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

Dataset for the histopathological reporting of carcinomas of the pancreas, ampulla of Vater and common bile duct

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Comments	This document supersedes the 2010 edition of the *Dataset for carcinomas of the pancreas, ampulla of Vater and common bile duct*. In accordance with the College's pre-publications policy, this document was on the College website for consultation from 1–29 November 2016. Seventeen items of feedback were received and the guidance was amended as appropriate. Please email publishing@rcpath.org if you wish to see the responses and comments. **Dr Lorna Williamson** **Director of Publishing and Engagement**

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Contents

Appendices

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 inflammation, 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 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 Dataset) 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 following stakeholders have been consulted during the preparation of the dataset:

- British Society of Gastroenterology – Pancreas Section (www.bsg.org.uk)
- British Society of Gastroenterology – Pathology Section (www.bsg.org.uk)
- Pancreas Society of Great Britain and Ireland (www.pancsoc.org.uk).

Evidence for the revised dataset was obtained from updates to classification systems and by electronically searching medical literature data bases for relevant research evidence, systemic reviews, and national or international publications on pancreatic/ampullary/bile duct cancer up to and including December 2016. The level of evidence for the recommendations has been summarised (see Appendix N). 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”.

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset for the core items.

A formal revision for all cancer datasets takes place on a three-year cycle. However, each year, the College will ask the authors of the dataset, in conjunction with the relevant sub-specialty 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 Clinical Effectiveness Department and the Working Group on Cancer Services. It was placed on the College website for consultation with the membership from 1–29 November 2016. All comments received from the Working Group and the membership have

been 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 of this document have declared that there are no conflicts of interest.

1 Introduction

Careful and accurate pathology reporting of pancreatic, ampulla of Vater and common bile duct cancers is important because pathology reports are used to:

- confirm the diagnosis
- inform prognosis
- select potential patients for future trials of adjuvant therapy
- audit pathology services
- evaluate the quality of other clinical services, e.g. radiology and surgery
- collect accurate data for cancer registration and epidemiology
- facilitate high-quality research
- plan service delivery.

In pancreatic/ampullary/bile duct cancer, the key reasons for high-quality pathology reporting include the following:[1]

- to identify the primary origin of the tumour, which, in turn, may determine further therapy and/or entry into clinical trials
- to determine the type, grade and stage of the tumour correctly
- to assess resection margin status accurately and comprehensively
- to document the presence of significant precursor lesions
- to provide accurate, good quality prognostic information
- to determine the effects of preoperative (neoadjuvant) therapy
- to evaluate any changes in surgical technique
- to provide information that will facilitate investigations into the epidemiological, biological and molecular characteristics of these tumours.

Communication of pathology information to the patient and the MDT is essential for optimal clinical management. Each department should have, as a minimum, a lead and deputy gastrointestinal pathologist, one of whom should attend MDT meetings. All reporting pathologists should provide pathology reports that are accurate, complete, understandable, timely and transferable. There is evidence that the use of proformas facilitates these requirements[2] and their use is strongly recommended, supplemented as necessary by free text. It is appreciated that electronic versions of the dataset are still not available in all pathology departments and there remain some laboratories that have to dictate or type the dataset into the pathology report.

1.1 Changes made to the third version of the dataset

- Addition of comments on the assessment of specimens following neoadjuvant therapy.
- Expansion of comments on cancer specimens with intraductal papillary mucinous neoplasm (IPMN) or mucinous cystic neoplasm (MCN).
- Addition of a section on pancreatic biopsy reporting.
- Updated to WHO 2010 classification of tumours and included TNM8.

The following specific changes have been made to the dataset proformas in Appendices E, F, and G for TNM7 and appendices H,I and J for TNM8:

- 'Date of surgery' has been added to the proformas to allow mapping to College key performance indicators relating to turnaround times (www.rcpath.org/clinical-effectiveness/kpi)
- specimen types have been listed
- response to neoadjuvant therapy has been added
- potential margins are now listed in table format
- TNM8 has been added.

The number of resections for pancreatic, ampullary or bile duct cancers continues to increase.[3] This has led to the identification of new pathological entities and investigation of numerous potential prognostic factors.

Pathological tumour characteristics that (in most studies) have significant prognostic value in resected pancreatic adenocarcinoma include tumour size, tumour differentiation, lymph node involvement and resection margin status.[4-9]

Histopathological tumour characteristics that have significant prognostic value in resected ampullary adenocarcinoma include pancreatobiliary differentiation, tumour stage and lymph node involvement,[10,11]

[Level of evidence C.]

The most important pathological prognostic factors identified to date for resected common bile duct adenocarcinoma are tumour stage, tumour grade and lymph node status.[12-16]

[Level of evidence D.]

1.2 Developments since the second edition

Since the second edition of this dataset in 2010 was published, there have been further requests for guidance particularly on dissection of the pancreatoduodenectomy specimen, identification of resection margins, definition of a positive resection margin, and assessment of resection specimens following neoadjuvant therapy. Many of these requests were sought following the publication of the British Society of Gastroenterology survey of 'Pathologists' approach to pancreatectomies for ampullary, pancreatic and bile duct cancer' in 2013.[17] These requests have been addressed, but it is emphasised that the dataset is for guidance and is not prescriptive. There is no single internationally recognised, standardised method for dissecting and sampling pancreatic cancer resection specimens. Moreover, there are also still many areas of controversy in reporting pancreatic cancer resection specimens, highlighting the need for international agreement and standardisation.[18]

The reporting proformas and guidance are based on the current WHO classifications of tumours of the exocrine pancreas, ampulla of Vater and extrahepatic bile duct[19] (Appendices

C and D) and the UICC TNM staging system, including both the 7th edition[20] and the imminent 8th edition[21] (Appendix A). The UICC TNM staging system has the advantage of being widely accepted and familiar, and is adhered to throughout this document.

These guidelines mainly apply to the reporting of pancreatic exocrine carcinomas, 90% of which are ductal adenocarcinomas, but similar principles may be applied to the reporting of carcinomas arising in the ampulla of Vater or common bile duct. The reporting of endocrine tumours is addressed in the College's separate *Dataset for endocrine tumours of the gastrointestinal tract including the pancreas*.[22]

1.3 Target users and health benefits of this guidance

The primary users of the dataset are cellular pathology trainees and consultants and, on their behalf, the suppliers of IT products to laboratories. Secondary users are surgeons, radiologists, oncologists, cancer registries and the National Cancer Intelligence Network (NCIN). MDT working and standardisation of cancer reporting 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 national/international benchmarking and research.

2 Clinical information required on the specimen request form

Patients often proceed to pancreatic surgery on the basis of imaging and/or cytology. It is therefore desirable for the pathologist to be aware of the specimen type, the presumed site and type of the tumour and whether or not pre-operative therapy has been given. The nature of the resection is usually obvious to the pathologist, but it is good practice to confirm this using the specimen request form. A diagram of the surgical procedure or a good clinical description can be very valuable in complex specimens. If there is doubt about the nature of the specimen or the procedure, advice or clarification should be sought from the surgeon.

[Level of evidence GPP.]

3 Preparation of specimens before dissection

Resection specimens should, preferably, be opened and partially sectioned by the pathologist immediately after resection, to aid fixation. The resection specimen should be received fresh in the laboratory if fresh tissue sampling is required for a biobank or other reasons. The stomach is opened along the greater curve. The duodenum is opened along the anti-mesenteric border, on the opposite aspect to the pancreas, being careful to avoid cutting through a duodenal or ampullary tumour.

The margins of the pancreas (see Section 5.2.4) should be painted with an agreed colour code before blocks are taken, either when the specimen is fresh or when fixed, according to the preference of the examining pathologist. The presence of a stent or a named vessel (e.g. portal vein, superior mesenteric vein) should be noted. Identification of a resected vessel, particularly if small in size, may be facilitated by painting it with an extra colour.

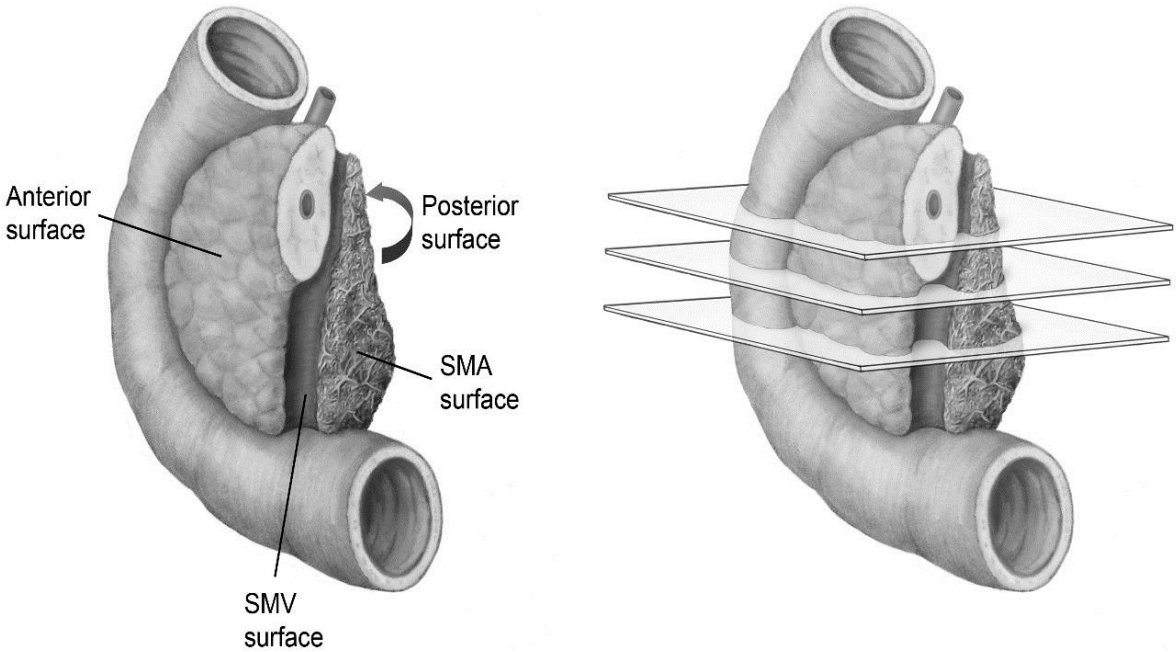
One or two slices may be made into the fresh pancreas, to allow tissue sampling for biobanking for example, and/or to aid fixation. The specimen may then be pinned to a cork board, but should always be placed in a large volume of formalin and allowed to fix for 24–48 hours.

[Level of evidence GPP.]

4 Specimen handling and block selection

Currently, several different techniques are used for dissecting pancreatoduodenectomy specimens.[23,24] A detailed dissection protocol is beyond the scope of these guidelines. However, a brief discussion of the axial dissection method is included because this technique has several advantages. After orientation of the specimen (Figure 1a), axial dissection (Figure 1b) serially slices the pancreatic head in an axial plane, i.e. perpendicular to the long axis of the duodenum. It is easy to perform, does not include longitudinal opening of the common bile duct or pancreatic duct and allows key anatomical structures (e.g. ampulla, common bile duct, main pancreatic duct) to be seen in the same slices. This dissection technique usually results in 8–10 slices, allowing thorough examination of the tumour and its relationship to the key anatomical structures and margins.[24]

[Level of evidence GPP.]



a **b**

Figure 1: (a) Head of the pancreas and (b) axial dissection, i.e. slicing perpendicular to the long axis of the duodenum

SMV = superior mesenteric vein, SMA = superior mesenteric artery

With acknowledgement to Paul Brown, St James's University Hospital, Leeds

For distal pancreatectomy specimens, in which the splenic artery and vein run along the superior (cranial) aspect, the anterior and posterior surfaces may be painted. Painting the superior (cranial) and/or inferior (caudal) aspects may also help with orientation. The entire specimen can then be serially sliced in the sagittal plane. For total pancreatectomy specimens, a combined approach of axial slicing of the pancreatic head followed by serial slicing of the body and tail in the sagittal plane is recommended.

Overview photographs of the lined-up specimen slices and close-up images of individual slices may be helpful for reporting (e.g. to identify the tumour origin), for multidisciplinary case discussion and for review of the gross findings if required (e.g. for audit or clinical trials).

Specimen measurements

Record the lengths of the duodenum, stomach (lesser curve and greater curve), gall bladder, cystic duct and extrapancreatic bile duct, and the maximum dimensions of the pancreas (craniocaudally, mediolaterally and anteroposteriorly). The diameters of the common bile duct and main pancreatic duct can indicate the location of an obstruction and are useful for correlation with radiology. Record the dimensions of any attached vessels (e.g. segment of superior mesenteric vein or portal vein), spleen or other structures (e.g. colon).

