been assessed. Classification should be undertaken using the WHO classification for resections and the updated biopsy classification.[7]
The rate of NSCLC not otherwise specified (NSCLC-NOS) should be around 10% at this point and no more than 15%.

– If the sample looks like small cell carcinoma, this can be confirmed, if felt necessary, by a panel of MNF116, CD56 and TTF-1, using the u/s sections.

– If there is no evidence of tumour on initial sectioning, then further sectioning should be undertaken.

– If tumour is present only in the first two levels, then discussion with a clinician and a molecular biologist about what testing may be needed and what is feasible on the sections should be undertaken. Re-biopsy may be required.

Step 2

Step 2 should ideally be undertaken on a second cutting from the block.

– In advanced disease, if clinically appropriate, testing for EGFR mutations should be done. Testing should take place according to local guidelines. In order to preserve tissue, if either clinically or histologically indicated, appropriate sections for ALK testing – via IHC and/or fluorescence *in situ* hybridisation (FISH) (see Figure 1) – may be taken at this cutting session. These must be taken in molecularly sterile conditions to prevent cross-contamination. Unused spares from step 1 can be used for ALK IHC. If a tumour load and percentage on the slide are requested by the molecular laboratory, these should be provided.

Step 3

Step 3 should be taken only if tissue is no longer needed for standard diagnostic purposes.

– Progress is sufficiently rapid in this field that further testing may be required in relation to clinical trials.

6.2 Handling of cytology specimens

Diagnosis and treatment of lung cancer can be safely based on cytological specimens. This requires the provision of all relevant clinical information to the pathologist (including previous malignancies and treatment) and a robust multidisciplinary assessment. The report should clearly indicate if the diagnosis is considered definite or equivocal. The diagnosis should be given with as much precision as possible. As for biopsies, particular effort should be given to determining differentiation of tumour subtype (adenocarcinoma versus squamous cell carcinoma) in non-small cell carcinoma, as well as distinguishing small cell carcinoma.

Primary diagnosis may be made using traditional exfoliative samples (bronchial washings and brushings, bronchoalveolar lavage, pleural fluid) or targeted fine-needle aspiration (FNA) specimens (lung FNA, transcarinal FNA, endobronchial ultrasound-guided FNA), but with all specimen types, the use of tissue should be optimised to allow adequate morphological assessment and ancillary testing on a single sampling. Except in special circumstances, such as immediate on-site assessment of FNA, Papanicolaou staining is mainly used for cytological preparations. Processing of material to cell block should be undertaken for immunocytochemistry and molecular tests, such as EGFR mutation analysis, this being the recommended methodology in international guidelines.[9] Results from all molecular tests must be incorporated in the pathology report. Direct smears for exfoliative specimens are not recommended. For aspirates of lymph nodes, specimens that are negative should be distinguished from those that are inadequate (i.e. do not contain lymphoid material).

6.3 Reporting of non-resection specimens (e.g. biopsies and cytology)

The 2015 WHO classification provides specific terminology for non-resection specimens[7] and there is therefore now a core dataset and reporting proforma to reflect this advance (Appendix E).

6.3.1 Core clinical data

Name, date of birth, hospital, hospital number, NHS/CHI number, specimen type, procedure, date of procedure and surgeon/physician should be supplied.

6.3.2 Core pathological data

Location of tumour

The location of the tumour, the site(s) of sampling and the type(s) of specimen should be recorded.

Histological type

If a common lung cancer is present, reporting should follow the recommendations of the 2015 WHO classification in relation to biopsy material,[7] as there is now a need for more precise separation of squamous cell carcinoma and adenocarcinoma from NSCLC not otherwise specified (NOS) in relation to therapeutic options.[5,6] The diagnosis should be recorded in a manner that makes it clear whether the pathologist made the determination based on light microscopy alone or light microscopy plus special studies, using recommended terminology (see Appendices A and E). In samples where morphological evidence is lacking, immunohistochemistry using TTF-1, Napsin A (NSCC, favour adenocarcinoma) and CK5/6, P40, P63 (NSCC, favour squamous cell carcinoma) is recommended, with TTF-1 and P40 being favoured if only two markers are used. Mucin stains are also of value.

Ancillary data, specifically EGFR mutation and ALK translocation status, should be recorded if testing is undertaken. Provision is made for reporting other molecular data within the form, although these are not yet viewed as core items.

If biopsies are positive for rarer lung tumours (e.g. carcinoid, mesenchymal tumours and lymphoproliferative disease), then these should be diagnosed as far as possible according to criteria in the WHO 2015 classification, with consideration of specialist referral if clinically relevant. For biopsies suggestive of a carcinoid tumour, the presence of atypical features (necrosis, between 2 and 10 mitoses per 2 mm^2) should be mentioned, although final classification should await resection, when undertaken. Tumours with more than 10 mitoses per 2 mm^2 with neuroendocrine morphology and immunophenotype should be reported as documented in Appendix A in relation to the possibility of large cell neuroendocrine carcinoma.

The above can also be applied to cell pellets derived from positive cytology specimens (see below).

7 Non-core data items

Various additional parameters have been recommended, but as yet there is insufficient evidence with regard to their influence on patient management for them to be included as core items. They may be prospectively recorded at a local level, according to needs and interest.

