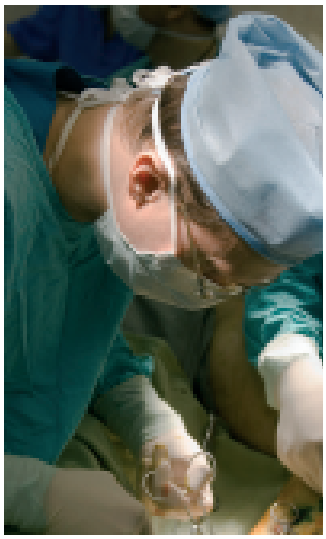
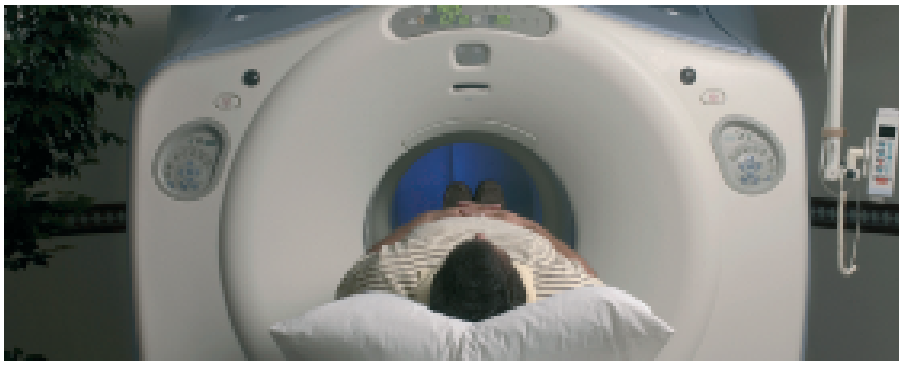
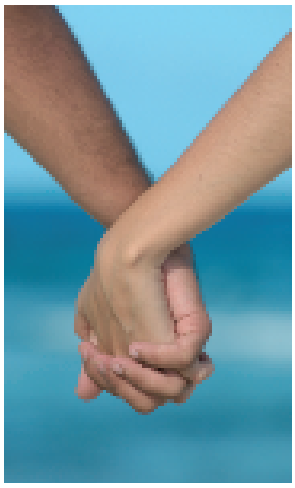
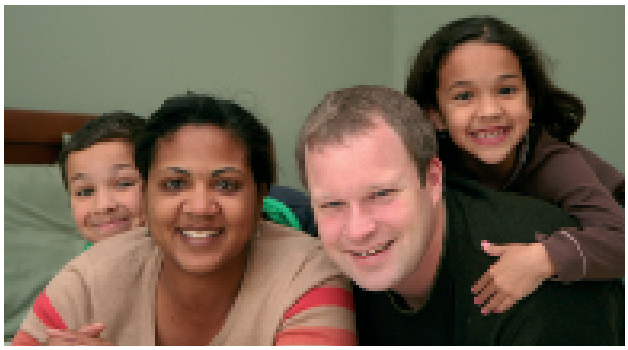
N. IRELAND Cancer Registry

Care of pancreatic cancer patients in Northern Ireland diagnosed 2007 (with comparisons 2001)









Queen's University Belfast

2007 Pancreas

Care of pancreatic cancer patients in Northern Ireland diagnosed 2007 (with comparisons 2001)

Edited by: **Deirdre Fitzpatrick, Arlene Connolly, and Anna Gavin**

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Available at http://www.qub.ac.uk/research-centres/nicr/Research/CancerServicesAudit/

FOREWORD

Cancer services in Northern Ireland have improved in recent years. Developments have spanned prevention, early detection and screening, diagnosis, management and palliative care. The N.Ireland Cancer Registry has played an important role in monitoring this progress.

This second report on pancreatic cancer is very welcome. It is the fifteenth in a series of reports on a wide range of cancers that examine in detail the pathways of care for patients. This report provides a detailed insight into the diagnosis and care received by pancreatic cancer patients in 2007 and compares that with 2001. In that period there is evidence of concentration of specialist expertise and an indication of improved survival for those patients whose cancer was suitable for surgery. This bears testament to the skills of the staff that treat these patients.

There has also been a significant increase in the proportion of patients offered palliative care services, which is important given that overall survival from this disease remains poor. Further improvement is still needed in the areas of multidisciplinary team discussion of all cases and there is a need for further research into causation and efforts to improve earlier diagnosis.

This work marks a significant step in the evaluation of cancer care and confirms the value of undertaking regular reports to monitor the changing process of diagnosis and treatment for cancer patients in Northern Ireland.

Dr Carolyn Harper
Director of Public Health for Northern Ireland

ACKNOWLEDGEMENTS

This report has been compiled in collaboration with the Northern Ireland Cancer Network (NICaN). I am grateful to the clinicians who helped with determining the data items to collect, their interpretation and final presentation.

The N.Ireland Cancer Registry is funded by the Public Health Agency of Northern Ireland and its audit work is facilitated by grants from the Guideline and Audit Implementation Network (GAIN).

The quality of data in this project is a result of the work of Bernadette Anderson (Tumour Verification Officer) who meticulously extracted detailed information from clinical records for analysis and presentation in this report. Data abstraction was facilitated by Colin Fox of the Registry's IT group. The analysis of data was undertaken by Dr Arlene Connolly and Mrs Deirdre Fitzpatrick. A special word of gratitude to the medical records staff of all the hospitals in Northern Ireland who have facilitated the Registry in this work, and the clinicians who have commented on this report.

The work of the N.Ireland Cancer Registry, including the production of this Report, is the result of the work of the Registry team. I wish also to record my thanks to the Steering Group and Council of the Registry who guide that work.

Dr Anna Gavin
Director, N.Ireland Cancer Registry
2011

SECTION I – INTRODUCTION, BACKGROUND & METHODS

INTRODUCTION

This Report is one of a series which examines in detail the pathway of care for cancer patients in Northern Ireland. Pancreatic cancer is a significant cause of cancer mortality and this report assesses change in service provision over a 7 year period.

Changes in service provision are driven by recommendations and guidance developed by several working groups and professional bodies. The key documents providing guidance for the optimum treatment and care of patients with pancreatic cancer are:

- In 1996 the Campbell Report[1], which resulted from the work of many clinicians, service planners and patients, made 14 recommendations with the aim of improving cancer services in Northern Ireland (see Appendix A).
- In 2001, the NHS produced a document outlining Guidance on Commissioning Cancer Services: **"Improving outcomes in upper gastro-intestinal cancers"**[2]. This document included cancers of the oesophagus, oesophago-gastric junction, stomach and pancreas. For the key recommendations see Appendix B. This guidance also provided a summary of recommendations in specific topic areas (see Appendix C).
- In 2005, the Pancreatic Section of the British Society of Gastroenterology published "**Guidelines for the management of patients with pancreatic cancer periampullary and ampullary carcinomas**" [3], a summary of which is included in Appendix D.

In 2005, the NICR produced a cancer services audit of pancreatic cancer patients diagnosed in Northern Ireland in 2001[4], which made the following recommendations:

a) One specialist pancreatic cancer team should be identified for Northern Ireland. All Trusts and GPs should be informed of this and have information on referral and advice protocols.
b) There should be one unit for Northern Ireland which should forge links with other similar centres outside Northern Ireland.
c) Research into the cause of pancreatic cancer and possibilities for earlier detection eg. via tumour markers should be funded.

PANCREATIC CANCER BACKGROUND

Aetiology and risk factors

The specific causes of pancreatic cancer are unknown, but cigarette smoking, nutritional, genetic/familial factors and pre-existing diseases are all associated with this cancer.

The risk factor consistently identified with pancreatic cancer is cigarette smoking, which may account for 25-29% of cases, with reported odds ratios ranging from 1.6 to 5.4[5].

Other factors including diet (high fat and protein, low fruit and vegetable intake), coffee consumption, alcohol, occupation, and the effects of other diseases such as diabetes mellitus, pernicious anaemia, chronic pancreatitis, cholelithiasis (gall stones), and previous gastric surgery, have also been studied in detail. Of these, only in chronic pancreatitis and adult onset diabetes of less than two years' duration does there seem to be clear evidence of an increased risk of pancreatic cancer[6-9]. Chronic pancreatitis is associated with an increased risk of cancer of the order of 5–15-fold[6, 7]. Hereditary pancreatitis is associated with a 50–70-fold risk and a cumulative lifetime risk to the age of 75 years of 40%[10, 11].

Pancreatic cancer may also occur in three other settings in which there is an inherited predisposition. Firstly, there appears to be an inherited component to pancreatic cancer in up to 10% of patients with pancreatic cancer in the absence of familial pancreatic cancer and other cancer syndromes[12, 13]. Secondly, there is an increased incidence of pancreatic cancer in individuals from families with familial pancreatic cancer in which the disease appears to be transmitted in an autosomal dominant manner with impaired penetrance. Two recent studies have shown that approximately 17–19% of these families may have disease linked with BRCA2 mutations in both Jewish and non-Jewish populations[14, 15]. Thirdly, an increased risk of pancreatic cancer may occur as part of another cancer syndrome, including familial atypical multiple mole melanoma, Peutz-Jeghers syndrome, hereditary non-polyposis colorectal carcinoma (HNPCC), familial breast-ovarian cancer syndromes, and familial adenomatous polyposis (FAP) but probably not Li-Fraumeni syndrome[16-22].

The diagnosis and management of genetic predispositions to pancreatic cancer are developing rapidly. Consensus Guidelines of the International Association of Pancreatology advise that patients with an inherited predisposition to pancreatic cancer should be referred to specialist centres capable of providing expert clinical assessment of pancreatic diseases, genetic counselling, and advice on secondary screening[23]. In the UK, the national co-coordinating centre for secondary screening for pancreatic cancer is the European Registry of Hereditary Pancreatic Diseases (EUROPAC)[24].

Pancreatic cancer in Northern Ireland

In Northern Ireland, from 1993-2007, on average 80 men and 80 women were diagnosed with pancreatic cancer each year, and 82 men and 83 women die annually

from this cancer (Appendices E and F). Age-standardised rates of disease are higher in men than women, as there are more older women in the population. There were no statistically significant trends in European age-standardised incidence (EASIR) (Figure 1) and mortality rates (EASMR) (Figure 2). (Note: more people are registered as dying from pancreatic cancer than diagnosed with it, as death certificates are not as accurate as cancer registration.)

Figure 1. EASIR pancreatic cancer in N.Ireland 1993-2007

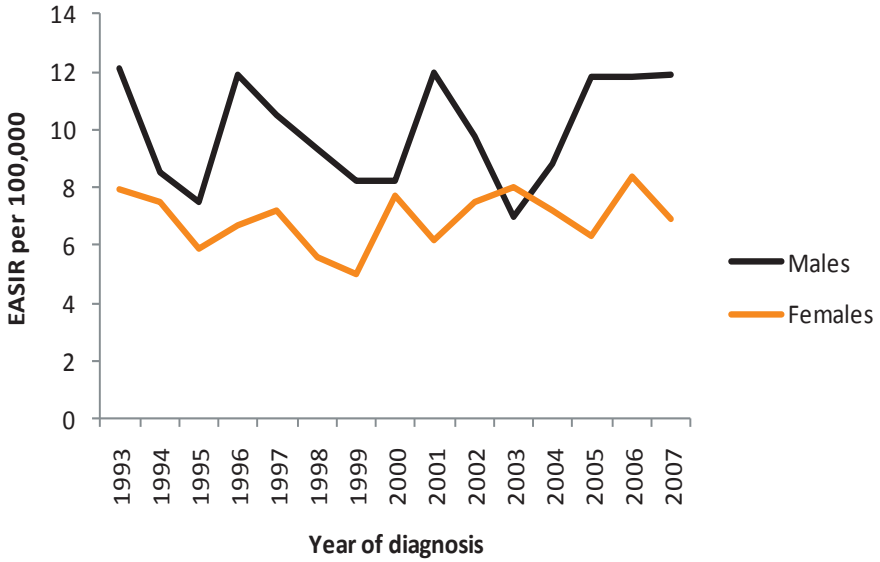
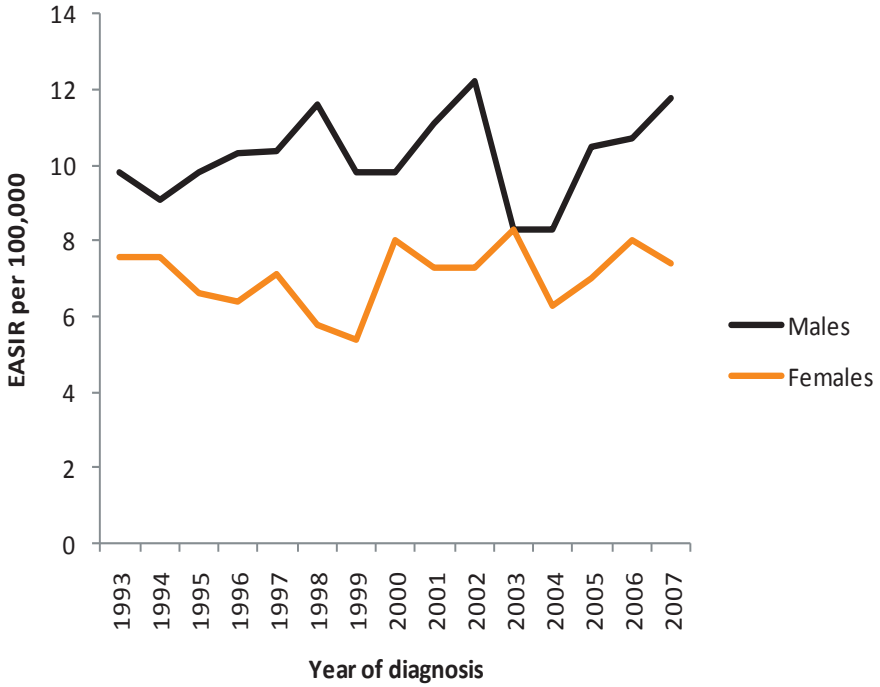