The following blocks of tissue are recommended as a minimum sampling

If not already submitted as separate samples for frozen section assessment, the transection margins of the pancreatic neck, common bile duct and duodenum/distal stomach are sampled (usually *en face*) prior to specimen dissection. Tissue blocks should include the tumour where it approaches or involves anatomical structures relevant to (UICC TNM) T-staging, e.g. duodenum, ampulla, common bile duct or peripancreatic tissue. Similarly, blocks should be taken from the tumour and the adjacent resection margin(s). It is often difficult to identify the invasive tumour front macroscopically, therefore extensive sampling of the tumour and the adjacent margins is recommended.[25] The importance of extensive sampling from the margins is supported by molecular studies.[26,27] If available, sampling with one or more wholemount blocks may be helpful for assessing the relationship of the tumour to anatomical structures and to margins, as well as allowing accurate measurement of tumour dimensions.

[Level of evidence D.]

Following neoadjuvant therapy, large parts of a tumour may be replaced by fibrosis. Macroscopic distinction between tumour, fibrotic areas of tumour regression, and fibrosis of obstructing pancreatitis (that is present in nearly all pancreatic cancer resection specimens) may be difficult or impossible.[28] Extensive sampling is required for accurate evaluation of the extent of viable tumour and its relationship to the margins. Extensive sampling is also necessary for a reliable diagnosis of complete response to neoadjuvant therapy, and sampling of the entire pancreas is recommended in this setting.[29]

[Level of evidence GPP.]

Macroscopic examination plays an important role in determining the presence of a **mucinous cystic neoplasm (MCN)** or **an intraductal papillary mucinous neoplasm (IPMN)** in association with a cancer. Macroscopic papillary areas and solid areas in an MCN are most likely to show invasive carcinoma and should always be sampled. Similarly, solid nodules and mucoid areas in the wall of an IPMN should always be sampled as they likely represent invasive carcinoma. However, invasive carcinoma in an MCN or IPMN may not be apparent macroscopically, and may also be multifocal in IPMN. In the absence of macroscopic invasive carcinoma, embedding the entire MCN or IPMN is recommended, particularly if microscopic examination reveals high-grade dysplasia but no invasion.[30]

[Level of evidence GPP.]

It is worth noting that an invasive adenocarcinoma and an IPMN may be present in the same pancreas, but the adenocarcinoma may not have arisen from the IPMN (i.e. the adenocarcinoma is a concomitant pancreatic ductal adenocarcinoma).[31] In this circumstance, the concomitant adenocarcinoma will not show transition from IPMN to invasive adenocarcinoma. For IPMNs, the resection specimen should also be assessed to determine whether the IPMN is of main duct type, branch duct type or mixed/combined duct type, as this has prognostic significance.[32] Placing a probe in the main pancreatic duct can help in this assessment.

When a segmental resection of the portal vein or superior mesenteric vein is removed *en bloc* with the pancreatoduodenectomy, then the proximal and distal ends of this vessel should be examined as additional transection margins. If a lateral sleeve resection of the vein is included in the specimen, then the entire edge of the vessel should be examined en bloc with the adjacent pancreas in the serial axial slices of the pancreas.

[Level of evidence GPP.]

All lymph nodes (see Figure 2 and Section 5.4.6) should be sampled in their entirety, because lymph node status is an important prognostic factor. Once lymph nodes have been identified and sampled individually, submission of the entire remaining peripancreatic fat and connective tissue may be considered to ensure that all lymph nodes are examined microscopically.

[Level of evidence GPP.]

Samples of the ampulla of Vater, common bile duct and background pancreas should be taken.

A block code should be recorded using an easily accessible method (e.g. within the final report, within the IT system or on a scanned bench worksheet). This will aid identification of block origin at later review (e.g. for MDT meetings or clinical trials).

[Level of evidence GPP.]

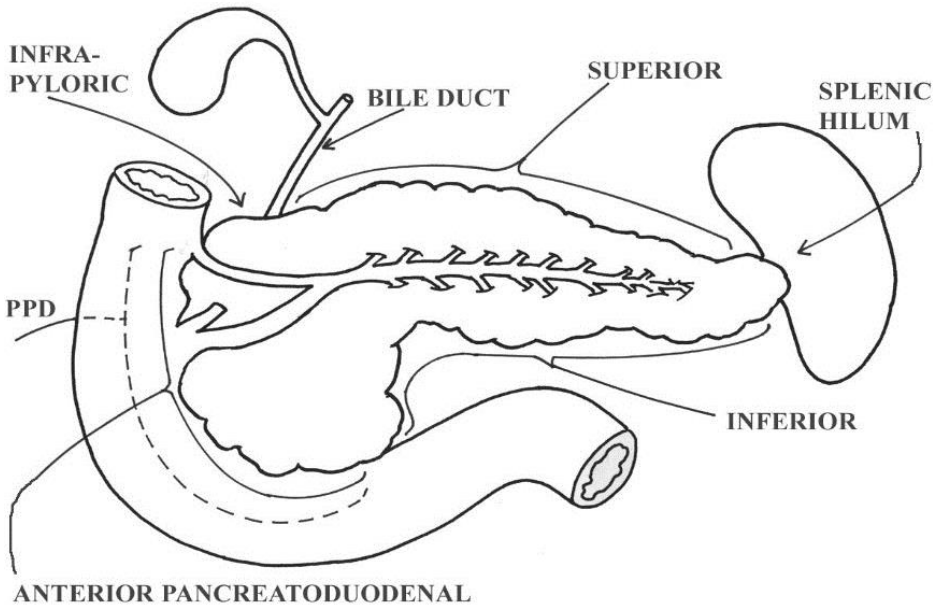


Figure 2: Lymph nodes. Inferior includes lymph nodes around superior mesenteric vessels

PPD = posterior pancreatoduodenal

5 Core data items

5.1 Macroscopic core data items

- Type of specimen
- Site of tumour
- Maximum tumour dimension (measurement confirmed microscopically)
- Resection margins (confirmed microscopically)
- Named vessel present
- Background pathology (e.g. intraductal papillary mucinous neoplasm, mucinous cystic neoplasm, adenoma of the ampulla)

5.2 Notes on macroscopic assessment

Measurements made on the gross specimen are recorded in millimetres. They are confirmed or amended, where appropriate, by microscopy.

5.2.1 Type of specimen

The type of specimen should be recorded, e.g. a standard Kausch-Whipple's pancreato-duodenectomy (PD), a pylorus-preserving PD, a total PD, a subtotal pancreatectomy or a left (distal) pancreatectomy. The standard Kausch-Whipple's PD includes the head of pancreas, duodenum, common bile duct, gall bladder and two thirds of the stomach. Modifications of this procedure include pylorus-preserving PD (stomach not included), total PD (also includes the body and tail of pancreas with or without the spleen and/or stomach) and subtotal pancreatectomy (includes the body of the pancreas with or without the stomach). A left (or distal) pancreatectomy consists of the body and tail of pancreas only, with or without the spleen.

The type of operation will depend upon the site and size of the tumour. Clinical trials, single-centre studies and a Cochrane Database Systematic Review have not shown any difference in patient survival between standard PD versus pylorus-preserving PD,[33-35] PD with or without vascular resection,[36] and PD with or without extended lymphadenectomy.[37,38]

5.2.2 Site of tumour (Appendix B)

State, when possible, whether the tumour appears to arise in the ampulla of Vater, in the intrapancreatic or extrapancreatic bile duct, or in the head, body or tail of the pancreas. Ampullary tumours are centred around the level of the ampulla and may involve the posterior or anterior pancreatoduodenal crevices. Common bile duct tumours arise along the route of the common bile duct, in the posterior-cranial aspect of the pancreatic head, above or at the level of the ampulla, and often involve the posterior pancreatic margin. Pancreatic tumours can occur in any part of the pancreatic head, body or tail.[1] The precise origin of a tumour in the head of the pancreas may be difficult to determine, particularly when the tumour is large and involves more than one potential site of origin. The tumour origin may then be determined by the location of the epicentre of the tumour.

[Level of evidence GPP.]

Microscopic confirmation of the site of origin of the tumour should be sought. In some cases, the presence of microscopic precursor lesions may be helpful (adenoma or flat dysplasia in the ampulla for ampullary carcinoma, dysplasia in the bile duct for distal bile duct cancer). However, note that pancreatic intraepithelial neoplasia (PanIN) is a frequent finding and can be found in the background pancreas of specimens with ampullary or bile duct cancer, as well as pancreatic cancer.[39,40] Moreover, cancerisation of background structures can mimic dysplasia.[41] An abrupt transition from highly atypical (cancer) epithelium to normal epithelium

is helpful in recognising cancerisation. Although immunohistochemistry may help distinguish intestinal-type carcinomas (CK20+, CDX2+, MUC2+) from pancreatobiliary-type carcinomas (CDX2-, MUC1+, MUC2-) arising in the ampulla of Vater,[42] there are currently no immunohistochemical markers that distinguish between pancreatobiliary-type carcinomas of the ampulla and pancreatic ductal adenocarcinoma or bile duct carcinoma.

Anatomically, the head is that part of the pancreas to the right of the left border of the superior mesenteric vein; the uncinate process is considered part of the head; the body lies between the left border of the superior mesenteric vein and the left border of the aorta; and the tail lies between the left border of the aorta and the hilum of the spleen. Carcinomas of the body or tail are usually more advanced than those of the head at the time of diagnosis, because of lack of obstructive symptoms, and because they usually spread into extrapancreatic tissue and metastasise before detection. They are therefore seldom resected. Note that pancreatic carcinomas may be multicentric (please complete a separate proforma for each carcinoma).

A recent study has subclassified ampullary carcinomas into four subtypes based upon their location (intra-ampullary, ampullary-ductal, periampullary-duodenal, and ampullary not otherwise specified) and has shown that the four clinicopathological subtypes are prognostically distinct.[43] It remains to be seen whether or not this site subclassification is adopted by the WHO or the UICC.

Following a good response to **neoadjuvant therapy**, it may be difficult or impossible to determine the site or origin of the cancer.[29] This should be stated in the report.

5.2.3 Tumour size

Tumour size is an independent prognostic factor for pancreatic carcinoma.[5-7]

[Level of evidence C.]

Optimally, three dimensions should be measured but, for staging purposes, at least the maximum dimension of the tumour should be measured. The tumour size is based on macroscopic assessment that is confirmed or amended on the basis of microscopy. This is often necessary for assessing tumour size in pancreatic cancer (which has a highly infiltrative growth pattern) and particularly following successful neoadjuvant therapy, when it can be very difficult to identify residual tumour macroscopically.[29] Use of wholemount blocks facilitates the measurement of tumour size.

In **IPMNs**, the size of the invasive component should be measured as accurately as possible. For unifocal invasive carcinoma, the largest dimension of the invasive focus should be measured. For multifocal invasive carcinomas in IPMN, it is recommended that both the maximum dimension of the largest invasive tumour and the overall estimated size of all invasive foci in aggregate should be provided.[44] It is not yet clear which of these reflects the tumour burden more accurately.

5.2.4 Distance from tumour to nearest margin

Completeness of excision should be assessed macroscopically and confirmed by microscopic examination. The transection margins are those of the pancreatic neck, common bile duct, superior mesenteric artery, jejunum and stomach/duodenum. The dissection or mobilisation margins are the superior mesenteric vein margin and the posterior margin (Figure 1a and Figure 3). The superior mesenteric vessel margin includes the superior mesenteric vein margin (defined as the smooth groove-like surface facing the superior mesenteric vein) and the superior mesenteric artery margin (defined as the rough area to the left of the superior mesenteric vein margin and facing the superior mesenteric artery) (Figure 1a). The superior mesenteric artery margin is also referred to as the medial or uncinate margin. Resected segment of superior mesenteric vein or portal vein will be found attached towards the cranial end of the mesenteric vein groove. The posterior margin is defined as the fibrous but smooth surface of the pancreatic head overlying the aorto-caval groove, which extends from the superior mesenteric artery margin to the posterior pancreatoduodenal groove.

The anterior surface of the pancreas (which extends from the superior mesenteric vein groove to the anterior pancreatoduodenal groove) is not a surgical margin but invasion of this surface has been shown to be associated with local recurrence and decreased survival time.[45,46]

The distance from the tumour to the nearest margins and surfaces should be recorded macroscopically, and refined by histological examination.

