# Survival, clinical practice and costs

# in patients with

# pancreatic, oesophageal and gastric cancer

**Oscar Max Bachmann**

A thesis submitted to the University of Bristol in accordance with the requirements of the degree of Doctor of Philosophy in the Faculty of Medicine, Department of Social Medicine, 1999.

# ABSTRACT

**Objectives**: To examine the relationships between specialisation of cancer care (indicated by volumes of patients managed annually by doctors and hospitals) and survival time, operative mortality, clinical practice, and costs of hospital care.

**Design**: Cohort study and cost analysis. Multiple linear and logistic regression models and Cox's proportional hazards models adjusted for relevant clinical and prognostic variables. Each cancer was examined separately.

**Setting and subjects**: 2294 patients newly diagnosed as having gastric, oesophageal or pancreatic cancer in hospitals in South and West England, and (for pancreas) south Wales, between June 1996 and May 1997.

**Results**: Patients of higher volume hospitals and doctors tended to have better prognostic factors. Several investigations were more likely with increasing doctor volume. Patients of higher volume doctors were more likely to have resections. "No active treatment" was more likely with lower doctor volumes for all three cancers and with lower hospital volumes for pancreatic cancer. Survival time was longer with higher doctor volumes for oesophageal cancer and with higher hospital volumes for gastric and pancreatic cancers (adjusted hazard ratios attributable to managing 40 more patients per year: 0.69 (95% CI (confidence intervals) 0.49-0.98), 0.78 (95% CI 0.62-0.97) and 0.64 (95% CI 0.49-0.83) respectively). Operative mortality was less likely with increasing doctor volume for oesophageal and gastric cancers (adjusted odds ratios attributable to managing 10 more patients per year: 0.68 (95% CI 0.52-0.96) and 0.60 (95% CI 0.39-1.0) respectively), but for pancreatic cancers was not associated with doctor or hospital volumes. Costs of hospital care, and costs per day of life, had U shaped relationships with doctor volumes for pancreatic and oesophageal cancers; for gastric cancer cost per day of life decreased with increasing doctor volume. Hospital costs were not associated with hospital volumes.

**Conclusions**: Specialist cancer care, as indicated by patient volumes, was significantly and substantially associated with lower mortality. Clinical practice and hospital costs were influenced more by doctor specialisation than by hospital specialisation. The study supports the specialisation of cancer care. Specialisation of doctors is at least as important as specialisation of hospitals, especially for oesophageal and gastric cancers.

# AUTHOR'S DECLARATION

The author was principal investigator in this study, taking the lead role in study design, raising research funds, supervision of data collection, data analysis and writing. Ian Harvey, Tim Peters, Derek Alderson, Gwyn Bevan and Barnaby Reeves contributed to study design and were co-applicants for the research grant. Ian Harvey, Tim Peters, and Derek Alderson were closely involved with the study throughout, and advised on any issues arising during its progress. Derek Alderson assisted especially with clinical aspects and with professional liaison. Tim Peters assisted especially with statistical methods. Ian Harvey was PhD supervisor initially and, after he left the University of Bristol, Tim Peters was PhD supervisor during the completion of the thesis. Deborah Edwards, Carol Bedford and Sandy Wotton collected the data from hospital records.

Max Bachmann

# ACKNOWLEDGEMENTS

The author is grateful to his PhD advisers, Ian Harvey and Tim Peters; to Carol Bedford, Deborah Edwards and Sandra Wotton who gathered most of the data; to Derek Alderson who helped design and interpret the study and who facilitated access to all collaborating hospitals; to Gwyn Bevan and Barney Reeves who contributed to the initial study design; to the NHS National Cancer Research and Development Programme for funding; to the Office of National Statistics' NHS Central Register for help in tracking survival; to the Wessex and South and West cancer registries and in particular to Jennifer Smith, David Etherington and Freddie Bray, for provision of data on cancer registrations; to Steven Oliver for help with census deprivation data; to Jonathan Pye and co-investigators of the Welsh Surgical Society's study of gastric and oesophageal cancers for advice and for permission to adapt their data collection form; to the clinical directors and consultants in surgery, pathology, radiotherapy and oncology, for permission to carry out the study, and to the personnel in medical records and audit departments who helped identify the patients, in the following hospitals: Cheltenham District Hospital; Frenchay Hospital, Bristol; Gloucestershire Royal Hospital, Gloucester; North Devon District Hospital, Barnstable; North Hampshire Hospital, Basingstoke; Plymouth Hospitals Trust; Poole General Hospital, Poole; Princess Margaret Hospital, Swindon; Queen Alexandra Hospital, Portsmouth; Royal Bournemouth Hospital; Royal Devon and Exeter Hospital; Royal Hampshire Hospital, Winchester; Royal United Hospital, Bath; Salisbury District Hospital; Southampton General Hospital; Southmead Hospital, Bristol; Musgrove Park Hospital, Taunton; Torbay Hospital, Torquay; Royal Cornwall Hospitals Trust, Truro; United Bristol Healthcare Trust; West Dorset Hospital, Dorchester; Yeovil Hospital; Weston-Super-Mare General Hospital; Llandough Hospital, Penarth; Morriston Hospital, Swansea; Princess of Wales Hospital, Bridgend; Royal Gwent Hospital, Newport; Singleton Hospital, Swansea; and University Hospital, Cardiff; to the hospital finance officers who provided cost data; and to his employers, Stephen Frankel and Paul Dieppe for encouragement to conduct and complete the study. The thesis is dedicated to my family: Catherine, Zack and Adam.

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# 1. INTRODUCTION

This study's immediate scope is limited to patients with three cancers diagnosed over one year in one region of the United Kingdom. Its interpretation, however, requires an understanding of national and international trends in cancer care, in hospitals and in specialisation of health care. The study's results, in turn, have implications for changes in cancer care and health care more generally. Given that this study is intended to inform and influence cancer care, its location and role at the interface between policy and knowledge must also be understood. This chapter will provide the background to the study by describing the current policy on cancer services in the United Kingdom's National Health Service (NHS), discussing wider and longer-term changes in hospitals and medical specialties, and considering the role of research evidence in making these changes.

## 1.1 Cancer services in the United Kingdom

### 1.1.1 A Policy Framework for Commissioning Cancer Services

The current programme of cancer services development in the NHS is aimed at providing a high and equitable quality of care for all patients.[1] This is to be achieved primarily by centralising selected services into a limited number of specialist cancer centres, and by ensuring good quality of care elsewhere. It provides a rare example of the application of epidemiological evidence to the design of health services on a national scale, although it can be argued that the limited evidence currently available does not directly support the scope of changes planned. The evidence used is also unusual because of its emphasis on the health effects of the configurations of facilities and personnel, rather than on effectiveness of specific technologies. Thus it exemplifies the application of the more broadly defined field of health services research, as opposed to the more narrowly defined field of health technology assessment.

The proposed design of NHS cancer services in England and Wales was outlined in May 1994, in a key document, A Policy Framework for Commissioning Cancer Services,

prepared by an Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales.[1] It came to be known as the Calman-Hine report, after two of its authors, Kenneth Calman, Chief Medical Officer in the Department of Health, and Deirdre Hine, Chief Medical Officer in the Welsh Office. The Advisory Group comprised fifteen people, including senior academics and representatives of the clinical disciplines contributing to cancer care: surgery, oncology, radiology, general practice and public health.

The first principle of cancer care stated in the document was that "All patients should have access to a uniformly high quality of care in the community or hospital wherever they may live to ensure the maximum possible cure rates and best quality of life."[2] Thus both equity and quality were emphasised. The first rationale for the change was that the potential effectiveness of both palliative and curative treatments had increased markedly in recent years. The second, related, rationale was that outcomes of cancer care were known to vary widely within the United Kingdom. Part of this variation was deemed likely to be due to differences in the quality of care, even though part was probably due to systematic differences in the types of patients treated. Finally, research increasingly showed that, for a limited range of cancers, outcomes were better for patients managed in hospitals or by doctors with large numbers of similar patients, or where multidisciplinary teams were available.

The framework proposed that cancer care be organised around three levels: primary care teams, cancer units and cancer centres. Cancer units would be based at district general hospitals, but would only manage common cancers, such as breast, lung and gastrointestinal cancers. At a higher level, cancer centres would be characterised by provision of care that was both comprehensive (covering all cancer care needs) and specialised. This would include "treatment programmes for less common and rare cancers, and those treatment regimens which are too specialised, technically demanding or capital intensive to be provided in the cancer unit".[2] Cancer centres would ideally be located in single hospitals, but could comprise a network of services provided by several hospitals. Centres would support cancer units, for example by managing referred patients and providing supervision. Cancer centres would each cover populations of at least two thirds of a million. Given the observed variations in patterns of practice, it "will be necessary for cancer units and cancer centres using different methods of treatment to justify them on scientific or logistic grounds".[2] At the other end of the spectrum, primary

care teams needed to relate as partners to cancer centres and units, with emphasis on developing good liaison and timely referrals.

Further indications of how cancer units and centres might be selected and developed were provided by a member of the Expert Advisory Group on Cancer, RA Haward, in a 1995 editorial in the British Journal of Cancer.[3] He suggested that the following factors should be considered in designating cancer units: potential volumes of work, local clinical interest and expertise, local attitudes, "the case for greater specialisation and its impact on other services; and the efficiency of the resulting service" as well as contracts and costs. He proposed that cancers such as breast, colorectal, lung and skin cancers were common enough to be managed in smaller cancer units, while moderately common cancers, including gastric and pancreatic cancers, could be managed at medium sized cancer units. Oesophageal cancer, although also moderately common, should probably be managed at cancer centres, because of the "current pattern of widely distributed and variable practice, with generally poor results". He stressed the importance of diagnostic as well as therapeutic abilities, referring specifically to the potential for earlier diagnosis of pancreatic and other gastrointestinal cancers.

The cancer policy was reinforced at the highest level by the first White Paper on health published by the new Labour government, in December 1997, in which its plans for the NHS were described. The document cited NHS policy on cancer services as an example of how the 'new NHS' would deliver a 'modern and dependable' service.[2] Cancer services, like paediatric intensive care, were being developed according to a National Service Framework, which would "set out what patients can expect to receive from the NHS in major care areas or disease groups", and function as a "care blueprint".[2] This model of National Service Frameworks would also be extended to care for coronary heart disease and mental health – two other major parts of NHS services.

Of relevance to this study is the increasing emphasis in the NHS of evaluation, including outcome surveillance, as a critical component of quality assurance. In the Policy Framework document the Expert Advisory Group on Cancer stated that "careful monitoring of treatment and outcomes is essential".[1] This was reinforced by the White Paper, which emphasised "clinical governance", with a key role for evaluation.[2] This meant that clinicians and health service managers were responsible for ensuring the quality of clinical care.

