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

Standards and datasets for reporting cancers

Dataset for histopathological reporting of oesophageal and gastric carcinoma

October 2019

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Unique document number	G006
Document name	Dataset for histopathological reporting of oesophageal and gastric carcinoma
Version number	3
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Date active	October 2019
Date for review	October 2022
Comments	This document supersedes the 2007 document, *Datasets for the histopathological reporting of oesophageal and gastric cancer.* In accordance with the College's pre-publications policy, this document was on the Royal College of Pathologists' website for consultation from 10 January to 7 February 2019. Responses and authors' comments are available to view on request. **Dr Brian Rous** **Clinical Lead for Guideline Review (Cellular Pathology)**

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Registered charity in England and Wales, no. 261035

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

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. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient.

Each dataset contains core data items (see Appendices C–J) 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 95% 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 following stakeholders were consulted for this document:

- British Society of Gastroenterology (BSG)
- Association of Upper Gastrointestinal Surgeons
- Association of Clinical Pathologists
- British Division of the International Academy of Pathology.

Evidence for the revised dataset was obtained from updates to international tumour grading, staging and classification systems and by electronically searching medical literature databases for relevant research evidence, systematic reviews and national or international publications on gastric and oesophageal cancer up to November 2017. The level of evidence for the recommendations has been summarised (Appendix K). Unless otherwise stated, the level of evidence corresponds to 'Good practice point (GPP): Recommended best practice based on the clinical experience of the authors of the writing group'. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in Appendix L.

No major organisational changes or cost implications 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 adviser 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 Clinical Effectiveness department, Working Group on Cancer Services and Lay Governance Group and was placed on the College website for consultation with the membership from 10 January to 7 February 2019. 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 Clinical Lead for Guideline Review (Cellular Pathology).

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 Clinical Effectiveness department and are available on request. The authors have declared no conflicts of interest.

1 Introduction

It is suggested that this dataset be used for the reporting of gastric and oesophageal cancer specimens to provide:

- prognostic information
- feedback to the multidisciplinary clinical team on the quality of resection and the effect of neoadjuvant therapy (if appropriate)
- information for audit of endoscopic and surgical procedures, medical therapies as well as quality of pathology reporting
- feedback for other specialties, e.g. radiology.

As a guiding principle, the World Health Organisation (WHO) classification of tumours of the digestive system (5th edition)[1] and the tumour-node-metastasis (TNM) classification of malignant tumours (8th edition)[2] from the Union for International Cancer Control are used throughout the document. In TNM 8, junctional cancers, e.g. tumours with a centre within 20 mm of the gastro-oesophageal junction (GOJ) and that extend into the oesophagus, are classified and staged using the oesophageal scheme. In TNM 8, the pT categories for oesophagus and stomach are aligned. The pN categories only differ in the pN3b stage for the stomach.

In an attempt to provide all the necessary information and avoid duplication between datasets, the oesophageal and gastric carcinoma datasets have been merged into a single oesophagogastric dataset.

This document has been developed to include the data required for adequate reporting of oesophageal, junctional and gastric carcinoma specimens. Separate datasets have already been published by RCPath for neuroendocrine cancers,[3] lymphomas[4] and gastrointestinal stromal tumours (GISTs).[5]

The dataset has been subdivided into core and non-core data items. Core data items represent a minimum requirement for appropriate patient management.

Since the publication of the second edition of the *Datasets for the histopathological reporting of oesophageal and gastric cancer* in 2007,[6] there have been a number of developments in the treatment of oesophageal and gastric carcinomas based on the results of major clinical trials.[7–11] The use of preoperative or pre- and postoperative chemo(radio)therapy is now the standard of care for patients with locally advanced, resectable disease in the UK. Furthermore, endoscopic resection has been increasingly used to cure early stage disease. This revised dataset has been adjusted to take such changes into account.

Some details regarding dissection techniques and histological interpretation are included in the current dataset. It is stressed that these are for guidance and are not meant to be prescriptive.

1.1 Target users and health benefits of these guidelines

The target primary users of the dataset are biomedical scientists, trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons, oncologists, cancer registries and the National Cancer Registration and Analysis Service (NCRAS). Standardised cancer reporting and multidisciplinary team (MDT) working reduce the risk of misdiagnoses and help ensure clinicians have all the relevant pathological information required for tumour staging, patient management decisions and prognosis prediction. 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

In the UK, preoperative chemo(radio)therapy has become the standard of care for patients with locally advanced, resectable oesophageal, junctional or gastric cancer since the publication of the results from three landmark trials.[7–9] Following neoadjuvant therapy, a tumour may no longer be macroscopically or microscopically visible. Furthermore, junctional cancers may shrink asymmetrically following neoadjuvant therapy such that they no longer appear to involve the GOJ and could potentially be misclassified as gastric cancer by the pathologist if no clinical information is provided with the specimen. Such misclassification after surgery could have a clinical impact as the postoperative treatment of locally advanced oesophageal and gastric cancer may differ according to local practice.

In all cases, and especially those after neoadjuvant treatment, standardised clinical information is very useful in optimising specimen sampling. Helpful clinical information includes:

- site of tumour at diagnosis (mid or lower oesophagus; junctional; proximal/mid/distal stomach)
- tumour involvement of the GOJ
- preoperative disease stage
- histological type of tumour
- previous histology (case number or name of the hospital where it was performed)
- history of neoadjuvant therapy
- type of resection
- if the patient is enrolled in a clinical trial as a specific pathology procedure may need to be followed
- if the patient is known to have hereditary diffuse-type gastric cancer as the pathology protocol varies from that for sporadic gastric cancer. Details about specimen handling for hereditary gastric cancer are provided elsewhere.[12]

3 Resection specimen handling and preparation before dissection

Where possible, photographs of the fresh, fixed, intact and sectioned specimen should be taken since these may be useful when reporting the microscopy for MDT discussions, comparison with radiological findings and surgical quality control purposes.

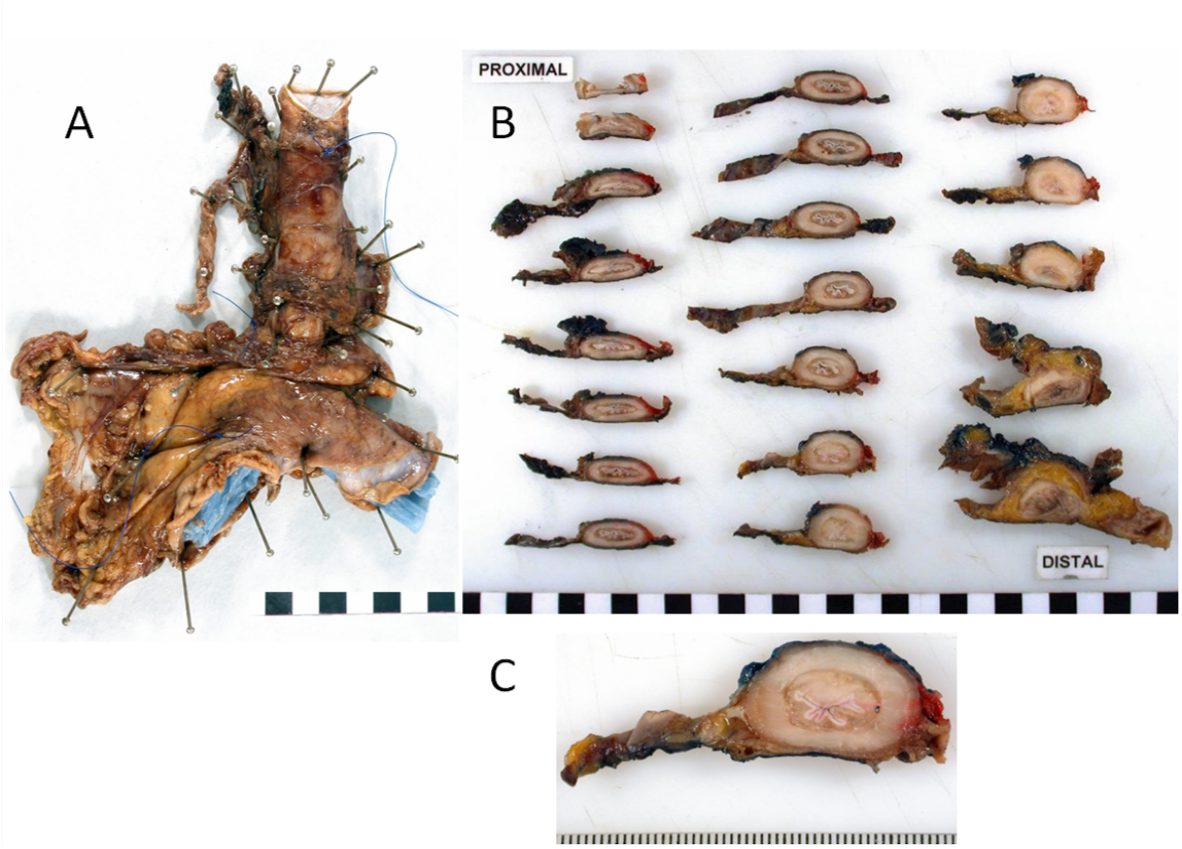
3.1 Oesophagectomy specimens

After dissection by the surgeon, oesophagectomy specimens contract immediately by a quarter of their in situ length and can shrink to a third of that length if fixed without being pinned.[13] Whether pleura is attached to the specimen will depend on the type of resection performed. A small patch of pleura is typically present anteriorly on the right side in so-called Ivor Lewis oesophagectomy specimens performed by open surgery, but may not be present if the same Ivor Lewis oesophagectomy is performed using a minimally invasive technique. Some surgeons will dissect the lymph nodes from the specimen themselves in the operating theatre. In such resection specimens, it may be impossible to assess the circumferential resection margin (CRM) and/or pleura for tumour involvement.

Ideally, the specimen should be received fresh in the pathology laboratory as soon as possible after resection. If this is not practicable, the specimen should at least be suitably incised by the surgeon along the distal resection margin to drain gastric contents and be placed in a large volume of formalin-based fixative**.** Alternatively, the surgeon may be asked to 'suture' the specimen onto some suitable support or pin in out in theatre to prevent shrinkage and distortion of the specimen.

If the oesophagectomy specimen is received fresh in the pathology laboratory, the stomach should be opened along the distal resection margin, the gastric contents removed and the whole specimen pinned to a cork board or rubber mat (Figure 1).

Figure 1: Handling of an Ivor Lewis-type oesophagectomy specimen.