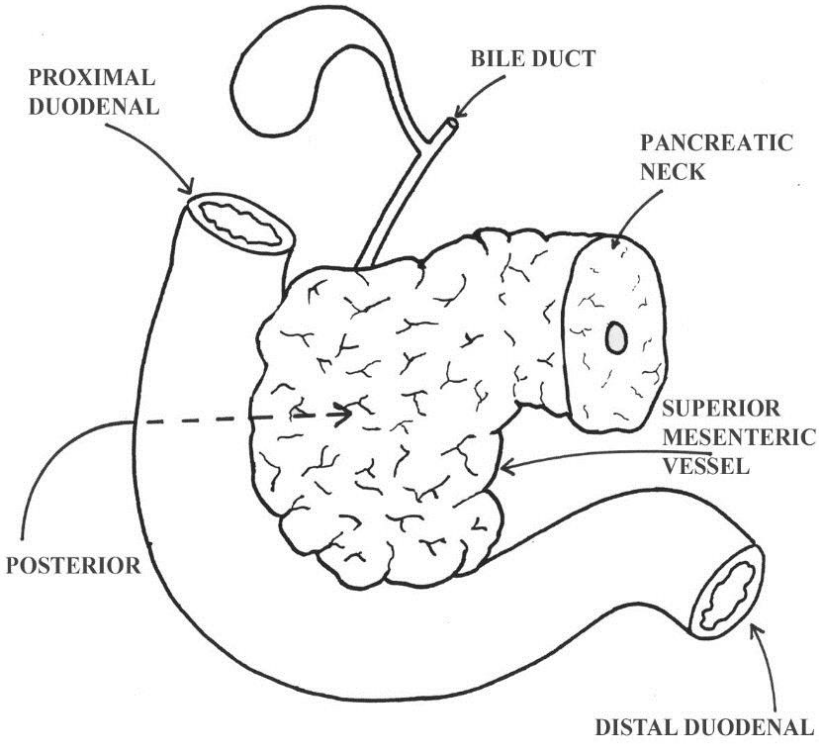


Figure 3: Resection margins for the head of the pancreas

5.3 Microscopic core data items

- Histological type of tumour
- Tumour grade/histological differentiation
- Size and maximum extent of local invasion
- Perineural invasion
- Named vessel involvement
- Lymph node status (number present, number involved)
- Resection margin status
- Regression following neoadjuvant therapy
- Histologically confirmed distant metastatic disease
- Background abnormalities
- UICC TNM stage (7th and/or 8th edition)
- Completeness of excision (R category)
- SNOMED codes.

5.4 Notes on microscopic assessment

5.4.1 Tumour type

The histological classification is based on the WHO typing of tumours of the exocrine pancreas, ampulla of Vater and extrahepatic bile duct[19] (Appendices C and D). Ductal adenocarcinoma, including its variants, accounts for 90% of the pancreatic tumours. Recognition of the variants of pancreatic ductal adenocarcinoma (PDAC) is important because they can differ in clinical behaviour, e.g. colloid carcinoma has a significantly better prognosis than conventional PDAC.[47]

[Level of evidence D.]

Unusual growth patterns of PDAC include clear cell,[48] foamy gland,[49] intestinal type,[50] large duct pattern, and cystic papillary pattern,[51,52] but none of these is currently included as a variant of PDAC in the WHO classification.[19]

It is important to recognise and state whether an adenocarcinoma has arisen from a **mucinous cystic neoplasm** (when the invasive tumour is typically a ductal type carcinoma) or from an **IPMN** (when the invasive carcinoma may be ductal type, colloid type or oncocytic type).[31,32] The five-year survival rate for resected invasive carcinoma arising in an MCN is 50–60%, which is much better than for non-MCN-related PDAC.[31,32] IPMNs with an associated invasive carcinoma may also have a better outcome than conventional PDAC, but this depends upon the subtype of the invasive carcinoma. The prognosis for IPMNs associated with a colloid carcinoma or an oncocytic carcinoma (five-year survival rates of 60–90%) is significantly better than for IPMNs with associated PDAC. IPMN with associated PDAC has a prognosis equivalent to that of conventional PDAC (five-year survival rate 37% *versus* 16%).[53-55]

[Level of evidence C.]

Adenocarcinomas originating in the ampulla of Vater have intestinal-type and/or pancreatobiliary-type differentiation, and this should be stated in the report. Immunohistochemistry may be helpful in making the distinction since intestinal-type carcinoma is CK20+, CDX2+ and MUC2+ while pancreatobiliary-type carcinoma is CDX2-, MUC1+ and MUC2-.[42] Pancreatobiliary-type adenocarcinoma of the ampulla has a poorer prognosis.[11]

5.4.2 Tumour grade

Histological grading of pancreatic ductal adenocarcinoma as well, moderately and poorly differentiated, according to the criteria of Klöppel *et al* [56] (Table 1), has prognostic significance in most studies.[2,57,58] and gives predictive values similar to those of the TNM grading system.[59]

[Level of evidence C.]

The criteria used for grading PDAC are detailed in Table 1. The tumour is graded according to the least differentiated area, regardless of prevalence. Duct structures and nuclei are usually the most informative criteria. There is no published guidance on whether this system can be used for grading bile duct carcinoma and pancreatobiliary type carcinoma of the ampulla.

Table 1: Histological grading of pancreatic ductal adenocarcinoma [19,56]

Tumour grade/ differentiation	Duct structures	Nuclei	Mitotic figures per 10 high power fields*	Mucin production
Grade 1, well differentiated	Well-formed duct-like structures and tubular glands	Little polymorphism, polar arrangement	≤ 5	Intensive
Grade 2, moderately differentiated	Some well-formed duct-like structures and tubular glands	Moderate polymorphism	6–10	Irregular
Grade 3, poorly differentiated	Abortive mucoepidermoid and pleomorohic structures	Marked polymorphism and increased size	> 10	Abortive

*High power field of Klöppel *et al* [48] measured 1356 µm^2

5.4.3 Local invasion (pT stage)

UICC TNM staging for pancreatic carcinoma requires assessment of the maximum size of the tumour and, in UICC TNM 7th edition,[20] whether or not tumour extends beyond the pancreas (Appendix A). The UICC pT stage correlates well with prognosis.[60] Tumour extension beyond the pancreas has been reported in up to 90% of cases[61] and correlates with poor prognosis.

[Level of evidence C.]

In the UICC TNM 7th edition,[20] pT1 and pT2 tumours are confined to the pancreas, but the pancreas has no capsule to delineate its limits, and often there are invaginations of peripancreatic fatty tissue in between lobules. For practical purposes, the boundary of the pancreas is determined by an imaginary line connecting the most peripheral acinar lobules and islets.[41] Extension beyond this into the peripancreatic fatty tissue would be considered pT3 in the UICC TNM 7th edition.[20] Since very small invasive carcinomas can be detected in MCNs and IPMNs, it has recently been proposed that such small tumours are subdivided into pT1a for those that are ≤0.5 cm, pT1b for those that are >0.5 cm and ≤1 cm, and pT1c for those that are 1–2 cm.[32,44] This proposal has now been adopted by the AJCC/UICC TNM 8th edition.[21]

There has been controversy over the UICC TNM 7th edition[20] pT staging of pancreatic carcinomas that invade the intrapancreatic common bile duct. While many would consider these to be pT3 tumours, others would consider these to be pT1/pT2 and would only consider invasion of the extrapancreatic bile duct as 'extension beyond the pancreas' and therefore pT3.[62] It is suggested that where there is no invasion of peripancreatic tissue, and invasion of the intrapancreatic bile duct is the only reason for calling a tumour pT3 in the UICC TNM 7th edition,[20] this is clearly stated in the report. Invasion of the duodenum (including the ampulla of Vater) by pancreatic carcinoma is staged as pT3, as is invasion of adherent portal vein or superior mesenteric vein, in the UICC TNM 7th edition.[20]

In the UICC TNM 8th edition,[21] the difficulties relating to invasion of the peripancreatic fat or the intrapancreatic bile duct are no longer an issue (Appendix A). Pancreas tumour staging as pT1, pT2 or pT3 in the UICC TNM 8th edition[21] is based entirely on the size of the tumour, which should be assessed by a combination of macroscopic and microscopic examination (see Section 5.2.3).

In both the 7th and 8th editions of UICC TNM,[20,21] T4 pancreatic tumours are locally advanced (involving the coeliac axis, superior mesenteric artery and/or common hepatic artery) and in the UK are considered to be unresectable.

If more than one invasive pancreatic cancer is present in the specimen, the specimen should be classified by the tumour with the highest T category, and the number of tumours should be indicated in parentheses after the T category (e.g. pT3[2]).

The UICC TNM staging systems for carcinomas of the distal extrahepatic bile duct and carcinomas of the ampulla of Vater are different from that for pancreatic carcinoma (Appendix A).[20] Controversies about the use and reproducibility of the UICC TNM 7th edition staging systems,[20] particularly for ampullary carcinomas, are discussed in the review by Adsay *et al*,[62] and have now also been addressed in the UICC TNM 8th edition.[21]

5.4.4 Perineural invasion

Perineural invasion is a histological characteristic of pancreatic carcinoma. There is a significant correlation between intrapancreatic neural invasion and extrapancreatic plexus invasion,[63] which is a major cause of local recurrence. Although the frequency of perineural invasion differs between studies, it remains a significant prognostic factor.[64-66]

[Level of evidence C.]

5.4.5 Vascular invasion

Large named-vessel involvement is a factor determining survival.[67] Radiological evidence of tumour extension into the coeliac axis (i.e. T4 tumour, Appendix A) is a contra-indication for surgery. Resection of pancreatic carcinoma infiltrating the superior mesenteric artery or hepatic artery is technically possible and performed in some European and American centres.[36] However, it is currently a contra-indication for surgery in the UK. Named-venous involvement (i.e. portal vein or superior mesenteric vein) is not a contra-indication to surgery, provided venous reconstruction is possible. Involvement is diagnosed histologically when there is a segment of vein wall attached to the resection specimen (in the superior mesenteric vein groove) that is clearly infiltrated by tumour (i.e. tumour invades into the media, with or without invasion of the intima). In a significant proportion of cases, however, there is no histological evidence of tumour invasion of the resected vessel wall, and the tethering of the vessel is caused by fibro-inflammatory changes. Controversy exists as to whether the presence or absence of microscopic tumour infiltration of the vessel wall influences survival.[36,66-68] Prognosis appears to be related to the depth of invasion of the vein wall; invasion of the media or intima (but not just the adventitia) is associated with a poor prognosis.[69]

5.4.6 Lymph node spread

The regional lymph nodes (Figure 2) **for the pancreas and ampulla of Vater** (according to UICC TNM) can be grouped into anterior pancreatoduodenal, posterior pancreatoduodenal, inferior (including the lymph nodes around the superior mesenteric vessels), common bile duct, infrapyloric (for tumours of head of pancreas or ampulla) and superior.[20] Coeliac lymph nodes (sent separately) are regional lymph nodes for tumours of the head of the pancreas only. Lymph nodes in the hilum of the spleen and tail of the pancreas are regional lymph nodes for tumours of the body and tail only.

The regional lymph nodes for the distal extrahepatic bile duct (according to UICC TNM) are along the common bile duct, common hepatic artery, back towards the coeliac trunk, posterior and anterior pancreaticoduodenal nodes, and nodes along the superior mesenteric vein and the right lateral wall of the superior mesenteric artery.[20]

In the Japan Pancreas Society (JPS) classification of lymph node stations[70] numbers are given to these groups of lymph nodes (Table 2). Lymph nodes 8 (around the common hepatic artery) and 16 (para-aortic) may be sent separately with pancreatoduodenectomy specimens.

Table 2: Japan Pancreas Society (JPS) classification of lymph node stations[70]

JPS node stations	Equivalent UICC node stations
6	Infrapyloric
8	Common hepatic artery
9	Coeliac
10	Splenic hilum
11	Superior/along splenic artery
12	Hepatoduodenal ligament (portal/bile duct)
13	Posterior pancreatoduodenal
14	Superior mesenteric vessel
16	Para-aortic
17	Anterior pancreatoduodenal
18	Inferior

Lymph nodes around the **common hepatic artery** are not specifically stated as regional for the pancreas and ampulla of Vater in the UICC TNM 7th edition,[20] but are considered to be regional lymph nodes in the AJCC TNM and JPS systems, and now in the UICC TNM 8th edition.[21] Para-aortic lymph nodes are not regional nodes, and metastases to these nodes are considered distant metastases (i.e. pM1).