The costs, or additional resource requirements, of the policy were not systematically estimated at a national level, and no targeted national funding was allocated. Another member of the Expert Advisory Group did however publish a simple cost estimate.[4] Assuming that each cancer centre would service a population of 1 to 2 million people and supervise 10 units, about 30 centres and 300 units would be needed nationally. About £100 million would be needed for capital investment, especially to refurbish cancer units. A further £100 million was needed annually for research (£15 million) and for training additional health professionals (£58 million), especially oncologists (who should increase from 350 to 520 nationally), cancer specialist nurses (600 more needed) and psychosocial professionals (300 more needed). Unfortunately no further justification is given for any of these numbers and the cost estimate excluded the most important cost item in any health service: the recurrent cost of employing professional staff. Given the national scale of the proposed reform, the absence of cost estimates appeared to be a deficiency of the plan. The implication is that it was the responsibility of health authorities and trusts to make marginal changes within existing budgets so as gradually to change cancer care, rather than to fund and implement a set of new services.

### 1.1.2 Developing NHS cancer services, 1995-1998

The organisational process for developing cancer services was not specified in detail and therefore was, by implication, to be as for any other centrally prescribed and locally implemented health service development. The key organisations to make the changes would be the local commissioners (purchasers) and providers of cancer care, namely district health authorities and hospital trusts. National and regional guidance would come from the National Health Service Executive, and sub-district input would be made through fundholding general practices and, in future, Primary Care Groups representing local general practitioners and community nurses. Plans for provision and funding of services would be specified in annual contracts or longer term agreements between purchasers and providers.

Progress towards implementation of the policy in Wales and in each region of England was reviewed superficially in an article in the Health Services Journal in April 1997.[5] Although regions varied, some common themes emerged. In some regions, plans were steered by regional working groups, having wide representation including leading clinicians and academics. In others, more action took place at the trust-health authority

level. Beneath this all-cancer umbrella, much activity focused on specific cancer sites, reflecting the varying needs of patients with different types of cancer. In Wales, a cancer services expert group was established, which set up eight cancer site-specific groups and nine generalist working groups. In some regions cancer site-specific groups of cancer nurses and professionals allied to medicine were formed in parallel to groups of doctors. In some regions health authorities and trusts were systematically developing their plans, standards and contracts on a cancer-by-cancer basis. Substantial effort was devoted to defining standards of care: both in terms of care pathways for patients with a particular cancer, and in terms of the infrastructure required at each level.

In the South and West of England the area covered by the study – the Regional Cancer Organisation emerged as having a key advisory and co-ordinating role. It was funded by a consortium of health authorities, with one authority acting as lead and making the greatest contribution initially, and the total number of funding authorities increasing from six from 1995-1998, to 12 from 1998-2000 (South & West Regional Cancer Organisation Newsletter 1998). By 1998 the organisation comprised an Oversight Management Committee, and eleven site-specific tumour panels, including one on upper gastrointestinal tract cancers, and employed three co-ordinators. The main outputs of the Organisation were advisory: informing purchasers, informing audits, and feedback of audit results to clinicians, through publications and oral presentations.

A key issue in implementing the strategy in the NHS was identifying which hospitals should be designated as cancer centres or as cancer units.[5] This was usually done by asking hospitals to apply to health authorities or regional committees for centre or unit status, and to supply supporting information. In some regions formal accreditation of centres or units was used, dependent on compliance with explicit criteria. Many hospital consultants and managers resisted their hospitals being designated as units rather than as centres, because they saw this as resulting in a loss of status and resources. In general, development of policies for common cancers and, correspondingly, of cancer units, preceded work on rarer cancers and on cancer centres. Cancer centres that were spread over a number of sites, rather than being based in one hospital, had been created in some regions.

## 1.1.3 Evidence, research and service development

For some rarer cancers the research evidence had clear implications for the desirable configurations of services, namely that they should be treated in a small number of highly specialised sites with specific facilities. For example, ovarian cancers and teratomas required a combination of several treatment modalities administered by experienced teams, which were clearly only available in certain hospitals.[6, 7] However for others the research evidence, where it existed, suggested that good quality care could be achieved in a number of different ways. For example for some common cancers such as breast cancer it seemed most important that individual surgeons, rather than hospitals, had experience in treating high volumes of similar cases or had a special interest in breast cancer surgery.[8 9] This could be achieved in smaller hospitals if individual doctors specialised in specific cancers or operations. The ability of doctors in smaller hospitals to specialise would depend on their other clinical responsibilities and their ability to attract enough suitable patients. The evidence of the relationships between the effectiveness, efficiency and source of care is critically reviewed in the literature review chapter of this thesis (Chapter 2). For the common upper gastrointestinal cancers investigated in this study, there has hitherto been little evidence on which to base service design.

The role of evidence in developing these policies is not entirely clear but there appears to be widespread and growing acceptance of a scientific basis for policy. The Expert Advisory Group published a paper in the Lancet in 1994, summarising supporting evidence and explicitly stating that it was pursuing an evidence-based policy.[10] The overall inference was that outcomes were better with larger volumes, implying that less common cancers should be treated at fewer sites. Some health authorities and trusts analysed hospital activity data to establish the numbers of patients treated by individual consultants and hospitals, with the implication that patient volumes would be a key accreditation criterion.[5] However for most cancers there was no evidence of precise volume cutpoints below which poorer outcomes would be expected. In parallel with discussion about service configurations, professional organisations or local groups developed clinical practice guidelines based to varying degrees on rigorous research evidence of clinical effectiveness.

Because of gaps in the evidence base for policy, the NHS Research and Development Directorate's National Cancer Programme in 1994 allocated substantial funding to

research that would inform the development of cancer services, including studies falling under the following three 'priority areas':

- "Studies designed to explain variations in disease outcomes, particularly in relation to variations in patterns of practice"
- "Comparison of care for common cancers (e.g. lung, breast, colorectal) in specialist and non-specialist treatment settings with respect to psychosocial and clinical outcomes; and the relative costs of managing each step of disease progression"
- "Factors influencing delayed presentation by patients (e.g. psychosocial) and variations in onward referrals by physicians to oncology specialists"

Most of these studies commenced in 1996 and most were scheduled to end in 1999. The present study was also funded by the Cancer Programme, and was included in the first of the above priority areas. Part of the study's role was to investigate whether the volume-outcome relationship which clearly did exist for some cancers also applied to three relatively common cancers with generally poor prognoses, namely oesophageal, gastric and pancreatic cancers. The study went further, disentangling influences on the clinical practice variations thought to contribute to differences in outcomes, examining the cost implications of different styles of practice, and investigating whether patients' socio-economic status affected access or outcome.

# 1.2 Specialisation of health professions and hospitals

## 1.2.1 Specialisation and subdivision of medical specialties

Cancer care is in many ways typical of the ways in which health care facilities and health professions are changing.[11] Services previously provided by medical specialists in hospitals are increasingly being provided by general medical practitioners or specialist nurses in primary care settings. Cancer specialist nurses have a growing role in palliative care based in patients' homes, while general practitioners co-ordinate a growing range of hospital and community care.[1] At the same time, medical specialties are changing, with increasing sub-specialisation. For example, the specialty of general surgery, already a subset of surgery, is increasingly being subdivided into sub-specialties such as upper gastrointestinal surgery.[12] Simultaneously, with multiple modalities of investigations

and treatments available, inter-specialty linkages are developing, for example between surgeons and physicians within gastroenterology, or between surgical and clinical oncologists and radiologists. Thus sub-specialists increasingly work together, cutting across traditional specialties.

The concept of a specialist has two interpretations. Conceptually, specialisation is a spectrum from lesser to greater depths of knowledge and expertise. Institutionally, it is a professional category, defined by regulations governing training, registration and permission to practice.[12] It may be inappropriate to focus primarily on the medical specialist and medical specialty, as exemplified by the consultant head of a firm: it has been argued that "the appropriate focus for rethinking the consultant's role is probably the specialist team because care – and its organisation – increasingly centres on teamwork".[11] However consultants remain at the core of specialised services in the NHS, both through their expertise and through their clinical and managerial responsibilities.

While at present NHS consultants are invariably employed by hospital trusts, the relationships between specialists and hospitals may become weaker in future. For example in the United States, where greater entrepreneurial experimentation is possible in a private sector environment, specialist practices are increasingly moving away from hospitals, because of high hospital costs and greater control of costs by the doctors concerned.[13] In the NHS, specialists are increasingly seeing patients in general practice-based outreach clinics.[14] However for investigations and surgical, chemotherapeutic and radiotherapeutic treatment of cancers, hospitals remain the main locus of care.

## 1.2.2 General hospitals and specialist services

The dominant model of hospitals in the NHS has shown remarkable durability since 1962, when the Hospitals Plan for England and Wales proposed the district general hospital as the fundamental unit.[15] At its basis were the assumptions that every district, with a population between 100 000 and 150 000, needed a basic range of medical specialties, and that combining these specialties in one location would allow sharing of resources, leading to better quality care at lower cost than if these services were provided at different sites.[15]

Despite the persistence of this model, the nature of the district general hospital has changed. Among the most dramatic changes have been the reduction in bed numbers, and

the increasingly intensive use of beds, together with more day case management. Between 1982 and 1992 the number of general and acute hospital beds decreased by 23%, while the number of patients treated increased by 27%.[12] During this period day cases increased by 160%, accounting for 30% of hospital cases treated in 1992.[12]

The other dramatic change has been the growing sophistication of diagnostic and therapeutic technology, accompanying the division of specialties into sub-specialties. While most marked in teaching hospitals, technological development and sub-specialisation have progressed unevenly across different general hospitals, resulting in variable quality of, and access to, specialist care across the country. Hence the Calman-Hine proposals for changing cancer care.

Over the past decade the concept of the hospital has been reconsidered, with vigorous debate about what a hospital should be, and how more specialised services should be located and co-ordinated in relation to more generalised services. It has been argued by Malcolm, in New Zealand, that "the overriding problem of hospitals, as organisational entities, is that they fragment the continuum of care". He therefore proposed that it was more useful to conceptualise the division of labour in health care "physiologically", that is according to services, rather than "anatomically", that is according to facilities.[16] In other words the "level" of care (on a specialist-generalist spectrum) was more important than the "location" of care.[16] He described how health system reforms in New Zealand led to services replacing hospitals as the key organisational units of the health service. In the United Kingdom, Vetter argued more radically that hospitals had largely outlived their usefulness and would be largely replaced by services provided in community settings.[17] However there clearly are advantages of concentrating services on a single site.