Figure 2. EASMR pancreatic cancer in N.Ireland 1993-2007



STUDY METHODS

Data Collection

Registry Tumour Verification Officers (TVOs) collected data by reviewing clinical notes of patients with a new primary pancreatic cancer already registered with the N. Ireland Cancer Registry. This, in many cases, involved review of notes from several hospitals. Data were then entered into an electronic proforma, which had been developed with the guidance of relevant clinicians; copy available at www.qub.ac.uk/nicr/racc.

Exclusions and analyses

Patients were excluded if their records lacked sufficient information, and/or when their cancer was diagnosed only by a death certificate (DCO). After cleaning and validation, data analysis was carried out using SPSS. Chi-square was used to test for significance, where appropriate, throughout the report. The Kaplan-Meier method was used for survival analysis.

Classification

The diseases covered by this report are ICD10 C25 (pancreatic cancer) except C25.4 (endocrine tumours of the pancreas). It also includes C22.1 (intrahepatic bile duct carcinomas), C24.0 (extrahepatic bile duct carcinomas) and C24.1 (peri-ampullary carcinomas). It excludes C23 (gallbladder tumours) and C24.8 (overlapping lesion of biliary tract). We acknowledge that pancreatic carcinomas, cholangiocarcinomas and peri-ampullary carcinomas may present the same clinically and in order to ensure that all pancreatic cancers have been captured, these tumours are reported on in separate sections.

Anatomical and Histopathological Key Features

The majority (85%) of malignant pancreatic tumours are ductal adenocarcinomas[25]. Rarer cancers include intraductal papillary tumours, neuroendocrine tumours, periampullary tumours and carcinomas of the intrapancreatic bile duct. 80-90% of tumours are located in the pancreatic head. Lymph node metastases are seen in 20 – 77% of resected specimens with tumours in the head of the pancreas[25]. Perineural (70%), vascular (45%) and lymphatic (80%) invasion are common[25]. The most common sites for metastases are liver and peritoneum and the most common extraperitoneal site for metastases is the lung[25].

SECTION II – RESULTS OF PANCREATIC CANCER AUDIT

Study patients

	Pancreas (C25 excl. C25.4)	
	2001	2007
Total number of patients	165	177
Exclusions – death certificate only*	3	2
Exclusions – insufficient information	10	2
Total exclusions	13	4
Total reported on (% of all patients)	152 (92%)	173 (98%)
Total reported on – male (%)	82 (54%)	96 (55%)
Total reported on – female (%)	70 (46%)	77 (45%)
Average age at diagnosis (age range (years) – male	70 (39-88)	69 (36-94)
Average age at diagnosis (age range (years) – female	75 (43-94)	74 (46- 94)

* Patients whose only record of cancer was on their death certificate

- There were 165 and 177 pancreatic cancers registered in 2001 and 2007 respectively.
- After exclusions 152 remained in 2001 and 173 in 2006.
- Pancreatic cancer was slightly more common in males.
- The average age at diagnosis was slightly older in females than in males.

Site of tumour

	Number of patients (%)	
	2001 (n=152)	2007 (n=173)
Head of Pancreas	100 (66%)	104 (60%)
Tail of Pancreas	12 (8%)	18 (10%)
Body of Pancreas	9 (6%)	16 (9%)
Overlapping lesion of pancreas	1 (<1%)	8 (5%)
Pancreatic duct	1 (<1%)	0
Pancreas, unspecified	29 (19%)	27 (16%)

- The percentage of pancreatic cancers with site unspecified has fallen from 19% in 2001 to 16% in 2007.

- Approximately two thirds of pancreatic cancers occurred in the head of pancreas.

Socio-economic residential area of patients

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Quintile 1 (Least affluent)	36 (24%)	35 (20%)
Quintile 2	25 (16%)	40 (23%)
Quintile 3	31 (20%)	46 (27%)
Quintile 4	24 (16%)	26 (15%)
Quintile 5 (Most affluent)	36 (24%)	26 (15%)

- The population of N.Ireland can be divided into five equally sized quintiles ranked by socio-economic deprivation level of residence. If a disease is not related to deprivation, it is expected that approximately 20% of all incidence would fall in each quintile. The data shows that in both 2001 and 2007 there was no significant difference in the levels of pancreatic cancer by socio-economic groups.

Risk Factors

Smoking History

	Number of patients (%)	
	2001 (n=152)	2007 (n=173)
Current		
> 20 per day	11 (7%)	24 (14%)
< 20 per day	14 (9%)	23 (13%)
< 5 per day	6 (4%)	4 (2%)
Unknown amount	4 (3%)	
Total	35 (23%)	51 (29%)
Ex-smoker		
> 1 year	7(5%)	6 (3%)
> 5 years	32 (21%)	41 (24%)
< 1 year	3 (2%)	4 (2%)
Unknown duration	6 (4%)	8 (5%)
Total	48 (32%)	59 (34%)
Non-smoker	53 (35%)	55 (32%)
Not Recorded	16 (11%)	8 (5%)

- There was better recording in 2007 of whether a patient had a history of smoking.
- In both years, approximately one third of patients were recorded as being non-smokers.
- The recorded level of current smokers is similar to the Northern Ireland average.

Alcohol Consumption

	Number of patients (%)	
	2001 (n=152)	2007 (n=173)
Drinker	58 (38%)	50 (29%)
Ex-drinker	13 (9%)	11 (6%)
Never	46 (30%)	58 (34%)
Occasional	-	30 (17%)
Not recorded	35 (23%)	24 (14%)

- In 2007, more than half of patients were recorded as having previously or currently consumed alcohol (47% in 2001), with 34% of patients recorded as consuming 20 or more units per week (12% in 2001).
- Over one third of patients were recorded as never having consumed alcohol (higher than the Northern Ireland average of 17%).

Family history of pancreatic and other cancers recorded in notes

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Pancreas, first degree relative	4 (3%)	3 (2%)
Pancreas, second degree relative	0	0
Other site, first degree relative	19 (13%)	32 (18%)
Other site, second degree relative	4 (3%)	3 (2%)
No family history of cancer	55 (36%)	71 (41%)
Family history not recorded	70 (46%)	62 (36%)

- Family history of pancreatic cancer or other site cancer was better recorded in 2007 (64%) than in 2001 (54%).
- 2% of patients had a family history of pancreatic cancer (3% in 2001).

Family history of previous malignancies recorded in notes

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
All sites combined	23 (15%)	35 (20%)
Breast	5 (3%)	4 (2%)
Lung	6 (4%)	7 (4%)
Colorectal	5 (3%)	7 (4%)
Stomach	1 (1%)	6 (3%)
Other	6 (4%)	8 (5%)
Unknown	1 (1%)	4 (2%)

- 20% of patients had a history of a family member having had a malignancy (15% in 2001).

- The most common cancers occurring in family members of pancreatic cancer patients are cancers of the lung (4%) and colon (4%).

Co-morbidities (Note: Patients may have had more than one co-morbidity)

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Hypertension	50 (33%)	85 (49%)
Diabetes mellitus	29 (19%)	47 (27%)
Ischaemic heart disease	49 (32%)	43 (25%)
Arthritis	32 (21%)	43 (25%)
Gallstones	37 (24%)	30 (17%)
Cerebrovascular disease	15 (10%)	21 (12%)
COPD*	24 (16%)	15 (9%)
Previous cholecystectomy	15 (10%)	15 (9%)
Chronic pancreatitis	8 (5%)	14 (8%)
Osteoporosis	7 (4%)	13 (8%)
Dementia	4 (3%)	12 (7%)
Other Malignancy	20 (13%)	31 (18%)

** COPD = Chronic Obstructive Pulmonary Disease*

- Almost half of patients in 2007 were recorded as suffering from hypertension (a third in 2001).
- Over a quarter of pancreatic patients in 2007 were recorded as diabetic compared to just under a fifth in 2001.
- An unexplained attack of acute pancreatitis is a condition associated with pancreatic cancer. In 2007, 8% of patients had a record of chronic pancreatitis in their notes.
- In 2007, 18% of patients had a personal history of malignancy. The most common malignancies reported were basal cell carcinoma in males and breast cancer in females (not shown).

Diabetes

	Number of patients (% of patients with diabetes)	
	2001 (n=29)	**2007 (n=47)**
Controlled - Insulin	7 (24%)	20 (43%)
Controlled - Tablet	9 (31%)	18 (38%)
Controlled - Diet	13 (45%)	9 (19%)
Median age when diagnosed with diabetes (years)	64	69

- In 2007, 19% of patients with a record of diabetes in their notes controlled their diabetes with diet (45% in 2001).
- Amongst those pancreatic patients recorded as being diabetic, the median ages that they were diagnosed as being diabetic were 64 years and 69 years respectively.

Duration between diagnosis of diabetes and diagnosis of pancreatic cancer

	Number of patients (%)	
	2001 (n=29)	**2007 (n=47)**
Up to 6 months	10 (34%)	11 (23%)
7-12 months	2 (7%)	2 (4%)
13-24 months	3 (10%)	3 (6%)
More than 24 months	14 (48%)	21 (45%)
Duration not recorded	0	10 (21%)

- Almost a quarter of pancreatic cancer patients with diabetes had their diagnosis of diabetes less than six months before their pancreatic cancer diagnosis (34% in 2001).

Drug History

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Antihypertensives	72 (47%)	97 (56%)
Aspirin	48 (31%)	73 (42%)
Respiratory	19 (13%)	20 (12%)
Steroids	11 (7%)	19 (11%)
Proton-pump inhibitor*	-	55 (32%)
Warfarin	8 (5%)	4 (2%)
Controlled**	4 (3%)	5 (3%)
Other NSAID***	9 (6%)	10 (6%)

**Not collected in 2001. **Includes morphine, diamorphine, pethidine. ***Non steroidal anti-inflammatory drugs*

- More than half of patients had a record in their notes of taking antihypertensives, whilst 11% were taking steroids.

Referral and presentation

Source of referral to hospital

Source	Number of patients (%)	
	2001 (n=152)	2007 (n=173)
GP	130 (86%)	129 (75%)
Self-presented	10 (7%)	22 (13%)
General physician	2 (1%)	11 (6%)
General surgeon	0	1 (<1%)
Non surgical consultant	5 (3%)	4 (2%)
Other*	0	6 (3%)
Not recorded	5 (3%)	0

**Other included nursing/care home nurse, inpatient, hepato clinic*

- Three quarters of patients in 2007 were referred by their GP (86% in 2001).
- In 2007, the percentage of self referrals has almost doubled (13% in 2007, 7% in 2001).

Mode of presentation of patients referred by their GP

Mode of presentation	Number of patients (% of those referred by GP)	
	2001 (n=130)	2007 (n=129)
Accident and Emergency	46 (35%)	67 (52%)
Outpatient	38 (29%)	40 (31%)
Elective	32 (25%)	15 (12%)
Other	11 (9%)	6 (5%)
Not Recorded	3 (2%)	1 (<1%)

- In 2007, more than half of pancreatic cancer patients referred by their GP presented in Accident and Emergency (35% in 2001), whilst almost a third presented as an outpatient (29% in 2001).