The number of examined lymph nodes has been shown to influence survival; inadequate lymph node sampling results in understaging.[71,72] All of the lymph nodes in the specimen should be examined histologically. A Whipple's resection should usually yield a minimum of 15 lymph nodes from the main specimen.[5,72-74]

Direct invasion of a lymph node by the primary tumour may occur in the absence of non-contiguous nodal metastasis in up to 20% of resections. It has been suggested by some authors that direct invasion does not represent a true lymph node metastasis (i.e. via lymphatic spread) and that it is equivalent to pN0 prognostically.[75] Others have shown that direct invasion is associated with an outcome equivalent to that of a 'true' pN1 resection.[76,77] Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis (pN1) in this dataset,[20] and in the UICC TNM.[20, 21]

There is conflicting evidence on whether **extracapsular lymph node spread** in pancreatic cancer or ampullary cancer is a prognostic factor.[76,78] A very recent meta-analysis suggests that extracapsular spread is associated with a poorer prognosis, but the authors acknowledge that a standard definition is required and that lymph nodes will need to be sampled with their entire surrounding fat to allow such assessment.[79] This assessment is not currently recommended for routine practice.

Multivariate analysis has shown lymph node involvement is a negative prognostic indicator in pancreatic carcinoma.[6, 80-82]

[Level of evidence B.]

The **lymph node ratio** (the ratio of the number of lymph nodes with metastatic cancer to the total number of lymph nodes examined) is considered a more powerful prognostic marker than the overall nodal status in resected pancreatic cancer, with a lymph node ratio >20% significantly correlating with a poorer survival.[73,83,84]

[Level of evidence C.]

The **total number of positive lymph nodes** also influences survival significantly.[77] Two very recent studies of pancreatic carcinoma have shown that, with high numbers of examined lymph nodes, the number of positive lymph nodes is superior to the lymph node ratio in predicting survival in N1 cases,[85,86] and can distinguish N-categories (N0, N1, N2, N3 proposed by Strobel *et al*;[85] N0, N1, N2 proposed by Basturk *et al*[86]) that improve prognostic accuracy. The UICC TNM 8th edition has now modified the N classification for pancreatic cancer to include pN1, metastases in 1–3 regional lymph nodes, and pN2, metastases in 4 or more regional lymph nodes.[21]

Two other recent studies have found that patients with pancreatic cancer and positive para-aortic lymph nodes (lymph node group 16) have significantly worse survival than cancer patients with negative para-aortic nodes.[87,88] This has led to the suggestion that detection of a positive para-aortic lymph node at frozen section should be a contra-indication to pancreatoduodenectomy, but this has not yet been adopted into clinical practice.

In **ampullary carcinoma**, lymph node involvement and lymph node ratio are independent prognosticators.[89,90] The number of positive lymph nodes in ampullary cancer also influences survival, leading to a proposed nodal classification of N0, N1 (for 1–2 positive lymph nodes) and N2 (for 3 or more positive lymph nodes).[91,92] In extrahepatic **bile duct** carcinoma, increasing numbers of lymph node metastases are also associated with poorer survival.[93,94]

The UICC TNM 8th edition has also modified the N classifications for ampullary cancer and bile duct cancer to include pN1 and pN2 categories (Appendix A).[21] Although lymph node involvement in ampullary carcinoma is associated with a poorer prognosis, survival figures are still better than for node-positive pancreatic adenocarcinoma.

Lymph node micrometastases, detected by immunohistochemistry, are an adverse prognostic factor in many, but not all, studies.[87,95] The use of immunohistochemistry, however, is not currently recommended for routine practice.

5.4.7 Margins

The rates of microscopic margin involvement (R1) vary markedly between studies.[96] Although resection margin status is believed to be a key prognostic factor, the rates of margin involvement and local tumour recurrence are often incongruous.[5,7,8,73,97] The disparities in R1 rate and its prognostic value may be due to differences in opinion on what constitutes a resection margin, controversy over the definition of microscopic margin involvement, and lack of standardisation of the histopathology examination of pancreatoduodenectomy specimens.[23] When a fully standardised, detailed pathology examination protocol is used, microscopic margin involvement is a common finding in pancreatic carcinoma (>75%) and correlates strongly with survival.[9,25,98,99]

[Level of evidence B.]

Compared to pancreatic carcinoma, the rate of margin involvement in common bile duct carcinoma is similar, and in ampullary carcinoma is lower.[99-104] Microscopic margin involvement is more frequent in extrapancreatic bile duct carcinoma than in intrapancreatic bile duct carcinoma, and more frequently affects the periductal margin.[104] In pancreatic carcinoma, the posterior and superior mesenteric vessel margins are involved the most frequently. [9,25,98,99]

Currently, there is controversy over the adequate minimum clearance for pancreatic, common bile duct and ampullary carcinoma. While some pathologists define margin involvement when carcinoma is present at the margin (i.e. 0 mm clearance), others use the 1 mm rule adopted from margin assessment in rectal carcinoma. The growth pattern of pancreatobiliary-type cancer is infiltrative and discontinuous, unlike colorectal cancer, and there is growing evidence that a cut-off point of 0 mm to distinguish between adequate and inadequate resection is inappropriate for pancreatic cancer.[105] Studies have shown no significant difference in survival for patients with pancreatic carcinoma less than 1 mm from a margin compared to those with

direct tumour involvement of a margin.[98,106] Other studies have shown that patients with a margin clearance of less than 1.5 mm have a long-term survival equivalent to those with directly involved resection margins (i.e. 0 mm clearance).[107,108] Moreover, involvement of transection margins (requiring lymphovascular division) is associated with a significantly shorter median survival than involvement of mobilisation margins.[109] Sampling is important, and there is a significant correlation between the number of tissue blocks taken and the likelihood of an R1 classification.[25]

In this dataset, carcinoma less than 1 mm from any resection margin is considered to be incompletely excised, while further studies are awaited.

[Level of evidence D.]

Since the anterior surface of the pancreatic head is an anatomical surface, rather than a surgical margin, the less than 1 mm rule does not apply, and this surface has to be breached by tumour to be considered involved.

[Level of evidence GPP.]

When there is no direct margin involvement by tumour, it is unclear whether those rare cases in which tumour cells are found within lymph nodes, lymphovascular channels or perineural clefts at, or less than 1 mm from, a resection margin should be classed as R1 resections.[9] In the UICC TNM classification, when tumour cells are found in the lumen of a lymphovascular channel at the resection margin, without contact with the endothelium, the classification is R0.[110] When tumour is attached to the lumen of the vessel wall or invades the vessel wall at the resection margin, a classification of R1 is appropriate.[110] In the current absence of evidence about lymph node or perineural involvement at a resection margin, it is recommended that such margin involvement should be considered as incomplete excision if it is the only reason to report a case as a R1 resection, but this should be clearly stated in the report.

[Level of evidence GPP.]

5.4.8 Regression following neoadjuvant therapy

Neoadjuvant therapy is now increasingly used as an alternative to the 'surgery-first' approach in the treatment of patients with potentially resectable pancreatic cancer, especially for patients with borderline-resectable disease. Neoadjuvant therapy potentially treats early micrometastatic disease and reduces tumour volume, increasing the likelihood of a complete resection. Pathologists have an important role in assessing the degree of tumour regression and completeness of excision in the resection specimen.

Several different schemes for assessing the degree of tumour regression have been proposed, based on assessment of either the amount of tumour destruction or the amount of residual tumour.[111-115] The histological grading of extent of residual tumour has been shown to be an independent prognostic factor for overall survival in multivariate analysis.[116]

[Level of evidence C.]

The most widely used tumour regression grading systems for pancreatic cancer are those proposed by Evans *et al* and the College of American Pathologists (CAP).[112,115] The system proposed by Evans *et al*, reproduced in Table 3, assesses the percentage of tumour cell destruction.[112] This requires the pathologist to be able to recognise the presumed area of initial (pre-therapy) tumour and assess the proportion now occupied by viable neoplastic cells. The Evans *et al* system does include the option to record abundant mucin pools. Acellular mucin pools are not regarded as residual tumour, but their presence should prompt the pathologist to search carefully for viable tumour cells.

Table 3: The tumour regression grading system of Evans *et al*[112]

Grade	Extent of tumour cell destruction/residual tumour
I	Little (<10%) or no tumour destruction
2a	Destruction of 10–50% of tumour cells
2b	Destruction of 51–90% of tumour cells
3 / 3M*	Few (<10%) viable-appearing tumour cells
4 / 4M*	No viable tumour cells

* Addition of the M suffix indicates abundant residual mucin pools.

CAP (2016) proposes a four-tiered system, reproduced in Table 4, and originally applied to rectal cancer.[115] It is based upon the amount of residual tumour, but there is no specific reference to acellular mucin pools.

Table 4: The CAP tumour regression grading system[115]

Grade	Proportion of residual viable tumour
0	No viable cancer cells (complete histological response)
1	Single cells or rare small groups of cancer cells (near complete response)
2	Residual cancer with evident tumour regression, but more than single cells or rare small groups of cancer cells (partial response)
3	Extensive residual cancer with no evident tumour regression (poor or no response)

Patients with a complete response (CAP grade 0, Evans grade 4) or minimal residual disease (CAP grade 1, Evans grade 3) have better disease-free and overall survival than patients with moderate or no response, while there is no difference in disease-free survival or overall survival between CAP grades 2 and 3. This has led Chatterjee *et al* to propose a modified (three-tiered) CAP grading system (Table 5),[116] which they suggest is simpler to use and more likely to improve inter-observer agreement.[117]

Table 5: The tumour regression grading system of Chatterjee *et al* [116]

Grade	Proportion of residual viable tumour
0	No residual cancer
1	Minimal residual cancer (single cells or small groups of cancer cells, <5% residual cancer)
2	5% or more residual cancer

The CAP scheme is recommended for this dataset since it is used for other organs and is simple to use, and it is easier to recognise and assess residual tumour than to estimate what tumour has been destroyed.

[Level of evidence GPP.]

Extensive sampling of resection specimens following neoadjuvant therapy is essential. After inadequate sampling, rates of complete tumour regression as high as 10–33% have been reported, but these fall to <3% with thorough sampling.[29,116,118]

Since neoadjuvant therapy can influence tumour morphology, the **grade of tumour differentiation** of residual cancer is not reported.

Assessing **resection margin status post neo-adjuvant therapy** is difficult, and reported R1 rates range from 0–100%.[29,119] Following a response to neoadjuvant therapy, the number of tumour cells is reduced, and the distances between remaining tumour cells increases. Therefore, the improved outcome of tumours greater than 1 mm from a given resection margin, compared to those less than 1 mm away, in the non-neoadjuvant therapy setting, may not be applicable in this circumstance.[29] The appropriate distance for a clear margin following neoadjuvant therapy is yet to be determined, but 5 mm has been proposed by Liu *et al*.[120] The prognostic significance of acellular mucin pools at resection margins is also unknown, but does suggest that, prior to neoadjuvant therapy, tumour is likely to have extended beyond the surgical resection field. This has led to the proposal in colorectal cancer management that the presence of mucin at the margin of a neoadjuvant resection is an indicator for further surgery (whenever possible) if detected at frozen section.[121] It seems prudent to adopt this approach for post-neoadjuvant therapy pancreatic resection margin assessment at frozen section. When assessing margins in the resection specimen following neoadjuvant therapy, it is suggested that the distance between tumour cells and the nearest resection margin is recorded in the final report. When acellular mucin pools are present at, or close to, the margin(s), this should also be noted in the report.

[Level of evidence GPP.]

For **tumour staging following pre-operative therapy**, only the presence of tumour cells in the resection specimen is used to determine the stage. Fibrosis, haemorrhage, necrosis, inflammation and acellular mucin are ignored. Cases with complete regression are therefore recorded as ypT0 ypN0.

5.4.9 Histologically confirmed distant metastatic disease

The presence of histologically confirmed distant metastases (pM1) and their site should be recorded.

Metastases to the liver, peritoneum, omentum or extra-abdominal sites are contra-indications for resection in pancreatic ductal adenocarcinoma.[122]

5.4.10 Background abnormalities

As stated in section 5.2.2, the presence of microscopic precursor lesions (e.g. ampullary adenoma, flat dysplasia) may be helpful in determining the primary origin of a tumour.

PanIN[39] is the most common precursor to pancreatic ductal adenocarcinoma but is a frequent finding in all pancreatic resections, including those for non-neoplastic disease.[39,40] The presence of an underlying IPMN or MCN should always be recorded.[44,123]

[Level of evidence C.]

6 Non-core data items

6.1 Macroscopic

- Specimen measurements for each organ included
- Stent in place
- Other organs.