Harrison and Prentice have neatly drawn together trends, policy options and evidence concerning the changing nature of hospitals in a simple conceptual model.[15] Their key concepts are repeatedly referred to in this thesis. Two central concepts underlying the rationale for hospitals are economies of scale and scope. Scale refers to the volume of activities performed and size of facilities in a hospital, while scope refers to the range of different activities and specialties available. "Economies of scale exist if costs fall or quality rises as scale increases", and "economies of scope exist if costs fall or quality rises as the range widens."[15] They went on to analyse the trade-offs that accompany varying scale and scope, according to three dimensions: quality, cost and access. For example, concentration of specialist services in fewer larger sites may increase the

effectiveness of care, but this may be at the expense of greater costs and decreased access. The literature review of this thesis (Chapter 2) shows that while there is some evidence of quality varying with scale and scope, there is less evidence of consistent cost variation. Although access to patients will predictably be decreased by distance as services are concentrated on fewer sites, it is not obvious whether this really is a serious problem for patients with rare or life-threatening conditions.[15] Despite gaps in our knowledge, the notion that quality, cost and access are likely to vary with the scale and scope of services is useful in conceptualising changes in cancer care. The challenge to scientists is to build the theory by providing more and better evidence.

### 1.2.3 Research on hospitals and specialisation

This raises the question as to what kind of research is most appropriate for understanding relationships between quality, access and costs of hospitals with respect to their scale and scope. Applying a systems framework to research on structural change in hospitals, Harrison stressed the interdependencies between the different parts of hospitals and of the wider health system.[18] He argued that because of these dependencies, in order to determine the best mix of specialists and generalists one needs to analyse "the performance of the hospital as a whole or at least substantial parts of this". He proposed that the data necessary for studying the complexities of health care systems should be, as outlined by Wolfson:

- "Multivariate - encompassing a broad range of domains and factors.
- Multilevel - covering both individuals and various aspects of their external milieux.
- Microdata the data have to be available at the level of individuals.
- Longitudinal – so that individual life paths can be analysed and the long-term lagged responses to changes can be identified and understood."[19]

This study attempts to do just that by collecting and analysing data that are:

- Multivariable: personal (pathology), ecological (sociodemographic), and health care (investigations and treatments as well as where and by whom they are provided) influences on survival, costs and access.
- Multilevel: individual, doctor and hospital level variations in care and survival

- Microdata: individuals as the principal units of analysis
- Longitudinal: following patients from time of hospital referral to time of death.

Thus the research is primarily an epidemiological study of individual patients, that also incorporates economic and organisational variables and analyses.

# 2. LITERATURE REVIEW

This chapter reviews three different areas of theory and evidence to which the study contributes, and which are necessary for interpretation of its results. Firstly, it addresses the question of whether care provided by specialist facilities or doctors, that is those that deal with large numbers of similar patients in similar ways, is more effective than care provided by non-specialist facilities or doctors. The outcomes considered in this review are limited to mortality and morbidity. Other important dimensions of health care quality, such as patients' subjective perceptions of the quality of care, and their impact on quality of life, are not reviewed because these dimensions are beyond the scope of the study.

Secondly the review examines the relationships between health care costs and the scale and scope of health services.

Thirdly, the review examines evidence of the effectiveness of the main types of investigation and treatment available for pancreatic, oesophageal and gastric cancers. This is necessary so as to help understand how variations in the use of specific investigations and treatments may influence patient outcomes, and to judge the treatment patterns of more and less specialised doctors and hospitals.

## 2.1 Patient outcomes, doctor volumes and hospital volumes

### 2.1.1 General considerations: causes and methods

#### 2.1.1.1 Reasons why volume and outcome may be associated

It is widely assumed that hospitals or doctors that manage larger numbers of patients will be more effective and thus obtain better health outcomes. This assumption underlies much of the regionalisation of health services over the past few decades, aiming to improving the quality of care by concentrating services into fewer, larger hospitals or centres.[20] The most significant development of this kind currently taking place in the National Health Service of the United Kingdom is the concentration of cancer services

into designated cancer units and cancer centres.[10] As the following literature review will show, there is substantial evidence showing better outcomes associated with larger hospital or doctor volumes, but there is almost as much evidence showing no such an association, and a few studies showing the opposite. Before reviewing the empirical literature, the arguments or reasoning as to why the management of larger volumes of patients by doctors or hospitals may be associated with better outcomes are considered. These arguments have been discussed in greater detail by Luft et al,[21] Sowden et al[20], and Black.[22]

The first reason is that "practice makes perfect".[21, 22] It is plausible that a surgeon who performs an operation hundreds of times is more manually dextrous when performing the operation than one who has only performed it a few times. However there is more to experience than manual dexterity. Skilful diagnostic workup and careful selection of appropriate patients for an operation may also reflect experience and expertise. The surgeon may be more experienced in managing rare complications, because lower volume surgeons may not have been exposed to them before.[21] The outcome may be influenced by other members of the health care team, such as the casualty officer who makes the earliest diagnosis, radiologists, theatre nurses and anaesthetists. The collective and individual experience of all of these team members could plausibly influence patient outcomes.

For the hospital there may be a cumulative learning effect or a current volume effect.[21] These could also apply to individual doctors and to whole teams. The cumulative numbers of patients ever treated or, as proxy measures, age and years of experience, may be most important. However, if skills and knowledge are rapidly lost without practice, then current patient numbers may be most relevant.

A second possible reason for an association between greater volumes and better outcomes is that those doctors or hospitals that are the most effective could attract the most patients.[20, 21] Thus causality could work in the opposite direction. At present, different hospitals' or doctors' patient outcomes are not routinely available or widely reported, but publicising league tables of hospitals' or doctors' mortality rates could increase this effect.

A third reason for observed volume-outcome rel tionships is that volume may simply be a marker for factors such as teaching hospital status, as teaching hospitals tend to have

larger volumes. Teaching hospitals may be able to attract more competent staff, or more resources, and it may be these factors rather than volumes that account for the association. If such volume-related factors that could influence outcomes are identified, it should be straightforward to separate the volume and other influences on outcomes by multivariable analysis.

A fourth reason is that particular hospitals or doctors may tend to treat patients that are more or less severely ill than average.[20, 22, 23] Those tending to attract patients with a worse prognosis from the outset - for example because poor quality local primary care leads to late diagnosis, or because they specialise in non-curative treatment for the severely ill - would have worse outcomes. Conversely those attracting patients with a better prognosis - for example because local screening leads to earlier diagnosis, or because they specialise in curative treatments for patients with early stage disease - would have better outcomes. Whether higher volume doctors or hospitals tend to attract patients with better or worse prognoses would depend on many factors about which it would be difficult to generalise. Thus selective referral could lead to biased positive or negative volume outcome relationships, owing to confounding by disease severity.

Selection bias is one of the fundamental problems of observational epidemiology applied to assessment of health care effectiveness. The best solution would be randomization of patients to low or high volume doctors of hospitals. This would eliminate any systematic differences between groups of patients being compared. However it would be difficult to persuade patients, doctors and hospitals to participate in such an experiment.[24] An exhaustive literature review[20, 25] only identified one such randomized trial. In that trial patients undergoing angiography were allocated either to a highly experienced or a less experienced doctor.[26]

An alternative solution to randomization is to measure relevant confounding variables and to take these confounders into account when comparing outcomes. This can either be done through stratified analysis - comparing like patients with like, one stratum at a time - or by multivariable analysis, in which the independent effects on outcome of doctor or patient volume, and that of confounding variables, are estimated simultaneously. In either case, substantial overlap in patient characteristics between comparison groups is required, and the main challenge in data collection is valid and reliable measurement of confounding variables. Severity of illness is usually the most important risk factor to control for. Measurement of, and adjustment for, confounders is never a perfect solution

however, because their identification will always be incomplete, their measurement will always be imperfect and, if the patient groups being compared are very different, then no amount of adjustment will allow valid comparison.[27]

### 2.1.1.2 Types of intervention or service studied

Most types of health care, including highly technical or interpersonal interventions, could in principle show volume-outcome relationships because 'practice makes perfect'. As shown in the systematic review below, the range of services evaluated have been mainly limited to surgery or intensive care. There are several likely reasons for this preference for evaluating surgery.[20, 25] Firstly, it is plausible that surgery, requiring manual skills, would be most susceptible to a learning effect. Secondly, a surgical procedure is a relatively well defined intervention package, occurring over a limited period, in contrast with management of chronic complex medical conditions, which tends to be more heterogeneous. Thus the evaluated intervention is fairly consistent between surgeons and hospitals. Thirdly, a minimum level of physiological functioning is necessary to undergo general anaesthesia, thus enhancing the comparability of patients by excluding those with the worst short-term prognosis and making short-term mortality more clearly attributable to treatment. Fourthly, morbidity or mortality resulting from complications of surgery is usually evident during the same hospital stay and does not require routine follow-up and surveillance mechanisms to detect the relevant outcomes.

For intensive care, detailed physiological measurements are available and are good prognostic indicators of mortality, especially when used in such indices as the APACHE score.[20] Short-term mortality is easy to measure in these patients. It is also plausible that practice would help perfect the skills required for physiological support and cardiorespiratory resuscitation. Intensive care is a good example of where economies of scale would improve quality of care, because large volume units would have relatively low excess capacity due to random variation in demand and thus could justify having advanced equipment and specialised staff. These issues are discussed later with regard to economies of scale.

For evaluation of cancer management as a whole, in contrast to specific surgical procedures on cancer patients, evaluation of volume-outcome relationships is less straightforward. Historically, such studies have appeared later than studies evaluating

surgical procedures. In a review written in 1990, Luft *et al*[21] comment that for patients admitted for palliation of terminal illnesses,

> "...the patient's health status on admission may be a more important determinant of short-term outcomes than the quality of care rendered. Thus, for example, there are no studies of the volume-outcome relationship for medical oncology patients, although we have included in our review some studies of surgical interventions for cancer".

Restriction of volume-outcome studies in cancer care to specific surgical procedures does allow relatively clear interpretation of results. However it provides limited information because it does not explicitly consider critical dimensions of the overall package of cancer care received by patients. It does not consider diagnostic practices, which may lead to curable cases not being identified and operated on. It also does not consider other therapeutic measures such as nutrition and hydration, pressure sore prevention, oncology and radiotherapy, which may themselves influence outcomes and may be associated with hospital volume. The main problem with including a wider spectrum of care is that it is difficult to identify which aspect of the care most influences outcomes. A solution, used in this study, is to do both types of analysis: examining volume-outcome relationships both for all patients with a given type of cancer, and for the limited numbers of patients undergoing surgery. If volume-outcome associations are shown for one type of analysis and not for the other, this would help distinguish surgical effects from the effects of the total care package.

### 2.1.1.3 Prognostic variables

The most important case mix variables to measure and adjust for are those that are most strongly associated with outcomes and that differ most between the hospitals or doctors being compared.[20, 21] Particularly important are diagnosis, and severity or stage of disease at the time of presentation.[20] Some of these data may be routinely collected, for example some cancer registries record disease stage for some types of cancer. In many cases however only diagnosis is recorded. In order to obtain more complete information, it may be necessary to examine patient's medical records. However data may not be recorded in the records, and it may be necessary to ask clinicians prospectively to record such information, using forms to ensure consistent collection. Even this may be inadequate if the disease stage cannot be known without invasive or costly investigations.