The size of the tumour can be measured and recorded in three dimensions. Histological grading can be provided, although there is no agreed system currently recommended. There is no evidence to indicate that perineural invasion affects outcome, but it may be included as a non-core item if desired locally.

Although the 7th TNM staging system maintains the same 'N' categories, a system of zones has been proposed for both pN1 and pN2 regions.[1] These are:

- hilar/intralobar zone (stations 10 and 11) and peripheral zone (stations 12–14) for pN1
- upper (superior mediastinal) zone (stations 2–4), aortic zone (stations 5 and 6) and subcarinal (station 7) and lower zone (stations 8 and 9) for pN2 disease.

Involvement of nodes may be by direct invasion or metastatic spread and this may be recorded for N1 nodes. The presence of extracapsular spread of nodal metastases may additionally be recorded. Actual numbers of positive and negative lymph nodes within each station may also be documented, if desired locally, although the pathologist would then have to ensure the nodes had been submitted without dissection.

Conditions such as emphysema and interstitial fibrosis should be noted, and further analysis (e.g. asbestos bodies) may be necessary if pneumoconiosis is suspected. Civil claims for personal injury due to industrial lung disease have increased in frequency and it is important to describe and sample non-neoplastic lung parenchyma – a minimum of three blocks per lobe is recommended.

If a pleural lavage is undertaken and is found to be positive, then the tumour should be additionally classified as R1(cy+).

With the advent of next-generation sequencing (NGS) and the identification of many other molecular abnormalities (e.g. ROS1, RET, BRAF, MET) that relate to specific targeted therapies and clinical trials, there are many additional tests being undertaken both nationally and internationally. The results, both positive and negative, should be documented by pathologists whenever possible.

8 Diagnostic coding and staging

The site and histological diagnosis should be coded using SNOMED codes (see Appendix C). SNOMED versions prior to SNOMED CT will cease to be licensed from April 2017, with a move to SNOMED CT in all health sectors.

The TNM stage is obtained by selecting the highest stage for each component from the completed data. The TNM subsets can be converted to the International Stage Groupings (TNM 7) (see Appendix B). However, clinical data will need to be taken into account before the final stage can be obtained, particularly for specimens smaller than a pneumonectomy.

The 7th TNM staging system is also now recommended for use in both small cell cancer when resectable and also for carcinoid tumours. Small cell lung carcinoma can be additionally staged as (i) limited or (ii) extensive disease for non-resectable disease (see Appendix D).

9 Reporting of frozen sections

The specimen should be measured. The location, type and size of lesion(s) should be recorded. The frozen section diagnosis should be recorded and confirmed in paraffin sections after fixation. At present, pathologists should not attempt to distinguish adenocarcinoma *in situ* from invasive lesions at frozen section with regard to limited (non-anatomic or wedge) resections, outside of a research setting.

10 Criteria for audit of the dataset

The following are recommended by the RCPath as key performance indicators (see *Key Performance Indicators – Proposals for Implementation,* July 2013*,* www.rcpath.org/profession/clinical-effectiveness/key-performance-indicators-kpi.html):

- cancer resections reported using a template or proforma, including items listed in the English COSD, which are, by definition, core data items in RCPath cancer datasets (English trusts were required to implement the structured recording of core pathology data in the COSD by January 2016)

  Standard: 95% of reports must contain structured data

- histopathology cases that are reported, confirmed and authorised within seven and ten calendar days of the procedure

  S*tandard:* 80% of cases must be reported within seven calendar days and 90% within ten calendar days.

The following standards are suggested as criteria that might be used in periodic reviews of the lung cancer pathology service:

- completeness of histopathology reports, expressed as the average proportion of the core data items recorded, or as the proportion of the reports that include 100% of the items (the standard is that all contain 100% of the items)
- value of subdivision of pleural invasions to PL0–PL3
- value of lymph node compartments
- inter- and intra-observer studies in classification of tumours, especially small biopsies, using recent recommendations
- percentage of cases showing EGFR mutations against morphology subtypes, proportion of cases sent for EGFR testing

- adequacy/failure rate of EGFR and other (e.g. ALK translocation) testing
- value of taking three blocks of background lung if macroscopically normal
- proportion of biopsy cases classified as NSCLC-NOS
- usage of immunohistochemistry in small sample diagnosis
- accuracy of cytology diagnosis via histology correlation.