6.2 Microscopic

Small vessel invasion is common in resections for pancreatic cancer and is considered by some to be an adverse prognostic factor.[124] Detection may be influenced by the number of tumour blocks sampled, and the use of additional stains, such as elastic van Gieson. Microvascular invasion may also be mistaken for PanIN when invasive tumour cells replace the endothelial cells, such that the vascular lumen is surrounded by neoplastic cells. The presence of smooth muscle around such a structure will confirm that it is vascular invasion.[125]

6.3 Other markers

A number of molecular markers, such as *k-ras*, *SMAD4, S100A6* and *cyclin E*, have prognostic value following resection, but use of such molecular or immunohistochemical studies in routine practice is currently not justified.[26,27,126–129]

7 Diagnostic coding

Tumours should be coded according to the SNOMED system (see Appendices B and C).

8 Pathological staging

Multivariate analysis shows that tumour stage is the most significant factor in predicting long-term survival in pancreatic carcinoma.[60] The UICC TNM classification obtained from the histopathological data can be converted to a stage grouping,[20] but full clinical data will need to be taken into account before the final stage can be determined.

9 Reporting of diagnostic biopsy specimens

Pre-operative diagnosis is usually made on cytology (including fine needle biopsy) in combination with imaging. Ampullary biopsies may be taken at upper endoscopy. Liver biopsies may be taken for exclusion of metastatic disease, and intra-operative pancreas biopsies may be taken to establish or confirm the diagnosis. Distinction between metastasis and benign biliary lesions in the liver, and distinction between pancreatic adenocarcinoma and chronic pancreatitis, are discussed in section 10 below.

10 Reporting of frozen sections

Histological confirmation of the primary diagnosis, assessment of the presence or absence of carcinoma or IPMN at the pancreatic transection margin, the presence of carcinoma at the bile duct margin, or histological confirmation of a potentially metastatic nodule in the liver, the peritoneum or a lymph node are the most common indications for intraoperative frozen section diagnosis.[130,131]

Distinction between a liver metastasis and a bile duct hamartoma or bile duct adenoma (peribiliary gland hamartoma) may be problematic. The presence of necrosis, desmoplastic stroma, irregularity of ducts, apoptosis, cellular atypia or mitoses in ducts all favour a diagnosis of malignancy,[131] as do extension of atypical glands into the adjacent liver or along portal tracts.

[Level of evidence GPP.]

The distinction between pancreatitis and adenocarcinoma in the pancreas may also be difficult on frozen section, because of cautery or freezing artefacts, or the distortion and reactive nuclear atypia in small residual ductules in chronic pancreatitis. Often a low-power microscopic view is most useful in order to appreciate the lack of a lobular distribution of the ducts and the irregularity of duct outline in adenocarcinoma. In chronic pancreatitis, the lobular architecture is preserved, the intralobular stroma is paler than the dense collagen that surrounds the lobules, and there is no cellular desmoplastic stroma. In the normal pancreas, ducts do not run alongside muscular blood vessels. Therefore, the presence of an atypical duct adjacent to a muscular blood vessel should be considered suspicious for adenocarcinoma.

[Level of evidence GPP.]

The distinction between adenocarcinoma and chronic pancreatitis on the basis of ductular architecture and cytological atypia can be difficult. The major and minor criteria established by Hyland *et al* in 1981[132] for distinguishing neoplastic from non-neoplastic ducts on frozen section are equally applicable to formalin-fixed, paraffin-embedded tissue.[131,132]

Assessment of the pancreatic transection (neck) margin or the bile duct margin for invasive carcinoma should include microscopic examination of the peripancreatic or periductal connective tissue (as well as the pancreas and bile duct), since this may be the only site of tumour infiltration.

It has been shown that PanIN-3 at the transection margin (in the absence of invasive carcinoma) does not influence outcome in patients with pancreatic ductal adenocarcinoma.[133] This reflects the fact that survival after resection for pancreatic carcinoma is generally too short for PanIN to become prognostically significant.[131] However, in patients with a small invasive carcinoma without evidence of lymph node metastases, or in those undergoing resection for benign disease, the presence of PanIN-3 at the transection margin may justify consideration of further resection, and this should be mentioned in the intra-operative report.

Frozen section of the transection margin may be used to determine whether an IPMN (with or without associated invasive carcinoma) is completely excised and to check if duct dilatation is due to tumour involvement or is secondary to obstruction.[131,134] Frozen section in IPMN, however, does have limitations, particularly because there may be erosion of the duct epithelium, duct inflammation and reactive epithelial atypia. The duct epithelium may be denuded, in which case deeper levels should be cut from the tissue block and/or further tissue samples should be requested from the surgeon. In the absence of any duct epithelium for assessment, the pathologist cannot state whether (non-invasive) neoplasm is present at the margin or not.[131]

11 Criteria for audit of the dataset

It is recommended that multidisciplinary teams and/or pathology departments audit their pathology reports at regular intervals (perhaps yearly) to ensure the completeness of data within pathology reports. As regards the standard of pathology, there is currently little evidence on the frequencies with which important adverse prognostic features are found by individual pathologists. It has been reported that the mean harvest of lymph nodes from a Whipple's resection should be at least 15 nodes[5,71-73] and that the number of retrieved lymph nodes does

influence survival.[71,72,90] Therefore, to evaluate the standard of pathology dissection, it is recommended that in a series of Whipple's resections for carcinoma, the mean number of lymph nodes examined should be 15. As more evidence accumulates, it may be possible to adjust this level and to introduce other outcome measures for pathology.

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Appendix A UICC TNM histopathological classification[20,21]

UICC TNM 7th edition[20] (use until 31 December 2017)

General	TX	Primary tumour cannot be assessed histologically
	T0	No histological evidence of primary tumour
	Tis	Carcinoma *in situ*
	NX	Regional lymph nodes cannot be assessed histologically
	N0	No regional lymph node metastasis histologically
	N1	Regional lymph node metastasis histologically*
	M1	Distant metastasis microscopically confirmed
Pancreas	T1	Tumour limited to the pancreas, 20 mm or less in greatest dimension
	T2	Tumour limited to the pancreas, more than 20 mm in greatest dimension
	T3	Tumour extends beyond pancreas, but without involvement of coeliac axis or superior mesenteric artery
	T4	Tumour involves coeliac axis or superior mesenteric artery
Ampulla of Vater	T1	Tumour limited to ampulla of Vater or sphincter of Oddi
	T2	Tumour invades duodenal wall
	T3	Tumour invades pancreas
	T4	Tumour invades peripancreatic soft tissues, or other adjacent organs or structures
Distal extrahepatic bile duct	T1	Tumour confined to the bile duct
	T2	Tumour invades beyond the wall of the bile duct
	T3	Tumour invades the gall bladder, liver, pancreas, duodenum, or other adjacent organs
	T4	Tumour involves the coeliac axis or the superior mesenteric artery

*For regional lymph nodes, see Section 5.4.6

UICC TNM 8th edition[21] (use from 1 January 2018)

General	TX	Primary tumour cannot be assessed histologically
	T0	No histological evidence of primary tumour
	Tis	Carcinoma *in situ*
	NX	Regional lymph nodes cannot be assessed histologically
	N0	No regional lymph node metastasis histologically
	M1	Distant metastasis microscopically confirmed
Pancreas	T1	Tumour 2 cm or less in greatest dimension
	T1a	Tumour 0.5 cm or less in greatest dimension
	T1b	Tumour greater than 0.5 cm and less than 1 cm in greatest dimension
	T1c	Tumour greater than 1 cm but no more than 2 cm in greatest dimension
	T2	Tumour more than 2 cm but no more than 4 cm in greatest dimension
	T3	Tumour more than 4 cm in greatest dimension
	T4	Tumour involves coeliac axis, superior mesenteric artery and/or common hepatic artery
	N1	Metastases in 1 to 3 regional lymph nodes histologically *
	N2	Metastases in 4 or more regional lymph nodes histologically *
Ampulla of Vater	T1a	Tumour limited to ampulla of Vater or sphincter of Oddi
	T1b	Tumour invades beyond the sphincter of Oddi (perisphincteric invasion) and/or into the duodenal submucosa
	T2	Tumour invades the muscularis propria of the duodenum
	T3	Tumour invades pancreas
	T3a	Tumour invades 0.5 cm or less into the pancreas
	T3b	Tumour invades more than 0.5 cm into the pancreas or extends into peripancreatic tissue or duodenal serosa but without involvement of the coeliac axis or superior mesenteric artery
	T4	Tumour with vascular involvement of the superior mesenteric artery, coeliac axis or common hepatic artery
	N1	Metastasis in 1 or 2 regional lymph nodes histologically *
	N2	Metastasis in 3 or more regional lymph nodes histologically *

Distal extrahepatic bile duct	T1	Tumour invades bile duct wall to a depth less than 5 mm
	T2	Tumour invades bile duct wall to a depth of 5 mm up to 12 mm
	T3	Tumour invades bile duct wall to a depth of more than 12 mm
	T4	Tumour involves coeliac axis, superior mesenteric artery and/or common hepatic artery
	N1	Metastases in 1 to 3 regional lymph nodes histologically *
	N2	Metastases in 4 or more regional lymph nodes histologically *

*For regional lymph nodes, see Section 5.4.6

Appendix B ICD-10 and SNOMED ‘T’ coding for tumour site

Tumour site	ICD-10	SNOMED code (version 2/ version 3.5)	SNOMED CT terminology	SNOMED CT code
Head of pancreas	C25.0	T-59100/T-65100	Structure of head of pancreas (body structure)	64163001
Body of pancreas	C25.1	T-59200/T-65200	Structure of body of pancreas (body structure)	40133006
Tail of pancreas	C25.2	T-59300/T-65300	Structure of tail of pancreas (body structure)	73239005
Whole pancreas	C25.8	T-59000/T-65000	Pancreatic structure (body structure)	15776009
Extrahepatic bile ducts	C24.0	T-58000/T-64000	Extrahepatic duct structure (body structure)	16014003
Ampulla of Vater	C24.1	T-58700/T-64700	Structure of ampulla of Vater (body structure)	67109009

Appendix C WHO classification of malignant exocrine pancreatic tumours[19] and SNOMED 'M' codes

Morphological codes	SNOMED code	SNOMED CT terminology	SNOMED CT code
Ductal adenocarcinoma	M8500/3	Infiltrating duct carcinoma (morphologic abnormality)	82711006
Adenosquamous carcinoma	M8560/3	Adenosquamous carcinoma (morphologic abnormality)	59367005
Colloid carcinoma (mucinous non-cystic carcinoma)	M8480/3	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Hepatoid carcinoma	M8576/3	Hepatoid adenocarcinoma (morphologic abnormality)	128706007
Medullary carcinoma	M8510/3	Medullary carcinoma (morphologic abnormality)	32913002
Signet-ring cell carcinoma	M8490/3	Signet ring cell carcinoma (morphologic abnormality)	87737001
Undifferentiated (anaplastic or sarcomatoid) carcinoma	M8020/3	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Undifferentiated carcinoma with osteoclast-like giant cells	M8035/3	Carcinoma with osteoclast-like giant cells (morphologic abnormality)	128631001
Acinar cell carcinoma	M8550/3	Acinar cell carcinoma (morphologic abnormality)	45410002
Acinar cell cystadenocarcinoma	M8551/3	Acinar cell cystadenocarcinoma (morphologic abnormality)	128703004
Intraductal papillary mucinous neoplasm with an associated invasive carcinoma	M8453/3	Intraductal papillary-mucinous carcinoma, invasive (morphologic abnormality)	128692006
Mixed acinar-ductal carcinoma	M8552/3	Mixed acinar-ductal carcinoma (morphologic abnormality)	450897002
Mixed acinar-neuroendocrine carcinoma	M8154/3	Mixed islet cell and exocrine adenocarcinoma (morphologic abnormality)	999000

Morphological codes (continued)	SNOMED code	SNOMED CT terminology	SNOMED CT code
Mucinous cystic neoplasm with an associated invasive carcinoma	M8470/3	Mucinous cystadenocarcinoma (morphologic abnormality)	79143006
Pancreatoblastoma	M8971/3	Pancreatoblastoma (morphologic abnormality)	53618008
Serous cystadenocarcinoma	M8441/3	Serous cystadenocarcinoma (morphologic abnormality)	90725004
Solid-pseudopapillary neoplasm	M8452/3	Solid pseudopapillary carcinoma (morphologic abnormality)	116061001

Procedure codes (P)

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 WHO classification of carcinomas of the ampulla of Vater and extrahepatic bile ducts[19] and SNOMED 'M' codes

WHO classification of carcinomas of the ampulla of Vater[10]