This is a key problem with advanced abdominal cancers. Doctors may make a clinical diagnosis of advanced cancer, and not consider it in the patient's interests to perform surgery or to perform costly or uncomfortable tests merely to confirm their poor prognosis. Pancreatic cancer would be a good example of this. Thus even in ideal circumstances it may be impossible adequately to obtain accurate staging or other prognostic information on all patients.

A further problem is differential misclassification of prognostic variables.[27] This arises if prognostic variables are measured systematically differently by the hospitals or doctors being compared.[28-30] A classic example is staging of gastric cancer, as discussed in the relevant section below. Japanese surgeons are known to be more aggressive than their Western counterparts in operating on these patients, performing more radical lymph node clearance to well beyond the most peripheral affected nodes. It is argued that because Japanese surgeons operate more radically, they are more likely to identify patients with distant lymphatic spread. More conservative Western surgeons, faced with similar patients, might classify their cancers as being of an earlier stage. Thus for each apparent stage of gastric cancer, Japanese surgeons obtain better outcomes. This is known as "stage migration".

Co-morbidity variables, reflecting the co-existence of other diseases, are commonly used as prognostic indicators, although they would usually be expected to be weaker predictors of outcome than stage or severity of a life-threatening illness such as cancer. However, where staging information is not available it may add to the predictive value of a statistical model and aid in adjustment for case mix. Where no staging information is available, co-morbidity may help to a limited extent with case mix adjustment. The commonest method of adjusting for case mix is simply to count the number of co-existing conditions, as these are often routinely recorded.[21] This variable could be sensitive to misclassification if minor conditions with no effect on mortality (for example backache) are given equal weight to life-threatening conditions (for example ischaemic heart disease). This problem arises with comorbidity indices routinely recorded in discharge abstracts in some United States hospitals.[31]

In summary, patients of different types of doctors and hospitals are likely to have different prognoses, which may partly account for observed differences in outcomes. If higher volume doctors or hospitals measure and record prognostic information in ways that are systematically different from lower volume doctor or hospitals, then this may

lead to biased estimates of treatment effectiveness, even if analyses attempt to control for prognostic variables. In other words, differential misclassification of confounding variables may lead to biased estimates of effectiveness.[27] Even if there were no systematic differences in methods of obtaining prognostic information, non-differential (unbiased) misclassification of prognostic variables could also lead to biased estimates of effectiveness, by reducing the ability to control for differences in prognostic variables.[27]

### 2.1.1.4 Outcome measures

The most relevant outcome of any treatment depends on the nature and severity of the illness, and the potential of the treatment to affect the respective outcome under ideal circumstances. Mortality is the most important variable for the three cancers included in this study because they have such high mortality rates. However outcome measures may be chosen primarily because of their availability and accuracy rather than their relevance to the treatment. The most commonly used outcome measures in volume-outcome studies are in-hospital or peri-operative mortality.[20] United States studies which are based on large administrative databases, primarily designed for billing and accounting purposes, tend to rely on routine in-hospital data, excluding deaths or morbidity after discharge.[21] Where individual patient data can be linked to routine mortality surveillance, as in the United Kingdom, survival might be relevant, accessible, valid and reliable. For many conditions, mortality is less important than factors that contribute to quality of life. However these may be difficult to collect, often requiring patient interviews. This may be difficult or impossible with rapidly fatal conditions such as cancers, and it may be necessary to interview patients' survivors, who may be unreliable or biased informants, or may be unwilling or unable to be interviewed.

### 2.1.1.5 Influence of methods of analysis on results

An analysis conducted as part of the York review of volume-outcome relationships, discussed below, elegantly demonstrates how poorer quality studies can lead to exaggerated estimates of the effect of hospital volume on outcome.[20, 32] The reviewers showed that, in the case of coronary artery bypass grafting, the magnitude of volume-outcome effects was inversely related to the adequacy of adjustment for case mix. In studies with no adjustment for disease severity or comorbidity, odds ratios for in-hospital mortality for hospitals with annual volumes of over 200 grafts per year, compared to

hospitals with smaller volumes, were less than 0.7. In those studies that adjusted for both disease severity and comorbidity, the equivalent odds ratios were all greater than 0.8. Meta-regression analysis, using each study as a unit of observation, showed that the association between estimated magnitude of effect and study quality score was statistically significant.

The 121 studies of volume-outcome relationships reviewed by Luft *et al* used a variety of statistical methods.[21] To investigate whether the variation in results was due to the different statistical methods, they analysed two large data sets in a variety of ways. These were routine data sets of coronary artery bypass grafts and cholecystectomies performed in California in 1983, included a range of case mix and hospital characteristic variables and used in-hospital mortality as the outcome measure. The same data were reanalysed using the following methods:

- categorisation of volumes without considering patient risk factors, or with minimal stratification by risk factor
- categorisation of volumes with risk adjustments
- grouping hospitals according to outcomes, then comparing volumes (analogous to case control design)
- regressions with the hospital as the unit of observation
- regressions with the patient as the unit of observation.

They showed that adjustment and stratification for risk factors made important differences to the results. Whereas unadjusted analyses showed a steadily decreasing risk of death with increasing volumes, adjustment showed that there was an excess mortality only in the lowest volume category of hospitals, with no trend across the other categories. Stratifying patients into high and low risk groups showed a strong volume-outcome relationship for high risk patients but no volume effect for low risk patients. This suggests that patient risk may modify rather than confound the effect of volume on outcome. In converting hospital volume from a continuous variable to an ordered categorical variable, choice of cutpoints affected the results, as the volume-outcome relationship was not linear. The other methods of analysis – comparing volumes of providers with high and low mortality rates, or using hospitals or patients as units of analysis - did not affect the overall evidence of decreasing mortality with increasing volume. Choice of outcome measure also did not appear to affect the main findings. Of 96 studies that used mortality

as the only outcome measure, 70% showed significant volume-outcome effects, while 72% of the 25 studies using morbidity measures as outcomes showed significant volume-outcome effects.

### 2.1.1.6 Summary

This section of the review has discussed several reasons why specialisation may improve the quality of health care. It has also discussed the use of patient volumes as an indicator of specialisation, and methodological issues inherent in research into volume-outcome relationships. Apparent volume-outcome associations may be at least partly due to selection bias, information bias, and confounding. It is necessary for researchers to measure and adjust for influential prognostic factors which may differ systematically between patients of specialists and non-specialists. However, such measurement may be difficult. Differential methods of obtaining prognostic information may themselves lead to biased estimates of effectiveness. It is necessary to examine those health outcomes that would be most affected by quality of care, but such information may be unobtainable or, if assessed in different ways, could also lead to biased results. Finally, methods of statistical analysis can influence results. Thus the selection and measurement of specialisation, prognostic and outcome variables, and the statistical methods employed, should all be critically appraised when examining empirical evidence. The following section will review the evidence regarding specific cancers.

## 2.1.2 Evidence about specific cancers

### 2.1.2.1 Interpreting the evidence

Empirical evidence of volume-outcome relationships will be discussed in the following sections. The relatively small number of studies involving pancreatic, gastric and oesophageal cancers are most relevant and will be critically analysed in detail. In order to make the results of these studies comparable with each other, where possible odds ratios and 95% confidence intervals have been calculated and tabulated by the reviewer, if they were not reported in the original studies. The more numerous studies involving all other cancers will then be critically examined, and generalisation of this evidence to cancer care will be discussed, but with less emphasis on alternative interpretations of each study. Finally, the much larger literature of volume-outcome relationships in all types of health

care will be reviewed, but as there are about 200 such studies, each study will not be discussed individually.

### 2.1.2.2 Pancreatic cancer

The only potentially curative treatment for pancreatic cancer is resection of the tumour, which usually entails resecting the entire pancreas and adjacent duodenum. This procedure is known as a pancreaticoduodenectomy, often known as a Whipple's procedure. Variations entail more radical resection of adjacent organs, and different ways of re-anastomosing the remaining bowel. Palliative procedures include bypass procedures, which allow gut contents to bypass obstructions, and stent insertions, which allow bile to be passed into the intestine.

Five studies were identified which examined volume-outcome relationships in pancreatic cancer care.[31, 33-36] All were conducted in the United States. All five studies showed significant volume-outcome associations: higher volume surgeons had significantly better outcomes in two of the studies, and higher volume hospitals had better outcomes in four of the studies. All five examined short-term outcomes: after pancreatic resections in four studies and after either resections, bypasses or stent insertions in one study. Four studies obtained their data from discharge abstracts from United States hospitals. Four adjusted for co-morbidity with varying degrees of rigour, but none systematically adjusted for cancer staging. Taken together, this evidence suggests that pancreatic procedures performed by high volume surgeons or hospitals are less likely to lead to in-hospital mortality and morbidity. An alternative interpretation is that these findings are artefacts of high volume hospitals and surgeons systematically attracting lower risk patients who have prognostic characteristics which were not taken into account.

*Comparing surgeons within Johns Hopkins Hospital*

Yeo et al[36] compared proportions of patients with pancreatic cancer who developed pancreatic fistulae after undergoing pancreaticoduodenectomies performed by five surgeons in one hospital. Data were obtained prospectively during a randomized controlled trial of 145 patients which compared two modifications of the procedure, namely pancreaticogastrostomy and pancreaticojejunostomy. The trial does not affect the comparison of surgeons because, although the paper does not report whether patients in each trial arm were equally distributed between surgeons, the modifications being compared were not associated with risk of pancreatic fistula. The study showed that

patients treated by the four surgeons who each performed 29 or fewer operations during the study period had significantly higher risks of developing pancreatic fistula than patients of the surgeon who performed 76. Logistic regression was used to obtain odds ratios, adjusting for location of tumour and type of anastomosis (Table 2.1). The effect of multivariable adjustment was to increase the odds ratios for two low volume surgeons, and for another surgeon to widen the lower 95% confidence interval to below 1.0.

**Table 2.1. Risk of pancreatic fistula after resection[37]**

| Number of patients per surgeon | Odds ratio (95% CI) of developing pancreatic fistula | |
|---|---|---|
| | Not adjusted | Adjusted |
| 9 | 7.0 (1.0-48.9) | 11.6 (1.3-105) |
| 14 | 6.6 (1.2-37.1) | 6.0 (0.9-41.3) |
| 17 | 10.1 (2.1-48.1) | 13.0 (2.1-78.3) |
| 29 | 3.9 (0.8-18.6) | 3.8 (0.7-20.8) |
| 76 | 1.0 | 1.0 |

Staging variables such as nodal involvement, tumour size and invasion and metastases were not collected or analysed, so one cannot exclude the possibility that the single high volume surgeon operated on earlier stage patients and therefore obtained better outcomes. The main limitation of this analysis is reliance on one high volume surgeon as the reference surgeon, especially as there is no obvious trend across the other four surgeons. It is plausible that the better outcomes obtained for this surgeon may be due to factors other than the number of operations performed during the course of the trial. Another limitation is the emphasis on pancreatic fistula, which was only one of 12 post-operative complications measured. It is possible that this volume-outcome relationship was a chance finding arising from multiple statistical comparisons.