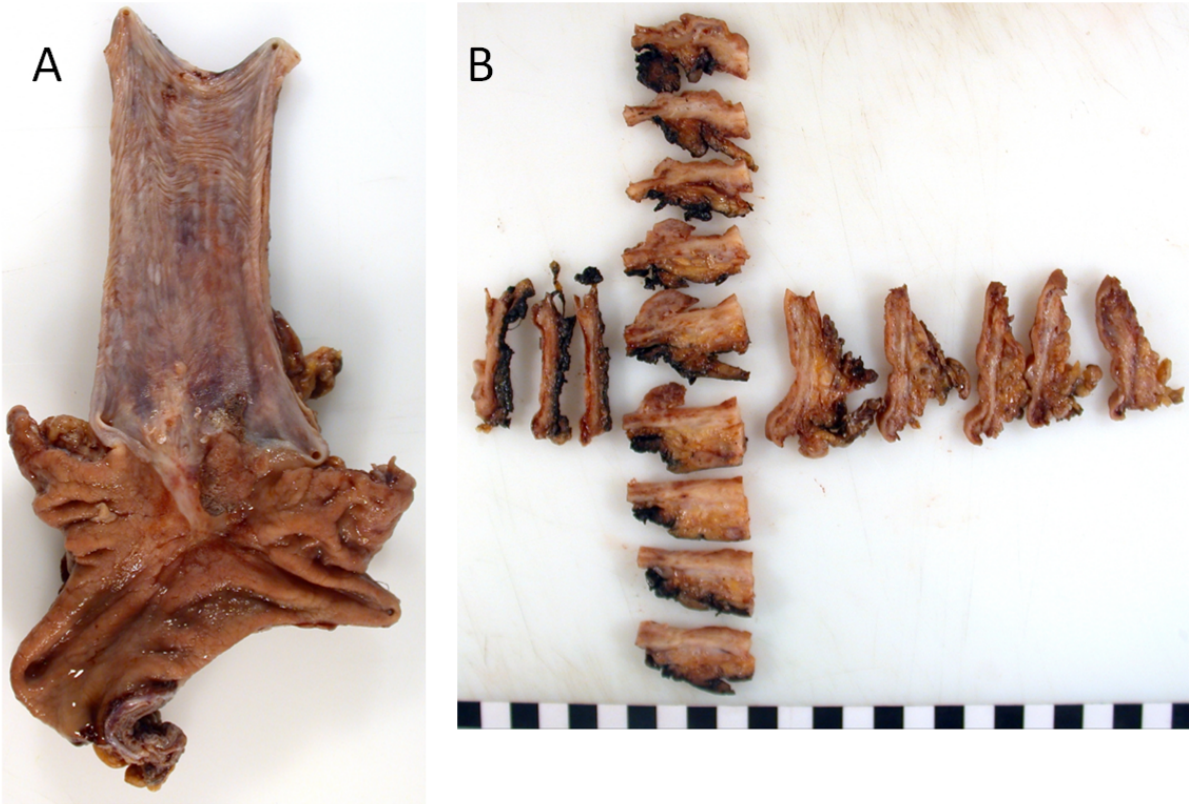
(A) The specimen is opened along the distal gastric resection margin, the oesophageal tube is left intact and the specimen is pinned out and fixed for up to 48 hours. **(B)** After fixation and inking of the CRM, the specimen is sliced perpendicular to its longitudinal axis. Ideally, slices are photographed. **(C)** Close-up photograph of a slice with tumour.

Ideally, the proximal (oesophageal) resection margin should be pinned through the full thickness of the oesophageal wall to minimise shrinkage of the oesophageal muscularis propria, which may result in 'pouting'/protrusion of the mucosa. The specimen should be fixed for a minimum of 24 hours (ideally 48 hours) in a sufficiently large volume of formalin-based fixative. When adequately pinned fresh and depending on the surgical procedure, the fixed oesophagus typically has a length of 100–120 mm.

Although longitudinal opening of the oesophagus may be required for sampling fresh tumour material for research or be preferred locally for macroscopic identification of potential dysplastic lesions in Barrett's oesophagus, it is preferable to fix the oesophagus intact. This allows assessment of the CRM by serial horizontal slicing and facilitates the comparison of macroscopic and radiological findings.

If the freshly received oesophagus is opened longitudinally (Figure 2A), staining of the mucosal surface with Lugol's iodine solution can help to identify small lesions as they will not be stained in contrast to the normal squamous epithelium. If the oesophagus is opened longitudinally before fixation, it is recommended that the outer surface is inked beforehand to facilitate macroscopic and microscopic CRM assessment. Inking of the outer surface can be performed after fixation if the oesophagus is left intact for fixation. In specimens where the surgeon has already dissected the lymph nodes, the CRM cannot be assessed confidently. Thus, inking the outer surface of the specimen is not necessary under such circumstances. When the specimen is measured, a note should be made of whether or not the specimen was pinned and measured before or after fixation.

Figure 2: Handling of an Ivor Lewis-type oesophagectomy specimen.



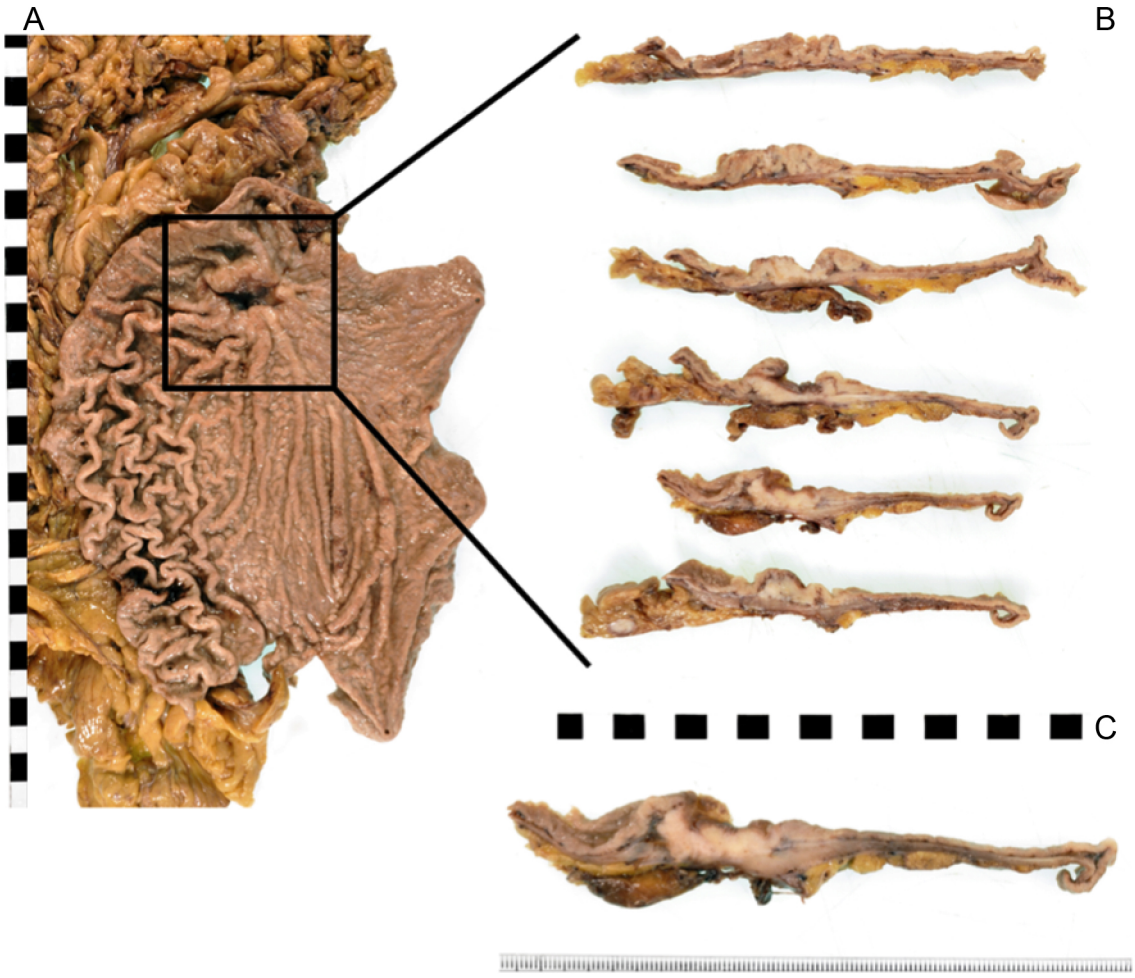
(A) The circumferential margin of the oesophagus was inked before opening of the oesophageal tube and pinning out for fixation. **(B)** The fixed specimen is cut in a combination of longitudinal and horizontal slices and photographed.

3.2 Gastrectomy specimens

Ideally, the specimen should be received fresh in the pathology laboratory as soon as possible after resection. If this is not practicable, the specimen should be suitably incised by the surgeon to drain gastric contents and then placed in a large volume of formalin-based fixative, preferably with insertion of a paper wick to ensure formalin access to the mucosal aspect of the specimen.

Specimens received fresh or partially fixed are usually opened along the anterior aspect of the greater curve. Cutting through the tumour should be avoided as this can compromise the assessment of serosal involvement. In such cases, the incision should be made in a wide arc around the tumour or the specimen should be opened along the anterior aspect of the lesser curve. After opening and removal of the stomach contents, the specimen should be pinned onto a cork/wooden board (Figure 3) and floated in a sufficiently large amount of formalin-based fixative for 24–48 hours. If feasible, pins should be removed after 24 hours of fixation and the specimen flipped over to allow adequate fixation of the serosal aspect.

Figure 3: Handling of a subtotal gastrectomy specimen.



(A) Specimen is opened along the greater curve, emptied, pinned out and fixed for up to 48 hours. **(B)** After fixation and inking of potentially present proximal/distal posterior CRM, the specimen is sliced perpendicular to its longitudinal axis. Ideally, slices are photographed. **(C)** Close-up photograph of a slice with tumour.

If the specimen is a so-called completion gastrectomy, e.g. a gastrectomy after a previous distal gastrectomy, one should avoid cutting across the anastomosis between the stomach and jejunum as tumours are often located in this area. In such cases, the attached small bowel loop should be opened longitudinally by a separate incision.

In specimens where tumours arise at/close to the gastric cardia or in the most distal part of the antrum on the posterior wall, the outer surface of the specimen should be carefully inspected. Areas that are not covered by serosa should be inked prior to block-taking as these areas represent true surgical ('circumferential') resection margins.

Where the stomach is received in formalin, handling will depend on the adequacy of fixation. If the surgeon has already opened the stomach and the specimen is sufficiently fixed, blocks can be taken immediately. Specimens that are received unopened and only partially fixed, should be opened, pinned out and fixed as described previously.

4 Tissue sampling

The following blocks of tissue are recommended as an absolute minimum sampling for oesophagectomy and gastrectomy specimens:

- proximal resection margin (please see comment regarding donuts in section 5.3.4)
- distal resection margin
- tumour – sufficient blocks (usually at least four, see comment regarding block-taking after neoadjuvant chemotherapy below) to assess:
  - deepest tumour penetration into/through the wall
  - serosal involvement
  - tumour proximity to the CRM (if present)
  - tumour proximity to the proximal and distal resection margin
- sampling of all lymph nodes
- sampling of background stomach, oesophagus and duodenum (if present)
- sampling of the spleen, omentum or other organs (if present).