Morphological codes	SNOMED code	SNOMED CT terminology	SNOMED CT code
Adenocarcinoma	M8140/3	Adenocarcinoma, no subtype (morphologic abnormality)	35917007
Invasive intestinal type	M8144/3	Adenocarcinoma, intestinal type (morphologic abnormality)	25190001
Pancreatobiliary type	M8163/3	Pancreatobiliary-type carcinoma (morphologic abnormality)	450894009
Adenosquamous carcinoma	M8560/3	Adenosquamous carcinoma (morphologic abnormality)	59367005
Clear cell adenocarcinoma	M8310/3	Clear cell adenocarcinoma (morphologic abnormality)	30546008
Hepatoid adenocarcinoma	M8576/3	Hepatoid adenocarcinoma (morphologic abnormality)	128706007
Invasive papillary adenocarcinoma	M8260/3	Papillary adenocarcinoma (morphologic abnormality)	4797003
Mucinous adenocarcinoma	M8480/3	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Signet ring cell carcinoma	M8490/3	Signet ring cell carcinoma (morphologic abnormality)	87737001
Squamous cell carcinoma	M8070/3	Squamous cell carcinoma, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	28899001
Undifferentiated carcinoma	M8020/3	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Undifferentiated carcinoma with osteoclast-like giant cells	M8035/3	Carcinoma with osteoclast-like giant cells (morphologic abnormality)	128631001

WHO classification of carcinomas of the extrahepatic bile ducts[19]

Morphological codes	SNOMED code	SNOMED CT terminology	SNOMED CT code
Adenocarcinoma	M8140/3	Adenocarcinoma, no subtype (morphologic abnormality)	35917007
Adenocarcinoma, biliary type	M8140/3	Adenocarcinoma, no subtype (morphologic abnormality)	35917007
Adenocarcinoma, gastric foveolar type	M8140/3	Well differentiated adenocarcinoma, gastric foveolar type (morphologic abnormality)	388676006
Adenocarcinoma, intestinal type	M8144/3	Adenocarcinoma, intestinal type (morphologic abnormality)	25190001
Clear cell carcinoma	M8310/3	Clear cell adenocarcinoma (morphologic abnormality)	30546008
Mucinous carcinoma	M8480/3	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Signet ring cell carcinoma	M8490/3	Signet ring cell carcinoma (morphologic abnormality)	87737001
Adenosquamous carcinoma	M8560/3	Adenosquamous carcinoma (morphologic abnormality)	59367005
Intraductal (bile duct) papillary neoplasm with an associated invasive carcinoma	M8503/3	Intraductal papillary adenocarcinoma with invasion (morphologic abnormality	64524002
Squamous cell carcinoma	M8070/3	Squamous cell carcinoma, no ICDO subtype (morphologic abnormality)	28899001
Undifferentiated carcinoma	M8020/3	Carcinoma, undifferentiated (morphologic abnormality)	38549000

Appendix E Reporting proforma for pancreatic carcinoma (use until 31 December 2017)

Surname: ..... Forename(s): ..... .Date of birth: ....…..... Sex:……

Hospital: .....…… Hospital no: .....…….. NHS no: .....…….…..…..

Date of surgery: ……..... Date of report authorisation:…….... Report number:: ....…….…….....

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

Specimen type †

Kausch-Whipple's pancreatoduodenectomy (PD) □ Pylorus preserving PD □

Total pancreatectomy□ Subtotal PD □ Left pancreatectomy □

Other □ (specify) …….

Gross description

Site of tumour ……..…… Maximum tumour diameter †……..…… mm

Macroscopic margin involvement: None □ Yes (R2) □ (which margin(s))……..

Identifiable named vessel(s) None □ Yes □ (which vessel)……

Background pathology None □ Yes □ (specify)……

Microscopic description

Histological type of tumour †**:** Ductal adenocarcinoma □ Other □ (specify)……..……..

Variant of PDAC (specify): ……..

Differentiation †: Not applicable *(post neoadjuvant therapy)* □

Well (Grade 1) □ Moderate (Grade 2) □ Poor (Grade 3) □

Asessment of size †**:** macroscopic appearances confirmed □
measured histologically □ …… mm

Maximum extent of invasion (pT) †**:**

pT0: No residual tumour □

pTis: Carcinoma *in situ* □

pT1: Tumour limited to the pancreas, 20 mm or less in greatest dimension □

pT2: Tumour limited to the pancreas, more than 20 mm in greatest dimension □

pT3: Tumour extends beyond pancreas but without involvement of coeliac axis / SMA □

pT4: Tumour involves coeliac axis or superior mesenteric artery (SMA) □

Response to neoadjuvant therapy †**:** Not applicable □

CAP Grade 0 (No residual tumour) □ CAP Grade 1 (Moderate / marked response) □

CAP Grade 2 (Minimal response) □ CAP Grade 3 (Poor / no response) □

Margin status †	**Involved**	**Not involved**	**Not sampled**	**Not applicable**	**Clearance***
Gastric transection margin:	□	□	□	□	..... mm
Duodenal transection margin:	□	□	□	□	..... mm
Pancreatic transection margin:	□	□	□	□	..... mm
Bile duct transection margin:	□	□	□	□	..... mm
SMV/SMA dissection margin:	□	□	□	□	..... mm
Posterior dissection margin:	□	□	□	□	..... mm
Anterior pancreatic surface:	□	□	□	□	..... mm

**Specify clearance of closest margin(s)*

Named vessel status: □ □ □ □

If named vessel involved, specify ……..

Perineural invasion: Present □ Not identified □

Regional lymph node status (pN)

Total number of nodes † ……

Number of involved nodes † ……

N stage †: pN0 (Regional lymph nodes not involved) □ pN1 (Regional lymph nodes involved) □

Distant metastasis (pM) †

Distant metastasis confirmed No□ Yes (pM1) □ specify site(s)……

Background pathology: Intraductal papillary mucinous neoplasm (IPMN) □

Mucinous cystic neoplasm (MCN) □ Other □……..

Comments

Pathological staging: (y)pT…. (y)pN…. (y)pM….. UICC Version **7**

Resection status †: Complete at all margins (R0) □ Incomplete microscopic (R1) □ macroscopic (R2) □

Signature:…… Date:…… SNOMED codes: T…… / M…….

† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7

Appendix F Reporting proforma for pancreatic carcinoma (use from 1 January 2018)

Surname: ..... Forename(s): ..... .Date of birth: ....…..... Sex:……

Hospital: .....…… Hospital no: .....…….. NHS no: .....…….….....

Date of surgery: ……..... Date of report authorisation:…….... Report number:: ....…….…….....

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

Specimen type †

Kausch-Whipple's pancreatoduodenectomy (PD) □ Pylorus preserving PD □

Total pancreatectomy□ Subtotal PD □ Left pancreatectomy □

Other □ (specify) …….

Gross description

Site of tumour ……..…… Maximum tumour diameter †……..…… mm

Macroscopic margin involvement: None □ Yes (R2) □ (which margin(s))……..

Identifiable named vessel(s) None □ Yes □ (which vessel)……

Background pathology None □ Yes □ (specify)……

Microscopic description

Histological type of tumour †**:** Ductal adenocarcinoma □ Other □ (specify)……..……..

Variant of PDAC (specify): ……..

Differentiation †: Not applicable *(post neoadjuvant therapy)* □

Well (Grade 1) □ Moderate (Grade 2) □ Poor (Grade 3) □

Asessment of size †**:** macroscopic appearances confirmed □
measured histologically □ …… mm

Maximum extent of invasion (pT) †**:**

pT0: No residual tumour □

pTis: Carcinoma *in situ* □

pT1a: Tumour 5 mm or less in greatest dimension □

pT1b: Tumour greater than 5 mm and less than 10 mm in greatest dimension □

pT1c: Tumour greater than 10 mm but no more than 20 mm in greatest dimension □

pT2: Tumour more than 20 mm but no more than 40 mm in greatest dimension □

pT3: Tumour more than 40 mm in greatest dimension □

pT4: Tumour involves coeliac axis, superior mesenteric artery and/or common hepatic artery □

Response to neoadjuvant therapy †**:** Not applicable □

CAP Grade 0 (No residual tumour) □ CAP Grade 1 (Moderate / marked response) □

CAP Grade 2 (Minimal response) □ CAP Grade 3 (Poor / no response) □

Margin status †	**Involved**	**Not involved**	**Not sampled**	**Not applicable**	**Clearance***
Gastric transection margin:	□	□	□	□	..... mm
Duodenal transection margin:	□	□	□	□	..... mm
Pancreatic transection margin:	□	□	□	□	..... mm
Bile duct transection margin:	□	□	□	□	..... mm
SMV/SMA dissection margin:	□	□	□	□	..... mm
Posterior dissection margin:	□	□	□	□	..... mm
Anterior pancreatic surface:	□	□	□	□	..... mm

**Specify clearance of closest margin(s)*

Named vessel status: □ □ □ □

If named vessel involved, specify ……..

Perineural invasion: Present □ Not identified □

Regional lymph node status (pN)

Total number of nodes † ……

Number of involved nodes † ……

N stage †: pN0 (Regional lymph nodes not involved) □

pN1 (Metastases in 1 to 3 regional lymph nodes) □

pN2 (Metastases in 4 or more regional lymph nodes) □

Distant metastasis (pM) †

Distant metastasis confirmed No□ Yes (pM1) □ specify site(s)……

Background pathology: Intraductal papillary mucinous neoplasm (IPMN) □

Mucinous cystic neoplasm (MCN) □ Other □……..

Comments

Pathological staging: (y)pT…. (y)pN…. (y)pM….. UICC Version **8**

Resection status †: Complete at all margins (R0) □ Incomplete microscopic (R1) □ macroscopic (R2) □

Signature:…… Date:…… SNOMED codes: T…… / M…….

† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7

Appendix G Reporting proforma for ampulla of Vater carcinoma (use until 31 December 2017)

Surname: ..... Forename(s): ..... .Date of birth: ....…..... Sex:……

Hospital: .....…… Hospital no: .....…….. NHS no: .....…….….....

Date of surgery: ……..... Date of report authorisation:…….…..... Report number:: ....…….…….....

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

Specimen type †

Kausch-Whipple's pancreatoduodenectomy (PD) □ Pylorus preserving PD □

Other □ (specify)

Gross description

Maximum tumour diameter †……..…… mm

Macroscopic margin involvement: None □ Yes (R2) □ (which margin(s))……

Identifiable named vessel(s) None □ Yes □ (which vessel)…….……

Background pathology None □ Yes □ (specify)……..……

Microscopic description

Type of tumour †**:** Adenocarcinoma □ Other □ (specify) ……..……..

Phenotype †**:** Pancreaticobiliary □ Intestinal □ Other □ (specify) ……

Differentiation †: Not applicable *(e.g. post neoadjuvant therapy)* □

Well (Grade 1) □ Moderate (Grade 2) □ Poor (Grade 3) □

Maximum depth of invasion (pT) †**:**

pT0: No residual tumour □

pTis: Carcinoma *in situ* □

pT1: Tumour limited to ampulla of Vater or sphincter of Oddi □

pT2: Tumour invades duodenal wall □

pT3: Tumour invades pancreas □

pT4: Tumour invades peripancreatic soft tissues / adjacent organs or structures □

Response to neoadjuvant therapy †**:** Not applicable □

CAP Grade 0 (No residual tumour) □ CAP Grade 1 (Moderate / marked response) □

CAP Grade 2 (Minimal response) □ CAP Grade 3 (Poor / no response) □

Margin status †	**Involved**	**Not involved**	**Not sampled**	**Not applicable**	**Clearance***
Gastric transection margin:	□	□	□	□	…… mm
Duodenal transection margin:	□	□	□	□	…… mm
Pancreatic transection margin:	□	□	□	□	…… mm
Bile duct transection margin:	□	□	□	□	…… mm
SMV/SMA dissection margin:	□	□	□	□	…… mm
Posterior dissection margin:	□	□	□	□	…… mm
Anterior pancreatic surface:	□	□	□	□	…… mm

**Specify clearance of closest margin(s)*

Named vessel status: □ □ □ □

If named vessel involved, specify ……..

Perineural invasion: Present □ Not identified □

Regional lymph node status (pN)

Total number of nodes † ……

Number of involved nodes † ……

N stage †: pN0 (Regional lymph nodes not involved) □ pN1 (Regional lymph nodes involved) □

Distant metastasis (pM)

Distant metastasis confirmed † No □ Yes (pM1) □ Specify site(s)……

Background pathology: Ampullary adenoma □ Other……..

Comments

Pathological staging: (y)pT…. (y)pN…. (y)pM….. UICC Version **7**

Resection status †:
Complete at all margins (R0) □ Incomplete microscopic (R1) □ macroscopic (R2) □

Signature:…… Date:…… SNOMED codes: T…… / M……..

† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7

Appendix H Reporting proforma for ampulla of Vater carcinoma (use from 1 January 2018)

Surname: ..... Forename(s): ..... .Date of birth: ....…..... Sex:……

Hospital: .....…… Hospital no: .....…….. NHS no: .....…….….....

Date of surgery: ……..... Date of report authorisation:…….…..... Report number:: ....…….…….....

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

Specimen type †

Kausch-Whipple's pancreatoduodenectomy (PD) □ Pylorus preserving PD □

Other □ (specify)

Gross description

Maximum tumour diameter †……..…… mm

Macroscopic margin involvement: None □ Yes (R2) □ (which margin(s))……

Identifiable named vessel(s) None □ Yes □ (which vessel)…….……

Background pathology None □ Yes □ (specify)……..……

Microscopic description

Type of tumour †**:** Adenocarcinoma □ Other □ (specify) ……..……..

Phenotype †**:** Pancreaticobiliary □ Intestinal □

Other □ (specify) ……

Differentiation †: Not applicable *(e.g. post neoadjuvant therapy)* □

Well (Grade 1) □ Moderate (Grade 2) □ Poor (Grade 3) □

Maximum depth of invasion (pT) †**:**

pT0: No residual tumour □

pTis: Carcinoma *in situ* □

pT1a: Tumour limited to ampulla of Vater or sphincter of Oddi □

pT1b: Tumour invades beyond the sphincter of Oddi and/or into the duodenal submucosa □

pT2: Tumour invades the muscularis propria of the duodenum □

pT3a: Tumour invades 5 mm or less into the pancreas □

pT3b: Tumour invades more than 5 mm into the pancreas or extends into peripancreatic tissue or duodenal serosa but without involvement of the coeliac axis or the superior mesenteric artery □

pT4: Tumour with vascular involvement of the superior mesenteric artery, coeliac axis, or common hepatic artery □

Response to neoadjuvant therapy †: Not applicable □

CAP Grade 0 (No residual tumour) □ CAP Grade 1 (Moderate / marked response) □

CAP Grade 2 (Minimal response) □ CAP Grade 3 (Poor / no response) □

Margin status †	**Involved**	**Not involved**	**Not sampled**	**Not applicable**	**Clearance***
Gastric transection margin:	□	□	□	□	..... mm
Duodenal transection margin:	□	□	□	□	..... mm
Pancreatic transection margin:	□	□	□	□	..... mm
Bile duct transection margin:	□	□	□	□	..... mm
SMV/SMA dissection margin:	□	□	□	□	..... mm
Posterior dissection margin:	□	□	□	□	..... mm
Anterior pancreatic surface:	□	□	□	□	..... mm
					**Specify clearance of closest margin(s)*
Named vessel status:	□	□	□	□	

If named vessel involved, specify ……..

Perineural invasion: Present □ Not identified □

Regional lymph node status (pN)

Total number of nodes † ……

Number of involved nodes † ……

N stage †: pN0 (Regional lymph nodes not involved) □

pN1 (Metastases in 1 or 2 regional lymph nodes) □

pN2 (Metastases in 3 or more regional lymph nodes) □

Distant metastasis (pM)

Distant metastasis confirmed † No □ Yes (pM1) □ specify site(s)……

Background pathology: Ampullary adenoma □ Other……..

Comments

Pathological staging: (y)pT…. (y)pN…. (y)pM….. UICC Version **8**

Resection status †: Complete at all margins (R0) □ Incomplete microscopic (R1) □ macroscopic (R2) □

Signature:…… Date:…… SNOMED codes: T…… / M……..

† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7

Appendix I Reporting proforma for common bile duct carcinoma (use until 31 December 2017)

Surname: ..... Forename(s): ..... Date of birth: ....…..... Sex:……

Hospital: .....…… Hospital no: .....…….. NHS no: .....…….…..…..

Date of surgery: ……..... Date of report authorisation:…….…..... Report number:: ....…….…….....

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

Specimen type †

Kausch-Whipple's pancreatoduodenectomy (PD) □ Pylorus preserving PD □

Other □ (specify) **……**

Gross description

Site of tumour ……..…… Maximum tumour diameter † …… mm

Macroscopic margin involvement: None □ Yes (R2) □ (which margin(s))……

Identifiable named vessel(s) None □ Yes □ (which vessel)……..…

Background pathology None □ Yes □ (specify)……

Microscopic description

Type of tumour †**:** Adenocarcinoma □ Other □ (specify) ……..……..

Differentiation †: Not applicable *(e.g. post neoadjuvant therapy)* □

Well (Grade 1) □ Moderate (Grade 2) □ Poor (Grade 3) □

Maximum depth of invasion (pT) †**:**

T0: No residual tumour □

Tis: Carcinoma *in situ* □

T1: Tumour confined to the bile duct □

T2: Tumour invades beyond the wall of the bile duct □

T3: Tumour invades gall bladder/liver/pancreas/duodenum/other adjacent organs □

T4: Tumour involves the coeliac axis or the superior mesenteric artery □

Response to neoadjuvant therapy †**:** Not applicable □

CAP Grade 0 (No residual tumour) □ CAP Grade 1 (Moderate / marked response) □

CAP Grade 2 (Minimal response) □ CAP Grade 3 (Poor / no response) □

Margin status †	**Involved**	**Not involved**	**Not sampled**	**Not applicable**	**Clearance***
Gastric transection margin:	□	□	□	□	…..… mm
Duodenal transection margin:	□	□	□	□	..…. mm
Pancreatic transection margin:	□	□	□	□	…..… mm
Bile duct transection margin:	□	□	□	□	…..… mm
SMV/SMA dissection margin:	□	□	□	□	…..… mm
Posterior dissection margin:	□	□	□	□	…..… mm
Anterior pancreatic surface:	□	□	□	□	…..… mm

**Specify clearance of closest margin(s)*

Named vessel status: □ □ □ □

If named vessel involved, specify ……..

Perineural invasion: Present □ Not identified □

Regional lymph node status (pN)

Total number of nodes † ……

Number of involved nodes † ……

N stage †: pN0 (Regional lymph nodes not involved) □ pN1 (Regional lymph nodes involved) □

Distant metastasis (pM)

Distant metastasis confirmed † No □ Yes (pM1) □ Specify site(s)……

Background pathology: Biliary IPMN □ Bil-IN □ Other……..

Comments

Pathological staging: (y)pT…. (y)pN…. (y)pM….. UICC Version **7**

Resection status †: Complete at all margins (R0) □ Incomplete microscopic (R1) □ Macroscopic (R2) □

Signature:…….… Date:…… SNOMED codes: T…… / M……..

† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7

Appendix J Reporting proforma for common bile duct carcinoma (use from 1 January 2018)

Surname: ..... Forename(s): ..... Date of birth: ....…..... Sex:……

Hospital: .....…… Hospital no: .....…….. NHS no: .....…….…..…..

Date of surgery: ……..... Date of report authorisation:…….…..... Report number:: ....…….…….....

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

Specimen type †

Kausch-Whipple's pancreatoduodenectomy (PD) □ Pylorus preserving PD □

Other □ (specify) **……**

Gross description

Site of tumour ……..…… Maximum tumour diameter † …… mm

Macroscopic margin involvement: None □ Yes (R2) □ (which margin(s))……

Identifiable named vessel(s) None □ Yes □ (which vessel)……..…

Background pathology None □ Yes □ (specify)……

Microscopic description

Type of tumour †**:** Adenocarcinoma □ Other □(specify) ……..……..

Differentiation †: Not applicable *(e.g. post neoadjuvant therapy)* □

Well (Grade 1) □ Moderate (Grade 2) □ Poor (Grade 3) □

Maximum depth of invasion (pT) †**:**

T0: No residual tumour □

Tis: Carcinoma *in situ* □

T1: Tumour invades bile duct wall to a depth less than 5 mm □

T2: Tumour invades bile duct wall to a depth of 5 mm up to 12 mm □

T3: Tumour invades bile duct wall to a depth of more than 12 mm □

T4: Tumour involves the coeliac axis, the superior mesenteric artery and/or the common hepatic artery □

Response to neoadjuvant therapy †**:** Not applicable □

CAP Grade 0 (No residual tumour) □ CAP Grade 1 (Moderate / marked response) □

CAP Grade 2 (Minimal response) □ CAP Grade 3 (Poor / no response) □

Margin status †	**Involved**	**Not involved**	**Not sampled**	**Not applicable**	**Clearance***
Gastric transection margin:	□	□	□	□	..... mm
Duodenal transection margin:	□	□	□	□	..... mm
Pancreatic transection margin:	□	□	□	□	..... mm
Bile duct transection margin:	□	□	□	□	..... mm
SMV/SMA dissection margin:	□	□	□	□	..... mm
Posterior dissection margin:	□	□	□	□	..... mm
Anterior pancreatic surface:	□	□	□	□	..... mm

**Specify clearance of closest margin(s)*

Named vessel status: □ □ □ □

If named vessel involved, specify ……..

Perineural invasion: Present □ Not identified □

Regional lymph node status (pN)

Total number of nodes † ……

Number of involved nodes † ……

N stage †: pN0 (Regional lymph nodes not involved) □

pN1 (Metastases in 1 to 3 regional lymph nodes) □

pN2 (Metastases in 4 or more regional lymph nodes) □

Distant metastasis (pM)

Distant metastasis confirmed † No □ Yes (pM1) □ Specify site(s)……

Background pathology: Biliary IPMN □ Bil-IN □ Other……..

Comments

Pathological staging: (y)pT…. (y)pN…. (y)pM….. UICC Version **8**

Resection status †: Complete at all margins (R0) □ Incomplete microscopic (R1) □ Macroscopic (R2) □

Signature:…… Date:…… SNOMED codes: T…… / M……..

† Data items which are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7

Appendix K Proforma for pancreatic carcinoma in list format

Element name	Values	Implementation notes
Specimen type	Single selection value list: • Kausch -Whipple's pancreatoduodenectomy (PD) • pylorus preserving PD • total pancreatectomy • subtotal PD • left pancreatectomy • other	
Specimen type, specify	Free text	Only applicable if 'Specimen type: other' selected
Site of tumour	Free text	
Maximum tumour diameter	Size in mm	
Macroscopic margin involvement	Single selection value list: • None • Yes (R2)	
Macroscopic margin involvement, which margin	Free text	Only applicable if 'Macroscopic margin involvement: yes' selected
Identifiable named vessel(s)	Single selection value list: • None • Yes	
Identifiable named vessel(s), which vessel	Free text	Only applicable if 'Identifiable named vessel(s): yes' selected
Background pathology	Single selection value list: • None • Yes	
Background pathology, specify	Free text	Only applicable if 'Background pathology: yes' selected
Histological type of tumour	Single selection value list: • Ductal adenocarcinoma • Other	
Histological type of tumour, other specify	Free text	Only applicable if 'Histological type of tumour: other' selected
Variant of PDAC	Free text	

Element name	Values	Implementation notes
Differentiation	Single selection value list: • not applicable (post neoadjuvant therapy) • well (Grade 1) • moderate (Grade 2) • poor (Grade 3)	
Assessment of size	Single selection value list: • macroscopic appearances confirmed • measured histologically	
Assessment of size measure histologically	Free text	Only applicable if 'Assessment of size: measured histologically' selected
Maximum extent of invasion	Single selection value list: • pT0 • pTis • pT1 • pT1a • pT1b • pT1c • pT2 • pT3 • pT4	pT1 only valid until 31/12/17. pT1a, pT1b, pT1c only valid from 01/01/18.
Response to neoadjuvant therapy	Single selection value list: • Not applicable • CAP Grade 0 (No residual tumour) • CAP Grade 1 (Moderate/marked response) • CAP Grade 2 (Minimal response) • CAP Grade 3 (Poor/no response)	
Margin status, gastric transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, gastric transection margin, clearance	Distance in mm	Only applicable if 'Margin status, gastric transection margin: Not involved' selected

Element name	Values	Implementation notes
Margin status, duodenal transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, duodenal transection margin, clearance	Distance in mm	Only applicable if 'Margin status, duodenal transection margin: Not involved' selected
Margin status, pancreatic transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, pancreatic transection margin, clearance	Distance in mm	Only applicable if 'Margin status, pancreatic transection margin: Not involved' selected
Margin status, bile duct transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, bile duct transection margin, clearance	Distance in mm	Only applicable if 'Margin status, bile duct transection margin: Not involved' selected
Margin status, SMV/SMA dissection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, SMV/SMA dissection margin, clearance	Distance in mm	Only applicable if 'Margin status, SMV/SMA dissection margin: Not involved' selected
Margin status, posterior dissection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	