*Comparing Johns Hopkins Hospital with other hospitals in Maryland*

Gordon et al[34] compared in-hospital mortality after pancreaticoduodenectomy between Johns Hopkins Hospital, which was the single high volume regional centre in the state of Maryland, and all other hospitals in the state, using discharge abstract data routinely collected between 1988 and 1993. Of the 502 patients included, 54% were treated by the regional centre and 46% by 38 other hospitals. Patients treated at the regional centre were significantly less likely to be black or to have state health insurance (both of which are

indicators of poorer social class), were less likely to have lung disease and more likely to have diabetes. These variables, together with age, gender, source of admission, and other comorbidities were included in a multiple linear regression model that provided an adjusted estimate of the difference in risk of in-hospital mortality between the regional centre and other hospitals.

Mortality in the regional centre was 2.2%, compared to 13.5% in the other hospitals, and so the risk difference was 11.3% ($p<0.001$). The adjusted risk difference was 11.4% ($p<0.001$). The crude odds ratio of death for other hospitals compared to the regional centre was 6.1 (95% CI 2.9-12.7), but no adjusted odds ratios were provided.

The main limitation of the study was the absence of cancer-specific prognostic variables. The paper reports that over time a greater proportion of patients were being referred to the regional centre, suggesting that patients were being selected for referral. If lower risk patients were being selectively referred, this could account for some of the difference in outcomes. Because only one hospital was compared with all other hospitals, it is a question of interpretation whether the lower mortality for the regional centre was because of the high patient volumes involved, or because of other unique features of this famous hospital.

The study also showed that the mean hospital charges for the regional centre were 17% lower than for other hospitals among all patients, and 22% less for patients discharged alive ($p<0.001$ for each comparison). These comparisons were also adjusted in multiple regression models, using the same prognostic variables, but adjustment did not affect the results. The authors argue that patient charges are a valid indicator of actual costs, because hospital charges are strictly regulated in Maryland.

Another, similar, study was conducted by members of the same research team, this time including all patients with pancreatic cancer and having bypass procedures, stent insertions or resections.[31] The study included 1236 patients in 48 hospitals. In-hospital mortality of patients managed by medium and low volume hospitals was compared with that of Johns Hopkins Hospital, and stratified according to whether patients had resections, bypass procedures or stents. The study showed that patients of medium and low volume hospitals had markedly and significantly higher mortality rates (relative risks ranging between 1.9 and 19.3) after adjustment for comorbidity. The main limitations of this study were, again, the absence of cancer-specific prognostic information, the

comparisons with only one high volume hospital, and reliance on hospital mortality as the primary outcome measure. For those prognostic variables that were known, patients of the high volume Johns Hopkins Hospital appeared to be systematically healthier at time of admission, and so it is likely that residual confounding persisted after adjustment. It is not clear whether one can generalise the study's findings from only one high volume hospital to others. Nevertheless, the magnitude of the relative risks, the suggestion of trends across low, medium and high volume hospitals, and the consistency of results for different types of treatment do suggest some benefits of specialisation for a wide range of pancreatic cancer patients.

*Comparing surgeons and hospitals in New York state*

Evidence that higher hospital volumes, but not higher surgeon volumes, were *associated* with fewer perioperative deaths, was obtained from another relatively high quality study.[35] The authors analysed discharge abstracts from all 1972 patients who had undergone pancreaticoduodenectomy or total pancreatectomy in New York State between 1984 and 1991. Perioperative death was defined as in-hospital death, and volumes were defined as the number of pancreaticoduodenectomies performed by the respective hospital or doctor in the same year as the patient's operation.

Case mix differences were controlled in two ways. Firstly, adjusted mortality rates were calculated, using multiple linear regression analysis to calculate a predicted probability of in-hospital death for each patient. Secondly, logistic regression was used to control for prognostic variables. Prognostic variables used in both models were age, sex, race, scheduled or unscheduled admission, referral from another hospital, number of secondary diagnoses, type of insurer and year of surgery. The single catch-all variable 'number of secondary diagnoses' is probably the most important, and includes cancer staging information (lymph node involvement, secondary neoplasm of other digestive organs), problems probably related to the cancer (postoperative infection, cholecystitis and disorders of the biliary tract) and unrelated comorbidities (diabetes, hypertension and coronary heart disease). It is unfortunate that these different categories were collapsed into a single variable, with equal weight given to each, especially as the most common secondary diagnoses were directly relevant to cancer staging and thus would probably be the best predictors of mortality. The number of secondary diagnoses was strongly associated with outcome using both chi square tests and logistic regression. Thus much highly relevant information was used to adjust for case mix, but the equating and

collapsing of strong and weak predictors probably weakened the overall control of case mix variation. The standardised in-hospital mortality rates and mean lengths of hospital stay associated with different hospital and doctor volumes were as shown in Table 2.2.

**Table 2.2. Standardised mortality rates and lengths of stay for different hospital and surgeon volumes[35]**

| Hospital volume | Percent of total patients | Standardised mortality (%) | Mean length of stay (days) |
|---|---|---|---|
| <10 | 24 | 18.9 | 35 |
| 10-50 | 54 | 11.8 | 32 |
| 50-80 | 3 | 12.9 | 22 |
| >80 | 19 | 5.5 | 27 |
| p value and comparison | | p<0.001 for lowest 2 vs. highest 2 categories | p<0.05 for lowest 2 vs. highest 2 categories |
| **Surgeon volume** | **Percent of total patients** | **Standardised mortality (%)** | **Mean length of stay (days)** |
| <9 | 67 | 13.0 | 34 |
| 9-41 | 18 | 9.7 | 26 |
| >41 | 15 | 6.0 | 27 |
| p value and comparison | | <0.001 for lowest vs. highest 2 categories | p<0.05 for lowest vs. highest 2 categories |

The authors report significant differences between volume categories, but their analyses were not ideal. They report comparing mean lengths of stay using a chi square test, but it is unclear how this test can be used for a continuous variable. In comparing standardised mortality rates they also use a chi square test, but instead of testing for trend across all volume categories, they compared various combinations of categories with each other. The choice of cutpoints for volume categories was not discussed in the paper and as these categories had quite different numbers of patients, with very few in the highest volume categories, it is possible that cutpoints could have been chosen so as to obtain the desired result. However it does appear from the above tables that there were clear trends of decreasing mortality and length of stay with increasing hospital and doctor volume. When both hospital and surgeon volumes were entered into a logistic regression model together with the other prognostic variables, only hospital volume was significantly independently associated with in-hospital mortality. Odds ratios from the logistic regression models were not reported.

A problem in interpretation arises from the definition of peri-operative mortality as in-hospital mortality rather than as death within a specified number of days since the operation. It is possible that deaths within, for example, a month of the operations were missed in patients discharged earlier. Because patients of higher volume hospitals and

surgeons had shorter lengths of stay, an undercount of deaths would be more likely for such patients. The overall bias would be to exaggerate the volume-mortality association.

*Comparing United States university hospitals*

The weakest study of volume-outcome relationships in pancreatic cancer resections used discharge coding data from 222 patients treated in 26 United States university hospitals in 1989 and 1990.[33] Types of resection included pancreaticoduodenectomy, distal pancreatectomy, total pancreatectomy and islet cell resection. The outcomes examined were in-hospital mortality and operative complications. There was no adjustment for case mix. Although there appeared to be weak trends of decreasing risk of death or operative complications with increasing hospital or surgeon volume, these were not statistically significant, with one exception. Surgeons performing four or more resections over two years were less likely to have complications than surgeons performing fewer (33% vs. 53%, p–0.01).

In summary, the four studies of volume-outcome relationships after major pancreatic cancer surgery suggest that higher volume surgeons or hospitals may obtain better outcomes. The only study including the full spectrum of pancreatic cancer patients found lower mortality in a large referral centre than in other hospitals. However these studies are flawed by limited adjustment for cancer-specific factors and by questionable choice of patients for comparison. Therefore these conclusions should be regarded as tentative.

### 2.1.2.3 Oesophageal cancer

The mainstay of treatment aimed at curing this cancer is resection, that is, oesophagectomy. The main palliative treatments are stent insertion and radiotherapy, which aim to reduce oesophageal obstruction and permit swallowing of food and drink. Three studies were identified that examined the relationship between hospital or surgeon volume and peri-operative mortality in patients undergoing oesophagectomy, and all of them considered cancer staging variables in some way.[38-40] Only one of them adequately adjusted for confounding prognostic variables in a multivariable model; it showed no relationship between hospital volume and peri-operative mortality. The other two showed that patients operated on by high volume surgeons had both significantly lower peri-operative mortality and worse prognostic variables, and so adjustment would be expected to strengthen the volume-outcome association. These studies suggest that high volume

surgeons tend to have lower peri-operative mortality but that hospital volume has no effect on peri-operative mortality.

*Hospitals in the Thames regions of England*

A United Kingdom cancer registry study found no association between hospital volume and perioperative mortality.[39] The study included 571 patients registered who had oesophagectomies at 68 hospitals during 1985-1989. Data were obtained from the Thames Cancer Registry. The broader study excluded 24% of the total of 3273 patients registered as having oesophageal cancer because of incomplete data. The proportion of oesophagectomy patients excluded because of incomplete data was not reported. Logistic regression was used to examine predictors of perioperative mortality, with age, sex, tumour stage, tumour morphology, tumour site and hospital volume as explanatory variables. Among those undergoing oesophagectomy, the adjusted odds ratios for peri-operative mortality for different levels of hospital volume are as shown in Table 2.3.

**Table 2.3. Risk of operative mortality and hospital volume[39]**

| No. oesophagectomies at hospital, 1985-9 | Adjusted odds ratio (95% CI) |
|---|---|
| >20 | 1.0 |
| 16-20 | 0.51 (0.26-1.01) |
| 11-15 | 0.85 (0.44-1.67) |
| 6-10 | 1.07 (0.51-2.24) |
| <6 | 0.37 (0.13-1.02) |

*Comparing surgeons in the West Midlands of England*

The most frequently cited study of volume-outcome relationships in oesophageal cancer surgery was reported by Matthews *et al.*[38] It included 1119 patients who underwent oesophageal resections for cancer between 1957 and 1976 and were reported to the West Midlands Cancer Registry, from which all data were obtained. 581 of the resections were performed by consultants doing 3 or fewer resections per year and were compared with 538 resections done by surgeons who performed 6 or more per year. No surgeons did 3 or 4 resections per year. Operative mortality (defined as any death within 30 days of operation) was 39.4% in the low volume group and 21.6% in the high volume group ($p<0.001$). Age-adjusted five year survival was 11.1% and 15.2%, respectively ($p<0.05$). When operative deaths were excluded, age adjusted five year survival rates were 18.0% and 19.0% respectively, which were not significantly different.