There are two major approaches to sampling the tumour. Probably the most widely utilised approach (in particular for oesophagectomy specimens) is the serial slicing of the specimen and tumour perpendicular to the longitudinal axis of the specimen (Figure 1B and 1C). This allows for correlation with radiological images for oesophagectomy specimens and easy assessment of circumferential margin. Blocking out the tumour with horizontal and longitudinal slices (Figure 2B) is recommended by some UK authors[14] and is the preferred method described in the datasets of the Royal College of Australasian Pathologists (RCPA)[15] and the Japanese classification of gastric[16] and oesophageal cancer.[17] This method probably best demonstrates the relationship of the tumour to the surrounding mucosa. Although this method is perhaps more applicable to the stomach, it may also be useful for the assessment of early neoplasia arising in Barrett's oesophagus and for sampling of the luminal aspect of fresh tumour for research purposes.

More extensive tumour sampling is indicated in patients after preoperative chemo(radio)therapy to confidently determine the degree of tumour regression. Depending on the tumour regression grading system used locally, the whole of the tumour, including surrounding fibrosis (presumed location of tumour before chemo(radio)therapy, e.g. 'tumour bed'), may need to be embedded. If no macroscopic tumour can be identified, blocking of the entire area showing macroscopic evidence of regression (fibrosis, necrosis, scarring) should always be considered.

If lymph nodes have not been dissected by station by the surgeon, the pathologist should ideally block the lymph nodes by location (e.g. para-oesophageal, junctional, lesser curve and greater curve). There is evidence that the location of the metastatic lymph nodes has prognostic value in patients with oesophageal cancer. Patients with metastatic nodes on both

sides of the diaphragm have a poorer prognosis than those with metastatic nodes only on one side of the diaphragm.[18,19]

5 Core data items

5.1 Summary of core items

5.1.1 Macroscopic

Macroscopic items include:

- specimen preparation: oesophagus (pinned/not pinned)
- specimen dimensions
- shape of tumour (oesophagus)
- tumour location: oesophagus (oesophagus only/involves GOJ), stomach (cardia/fundus/body/antrum)
- epicentre of tumour above or below GOJ: oesophagus (above/below)
- distance of tumour epicentre from GOJ: oesophagus
- closest distance from the tumour edge to the proximal and distal margin
- maximum three dimensions of tumour (and/or tumour bed dimension in regressed tumours after neoadjuvant therapy)
- Siewert type: oesophagus (type 1/type 2).

It is strongly recommended that a 'block key' stating the site of tissue origin and other relevant information of individual blocks is included in the macroscopic specimen description and final report. If the entire tumour or tumour bed has been submitted for histological examination, this should be documented.

5.1.2 Microscopic

Microscopic items include:

- tumour type: oesophagus (squamous/adenocarcinoma/other), stomach (intestinal/diffuse/mixed/indeterminate)
- maximum depth of invasion of the primary tumour in the wall (TNM 8 pT category), including serosal involvement if present
- longitudinal and circumferential resection margin status
- histological tumour type according to Laurén classification[20]
- predominant grade of differentiation according to WHO classification[1]
- presence of lymphovascular invasion
- lymph node status (total number of nodes, number of positive nodes)
- presence of M1 disease (peritoneal seedlings, omental tumour, positive peritoneal cytology [if performed]) or distant metastases
- tumour regression grade for patients after preoperative therapy.

5.2 Macroscopic

5.2.1 Specimen measurements

All measurements should be recorded in millimetres and ideally it should be stated in the macroscopic description whether measurements were taken on a pinned or unpinned specimen.

The overall dimensions of the specimen, including the length of the oesophagus, lesser/greater curve of the stomach and duodenum as well as distance of the GOJ to the distal (gastric) resection margin, should be recorded.

The maximum diameter of the tumour in three dimensions (if visible) and/or tumour bed (in patients treated with preoperative therapy), as well as distance from the tumour (bed) edge to all longitudinal and circumferential resection margins and GOJ (if present) should be measured. Tumour size has been related to oesophageal cancer patient prognosis.[21,22] Some studies found tumour size to be an independent prognostic factor in gastric adenocarcinoma,[23,24] but others suggest that this is not the case.[25]

[Level of evidence C – tumour size affects prognosis.]

5.2.2 Site of tumour

The location of the tumour should be recorded as oesophageal or junctional and in the stomach as cardia, fundus, body or antrum. Patients with proximal gastric cancer have a worse prognosis than those with more distal cancers.[23,24,26]

[Level of evidence B – location of tumour in oesophagus, GOJ or stomach has an effect on prognosis.]

5.2.3 Cardia/GOJ tumours

The TNM classification of carcinomas involving the GOJ has been problematic in the past owing to differences in the TNM staging systems of the oesophagus and stomach, and the lack of a separate TNM staging system in some countries for junctional cancers. This staging difficulty was addressed with the seventh edition of the Union for International Cancer Control (UICC) TNM classification and further clarified in the eighth edition.[2] According to TNM 8, tumours with an epicentre within 20 mm of the GOJ that extend into the oesophagus are classified and staged according to the oesophageal carcinoma scheme. All other tumours with an epicentre within 20 mm of the GOJ without extension into the oesophagus are staged using the gastric carcinoma scheme. Tumours located in the stomach with an epicentre below 20 mm of the GOJ are staged using the gastric carcinoma scheme irrespective of oesophageal involvement.

However, TNM 8 fails to provide a clear statement as to which definition of the GOJ should be used in this context, thus leaving some uncertainty. Endoscopists in the UK use the proximal limit of the gastric rugal folds as the definition of the GOJ, which is also supported by the BSG.[23] In situations where the tumour completely effaces the GOJ, the peritoneal reflection on the serosal aspect of the specimen approximates to the level of the GOJ (proximal limit of the rugal folds).

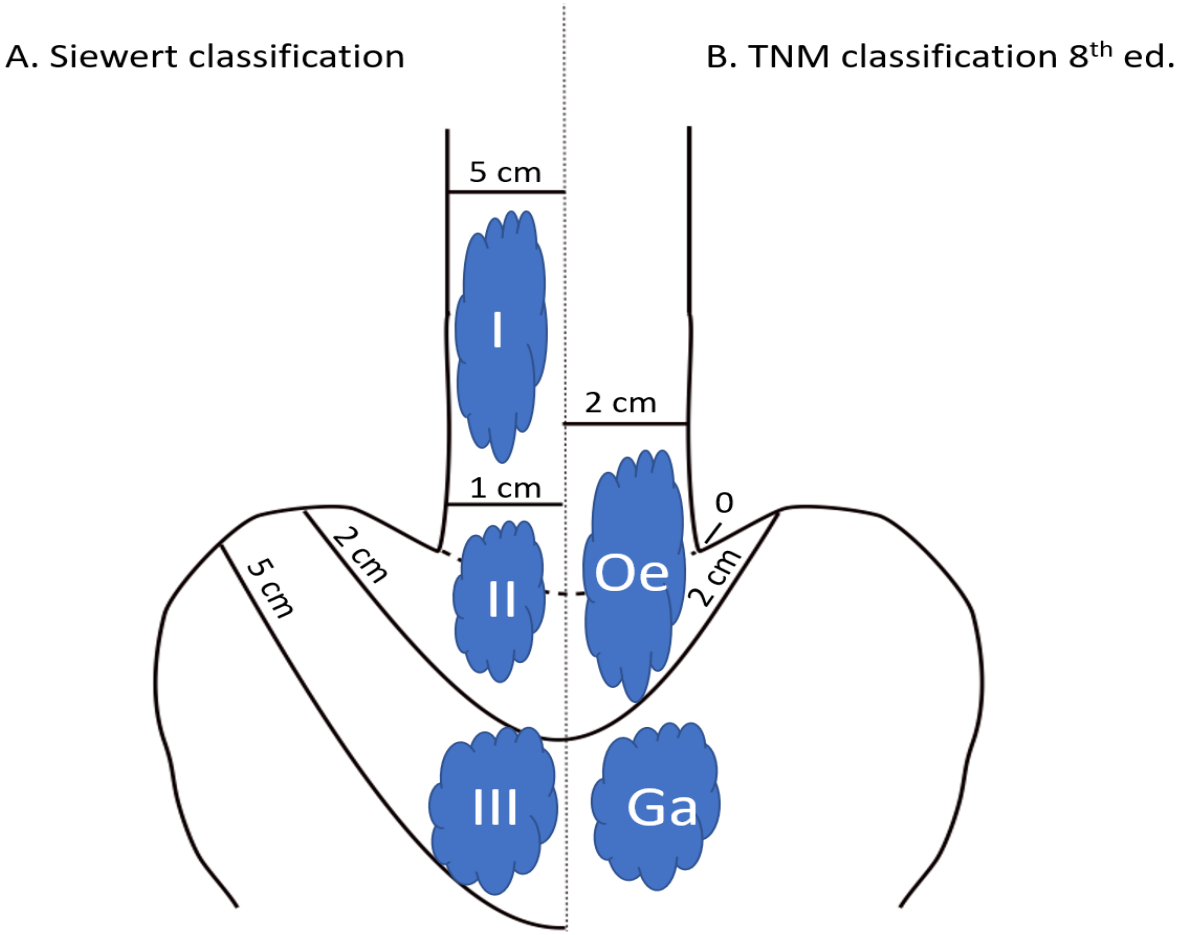
While TNM 7 and TNM 8 have solved the problem of how to stage junctional cancers in resection specimens and been shown to be superior to the sixth edition of the TNM classification in stratifying oesophagogastric cancer patients by survival,[27–34] there is an ongoing debate among clinicians regarding the usefulness of TNM changes for treatment decisions. Some of the junctional cancers would have previously been classified as gastric cancer and therefore treated with pre- and postoperative chemotherapy. These cancers are now classified as oesophageal cancers and therefore may be treated by preoperative chemotherapy or chemoradiotherapy alone.

UK clinicians classify cancers involving the GOJ according to the Siewert classification, which distinguishes three types:

- type I: cancers with their centre located 1–5 cm above the GOJ
- type II: cancers with their centre located between 1 cm above and 2 cm below the GOJ
- type III: cancers with their tumour centre located 2–5 cm below the GOJ.[35]

As the use of this classification has been recommended by the BSG, the Siewert type remains a core data item for oesophageal cancers in this dataset.[23] Type III cancers will, in concordance with TNM 8, be classified as gastric cancers (see Figure 4).

Figure 4: Comparison between Siewert classification and TNM 8 classification for junctional adenocarcinomas.



(A) Siewert classification. Type I (adenocarcinoma of the distal oesophagus): adenocarcinoma with the centre located within 1–5 cm above the GOJ (0, dashed line). Type II (true carcinoma of the cardia): adenocarcinoma with the centre located within 1 cm above and 2 cm below the GOJ. Type III (subcardial cancer): adenocarcinoma with the centre located between 2 and 5 cm below the GOJ infiltrating the GOJ from below. **(B)** TNM 8 classification: a cancer with an epicentre within 2 cm of the GOJ extending into the oesophagus is classified and staged using the oesophageal scheme (Oe). Cancers with an epicentre more than 2 cm distal from the GOJ are classified and staged using the gastric scheme (Ga).