Hospital of Presentation

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Belfast City Hospital	15 (10%)	17 (10%)
Royal Victoria Hospital	13 (9%)	15 (9%)
Mater Hospital	8 (5%)	20 (12%)
Belfast HSCT	**36 (24%)**	**52 (30%)**
Ulster Hospital	24 (16%)	18 (10%)
Downe Hospital	3 (2%)	2 (1%)
Ards Hospital	0	1 (1%)
Lagan Valley Hospital	7 (5%)	4 (2%)
Bangor Community Hospital	1 (<1)	0
South-Eastern HSCT	**35 (23%)**	**25 (14%)**
Causeway (Coleraine) Hospital	4 (3%)	13 (7%)
Antrim Hospital	16 (11%)	9 (5%)
Mid-Ulster Hospital	4 (3%)	6 (3%)
Whiteabbey Hospital	7 (5%)	6 (3%)
Braid Valley Hospital	0	1 (1%)
Moyle Hospital	1 (<1%)	0
Waveney Hospital	1 (<1%)	0
Northern HSCT	**33 (22%)**	**35 (20%)**
Craigavon Area Hospital	8 (5%)	21 (12%)
Daisy Hill Hospital	11 (7%)	13 (8%)
Lurgan Hospital	1 (<1%)	1 (1%)
South Tyrone Hospital	2 (1%)	0
Southern HSCT	**22 (15%)**	**35 (20%)**
Altnagelvin Hospital	8 (5%)	13 (8%)
Erne Hospital	11 (7%)	10 (6%)
Tyrone County Hospital	2 (1%)	2 (1%)
Western HSCT	**21 (14%)**	**25 (14%)**
Private Patients	4 (3%)	1 (1%)
Outside N. Ireland	1 (<1%)	0

- In 2007, 173 patients with cancer of the pancreas presented to 19 hospitals, whilst 152 patients with the same disease presented to 23 hospitals in 2001.
- The percentage of patients presenting at the Mater increased from 5% in 2001 to 12% in 2007.
- Of patients resident in the Belfast HSCT (Health and Social Care Trust), 38% presented at the Mater; of those resident in the South-Eastern HSCT 42% presented at the Ulster Hospital. 53% of patients resident in the Southern HSCT presented at Craigavon Area Hospital and 46% of patients in the Western HSCT presented at Altnagelvin Hospital (not shown).

Patients presenting within their own Trust of residence

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Belfast HSCT		29 (85%)
South-Eastern HSCT		20 (65%)
EHSSB*	63 (95%)	
Northern HSCT		33 (72%)
NHSSB*	29 (78%)	
Southern HSCT		31 (91%)
SHSSB*	22 (88%)	
Western HSCT		25 (89%)
WHSSB*	21 (95%)	

**EHSSB, NHSSB, SHSSB and WHSSB were the Eastern, Northern, Southern and Western Health and Social Services Boards. Following reorganisation the EHSSB geographical area is now covered by Belfast and South-Eastern HSCT. The NHSSB, SHSSB and WHSSB areas are equivalent to the Trusts.*

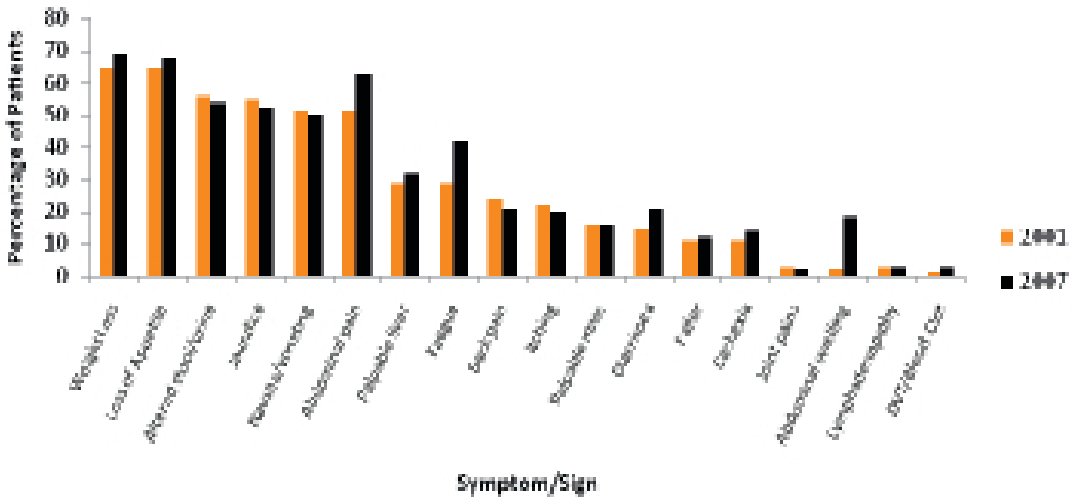
- The analysis has shown that 85% of persons living in Belfast HSCT presented within that Trust. However, the remaining 15% of patients presented at the Ulster Hospital which geographically sits on the outskirts of Belfast but falls within the South-Eastern HSCT.
- The Northern and South-Eastern HSCT are the closest neighbours to Belfast HSCT. Almost a quarter of patients resident in the Northern HSCT and South-Eastern HSCT presented at Belfast HSCT.

Symptoms/signs at presentation (Note: Patients may have more than one symptom)

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Weight Loss	97 (64%)	120 (69%)
Loss of Appetite	99 (65%)	118 (68%)
Abdominal pain	78 (51%)	109 (63%)
Altered stool/urine	85 (56%)	93 (54%)
Jaundice	84 (55%)	90 (52%)
Nausea/vomiting	78 (51%)	87 (50%)
Fatigue	44 (29%)	72 (42%)
Palpable liver mass	44 (29%)	56 (32%)
Back pain	36 (24%)	36 (21%)
Diarrhoea	23 (15%)	36 (21%)
Itching	33 (22%)	34 (20%)
Abdominal swelling	3 (2%)	32 (18%)
Palpable abdominal mass	25 (16%)	27 (16%)
Cachexia	16 (11%)	24 (14%)
Pallor	17 (11%)	20 (12%)
Joint pains	4 (3%)	3 (2%)
Lymphadenopathy	4 (3%)	5 (3%)
DVT/Blood Clot	1 (<1%)	5 (3%)

- Patients presented with similar symptoms in both years. However, a higher percentage of patients reported abdominal pain, fatigue, diarrhoea and/ or abdominal swelling in 2007.
- The most frequently recorded symptoms were weight loss (69% in 2007 and 64% in 2001) and loss of appetite (68% in 2007 and 65% in 2001).
- Over half of patients presented with altered stool/urine.
- On examination 16% of patients had a palpable abdominal mass at presentation.

Figure 3: Symptoms/signs for pancreatic cancer patients diagnosed 2001 and 2007



Weight loss

Weight loss (kg)	Number of patients (% experiencing weight loss)	
	2001 (n=99)	2007 (n=120)
Weight loss less than 4	13 (13%)	14 (12%)
Weight loss between 4 and 8	22 (22%)	37 (31%)
Weight loss between 8 and 12	23 (23%)	11 (9%)
Weight loss between 12 and 16	2 (2%)	14 (12%)
Weight loss more than 16	10 (10%)	4 (3%)
Not recorded	29 (29%)	40 (33%)

- Marked and rapid weight loss is a clinical feature of pancreatic cancer. In 2007, 32 patients were recorded as having lost up to 8 kg in weight in less than 3 months (not shown).

Patients Investigations
Blood tests at presentation

Test	Number of patients (%)	
	2001 (n=152)	2007 (n=173)
Bilirubin	141 (93%)	167 (97%)
ALP*	141 (93%)	167 (97%)
Albumin	139 (91%)	166 (96%)
Haemoglobin	139 (91%)	163 (94%)
Urea	140 (92%)	161 (93%)
Creatinine	136 (89%)	152 (88%)
ALT*	113 (74%)	148 (86%)
AST*	126 (83%)	141 (82%)
CRP*	63 (41%)	140 (81%)
CA19-9*	73 (48%)	137 (79%)
Serum	96 (63%)	112 (65%)
Prothrombin time	106 (70%)	100 (58%)
CEA*	35 (23%)	94 (54%)
CA125*	18 (12%)	55 (32%)
ESR*	63 (41%)	50 (29%)

*ALP = Alkaline phosphate, AST = Aspartate transaminase, ALT = Alamine aminotransferase, CRP = Creactive protein, ESR = Erythrocyte sedimentation rate, CEA = Carcinoembryonic antigen, CA19-9 = Carbohydrate antigen 19-9, CA125 = Carbohydrate antigen 125

- More patients had blood tests in 2007 than 2001, with the exception of Prothrombin time and ESR.
- There was a marked increase in the numbers of patients tested using CRP, CA19-9, CA125 and/or CEA.

Investigation procedure

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
CT Scan	123 (81%)	161 (93%)
Ultrasound	135 (89%)	146 (84%)
ERCP[1]	110 (71%)	84 (49%)
OGD[2]	24 (16%)	30 (17%)
EUS*[3]	-	21 (12%)
PTC[4]	21 (14%)	17 (10%)
MRCP[5]	4 (3%)	18 (10%)
X-Ray*	-	13 (8%)
Colonoscopy*	-	11 (6%)
Barium*	-	10 (6%)
PET[6] Scan	-	8 (5%)
MRI[7] Scan	-	6 (3%)

*[1]ERCP – Endoscopic Retrograde Cholangiopancreatography , [2]OGD – Oesophagogastroduodenoscopy, [3]EUS – Endoscopic Ultrasound, [4]PTC – PercutaneousTranshepatic Cholangiogram, [5] MRCP – Magnetic Resonance Cholangiopancreatography , [6]PET – Positron Emission Tomography,[7] MRI – Magnetic Resonance Imaging, *Not collected in 2001.*
Note: not all tests recorded in 2007 were recorded in 2001

- In 2007, more patients had a CT scan (93% in 2007, 81% in 2001).
- There were fewer patients in 2007 investigated by ERCP.

Complications of ERCP

	Number of patients (% of ERCP patients)	
	2001 (n=110)	**2007 (n=84)**
Pancreatitis	2 (2%)	2 (2%)
Bleeding	3 (3%)	0
Cholangitis	2 (2%)	1 (1%)

- Few patients were recorded as having had a complication post ERCP.

Method of Diagnosis

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Clinical opinion	32 (21%)	22 (13%)
ERCP	21 (14%)	6 (3%)
CT scan	18 (12%)	35 (20%)
Ultrasound	13 (9%)	22 (13%)
Other*	4 (3%)	
Total	**88 (58%)**	**85 (49%)**
Histopathology	30 (20%)	41 (24%)
Cytology	25 (16%)	21 (12%)
Secondary histology	9 (6%)	26 (15%)
Total	**64 (42%)**	**88 (51%)**

** Other includes X-ray and surgery*

- There were fewer patients diagnosed on clinical opinion alone in 2007 compared with 2001.
- By 2007, more patients had a histological/cytological confirmation of their diagnosis (51% in 2007, 42% in 2001).

Histopathological Type

	Number of patients (% of patients diagnosed histologically/cytologically)	
	2001 (n=64)	**2007 (n=88)**
Adenocarcinoma	47 (73%)	48 (55%)
Adenocarcinoma, metastatic	10 (16%)	30 (34%)
Carcinoma	5 (8%)	2 (2%)
Carcinoma, metastatic	1 (2%)	3 (3%)
Neoplasm, malignant		5 (6%)
Stromal tumour	1 (2%)	0

- For those patients that had a histological/cytological verification of their diagnosis about 90% had adenocarcinoma.

Staging (see also Appendix G)
Recording….

When stage was not recorded and there was sufficient information available in the clinical notes, Registry TVOs were able to assign a stage group (Registry-assigned stage). The American Joint Committee on Cancer (AJCC) staging classification[26] was applied.

Stage

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
I	9 (6%)	2 (1%)
II	1 (<1%)	15 (9%)
III	8 (5%)	15 (9%)
IV	59 (39%)	92 (53%)
Unstaged	75 (49%)	49 (28%)

- Staging improved by 2007, with 72% of tumours staged (51% in 2001).
- In both years the overall percentage of Stage I/II was similar; the increased numbers of Stage II patients possibly reflects better staging information.
- At least 80% of patients presented with Stage IV disease or were unstaged.

Site of metastatic disease

	Number of patients (% of Stage IV patients)	
	2001 (n=59)	**2007 (n=92)**
Liver	52 (88%)	66 (72%)
Lung	4 (7%)	8 (9%)
Peritoneum	3 (5%)	22 (24%)
Other Sites/Combination of sites	4 (7%)	9 (10%)

- In 2007, of those patients with Stage IV pancreatic disease, 72% had metastasis to the liver, 24% peritoneum and 9% lung.