The following prognostic variables were reported: age, sex, site of tumour, nodal or other metastasis at operation, duration of symptoms, whether surgery was curative, and adjuvant therapy. The authors tabulate these figures and state that "none of the differences was statistically significant and the groups can therefore legitimately be compared with regard to operative results". They do not provide any p values for the table and do not perform any multivariable analyses. This is unfortunate as the quoted statement is incorrect. Patients of high volume surgeons were more likely to have had tumours in the middle than the lower third of the oesophagus. The author of this thesis tested this comparison with a $\chi^2$ test and found p=0.00001. Patients of high volume surgeons were significantly more likely to have nodal or other metastases at the time of the operation (44.9% vs. 43.7%, p 0.04). As both metastases and location of tumour were associated with mortality,[39] the unadjusted comparisons could therefore be confounded. However as these indicators of poor prognosis were both more common in the high volume patients, the direction of bias would have been to reduce the strength of association between volume and outcome. Another limitation of the study was that it covered a 20 year period and did not take date of surgery into account. It is plausible that both surgical techniques and average surgeon volumes changed over time, and thus volume could be an indicator of secular trends in surgery.

*Comparing surgeons within a Canadian hospital*

A small Canadian study[40] of 74 patients undergoing oesophagectomy for cancer in one centre found that the risk of operative mortality for the three surgeons who did 6 or more oesophagectomies per year was significantly lower than for the 17 surgeons who did fewer oesophagectomies (0% vs. 22%, p=0.001). Anastomotic leaks were also less common for high volume surgeons, although this difference was not significant (7% vs. 22%, p 0.07). The authors state that stage and location of tumours were "similar" between the groups but do not report statistical tests and do not make any adjustments. Re-analysis by the author of this thesis found that patients of high volume surgeons tended to have more tumours in the middle third of the oesophagus (p=0.065) which is associated with a worse prognosis[39] and thus this should have been controlled in a multivariable analysis. Cancer stage was indeed not significantly different between the groups (p=0.5). Adjustment for tumour location would be expected to increase the strength of association between doctor volume and mortality. The above-mentioned comparison of operative mortality should have been tested with Fisher's exact test instead

of a $\chi^2$ test because of small numbers in some cells, but this author's reanalysis still showed a highly significant difference (p=0.002).

In summary, the best of these studies showed no advantage of high volume hospitals or surgeons, while the poorer quality studies did suggest benefits of higher surgical volumes. All of the studies were limited to examining complications after resection, which is not relevant to the majority of oesophageal cancer patients. Thus studies with good case mix adjustment, and including a wider spectrum of patients, are needed.

### 2.1.2.4 Gastric cancer

Only one study was identified that examined volume-outcome relationships in gastric cancer surgery it adjusted thoroughly for case mix and found no advantage of having resections performed by higher volume surgeons or in higher volume hospitals. This study is now over 20 years old. A second study merely showed moderate variation in case-mix adjusted outcomes between surgeons within one hospital. There is thus clearly a shortage of evidence about this common cancer.

*Comparing surgeons in 69 United States hospitals*

The only study of gastric cancer surgery to examine the relationship between hospital mortality and doctor and hospital volume, adequately adjusting for prognostic variables, found no volume-outcome relationship.[41] Kelly and Hellinger examined 1977 data derived from discharge abstracts derived from 373 non-Federal United States hospitals. Analysis of outcomes for gastric cancer surgery was restricted to 69 hospitals who also provided information on physician characteristics. 193 doctors were included. The authors do not discuss how representative these 69 hospitals were of the 373 hospitals in the sample, or of all hospitals in the country, limiting the generalisability of the study. The overall hospital mortality was 12% (41/341) and the most common surgical procedures were types of gastrectomy. They used a logistic regression model which included as explanatory variables hospital characteristics (hospital volume, teaching hospital status, geographical region, urban or rural location, public or private hospital, total admissions per year), surgeon characteristics (doctor volume, surgeons' board certification), and patient characteristics (cancer stage, number of diagnoses, age, sex, daily costs, insurance cover). The paper only reports coefficients and t ratios from the logistic regression analysis, and so this author calculated the odds ratio and 95% confidence intervals (Table 2.4). Table 2.4 shows only the odds ratios for selected

explanatory variables, although all of the above variables were included in the model. It is apparent that there was no significant association between hospital mortality and doctor or hospital volumes, or teaching hospital status, but mortality was significantly lower in urban hospitals and significantly higher in hospitals with more admissions.

**Table 2.4. Odds ratios for in-hospital mortality for selected explanatory variables included in the logistic regression model.[41]**

| Explanatory variable | Coefficient | t | OR | 95% CI |
|---|---|---|---|---|
| Hospital volume* | -0.0043 | 0.8190 | 1.00 | 0.99-1.01 |
| Doctor volume* | 0.0050 | 0.5390 | 1.01 | 0.99-1.02 |
| Teaching hospital | -0.0885 | 1.2570 | 0.92 | 0.80-1.05 |
| Urban hospital | -0.1868 | 2.4120 | 0.83 | 0.71-0.97 |
| No. of admissions (thousands) | 0.0105 | 2.2070 | 1.01 | 1.00-1.02 |

* Number of operations for gastric cancer performed during 1977

The main strength of the study was the availability of detailed data on cancer staging and the number of diagnoses per patient. The main limitations of the study were its restriction to in-hospital mortality, as in most United States studies based on discharge abstracts, and the low proportion of eligible hospitals that were included.

*Comparing surgeons in one Scottish hospital*

McArdyle and Hole[42] studied 328 patients receiving gastric cancer surgery in one hospital over eleven years (1974-1984). They showed moderate variation in survival between surgeons, none of whom had a specific interest in gastric cancer surgery, after adjusting for duration of symptoms, serosal involvement, involvement of resection margins and lymph node infiltration, in a proportional hazards model. Adjusted hazard ratios were obtained for each surgeon by comparison of their patients with all other patients, and ranged from 0.69 to 1.61 for all patients, and between 0.74-1.76 for curative resections only. However no surgeon had a significantly higher or lower hazard ratio than their colleagues. There was no trend of better outcomes for higher volume surgeons. The variation in case mix, clinical practice and survival are not surprising, and could be as much due to random variation as to expertise. Thus this study does not provide support for specialisation of gastric cancer surgery within a hospital.

### 2.1.2.5 Other cancers

While there is limited evidence about upper gastrointestinal cancers, there are substantially more high quality studies of colorectal and breast cancers. It may be that patients with these latter cancers tend to present earlier, and staging may thus be easier or more clinically desirable. The evidence regarding colorectal cancer, however, is highly variable, and the most recent United Kingdom study showed no advantages of higher surgeon or hospital volumes. The evidence concerning breast cancer is more encouraging. For rarer cancers the evidence is more scanty, often with only one study on a particular cancer showing either an advantage or no advantage of specialisation. Given the limited number of studies on cancers other than colorectal or breast cancer, and their variable methods, it is difficult to generalise as to whether the differences in results are due to differences between cancers or to differences in research methods.

#### Colorectal cancer

There is little evidence of benefits of specialisation for colorectal cancer surgery. Of the studies that adjusted for case mix, one showed worse survival in higher volume hospitals, and another showed worse outcomes in low volume hospitals; one showed worse outcomes among low volume surgeons; three studies showed no independent effect on outcome of surgeon volume and two showed no independent effect of teaching or specialist hospitals. One further study showed no benefits of treatment in a teaching hospital but did not adjust for case mix.

The most recent and highest quality study was conducted in Northern Ireland and reported in 1999.[43] It included 3217 patients newly diagnosed between 1990 and 1994 and followed up for a median of 54 months. The prognostic variables measured and adjusted for included tumour invasion, liver metastases, tumour differentiation, and type of intervention. Analysis was by multiple logistic regression (for 2-year survival) and Cox's proportional hazards modelling. Patients were grouped into quintiles of consultants' current workload per year, consultants' years of experience, and hospitals' annual workload. Consultants' patient volumes and years of experience were not independently associated with survival. There was a suggestion of higher mortality among higher volume hospitals: compared to patients in hospitals with volumes of 23 per year or less, patients in hospitals with volume of between 33 and 54 were about 50% more likely to die within two years. The hospital volume-survival association was

statistically significant whether data were analysed by ordinary logistic regression (P 0.01), multilevel logistic regression (P 0.02) or Cox's proportional hazards model (P 0.002).

The best evidence favouring high volume hospitals is provided by Flood *et al* who studied 17,872 patients with colon cancer treated in 1040 United States hospitals during 1972.[44] Data were obtained from routine hospital chart abstracts. They showed a higher risk of in-hospital mortality in hospitals with lower than average volumes than in higher volume hospitals (standard mortality ratios (SMRs) 1.14 and 0.94; $p<0.05$) after adjusting for biochemical, physiological and severity variables in a logistic regression model. Stage of disease was reportedly included in the analysis but was not defined in the paper. When high:low volume comparisons were stratified into three risk categories, the ratio was much greater for low and medium risk patients than for high risk patients. This pattern, whereby advantages of high volume hospitals disappeared for high risk patients, was also found for most other surgical categories studied, but no statistical tests of interaction were reported.

McArdyle and Hole studied 645 patients clinically diagnosed as having colorectal cancer and presenting to the Glasgow Royal Infirmary between 1974 and 1979.[45] They compared the 13 surgeons who treated them, each with between 98 and 21 patients over the study period, and none of whom having a special interest in colorectal surgery. After adjusting for case mix (including emergency admission, tumour invasion and differentiation, metastasis, age and sex) they found substantial variation between the surgeons in choice of procedure, mortality and morbidity. They did not show any volume-outcome association, however, but did not explicitly examine this relationship. A study such as this which shows wide variation in clinical practice and in outcomes, but no association between process and outcome, is difficult to interpret.

United States experience of surgery for colorectal cancer during the 1980s was examined in the study by Kelly and Hellinger[41] discussed before under gastric cancer surgery. The study included 170 in-hospital deaths among 2612 patients treated by 434 doctors in 116 hospitals, and adjusted for cancer stage, number of diagnoses, age, sex, insurance coverage, and several hospital and doctor characteristics in a logistic regression model. There was no association between mortality and nu nbers of patients with the same condition treated by their hospital or their doctor. There was however a slightly lower mortality in teaching hospitals than in other hospitals (OR=0.96; 0.93-0.99) and a higher

mortality in public hospitals than in private hospitals (OR=1.04; 1.01-1.08) in the same multiple logistic regression model.

A German study included 600 patients and compared outcomes in those operated on by surgeons who performed more than 15, versus 15 or fewer, colorectal resections over two years (between 1984 and 1986).[46] Although there was no significant difference in surgical mortality, the risk of loco-regional recurrence was significantly higher in the low volume group (OR 1.71; 95% CI 1.06-2.78) after adjustment for site, stage, grade, operation, and local spillage of tumour cells.

A French study of colorectal cancers based on data from the cancer registry in the department of Calvados found that rural patients were less likely than urban patients to be treated in specialised centres (45% vs. 55%; $p<0.05$) and, among females only, were more likely to have metastases at the time of presentation (19% vs. 12%; $p<0.05$).[47] However, after adjustment for tumour extension, type of surgery, age and symptoms in a proportional hazards model, treatment in a specialist centre was not associated with survival.