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Appendix A Table of revised classification of lung cancers on resection and biopsy (may also be used for cytology preparations/cell pellets) (adapted from references 2 and 10)

2015 WHO classification in resection specimens	Morphology/stains	Small biopsy/cytology terminology
ADENOCARCINOMA (predominant pattern) **Acinar** **Papillary** **Solid** **Micropapillary**	Morphological adenocarcinoma patterns clearly present	Adenocarcinoma (describe identifiable patterns present)
Lepidic (non-mucinous)		Adenocarcinoma with lepidic pattern (if pure, add note: an invasive component cannot be excluded)
Invasive mucinous adenocarcinoma		Invasive mucinous adenocarcinoma (describe patterns present; use term 'mucinous adenocarcinoma with lepidic pattern' if pure lepidic pattern – see text)
Colloid adenocarcinoma		Adenocarcinoma with mucinous features
Fetal adenocarcinoma		Adenocarcinoma with fetal features
Enteric adenocarcinoma		Adenocarcinoma with enteric features††
SQUAMOUS CELL CARCINOMA	Morphological squamous cell patterns clearly present	Squamous cell carcinoma
SMALL CELL CARCINOMA		Small cell carcinoma
Adenocarcinoma (solid pattern may be just one component of the tumour)‡	Morphological adenocarcinoma patterns not present, but supported by special stains, i.e. +TTF-1	Non-small cell carcinoma, favour adenocarcinoma‡
Squamous cell carcinoma, (non-keratinising pattern may be just one component of the tumour)‡	Morphologic squamous cell patterns not present, but supported by stains, i.e. +p40 (or p63)	Non-small cell carcinoma, favour squamous cell carcinoma
LARGE CELL CARCINOMA	No clear adenocarcinoma, squamous or neuroendocrine morphology or staining pattern	‡Non-small cell carcinoma, not otherwise specified (NSCC-NOS)‡‡

LARGE CELL NEUROENDOCRINE CARCINOMA (LCNEC)	Non-small cell carcinoma with neuroendocrine (NE) morphology and positive NE markers	NSCC, possible LCNEC
ADENOSQUAMOUS CARCINOMA	Morphological squamous cell and adenocarcinoma patterns present	NSCC-NOS (comment that adenocarcinoma and squamous components are present and this could represent adenosquamous carcinoma)
Pleomorphic, spindle and/or giant cell carcinoma		NSCC with spindle and/or giant cell carcinoma (mention if adenocarcinoma or squamous carcinoma are present)

Notes

†† Metastatic carcinomas should be carefully excluded with clinical and appropriate but judicious immunohistochemical examination.

‡ The categories do not always correspond to solid predominant adenocarcinoma or non-keratinising squamous cell carcinoma respectively. Poorly differentiated components in adenocarcinoma or squamous cell carcinoma may be sampled.

‡‡ NSCLC-NOS pattern can be seen not only in large cell carcinomas but also when the solid poorly differentiated component of adenocarcinomas or squamous cell carcinomas are sampled but do not express immunohistochemical markers or mucin.

TTF-1 Thyroid transcription factor-1.

Appendix B Staging of lung carcinomas*

* Small cell carcinomas: Staging via 7th TNM is now recommended for those with limited disease

* Carcinoid tumours: Staging via 7th TNM is now recommended for all cases

Limited disease	**Extensive disease**
Disease confined to one hemithorax, including involvement of ipsi- and/or contralateral hilar, mediastinal or supraclavicular lymph nodes Patients with ipsilateral pleural effusion, regardless of pleural cytology, should be included in this group	Any disease beyond the definition of limited stage

Non-small cell carcinoma (TNM 7th edition)[1]

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma *in situ*
T1a Tumour ≤20 mm diameter
T1b Tumour >20–≤30 mm

T2 Tumour ≥ 20 mm from the carina, invades visceral pleura, partial atelectasis
T2a >30–≤50 mm
T2b >50–≤70 mm

T3 >70 mm; involvement of parietal pleura, mediastinal pleura, chest wall, pericardium or diaphragm; tumour within 20 mm of the carina; atelectasis/obstructive pneumonitis involving whole lung; separate nodule(s) in the same lobe

T4 Involvement of great vessels, mediastinum, carina, trachea, oesophagus, vertebra, or heart
Separate tumour nodule(s) in different ipsilateral lobe

NX Regional lymph nodes cannot be assessed
N0 No regional node involvement
N1 Ipsilateral hilar/intrapulmonary nodes (node stations 10–14)
N2 Ipsilateral mediastinal nodes (node stations 1–9)
N3 Contralateral mediastinal, hilar, ipsilateral or contralateral scalene, supraclavicular nodes

M1 Distant metastasis
M1a Separate tumour nodule(s) in a contralateral lobe; pleural nodules or malignant pleural or pericardial effusion
M1b Distant metastasis

TNM stage groupings

Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a, b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a, b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a, b, T2a, b	N2	M0
	T3	N1, N2	M0
	T4	N0, N1	M0
Stage IIIB	T4	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

Appendix C SNOMED codes

SNOMED T and CT codes

Topographical code	SNOMED	SNOMED CT terminology	SNOMED CT code
Trachea, NOS	T25000	Tracheal structure (body structure)	44567001
Bronchus, NOS	T26000	Bronchial structure (body structure)	955009
Lung, NOS	T28000	Lung structure (body structure)	39607008
Pleura, NOS	T29000	Pleural membrane structure (body structure)	3120008
FNA Lung	T20250 (SNOMED 3) T2Y010 (SNOMED 2)	Lower respiratory fluids (substance)	87200008

SNOMED M and CT codes for epithelial tumours (see WHO book for SNOMED codes of other tumours)

