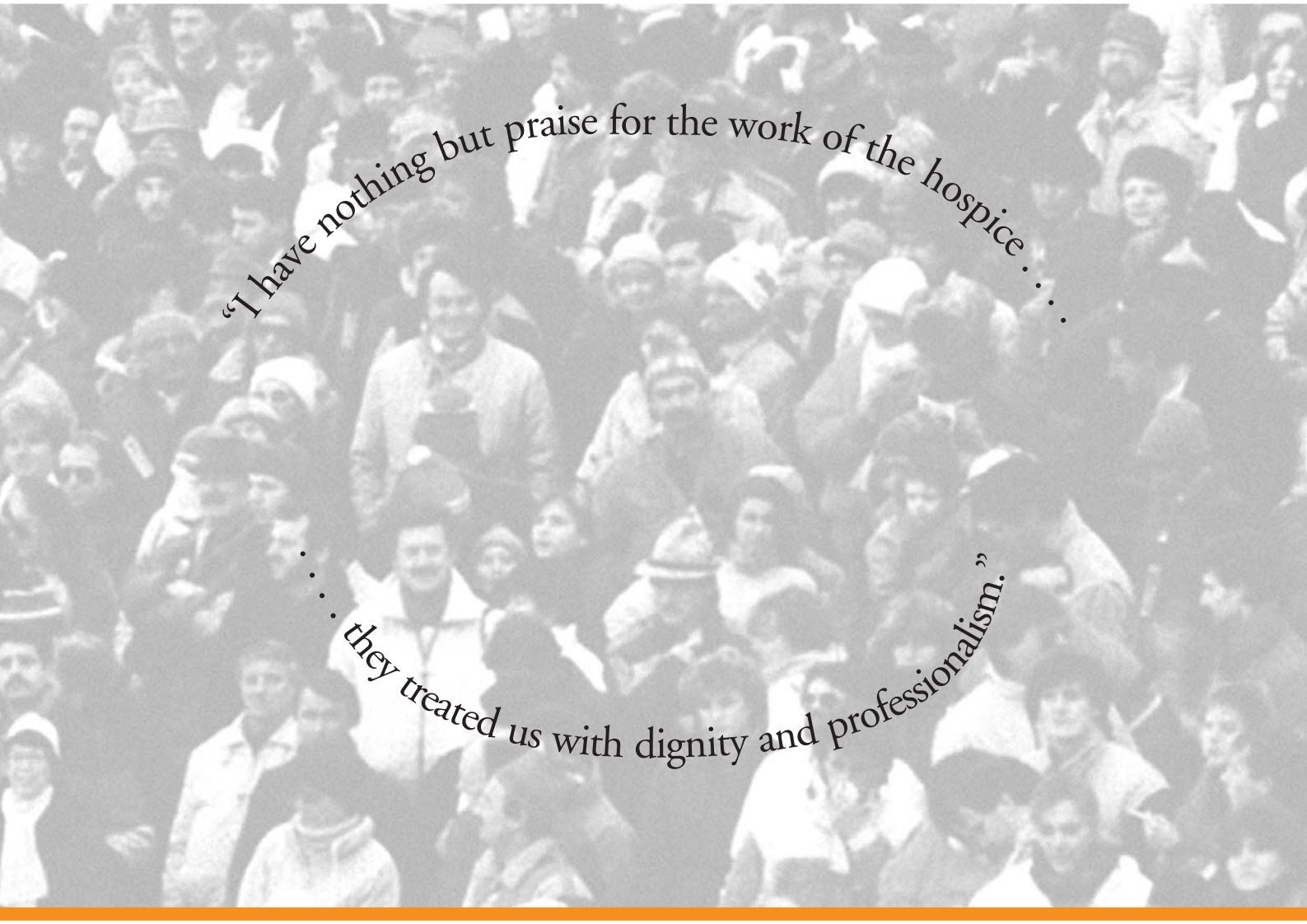
N. IRELAND Cancer Registry

Cancer Services Audit 2001

Pancreas



Queen's University Belfast

Cancer Services Audit 2001
PANCREAS
(also includes cholangiocarcinomas and ampulla of Vater carcinomas)

Edited by: **Heather Kinnear, Anna Gavin, Damian Mole, and Lisa Ranaghan.**

This report should be cited as; Kinnear H, Gavin A, Mole D, Ranaghan L, 2005.
Cancer Services Audit 2001, Pancreas.
N. Ireland Cancer Registry

available at www.qub.ac.uk/nicr/racc.htm

CONTENTS

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 and made a vital contribution in monitoring this progress.

Since 1996 we have seen the establishment of five Cancer Units at Altnagelvin, Antrim, Belfast City, Craigavon, and Ulster hospitals and a regional Cancer Centre at the Belfast City Hospital working closely with the Royal Group of Hospitals. The Cancer Units are now the main focus for the delivery of services for people with the more common cancers. In addition, some services for other less common cancers are provided from Cancer Units, in conjunction with the Cancer Centre, on a shared care basis. These organisational changes have already made an impact on care.

This report on pancreatic cancer is very welcome. It is the sixth in a series that will examine in detail the pathways of care for patients with cancer and to make service recommendations. This report provides a fascinating insight into the care received by pancreatic cancer patients in 2001. I recognise that the service has developed since then and see this report as facilitating the ongoing work of improving services and patient care.

This work marks a significant step in the evaluation of cancer care and confirms the great value of the Registry as a public health tool. I look forward to future reports in this series and regular five yearly snapshots of the changing process of cancer care.

Dr Henrietta Campbell
Chief Medical Officer

ACKNOWLEDGEMENTS

The N. Ireland Cancer Registry is funded by the Department of Health, Social Services & Public Safety Northern Ireland (DHSSPSNI).

The work of this project would not have been possible without the additional funding received from the various sources outlined below:

- Department of Health, Social Services & Public Safety (DHSSPS)
- Eastern Health and Social Services Board
- Northern Health and Social Services Board
- Regional Medical Audit Group
- Research and Development Office
- Southern Health and Social Services Board
- Western Health and Social Services Board

The quality of data in this project is a result of the work of the present Registry Tumour Verification Officers, especially Carmel Canning and Bernadette Anderson, who meticulously extracted detailed information from clinical records for analysis and presentation in this report. The analysis of data was largely undertaken by Heather Kinnear and Mr Damian Mole (SpR in surgery) after data preparation by Dr Richard Middleton. We would like to express our gratitude to the Medical Records staff from all the hospitals in Northern Ireland, who, in the course of the audit for all sites, pulled an estimated 10,000 charts.

We are grateful to the clinicians who commented on the detail of data to be collected, its interpretation and final presentation. We are also grateful to Dr Peter Kennedy (Consultant Radiologist) in the Royal Victoria Hospital.

The work of the N. Ireland Cancer Registry including the production of this report is the result of the work of the team listed below:

Bernadette Anderson	Carmel Canning	Dr Denise Catney	Kate Donnelly
Patricia Donnelly	Deirdre Fitzpatrick	Colin Fox	Wendy Hamill
Helen Hanlon	Anita Jones	Jackie Kelly	Heather Kinnear
Julie McConnell	Susan McGookin	Dr Richard Middleton	Pauline Monaghan
Dr Liam Murray	Giulio Napolitano	Dr Lisa Ranaghan	Dr Jeffrey Robertson
Breige Torrans	Rosemary Ward		

I wish also to record my thanks to the Management Group and Council of the Registry who guide the work.

This presentation, I feel, has been enhanced by the stories from patients who have walked the patient journey. We have attempted to analyse and quantify this journey with a view to identifying current practice, in order that clinicians may be facilitated in improving care.

A Gavin
Director, NICR
2005

PATIENT STORIES

"My wife, a vibrant lady with red hair, in her early forty's became ill in April when she vomited up blood. She was on medication for arthritis and it was felt this had upset her stomach. The second time this happened she was admitted to hospital. She was then seen by a gastroenterologist and had investigations including an ultrasound and a gastroscopy. The results from these were not discussed with her at the hospital but she knew something was wrong when she was told her GP would be contacted and would discuss the results with her.

We were counselled appropriately by the GP and while we waited to see the consultant my wife developed a clot in her leg. We went to see the consultant, I realised that when I saw the chairs beside the table with a box of tissues the diagnosis was not good.

A biopsy was required to confirm the diagnosis of pancreatic cancer which had spread to the liver. That was 12 weeks before she died. This was the one and only time my wife showed raw emotion. She would not see our teenage daughter growing up.

We saw the consultant oncologist. He knew that we wanted to make the 'landing' as smooth as possible and that we did not want 'an estimated time of arrival'. My wife was to have chemotherapy but she was only able to have this once as she had problems with her blood clotting. She was hospitalised again and on the eve of her 44th birthday she suffered a stroke that deprived her of much of her memory but not of her great determination.

She was not expected to live through the weekend but was eventually able to come home for about 10 days. She was a shell of her former self with little memory of her past. This was torture for her family because as we knew her time was short we had expected to be able to say those things that needed to be said.

My wife was admitted to the local hospice on our 20th wedding anniversary and she passed away peacefully five days later. I have nothing but praise for the work of the hospice, not only with my wife whom they treated with dignity and professionalism but also with our daughter and me. The 'landing' was smooth even if the arrival was four decades too soon."

~

The following quotes have been adapted from actual stories.