It is important to note that the location of the epicentre of the tumour and hence the Siewert type may change after preoperative therapy owing to asymmetric shrinkage of the tumour. This can lead to a clinically classified and treated oesophageal cancer becoming a gastric cancer in the resection specimen, potentially confusing clinicians involved in the patient management. The 'TNM helpdesk' advises that the clinically determined tumour type (oesophageal or gastric cancer, Siewert type) should not be changed after preoperative chemotherapy.

5.3 Microscopic

5.3.1 Depth of invasion

Depth of direct tumour invasion is assessed according to TNM 8 (see Appendix A). Tumour present in vessels or nerves outside and deeper in the wall than the primary cancer does not influence the pT stage. Depth of invasion has been repeatedly shown to be a predictor of prognosis in multivariate analysis in both patients with oesophageal or gastric cancer treated by surgery alone[36–41] and after neoadjuvant treatment.[42]

Tumours of the oesophagus may involve the pleura, pericardium or the peritoneum (after invading the stomach). Tumours of the stomach may involve the peritoneum. While there is no evidence to confirm or refute serosal involvement as an important prognostic factor in oesophageal carcinomas, it is undoubtedly important in stomach carcinomas[43] where serosal involvement has been shown to be an independent prognostic factor in multivariate analysis.[44] Serosal involvement has also been shown to be predictive of the likely site of gastric cancer recurrence (peritoneal versus haematogenous).[45]

With the introduction of TNM 7, the T categories were aligned for oesophageal and gastric cancer (see Appendix A). The same TNM system is currently used for staging after preoperative therapy in conjunction with the 'y' prefix.

5.3.2 Histological tumour type

The vast majority of oesophageal cancers resected in the UK will be adenocarcinomas; however, some squamous cell carcinomas and a few rare tumour subtypes, such as adenosquamous and small cell carcinomas, are also reported. TNM 8 details different clinical stage and prognostic grouping categories for adenocarcinoma and squamous cell carcinoma of the oesophagus.

Gastric cancers are usually adenocarcinomas and show considerable morphological diversity, which is likely why at least seven different classification systems have been proposed (Laurén,[20] Ming,[46] WHO,[1] Nakamura,[47] Mulligan,[48] Goseki[49] and Carneiro).[50] The Laurén classification (diffuse, intestinal and mixed/unclassifiable types) is probably the classification system most widely used outside Japan,[51] but the Ming classification (expansive and infiltrative) is perhaps the most prognostically relevant.[52,53] Since UK pathologists and clinicians are most familiar with the Laurén classification system, it is suggested that this is used for oesophageal and gastric cancers. Furthermore, there is evidence that the Laurén classification is of prognostic value in gastric cancer[51] and useful for clinical decision-making. As the spread of intestinal and diffuse-type gastric adenocarcinoma into the neighbouring structures is different, it has been suggested that different surgical approaches with respect to margin clearance are necessary.[54] There is evidence that with diffuse-type gastric adenocarcinomas longitudinal resection margins should ideally be >30 mm from the tumour.[55]

Many UK pathologists will also use the Laurén classification to classify oesophageal adenocarcinomas since there is currently no separate classification system for these tumours.

[Level of evidence C – the Laurén classification provides useful prognostic and management-related information.]

5.3.3 Grade of tumour differentiation

Using the fifth edition of the WHO classification,[1] carcinomas are graded based on cytological and architectural similarity to the presumed tissue of origin – preferably using a two-tiered system: low grade (formerly well or moderately differentiated) versus high grade (formerly poorly differentiated). While all squamous cell carcinomas should be graded, according to the WHO classification, only tubular and papillary carcinomas (e.g. intestinal-type adenocarcinomas according to the Laurén classification) should be graded.[1]

Opinion on the prognostic significance of tumour differentiation in oesophageal cancer is divided. Some studies have shown the prognostic significance of tumour differentiation in squamous cell carcinomas,[56] adenocarcinomas[57] or both.[38,58] However, in one large study, tumour differentiation failed to reach statistical significance.[37] The degree of tumour differentiation (well and moderately versus poorly differentiated) has been shown to be an independent prognostic factor in gastric cancer.[59]

As grade of tumour differentiation may be important prognostically, it is included in the core dataset. The WHO classification (second edition) in the *International Histological Classification of Tumours* series[60] specifies that 'when a tumour shows different grades of differentiation the higher grade should determine the final categorisation'. In addition, the fifth edition of the WHO classification[1] does not specify how to classify the grade of differentiation in tumours consisting of more than one grade. There is uncertainty in the literature whether grading of differentiation should be based on the predominant area or the worst area. In view of this uncertainty, it is recommended that grading of differentiation in resection specimens should be based on the predominant area until the situation is clarified by further research. Note that according to the TNM helpdesk, grading of differentiation after preoperative treatment should not be performed. Also note that it is currently recommended to provide the worst grade of differentiation to the clinicians for biopsies and endoscopic resection specimens as treatment decisions for endoscopic resections or further treatment after endoscopic resection are currently based on the size of the lesion, presence of ulceration and presence of 'undifferentiated' carcinoma.[61]

[Level of evidence C – grade of differentiation is an independent prognostic indicator.]

5.3.4 Resection margins

Complete surgical removal of the invasive tumour is the primary aim of curative surgery, with surgical resection still considered the only potentially curative option for patients with oesophageal and gastric cancer.[62] Complete macroscopic and microscopic resection of tumours (R0 resection) has been shown to be one of the strongest independent predictors of outcome in patients with oesophageal and gastric cancer and as R0 resection rates have improved, so has survival.[63] There is good evidence that involved proximal margins increase the likelihood of oesophageal cancer recurrence,[56,57,64,65] but less evidence for distal margins.[45,66]

In all cases, the proximal and distal resection margins of oesophagectomy and gastrectomy specimens require histological exclusion of tumour involvement. The entire proximal margin of the oesophagus should always be examined, regardless of distance from the tumour, because of the risk of discontinuous foci or well-hidden intramural spread of the carcinoma in the proximal oesophagus.[67,68] Proximal resection margin involvement by Barrett's metaplasia or dysplasia may inform decisions about endoscopic surveillance. As the distal resection margin of an oesophagectomy specimen can be very wide, blocking of the distal resection margin might be restricted to the part nearest to the primary tumour. The same approach could be applied for the proximal/distal resection margins of partial distal/proximal gastrectomy specimens. There are recommendations for clearance of tumour from proximal and distal margins, but this may vary depending on the type of tumour.[65,66]

For oesophageal and gastric cancer specimens, a resection margin is currently classified as 'positive' (e.g. involved) if there is direct extension of the primary tumour, or tumour present in lymphatic vessels or veins with adherence of the tumour cells to the endothelium, or tumour present in lymph nodes or soft tissue within equal or less than 1 mm of the resection margin. For audit purposes, the distance between the tumour and the resection margin should be measured regardless of whether the margin is classified as 'involved' or 'not involved'. Depending on local practice, surgeons and oncologists may request that the pathologist distinguishes between 'at the margin' (e.g. 0 mm), within 1 mm and more than 1 mm from the resection margin to enable comparison of local (UK) data to the international literature.

Depending on local practice, some oesophageal and gastric cancer resection specimens will be submitted to the laboratory together with 'donuts' in a separate specimen pot. These donuts are either submitted still attached to an anvil (a metal device with a conical end and a shaft with a pointed end) or 'free floating' in the specimen pot. In oesophagectomies and gastrectomies the anastomosis is usually constructed end-to-side. Thus, only one of the donuts represents a true longitudinal, in this case proximal, resection margin, which should be processed completely into paraffin to assess presence of abnormalities and completeness of the wall. This donut can be identified as the one containing suture material and located closest to the conical end of the anvil (if submitted on the device) whereas the other donut contains staples. In resection specimens without donuts, the true proximal margin is the proximal end of the specimen.

In tumours arising in the oesophagus, the gastric cardia/GOJ and the posterior wall of the gastric antrum, there is the potential for involvement of the circumferential (radial) surgical resection margin (CRM). There is an expanding literature showing that tumour involvement of the CRM is associated with poor prognosis.[69–72] CRM status also provides surgical[73] and radiological feedback and may therefore be a useful audit tool. The evidence is variable on whether confirmation of CRM involvement requires direct involvement of the margin by the tumour or the tumour being within 1 mm of the margin.[70–72,74–78] Others have suggested a distance other than 1 mm for the cut-off.[66,69] Given the level of uncertainty, it is recommended that the nearest distance of tumour from margin is documented for all tumours, rather than just those more than 1 mm away, and that the category R1 is used for tumours equal to or less than 1 mm from the margin.

If surgeons remove lymph nodes from the resection specimen themselves before sending the specimen to the laboratory, depending on the tumour location, the CRM status cannot be assessed reliably and should be recorded as 'not assessable'.

[Level of evidence B – resection margin involvement is an independent prognostic indicator.]

5.3.5 Lymphatic, vascular and perineural invasion

In oesophageal cancer, vascular invasion has been shown to be related to patient prognosis. It is worth noting, however, that different studies detected vascular involvement in different ways. Some used special stains, some distinguished venous and lymphatic vessel invasion, and some provided no details on how vascular invasion was identified. Many showed a significant relationship between 'vascular invasion' and patient prognosis in univariate analysis.[40,44,45,72,76,79] In three studies using multivariate analyses, vascular invasion was shown to be an independent prognostic marker.[42,57,58,80,81] In particular, lymphatic invasion has been shown to indicate a poor prognosis in oesophageal cancer patients.[82,83] There are currently no data comparing intra- and extramural vascular invasion. It is recommended that invasion of any vascular space is recorded, preferably together with its location (intramural versus extramural) and whether it is considered to be venous or lymphatic vessel invasion.

There is less evidence for perineural invasion as a prognostic indicator in oesophageal cancer. In some studies,[57,84] significance was shown in univariate analysis but not in multivariate analysis. However, in other studies,[42,85] perineural invasion was found to be an important prognostic factor, including in the stomach.[86] A recent meta-analysis[87] suggested perineural invasion was an independent factor for poor prognosis.

In gastric carcinoma, univariate analyses have demonstrated that the presence of perineural,[88] lymphatic[41,59] and vascular invasion[41,52,59] are all associated with a poor prognosis. However, perineural invasion was not found to be an independent prognostic factor in multivariate analysis.[88] Results for lymphatic and vascular invasion are variable, with some multivariate analysis studies showing them to be independent prognostic factors,[52,59] but a more recent large study failed to confirm these results.[41]

5.3.6 Lymph node staging

All studies that assessed lymph node status showed it to be a significant indicator of prognosis in oesophageal cancer treated by surgery alone or preoperative chemotherapy followed by surgery.[36–38,56–58,79,84,86,89] In many of these studies, it was the most significant prognostic indicator.