Morphological code	SNOMED	SNOMED CT terminology	SNOMED CT code
Adenocarcinoma	M81403	Adenocarcinoma, no subtype (morphological abnormality)	35917007
Lepidic adenocarcinoma	M82503	Bronchiolo-alveolar adenocarcinoma (morphological abnormality)	112677002
Acinar adenocarcinoma	M85513	Acinar cell cystadenocarcinoma (morphological abnormality)	128703004
Papillary adenocarcinoma	M82603	Papillary adenocarcinoma (morphological abnormality)	4797003
Micropapillary adenocarcinoma	M82653	Micropapillary carcinoma (morphological abnormality)	450895005
Solid adenocarcinoma	M82303	Solid carcinoma (morphological abnormality)	81920005
Mixed non-mucinous and mucinous or indeterminate	M82543	Bronchiolo-alveolar carcinoma, mixed mucinous and non-mucinous (morphological abnormality)	128661009
Invasive mucinous adenocarcinoma	M82533	Bronchiolo-alveolar carcinoma, mucinous (morphological abnormality)	128660005

Morphological code	SNOMED	SNOMED CT terminology	SNOMED CT code
Fetal adenocarcinoma	M83333	Fetal adenocarcinoma (morphological abnormality)	128893004
Colloid adenocarcinoma	M84803	Mucinous adenocarcinoma (morphological abnormality)	72495009
Enteric adenocarcinoma	M81443	Adenocarcinoma, intestinal type (morphological abnormality)	25190001
Minimally invasive adenocarcinoma, non-mucinous	M82563		No code yet
Minimally invasive adenocarcinoma, mucinous	M82573		No code yet
Adenocarcinoma *in situ*	M81402	Adenocarcinoma *in situ* (morphological abnormality)	51642000
Adenocarcinoma *in situ*, non-mucinous	M8250/2		No code yet
Adenocarcinoma *in situ*, mucinous	M82532		No code yet
Squamous cell carcinoma (SQCC)	M80703	Squamous cell carcinoma, no International Classification of Diseases for Oncology (ICD-O) subtype (morphological abnormality)	28899001
Keratinising SQCC	M80713	Squamous cell carcinoma, keratinising (morphological abnormality)	18048008
Non-keratinising SQCC	M80723	Squamous cell carcinoma, large cell, non-keratinising (morphological abnormality)	45490001
Basaloid SQCC	M80833	Basaloid squamous cell carcinoma (morphological abnormality)	128634009
SQCC *in situ*	M80702	Squamous cell carcinoma *in situ*, no ICD-O subtype (morphological abnormality)	59529006
Small cell carcinoma	M80413	Small cell carcinoma (morphological abnormality)	74364000
Combined small cell carcinoma	M80453	Combined small cell carcinoma (morphological abnormality)	21326004
Large cell neuroendocrine carcinoma	M80133	Large cell neuroendocrine carcinoma (morphological abnormality)	128628002
Combined large cell neuroendocrine carcinoma	M80133	Large cell neuroendocrine carcinoma (morphological abnormality)	128628002

Morphological code	SNOMED	SNOMED CT terminology	SNOMED CT code
Typical carcinoid	M82403	Carcinoid tumour no ICD-O subtype (morphological abnormality)	81622000
Atypical carcinoid	M82493	Atypical carcinoid tumour (morphological abnormality)	128658008
Diffuse idiopathic neuroendocrine cell hyperplasia	M80400		No code yet
Large cell carcinoma	M80123	Large cell carcinoma (morphological abnormality)	22687000
Adenosquamous carcinoma	M85603	Adenosquamous carcinoma (morphological abnormality)	59367005
Pleomorphic carcinoma	M80223	Pleomorphic carcinoma (morphological abnormality)	16741004
Spindle cell carcinoma	M80323	Spindle cell carcinoma (morphological abnormality)	65692009
Giant cell carcinoma	M80313	Giant cell carcinoma	42596004
Carcinosarcoma	M89803	Carcinosarcoma (morphological abnormality)	63264007
Pulmonary blastoma	M89723	Pulmonary blastoma (morphological abnormality)	43149009
Lympho-epithelial carcinoma	M80823	Lymphoepithelial carcinoma (morphological abnormality)	7300000
NUT-carcinoma	M80233		No code yet
Mucoepidermoid carcinoma	M84303	Mucoepidermoid carcinoma (morphologic abnormality)	4079000
Adenoid cystic adenocarcinoma	M82003	Adenoid cystic carcinoma (morphological abnormality)	11671000
Epithelial-myoepithelial carcinoma	M85623	Epithelial-myoepithelial carcinoma (morphological abnormality)	9618003
Pleomorphic adenoma	M89400	Pleomorphic adenoma (morphological abnormality)	8360001
Squamous cell papilloma	M80520	Squamous cell papilloma (morphological abnormality)	63451008
Glandular papilloma	M82600	Papillary adenoma (morphological abnormality)	86143001
Mixed squamous and glandular papilloma	M85600	Mixed squamous cell and glandular papilloma (morphological abnormality)	107692003
Sclerosing pneumocytoma	M88320	Dermatofibroma, no ICD-O subtype (morphological abnormality)	72079004

Morphological code	SNOMED	SNOMED CT terminology	SNOMED CT code
Alveolar adenoma	M82510	Alveolar adenoma (morphological abnormality)	8097004
Papillary adenoma	M82600	Papillary adenoma (morphological abnormality	86143001
Mucinous cystadenoma	M84700	Mucinous cystadenoma (morphological abnormality)	67182003
Mucus gland adenoma	M84800	Mucinous adenoma (morphological abnormality)	33170000

SNOMED P (Procedure) codes

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure.

Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

Appendix D Reporting proforma for lung cancer resection specimens

Surname……. Forenames……... Date of birth……... Sex…

Hospital…….……..……..... Hospital no…….…….. NHS/CHI no…….……..

Date of surgery…….…..... Date of report authorisation……. Report no…….….....

Date of receipt……..…….. Pathologist…….……. Surgeon…….…….

Previous treatment (neoadjuvant chemotherapy/radiotherapy)* Yes □ No □ Not known □

Specimen type

Laterality ±*

Right lung □
Left lung □
Not known □

Surgical access

VATS □
VATS converted to open □
Open □
Not known □

Resection type ±*

Single wedge resection □
Multiple wedge resections □
Segmentectomy □
Sleeve resection □
Pneumonectomy (extra-pericardial) □
Pneumonectomy (intra-pericardial) □
Lobectomy/bi-lobectomy □
Other □ (specify) ……..……...……..

Attached anatomical structures

None submitted □
Submitted □ (specify) ……..

Macroscopic features

Location of tumour ±*

Hilar/endobronchial/central □

Right upper lobe □ Right middle lobe □ Right lower lobe □
Left upper lobe □ Left lower lobe □ Cannot be assessed □

Other (please state): ……

Relationship to carina ±*

Involves carina (pT4) □
≤ 20 mm from carina (pT3) □
> 20 mm from carina (pT2) □
Cannot be assessed □

Measurements ±*

Tumour size …….mm (maximum dimension)

(pT1a ≤20 mm; pT1b 21–≤30 mm; pT2a 31–≤50 mm; pT2b 51–≤70 mm; pT3 >70 mm)

Not assessable □

Extent of atelectasis/obstructive pneumonia ±*

None/less than the two categories below □
Involving hilar region but not whole lung (T2) □
Involving whole lung (T3) □

Microscopic features

Histological type ±*

Squamous cell carcinoma □

Large cell undifferentiated carcinoma □

Small cell carcinoma □

Carcinoid □

Adenocarcinoma: Invasive adenocarcinoma, not otherwise specified □

(If yes: predominant pattern (as percentages to total of 100%): Lepidic ... Acinar ...

Papillary ... Micropapillary ... Solid ... Cribriform …)

Mucinous □ Non-mucinous □

Mixed mucinous/non-mucinous (>10% of each) □

Adenocarcinoma *in situ* □

Minimally invasive adenocarcinoma (invasive component less than 5 mm) □

Variants of adenocarcinoma □ (If yes: Mucinous (colloid) □ Fetal □ Enteric □)

Combined tumours □ (specify …….....)

Other tumour □ (specify …….....)

Local invasion ±

Extent of pleural invasion *	No pleural invasion □		
	Visceral pleura only □		
	Parietal pleura/chest wall □		
	Mediastinal pleura □		
Pericardium (pT3) ±*	Yes □	No □	Cannot be assessed □
Diaphragm (pT3) ±*	Yes □	No □	Cannot be assessed □
Great vessel (aorta, central pulmonary artery or vein) (T4) ±*	Yes □	No □	Cannot be assessed □
Atrium, heart (pT4) ±*	Yes □	No □	Cannot be assessed □
Malignant pleural effusion (pM1a) *	Yes □	No □	Cannot be assessed □

Separate tumour nodules

Cannot be assessed □	Absent □	Present □
Synchronous primary tumours	Absent □	Present □

(Core items should be reported for each synchronous primary tumour)

Satellite nodules (intrapulmonary metastases)*

Satellite tumour nodules in same lobe (pT3) □

Satellite tumour nodules in different ipsilateral lobe (pT4) □

Satellite tumour nodules in contralateral lobe (pM1a) □

Pleural invasion ±*

PL0 (no pleural involvement) □

PL1 (breaching of the outer layer of the visceral pleura but no extension to the pleural surface) □

PL2 (breaching of the outer layer of the visceral pleura **and** extension to the pleural surface) □

PL3 (involvement of the parietal pleura) □

Extent of pleural invasion cannot be assessed □

Lymph node spread ±

Ipsilateral hilar/intrapulmonary (node stations 10–14)	Submitted □ Not submitted □	Involved (N1) □ Not involved □
Ipsilateral mediastinal (node stations 1–9)	Submitted □ Not submitted □	Involved (N2) □ Not involved □
Contralateral mediastinal, hilar nodes	Submitted □ Not submitted □	Involved (N3) □ Not involved □
Ipsilateral or contralateral scalene or supraclavicular nodes	Submitted □ Not submitted □	Involved (N3) □ Not involved □

Margins ±*

Bronchial	Not involved □	Involved □	Uncertain □	Not applicable □
Mediastinal	Not involved □	Involved □	Uncertain □	Not applicable □
Vascular	Not involved □	Involved □	Uncertain □	Not applicable □
Chest wall	Not involved □	Involved □	Uncertain □	Not applicable □

Distance of tumour to closest resection margin …….mm. Specify margin ……..