"The fatigue is overwhelming. I can hardly describe the effect it has had on me and my life. Because of my continued sickness and pain I feel my relationship with my family has changed – I don't know if they love me anymore."

~

"I have had constant back pain and itch, my energy levels are so low. It has affected my mood badly. The itch was throughout my head, in my nostrils down to my toes – even inside my eyes – it was unbearable for weeks."

~

"I had lost a lot of sleep before coming into hospital. The sickness, stomach pain and itch were terrible. I don't know which one was worse, they were all bad. For months I was truly miserable. It has affected all of the family and brought out the worst in us all."

~

"I have decided against further treatment – I just remember feeling I had been to hell and back when I had it before."

~

INTRODUCTION

This Report is the sixth in a series which examines in detail the pathway of care for cancer patients in Northern Ireland. Pancreatic cancer is a significant cause of cancer death. The Campbell Report **"Cancer Services - Investing for the Future"**[1], while not dealing directly with pancreatic cancer 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. Key recommendations are as follows:

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.

This guidance also provided a summary of recommendations in specific topic areas (see Appendix B). We acknowledge that the guidelines given in 2001 have been superceded by more recent advice (see Appendix C), but the principles, if not particular details remain highly relevant. The following relates specifically to pancreatic cancer:

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.

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, gemcitabine, capecitabine or combinations of these drugs may be beneficial, but adjuvant radiotherapy (with or without chemotherapy) is not recommended.
- Palliative treatment with chemotherapy should be considered. There is no clear evidence to guide the choice of therapy, but ongoing trials will soon provide an evidence base for choosing an optimum drug regime. 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.

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.

At present, surgery offers the only possibility of cure from pancreatic cancer although the majority, usually over 90%, present too late for curative resection. Palliative interventions are frequently required to relieve the major symptoms: jaundice due to bile duct obstruction, and severe pain. Pancreatic cancer surgery, whether palliative or carried out with curative intent, is technically demanding high-risk surgery usually performed on elderly, malnourished patients. Life-threatening complications are common after surgery so adequate intensive care, high-dependency facilities and specialist postoperative care play an important part in the surgical management[2]. Postoperative complication rates are high. Cancer Centres should aim to achieve perioperative (30-day) mortality rates for both radical and palliative surgery of less than 5%[2].

The Pancreatic Section of the British Society of Gastroenterology published further guidelines in 2005 **"Guidelines for the Management of patients with Pancreatic cancer periampullary and ampullary carcinomas"**[3] a summary of which is included as Appendix C.

PROJECT AIM

This Report aims to document care for patients diagnosed with pancreatic cancer in 2001, and provide a baseline from which service development may be measured.

BACKGROUND

The pancreas is a glandular organ which lies just under the curvature of the stomach and deep within the abdomen. The pancreas produces enzymes which are essential for the digestion of food and it secretes hormones (insulin, glucagon, somatostatin) which regulate blood sugar levels[4], body energy stores and growth.

Pancreatic cancer is one of the less common cancers (2% of all cancers diagnosed in males and females in 2001, excluding non melanoma skin cancers). It is predominantly a disease of the elderly. The likelihood of developing pancreatic cancer rises steeply with age[5]. The average age at presentation is 69 years[6] and three-quarters of pancreatic cancer deaths occur in people over 65 years old. Of all the solid tumours, pancreatic cancer carries one of the most dismal prognoses, with rarely more than a few months between diagnosis and death[2]. The incidence of pancreatic cancer in the UK is 10 per 100,000 population[5]. There are 160 – 180 new cases each year in Northern Ireland and 6000 new cases each year in the UK. No dramatic change in levels have been observed in recent years[6]. Males are affected 1.2 – 1.5 times more commonly than females.

Pancreatic cancer can cause jaundice, nausea, weight loss, loss of appetite, and severe pain; it may also cause diabetes, diarrhoea and profound depression. Surgical resection offers the possibility of cure for a small minority of patients, particularly those with unusual types of tumour. Effective palliation of symptoms is often possible but may require specialist interventions[2].

Pancreatic cancer usually presents late, with pain, when only palliative treatment is possible. It can be diagnosed at an early (painless) stage if the tumour presses on the bile duct, causing jaundice[2].

Risk Factors

Pancreatic cancer incidence and mortality are highest in developed countries. In the USA, it is the 4th most common cause of cancer deaths and the 6th in Europe[7]. International variation lends weight to suggestions that environmental factors play a key role in the development of pancreatic cancer[8].

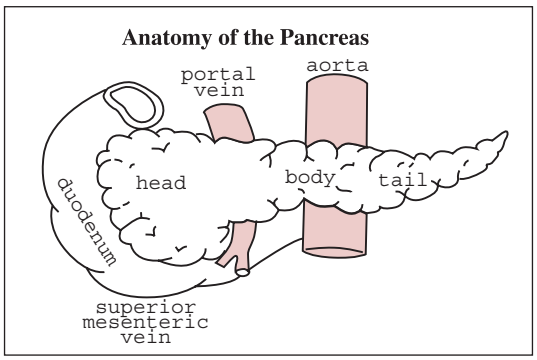
Having a close relative with pancreatic cancer doubles the risk. Smoking is the most important known risk factor, with an attributable risk of 20-40% for men and 10-20% for women[9]. Smokers who are related to a patient who developed pancreatic cancer prior to the age of 60, have an 8-fold increased risk[8]. As with other types of cancer, higher consumption of fruit and vegetables appears to be protective; nine out of ten case-control studies have found significant effects, although three cohort studies have failed to demonstrate significant benefits[8].

Dietary links have been more difficult to establish. High calorific diets, low in fruits and vegetables, with a high fat content derived from animal sources, show a strong correlation with pancreatic cancer risk[8]. There is a putative role association between charred or grilled food and an increased risk of pancreatic cancer[6]. No consistent relationship has been shown between risk of pancreatic cancer and alcohol or coffee intake, despite occasional small studies showing a detrimental effect[8]. Occupational effects are small and where present, relate to the use of formaldehyde, organic solvents and noxious pesticides[8].

Rare hereditary, genetic and medical conditions, including hereditary pancreatitis, hereditary non-polyposis colorectal cancer, ataxia-telangectasia, Peutz-Jeghers syndrome, familial breast cancer, familial atypical multiple mole melanoma, chronic pancreatitis, previous gastrectomy and DNA repair disorders show an association, when present. The majority of pancreatic cancers, however, are not associated with any of these conditions[6].

Anatomical and Histopathological Key Features

The majority (85%) of malignant pancreatic tumours are ductal adenocarcinomas[9]. 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[9]. Perineural (70%), vascular (45%) and lymphatic (80%) invasion are common[9]. The most common sites for metastases are liver and peritoneum and the most common extraperitoneal site for metastases is the lung[9].



METHODS

DATA COLLECTION

The diseases covered by this Report are ICD10 C25 (Pancreatic cancer) except C25.4 (Endocrine tumours of the pancreas). It also includes C24.0 (Extrahepatic bile duct tumours) and C24.1 (Periampullary carcinomas). It excludes C23 (Gallbladder tumours) and C24.8 (Overlapping lesion of biliary tract).

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.htm

To verify the accuracy of the radiological data collection, a representative sample of 46% (70 of 152) electronic radiology records for each patient were checked and correlated with reports held in the notes.

We acknowledge that pancreatic carcinomas, cholangiocarcinomas and periampullary carcinomas may present the same clinically so in order to ensure that all pancreatic cancers have been captured, we have included these other tumours in separate sections to make sure none have been miscoded.

EXCLUSIONS & ANALYSES

Patients were excluded if their records lacked sufficient information or if information was available only from 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.

PANCREAS RESULTS

Study Patients

Patients	Number of Patients in 2001
Total patients registered with NICR	165
Exclusions – Death certificate only	3
Exclusions – Lack of information	10
Total exclusions	13
Total reported on	152
Total reported on - Male	82 (54%)
Total reported on - Female	70 (46%)
Average age at diagnosis - Male	70
Average age at diagnosis - Female	75
Median age at diagnosis - Male	70
Median age at diagnosis - Female	77

- Data were available on 152 individuals in 2001, just over half (54%) were male.
- Levels were the same in deprived and affluent populations.

Site of Tumour

Site	Number of Patients (%) *(n=152)*
Head of pancreas	100 (66%)
Body of pancreas	9 (6%)
Tail of pancreas	12 (8%)
Overlapping lesion of pancreas	1 (<1%)
Pancreatic duct	1 (<1%)
Pancreas, unspecified	30 (20%)

- Two thirds of pancreatic cancers were recorded as head of the pancreas with 20% pancreas unspecified.

Source of referral to specialist care

Source	Number of Patients (%) *(n=152)*
GP	130 (86%)
Self (via A&E)	10 (7%)
Not recorded	5 (3%)
Non-HPB * surgeon	5 (3%)
Physician	2 (1%)

- Over 80% of all diagnosed pancreatic cancer cases in 2001 came from GP referrals.

** HPB=Hepatobilliary*

Details of GP referrals

Mode of presentation	Number of Patients (%) *(n=130)*
Accident & Emergency	46 (35%)
Elective admission*	32 (25%)
Outpatient	38 (29%)
Not recorded	3 (2%)
Other **	11 (9%)

- Just over one third (35%) presented as emergencies.
- Over one quarter presented via outpatients (29%).