Lymph node involvement has also been shown to be one of the strongest prognostic indicators in gastric carcinoma.[41,45,90,91]

According to TNM 8, seven and 16 lymph nodes are the minimum number of lymph nodes that should ordinarily be retrieved from an oesophagectomy specimen and gastrectomy specimen, respectively.

The lymph node classification in TNM 8 has been updated and is very similar between oesophageal and gastric cancer. This was based on evaluation of data from 4,627 patients treated by surgery alone using advanced statistical methodology.[33] The definition of what constitutes regional lymph nodes rather than distal lymph nodes has also been updated. While, in TNM 6, regional lymph nodes in relation to oesophagectomies were defined depending on the location of the primary cancer, in TNM 7 onwards regional nodes are those in the oesophageal drainage area including coeliac axis nodes and para-oesophageal nodes in the neck, irrespective of the site of the primary tumour. Only supraclavicular nodes are non-regional nodes in patients with oesophageal cancer, warranting the classification of M1 (distant metastasis) if involved by tumour.

There has been no change in the definition of regional lymph nodes in relation to gastric resections; however, the N category has been redefined with new thresholds. TNM 8 categories for gastric cancer are N0 (no regional lymph node metastases), N1 (one to two regional lymph nodes with metastatic tumour), N2 (three to six regional lymph nodes with metastatic tumour) and N3 (more than six nodes), which is subdivided into N3a (seven to 15 regional nodes with metastatic tumour) and N3b (16 or more regional nodes with metastatic tumour). TNM 8 categories for oesophageal cancer are N0 (no regional lymph node metastases), N1 (one to two regional lymph nodes with metastatic tumour), N2 (three to six regional lymph nodes with metastatic tumour) and N3 (more than six nodes). There is no subdivision of the N3 category in oesophageal cancer.

A number of studies have shown the ratio of involved to uninvolved nodes to be important in oesophageal and gastric cancer.[24,92] This reinforces the importance of documenting not only the number of involved nodes, but also the total numbers examined.

There is emerging evidence that the location of involved lymph nodes (on one side of the diaphragm versus on both sides of the diaphragm) is related to patient prognosis in oesophageal cancer.[18,93,94]

Furthermore, there is increasing evidence that extracapsular invasion is a significant indicator of poor prognosis, independent of the numbers of involved nodes.[95,96] If this is confirmed, this will need to be documented in future versions of this dataset.

The search for involved lymph nodes has been refined in some centres by the use of immunohistochemistry and serial sections to detect ‘micrometastases’. Such techniques have demonstrated micrometastases in some patients identified as being node negative using conventional histology.[97–99] Some studies suggest that the presence of micrometastases provides important prognostic information,[100–102] while others have reported the opposite.[97,99,103] Immunohistochemistry and cutting of serial sections are currently not recommended in the routine workup of lymph nodes, although this may be of use in specimens that have undergone neoadjuvant treatment. Other techniques, such as reverse transcriptase polymerase chain reaction,[104] are beyond the scope of this dataset.

According to TNM 7 and TNM 8, cases with micrometastases only, i.e. no metastasis larger than 2 mm, should be identified by the addition of 'mi' (e.g. pN1 [mi]) if these are the only lymph node metastases present. Micrometastases need to be distinguished from isolated tumour cells (ITCs), which are defined as single tumour cells or small clusters of cells not more than 0.2 mm in greatest dimension. Cases that only show ITCs in lymph nodes or at distant sites should be classified as pN0(i+) and pM0(i+), respectively, as there is currently no conclusive evidence of true metastatic activity of ITCs.

[Level of evidence A – lymph node involvement is an independent prognostic indicator.]

5.3.7 Distant metastasis

In TNM 8, peritoneal seedlings, omental tumour not part of continuous tumour extension and positive cytology are classified as pM1 (distant metastasis). Note that a tumour in the coeliac axis nodes in a patient with oesophageal cancer is no longer classified as distant metastasis, but as regional lymph node metastasis.

5.3.8 Tumour regression grading after preoperative chemo(radio)therapy

Preoperative and perioperative treatment with chemotherapy or chemoradiotherapy is now considered standard of care for all oesophageal and gastric cancer patients with clinically detected disease greater than T2N0, provided the patient is considered 'fit for multimodal treatment'.

In such pre-treated patients, pathologists may be asked to provide the clinicians with a tumour regression grade as the pathological response to chemotherapy in the primary tumour has been shown to be of prognostic value in gastric and oesophageal cancer.[105–107] There is also some evidence that the response in lymph nodes may be prognostically informative.[108,109]

The histopathological changes after chemotherapy are variable and include ulceration, mucosal oedema, inflammation, foamy histocytes, haemorrhage, necrosis, acellular mucus, fibrosis, vascular changes, and the presence of keratin, giant cells and multinucleated cells. There have been more than ten different systems published about grading of the regression of the primary tumour (including Mandard, Japanese, Dworak, Wheeler, Becker, Junker and Mueller, Rubbia-Brandt, Ryan, Le Sodan, Schneider, Lowy and Mansourd).[110,111] In all grading systems, a qualitative or quantitative assessment is made regarding the proportion of 'residual primary tumour tissue' after preoperative therapy. Tumour regression grading in lymph nodes is currently not part of any of the regression grading systems. The published grading systems propose either different percentages of residual tumour as being significantly related to prognosis or different qualitative measures, such as 'rare residual cancer cells' or 'fibrosis outgrowing residual cancer' in the Mandard classification.[112] None of the proposed systems provide a reproducible method of how to determine the size of the pre-treatment tumour. However, most of these regression grading systems are based on completely embedding the presumed area of the pre-treatment tumour (tumour bed) and based on comparing presumed viable tumour areas with fibrosis. It is unclear how areas with necrosis or mucin lakes after chemotherapy are incorporated into the tumour regression grade.

As there is no national or international consensus on which regression grading system should be used; this dataset cannot be prescriptive in this area and the regression system to be used should be determined by the pathologist locally after discussion with the clinical team. The regression system used should be specified in the histopathology report/proforma.

A specimen in which no tumour is identified following neoadjuvant treatment and which has been sampled extensively is staged as ypT0N0.

[Level of evidence B – response to neoadjuvant treatment provides important prognostic and treatment related information.]

6 Non-core data items

6.1 Summary of non-core items

6.1.1 Macroscopic

These include:

- type of resection
- tumour type according to the Borrmann classification.[113]

6.1.2 Microscopic

These include:

- presence of Barrett's metaplasia in the lower oesophagus
- presence of atrophy/intestinal metaplasia in the stomach
- presence of dysplasia in the background
- presence of *Helicobacter pylori*
- site (intramural/extramural) and nature (venous/lymphatic) of lymphovascular invasion
- molecular data (where applicable).

6.2 Macroscopic assessment

6.2.1 Type of resection specimen

The type of resection (e.g. oesophagogastrectomy; total, subtotal or partial [proximal or distal] gastrectomy; completion gastrectomy [gastrectomy after previous partial gastrectomy]; or extended gastrectomy [total gastrectomy with up to 5 cm oesophagus]) should be recorded if possible. This information is helpful when auditing lymph node yield from specimens, as the expected number of lymph nodes will vary with the type of resection.[114–116]

[Level of evidence C – type of operation affects lymph node yield.]

6.2.2 Macroscopic tumour type

With the exception of polypoid tumours, the macroscopic appearance of the tumour according to the Borrmann classification (polypoid, ulcerative, fungating, diffusely infiltrative) makes little difference to the prognosis in oesophageal and junctional tumours.[117,118] If gastric cancers are classified into Borrmann types (type 1 – polypoid, type 2 – fungating, type 3 – ulcerated and type 4 – diffusely infiltrating), patients with types 3 and 4 gastric cancer have a poorer prognosis.[51]

[Level of evidence D – polypoid tumours of the oesophagus have a better prognosis.]

6.3 Microscopic assessment

6.3.1 Barrett's metaplasia

Some studies indicate that the presence of metaplastic columnar mucosa in the adjacent oesophagus is a positive prognostic marker.[119] While this may identify less advanced tumours, many of these patients may have been screened for Barrett's oesophagus and documentation of its presence is useful for audit. It is therefore included as a non-core data item.

6.3.2 Other markers

Many other markers of prognosis have been investigated, including ploidy,[56,120,121] angiogenesis,[122] CD44[123] and epidermal growth factor receptor (EGFR).[124] Many show some prognostic significance, but without confirmatory evidence in larger studies the use of such special techniques is not justified in a core dataset.

HER2 status may be associated with prognosis in the oesophagus[125] and stomach.[126] The College of American Pathologists has produced guidelines on the application of HER2 in advanced gastric cancer.[127] The National Institute for Health and Care Excellence (NICE) has indicated that trastuzumab should be an option for treatment in patients with HER2-positive metastatic gastric adenocarcinoma. Inevitably, the vast majority of resection specimens will have been taken from patients with no evidence of distant metastases. There is therefore no need to document HER2 status as part of this dataset.[128]

7 Diagnostic staging and coding

Tumours should be coded using SNOMED codes (Appendix B). It is noted, however, that SNOMED is now in a practical transition phase, as part of the intended full implementation by the NHS and Public Health England (PHE) of SNOMED CT. SNOMED ceased to be licensed by the International Health Terminology Standards Development Organisation from 26 April 2017.

A list of applicable T and M SNOMED and SNOMED CT codes is provided in Appendix B.

Mapping SNOMED CT terminology is provided.

8 Reporting of oesophageal and gastric cancer biopsies

In the clinical context of an endoscopically or radiologically identified lesion, the primary role of the biopsy is to confirm the presence of a carcinoma and exclude benign conditions. The initial biopsy report should identify the histological tumour type: squamous cell cancer, adenocarcinoma or others (endocrine tumour, GIST, lymphoma, etc.) In the case of poorly differentiated cancers, this may only be possible using special stains and appropriate immunohistochemical markers. An attempt should be made to grade the tumour differentiation (well/moderately differentiated versus poorly) by worst area and, in the case of adenocarcinomas, to determine the histological subtype according to Laurén.[20]

The presence of dysplasia in squamous, glandular or metaplastic columnar mucosa may provide support for a primary oesophagogastric origin and should therefore be included in the report if present. In the clinical context of an early (intramucosal) cancer that might be amenable to curative endoscopic resection, it may also be useful to comment on the presence of lymphovascular invasion, ulceration and scarring as well as submucosal invasion (if present) since these factors may be taken into consideration by the endoscopist when considering further treatment options.[129]

There is evidence that some types of adenocarcinomas, such as mucinous or signet ring cell types (assessed in post-therapy and pre-treatment specimens),[130] may respond differently to chemotherapy. If the patient is younger than 40 years at the time of diagnosis, a diffuse type/poorly cohesive type including signet ring cell carcinoma has to be referred to the geneticist for genetic counselling and genetic testing for hereditary diffuse-type gastric cancer (CDH1 mutation carrier) before any surgery is performed. Patients with proven hereditary diffuse gastric cancer always require a total gastrectomy irrespective of tumour location or site.[12]

For further guidance on reporting of endoscopic biopsies please see RCPath's *Tissue pathways for gastrointestinal and pancreaticobiliary pathology.*[131]

9 Reporting of endoscopic resection specimens

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are becoming increasingly popular in the UK for the treatment of early cancers and dysplasia in the gastrointestinal (GI) tract.[132] All existing guidelines for the assessment of endoscopic resection specimens are based on the guidelines/criteria for early gastric cancer resections performed in Japan,[133,134] which are also now being applied to oesophageal endoscopic resections in other countries. The following is intended to provide pathologists with some guidance on the reporting of endoscopic resection specimens.