Patient management and treatment

Multidisciplinary Team Meetings
The diagnosis and treatment of patients is most effectively managed by input from a range of healthcare professionals meeting at multidisciplinary team meetings (MDT). In many cases discussions among healthcare professionals may have taken place but a recognised meeting date may not have been recorded in the patient notes.

Multidisciplinary team meeting recorded in patient notes

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Yes	20 (13%)	82 (47%)
No/ not recorded	132 (87%)	98 (57%)

- In 2007, almost half of pancreatic cancer patients had a record in their notes of being discussed an MDT (13% 2001).

Preoperative surgical plan

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Diagnostic laparoscopy	4 (3%)	2 (1%)
Diagnostic laparotomy	6 (4%)	12 (7%)
No surgery planned	18 (12%)	124 (72%)
Planned curative resection	5 (3%)	22 (13%)
Planned palliative biliary bypass	0	6 (4%)
Not Recorded	119 (78%)	7 (4%)

- There was better recording of a preoperative surgical plan (96% 2007, 12% 2001).
- In 2007, 13% had a planned curative resection (3% 2001).

Surgical procedure

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Curative resection	4 (3%)	14 (8%)
Biliary bypass	22 (14%)	17 (10%)
Gastric bypass	17 (11%)	17 (10%)
Total number of surgery patients	31	45
Total number of operators	17	14

- In 2007, of the 22 patients for whom it was planned at MDT to undertake a curative surgical resection, this was only possible for 14 (64%).
- In 2007, there were more curative resections performed for pancreatic cancer patients, with 79% performed in the Mater Hospital (50% in 2001). The remaining 3 curative resections were performed in the Royal Victoria and Ulster Hospitals. In 2007, there were more patients having surgery by fewer surgeons
- Three quarters of patients had their surgery performed by one of four surgeons, whilst in 2001 it was 11 surgeons who performed three quarters of the surgery.

Hospital of surgery

	Number of patients (% of surgery patients)	
	2001 (n=31)	**2007 (n=45)**
Altnagelvin	2 (6%)	2 (4%)
Antrim	1 (3%)	
Belfast City	1 (3%)	2 (4%)
Craigavon	2 (6%)	
Causeway	1 (3%)	
Downe	2 (6%)	
Daisy Hill	2 (6%)	1 (2%)
Erne		2 (4%)
Lagan Valley	1 (3%)	
Mater	12 (39%)	27 (60%)
Royal Victoria	4 (13%)	9 (20%)
Ulster	3 (10%)	2 (4%)

- More patients with pancreatic cancer had surgery in 2007 than in 2001.
- In 2001, 31 pancreatic cancer patients had surgery in one of 11 hospitals. By 2007, more patients received surgery in fewer hospitals, with 60% taking place in the Mater Hospital.
- In 2007, 42% of surgery patients had a record of metastatic disease (24% in 2001); hence treatment is presumed to be palliative (not shown).

Direct tumour invasion found at surgery

	Number of patients (% of surgery patients)	
	2001 (n=31)	**2007 (n=45)**
Duodenum	9 (29%)	5 (11%)
Peritoneal spread	7 (23%)	1 (2%)
Superior mesenteric vein	3 (10%)	5 (11%)
Portal vein	2 (6%)	6 (13%)
Colon	1 (3%)	2 (4%)
Gallbladder/ Liver/ Stomach/ Bowel		5 (11%)
Aorta/ IVC		3 (7%)

- In 2001, almost a third of all surgical patients were found to have tumour invasion of the duodenum and 23% to have tumour spread into the peritoneum. Both these figures are substantially higher than the 2007 findings, 11% and 2% respectively.
- In 2007, 27 (60%) surgical patients had no record of direct tumour invasion found during surgery. Of the remaining 18 (40%) patients, 11 had one recorded tumour invasion site, 5 had two sites invaded and 2 patients had 3 recorded invaded sites (not shown).

Reconstruction during surgery

	Number of patients (% of surgery patients)	
	2001 (n=31)	**2007 (n=45)**
Gastrojejunostomy	12 (39%)	28 (62%)
Hepaticojejunostomy	11 (35%)	24 (53%)
Roux en Y	10 (32%)	18 (40%)
Pancreatic anastomosis	3 (10%)	11 (24%)
Other	17 (55%)	17 (38%)
Total reconstructions	56	98
Total number of patients	**19 (61%)**	**38 (84%)**

- In 2007, 38 (84%) of surgical patients underwent reconstructive surgery. Surgical notes indicate that these procedures were carried out in the majority of cases when a planned Whipples procedure was abandoned due to advanced disease spread.
- Surgical procedures were described as palliative for 27 patients, curative for 15 and not recorded for the remaining 3 patients in 2007.

Biliary decompression

Drains	Number of patients (% of surgery patients)	
	2001 (n=31)	**2007 (n=45)**
0	18 (58%)	15 (33%)
1	10 (32%)	22 (49%)
2	2 (6%)	7 (16%)
3	1 (3%)	1 (2%)

- The majority of surgery patients in 2001 (58%) did not have a drain, whereas the majority of patients in 2007 (67%) did receive one or more drains.

Postoperative outcome (Note: patients may have had more than one complication)

Complications	Number of patients (% of surgery patients)	
	2001 (n=31)	2007 (n=45)
Chest infection	3 (10%)	3 (7%)
Cardiac complications	2 (6%)	1 (2%)
Pancreatic leak	1 (3%)	0 (0%)
Biliary/Other leak	1 (3%)	1 (2%)
Renal failure	1 (3%)	2 (4%)
Wound Infections	1 (3%)	3 (7%)
Delayed gastric emptying	0	5 (11%)
Urinary Tract Infection	0	1 (2%)
General complications*	6 (19%)	8 (18%)
Return to theatre	3 (10%)	5 (11%)
Death within 30 days	3 (10%)	2 (4%)

** General complications include septic shock, tachycardia, surgical emphysema, confusion*

- In 2007, the percentage of surgery patients recorded as having a post-surgical complication was less than 2001 (36%, 48% respectively).
- The number patients admitted to ICU following surgery for pancreatic cancer increased in 2007 to 32 (71%) from 16 (52%) in 2001.

Patient referred to oncology

	Number of patients (%)	
	2001 (n=152)	2007 (n=173)
Yes	50 (33%)	87 (50%)
No/ not recorded	102 (67%)	86 (50%)

- In 2007, half of pancreatic cancer patients had a record in their notes of a referral to oncology (33% in 2001).

Reason for referral to oncology

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Assessment	48 (32%)	75 (43%)
Pain relief	3 (2%)	0
Symptom relief	3 (2%)	1 (<1%)
Radiotherapy	4 (3%)	3 (2%)
Chemotherapy	45 (30%)	72 (42%)

- In 2007, more pancreatic cancer patients had a record in their notes of a referral to oncology for chemotherapy (42% 2007, 30% 2001).

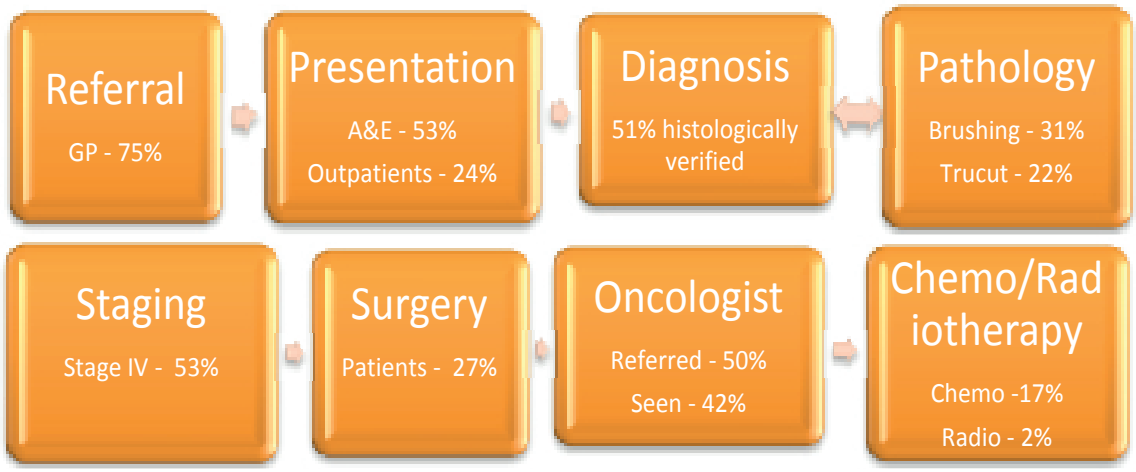
Chemotherapy

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Gemcitabine	22 (15%)	22 (13%)
Clinical trial	3 (2%)	1 (<1%)
Other	2 (1%)	7 (4%)

- In both years, less than half of those patients referred to oncology for chemotherapy received it. The reasons noted were patient refusal, or the patient was too ill.

Timelines in the patient pathway

A patient diagnosed with pancreatic cancer may expect to follow the investigative and treatment pathway below. The timescales involved as a patient moves along each step are significant in terms of service targets to ensure that pancreatic cancer patients are investigated, diagnosed and treated within acceptable timescales.



Summary timeline for pancreatic patients

Duration (Days)	Number of patients (%)					
	Referral to presentation		Presentation to diagnosis		Presentation to surgery	
	2001 (n=152)	2007 (n=173)	2001 (n=152)	2007 (n=173)	2001 (n=31)	2007 (n=45)
Not recorded	13 (9%)	0	6 (4%)	0	0	0
	Number of patients (% of patients with timeline recorded)				Number of patients (% of surgery patients)	
	2001 (n=139)	2007 (n=173)	2001 (n=146)	2007 (n=173)	2001 (n=31)	2007 (n=45)
Same day	85 (61%)	102 (60%)	38 (26%)	17 (10%)	0	0
Day 14	126 (91%)	153 (88%)	93 (64%)	110 (64%)	9 (29%)	9 (20%)
Day 31	133 (96%)	162 (94%)	115 (79%)	133 (77%)	16 (52%)	20 (44%)
Day 62	139 (100%)	169 (98%)	129 (88%)	156 (90%)	24 (77%)	35 (78%)

- The majority of pancreatic cancer referrals are urgent (76%) accounting for the very high proportion of patients seen at hospital on the same day as they are referred (60% in 2007, 61% in 2001).
- In 2001, 26% of patients with dates recorded had their cancer diagnosed on the same day as presenting at hospital. This fell in 2007 to only 10%, which accounts in part for the increased numbers of patients having their diagnosis histologically verified.
- Over three quarters of patients were diagnosed within 31 days of presenting at hospital in 2001 and 2007.
- More than three quarters of surgery patients had their surgery within 62 days of first presenting at hospital.
- The completeness of dates recorded in the notes improved since 2001.

Information and after care

Follow-up care details
After care recorded (Note: patients may have had more than one type of referral).

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
General practitioner	103 (68%)	139 (80%)
Dietician	2 (1%)	112 (65%)
Community nurse	69 (45%)	103 (60%)
Hospital palliative team	3 (2%)	90 (52%)
Occupational therapist	17 (11%)	70 (40%)
Palliative care specialist	23 (15%)	59 (34%)
Macmillan nurse	30 (20%)	51 (29%)
Physiotherapist	16 (11%)	40 (23%)
HPB* nurse	0	32 (18%)
Education supplied	1 (<1%)	32 (18%)
Hospice	34 (22%)	27 (16%)
Pain management	0	8 (5%)
Speech and language therapist	1 (<%)	5 (3%)
Psychologist	1 (<1%)	3 (2%)
Diabetic nurse	3 (2%)	1 (1%)
Marie Curie nurse	8 (5%)	1 (<1%)

** HPB – Hepato Pancreato Biliary*

- There was increased referral to GP and community nurse. In 2001, 68% of patients received care from their GP which increased to 80% in 2007. Similarly, community nurses treated 45% of patients in 2001 and 60% of patients in 2007.
- In 2007, there was a significant increase in the referral to dietician (65% in 2007, 1% in 2001).
- There has been a substantial increase in the number of patients being referred to a palliative care specialist; 15% of patients in 2001 and 34% in 2007.
- In 2007, 90 patients (52%) were referred to the hospital palliative team at some stage in their treatment journey. A further 5 patients refused the help from palliative care health professionals or the social services. Hospital notes in 2001 indicated that only 3 patients were referred to a palliative team.

Information in GP letter

This relates to information recorded in the discharge letter from the hospital to GP.