A Finnish study of 7507 cases of colon cancer diagnosed between 1970 and 1981 compared 5 year relative survival between those living in different hospital districts.[48] Districts were classified according to whether the respective hospitals had radiotherapy facilities or were teaching hospitals. The study found a higher risk of death among patients from districts with no teaching hospital or radiotherapy unit, compared to districts with both (RR=1.14, 95% CI 1.05-1.23), after adjusting for age, sex and tumour invasion in a proportional hazards model. The key problems with this study are the assumption that patients were treated in the districts in which they lived, and the limited staging data used (i.e. excluding nodal involvement and metastases). Volume indicators of specialisation were not used.

A study of 10,297 patients who had colectomies in New York State in 1986, mostly for cancer, showed that physician volume was inversely associated with in-hospital mortality.[49] This association remained after adjustment for a range of risk factors (including presence of cancer, number of secondary diagnoses, mode of admission, age, sex, race, and hospital characteristics) in a multiple logistic regression model. Smaller hospital volume was significantly and independently, but less strongly, associated with

greater risk. The limited measurement and control of cancer-specific variables, however, could have allowed for substantial confounding by case mix to persist.

Sagar and colleagues studied 438 patients who had colorectal resections by one of five surgeons, each of whom performed between 44 and 110 resections.[50] There was no difference in postoperative mortality or morbidity between surgeons after adjusting for physiological status, operative severity and malignancy.

A Manchester study compared outcomes between 272 patients treated by six surgeons working in a district general hospitals and 295 patients treated by six surgeons in a teaching hospital between 1981 and 1983.[51] All surgeons had an interest in coloprocotology. There was no significant difference in operative or five-year mortality between teaching hospital and district general hospital patients, although teaching hospital patients had poorer 'performance status' at admission, were less likely to be 'unstaged inoperable' and were more likely to have a curative resection. The combination of unfavourable and favourable prognostic characteristics makes it difficult to establish whether teaching hospital patients had a better or worse prognosis at the time of presentation. Although this study had high quality data including Duke's staging, and substantial statistical power, it is unfortunate that no multivariable analysis was performed, and thus the independent effect of any patient, surgeon or hospital characteristic was not determined.

### Breast cancer

Two companion studies of breast cancer surgery in Yorkshire provide relatively strong evidence of better survival with larger surgeon volumes. These studies are supported by a Scottish study showing better survival among patients of surgeons with a special interest in breast cancer surgery. Two other studies – one Finnish and one from the United States provide indirect evidence of advantages of specialisation.

The earlier Yorkshire study covered 27000 patients with breast cancer registered with the cancer registry from 1978 to 1992 and treated by 60 surgeons in 16 districts.[52] It showed that surgeons who expressed an interest in breast cancer treated larger numbers of patients, and were more likely to provide chemotherapy, hormone therapy and radiotherapy. The second study was confined to 12891 patients registered between 1979 and 1988 and treated by surgery of curative intent.[8] Patients of surgeons treating over 30 patients per year had significantly better survival than patients of surgeons treating fewer

than 10 patients per year (RR 0.85, 95% CI 0.77-0.93), after adjusting for nodal involvement, metastases, histological tumour differentiation, ward deprivation index, year of diagnosis, and type of treatment given, in a proportional hazards model. There was however no gradient of decreasing risk with increasing volume, and no single statistical test of an association between volume and outcome for the full range of volumes. Compared to surgeons treating fewer than ten patients per year, the adjusted relative risk for those treating 10-29 per year was 0.97 (95% CI 0.90-1.06). Survival was similar for those treating 30-49 per year (RR=0.85, 95% CI 0.77-0.93) and those treating 50 or more per year (RR 0.86, 95% CI 0.79-0.94). After controlling for patient level prognostic factors, consultant variables, of which case load and use of chemotherapy were most important, accounted for 8% of the variance in survival.

Another British study provides similar evidence, although the main comparison is between specialist and non-specialist breast cancer surgeons.[9] The study examined five year survival in all 3786 patients with breast cancer registered with the west of Scotland cancer registry between 1980 and 1988. A third of patients were treated by specialist surgeons, all of whom had a dedicated breast clinic, had a defined association with pathologists and oncologists, were involved in clinical trials and maintained a separate record for all of their breast cancer patients. The relative risk of death for patients of specialist surgeons was significantly lower than for other patients (RR=0.83, 95% CI 0.75-0.94) after adjustment for age, tumour size, socioeconomic status and nodal involvement in a proportional hazards model. Patients treated by specialist and non-specialist surgeons had similar prognostic characteristics and multivariable adjustment made little difference to the relative risks. The survival advantage persisted when the comparison was stratified by age group, tumour size, nodal involvement and socioeconomic status.

A Finnish cancer registry study of 16754 patients diagnosed between 1970 and 1981 found that 5 year relative survival rates were significantly higher in patients who lived in university hospital districts, where radiotherapy was provided, than in other districts.[53] This was true of both localised and non-localised tumours. The main limitation of this study is its ecological design – because individual patients' hospitals or their experience of radiotherapy were not identified, the evidence of an effect of teaching hospital status or radiotherapy is weak. Also, stratification into two risk strata and adjustment for age are probably inadequate to control for confounding by case mix.

A United States study similarly showing care to vary according to hospital access[54] found that patients with Stage I or II breast cancer were less likely to receive breast-conserving surgery if they lived in counties outside the region's main urban centre, and were less likely to receive radiotherapy if they lived in counties with no radiotherapy facilities. Comparisons were controlled for stage, age, year of diagnosis, marital status, education level, income and race in multiple logistic regression models. Outcomes were not examined, however.

### Ovarian cancer

Three United Kingdom studies have shown advantages of management in teaching hospitals or by gynaecologists or multidisciplinary teams, compared to less specialised care. None of these studies used patient volumes as indicators of specialisation.

Two Scottish studies by Gillis, Hole and colleagues show the advantages of treatment in a teaching hospital and by a multidisciplinary team. In the first study, survival was compared between patients treated in teaching and non-teaching hospitals in the west of Scotland.[55] Of patients diagnosed in 1974 as having early stage disease (II or below) survival up to 10 years was significantly greater for teaching hospital patients, after adjusting for stage, tumour type and age in a proportional hazards model. Patients diagnosed during the subsequent years between 1975 and 1987 experienced improvements in survival, with greater improvements among teaching hospital patients than among non-teaching hospital patients. In the later period, survival differences were significant only for patients aged under 55 years (13% vs. 1%, $p<0.05$), which may be a chance finding arising from subgroup analyses.

A second study by the same authors investigated survival in all 533 cases of ovarian cancer registered in Scotland during 1987.[6] Survival analyses using proportional hazards models and adjusting for stage, tumour differentiation, postoperative residual disease, presence of ascites and age, showed significantly raised hazards ratios for non-gynaecologists versus gynaecologists (HR=1.34, 95% CI 1.05-1.70) and for surgeons versus gynaecologists (HR=1.37, 95% CI 1.05-1.77), and showed significantly lower risk associated with attendance at a combined clinic (HR=0.66, 95% CI 0.46-0.78). A combined clinic was defined as one in which "gynaecologists and oncologists agreed the most appropriate management throughout the entire post-operative treatment". Combined clinics tended to see earlier stage patients.

A West Midlands Cancer Registry study examined 1654 patients with ovarian cancer diagnosed between 1985 and 1987, and compared survival of those treated by gynaecologists with those treated by general surgeons.[56] Twenty eight percent of eligible patients were excluded because of missing data. Risk of death was significantly higher among patients treated by general surgeons (RR=1.34, 95% CI 1.05-1.71) after adjusting for stage, age, tumour grade, surgical tumour clearance and amount of residual disease in a proportional hazards model. General surgeons were significantly more likely than gynaecologists to perform oopherectomies alone, and in stage III disease were significantly more likely to perform gastrointestinal resections but were less likely to perform radical gynaecological resections.

## Other cancers

Several studies of rarer cancers have suggested advantages of specialist cancer care. Most of the studies have serious design flaws, however, and they use various different indicators of specialisation.

### *Soft tissue sarcoma*

Evidence of benefits of treatment in a cancer centre comes from a Swedish study that examined outcomes among patients with soft tissue sarcoma in a health care region, and compared patients referred to a cancer centre before and after surgery, and patients not referred.[57] Local recurrence rates were higher for patients not referred, or referred after surgery, compared to those referred before surgery (RR=2.4 and 1.4 respectively; P 0.0001 for the first comparison but P>0.05 for the second). Survival did not differ between the three groups. Although data on disease stage, depth, location and size were presented, no multivariable analysis was conducted. Patients referred before surgery did not have better prognostic indicators, and for some variables had worse indices, than patients not referred. Thus the bias in this comparison is likely to have underestimated the benefits of early referral to a cancer centre. However cancer centre patients were followed up for shorter periods, which may account for some of the difference.

### *Testicular cancer*

A study of 200 patients with nonseminomatous metastatic testicular cancer treated in 14 hospitals in Sweden and Norway between 1981 and 1986[58] showed that survival was better in the specialist and highest-volume Norwegian Radium Hospital than in all other hospitals combined (HR=2.1; 95% CI 1.9-2.2). This estimate was derived from a

proportional hazards model after adjusting for tumour size, patient age, pre-treatment interval, and prechemotherapeutic doses of alpha-fetoprotein and human chorionic gonadotropin.

*Paediatric oncology*

Survival of children with a range of cancers diagnosed between 1977 and 1984 at selected sites across Great Britain was compared between specialist paediatric oncology centres and other settings.[59] Three year survival was significantly better at oncology centres then at other hospitals for patients with acute non-lymphoblastic leukaemia, non-Hodgkin's lymphoma, Ewing's tumour and rhabdomyosarcoma, but not for those with Hodgkin's disease, neuroblastoma, Wilm's tumour and osteosarcoma. For tumours showing significantly better survival in oncology centres, there appeared to be a gradient of effect, with survival in other teaching hospitals intermediate between oncology centres and non-teaching hospitals. The study did not account for case mix, other than to report that oncology centres tended to treat more advanced stages of neuroblastoma and, for some tumours, to report separate analyses for different age strata.

*Leukaemia*

The same author analysed survival in a large (n=4070) and representative group of children with acute lymphoblastic leukaemia, including all those ages under 15 years and registered with cancer registries in Great Britain between 1971 and 1982.[60] There was no adjustment for case mix. Five year survival was better in hospitals treating at least six patients per year (67% in 1988-2) than in hospitals treating between one and five per year (66%) or fewer than one per year (58%), but these small differences were not statistically significant. Patients entered into clinical trials had significantly better five year survival, but this could be due to exclusion of more severe cases from trials. Five year survival improved steadily during the study period, from 37% overall for 1971-3 cases to 66% for 1980-2 cases.