**** A patient who was admitted for further investigations***

***** 6 after a domicilary visit by a hospital consultant; 5 from the private sector***

Risk factors

- 12 patients (8%) self declared that they drank more than 30 units of alcohol per week.
- 34 patients (22%) were current smokers, 49 (32%) were ex-smokers and 53 (35%) were non-smokers. The remaining 16 patients had no smoking history recorded.

Family history of pancreatic and other cancers recorded in notes

Family history	Number of Patients (%) *(n=152)*
Pancreas, first degree relative	4 (3%)
Pancreas, second degree relative	0
Other site, first degree relative	19 (13%)
Other site, second degree relative	4 (3%)
No family history of cancer	55 (36%)
Family history not recorded	70 (46%)

- 3% of all patients had a positive record of a family history of pancreatic cancer in a first degree relative in their hospital notes (5% of those with a record).

Personal history of other previous malignancies

Site	Number of Patients (%) *(n=152)*
All sites combined	23 (15%)
Breast *	5 (3%)
Basal cell skin carcinoma	4 (3%)
Other **	13 (9%)

- 15% (1 in 7) had a history of previous malignancy.

**** Some patients had more than one type of cancer***

***** Other includes bladder, brain, colorectal, lung, renal, stomach, prostate with numbers less than 4***

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

Co-morbidities	Number of Patients (%) *(n=152)*		
	Yes	No	Not recorded
COPD *	24 (16%)	117 (77%)	11 (7%)
Ischaemic heart disease	49 (32%)	93 (61%)	10 (7%)
Dementia	4 (3%)	130 (85%)	18 (12%)
Cerebrovascular disease	15 (10%)	121 (80%)	16 (10%)
Chronic pancreatitis	8 (5%)	134 (88%)	10 (7%)
Arthritis	32 (21%)	105 (69%)	15 (10%)
Gallstones ± cholecystectomy	37 (24%)	101 (67%)	14 (9%)
Previous cholecystectomy	15 (10%)	128 (84%)	9 (6%)
Diabetes mellitus	29 (19%)	115 (76%)	8 (5%)
Diabetes - diet controlled	13 (9%)	-	-
- insulin	7 (5%)	-	-
- tablet controlled	9 (6%)	-	-
Hypertension	50 (33%)	89 (58%)	13 (9%)
Osteoporosis	7 (4%)	126 (83%)	19 (13%)

**** COPD = Chronic Obstructive Pulmonary Disease***
NOTE: 9 patients also had comorbidities of ulcerative colitis, psychiatric disease, Parkinson's disease or learning disability

- 5% of patients had a history of chronic pancreatitis.
- One third of patients had a record in their hospital notes of ischaemic heart disease and a further third had hypertension.
- A quarter had a history of gallstones. One fifth of patients had gallstones but had not had a cholecystectomy.

Duration of diabetes

Duration	Number of Patients (%) *(n=29)*
Up to 6 months	10 (34%)
7 – 12 months	2 (7%)
13 – 24 months	3 (10%)
More than 24 months	14 (48%)

- One fifth of patients had diabetes. Of these, one third (34%) experienced it for a period up to 6 months before diagnosis, while half were diagnosed for more than two years (maximum period was 13 years).

Drug History at Presentation

Drug/Drug class	Positive record	Negative record	Not recorded
Steroids	11 (7%)	107 (70%)	34 (23%)
Antihypertensives	72 (47%)	56 (37%)	24 (16%)
Controlled*	4 (3%)	110 (72%)	38 (25%)
Inhalers	19 (13%)	101 (66%)	32 (21%)
Aspirin	48 (31%)	85 (56%)	19 (13%)
Warfarin	8 (5%)	127 (84%)	17 (11%)
Other NSAID**	9 (6%)	107 (70%)	36 (24%)

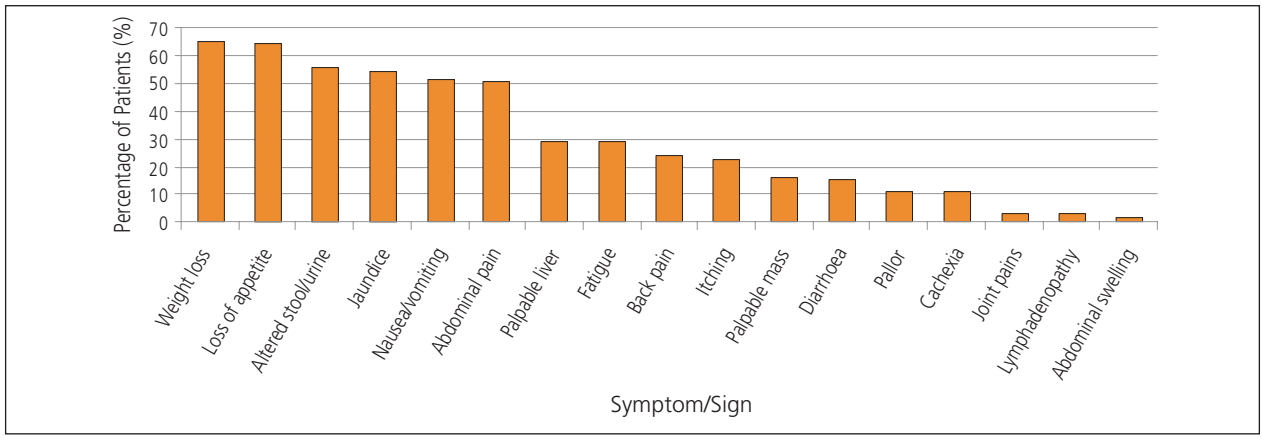
** Includes morphine, diamorphine, pethidine*
*** NSAID = Non Steroidal Anti-Inflammatory Drug*

Symptoms/Signs at presentation (NOTE: Patients may present with more than one symptom/sign)

Symptom/Signs	Number of Patients (%) *(n=152)*
Altered stool/urine colour	85 (56%)
Weight loss	99 (65%)
Back pain	36 (24%)
Fatigue	44 (29%)
Abdominal pain	78 (51%)
Nausea/vomiting	78 (51%)
Loss of appetite	99 (65%)
Itching	33 (22%)
Diarrhoea	23 (15%)
Abdominal swelling	3 (2%)
Joint pains	4 (3%)
Lymphadenopathy	4 (3%)
DVT/Blood clot	1 (<1%)
Jaundice	84 (55%)
Cachexia	16 (11%)
Pallor	17 (11%)
Palpable liver	44 (29%)
Palpable mass	25 (16%)

- Almost two thirds of patients had weight loss associated with a loss of appetite.
- Over half of patients presented with jaundice (53% male, 47% female).
- One fifth of patients had itching.
- Almost one quarter of patients had back pain.
- 15% of patients had both back pain and abdominal pain (not shown).
- There were significantly more males than females who presented with altered stool/urine colour (50 males, 35 females) and palpable livers (30 males, 14 females) ($p<0.05$). The other symptoms occurred equally among both sexes.

Symptoms/Signs for pancreatic cancer patients



- There was poor recording of symptom duration.
- Of those patients who presented with weight loss, one quarter experienced it for one month or less, over half for two to six months with only 15% experiencing it for more than 7 months (maximum period was 24 months).
- 97% of pancreatic cancer patients who presented with jaundice had it for one month or less, with a further 3% experiencing it for a period up to 2 months.
- Over half (52%) of those patients who presented with abdominal pain had it for one month or less with almost two fifths experiencing it for two to six months after presentation and a further 10% having it for more than 7 months (maximum period was 24 months).
- Over half (53%) of those patients who presented with back pain experienced it for one month or less, 37% experienced it between two and six months, with a further 11% experiencing it for a period of up to 12 months.

Blood tests at presentation

Test	Number of Patients tested (%) *(n=152)*
Bilirubin	141 (93%)
Albumin	139 (91%)
ALP*	141 (93%)
AST*	126 (83%)
ALT*	113 (74%)
CRP*	63 (41%)
ESR*	63 (41%)
CEA*	35 (23%)
CA19-9*	73 (48%)
CA125*	18 (12%)
Haemoglobin	139 (91%)
PT*	106 (70%)
Creatinine	136 (89%)

- Over 90% of pancreatic cancer patients had the following blood tests performed – Bilrubin, Albumin and ALP and a third of patients tested were within the normal reference range (not shown).

* ***ALP=Alkaline phospatase, AST=Aspartate transaminase, ALT=Alamine aminotransferase, CRP=Creactive protein, ESR=Erythrocyte sedementation rate, CEA=Carcinoembryonic antigen, CA19-9=Carbohydrate antigen 19-9, CA125=Carbohydrate antigen 125, PT=Prothrombin time***

Patients presenting within their own Board

Board of residence	Number of Patients (% presenting within own Board) *(n=152)*
NHSSB	29 (78%)
EHSSB	63 (95%)
SHSSB	22 (88%)
WHSSB	21 (95%)

- The majority of patients presented to a hospital within their own Board of residence in 2001. Patients who presented elsewhere, mostly went to a Hospital in the Eastern Board.