	Number of patients (%)	
	2001 (n=152)	**2007 (n=173)**
Management plan	103 (68%)	146 (84%)
Letter includes prognosis	53 (35%)	66 (38%)
Discussed prognosis with patient	75 (49%)	112 (65%)
Discussed prognosis with family	68 (45%)	100 (58%)

- Overall, information contained in the GP letter has improved with a substantial increase in the number of GP letters containing details of the patient management plan and whether or not a diagnosis has been discussed with the patient and/or family members.

Patient survival

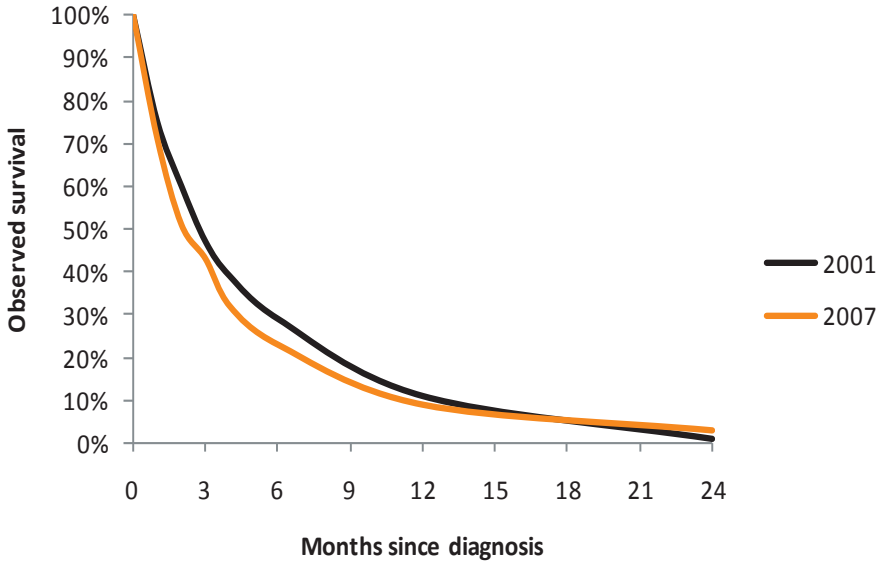
Survival analysis was performed on patients diagnosed in 2001 and 2007, with follow up for 2 years using the Kaplan Meier method. Sub-group analysis was carried out for year of diagnosis, surgery and stage of disease.

Percentage of patients alive at various times after diagnosis

Time	Observed survival (%)		
	Both diagnosis years (n=325)	Diagnosed 2001 (n=152)	Diagnosed 2007 (n=173)
30 days	73%	78%	71%
60 days	56%	60%	51%
6 months	26%	29%	23%
1 year	10%	11%	9%
2 years	3%	1%	3%

- Survival from pancreatic cancer is very poor with around 10% of patients surviving one year after diagnosis. There was no significant improvement in overall survival between 2001 and 2007 (P>0.05) (Figure 4).

Figure 4: Observed survival of patients diagnosed with pancreatic cancer in 2001 and 2007

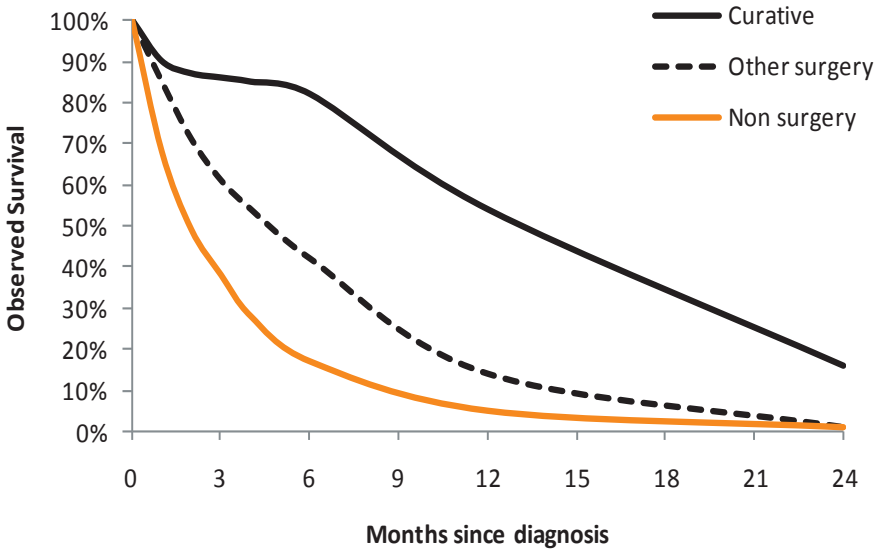


Percentage of patients alive at various times after diagnosis by surgery

Time	Observed survival (%)			
	Non-surgery (n=249)	Curative resection (n=18)	Other surgery (n=58)	All surgery (n=76)
30 days	68%	90%	85%	88%
60 days	49%	87%	71%	75%
6 months	17%	82%	42%	52%
1 year	5%	54%	14%	24%
2 years	1%	16%	1%	5%

- Patients who had surgery had better survival than those who did not. This is as expected, as patients selected for surgery tend to be clinically different than those who aren't selected.
- Patients who had a curative resection had a one year survival of 54%.

Figure 5: Observed survival of pancreatic cancer patients who did/ did not have surgery

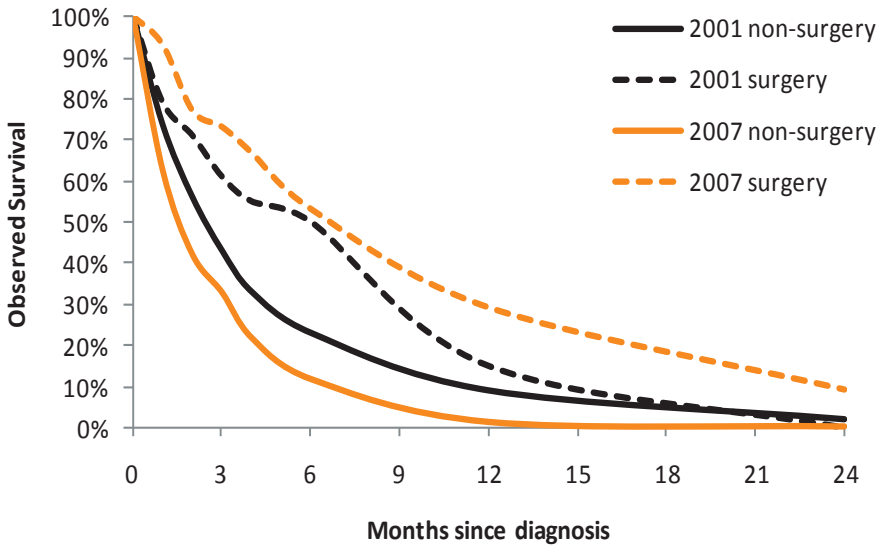


Percentage of patients alive at various times after diagnosis by surgery

Time	Observed survival (%)			
	2001		2007	
	Non-surgery patients (n=121)	Surgery patients (n=31)	Non-surgery patients (n=128)	Surgery patients (n=45)
30 days	74%	79%	63%	93%
60 days	56%	71%	42%	77%
6 months	23%	50%	12%	53%
1 year	9%	15%	2%	29%
2 years	2%	<1%	<1%	9%

- Surgery patients diagnosed in 2007 had significantly higher survival than those who did not have surgery (P<0.001) (two year survival was 9% and <1% respectively) (Figure 6). In 2001, there was no significant improvement in survival for patients who had surgery compared to those who did not.
- Patients diagnosed in 2007 who had surgery had better survival (but not statistically significant P>0.05) than those in 2001.

Figure 6: Observed survival of pancreatic cancer patients who did/ did not have surgery

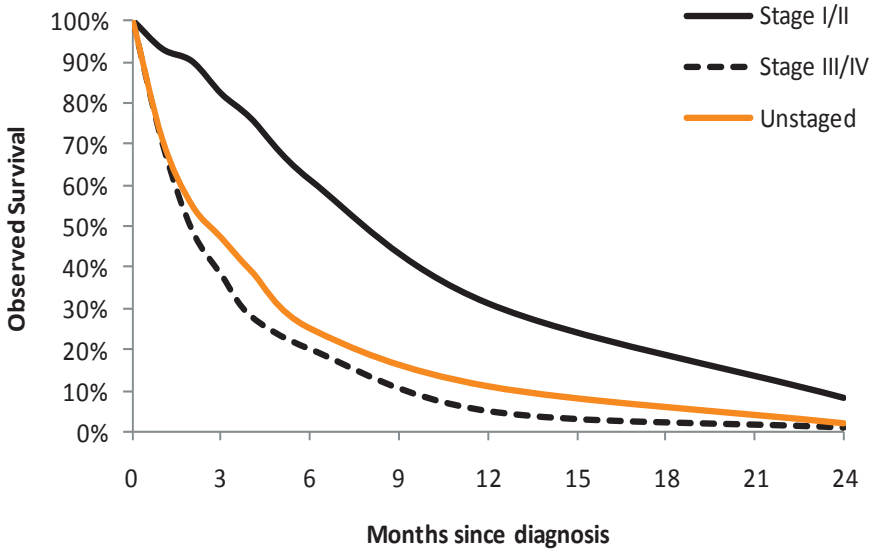


Percentage of patients alive at various times after diagnosis by stage of disease

Time	Observed survival (%)		
	Stage I & II (n=27)	Stage III & IV (n=174)	Unstaged (n=124)
30 days	93%	70%	71%
60 days	89%	49%	55%
6 months	62%	20%	24%
1 year	32%	5%	11%
2 years	7%	<1%	2%

- Overall survival for patients with early stage pancreatic cancer was significantly better than that of patients with late stage (P<0.001) and unstaged (P<0.01) disease.
- Patients with Stage I/II disease had a one-year survival of 32% (5% for Stage III/IV).

Figure 7: Observed survival of pancreatic cancer patients by stage of disease.



CONCLUSIONS

- There was information on stage of disease, with staging possible for almost three quarters of patients.
- There were fewer surgeons operating on more patients.
- More patients received surgery in fewer hospitals, with evidence of centralisation of services to the Mater Hospital.
- Less than half of patients with pancreatic cancer had a record in their notes of a multidisciplinary team discussion. An improvement on 2001, but all patients should be discussed at a multidisciplinary team meeting.
- More patients were referred to the hospital palliative care team.
- Survival for patients with early stage disease was better than that of patients with late stage and unstaged disease.
- Overall, patients who had a curative resection had a one-year survival of 54%.

SECTION III – CHOLANGIOCARCINOMA

BACKGROUND

Cholangiocarcinoma is a malignant growth arising from the cells which line the bile ducts. These are the vessels which carry bile from the liver to the small intestine. Cholangiocarcinoma is rare, with 2 new cases per 100,000 population per year in Northern Ireland. It is the second most common primary liver tumour after hepatoma. Malignant tumours of the bile ducts are usually slow growing, infiltrate locally and are late to metastasise but because they do not generate symptoms until fairly late in the course of the disease, many of these tumours are too advanced to be removed surgically by the time the diagnosis is made. Recent reports, however, have suggested an improved outcome for extensive surgical removal, even for large tumours[27]. A cholangiocarcinoma can arise anywhere in the biliary system and produces symptoms when it blocks the ducts. More than 90% are adenocarcinomas, with the remainder being squamous cell tumours. They affect both sexes, and the majority of cases are found in patients above the age of 65 years (intrahepatic occurs more often in those aged 50-60 years, extrahepatic in 60-70 years)[28].

TYPES

Cholangiocarcinomas may be classified as extrahepatic (87-92%) or intrahepatic (8-13%), and recent reports indicate that there is a trend towards an increase in the proportion of intrahepatic tumours. Whether this is due to increased diagnosis with improved cross-sectional imaging or a true secular trend, is unclear. Extrahepatic tumours are divided into proximal, middle, or distal ductal tumours. Tumours located where the right and left hepatic ducts meet with the proximal common hepatic duct are called Klatskin tumours. Intrahepatic tumours arise from the small ducts and are often diffuse and multicentric; satellite nodules occur in about 65% of patients. Solitary well-demarcated tumours are difficult to differentiate from primary hepatocellular carcinomas[28].

Lymphatic spread of these tumours is common and occurs in the cystic and common bile duct nodes in about 32% of extrahepatic tumours and 15% of intrahepatic tumours. Extrahepatic tumours also spread to the celiac nodes in about 16% of cases and to the peripancreatic and superior mesenteric nodes. Infiltration of adjacent liver occurs in 23% of cases, with peritoneal seeding, in 9%. True distant metastasis to the liver, peritoneum, or lung is extremely rare[29].