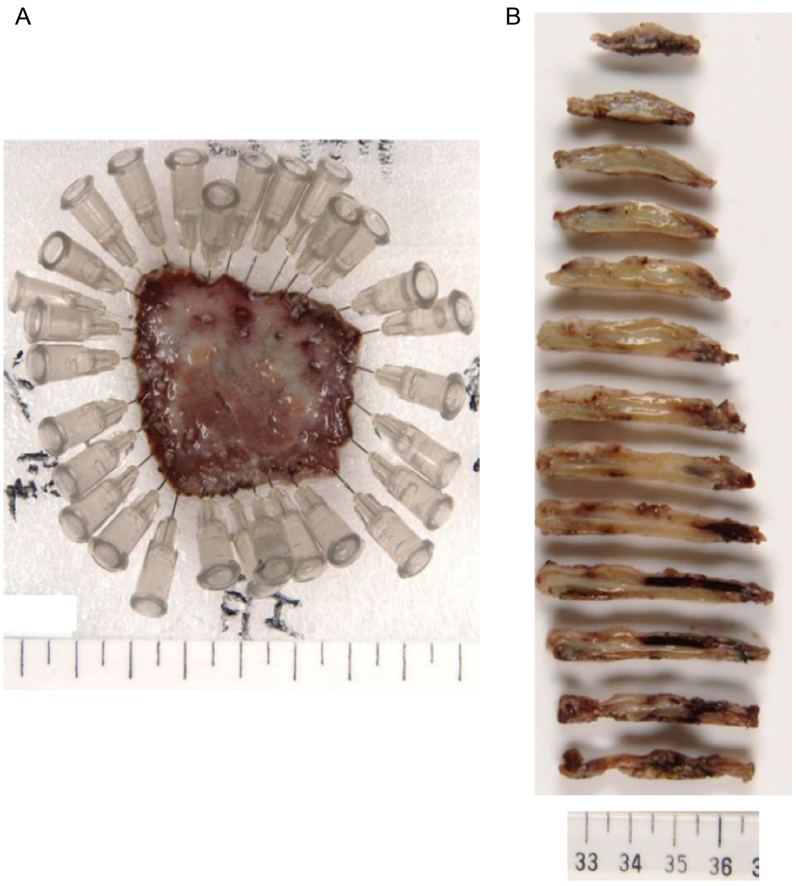
9.1 Specimen type

With current technology the maximum size of EMRs is limited to approximately 15 mm diameter, meaning that resections of lesions >15 mm diameter will arrive in the laboratory as piecemeal. To save performing multiple intubations at endoscopy, when multiple EMRs are performed, the EMR tissue pieces are usually dropped into the stomach and then collected all together at the end of the procedure. This makes it impossible to orientate the relative positions of individual EMRs and to assess the lateral resection margins of the lesion as a whole.

9.2 Specimen preparation

Ideally, EMR specimens should be pinned out on cork boards/wax blocks (Figure 5) or flattened out between sponges in cassettes before placing into formalin, otherwise they tend to distort on fixation, making assessment of resection margins difficult.

Figure 5: Handling of endoscopic resection specimens.



(A) Ideally, the specimen should be received pinned out onto some support. **(B)** After fixation, the specimen is sliced at 2 mm intervals and completely processed into paraffin for assessment.

9.3 Macroscopic description

The specimen should be measured in three dimensions and if several pieces are received, all pieces should be measured and processed separately. If there is a visible lesion on the surface of the EMR, its appearances should be described as polypoid, elevated, flat or depressed and the distance to the nearest lateral margin should be measured. The specimen should then be cut serially at 2–3 mm intervals. The cutting direction should be optimised to allow assessment of the distance of the lesion to the closest lateral margin. If possible, the specimen should be photographed, and cut slices should be numbered and referred to in the block key to optimise feedback provided to the endoscopist.

9.4 Microscopic features

The distance from the edge of the lesion to the lateral and deep margins should be assessed.

Apart from classifying an invasive tumour located directly at the margin as 'involved margin', there are currently no guidelines clarifying whether or not a tumour within 1 mm should also be classified as 'involved'.

The size of the invasive tumour needs to be confirmed on histology as macroscopy may underestimate its size. The size of the invasive part of the tumour is one of the factors that will determine if the patient requires further therapy.[135,136]

The depth of invasion has been associated with risk of lymph node metastases in a number of studies.[137,138] Endoscopic resection specimens will normally include the mucosa and part of the submucosa. Using TNM 8, cancers in the mucosa (including the muscularis mucosae) are classified as pT1a, whereas those in the submucosa are classified as pT1b. However, there are several additional subclassifications where the depth of mucosal (M) and submucosa (SM) invasion is considered.

Depth of invasion in specimens from adenocarcinomas in Barrett's oesophagus can be difficult to determine owing to the potential presence of a duplicated muscularis mucosae in up to 87.5% of patients.[139] The new duplicated muscularis mucosae is typically thinner, often splayed and less well defined than the original muscularis mucosae. If the resection has been performed between the two muscularis mucosae layers, it may appear histologically as if the plane of resection is in the submucosa. The presence of thick-walled blood vessels and submucosal glands in the submucosa act as useful landmarks/clues that can be used to avoid this potential pitfall.[140]

Assessment of the depth of invasion into the submucosa is clinically much more important than assessment of intramucosal depth of invasion. The depth of submucosal invasion is subdivided into thirds (in a similar way to Kikuchi staging in the colorectum) – SM1/SM2/SM3 – and is strongly associated with the risk of lymph node metastases.[137] However, when examining an EMR or ESD specimen the muscularis propria is usually absent, therefore it is not possible to accurately divide the submucosa into thirds. As a proxy, measurements of the depth of invasion below the original (deepest) muscularis mucosae are used to determine SM staging. However, there are a variety of classifications currently in use, the choice of which may affect clinical management decisions.[141] The staging system likely to be the most commonly used for oesophageal adenocarcinomas proposes cut-offs of 500 µm for SM1 and 1000 µm for SM2 (SM1: >0 to ≤ 500 µm, SM2: >500 µm to ≤ 1,000 µm, SM3: >1,000 µm).

It should be noted that a cut-off of 200 µm for SM1 has been suggested for squamous cell carcinomas, perhaps reflecting the more biologically aggressive nature of this tumour.[142]

Two competing subclassifications for the depth of intramucosal invasion have been suggested for oesophageal adenocarcinomas that divide the mucosa into three (M1/M2/M3)[143] or four levels (M1/M2/M3/M4).[144] The second of these classifications takes the duplicated muscularis

mucosae into account.[144] Currently, there is little, if any, evidence favouring one classification over the other.

There is also some evidence that the width and the pattern of invasion into the SM are related to the risk of lymph node metastases.[135]

The subclassification system used to determine depth of invasion of the M and SM should be decided locally according to the preference of the endoscopist making the clinical management decisions.

The importance of histological subtype has only been demonstrated for early gastric cancer where the pathologist has to distinguish between 'differentiated type' (papillary adenocarcinoma, well and moderately differentiated tubular adenocarcinoma, e.g. well to moderately differentiated intestinal type cancer) and 'undifferentiated type' (poorly differentiated intestinal type cancer, signet ring cancer). If there is more than one histological subtype, the most predominant should be reported. If there is invasion into the SM, the histological type of the invasive portion should be reported.

The presence of intratumoural ulceration or an intratumoural scar is part of the criteria used to determine further clinical management in gastric cancer.[145] The pathologist needs to distinguish between ulceration due to previous biopsy and genuine ulceration of the tumour, which can be challenging. The presence of ulceration is related to an incomplete resection of the lesion,[145] hence the necessity to report the presence of ulceration already in the endoscopic biopsies.

The presence of lymphatic channel or venous invasion has been related to the presence of lymph node metastasis[80] and is often used as an indication to perform a full resection.[146] The risk of lymph node metastasis increases with increasing depth of infiltration. Special stains (D2-40 for lymphatic channels and CD31 for blood vessels) may be helpful.

An endoscopic resection from the stomach is considered 'curative' if the lesion was excised en bloc (in one piece), the tumour size is ≤2 cm, the lesion has a differentiated histology type, the lesion is intramucosal, the resection margin is negative, and there is no lymphovascular invasion, no ulcer or ulcer scar.[147]

An endoscopic resection from the oesophagus is considered curative if the lesion was excised en bloc (in one piece), the maximum tumour size was less than one third of the circumference (no maximum tumour size established), the lesion has a well/moderately differentiated histology, the lesion is intramucosal (adenocarcinoma) or intramucosal but not involving the muscularis mucosae (squamous cancer), the resection margin is negative and there is no lymphovascular invasion.[147]

10 Criteria for audit

As recommended by the RCPath as key performance indicators (see *Key Performance Indicators – Proposals for implementation,* July 2013*,* www.rcpath.org/profession/quality-improvement/kpis-for-laboratory-services.html):

- cancer resections must be 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 and to update their systems in line with subsequent COSD updates:
  - standard: 95% of reports must contain structured data

- histopathology cases must be reported, confirmed and authorised within seven and ten calendar days of the procedure:
  - standard: 80% of cases must be reported within seven calendar days and 90% within 10 calendar days.

The following standards are suggested as some of criteria that might be used in periodic reviews of oesophageal and gastric carcinoma cancer in pathology service:

- total number of lymph nodes retrieved from oesophagectomy specimens
- total number of lymph nodes retrieved from partial gastrectomy specimens
- total number of lymph nodes retrieved from total gastrectomy specimens
- proportion of pT3 resections that are N1
- proportion of R0 oesophagectomy specimens
- proportion of specimens showing lymphovascular and/or perineural invasion
- proportion of R0 EMR/ESD specimens.