Hospital of presentation & Hospital of treatment (Number of patients attending hospital at some point during treatment) (NOTE: Patients may have attended more than one hospital during treatment)

Hospital of presentation	Number of Patients (%) *(n=152)*	Hospital of treatment	Number of Patients (%) *(n=152)*
Ulster (UH)	24 (16%)	Ulster (UH)	30 (20%)
Antrim (ANT)	16 (11%)	Antrim (ANT)	26 (17%)
Belfast City (BCH)	14 (9%)	Belfast City (BCH)	49 (32%)
Royal Victoria (RVH)	12 (8%)	Royal Victoria (RVH)	36 (24%)
Daisy Hill (DHH)	11 (7%)	Daisy Hill (DHH)	12 (8%)
Erne (ERN)	11 (7%)	Erne (ERN)	10 (7%)
Altnagelvin (AH)	8 (5%)	Altnagelvin (AH)	24 (16%)
Craigavon Area (CAH)	8 (5%)	Craigavon Area (CAH)	20 (13%)
Lagan Valley (LVH)	7 (5%)	Lagan Valley (LVH)	9 (6%)
Mater (MIH)	7 (5%)	Mater (MIH)	37 (24%)
Whiteabbey (WHA)	7 (5%)	Whiteabbey (WHA)	9 (6%)
Causeway (CAU)	4 (3%)	Causeway (CAU)	4 (3%)
Mid Ulster (MUH)	4 (3%)	Mid Ulster (MUH)	3 (2%)
Downe (DH)	3 (2%)	Downe (DH)	5 (3%)
Ulster Independent (UIC)*	3 (2%)	Ulster Independent (UIC)*	2 (1%)
Tyrone County (TCH)	2 (1%)	Tyrone County (TCH)	4 (3%)
South Tyrone (STH)	2 (1%)	Lurgan (LGH)	1 (<1%)
Lurgan (LGH)	1 (<1%)	Belvoir Park (BPH)	38 (25%)
Bangor Community (BGR)	1 (<1%)	Musgrave (MPH)	2 (1%)
Moyle (MLE) **	1 (<1%)		
Waveney (WAV)	1 (<1%)		
Outside N. Ireland	1 (<1%)		
North West Clinic (NWC) *	1 (<1%)		

The Ulster Independent Clinic and the North West Independent Clinic are private hospitals **Facility still had 2 palliative beds in 2001

- 152 patients with cancer of the pancreas presented to 23 hospitals in 2001.
- Patients attended 19 hospitals throughout the course of their treatment.
- Belfast City Hospital saw the highest attendance with one third of patients attending for some form of treatment.
- Almost two thirds (61%) of patients attended either the Cancer Centre or Cancer Units (Antrim, Altnagelvin, Craigavon, Ulster) during some point of their treatment.

HOSPITALS ATTENDED

- Half (51%) of patients attended only one hospital, almost one third (32%) attended two hospitals and 17% attended three hospitals for their investigations and treatment of pancreatic cancer (not shown).

Investigations (NOTE: Patients may have received more than one type of investigation)

Investigation	Number of Patients (%) *(n=152)*
Ultrasound scan	135 (89%)
CT scan	123 (81%)
ERCP *	110 (71%)
Successful cannulation	68 (62% of ERCPs)
Sphincterotomy	30 (27% of ERCPs)
MRCP **	4 (3%)

**** Endoscopic Retrograde Cholangiopancreatography***
***** Magnetic Resonance Cholangiopancreatography***

- Almost 90% of pancreatic cancer patients had an ultrasound investigation, while over three quarters had a CT scan.
- Almost three quarters of patients had an ERCP of whom a fifth had a complication recorded.
- Staging laparoscopy was performed on 4% of patients and in every case liver metastases and/or ascites were detected that had not been noted previously (not shown).

Complications of ERCP

Complications	Number of Patients (% of total ERCPs) *(n=110)*
Pancreatitis	2 (2%)
Bleeding	3 (3%)
Cholangitis	2 (2%)
Other complications*	15 (14%)

**** These included sepsis as well as developing pleural effusion after the procedure and perforation of the upper oesophagus***

Results of examination and investigations at presentation (NOTE: Patients may be counted in more than one category)

Finding	Number of Patients (%) *(n=152)*
Mass in pancreas	93 (61%)
Dilated bile ducts	91 (60%)
Multiple liver lesions	47 (31%)
Lymphadenopathy	30 (20%)
Ascites	15 (10%)
Pleural effusion	13 (9%)
Evidence of secondary spread*	106 (70%)

**** Each patient has been counted only once here depending on whether they have had multiple liver lesions, lymphadenopathy, ascites or pleural effusion.***

- 70% of patients had evidence of secondary spread at presentation.
- Of those patients who had a mass in the pancreas, almost one quarter (23%) had a palpable abdominal mass at presentation and one third had a palpable liver at presentation (14% and 20% of all patients respectively).
- 61% of patients had a radiologically identifiable mass detected at presentation.

STAGING (see also Appendix D)

TNM stage was recorded in the clinical notes for 42% of patients. 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) using the AJCC Cancer Staging Handbook[10].

- With Registry staff assigning a stage, it was possible to achieve staging in another 7% of patients. Staging varied little between Boards.

Stage (recorded in notes or registry-assigned)

TNM stage	Stage recorded in notes	Registry assigned stage
	Number of Patients (%)	Number of Patients (%)
I	7 (5%)	9 (6%)
II	1 (<1%)	1 (<1%)
III	2 (1%)	1 (<1%)
IVa	0	8 (5%)
IVb	54 (36%)	55 (36%)
Unstaged *	88 (58%)	78 (51%)

**** Staging for these patients was not possible due to a lack of information recorded in the notes***

- Staging was possible for only 49% of patients and of these 85% were late, Stage IV disease. However, there was evidence from investigations and surgery that 70% of all patients had evidence of secondary spread at investigation.
- Stage was available for 41% of the surgery patients of which 60% were Stage IVb (i.e. metastatic disease).

Site of metastatic disease

Site	Number of Patients (% of Stage IV patients with metastases) *(n=63)*
Liver	52 (83%)
Lung	4 (6%)
Peritoneum	3 (5%)
Other combinations	4 (6%)
Total patients staged as IV	63 (41% of all patients)

- 41% of all patients were recorded as having Stage IV disease and of these, 83% had metastases in the liver.

HISTOPATHOLOGY

- Over half of all patients (57%) had a histological/cytological confirmation of their diagnosis. The remainder, 43%, had their diagnosis confirmed solely by clinical or radiological means (not shown).

Histopathology Type

Sub-type	Number of Patients (%) *(n=87)*
Adenocarcinoma	54 (62%)
Carcinoma, NOS*	8 (9%)
Stromal tumour	1 (1%)
Malignant neoplasm	3 (3%)
Other, NOS*	21 (24%)

**** NOS=Not otherwise specified***

- 54 of 87 (62%) patients with a histological diagnosis were confirmed as adenocarcinoma of the pancreas.

Source of Histopathology (NOTE: Patients may have had more than one source)

Source	Number of Patients (%) *(n=152)*
Resection specimen	3 (2%)
Fine needle aspiration	8 (5%)
Trucut biopsy	36 (24%)
Brushings at ERCP	31 (20%)
Ascites cytology	6 (4%)
Bile cytology	1 (<1%)
Wedge biopsy	2 (1%)
TOTAL	87 (57%)

MULTIDISCIPLINARY TEAM MEETINGS

The effective management of pancreatic cancer patients requires input from a range of experts. Multidisciplinary team meetings (MDMs) involve a group of healthcare professionals meeting to discuss the diagnosis and treatment of patients. As there are a range of potential treatments that could be carried out, multidisciplinary discussions are of great importance. With respect to MDMs it should be noted that discussions among healthcare professionals, regarding the diagnosis and treatment of patients, may have taken place but may not have been in recognised MDM format.

Multidisciplinary Team Meetings recorded in the notes

MDM	Number of Patients (%) *(n=152)*
Yes	20 (13%)
No/Not recorded	132 (87%)

- Recording in the clinical notes that discussion at an MDM had taken place was very poor with only 13% of patients having a record of an MDM.
- MDMs were recorded for 7 surgery patients and 13 non-surgery patients.
- 40% of the MDMs that took place were for Stage IV patients.

Outcome of MDM discussion (NOTE: Patients may have had more than one planned outcome)

MDM	Number of Patients (%) *(n=20)*
Planned curative resection	2 (10%)
Planned staging laparoscopy	3 (15%)
Planned exploratory laparotomy	1 (5%)
Planned palliative chemotherapy	2 (10%)
Planned best support care	12 (60%)

- Recording of information that was discussed during an MDM was poor.

SURGERY

Hospitals performing surgery* for pancreatic cancer (Patients may have had more than one type of surgery but patients are counted only once)

Hospital	Number of Patients (%)	Curative resection	Biliary bypass	Gastric drainage	Surgery not specified
Altnagelvin (AH)	2 (6%)	0	1	2	0
Antrim (ANT)	1 (3%)	0	1	0	0
Belfast City (BCH)	1 (3%)	0	0	1	0
Craigavon (CAH)	2 (6%)	0	0	1	1
Causeway (CAU)	1 (3%)	0	0	0	1
Downe (DH)	2 (6%)	0	0	1	1
Daisy Hill (DHH)	2 (6%)	0	1	1	0
Lagan Valley (LVH)	1 (3%)	0	1	0	0
Mater (MIH)	12 (39%)	2	10	4	0
Royal Victoria (RVH)	4 (13%)	2	7	7	0
Ulster (UH)	3 (10%)	0	1	0	2
Total	31 patients	4	22	17	5

NOTE: This excludes pancreaticoduodenectomies performed for other reasons e.g. inflammatory mass, complications related to chronic pancreatitis and periampullary or ampullary carcinomas. Includes curative resection, biliary bypass and/or gastric drainage for pancreatic cancer

- In 2001, 48 surgical procedures were carried out on 31 patients with pancreatic cancer, by 18 surgeons in 11 hospitals.
- Only 4 (3%) patients were recorded as having a completed pancreatic resection. These took place in two hospitals (Mater and Royal Victoria).
- 24% of surgical procedures were on patients who had a record of metastatic disease and are presumed to be palliative.