RISK FACTORS

Cholangiocarcinoma is usually associated with environmental exposures such as polyvinyl chloride (widely used plastic) or Thorotrast (thorium dioxide), a radioactive compound. It is also associated with Opisthorchis viverrini (a parasite that attacks the area of the bile duct). Other high risk groups predisposed to cholangiocarcinomas include patients with the following[30]:

1. Congenital choledochal cysts
2. Inflammatory bowel disease
3. History of other malignancies
4. Previous surgery for choledochal cyst or biliary atresia
5. Alpha1-antitrypsin deficiency
6. Autosomal dominant polycystic kidney disease
7. Gallstones
8. Papillomatosis of the bile ducts
9. Chronic typhoid carrier status

Cholangiocarcinoma is also associated with ulcerative colitis (8%), primary sclerosing cholangitis (PSC) and chronic infestation with the liver fluke 'Clonorchis sinensis'[30].
No specific race-related increase in prevalence is thought to exist, although the incidence in the Far Eastern countries is increased due to increased prevalence of risk factors e.g. parasitic infections[29].

SYMPTOMS

Symptoms are usually due to biliary obstruction, and therefore include jaundice, pale stools, dark urine, pruritus (itching), weight loss and abdominal pain. Jaundice is the most common manifestation of cholangiocarcinoma. The obstruction and subsequent cholestasis tends to occur early if the tumour is located in the common bile duct or common hepatic duct. Jaundice often occurs later in perihilar or intrahepatic tumours and is often a marker of advanced disease. Pruritus usually is preceded by jaundice, but itching may be the initial symptom of cholangiocarcinoma. Weight loss is a variable finding and may be present in one third of patients at the time of diagnosis. Abdominal pain is relatively common in advanced disease and often is described as a dull ache in the right upper quadrant[31].

TREATMENT

Less than 20% of intrahepatic tumours are resectable. Distal and periampullary extrahepatic tumours are more amenable to surgery and carry a better prognosis, with a five-year survival rate of 39%. The reported five-year survival rate in patients with resected proximal tumours is 5-15%. Most patients die within a year of diagnosis.[29]
The type of treatment given depends on a number of factors, including general health, the position and size of the cancer in the bile duct and whether the cancer has spread beyond the bile duct. If the intrahepatic cholangiocarcinoma is limited to a portion of the liver that can safely be removed, then resection or removal of this part of the liver is the preferred treatment. If the cancer has spread outside the liver to lymph nodes or other organs, then surgery is unlikely to prolong life. Chemotherapy and radiation therapy have been tried in patients who are not candidates for surgery. For most of these patients biliary drainage is the mainstay of palliation. However, shrinkage of the cancer and prolongation of life only occurs in a minority of patients. Data suggest that liver transplantation could offer long-term survival in selected patients when combined with neoadjuvant chemoradiotherapy. Photodynamic treatment to treat bilirubin build up is a palliative technique that might improve quality of life[32].

RESULTS

Study patients

	Cholangiocarcinoma (C22.1, C24.0, C24.9)	
	2001	**2007**
Number of patients reported on	45	49
Number of male (%)	23 (51%)	20 (41%)
Number of female (%)	22 (49%)	29 (59%)
Average age at diagnosis (age range)–male	70 (47-92)	72 (46-89)
Average age at diagnosis (age range)–female	77 (57-95)	74 (57-99)

- There were 45 and 49 patients with cholangiocarcinoma registered in 2001 and 2007 respectively.
- The average age at diagnosis was slightly higher in females.
- Over half of patients presented through Accident & Emergency with others including elective admissions, outpatients and radiology.
- Patients mostly presented within their Health Board/ Trust of residence.

Risk Factors

- In both years about a third of patients were recorded as non-smokers.
- Similarly just under a third of patients were recorded as having never consumed alcohol.
- In 2007, two patients had a family history of pancreatic cancer (none in 2001).

Co-morbidities (Note: Patients may have had more than one co-morbidity)

	Number of patients (%)	
	2001 (n=45)	**2007 (n=49)**
Gallstones	20 (44%)	15 (30%)
Arthritis	13 (29%)	16 (33%)
Ischaemic heart disease	13 (29%)	12 (25%)
Hypertension	11 (24%)	20 (41%)
Cerebrovascular disease	7 (16%)	2 (4%)
Diabetes mellitus	5 (11%)	6 (12%)
Osteoporosis	4 (9%)	7 (14%)
COPD*	4 (9%)	4 (8%)
Previous cholecystectomy	3 (7%)	4 (8%)
Dementia	2 (4%)	4 (8%)
Chronic pancreatitis	1 (2%)	1 (2%)
Other Malignancy	8 (18%)	5 (10%)

* *COPD = Chronic Obstructive Pulmonary Disease*

- Co-morbidities were similar in both years, reflecting the age group of the patients.

Symptoms/signs at presentation (Note: Patients may have had more than one symptom)

	Number of patients (%)	
	2001 (n=45)	**2007 (n=49)**
Altered stool/urine	37 (82%)	31 (63%)
Jaundice	35 (78%)	36 (74%)
Loss of Appetite	25 (56%)	31 (63%)
Nausea/vomiting	25 (56%)	22 (45%)
Weight Loss	22 (49%)	26 (53%)
Abdominal pain	22 (49%)	23 (47%)
Fatigue	15 (33%)	21 (43%)
Palpable liver mass	14 (31%)	22 (45%)
Itching	14 (31%)	18 (37%)
Back pain	11 (24%)	6 (12%)
Diarrhoea	6 (13%)	7 (14%)
Cachexia	5 (11%)	5 (10%)
Palpable abdominal mass	3 (7%)	8 (16%)
Pallor	3 (7%)	5 (10%)
Abdominal swelling	2 (4%)	8 (16%)

- The most frequently recorded symptoms were altered stool/ urine (63% in 2007 and 82% in 2001) and jaundice (74% in 2007 and 78% in 2001).
- Approximately half of patients presented with loss of appetite, nausea/vomiting, weight loss and /or abdominal pain.
- On examination 45% of patients had a palpable liver mass.

Multidisciplinary Team Meetings

- In both years just over one half of patients had a record in their notes that a multidisciplinary meeting had taken place.

Staging

- In 2007, 8% of cholangiocarcinoma patients had a staging laparoscopy (4% in 2001).
- There was better recording of stage in 2007, with 49% of patients staged (29% in 2001).
- In 2007, more than one third of cholangiocarcinoma patients were Stage IV.

Treatment

- In 2007, 77% of cholangiocarcinoma patients had non-surgical biliary drainage either at an ERCP or PTC (27% in 2001).
- In 2007, 8 patients had surgery (4 patients in 2001), 2 of which were surgical resections with curative intent in 2007 (none in 2001). All 8 surgical procedures were performed in the Mater Hospital.

Oncology

Reason for referral to oncology

	Number of patients (%)	
	2001 (n=45)	**2007 (n=49)**
Assessment	12 (27%)	19 (39%)
Radiotherapy	3 (7%)	-
Chemotherapy	9 (20%)	18 (37%)

- More patients were referred to oncology in 2007.

After care recorded (Note: patients may have had more than one type of referral).

	Number of patients (%)	
	2001 (n=45)	**2007 (n=49)**
General practitioner	35 (78%)	38 (77%)
Community nurse	17 (38%)	23 (47%)
Hospice	9 (20%)	7 (14%)
Macmillan nurse	9 (20%)	6 (12%)
Palliative care team/specialist	5 (11%)	26 (53%)
Dietician	2 (4%)	5 (10%)
HPB* nurse	0	10 (20%)

** Hepato Pancreato Biliary*

- Three quarters of patients had a record of onward referral to their GP.
- In 2007, 53% of patients were referred to the hospital palliative team at some stage in their treatment journey. Hospital notes in 2001 indicated that only 11% of patients were referred to a palliative team.
- In 2007, 20% of patients were referred to the HPB nurse at the Mater Hospital.

Information in GP letter

This relates to information recorded in the discharge letter from the hospital to GP.

	Number of patients (%)	
	2001 (n=45)	2007 (n=49)
Management plan	38 (84%)	39 (80%)
Letter includes prognosis	22 (49%)	19 (39%)
Discussed prognosis with patient	22 (49%)	43 (88%)
Discussed prognosis with family	17 (38%)	22 (90%)

- Overall, information contained in the GP letter has improved with a substantial increase in the number of GP letters containing details of whether or not a diagnosis has been discussed with the patient and/or family members.

Patient survival

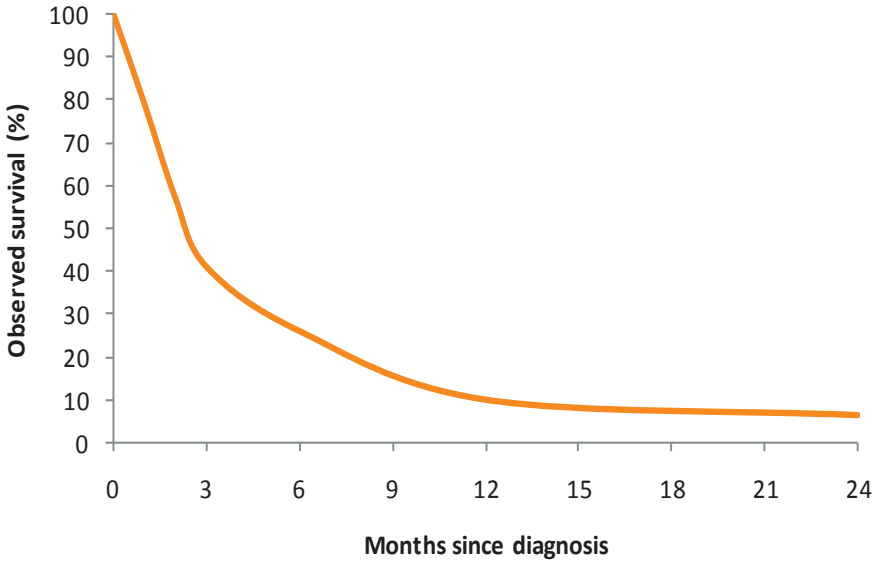
Survival analysis was performed on patients diagnosed in 2001 and 2007, with follow up for 2 years using the Kaplan Meier method.

Percentage of patients alive at various times after diagnosis

Time	Observed survival (%)		
	Both years (n=94)	2001 (n=45)	2007 (n=49)
30 days	79%	82%	74%
60 days	57%	52%	60%
6 months	26%	22%	29%
1 year	10%	9%	9%
2 years	7%	5%	5%

- Survival from cholangiocarcinoma is very poor with around 10% of patients surviving one year after diagnosis (Figure 8).
- There was no significant improvement in overall survival between 2001 and 2007 ($P>0.05$).

Figure 8: Observed survival of patients diagnosed with cholangiocarcinoma



SECTION IV - AMPULLA OF VATER CARCINOMAS

BACKGROUND

Carcinoma of the ampulla of Vater is defined as a malignant tumour arising in the last centimetre of the common bile duct where it passes through the wall of the duodenum and ampullary papilla. The pancreatic duct and common bile duct merge and exit by way of the ampulla into the duodenum. The ductal epithelium in these areas is columnar and resembles that of the lower common bile duct[33].

Adenocarcinoma of the ampulla of Vater is a relatively uncommon tumour that accounts for approximately 0.2% of gastrointestinal tract malignancies and approximately 7% of all ampulla of Vater carcinomas[33].

RISK FACTORS

Both benign and malignant ampullary tumours can occur sporadically, or in the setting of a genetic syndrome. The incidence is increased among patients with hereditary polyposis syndromes, such as familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC)[33].

SYMPTOMS

The usual symptoms are painless jaundice, intermittent or constant fatigue, pruritus, fever and non-specific abdominal pain. Intestinal haemorrhage or pancreatitis are also possible. The clinical signs and symptoms of cancers of bile duct cancer (including the ampulla of Vater) can mimic cancers of the common bile duct, the duodenum or even the pancreas. In some ways they partake of features of each of these, and can also involve these organs. But they have some features that set them apart. For instance, the surface of these tumours is frequently necrotic or ulcerated. They are occasionally infiltrating, mucous producing type, or undifferentiated adenocarcinomas[34].

SPREAD

Ampulla of Vater carcinomas tend to spread by a local infiltration of the walls of the adjacent common bile ducts, or the second portion of the duodenum, or the head of the pancreas. If it spreads further it may involve the portal or splenic veins, and clots within these vessels may occur. It is said that local lymph nodes are involved in about one in every four patients at the time of surgical diagnosis[34].

TREATMENT

True ampullary tumours have a better prognosis than ampulla of Vater malignancies of pancreatic origin. Resectability rates are higher (over 90% in contemporary series) and 5-year survival rates are approximately 30-50%, even in patients with lymph node involvement. In contrast, fewer than 10% of patients with completely resected node-positive pancreatic cancer are alive at two years. Because it can be difficult to distinguish a primary ampullary carcinoma from other ampulla of Vater tumours preoperatively, an aggressive approach to diagnosis and treatment is needed to ensure

that patients with these comparatively favourable and treatable cancers are treated optimally[35].