Lymphovascular invasion

Present □ Absent □ Indeterminate □

Response to neoadjuvant therapy

Not applicable □ Less than 10% residual viable tumour □ More than 10% residual viable tumour □

Treatment history not known □

Metastases*

Not identified in this specimen □ Present (M1a) □ Present (M1b) □

Details: …….....

Ancillary data

Epidermal growth factor mutation present ±	Yes □	No □	Not assessed □
ALK translocation present	Yes □	No □	Not assessed □

Summary of pathological staging, stating version of TNM used [±] *

(Select highest stage from above data; for synchronous primaries, use protocol above.

Use prefix 'y' for resection during or following treatment and 'r' for recurrence after treatment)

……pT ……..pN ……pM (if known) ……

Complete resection at all margins Yes (R0) □ No (R1 □ R2 □)

SNOMED codes*:

Signature .....……

Date ……../……../……...

Notes:

[±] Data items included in 1st edition ICCR lung cancer resection dataset.

*Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) v6.

Appendix E Reporting proforma for lung cancer biopsy/cytology specimens

Surname……..	Forenames……..…	Date of birth……... Sex….....
Hospital……..……..……	Hospital no…….……..	NHS/CHI no……..…….
Date of procedure…….....	Date of report authorisation…….	Report no…….….....
Date of receipt…….…….	Pathologist…….……..	Clinician…….…….....

Previous treatment (neoadjuvant chemotherapy/radiotherapy)* Yes □ No □ Not known □

Specimen origin*

Right lung, NOS	□	Left lung, NOS	□	Right lower lobe	□
Right upper lobe	□	Right middle lobe	□	Other …….	□
Left upper lobe	□	Left lower lobe	□	Not known	□

Sample type* (more than one box may be ticked)

*It is recommended that residual positive cytology samples be processed to histology blocks for potential further analysis.

Biopsy

Endobronchial biopsy	□	
Transbronchial biopsy	□	
Transthoracic needle biopsy	□	
Lymph node biopsy	□	Specify site(s) ……..…….….....
Pleural biopsy	□	
Other metastatic site(s)	□	Details .....…….....

Cytology

Transthoracic FNA lung	□	
Bronchial washings/traps/lavages	□	
Bronchial brushings	□	
Transbronchial or endoscopic needle aspirate	□	Details of site(s) ……..…….....
Pleural fluid	□	
Other cytology	□	Specify….....……..……..…..

Microscopic features

Histological/cytological type†

Adenocarcinoma (*morphological adenocarcinoma patterns clearly present)* □

Specify patterns present or variants .....…….....

Non-small cell carcinoma, favour adenocarcinoma *(morphological adenocarcinoma patterns not present but adenocarcinomatous differentiation supported by stains such as TTF-1, D-PAS)* □

Squamous cell carcinoma *(morphological squamous cell patterns clearly present)* □

Non-small cell carcinoma, favour squamous cell carcinoma *(morphological squamous cell patterns not present but squamous differentiation supported by stains such as p40, CK5/6)* □

Small cell carcinoma □

Non-small cell carcinoma, not otherwise specified □

Non-small cell carcinoma with neuroendocrine morphology (NE markers positive) □

Non-small cell carcinoma with neuroendocrine morphology (NE markers negative) □

Non-small cell carcinoma, not otherwise specified, possible adenosquamous carcinoma *(when both glandular and squamous components are morphologically present or both are suggested by special stains)* □

Non-small cell carcinoma with spindle and/or giant cell carcinoma and/or pleomorphic features *(mention if adenocarcinoma or squamous carcinoma are present morphologically or with stains)* □

Evidence of differentiation if pleomorphic NSCC …….

Combined tumour □ (Specify) …….

Other tumour □ (Specify, e.g. carcinoid, etc.) …….....……..

Ancillary data

Epidermal growth factor (EGFR) mutation present	Yes □	No □	Not assessed □
ALK translocation present	Yes □	No □	Not assessed □

SNOMED codes:

Comments

Signature **.....……**

Date **……../……../……...**

Note:

†Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) v6.

Appendix F Reporting proforma lung cancer resection specimens in list format

Element name	Values	Implementation comments
Previous treatment (neoadjuvant chemotherapy/radiotherapy)	Single selection value list: • Yes • No • Not known	
Laterality	Single selection value list: • Right lung • Left lung • Not known	
Surgical access	Single selection value list: • VATS • VATS converted to open • Open • Not known	
Resection type	Single selection value list: • Single wedge resection • Multiple wedge resections • Segmentectomy • Sleeve resection • Pneumonectomy (extra=pericardial) • Pneumonectomy (intra-pericardial) • Lobectomy/bi-lobectomy • Other	
Resection type, other (specify)	Free text	Only applicable if 'Resection type, Other' is selected.
Attached anatomical structures	Single selection value list: • None submitted • Submitted	
Attached anatomical structures, submitted (specify)	Free text	Only applicable if ' Attached anatomical structures, submitted' is selected.
Location of tumour	Multiple selection value list: • Hilar/endobronchial/central • Right upper lobe • Right middle lobe • Right lower lobe • Left upper lobe • Left lower lobe • Cannot be assessed • Other	