Direct tumour invasion found at surgery

Site	Number of Patients (% of all surgery patients) *(n=31)*
Duodenum	9 (29%)
Portal vein	2 (6%)
Superior mesenteric vein	3 (10%)
Colon	1 (3%)
Peritoneal spread	7 (23%)

- For almost one third of pancreatic surgery patients (29%) the tumour was found to have invaded the duodenum. A further 23% of surgical tumours showed direct peritoneal spread.

Interventions

Intervention	Number of Patients (%) *(n=152)*
Surgery + prior stent	31 (20%)
Stent alone	55 (36%)
No intervention	60 (39%)

- While one fifth of patients had surgery, almost two fifths had no intervention.

Biliary decompression (NOTE: Patients may have had more than one type)

Drain/Stent type	Number of Patients (%) *(n=74)*
Patients decompressed (Biliary decompression)	74 (100%)
Plastic stent	53 (72%)
Metal stent	9 (12%)
External drain	2 (3%)
Combined External/Internal drain	10 (14%)

- Almost half of patients (49%) underwent biliary decompression with 53 of 74 (72%) receiving a plastic stent.
- Of the 53 who received a plastic stent, one had a curative resection, biliary bypass and gastric drainage, four had a biliary bypass, three had gastric drainage, three had a staging laparoscopy, one had a staging laparoscopy, biliary bypass and gastric drainage, three had biliary bypass and gastric drainage and one had a curative resection and biliary bypass. 37 of the 53 (70%) received no other interventions.

Surgical Interventions (NOTE: Patients may have had a combination of care)

Procedure	Number of Patients (%) *(n=152)*
Curative resection	4 (3%)
Biliary bypass	22 (14%)
Gastric drainage procedure	17 (11%)

Postoperative course/outcomes – Surgery only patients (NOTE: Patients may have had more than one outcome)

Complications	Number of Patients (%) *(n=31)*
ICU* admission	16 (52%)
Pancreatic leak	1 (3%)
Biliary leak	1 (3%)
General complications	13 (42%)
Return to theatre	3 (10%)
Deaths within 30 days	3 (10%)

**** ICU = Intensive Care Unit***

- Over half (52%) of all surgery patients were admitted to the Intensive Care Unit following surgery (this was made up of 3 curative resections, 14 biliary bypass procedures and 11 gastric drainage procedures).
- Two fifths (42%) of all surgery patients had general complications.
- 10% were returned to theatre while 10% died within 30 days of their operation.

Frequency of operations carried out by surgeon (NOTE: Includes curative resection, biliary bypass and gastric drainage procedures)

Procedures*	Number of Surgeons (% of procedures)
6 – 10 procedures	3 (54%)
2 – 5 procedures	3 (19%)
1 procedure	12 (25%)
Total named operators	18
Total unnamed operators	- (2%)
Total procedures	48

(NOTE: 'Total named surgeons' are fully appointed consultant surgeons operating on patients with pancreatic cancer. Where trainee surgeons were supervised by Consultant trainers, these operations have been credited to the Consultant)
**** In one procedure in the Mater Hospital and one procedure in Causeway Hospital the operation note was not all available***

- The 4 resections were performed by three different Consultant surgeons.

  (NOTE: There are other indicators for pancreatic resections and so surgeons may have performed more of these on diseases other than pancreatic cancer).
- There were 18 surgeons who collectively performed 48 surgical procedures on 31 patients with pancreatic cancer in 2001.
- The 12 single operators performed 4 bypass procedures and 4 gastric drainage procedures. The other 4 procedures were "open and close" laparotomies.
- Two surgeons each performed 10 surgical procedures in 2001 for pancreatic cancer patients, accounting for 42% of all procedures performed.

ONCOLOGY

There were 49 pancreatic cancer patients referred to an oncologist in 2001.

Oncology unit attended

Centre	No of Patients (%) *(n=49)*
Altnagelvin	6 (12%)
Antrim	3 (6%)
Belfast City	25 (51%)
Belvoir Park	9 (18%)
Craigavon	3 (6%)
Not recorded	3 (6%)

- Almost 70% of patients referred to an oncology unit attended the Cancer Centre.

Reasons for referral to oncology (NOTE: Patients may have been counted more than once)

Type of Input	Number of Patients (%) *(n=152)*
Management discussed	58 (38%)
Palliative treatment	37 (24%)
Radiotherapy	4 (3%)
Chemotherapy	45 (30%)
Symptom relief	3 (2%)

- Almost two fifths had their management discussed with an oncologist.
- 34% of all pancreatic cancer patients were referred to an oncologist.
- Almost one third (30%) of patients had chemotherapy while 3% had radiotherapy.
- 10 patients (7%) were entered into clinical trials (not shown).
- Of the 45 patients who received chemotherapy, 49% received gemcitabine, a further 7% were entered into a chemotherapy clinical trial and a further 9% received other drugs including capecitabine, docetaxel and sandostatin.

TIMELINES/WAITING TIMES

Time	Referral – first seen at hospital *(n=152)*	First seen – diagnosis confirmed *(n=152)*	Diagnosis confirmed – surgery *(n=31)*
Same day	86 (57%)	39 (26%)	7 (23%)
1- 14 days	41 (27%)	56 (37%)	5 (16%)
15 – 42 days	10 (7%)	26 (17%)	4 (13%)
43 – 84 days	2 (1%)	15 (10%)	0
More than 84 days	0	11 (7%)	1 (3%)
Minus values*	1 (<1%)	3 (2%)	11 (35%)
Not recorded	12 (8%)	2 (1%)	3 (10%)

**** Surgery was performed for symptom control and cancer was confirmed during surgery***

- 84% of patients were seen within two weeks of referral reflecting the emergency nature of presentation.
- 63% of patients had their diagnosis confirmed within two weeks of presentation to hospital.
- One fifth (20%) of pancreatic cancer patients underwent surgery and of these over one third (38%) received surgery within two weeks of diagnosis.

FOLLOW-UP CARE DETAILS

This relates to information recorded in the discharge letter from hospital to GP. Patients may have had more than one referral.

GP Letter (NOTE: A patient may have had more than one type of information recorded)

Information	Positive record
Management plan	103 (68%)
Prognosis recorded	53 (35%)
Patient awareness	75 (49%)
Family awareness	68 (45%)

- Overall, information in the GP letter was quite well recorded with two thirds having a positive record of a management plan.

After Care/Follow Up (NOTE: Patients may have had more than one type of follow up recorded)

After care	Number of Patients (%) *(n=152)*
General Practitioner	103 (68%)
Palliative care physician*	23 (15%)
Community nurse	69 (45%)
Macmillan nurse*	30 (20%)
Marie Curie nurse*	8 (5%)
Hospice*	34 (22%)
Psychologist	1 (<1%)
Support groups	3 (2%)
Dietician	2 (1%)

**** Palliative care***

- 68% had a record of some form of palliative care follow up.

SURVIVAL

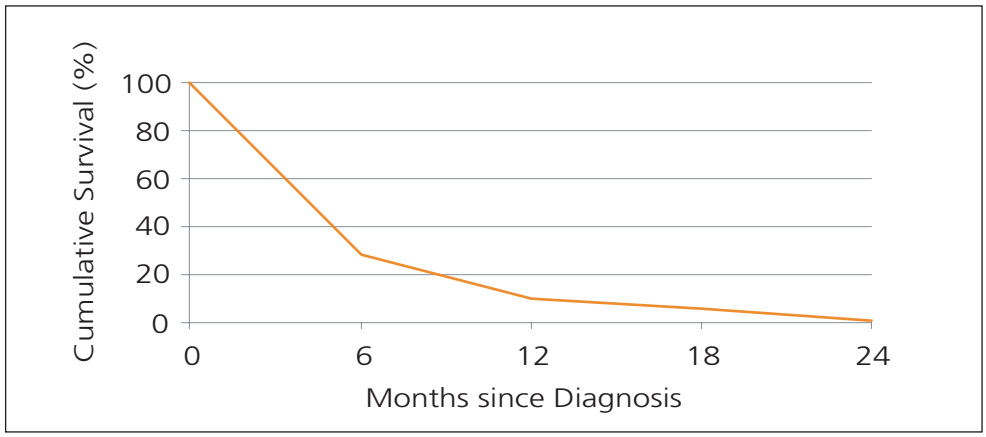
Survival analysis was performed on all patients with subgroup analysis for surgery and non surgery patients and for stage.