Sometimes, ampulla of Vater carcinomas with necrosis or ulceration may have potentially troublesome and occasionally life-threatening bleeding. For these tumours a pancreaticoduodenectomy is a formidable operation, and the morbidity and mortality rates associated with this procedure historically have been high[36].

RESULTS

- There were 14 and 16 patients with ampulla of Vater carcinoma registered in 2001 and 2007 respectively.
- Ampulla of Vater is more common in males[37]. In 2007, 88% of patients were male (50% in 2001) (variation likely due to small numbers).
- Almost 80% of patients presented to a hospital within their Health Board/Trust of residence.
- In 2007, 94% of patients were diagnosed on the basis of histopathology (64% in 2001).
- In 2007, 81% of patients had a stage assigned (71% in 2001). Where staging was possible 38% of patients were Stage III/ IV (20% in 2001).
- In 2007, 44% of patients had surgery (93% in 2001).
- In 2007, 6 of the 7 patients had their surgery in the Mater Hospital (the remaining one was carried out in the Ulster Hospital). In 2001 surgery was carried out in 7 different hospitals.

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APPENDICES

APPENDIX A:

Summary of recommendations of the 'Campbell Report', that is, Cancer Services: Investing for the Future[1], 1996.

1. The management of patients with cancer should be undertaken by appropriately trained, organ and disease specific medical specialists.

2. All patients with cancer should be managed by multidisciplinary, multiprofessional specialist cancer teams.

3. A Cancer Forum should be established involving all key interests in the delivery of cancer services.

4. Cancer Units should, in conjunction with local GPs and other providers, develop an effective communication strategy.

5. Northern Ireland should have one Cancer Centre, which in addition to its regional role, should act as a Cancer Unit to its local catchment population of around half a million.

6. There should be four other Cancer Units, one in each Board area, each serving a population of around a quarter of a million.

7. Radiotherapy services, together with chemotherapy services, should be moved as soon as possible to the Belfast City Hospital and become an integral part of the regional Cancer Centre.

8. Each Cancer Unit should develop a chemotherapy service. This service should be staffed by designated specialist nurses and pharmacists, and should be overseen by the non-surgical oncologist attached to the unit, with back-up from a haematologist.

9. There should be a minimum target of 13 consultants in non-surgical oncology for Northern Ireland by 2005.

10. Any new appointments of trained cancer specialists should be to Cancer Units or to the Cancer Centre.

11. Guidelines should be drawn up and agreed for the appropriate investigation and management of patients presenting to non-Cancer Unit hospitals who turn out to have cancer.

12. The Cancer Centre and Cancer Units should each develop a specialist multiprofessional palliative care team.

13. There should be a comprehensive review of palliative care services in Northern Ireland.

14. The Northern Ireland Cancer Registry should be adequately resourced.

APPENDIX B:

Key recommendations of the Guidance on Commissioning Cancer Services: "Improving Outcomes in upper gastro-intestinal cancers"[2]

1. All hospitals which intend to provide services for patients with upper gastrointestinal cancer should be fully involved in appropriate Cancer Networks which include inter-linked Cancer Centres and Cancer Units. Each region should review proposals for these services, to ensure that proposed local arrangements reflect the recommendations in this guidance manual accurately.

2. There should be documented local referral policies for diagnostic services for suspected upper gastro-intestinal cancer. These should be jointly agreed between General Practitioners (GPs) in Primary Care Groups and Trusts, and appropriate specialists in local hospitals and Cancer Units and Centres in each Network.

3. Specialist treatment teams should be established at appropriate Cancer Centres or Units. Pancreatic Cancer Teams should aim to draw patients from populations of two to four million. Special arrangements need to be made where geographical constraints and boundaries define populations, e.g. in Northern Ireland and the Scottish Highlands.

4. There should be clear documented policies for referral of patients between hospitals, and for processes by which clinicians in local hospitals seek advice from specialist treatment teams about the management of individual patients for whom referral may not be appropriate.

5. Palliative support and specialist care should be available to all who need it. This will require effective co-ordination and communication between primary care, social and voluntary services, local palliative care teams, hospital services and those who provide specialist advice and interventions.

6. Monitoring systems using common data-sets should be established throughout each Cancer Network to audit patient management, key communications, referral processes, and key outcomes of treatment.

APPENDIX C:

Summary recommendations in specific topic areas of the Guidance on Commissioning Cancer Services: *"Improving Outcomes in upper gastro-intestinal cancers"*[2]

1. Primary Care in Diagnosis and Referral

- Patients with symptoms that could be due to upper gastro-intestinal cancer should either be referred for endoscopy, or for investigation by a designated Upper Gastro-intestinal Diagnostic Team at a local District General Hospital (DGH). Symptoms of uncomplicated dyspepsia in patients under the age of 55 should be managed empirically.
- Fast-track endoscopy services (which may be provided within primary care) should be established.
- Patients with dysphagia, dyspepsia, jaundice or upper abdominal mass should be referred to the Upper Gastro-intestinal Diagnostic Team for investigation within two weeks.

2. Patient-centred Care

- Patients should be given as much information as they wish to have, in language they are likely to understand, and in both verbal and written forms. This should include realistic information about the disease, and about the aims and likely effects of diagnostic procedures and treatment options.
- Since these are disorders that directly affect patients' ability to eat and drink, help with nutrition can be vital. All patients should be given practical information about appropriate diets and advice on minimising problems with eating.
- The majority of patients are over 70 years of age. Many will require both practical and social support. Additional support may also be necessary for carers who look after patients at home.

3. Specialist Services and Multiprofessional Teams

- All levels of service should work closely together to form an integrated Cancer Network which offers efficient and consistent delivery of high standards of care.
- Diagnostic services should be established at local District General Hospitals (DGHs). Those who are believed to have, or might have, pancreatic cancer should normally be referred to the Specialist Pancreatic Cancer Team – this includes patients with distal bile duct stricture.

4. Diagnosis and Assessment

- The lead clinicians of Upper Gastro-intestinal Diagnostic Teams in each Network should collaborate with the Specialist Pancreatic Cancer Team to produce agreed assessment and referral guidelines which specify the nature and sequence of diagnostic procedures to be used throughout the Network for patients with suspected cancer of the pancreas.

- It may not be appropriate for frail patients with advanced disease to be referred to the Cancer Centre for direct assessment; the management of such patients should be discussed with the Specialist Pancreatic Cancer Team.
- Patients with jaundice should only be given biliary stents by, or with the specific agreement of, the Specialist Pancreatic Cancer Team.

5. Treatment for Pancreatic Cancer

- Treatment for patients with pancreatic cancer should be the responsibility of Specialist Pancreatic Cancer Teams. These should be based in Cancer Centres and should serve populations of two to four million.
- Patients for whom radical interventions would not be appropriate may be treated in local hospitals with Cancer Units which offer palliative care, but the Specialist Pancreatic Cancer Team should be informed of every case and should normally be involved in working out an appropriate care plan. There should be arrangements to allow for members of Specialist Pancreatic Cancer Teams to see patients in local hospitals.
- Post-operative chemotherapy using 5-FU may be beneficial, but adjuvant radiotherapy (with or without chemotherapy) is not recommended.
- Palliative treatment with chemotherapy should be considered. 5-FU is probably as effective as other drug regimes but there is no clear evidence to guide the choice of therapy. Hormone treatment should not normally be used in the primary treatment of patients with pancreatic cancer.
- Chemo-radiotherapy may be considered for fitter patients with inoperable localised disease, but the risk of adverse effects must be carefully balanced against potential benefits.
- Radiotherapy alone is not recommended.

6. Palliative Interventions and Care

- Palliative care should be an integral part of patient management. Specialist multiprofessional palliative care teams should be available to arrange the provision both of relief from symptoms and social and psychological support for patients and their carers when these needs cannot be met by primary care teams.

APPENDIX D:

Guidelines for the management of patients with pancreatic cancer periampullary and ampullary carcinomas[3], June 2005 – Issued by the Pancreatic Section of the British Society of Gastroenterology
(Summary of recommendations)

1. Incidence, mortality rates, and aetiology

- Continued health education to reduce tobacco consumption should lower the risk of developing pancreatic carcinoma.
- All patients at increased inherited risk of pancreatic cancer should be referred to a specialist centre offering specialist clinical advice and genetic counselling and appropriate genetic testing.
- Secondary screening for pancreatic cancer in high risk cases should be carried out as part of an investigational programme coordinated through specialist centres.
- Examination and biopsy of the periampullary region is important in patients with longstanding familial adenomatous polyposis. The frequency of endoscopy is determined by the severity of the duodenal polyposis.
- Patients with Stage IV duodenal polyposis who are fit for surgery should be offered resection.

2. Pathology

- Proper recognition of variants of ductal carcinomas and other malignant tumours of the pancreas require specialist pathological expertise.
- The minimum dataset proposed by the Royal College of Pathologists should be used for reporting histological examination of pancreatic resection specimens.

3. Clinical features

- The diagnosis of pancreatic cancer should be considered in patients with adult onset diabetes who have no predisposing features or family history of diabetes.
- Pancreatic cancer should be excluded during the investigation of patients who have had an unexplained episode of acute pancreatitis.

4. Investigations

- Clinical presentation suggesting cancer of the pancreas should lead without delay to ultrasound of the liver, bile duct, and pancreas.
- When the diagnosis of pancreatic malignancy is suspected from clinical symptoms and/or abdominal ultrasound findings, the selective use of computerised tomography (CT), endoscopic retrograde cholangio-pancreatography (ERCP), and/or magnetic resonance (MR), including magnetic resonance cholangiopancreatography (MRCP) and occasionally magnetic resonance angiography (MRA), will accurately delineate tumour size, infiltration, and the presence of metastatic disease in the majority of cases.
- Where available, endosonography and/or laparoscopy with laparoscopic ultrasonagraphy may be appropriate in selected cases.

5. Tissue diagnosis

- Attempts should be made to obtain a tissue diagnosis during the course of investigative endoscopic procedures.
- Failure to obtain histological confirmation of a suspected diagnosis of malignancy does not exclude the presence of a tumour, and should not delay appropriate surgical treatment.
- Efforts should be made to obtain a tissue diagnosis in patients selected for palliative forms of therapy.

6. Treatment

a. Stent or surgical palliation

- Most patients requiring relief of obstructive jaundice will be adequately treated by placement of a plastic stent; surgical bypass may be preferred in patients likely to survive more than six months.
- Duodenal obstruction should be treated surgically.

b. Stent insertion

- Endoscopic stent placement is preferable to trans-hepatic stenting.
- After failure of endoscopic stent placement, percutaneous placement of a self expanding metal stent, or a combined radiological/endoscopic approach, will increase the number of patients who can be successfully stented.
- Both plastic and self expanding metal stents are effective in achieving biliary drainage but require further development. Currently, the choice between these stents depends on clinical factors, local availability, and local expertise.
- If a stent is placed prior to surgery, this should be of the plastic type and it should be placed endoscopically. Self expanding metal stents should not be inserted in patients who are likely to proceed to resection.
- Resectional surgery should be confined to specialist centres, to increase resection rates and reduce hospital morbidity and mortality.
- Pancreaticoduodenectomy (with or without pylorus preservation) is the most appropriate resectional procedure for tumours of the pancreatic head.
- Extended resections involving the portal vein or total pancreatectomy may be required in some cases but do not increase survival when carried out routinely.
- Percutaneous biliary drainage prior to resection in jaundiced patients does not improve surgical outcome and may increase the risk of infective complications.
- Left sided resection (with splenectomy) is appropriate for localised carcinomas of the body and tail of the pancreas. Involvement of the splenic vein or artery is not in itself a contraindication to such resection.

c. Palliative surgery

- Duodenal bypass should be used during palliative surgery.
- Biliary bypass should be constructed with the bile duct in preference to the gall bladder.

d. Non-surgical therapies

- Adjuvant or neoadjuvant therapies in conjunction with surgery should ideally be administered in the context of a clinical trial. Outside a trial the use of 5FU and folinic acid based treatment is recommended.
- If chemotherapy is used for palliation, gemcitabine single agent treatment is recommended.
- Therapy with novel treatments should only be offered to patients within clinical trials.

e. Relief of pancreatic pain/ palliative care

- Patients should have access to palliative care specialists.
- Pain relief should be achieved using a progressive analgesic ladder.
- Neurolytic coeliac plexus block is effective for the treatment and prevention of pain. Its use should be considered at the time of palliative surgery, or by percutaneous or endoscopic approach in non-surgical patients.
- Chemoradiation should be considered for severe pain.
- Pancreatic enzyme supplements should be used to maintain weight and increase quality of life.
- Attention to dietary intake and the use of specific nutritional supplements may improve well being.