Element name	Values	Implementation comments
Location of tumour, Other (please state)	Free text	Only applicable if 'Location of tumour, Other' is selected.
Relationship to carina	Single selection value list: • Involves carina (pT4) • ≤20 mm from carina (pT3) • >20 mm from carina (pT2) • Cannot be assessed	
Tumour size	Size in mm	
Tumour size, assessable	Single selection value list: • Assessable • Not assessable	'Assessable' if value given for tumour size.
Extent of atelectasis/obstructive pneumonia	Single selection value list: • None/less than the two categories below • Involving hilar region but not whole lung (T2) • Involving whole lung (T3)	
Histological type	Single selection value list: • Squamous cell carcinoma • Large cell undifferentiated carcinoma • Small cell carcinoma • Carcinoma • Adenocarcinoma • Combined tumours • Other tumour	
Adenocarcinoma, type	Single selection value list: • Invasive adenocarcinoma • Adenocarcinoma in situ • Minimally invasive adenocarcinoma • Variants of adenocarcinoma	Only applicable of 'Histological type, adenocarcinoma' selected
Lepidic	Numeric value (0–100)	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected
Acinar	Numeric value (0–100)	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected
Papillary	Numeric value (0–100)	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected
Micropapillary	Numeric value (0–100)	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected

Element name	Values	Implementation comments
Solid	Numeric value (0–100)	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected
Cribriform	Numeric value (0–100)	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected
Mucinous/Non-mucinous	Single value selection list: • Mucinous • Non-mucinous • Not applicable	Only applicable of 'Adenocarcinoma type, invasive adenocarcinoma' selected
Variants of adenocarcinoma, specify	Single value selection list: • Mucinous (colloid) • Fetal • Enteric • Not applicable	Only applicable of 'Adenocarcinoma type, variants of adenocarcinoma' selected
Combined tumour, specify	Free text	Only applicable of 'Histological type, combined tumour' selected
Other tumour, specify	Free text	Only applicable of 'Histological type, other tumour' selected
Extent of pleural invasion	Single value selection list: • No pleural invasion • Visceral pleura only • Parietal pleura/chest wall • Mediastinal pleura	
Pericardium (pT3)	Single value selection list: • Yes • No • Cannot be assessed	
Diaphragm (pT3)	Single value selection list: • Yes • No • Cannot be assessed	
Great vessel (Aorta, central pulmonary artery or vein) (T4)	Single value selection list: • Yes • No • Cannot be assessed	
Atrium, heart (pT4)	Single value selection list: • Yes • No • Cannot be assessed	

Element name	Values	Implementation comments
Malignant pleural effusion (pM1a)	Single value selection list: • Yes • No • Cannot be assessed	
Separate tumour nodules	Single value selection list: • Absent • Present • Cannot be assessed	
Synchronous primary tumours	Single value selection list: • Absent • Present	
Satellite nodules (intrapulmonary metastases)	Multiple value selection list: • Satellite tumour nodules in same lobe (pT3) • Satellite tumour nodules in different ipsilateral lobe (pT4) • Satellite tumour nodules in contralateral lobe (pM1a)	
Pleural invasion	Single value selection list: • PL0 (no pleural involvement) • PL1 (breaching of the outer layer of the visceral pleura but no extension to the pleural surface) • PL2 (breaching of the outer layer of the visceral pleura and extension to the pleural surface) • PL3 (involvement of the parietal pleura) • Extent of pleural invasion cannot be assessed	
Ipsilateral hilar/intrapulmonary (node stations 10–14)	Single value selection list: • Submitted • Not submitted	
Ipsilateral hilar/intrapulmonary (node stations 10–14), involved	Single value selection list: • Involved (N1) • Not involved • Not applicable	Not applicable if “Ipsilateral hilar/intrapulmonary (node stations 10–14): not submitted”
Ipsilateral mediastinal (node stations 1–9)	Single value selection list: • Submitted • Not submitted	
Ipsilateral mediastinal (node stations 1–9), involved	Single value selection list: • Involved (N2) • Not involved • Not applicable	Not applicable if “Ipsilateral mediastinal (node stations 1–9): not submitted”

Element name	Values	Implementation comments
Contralateral mediastinal, hilar nodes	Single value selection list: • Submitted • Not submitted	
Contralateral mediastinal, hilar nodes, submitted	Single value selection list: • Involved (N3) • Not involved • Not applicable	Not applicable if “Contralateral mediastinal, hilar nodes: not submitted”
Ipsilateral or contralateral scalene or supraclavicular nodes	Single value selection list: • Submitted • Not submitted	
Ipsilateral or contralateral scalene or supraclavicular nodes, submitted	Single value selection list: • Involved (N3) • Not involved • Not applicable	Not applicable if “Ipsilateral or contralateral scalene or supraclavicular nodes: not submitted”
Bronchial margin	Single value selection list: • Not involved • Involved • Uncertain • Not applicable	
Mediastinal margin	Single value selection list: • Not involved • Involved • Uncertain Not applicable	
Vascular margin	Single value selection list: • Not involved • Involved • Uncertain • Not applicable	
Chest wall margin	Single value selection list: • Not involved • Involved • Uncertain • Not applicable	
Distance of tumour to closest resection margin	Size in mm	
Distance of tumour to closest resection margin, specify	Free text	
Lymphovascular invasion	Single value selection list: • Present • Absent • Indeterminate	