Percentage of patients alive at various times after diagnos

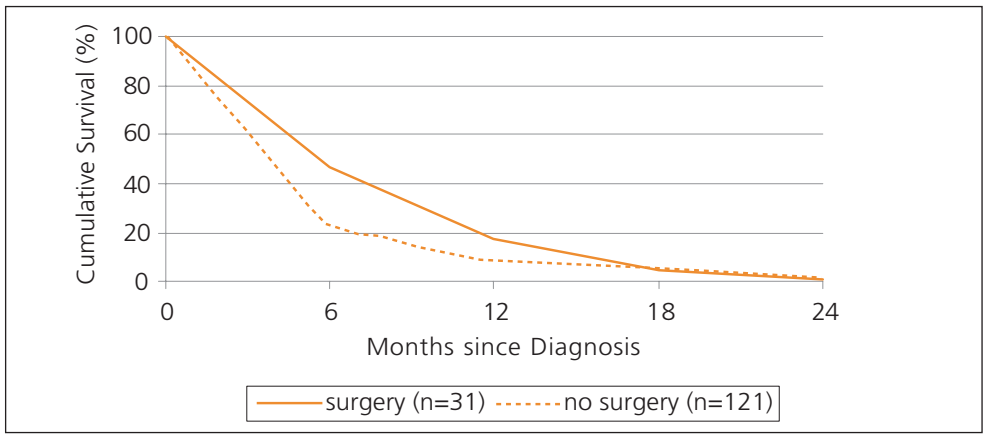
Time	Surgery only Patients *(n=31)*	Non surgery Patients *(n=121)*	All Patients *(n=152)*
30 days	78%	73%	74%
60 days	64%	54%	58%
6 months	47%	22%	28%
1 year	17%	8%	10%
2 years	<1%	<1%	<1%

- Observed survival from pancreatic cancer is very poor with only 10% of all 2001 patients alive at one year after diagnosis.

Pancreatic cancer observed survival for all patients diagnosed in 2001 *(n=152)*



Pancreatic cancer observed survival for surgery (vs) no surgery

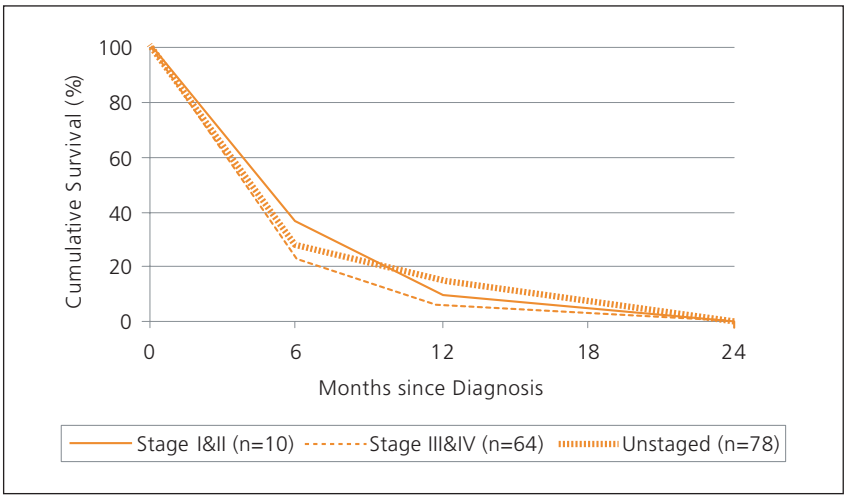


- The subgroup selected for surgery had better observed survival of 17% at one year. This difference was apparent only until 18 months after diagnosis. Even though only 4 of this surgery group received a curative resection and the remainder received palliative care, they still showed better survival than those who did not have any surgical intervention. This probably reflects selection of patients fit for palliation.

Percentage of patients alive at various times after diagnosis with different recorded stage of disease at presentation

Time	Stage I &II	Stage III & IV	Unstaged
30 days	90%	73%	71%
60 days	80%	52%	56%
6 months	37%	23%	28%
1 year	10%	6%	15%
2 years	0	0	1%
Total patients	10	64	78

Pancreatic cancer observed survival by stage



- There was no significant difference in survival across patients with different recorded stages of disease ($p>0.05$). This reflects low levels of resections for early stage disease.

PANCREAS SUMMARY

PRESENTATION

- 35% presented as emergencies.
- 152 patients with cancer of the pancreas presented to 23 hospitals in 2001.
- Patients attended 19 hospitals throughout the course of their treatment.
- Belfast City Hospital saw the highest attendance with one third of patients attending for some form of treatment. 61% of patients attended either the Cancer Centre or Cancer Units (Antrim, Altnagelvin, Craigavon, Ulster) during some point of their treatment.
- The majority of patients presented to a hospital within their own Board of residence in 2001. Patients who presented elsewhere mostly went to a Hospital in the Eastern Board.

CO-MORBIDITY AND RISK FACTORS

- 5% of patients had a history of chronic pancreatitis.
- 19% of patients had diabetes. Of these, 34% experienced it for a period up to 6 months before diagnosis, while 48% were diagnosed more than two years ago (maximum period was 13 years).
- 12 patients (8%) self declared that they drank more than 30 units of alcohol per week.
- 34 patients (22%) were current smokers, 49 (32%) were ex-smokers and 53 (35%) were non-smokers. The remaining 16 patients had no smoking history recorded.

SYMPTOMS AND SIGNS

- 65% of patients had weight loss associated with a loss of appetite.
- 55% of patients presented with jaundice.
- 24% of patients had back pain.
- 15% of patients had both back and abdominal pain.

INVESTIGATIONS

- 89% of pancreatic cancer patients had an ultrasound investigation, while 81% had a CT scan.
- 71% of patients had an ERCP of whom a fifth had a complication recorded.
- 61% of patients had a radiologically identifiable mass detected at presentation.

HISTOPATHOLOGY

- 54 of 87 (62%) histological diagnoses were confirmed as adenocarcinoma of the pancreas.
- 43% had their diagnosis confirmed non pathologically i.e by clinical or radiological diagnosis only.

STAGING AND NODAL INVOLVEMENT

- 70% of patients had evidence of secondary spread at investigation.
- Of those patients who had a mass in the pancreas, 23% had a palpable abdominal mass at presentation and one third had a palpable liver at presentation (14% and 20% of all patients respectively).

- TNM stage was recorded in the clinical notes for 42% of patients and was possible from the notes for 49% of patients and of these 85% were late Stage IV disease.
- Staging varied little between Boards.
- Staging laparoscopy was performed in 4% of all patients in three hospitals (Lagan Valley, Mater and Royal Victoria hospitals).

RECORDING OF MULTIDISCIPLINARY TEAM MEETINGS

- Recording in the clinical notes that discussion at an MDM had taken place was very poor with only 13% of patients having such a record.
- MDMs were recorded for 23% of surgery patients and 11% of non surgery patients.
- 40% of the MDMs that took place were for Stage IV patients.

SURGERY

- In 2001, 48 surgical procedures were carried out on 31 patients with pancreas cancer, by 18 surgeons in 11 hospitals.
- Only 4 (3%) patients were recorded as having a completed pancreatic resection. These took place in two hospitals (Mater and Royal Victoria hospitals).
- 24% of surgical procedures (n=7) were on patients who had metastatic disease.
- For 29% the tumour had invaded the duodenum. A further 23% of surgical tumours showed peritoneal spread.
- 52% of all surgery patients were admitted to the Intensive Care Unit following surgery.
- 42% of all surgery patients had general complications.
- 10% were returned to theatre while 10% died within 30 days of their operation.

SURGEON WORKLOAD

- The 4 resections were performed by three different Consultant surgeons.
- There were 18 surgeons who collectively performed 48 surgical procedures on 31 patients with pancreatic cancer in 2001.
- The 12 single operators performed 4 bypass procedures and 4 gastric drainage procedures. The other 4 procedures were not specified.
- Two surgeons each performed 10 surgical procedures in 2001 for pancreatic cancer patients, accounting for 42% of all procedures performed.

ONCOLOGY

- 49 pancreatic cancer patients were referred to oncology in 2001.
- 69% of patients referred to an oncology unit attended the Cancer Centre.
- 38% had their management discussed with an oncologist while 34% of all pancreatic cancer patients were referred to an oncologist.
- 30% of patients had chemotherapy while 3% had radiotherapy.
- 10 patients (7%) were entered into clinical trials.
- Of the 45 patients who received chemotherapy, 49% received the drug gemcitabine, a further 7% were entered into a chemotherapy clinical trial and a further 9% received other drugs including capecitabine, docetaxel and sandostatin.

TIMELINES

- 84% of patients were seen within two weeks of referral.
- 63% of patients had their diagnosis confirmed within two weeks of presentation to hospital.
- 20% of pancreatic cancer patients underwent surgery and of these 38% received surgery within two weeks of diagnosis.

ONWARD REFERRAL

- 68% of patients were referred back to their own GP and 45% were referred to a community nurse.
- Uptake of all other services was poorly recorded.
- 68% had a record of same form of palliative care follow up.

COMMUNICATION

- Overall, information in the GP letter was quite well recorded with the best recorded piece of information being the patients' management plan with over two thirds having a positive record.

SURVIVAL

- Observed survival from pancreatic cancer is very poor with only 10% of the 2001 patients alive at one year after diagnosis. The subgroup selected for surgery had better observed survival of 17% at one year. This difference was apparent only until 18 months after diagnosis.
- There was no significant difference in survival across patients with different recorded stages of disease ($p>0.05$). This reflects low levels of resections for early stage disease.

PANCREAS CONCLUSION, KEY ISSUES AND RECOMMENDATIONS

Key Issues

- At least 69% of patients had evidence of metastatic disease at presentation to hospital.
- Survival for pancreatic cancer patients is very poor with only 10% of patients alive at one year after diagnosis.
- 48 surgical procedures for pancreatic cancer were performed on 31 patients by 18 surgeons in 11 hospitals in 2001 reflecting lack of service centralisation.