APPENDIX E: Incidence of pancreatic cancer in Northern Ireland

Sex	Year of diagnosis	Number of cases	% of all cancers exc. NMSC	Crude rate per 100,000	EASR per 100,000	95% CI	WASR per 100,000	95%CI
Males	1993	90	2.9	11.3	12.1	(9.6,14.6)	8.1	(6.3,9.8)
	1994	62	2.0	7.7	8.5	(6.4,10.7)	5.7	(4.3,7.2)
	1995	57	1.9	7.1	7.5	(5.5,9.5)	4.8	(3.5,6.1)
	1996	92	2.9	11.4	11.9	(9.5,14.4)	7.6	(6.0,9.3)
	1997	80	2.6	9.8	10.5	(8.2,12.9)	6.9	(5.3,8.4)
	1998	71	2.3	8.7	9.3	(7.1,11.5)	6.3	(4.8,7.8)
	1999	63	2.1	7.7	8.2	(6.2,10.3)	5.3	(4.0,6.7)
	2000	64	2.0	7.8	8.2	(6.2,10.2)	5.3	(3.9,6.6)
	2001	96	2.9	11.6	12.0	(9.6,14.5)	8.0	(6.4,9.7)
	2002	83	2.5	10.0	9.8	(7.7,11.9)	6.4	(4.9,7.8)
	2003	60	1.7	7.2	7.0	(5.2,8.8)	4.6	(3.4,5.8)
	2004	75	2.1	9.0	8.8	(6.8,10.9)	6.0	(4.6,7.4)
	2005	100	2.8	11.8	11.8	(9.5,14.2)	7.9	(6.3,9.5)
	2006	104	2.8	12.2	11.8	(9.5,14.0)	8.0	(6.4,9.6)
	2007	107	2.7	12.4	11.9	(9.6,14.1)	7.9	(6.3,9.4)
Females	1993	85	2.7	10.2	7.9	(6.1,9.7)	5.3	(4.0,6.5)
	1994	78	2.5	9.3	7.5	(5.8,9.3)	5.0	(3.8,6.3)
	1995	65	2.1	7.7	5.9	(4.4,7.5)	3.9	(2.8,5.0)
	1996	73	2.2	8.6	6.7	(5.1,8.3)	4.2	(3.1,5.4)
	1997	82	2.5	9.6	7.2	(5.5,8.8)	4.7	(3.5,5.8)
	1998	65	2.0	7.6	5.6	(4.2,7.0)	3.6	(2.6,4.7)
	1999	58	1.7	6.7	5.0	(3.6,6.4)	3.2	(2.2,4.1)
	2000	81	2.4	9.4	7.7	(6.0,9.5)	5.3	(4.0,6.5)
	2001	75	2.3	8.7	6.2	(4.7,7.7)	4.0	(3.0,5.0)
	2002	87	2.5	10.0	7.5	(5.9,9.2)	4.8	(3.7,6.0)
	2003	97	2.7	11.2	8.0	(6.3,9.7)	5.2	(4.0,6.3)
	2004	83	2.3	9.5	7.2	(5.5,8.8)	4.8	(3.6,5.9)
	2005	81	2.2	9.2	6.3	(4.9,7.8)	4.0	(3.0,4.9)
	2006	103	2.8	11.6	8.4	(6.7,10.1)	5.5	(4.3,6.6)
	2007	85	2.2	9.5	6.9	(5.4,8.5)	4.6	(3.5,5.7)
Both	1993	175	2.8	10.7	9.7	(8.3,11.2)	6.5	(5.4,7.5)
	1994	140	2.3	8.5	7.9	(6.6,9.3)	5.3	(4.4,6.3)
	1995	122	2.0	7.4	6.6	(5.4,7.8)	4.2	(3.4,5.1)
	1996	165	2.6	9.9	8.9	(7.5,10.2)	5.7	(4.7,6.6)
	1997	162	2.6	9.7	8.6	(7.3,10.0)	5.6	(4.7,6.5)
	1998	136	2.1	8.1	7.5	(6.2,8.8)	5.0	(4.1,5.9)
	1999	121	1.9	7.2	6.3	(5.2,7.5)	4.1	(3.3,4.9)
	2000	145	2.2	8.6	7.8	(6.5,9.1)	5.2	(4.3,6.1)
	2001	171	2.6	10.1	8.8	(7.4,10.2)	5.8	(4.9,6.7)
	2002	170	2.5	10.0	8.5	(7.2,9.9)	5.5	(4.6,6.4)
	2003	157	2.2	9.2	7.7	(6.4,8.9)	5.0	(4.1,5.8)
	2004	158	2.2	9.2	8.0	(6.7,9.3)	5.3	(4.4,6.2)
	2005	181	2.5	10.5	8.8	(7.5,10.2)	5.8	(4.9,6.7)
	2006	207	2.8	11.9	10.1	(8.7,11.5)	6.7	(5.7,7.7)
	2007	192	2.4	10.9	9.2	(7.8,10.5)	6.1	(5.2,7.0)

NMSC – Non Melanoma Skin Cancer, EASR – European Age Standardised Rates, WASR – World Age Standardised Rates, CI – Confidence Interval

APPENDIX F: Mortality from pancreatic cancer in Northern Ireland

Sex	Year of diagnosis	Number of cases	% of all cancers exc. NMSC	Crude rate per 100,000	EASR per 100,000	95% CI	WASR per 100,000	95%CI
Males	1993	72	3.8	9.0	9.8	(7.5,12.1)	6.4	(4.8,7.9)
	1994	69	3.7	8.6	9.1	(7.0,11.3)	6.2	(4.7,7.7)
	1995	72	3.8	9.0	9.8	(7.5,12.1)	6.2	(4.7,7.7)
	1996	79	4.2	9.7	10.3	(8.0,12.7)	6.6	(5.1,8.1)
	1997	80	4.3	9.8	10.4	(8.1,12.7)	6.8	(5.2,8.3)
	1998	88	4.6	10.7	11.6	(9.1,14.0)	7.7	(6.0,9.3)
	1999	75	4.2	9.2	9.8	(7.5,12.0)	6.4	(4.9,7.9)
	2000	78	4.4	9.5	9.8	(7.6,12.0)	6.4	(4.9,7.9)
	2001	90	4.7	10.9	11.1	(8.8,13.5)	7.1	(5.6,8.6)
	2002	101	5.3	12.2	12.2	(9.8,14.6)	8.1	(6.4,9.7)
	2003	71	3.7	8.5	8.3	(6.4,10.3)	5.3	(4.0,6.6)
	2004	72	3.7	8.6	8.3	(6.4,10.3)	5.5	(4.2,6.8)
	2005	89	4.7	10.5	10.5	(8.3,12.7)	6.9	(5.4,8.4)
	2006	96	4.8	11.2	10.7	(8.6,12.9)	7.2	(5.7,8.7)
	2007	106	5.2	12.3	11.8	(9.5,14.0)	8.0	(6.4,9.6)
Females	1993	83	4.8	9.9	7.6	(5.8,9.3)	5.0	(3.8,6.2)
	1994	80	4.6	9.5	7.6	(5.8,9.3)	5.0	(3.8,6.1)
	1995	72	4.3	8.5	6.6	(5.0,8.2)	4.3	(3.2,5.3)
	1996	74	4.3	8.7	6.4	(4.9,8.0)	4.1	(3.0,5.1)
	1997	81	4.6	9.5	7.1	(5.4,8.7)	4.5	(3.4,5.6)
	1998	68	3.9	7.9	5.8	(4.4,7.3)	3.8	(2.7,4.8)
	1999	64	3.7	7.4	5.4	(4.0,6.8)	3.5	(2.5,4.4)
	2000	86	4.8	10.0	8.0	(6.2,9.8)	5.3	(4.1,6.6)
	2001	87	5.0	10.1	7.3	(5.7,9.0)	4.7	(3.6,5.8)
	2002	90	5.1	10.4	7.3	(5.7,8.9)	4.5	(3.5,5.6)
	2003	102	5.6	11.7	8.3	(6.6,10.0)	5.2	(4.0,6.3)
	2004	79	4.4	9.0	6.3	(4.8,7.8)	4.1	(3.1,5.1)
	2005	87	4.8	9.9	7.0	(5.5,8.6)	4.4	(3.4,5.5)
	2006	102	5.6	11.5	8.0	(6.3,9.6)	5.1	(4.0,6.3)
	2007	95	5.3	10.6	7.4	(5.8,9.0)	4.7	(3.7,5.8)
Both	1993	155	4.3	9.5	8.5	(7.1,9.9)	5.6	(4.6,6.5)
	1994	149	4.1	9.1	8.3	(6.9,9.7)	5.5	(4.6,6.5)
	1995	144	4.0	8.7	7.9	(6.6,9.2)	5.0	(4.2,5.9)
	1996	153	4.2	9.2	8.1	(6.7,9.4)	5.1	(4.2,6.0)
	1997	161	4.5	9.6	8.6	(7.2,10.0)	5.5	(4.6,6.4)
	1998	156	4.3	9.3	8.5	(7.1,9.8)	5.6	(4.6,6.5)
	1999	139	3.9	8.3	7.3	(6.0,8.5)	4.8	(3.9,5.6)
	2000	164	4.6	9.7	8.8	(7.4,10.1)	5.8	(4.8,6.7)
	2001	177	4.8	10.5	8.8	(7.5,10.1)	5.7	(4.8,6.6)
	2002	191	5.2	11.3	9.6	(8.2,11.0)	6.2	(5.2,7.1)
	2003	173	4.6	10.2	8.4	(7.1,9.6)	5.3	(4.4,6.1)
	2004	151	4.0	8.8	7.3	(6.1,8.5)	4.8	(3.9,5.6)
	2005	176	4.7	10.2	8.6	(7.3,9.9)	5.6	(4.7,6.4)
	2006	198	5.1	11.4	9.4	(8.0,10.7)	6.1	(5.2,7.1)
	2007	201	5.3	11.4	9.5	(8.2,10.9)	6.3	(5.4,7.3)

NMSC – Non Melanoma Skin Cancer, EASR – European Age Standardised Rates, WASR – World Age Standardised Rates, CI – Confidence Interval

APPENDIX G:

Staging of Pancreatic Cancer

Accurate staging
Accurate staging is essential for the planning of appropriate treatment and for the comparison of the outcomes of such treatment (surgical and non-surgical).

The TNM classification of exocrine pancreatic carcinoma (6th Edition[26]) is shown in Table 1.

Since only a minority of patients with pancreatic cancer undergo surgical resection, a single TNM classification applying to both clinical and pathological staging has been introduced in the 6th edition of TNM.

Clinical staging

Sufficient information for clinical staging can be obtained from clinical examination, high quality CT imaging (contrast-enhanced multislice CT) and chest X-ray. On the basis of these findings, patients can be classified as having locally resectable (Stage I or II) locally advanced (Stage III), or metastatic (Stage IV) pancreatic cancer. Endoscopic ultrasound also provides additional information on clinical stage and also permits fine needle aspiration biopsy. Laparoscopy is often performed on patients believed to have localized resectable tumours (Stage I or II). It can detect small liver or peritoneal metastases and result in upstaging to Stage IV in 10 - 40% of patients believed to have Stage I or II disease on the basis of CT alone.

Pathological staging
Pathological staging adds significant information to this process. It is usually only possible if partial resection (pancreaticoduodenectomy/distal pancreatectomy) or complete resection of the tumour (total pancreatectomy) and the regional nodes. This gives more exact information on the extent of the tumour (T) and detects the presence of metastatic tumour within the examined lymph nodes (N) and the presence of distant metastases e.g. Peritoneal or liver seeding (M). The presence of malignant cells in peritoneal fluid is considered M1.

Table 1 TNM classification of pancreatic cancer[26]

Primary Tumour (T)

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour limited to the pancreas, 2cm or less in greatest dimension
T2	Tumour limited to the pancreas, more than 2cm in greatest dimension
T3	Tumour extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
T4	Tumour involves the celiac axis or the superior mesenteric artery (unresectable tumour)

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant Metastasis (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastases

In order to facilitate survival analysis the assigned TNM profile is condensed into a stage group category (Table 2).

Table 2 Stage Group Pancreatic Cancer

Stage	***T***	***N***	***M***
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIIB	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
III	T4	any N	M0
IV	any T	any N	M1

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