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Appendix A UICC TNM 8th edition classification of oesophageal and gastric carcinoma[2]

pT Primary tumour

pTX Primary tumour cannot be assessed

pT0 No evidence of primary tumour

pTis Carcinoma in situ

pT1 Tumour invades lamina propria or submucosa

- pT1a Tumour invades lamina propria or muscularis mucosae
- pT1b Tumour invades the submucosa

pT2 Tumour invades muscularis propria

pT3 Tumour invades adventitia/subserosa

pT4 Gastric cancer: Tumour invades serosa or adjacent structures

- pT4a Tumour invades the serosa
- pT4b Tumour invades adjacent structures (spleen, transverse colon, liver, pancreas, diaphragm, adrenal glands, kidney)

pT4 Oesophageal cancer: Tumour invades adjacent structures

- pT4a Tumour invades pleura, pericardium, peritoneum or diaphragm
- pT4b Tumour invades aorta, vertebra or trachea

pN Regional lymph nodes

pNX Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 1–2 regional lymph node metastasis

pN2 3–6 regional lymph node metastasis

pN3 7 or more regional lymph node metastasis

- pN3a (gastric cancer only): 7–15 regional lymph node metastasis
- pN3b (gastric cancer only): more than 15 regional lymph node metastasis

M Distant metastasis

M1 Distant metastasis microscopically confirmed

Note that pM0 and pMx are not valid categories.

Regional lymph nodes for the oesophagus are those in the oesophageal drainage area, including coeliac axis, paraoesophageal nodes in the neck, but not the supraclavicular nodes.

Regional lymph nodes for the stomach are the perigastric nodes along the lesser and greater curvatures, the nodes along the left gastric, common hepatic, splenic and coeliac arteries, and the hepatoduodenal nodes.

TNM staging after neoadjuvant therapy

If there is a history of neoadjuvant chemotherapy, radiotherapy or combined chemoradiotherapy, the prefix y should be added to the TMN stage (e.g. ypT2 N1), otherwise the same staging system is used. The presence of fibrosis, haemorrhage, necrosis or acellular mucin is not considered in the tumour staging, neither in the T nor the N category. Only viable tumour/tumour cells are assessed for staging. A specimen in which no tumour is identified following neoadjuvant treatment is staged as ypT0 N0.

Appendix B SNOMED codes for reporting oesophageal and gastric carcinoma

SNOMED 'T' codes

Topographical codes	SNOMED code (SNOMED 3.5/ SNOMED 2)	SNOMED CT terminology	SNOMED CT code
Oesophagus	T-56000/T-62000	Esophageal structure (body structure)	32849002
Oesophageal mucosa	T-56010/T-62010	Esophageal mucous membrane structure (body structure)	82082004
Stomach	T-57000/T-63000	Stomach structure (body structure)	69695003
Gastric mucosa	T-57010/T-63010	Gastric mucous membrane structure (body structure)	78653002
GOJ	T-56350/T-62350	Cardioesophageal junction structure (body structure)	25271004
Pylorus	T-57700/T-63700	Pylorus structure (body structure)	78987009

SNOMED 'M' codes

Note: This is not a comprehensive list of all malignancies and other codes should be used as necessary.

Morphological codes	SNOMED code (SNOMED 3.5/ SNOMED 2)	SNOMED CT terminology	SNOMED CT code
Metaplasia	M-73000	Metaplasia (morphologic abnormality)	17665002
Dysplasia	M-74000	Dysplasia (morphologic abnormality)	25723000
Adenocarcinoma in situ	M-81402	Adenocarcinoma in situ (morphologic abnormality)	51642000
Adenocarcinoma	M-81403	Adenocarcinoma, no subtype (morphologic abnormality)	35917007
Adenocarcinoma, mucinous	M-84803	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Carcinoma	M-80103	Carcinoma, no subtype (morphologic abnormality)	68453008

Morphological codes (continued)	SNOMED code (SNOMED 3.5/ SNOMED 2)	SNOMED CT terminology	SNOMED CT code
Undifferentiated carcinoma	M-80203	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Small cell carcinoma	M-80413	Small cell carcinoma (morphologic abnormality)	74364000
Squamous intraepithelial neoplasia grade III	M-80772	Squamous intraepithelial neoplasia, grade III (morphologic abnormality)	20365006
Squamous carcinoma	M-80703	Squamous cell carcinoma, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	28899001
Basaloid squamous cell carcinoma	M-80833	Basaloid squamous cell carcinoma (morphologic abnormality)	128634009
Spindle cell squamous carcinoma	M-80743	Squamous cell carcinoma, spindle cell (morphologic abnormality)	10288008
Glandular intraepithelial neoplasia grade III	M-81482	Glandular intraepithelial neoplasia, grade III (morphologic abnormality)	128640002
Adenosquamous carcinoma	M-85603	Adenosquamous carcinoma (morphologic abnormality)	59367005
Malignant melanoma	M-87203	Malignant melanoma, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	2092003

SNOMED P 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 C Reporting proforma for oesophageal carcinoma resections

Surname……	Forenames……	Date of birth……
Hospital……..	Hospital no……..	NHS no……
Date of procedure……	Date of receipt……	Date of reporting……
Report no……	Pathologist……	Surgeon……..
Gender……		

GROSS DESCRIPTION

Specimen	Pinned	☐	Not pinned	☐
Oesophagus length	…….mm			
Stomach length	Lesser curve	…….mm	Greater curve	…….mm
Tumour location	Oesophageal only	☐	Junctional	☐
Tumour epicentre distance from GOJ	…….mm above		…….mm below	
Length of tumour	…….mm		Width of tumour	…….mm
Tumour edge to nearest margin	Distal	…….mm	Proximal	…….mm
Shape of tumour	Polypoid	☐	Non-polypoid	☐
Siewert tumour type (cardiac cancers only)	1	☐	2	☐

HISTOLOGY

Type of tumour†

Squamous cell carcinoma	☐	Adenocarcinoma	☐	Other (specify) ……..	☐
Differentiation by predominant area		Well	☐	Moderate	☐
		Poor	☐	Not applicable	☐

Depth of invasion†

T0	No tumour identified	☐
Tis	High-grade dysplasia	☐
T1a	Invasion of lamina propria	☐
T1b	Invasion of submucosa	☐
T2	Invasion of muscularis propria	☐
T3	Invasion beyond muscularis propria	☐
T4a	Invades pleura, pericardium or diaphragm	☐
T4b	Invades aorta, vertebrae or trachea	☐

Serosal involvement	Yes	☐	No	☐

History of neoadjuvant therapy	Yes	☐	No	☐
	Unknown	☐		
Tumour regression grade if neoadjuvant treatment used	System used: ……		Grade: ……	
			Not applicable	☐
Proximal margin	Normal	☐	Barrett's	☐
	Dysplasia	☐	Carcinoma	☐
Distal margin	Normal	☐	Dysplasia	☐
	Carcinoma	☐		
Circumferential margin†	Involved: carcinoma equal or less than 1 mm from CRM (R1)			
	Not involved: carcinoma more than 1 mm from CRM (R0)	☐		
	Not applicable	☐		
	Distance of carcinoma to nearest circumferential margin (if not involved) …….mm			

Other features				
Lymphovascular space invasion	Present	☐	Not identified	☐
Perineural invasion	Present	☐	Not identified	☐
Lymph nodes	Total examined	…….	Positive	…….
Presence of pM1 disease	Yes	☐	No	☐

PATHOLOGICAL STAGING

TNM … ed.	**(y)pT….**	**N….**	**M**….
SNOMED† codes	**T ….**	**M….**	
Signature……..		Date	…../……/…..

†Data items that are currently part of the COSD version 8.

Appendix D Reporting proforma for gastric carcinoma resections

Surname……	Forenames……	Date of birth……
Hospital……..	Hospital no……	NHS no……
Date of procedure……	Date of receipt……	Date of reporting……
Report no……	Pathologist……	Surgeon……..
Gender……		

GROSS DESCRIPTION

Specimen	Pinned	☐	Not pinned	☐
Specimen type	Total gastrectomy	☐	Subtotal gastrectomy	☐
Tumour location	Cardia	☐	Fundus	☐
	Body	☐	Antrum	☐
Specimen dimensions	Length lesser curvature …..mm			
	Length greater curvature …..mm			
	Length duodenum …….mm			
	Length oesophagus …….mm			
Maximum tumour diameter	…….mm			
Tumour edge to distal margin	…….mm			
Tumour edge to proximal margin	…….mm			

HISTOLOGY

Type of tumour†	Adenocarcinoma	☐	Other (specify)	☐
Laurén classification	Intestinal	☐	Diffuse	☐
	mixed	☐	Indeterminate	☐
Differentiation by predominant area	Well	☐	Moderate	☐
	Poor	☐	Not applicable	☐

Depth of invasion†

T0	No tumour identified	☐
Tis	High-grade dysplasia	☐
T1	Invasion of lamina propria/submucosa	☐
T1a	Invasion of lamina propria	☐
T1b	Invasion of submucosa	☐
T2	Invasion of muscularis propria	☐
T3	Invasion beyond muscularis propria	☐
T4a	Invades pleura, pericardium or diaphragm	☐
T4b	Invades aorta, vertebrae or trachea	☐

History of neoadjuvant therapy	Yes ☐ Unknown ☐		No	☐
Tumour regression grade if neoadjuvant treatment used	System used: ……		Grade: …… Not applicable	☐ ☐
Proximal margin†	Involved	☐	Not involved	☐
Distal margin†	Involved	☐	Not involved	☐

Circumferential margin lower oesophagus†

Involved: carcinoma equal or less than 1 mm from CRM ☐
Not involved: carcinoma more than 1 mm from CRM ☐
Not applicable ☐

Distance of carcinoma to nearest circumferential margin (if not involved) …….mm

Lymphovascular space invasion†	Present	☐	Not identified	☐
Lymph nodes	Total examined†	…….	Number positive†	…….
Presence of pM1 disease	Yes	☐	No	☐

PATHOLOGICAL STAGING

Complete resection†	Yes (R0)	☐	No (R1 or R2)	☐	
TNM†… ed.	(y)pT….	N….		M….	
SNOMED† codes	T ……	M……			
Signature……..		Date		…../……/…..	

†Data items that are currently part of the COSD version 8.

Appendix E Reporting proforma for gastric/oesophageal carcinoma biopsies

Surname……	Forenames……	Date of birth……
Hospital……..	Hospital no……..	NHS no……
Date of procedure……	Date of receipt……	Date of reporting……
Report no……	Pathologist……	Surgeon……..
Gender……		

TUMOUR LOCATION†

Oesophagus	☐	Stomach	☐
Oesophagogastric junction	☐	Unknown	☐

HISTOLOGY

Type of tumour†	Adenocarcinoma	☐	Squamous cell carcinoma	☐
	Other (specify)	☐	……	
Laurén classification	Intestinal	☐	Diffuse	☐
	Mixed	☐	Indeterminate	☐
Differentiation by worst area†	Well	☐	Moderate	☐
	Poor	☐	Not applicable	☐
Adjacent dysplasia				
Glandular	High grade	☐	Low grade	☐
	None	☐		
Squamous	High grade	☐	Low grade	☐
	None	☐		

SNOMED† codes T …… M……

Signature…….. Date …../……/…..