Recommendations

- 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.
- There should be one hepatopancreatobiliary unit for Northern Ireland which should forge links with other similar centres outside Northern Ireland.
- Research into the cause of pancreatic cancer and possibilities for earlier detection e.g. via tumour markers should be funded.

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[11]. 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)[12].

Types

Cholangiocarcinomas may be classified as extrahepatic (87-92%) or intraheptic (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[12].

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 coeliac 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[13].

Risk Factors

Cholangiocarcinoma is usually associated with environmental exposures such as polyvinyl chloride (a widely used plastic) or Thorotrast (thorium dioxide), a radioactive compound. It is also associated with Opisthorchis viverrini infection (a parasite that attacks the area of the bile duct). Other high risk groups predisposed to cholangiocarcinomas include patients with the following[14]:

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 in 8% of cases, primary sclerosing cholangitis (PSC) and chronic infestation with the liver fluke 'Clonorchis sinesis'[14].

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[13].

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[15].

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[15].

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 new palliative technique that might improve quality of life[15].

CHOLANGIOCARCINOMA RESULTS

Study patients

In Northern Ireland in 2001 there were 45 cases of cholangiocarcinoma registered with the N. Ireland Cancer Registry (51% male, 49% female). 38% were diagnosed at age 80 years or over. There was no association with social deprivation index, although the small numbers of cases precludes satisfactory confirmation of this ($p>0.05$). 58% presented through Accident & Emergency with others including elective admissions, outpatients and radiology.

Health board of residence	Health Board of Presentation				
	EHSSB	NHSSB	SHSSB	WHSSB	Total
EHSSB	13 (93%)	1 (7%)	0	0	14
NHSSB	1 (6%)	17 (94%)	0	0	18
SHSSB	0	0	5 (100%)	0	5
WHSSB	0	1 (13%)	0	7 (87%)	8
Total	14	19	5	7	45

- There was an over representation of patients residing in the Northern Board (40%) in 2001. This is an artefact of 2001 data as patients diagnosed with cholangiocarcinoma and registered with the N. Ireland Cancer Registry from 1993 – 2003 were investigated and there was no over representation in any Health Board area.
- Patients mostly presented within their health board of residence.

Risk Factors

Where smoking history was recorded (91% of patients), 34% were current smokers, 27% were ex-smokers and 39% were recorded as non-smokers. This was similar to the general population of that age. Alcohol use was recorded in 64% of patients of which 59% were current drinkers, 10% were ex-drinkers and the remaining 31% had never drank alcohol.

- 4 patients (9%) self declared that they drank more than 30 units of alcohol per week.
- There were no positive records of family history of pancreatic cancer or cholangiocarcinoma but 16% (24 patients) of patients had positive record of a family history of other cancers.

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

Co-morbidity	Number of Patients (%) *(n=45)*
COPD*	4 (9%)
Cardiovascular disease	13 (29%)
Dementia	2 (4%)
Learning disability	5 (11%)
Cerebrovascular disease	7 (16%)
Arthritis	13 (29%)
Proven gallstones	20 (44%)

**** COPD = Chronic Obstructive Pulmonary Disease***

- The co-morbidities reflect the age group of the sample.

Previous conditions/investigative procedures (NOTE: Patients may be counted more than once)

Procedure/Condition	Number of Patients (%) *(n=45)*
Previous cholestectomy	3 (7%)
Previous ERCP	2 (4%)
Previous colectomy	2 (4%)
Primary sclerosing cholangitis	3 (7%)
Known biliary abnormalities	1 (2%)
Diabetes	5 (11%)
Obesity	5 (11%)
Hypertension	11 (24%)
Osteoporosis	4 (9%)
Alzheimers	1 (2%)
Ulcerative colitis	2 (4%)
Crohn's disease	1 (2%)
Other malignancy	8 (18%)
Other morbidity*	29 (64%)

**** Includes diverticular disease, renal failure, oesophagitis, varicose veins***

Multi-disciplinary Team Meetings

- Multidisciplinary team meetings (MDM) were recorded as having taken place in 24 patients (53%). The remaining patients had no record of such a meeting.

Staging

- 4% of 2001 cholangiocarcinoma patients had a staging laparoscopy.
- Very few cholangiocarcinoma cancer patients were staged (29%). The majority of those staged were Stage IVb.

Treatment

- Over one quarter (27%) had non-surgical biliary drainage either at an endoscopic retrograde cholangiopancreatography (ERCP) or a percutaneous transhepatic cholangiogram (PTC). There were no surgical resections with curative intent in 2001.
- 51% of all patients required repeated admissions to hospital for symptom control.

Readmissions

Number of readmissions	Number of Patients (%) *(n=45)*
1	17 (38%)
2	3 (7%)
3	2 (4%)
4	1 (2%)

- Reasons for readmission included progression of the patient's disease and adverse effects of the patients main treatment while other reasons included blocked stent, nausea, vomiting and weight loss.

Oncology

- The management was discussed with an oncologist in 29% of cases. 27% of all patients were referred to an oncologist unit (Belvoir Park/Belfast City (n=6),Antrim (n=2), Altnagelvin (n=2), Craigavon (n=2)).

Reason for referral to oncology	Number of Patients (%) *(n=45)*
Assessment	12 (27%)
Radiotherapy	3 (7%)
Chemotherapy	9 (20%)

- The treatment intent was poorly recorded but was recorded as being palliative in about one fifth of all patients (18%) (not shown)

Follow-up care

- 9% of patients had a record of referral to a Macmillan nurse for counselling and 20% were referred for other reasons.
- Over three quarters (78%) were referred back to their own GP while over one third (38%) were referred to a community nurse.
- 13% were referred to a hospice, 4% to a Marie Curie nurse, 11% to a palliative care specialist and 9% to social services.
- 4% of patients were entered into a clinical trial using the drug Xelox (oxaliplatin/capecitabine).

Information recorded in letter to GP (NOTE: A patient may have had more than one type of information recorded)

Information	Number of Patients (%) *(n=45)*
Management plan	38 (84%)
Prognosis	22 (49%)
Diagnosis discussed with patient	22 (49%)
Diagnosis discussed with family	17 (38%)

- In almost half of letters to GP (49%) there was a record that the information had been discussed with patients.
- The management plan was recorded in over three quarters of letters to the GP (84%).

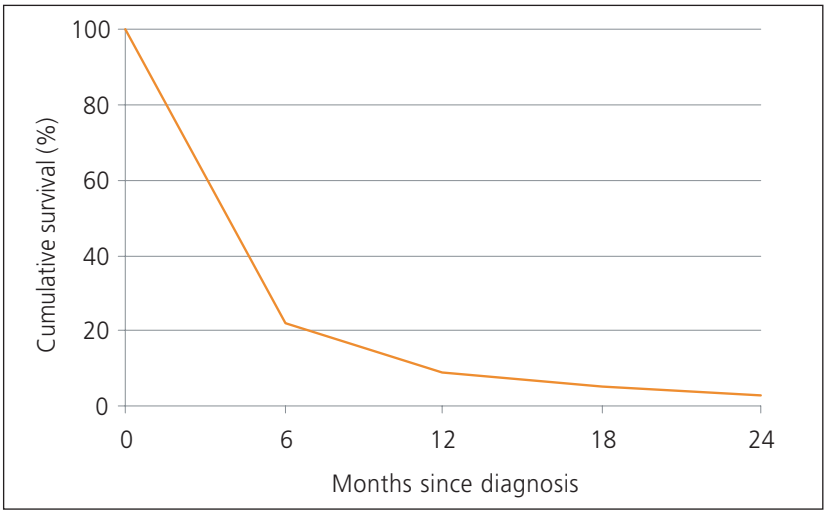
Survival

- Survival from cholangiocarcinoma is very poor with only 9% of all 2001 diagnosed patients alive one year after diagnosis and 3% alive at two years after diagnosis.

Percentage of patients alive at various times after diagnosis

Time after diagnosis	Percentage of Patients
30 days	81%
60 days	48%
6 months	22%
1 year	9%
2 years	3%
Total patients	45

Cholangiocarcinoma observed survival for all patients diagnosed in 2001 *(n=45)*



AMPULLA OF VATER CARCINOMAS **(Numbers are small (n=14) but are included for completeness)**

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[16].

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[16].

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)[16].

Symptoms

The usual symptoms are painless jaundice, intermittent or constant fatigue, itching, fever and non-specific abdominal pain. Intestinal haemorrhage or pancreatitis are also possible. The clinical signs and symptoms 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[17].

Spread

Ampulla of Vater carcinomas tend to spread by a local infiltration of the walls of the adjacent common bile ducts, 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 4 patients at the time of surgical diagnosis[17].

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 ampullary 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[18].

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[19].

AMPULLA OF VATER RESULTS

Study patients

In Northern Ireland in 2001 there were 14 cases of ampulla of Vater carcinoma registered with the N. Ireland Cancer Registry (50% male, 50% female). 29% were diagnosed at age 80 years or over but ages ranged from 50 – 98 years. Patients resided in the Eastern (36%), Northern (29%) and Southern (36%) Boards. No patient presented from the Western Board. 79% of patients presented to a Hospital within their Board of residence and those who did not, presented to a Hospital within the Eastern Board area. 64% of patients were diagnosed on the basis of histopathology with 30% by cytology. Others included hospital admission system (PAS) and ERCP. A fifth (21%) of patients had a previous personal history of other malignancy including skin and colon cancers.