Element name	Values	Implementation notes
Margin status, posterior dissection margin, clearance	Distance in mm	Only applicable if 'Margin status, posterior dissection margin: Not involved' selected
Margin status, anterior pancreatic surface	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, anterior pancreatic surface, clearance	Distance in mm	Only applicable if 'Margin status, anterior pancreatic surface: Not involved' selected
Named vessel status	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Named vessel, specify	Free text	Only applicable if 'Named vessel status: involved' selected
Perineural invasion	Single selection value list: • Present • Not identified	
Total number of nodes	Integer	
Number of involved nodes	Integer	
N stage	Single selection value list: • pN0 • pN1 • pN2	pN2 only valid from 01/01/18.
Distant metastasis confirmed	Single selection value list: • No • Yes	
Distant metastasis confirmed, specify site	Free text	Only applicable if 'Distant metastasis confirmed: Yes' selected
Background pathology	Single selection value list: • Intraductal papillary mucinous neoplasm (IPMN) • Mucinous cystic neoplasm (MPN) • Other • None	

Element name	Values	Implementation notes
Background pathology, other specify	Free text	Only applicable if 'Background pathology: Other' selected.
Comments	Free text	
T stage	Single selection value list: • pTX • pT0 • pTis • pT1 • pT1a • pT1b • pT1c • pT2 • pT3 • pT4 • ypTX • ypT0 • ypTis • ypT1 • ypT1a • ypT1b • ypT1c • ypT2 • ypT3 • ypT4	pT1, ypT1 only valid until 31/12/17. pT1a, pT1b, pT1c, ypT1a, ypT1b, ypT1c only valid from 01/01/18.
N stage	Single selection value list: • pNX • pN0 • pN1 • pN2 • ypNX • ypN0 • ypN1 • ypN2	pN2, ypN2 only valid from 01/01/18
M stage	Single selection value list: • Not applicable • pM1 • ypM1	
UICC version	Single selection value list: • 7 • 8	

Element name	Values	Implementation notes
Resection status	Single selection value list: • Complete at all margins (R0) • Incomplete microscopic (R1) • Incomplete macroscopic (R2)	
SNOMED T code	May have multiple codes. Look up from SNOMED tables.	
SNOMED M code	May have multiple codes. Look up from SNOMED tables.	

Appendix L Proforma for ampulla of Vater carcinoma in list format

Element name	Values	Implementation notes
Specimen type	Single selection value list: • Kausch -Whipple's pancreatoduodenectomy (PD) • pylorus preserving PD • other	
Specimen type, specify	Free text	Only applicable if 'Specimen type: other' selected
Maximum tumour diameter	Size in mm	
Macroscopic margin involvement	Single selection value list: • None • Yes (R2)	
Macroscopic margin involvement, which margin	Free text	Only applicable if 'Macroscopic margin involvement: yes' selected
Identifiable named vessel(s)	Single selection value list: • None • Yes	
Identifiable named vessel(s), which vessel	Free text	Only applicable if 'Identifiable named vessel(s): yes' selected
Background pathology	Single selection value list: • None • Yes	
Background pathology, specify	Free text	Only applicable if 'Background pathology: yes' selected
Histological type of tumour	Single selection value list: • Adenocarcinoma • Other	
Histological type of tumour, other specify	Free text	Only applicable if 'Histological type of tumour: other' selected
Phenotype	Single selection value list: • Pancreatobiliary • Intestinal • Other	Only applicable if 'Histological type of tumour: adenocarcinoma is selected'
Phenotype, other	Free text	Only applicable if 'Phenotype: other' selected

Element name	Values	Implementation notes
Differentiation	Single selection value list: • not applicable (post neoadjuvant therapy) • Well (Grade 1) • Moderate (Grade 2) • Poor (Grade 3)	
Maximum extent of invasion	Single selection value list: • pT0 • pTis • pT1 • pT1a • pT1b • pT2 • pT3 • pT3a • pT3b • pT4	pT1, pT3 only valid until 31/12/17. pT1a, pT1b, pT3a, pT3b only valid from 01/01/18.
Response to neoadjuvant therapy	Single selection value list: • Not applicable • CAP Grade 0 (No residual tumour) • CAP Grade 1 (Moderate/marked response) • CAP Grade 2 (Minimal response) • CAP Grade 3 (Poor/no response)	
Margin status, gastric transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, gastric transection margin, clearance	Distance in mm	Only applicable if 'Margin status, gastric transection margin: Not involved' selected
Margin status, duodenal transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, duodenal transection margin, clearance	Distance in mm	Only applicable if 'Margin status, duodenal transection margin: Not involved' selected

Element name	Values	Implementation notes
Margin status, pancreatic transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, pancreatic transection margin, clearance	Distance in mm	Only applicable if 'Margin status, pancreatic transection margin: Not involved' selected
Margin status, bile duct transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, bile duct transection margin, clearance	Distance in mm	Only applicable if 'Margin status, bile duct transection margin: Not involved' selected
Margin status, SMV/SMA dissection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, SMV/SMA dissection margin, clearance	Distance in mm	Only applicable if 'Margin status, SMV/ SMA dissection margin: Not involved' selected
Margin status, posterior dissection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, posterior dissection margin, clearance	Distance in mm	Only applicable if 'Margin status, posterior dissection margin: Not involved' selected
Margin status, anterior pancreatic surface	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	

Element name	Values	Implementation notes
Margin status, anterior pancreatic surface, clearance	Distance in mm	Only applicable if 'Margin status, anterior pancreatic surface: Not involved' selected
Named vessel status	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Named vessel, specify	Free text	Only applicable if 'Named vessel status: involved' selected
Perineural invasion	Single selection value list: • Present • Not identified	
Total number of nodes	Integer	
Number of involved nodes	Integer	
N stage	Single selection value list: • pN0 • pN1 • pN2	pN2 only valid from 01/01/18.
Distant metastasis confirmed	Single selection value list: • No • Yes	
Distant metastasis confirmed, specify site	Free text	Only applicable if 'Distant metastasis confirmed: Yes' selected
Background pathology	Single selection value list: • Ampullary adenoma • Other • None	
Background pathology, other specify	Free text	Only applicable if 'Background pathology: Other' selected.
Comments	Free text	

Element name	Values	Implementation notes
T stage	Single selection value list: • pTX • pT0 • pTis • pT1 • pT1a • pT1b • pT2 • pT3 • pT3a • pT3b • pT4 • ypTX • ypT0 • ypTis • ypT1 • ypT1a • ypT1b • ypT2 • ypT3 • ypT3a • ypT3b • ypT4	pT1, pT3, ypT1, ypT3 only valid until 31/12/17. pT1a, pT1b, ypT1a, ypT1b, pT3a, pT3b, ypT3a, ypT3b only valid from 01/01/18.
N stage	Single selection value list: • pNX • pN0 • pN1 • pN2 • ypNX • ypN0 • ypN1 • ypN2	pN2, ypN2 only valid from 01/01/18
M stage	Single selection value list: • Not applicable • pM1 • ypM1	
UICC version	Single selection value list: • 7 • 8	

Element name	Values	Implementation notes
Resection status	Single selection value list: • Complete at all margins (R0) • Incomplete microscopic (R1) • Incomplete macroscopic (R2)	
SNOMED T code	May have multiple codes. Look up from SNOMED tables.	
SNOMED M code	May have multiple codes. Look up from SNOMED tables.	

Appendix M Proforma for common bile duct carcinoma in list format

Element name	Values	Implementation notes
Specimen type	Single selection value list: • Kausch-Whipple's pancreatoduodenectomy (PD) • pylorus preserving PD • other	
Specimen type, specify	Free text	Only applicable if 'Specimen type: other' selected
Site of tumour	Free text	
Maximum tumour diameter	Size in mm	
Macroscopic margin involvement	Single selection value list: • None • Yes (R2)	
Macroscopic margin involvement, which margin	Free text	Only applicable if 'Macroscopic margin involvement: yes' selected
Identifiable named vessel(s)	Single selection value list: • None • Yes	
Identifiable named vessel(s), which vessel	Free text	Only applicable if 'Identifiable named vessel(s): yes' selected
Background pathology	Single selection value list: • None • Yes	
Background pathology, specify	Free text	Only applicable if 'Background pathology: yes' selected
Histological type of tumour	Single selection value list: • Adenocarcinoma • Other	
Histological type of tumour, other specify	Free text	Only applicable if 'Histological type of tumour: other' selected
Differentiation	Single selection value list: • not applicable (post neoadjuvant therapy) • Well (Grade 1) • Moderate (Grade 2) • Poor (Grade 3)	

Element name	Values	Implementation notes
Maximum extent of invasion	Single selection value list: • pT0 • pTis • pT1 • pT2 • pT3 • pT4	
Response to neoadjuvant therapy	Single selection value list: • Not applicable • CAP Grade 0 (No residual tumour) • CAP Grade 1 (Moderate/marked response) • CAP Grade 2 (Minimal response) • CAP Grade 3 (Poor / no response)	
Margin status, gastric transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, gastric transection margin, clearance	Distance in mm	Only applicable if ‘Margin status, gastric transection margin: Not involved’ selected
Margin status, duodenal transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, duodenal transection margin, clearance	Distance in mm	Only applicable if ‘Margin status, duodenal transection margin: Not involved’ selected
Margin status, pancreatic transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, pancreatic transection margin, clearance	Distance in mm	Only applicable if ‘Margin status, pancreatic transection margin: Not involved’ selected

Element name	Values	Implementation notes
Margin status, bile duct transection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, bile duct transection margin, clearance	Distance in mm	Only applicable if 'Margin status, bile duct transection margin: Not involved' selected
Margin status, SMV/SMA dissection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, SMV/SMA dissection margin, clearance	Distance in mm	Only applicable if 'Margin status, SMV/SMA dissection margin: Not involved' selected
Margin status, posterior dissection margin	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, posterior dissection margin, clearance	Distance in mm	Only applicable if 'Margin status, posterior dissection margin: Not involved' selected
Margin status, anterior pancreatic surface	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Margin status, anterior pancreatic surface, clearance	Distance in mm	Only applicable if 'Margin status, anterior pancreatic surface: Not involved' selected
Named vessel status	Single selection value list: • Involved • Not involved • Not sampled • Not applicable	
Named vessel, specify	Free text	Only applicable if 'Named vessel status: involved' selected

Element name	Values	Implementation notes
Perineural invasion	Single selection value list: • Present • Not identified	
Total number of nodes	Integer	
Number of involved nodes	Integer	
N stage	Single selection value list: • pN0 • pN1 • pN2	pN2 only valid from 01/01/18
Distant metastasis confirmed	Single selection value list: • No • Yes	
Distant metastasis confirmed, specify site	Free text	Only applicable if 'Distant metastasis confirmed: Yes' selected
Background pathology	Single selection value list: • Biliary IPMN • Bil-IN • Other • None	
Background pathology, other specify	Free text	Only applicable if 'Background pathology: Other' selected.
Comments	Free text	
T stage	Single selection value list: • pTX • pT0 • pTis • pT1 • pT2 • pT3 • pT4 • ypTX • ypT0 • ypTis • ypT1 • ypT2 • ypT3 • ypT4	

Element name	Values	Implementation notes
N stage	Single selection value list: • pNX • pN0 • pN1 • pN2 • ypNX • ypN0 • ypN1 • yPN2	pN2, ypN2 only valid from 01/01/18
M stage	Single selection value list: • Not applicable • pM1 • ypM1	
UICC version	Single selection value list: • 7 • 8	
Resection status	Single selection value list: • Complete at all margins (R0) • Incomplete microscopic (R1) • Incomplete macroscopic (R2)	
SNOMED T code	May have multiple codes. Look up from SNOMED tables.	
SNOMED M code	May have multiple codes. Look up from SNOMED tables.	

Appendix N Summary table – explanation of levels 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 control trials or a randomised control 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 control trials or randomised control 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 casual 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 O AGREE compliance monitoring sheet

The cancer datasets of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines (www.agreecollaboration.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 dataset
Scope and purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	Foreword
2. The clinical question(s) covered by the guidelines is (are) specifically described.	1
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	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
Rigor 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.	All
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.	All
16. The different options for management of the condition on health issue are clearly presented.	All
17. Key recommendations are easily identifiable.	4–9, 11
Applicability	
18. The guideline describes facilitators and barriers to its application.	Foreword
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Foreword
20. The potential resource implications of applying the recommendations have been considered.	Foreword
21. The guideline presents monitoring and/or auditing criteria.	11
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