†Data items that are currently part of the COSD version 8.

Appendix F Reporting proforma for gastric/oesophageal carcinoma EMR specimens

Surname……	Forenames……	Date of birth……
Hospital……..	Hospital no……..	NHS no……
Date of procedure……	Date of receipt……	Date of reporting……
Report no……	Pathologist……	Surgeon……..
Gender……		

TUMOUR LOCATION†

Oesophagus	☐	Stomach	☐
Oesophagogastric junction	☐	Unknown	☐

HISTOLOGY

Type of tumour†	Adenocarcinoma	☐	Squamous cell carcinoma	☐
	Other (specify)	☐	……	
Laurén classification	Intestinal	☐	Diffuse	☐
	Mixed	☐	Indeterminate	☐
Differentiation by worst area†	Well	☐	Moderate	☐
	Poor	☐	Not applicable	☐
Size of invasive tumour	Not measurable	☐		
	Width of invasive tumour			……mm
	Depth of invasion below original muscularis mucosae (for pT1b lesions)			…..mm
	Depth of invasive tumour from luminal surface (when cannot be measured from muscularis mucosae)			…..mm

Adjacent dysplasia

Glandular	High grade	☐	Low grade	☐
	None	☐		
Squamous	High grade	☐	Low grade	☐
	None	☐		

Depth of invasion†

Tis	High-grade dysplasia	☐
T1a	Invasion of lamina propria	☐
T1b	Invasion of submucosa	☐
T2	Invasion of muscularis propria	☐

Lymphovascular space invasion†	Present	☐	Not identified	☐

Completeness of excision

Distance of invasion from mucosal peripheral margins …….mm

Distance of invasion from deep margin …….mm

SNOMED† codes T …… M……

Signature…….. Date …../……/…..

†Data items that are currently part of the COSD version 8.

Appendix G Reporting proforma for oesophageal carcinoma resections in list format

Element name	Values	Implementation comments
Specimen	Single selection value list: • Pinned • Not pinned	
Oesophagus length	Size in mm	
Stomach length, Lesser curve	Size in mm	
Stomach length, Greater curve	Size in mm	
Tumour location	Single selection value list: • Oesophageal only • Junctional	
Tumour epicentre, distance above GOJ	Size in mm	
Tumour epicentre, distance below GOJ	Size in mm	
Length of tumour	Size in mm	
Width of tumour	Size in mm	
Tumour edge to nearest distal margin	Size in mm	
Tumour edge to nearest proximal margin	Size in mm	
Shape of tumour	Single selection value list: • Polypoid • Non-polypoid	
Siewert tumour type	Single selection value list: • 1 • 2	
Type of tumour	Single selection value list: • Squamous carcinoma • Adenocarcinoma • Other	
Type of tumour, Other, specify	Free text	Only applicable if 'Type of tumour, Other' is selected.
Differentiation by predominant area	Single selection value list: • Well • Moderate	

	• Poor • Not applicable	
Depth of invasion	Single selection value list • No tumour identified • High-grade dysplasia • Invasion of lamina propria • Invasion of submucosa • Invasion of muscularis propria • Invasion beyond muscularis propria • Invades pleura, pericardium or diaphragm • Invades aorta, vertebrae or trachea	
Serosal involvement	Single selection value list: • Yes • No	
History of neoadjuvant therapy	Single selection value list: • Yes • No • Unknown	
Tumour regression grade	Free text	Only applicable if 'History of neoadjuvant therapy, Yes' is selected.
Tumour regression grade, System used	Free text	Only applicable if 'History of neoadjuvant therapy, Yes' is selected.
Proximal margin	Single selection value list: • Normal • Barrett's • Dysplasia • Carcinoma	
Distal margin	Single selection value list: • Normal • Dysplasia • Carcinoma	
Circumferential margin	Single selection value list: • Involved: carcinoma equal or less than 1 mm from CRM	

	• Not involved: carcinoma more than 1 mm from CRM • Not applicable	
Distance of carcinoma to nearest circumferential margin	Size in mm	Only applicable if 'Not involved' is selected for 'Circumferential margin'.
Lymphovascular space invasion	Single selection value list: • Present • Not identified	
Perineural invasion	Single selection value list: • Present • Not identified	
Lymph nodes, Total examined	Integer	
Lymph nodes, Positive	Integer	
Presence of pM1 disease	Single value selection list: • Yes • No	
TNM edition	Single value selection list: • UICC TNM 8	
pT category	Single selection value list: • TX • T0 • Tis • T1a • T1b • T2 • T3 • T4a • T4b • yTX • yT0 • yTis • yT1a • yT1b • yT2 • yT3 • yT4a • yT4b	

pN category	Single selection value list: • NX • N0 • N1 • N2 • N3	
pM category	Single selection value list: • Not applicable • M1	
SNOMED codes	May have multiple codes. Look up from SNOMED tables.	

Appendix H Reporting proforma for gastric carcinoma resections in list format

Element name	Values	Implementation comments
Specimen	Single selection value list: • Pinned • Not pinned	
Specimen type	Single selection value list: • Total gastrectomy • Subtotal gastrectomy	
Tumour location	Single selection value list: • Cardia • Fundus • Body • Antrum	
Specimen dimensions, Length lesser curvature	Size in mm	
Specimen dimensions, Length greater curvature	Size in mm	
Specimen dimensions, Length duodenum	Size in mm	
Specimen dimensions, Length oesophagus	Size in mm	
Maximum tumour diameter	Size in mm	
Tumour edge to nearest distal margin	Size in mm	
Tumour edge to nearest proximal margin	Size in mm	
Type of tumour	Single selection value list: • Adenocarcinoma • Other	
Type of tumour, Other, specify	Free text	Only applicable if 'Type of tumour, Other' is selected.
Laurén classification	Single selection value list • Intestinal • Diffuse • Mixed • Indeterminate	
Differentiation by predominant area	Single selection value list	

	• Well • Moderate • Poor • Not applicable	
Depth of invasion	Single selection value list • No tumour identified • High-grade dysplasia • Invasion of lamina propria/submucosa • Invasion of lamina propria • Invasion of submucosa • Invasion of muscularis propria • Invasion beyond muscularis propria • Invades pleura, pericardium or diaphragm • Invades aorta, vertebrae or trachea	
History of neoadjuvant therapy	Single selection value list: • Yes • No • Unknown	
Tumour regression grade	Free text	Only applicable if 'History of neoadjuvant therapy, Yes' is selected.
Tumour regression grade, System	Free text	Only applicable if 'History of neoadjuvant therapy, Yes' is selected.
Proximal margin	Single selection value list: • Involved • Not involved	
Distal margin	Single selection value list: • Involved • Not involved	
Circumferential margin lower oesophagus	Single selection value list: • Involved: carcinoma equal or less than 1 mm from CRM • Not involved: carcinoma more than 1 mm from CRM • Not applicable	

Distance of carcinoma to nearest circumferential margin	Size in mm	Only applicable if 'Not involved' selected for 'Circumferential margin lower oesophagus'.
Lymphovascular space invasion	Single selection value list: • Present • Not identified	
Lymph nodes, Total examined	Integer	
Lymph nodes, Number positive	Integer	
Presence of pM1 disease	Single value selection list: • Yes • No	
Complete resection	Single value selection list: • Yes (R0) • No (R1 or R2)	
TNM edition	Single value selection list: • UICC TNM 8	
pT category	Single selection value list: • TX • T0 • Tis • T1a • T1b • T2 • T3 • T4a • T4b • yTX • yT0 • yTis • yT1a • yT1b • yT2 • yT3 • yT4a • yT4b	
pN category	Single selection value list: • NX	

	• N0 • N1 • N2 • N3a • N3b	
pM category	Single selection value list: • Not applicable • M1	
SNOMED codes	May have multiple codes. Look up from SNOMED tables.	

Appendix I Reporting proforma for gastric/oesophageal carcinoma biopsies in list format

Element name	Values	Implementation comments
Tumour location	Single selection value list: • Oesophagus • Oesophagogastric junction • Stomach • Unknown	
Type of tumour	Single selection value list: • Adenocarcinoma • Squamous carcinoma • Other	
Type of tumour, Other, specify	Free text	Only applicable if 'Type of tumour, Other' is selected.
Lauren classification	Single selection value list • Intestinal • Diffuse • Mixed • Indeterminate	
Differentiation by worst area	Single selection value list • Well • Moderate • Poor • Not applicable	
Adjacent glandular dysplasia	Single selection value list • High grade • Low grade • None	
Adjacent squamous dysplasia	Single selection value list • High grade • Low grade • None	
SNOMED codes	May have multiple codes. Look up from SNOMED tables.	

Appendix J Reporting proforma for gastric/oesophageal carcinoma EMR specimens in list format

Element name	Values	Implementation comments
Tumour location	Single selection value list: • Oesophagus • Oesophagogastric junction • Stomach • Unknown	
Type of tumour	Single selection value list: • Adenocarcinoma • Squamous carcinoma • Other	
Type of tumour, Other, specify	Free text	Only applicable if 'Type of tumour, Other' is selected.
Laurén classification	Single selection value list • Intestinal • Diffuse • Mixed • Indeterminate	
Differentiation by worst area	Single selection value list • Well • Moderate • Poor • Not applicable	
Size of invasive tumour, measurable	Single selection value list • Not measurable • Measurable	Measurable automatically selected if size given for 'Size of invasive tumour, Width of invasive tumour', 'Size of invasive tumour, Depth of invasion below original muscularis mucosa (for pT1b lesions)' or 'Size of invasive tumour, Depth of invasive tumour from luminal surface (when cannot be measured from muscularis mucosae)'.
Size of invasive tumour, Width of invasive tumour	Size in mm	
Size of invasive tumour, Depth of invasion below original muscularis mucosa (for pT1b lesions)	Size in mm	
Size of invasive tumour, Depth of invasive tumour from luminal	Size in mm	

surface (when cannot be measured from muscularis mucosae)		
Adjacent glandular dysplasia	Single selection value list • High grade • Low grade • None	
Adjacent squamous dysplasia	Single selection value list • High grade • Low grade • None	
Depth of invasion	Single selection value list • High grade dysplasia pTis • Invasion of lamina propria pT1a • Invasion of submucosa pT1b • Invasion of muscularis propria pT2	
Lymphovascular space invasion	Single selection value list • Present • Not identified	
Distance of invasion from mucosal peripheral margins	Size in mm	
Distance of invasion from deep margin	Size in mm	
SNOMED codes	May have multiple codes. Look up from SNOMED tables.	

Appendix K Summary table – Explanation of grades of evidence

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

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

Appendix L AGREE II guideline monitoring sheet

The cancer datasets of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. 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	Foreword, 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
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	1
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword,1
12 There is an explicit link between the recommendations and the supporting evidence	2–9
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	2–9
16 The different options for management of the condition or health issue are clearly presented	2–9
17 Key recommendations are easily identifiable	2–9
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	Appendices A–J
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