Type

71% of patients presented with an adenocarcinoma. Almost half (43%) of patients had a tumour that was well differentiated, 29% were moderately differentiated and 7% were poorly differentiated with the remaining 21% not recorded.

Stage

From information available in the clinical notes for 71% of patients, it appeared that 80% of these were early tumours and the remaining 20% were late tumours.

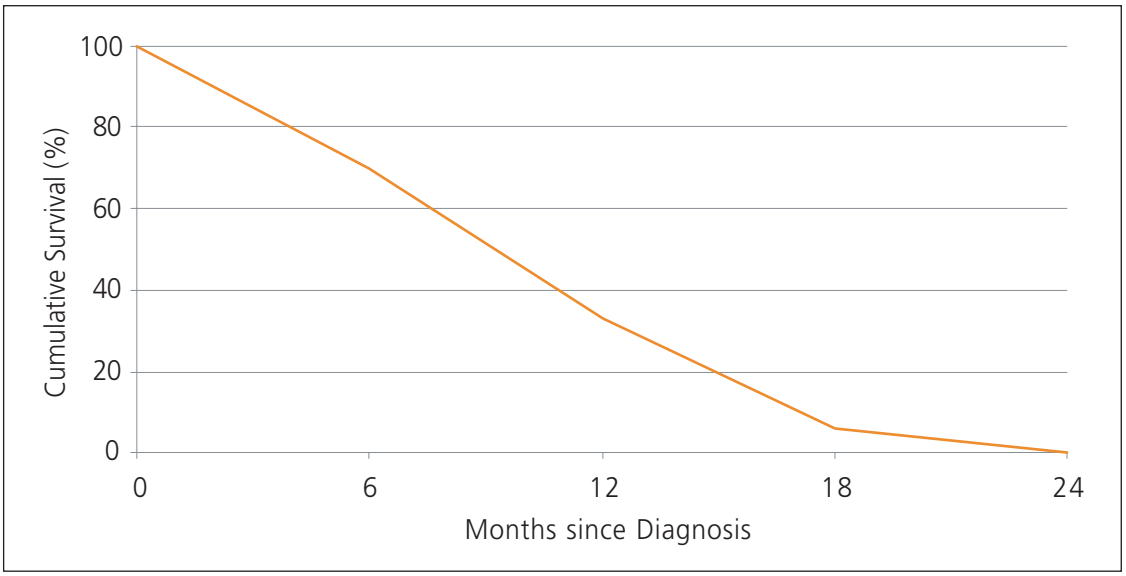
Surgery

93% of all patients had surgery and for 77% of these, this was performed within their own Board of residence. Surgery was performed in 7 different hospitals by 10 different consultant surgeons. Types of surgical procedures included pancreaticoduodenectomy, endoscopic examination, ERCP, PTC and the Whipple procedure.

Survival

Survival from ampulla of Vater carcinoma was poor with 33% of patients alive one year after diagnosis but none alive at two years.

Observed survival for patients with periampullary carcinomas *(n=14)*



REFERENCES

1. Campbell Report. *Cancer Services – Investing for the Future*. Department of Health and Social Services, 1996.
2. NHS Improving Outcomes. *'Guidance on Commissioning Cancer Services – Improving Outcomes in Upper Gastro-intestinal Cancers – The Manual'* . NHS Executive, 2001. Available at www.dh.gov.uk/assetRoot/04/08/02/78/04080278.pdf
3. *Guidelines for the Management of patients with Pancreatic cancer periampullary and ampullary carcinomas*. Issued by the Pancreatic Section of the British Society of Gastrenterology, June 2005.
4 Fuller H. *Confronting Pancreatic Cancer.* Stanford University Medical Centre. Available at www.pancreatica.org/faq.html
5 Takhar A.S, Palaniappan P, Dhingsa R, Lobo D.N. *Recent developments in diagnosis of pancreatic cancer.* British Medical Journal 2004; 329 (7467): 668-73.
6 Li D, Xie K, Wolff R, Abbruzzesse J.L. *Pancreatic cancer.* Lancet 2004; 363 (9414): 1049-57.
7 Lowenfels A.B, Maisonneuve P. *Epidemiologic and etiologic factors of pancreatic cancer.* Hematol Oncol Clin North Am 2002; 16 (1): 1-16.
8 Lowenfels A.B, Maisonneuve P. *Environmental factors and risk of pancreatic cancer.* Pancreatology 2003; 3 (1): 1-7.
9 Alexakis N, Halloran C, Raraty M, Ghaneh P, Sutton R, Neoptolemos J.P. *Current standards of surgery for pancreatic cancer.* British Journal of Surgery 2004; 91 (11): 1410-27.
10 Greene F.L, Page D.L, Fleming I.D, Fritz A.G, Balch C.M, Haller D.G, Morrow M. *AJCC Cancer Staging Handbook TNM Classification of Malignant Tumours.* 5th Edition, New York: Springer-Verlag, 1997.
11 Jamagin W.R, Fong Y, DeMatteo R.P, Gonen M, Burke E.C, Bodniewicz J.B.S, Youssef M.B.A, Klimstra D, Blumgart L.H. *Staging, Resectability and Outcome in 225 patients with Hilar Cholangiocarcinoma.* Annals of Surgery 2001; 234 (4): 507-519.
12 Y Abeloff. *Clinical Oncology,* 2nd Edition, Churchill Livingston, 2000.
13 Anand M.K.N. *Cholangiocarcinoma.* Available at www.emedicine.com
14 Greenwood N.N, Earnshaw A. *Chemistry of the Elements*. Pergamon Press, Oxford, UK 1984: 1425-1546.
15 CancerBacup: *Helping people live with cancer: Bile duct cancer (Cholangiocarcinoma).* Available at www.cancerBACUP.com
16 Mehta V.K. *Ampullary Carcinoma.* Available at www.emedicine.com
17 Chaturvedi P. *Carcinoma of the Ampulla of Vater.* Available at www.emedicine.com/med/topic2676.htm
18 Moss R. *Treatment of Cancer of the Ampulla of Vater.* Available at www.ralphmoss.com/html/ampulla-vater.shtml
19 Gold M.S, Bordley J. *Pancreaticoduodenectomy for bleeding periampullary tumours.* Department of Surgery, Mary Imogene Bassett Hospital, Cooperstown, NY 13326-1394.

APPENDIX A

Campbell Report[1]: Recommendations regarding Cancer Services in N. Ireland, 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 4 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.

The above recommendations outlined the change that was necessary to improve cancer care.

APPENDIX B

NHS Improving Outcomes in Upper Gastro-intestinal Cancer[2], 2001.

(Summary Recommendations in specific topic areas).

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 C

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 guidelines)

1 Prevention and Early Detection

- 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 (FAP). The frequency of endoscopy is determined by the severity of the duodenal polyposis.
- 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.
- Patients with Stage IV duodenal polyposis who are fit for surgery should be offered resection.

2 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 cholangiopancreatography (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.

3 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.
- Transperitoneal techniques to obtain a tissue diagnosis have limited sensitivity in patients with potentially resectable tumours and should be avoided in such patients.

4 Pathology

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

5 Treatment

- 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 6 months.
- Duodenal obstruction should be treated surgically.
- 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.
- Duodenal bypass should be used during palliative surgery.
- Biliary bypass should be constructed with the bile duct in preference to the gall bladder.
- 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.
- 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 D

Staging of pancreatic cancer

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[10]) 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 between 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 in partial resection (pancreaticduodenectomy/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**[10]

	Tumour		
T0	**T0**		no evidence of primary tumour
T1	**T1**		tumour limited to the pancreas, 2cm or less in greatest diameter
T2	**T2**		tumour limited to the pancreas more than 2cm in greatest diameter
T3	**T3**		tumour extends directly into any of the following: duodenum, bile duct, peripancreatic tissues
T4	**T4**		tumour extends directly into any of the following: stomach, spleen, colon, adjacent large vessels
	Nodes		
NX	**NX**		regional nodes not assessed
N0	**N0**		no regional node metastasis
N1	**N1**		regional lymph node metastases
		pN1a	metastasis in a single regional lymph node
		pN1b	metastasis in multiple regional lymph nodes
	Metastases		
M0	**M0**		no distant metastases
M1	**M1**		distant metastases

In order to facilitate survival analysis the assigned TNM profile is condensed into a stage group category of which there are 5 stages (I, II, III, IVa, IVb, Table 2)

Example :

- 3cm tumour in head of pancreas, no evidence of arterial involvement. Therefore **T** = T2
- At pancreaticoduodenectomy regional nodes sampled and are negative for metastases, therefore **N** = N0
- At pancreaticoduodenectomy, no evidence of distant metastases in peritoneum or liver, peritoneal fluid negative, therefore **M** = M0

TNM profile is **pT2 pN0 pM0** (p = determined pathologically)

This TNM profile is assigned to stage group I.

Table 2 Stage Group Pancreatic Cancer

Stage	T	N	M
I	T1	N0	M0
	T2	N0	M0
II	T3	N0	M0
III	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
IVa	T4	Any N	M0
IVb	Any T	Any N	M1

N. Ireland Cancer Registry
Centre for Clinical and Population Sciences
Mulhouse Building
Grosvenor Road
Belfast BT12 6BJ

Tel: (44) 028 9063 2573
Fax: (44) 028 9024 8017
Email: nicr@qub.ac.uk
Website: www.qub.ac.uk/nicr