Element name	Values	Implementation comments
Response to neoadjuvant therapy	Single value selection list: • Not applicable • Less than 10% residual viable tumour • More than 10% residual viable tumour • Treatment history not known	
Metastases	Single selection value list: • Not identified in this specimen • Present (M1a) • Present (M1b)	
Metastases, details	Free text	
Epidermal growth factor mutation present	Single selection value list: • Yes • No • Not assessed	
ALK translocation present	Single selection value list: • Yes • No • Not assessed	
pT stage	Single selection value list: • X • 0 • 1a • 1b • 2a • 2b • 3 • 4	
pN stage	Single selection value list: • X • 0 • 1 • 2 • 3	
pM stage	Single selection value list: • Not applicable • 1a • 1b	
TNM version	Single selection value list: • 7 • 8	

Element name	Values	Implementation comments
Complete resection at all margins	Single selection value list: • Yes (R0) • No (R1) • No (R2)	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables.	
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables.	

Appendix G Reporting proforma lung cancer biopsy/cytology specimens in list format

Element name	Values	Implementation comments
Previous treatment (neoadjuvant chemotherapy/radiotherapy)	Single selection value list: • Yes • No • Not known	
Specimen origin	Single selection value list: • Right lung, NOS • Left lung, NOS • Right upper lobe • Right middle lobe • Right lower lobe • Left upper lobe • Left lower lobe • Other • Not known	
Specimen origin, other specify	Free text	Only applicable if 'Specimen origin: other' is selected
Sample type	Multiple selection value list: • Endobronchial biopsy • Transbronchial biopsy • Transthoracic needle biopsy • Lymph node biopsy • Pleural biopsy • Other metastatic site(s) • Transthoracic FNA lung • Bronchial washings/traps/lavages • Bronchial brushings • Transbronchial or endoscopic needle aspirate • Pleural fluid • Other cytology	
Lymph node biopsy, specify sites	Free text	Only applicable if 'Sample type: lymph node biopsy' selected
Other metastatic site(s), details	Free text	Only applicable if 'Sample type: Other metastatic site(s)' selected
Transbronchial or endoscopic needle aspirate, Details of site(s)	Free text	Only applicable if 'Sample type: Transbronchial or endoscopic needle aspirate' selected

Element name	Values	Implementation comments
Histological/cytological type	Single selection value list: • Adenocarcinoma (morphological adenocarcinoma patterns clearly present) • Non-small cell carcinoma, favour adenocarcinoma (morphological adenocarcinoma patterns not present but adenocarcinomatous differentiation supported by stains such as TTF-1, D-PAS) • Squamous cell carcinoma (morphological squamous cell patterns clearly present) • Non-small cell carcinoma, favour squamous cell carcinoma (morphological squamous cell • patterns not present but squamous differentiation supported by stains such as p40, CK5/6 • Small cell carcinoma • Non-small cell carcinoma, not otherwise specified • Non-small cell carcinoma with neuroendocrine morphology (NE markers positive) • Non-small cell carcinoma with neuroendocrine morphology (NE markers negative) • Non-small cell carcinoma, not otherwise specified, possible adenosquamous carcinoma (when both glandular and squamous components are morphologically present or both are suggested by special stains) • Non-small cell carcinoma with spindle and/or giant cell carcinoma and/or pleomorphic features (mention if adenocarcinoma or squamous carcinoma are present morphologically or with stains) • Combined tumour • Other tumour	
Adenocarcinoma, specify patterns present or variants	Free text	Only applicable of 'Histological/cytological type: Adenocarcinoma (morphological adenocarcinoma patterns clearly present)' selected

Element name	Values	Implementation comments
Evidence of differentiation if pleomorphic NSCC	Free text	Only applicable of 'Histological/cytological type: Non-small cell carcinoma with spindle and/or giant cell carcinoma and/or pleomorphic features (mention if adenocarcinoma or squamous carcinoma are present morphologically or with stains)' selected
Combined tumour, specify	Free text	Only applicable of 'Histological/cytological type: combined tumour' selected
Other tumour, specify	Free text	Only applicable of as 'Histological/cytological type: other tumour' selected
Epidermal growth factor mutation present	Single selection value list: • Yes • No • Not assessed	
ALK translocation present	Single selection value list: • Yes • No • Not assessed	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables.	
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables.	

Appendix H Summary table – Explanation of levels of evidence

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

Level of evidence	Nature of evidence
Level 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 cancer type 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
Level 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 cancer type or Extrapolation evidence from studies described in A
Level C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B
Level 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 I AGREE II compliance monitoring sheet

The cancer datasets of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines (www.agreetrust.org). The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	1
2 The health question(s) covered by the guideline is (are) specifically described	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	N/A
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	Foreword
12 There is an explicit link between the recommendations and the supporting evidence	4–10
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	4–10
16 The different options for management of the condition or health issue are clearly presented	4–10
17 Key recommendations are easily identifiable	4–10
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword, 1
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices A–E
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	10
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