*Hodgkin's disease*

A United States study compared survival in Hodgkin's disease between 2278 patients treated at 21 comprehensive cancer centres and 3607 patients registered with 9 state or metropolitan cancer registries.[61] Survival was significantly worse among the latter patients than among cancer centre patients (RR=1.5, 95% CI 1.3-1.7), after adjusting for

disease stage and histology, age, sex, and race in a proportional hazards model. A survival advantage for cancer centres was shown for each stage of the disease.

*Malignant teratoma*

A Scottish study of 440 patients with malignant teratoma treated in five tertiary referral units compared case mix, treatment and survival in patients treated in the largest unit, with patients treated in the other four smaller units.[7] Patients in the largest unit were more likely to have poor prognoses, with metastatic disease, and were more likely to receive treatment according to nationally agreed protocol (97% versus 61%). Among those patients receiving protocol treatment, patients in the four smaller units had a significantly higher risk-adjusted death rate (rate ratio 2.82, 95% CI 1.53-5.19). Thus the survival advantage of treatment in the highest volume unit was attributable to factors other than choice of treatment.

In summary, the evidence of survival advantages attributable to specialist cancer care is at times compelling but is uneven overall, and often impaired by poor study design, data or analysis. Thus one may question the extent to which the centralisation and specialisation of care for all types of cancer, and especially common cancers, is supported by good evidence. In order to see the evidence about cancers in perspective, it is necessary briefly to consider evidence from a wider range of clinical conditions.

## 2.1.3 Volume-outcome relationships beyond cancer care

Most evidence of better outcomes with larger volumes comes from non-cancer care. In recent years, several literature reviews have appraised and summarised research evidence on volume-outcome relationships in health care.[20-22, 25] These three reviews overlap with regard to the studies reviewed, the methodological issues discussed, their explanations for observed volume-outcome relationships, and their main conclusions. In general, they all show significant relationships between outcomes and hospital and/or doctor volumes, but only for certain diseases and procedures, and with varying degrees of uncertainty about residual confounding. Most studies that show significant associations examined short-term outcomes of surgery. Their main explanations - 'practice makes perfect' or 'selective referral' - are discussed above in section 2.1.1.1.

The most systematic and recent review was conducted by Sowden and colleagues at the Centre for Reviews and Dissemination, University of York, and reported in 1996 and

1997.[20, 25] This review provides the broadest overview, but does not report on any study that did not adjust at least for demographic variables and comorbidity, or stage or severity of illness. Thus some suggestive but inconclusive evidence was not reported in the review. An earlier review of United States studies by Luft and colleagues was published as a book-length report in 1990.[21] Strengths of this review include an exhaustive examination of the effects of different statistical methods on results, and its inclusion of the full texts and tables of 12 published journal articles, each illustrating a different methodological issue. In a journal article published in 1990, Black and Johnston reviewed a similar range of studies, mainly drawn from the United States, and excluding cancer care.[22] Neither of the latter two reviews appears to have been conducted systematically, however. The York review was largely in agreement with, but superseded, the Luft and Black reviews.

The York review by Sowden and colleagues identified over 200 studies of volume-outcome relationships.[20, 25] Of these, only 41 were of the highest methodological standard, meaning that case mix was adjusted for using disease stage or severity variables. Of these 41 studies, 24 showed significantly better outcomes with larger hospital or doctor volumes, or with specialist care, 2 showed significantly worse outcomes, and 15 showed no significant effect. These 41 highest quality studies could be divided into 29 that examined hospital, ward or unit volumes, and 15 that examined doctor volumes or specialisation. Of the 29 studies of hospital, ward or unit volume effects, 16 showed significantly better outcomes in high volume or specialist facilities, one showed significantly worse outcomes, and 12 showed no significant effect. Of the 15 studies that examined doctor level effects, 8 showed significantly better outcomes with high volume or specialist doctors, one showed significantly worse outcomes, and 6 showed no significant effect. This crude numerical breakdown provides an overall impression that high volume or specialist care is generally better, but could be misleading because the strengths of evidence varied between studies.

For the following types of care, high volume or specialist care was significantly associated with better outcomes:

- coronary bypass graft surgery (hospital volume),[32]
- paediatric heart surgery (hospital volume),[62]
- percutaneous transluminal coronary angioplasty (hospital and doctor volumes),[26, 63, 64]
- abdominal aortic aneurysm (hospital volume),[7, 41, 65, 66]

- lower limb amputation (hospital volume),[44]
- gastric surgery (hospital and doctor volumes),[41, 44, 49]
- cholecystectomy (hospital volume),[44, 49]
- non-cancer intestinal operations (doctor and hospital volumes),[49]
- acute myocardial infarction (doctor but not hospital volume),[67]
- cardiac recatheterisation (hospital volume),[67]
- neonatal care (unit volume), [8]
- AIDS care (experienced hospitals)[69]
- knee replacement (hospital volume),
- cancers:
  - malignant teratoma (hospital volume),[7]
  - colorectal cancer (hospital volume),[44]
  - oesophageal cancer (doctor volume),[38]
  - pancreatic cancer (doctor volume),[36] and
  - breast cancer (doctor volume).[8]

Most of the above conditions or types of care involve surgery. This is not surprising, because one would expect that the manual skills required would improve with practice. The non-surgical conditions listed above would also be expected to require specialist expertise and technology for diagnosis and treatment because of the complexity of the conditions or because of the cost, complexity or recent development of effective technologies.

Only 3 of the 41 high quality studies studied long term survival (one year or more), the rest using only in-hospital, or short term, mortality or morbidity as outcome measures. Short term outcomes may be reasonable indicators of surgical skill or quality of emergency care, but they are less relevant than long-term survival to assessment of the overall management of complex conditions aiming to prolong life.

A similar crude 'head count' is provided by the earlier review by Luft *et al.*[21] 121 studies were reviewed, mainly concerning non-cancer surgery in the United States, with in-hospital mortality as the main outcome measure. Of these, about three quarters showed significantly better outcomes with increasing volume. Only studies of stomach operations and femoral fractures consistently showed no volume-outcome relationship. 99 of the 121 studies only examined hospital volumes, mainly because doctor volumes were difficult to

obtain. Of these 99, three quarters showed a significant volume-outcome relationship. Of the 22 studies including both doctor and hospital volumes, half showed a significant hospital volume effect, but no significant doctor volume effect, and three quarters showed either a doctor volume or hospital volume effect. In general, this review supports the observation from the York review that there is more evidence of a hospital volume effect than a doctor volume effect. However this difference may be due to the greater difficulty of obtaining doctor volume data.

It is possible that publication bias may have contributed to more studies with significant associations being published, but this would not explain the scarcity of studies showing worse outcomes with low volume or non-specialised care. Other possible artefactual explanations are inadequate adjustment for case mix, which would only bias results in this direction if high volume or specialist centres tended to treat less severe cases, or if their more rigorous clinical investigation resulted in stage migration.[28]

In summary, there is substantial evidence supporting efforts to increase the scale and scope of health services by centralising and specialising services, so as to improve the quality of care. However there is also substantial evidence showing no such advantages, and large areas of health care that have never been adequately investigated. With no clearly generalisable evidence, it is thus necessary to consider each disease and each type of service separately. As more high quality evidence accumulates, clearer patterns may emerge. Meanwhile one needs to consider a key determinant and effect of differences in quality, namely the funding and cost of care.

# 2.2 Economies of scale and scope

The development of cancer services is ultimately constrained by scarce resources and finance. It is therefore necessary, when planning services changes, to estimate the costs of the changes, which in turn requires knowledge of the costs of current services. It would be especially desirable to know how costs varied between different types of services and different types of patients. It is plausible that the costs of care would differ between patients managed in more or less specialised facilities, or by more or less specialised professionals. The determinant of quality and of costs most directly relevant to this study is scale, as indicated by doctor and hospital volumes. The volumes of patients managed annually by consultants and hospitals have direct implications for the size of organisational units and facilities, which is likely to affect costs. The range of services provided may also influence costs. This section will first discuss theoretical arguments concerning costs of care in relation to economies of scale and scope, and will then review the empirical evidence.

## 2.2.1 Theoretical arguments why larger health facilities may be more or less efficient.

### 2.2.1.1 Economies of scale

Economies of scale are widely assumed to exist in health care, but this assumption is based on little empirical evidence.[70] Microeconomic theory concerning economies of scale is useful in understanding why concentration of health services may or may not be efficient.[71] This theory would consider a hospital trust to be a firm engaged in a production process, producing, for example, a treated patient or health improvement. It may also be appropriate to consider an organisational unit within a hospital – for example, a department or a consultant-led team – as a firm producing a narrower range of products. In the simplest version of the theory a firm is assumed to produce a single homogenous product. A graph plotting the average cost of the product against the scale of production is assumed by economists generally to be U shaped, with long run average costs decreasing as scale increases, up to a point, after which average costs increases.[72] The lowest point of the curve indicates the most efficient scale of production.

There are four main factors influencing whether it may be more efficient to provide a homogenous unit of health care on a larger scale: technology, specialisation, indivisibilities, and reserve capacity.[72] Firstly, new technology may allow an increased volume of work or an increased effect on health that exceeds the extra cost of the new technology. Thus the average cost per unit of care provided, or per unit of health gain obtained, may decrease with increasing scale, at least up to a point. Specialisation is a familiar concept in health care, and refers more generally to the division of labour which allows each component of the production process to be performed more effectively and efficiently, as for example in car assembly line production. In cancer surgery, for example, specialisation in certain operations may make surgeons and their teams more effective and efficient. Specialisation is more feasible with larger scale hospitals or units. Indivisibilities exist when a production unit has a minimum size below which it would be ineffective. For example, certain operations may require a large surgical team for treatment to be effective. A smaller hospital would not be able to afford what is regarded as minimal requirements. Technology, specialisation and indivisibilities are all interrelated factors.

A further reason for economies of scale in health care concerns the need for reserve capacity which is required to deal with random demands for urgent care. Smaller units require proportionately more reserve capacity, because of the relatively greater amount of random variation in demand of urgent care. In other words larger firms may be better able to match workload to capacity and thus be more efficient.[15] For example, an intensive care unit with two beds would require 50% of its capacity to be unused and held in reserve at any time be able to accept an urgent new case; a 20 bed unit would only require 5% of its capacity to be held in reserve.[15]

Furthermore, queuing theory demonstrates that channelling patients into separate queues with more predictable service times (for example duration of operations or lengths of stay) can decrease the overall waiting time.[73] Larger hospitals will be able to create more channels and could thus potentially manage waiting times more efficiently. To the extent that decreased waiting times represent an improvement in quality of care without increasing costs, this could be another reason for economies of scale. However, because the gain in quality is difficult to quantify and combine with other outputs of health care, this dimension has not been explicitly studied in the economies of scale literature discussed below.

There are also, however, several reasons why diseconomies of scale may exist.[72] The most commonly cited reason is managerial diseconomies of scale: the difficulty and cost of management become proportionately greater as organisations become larger and more complex. Also important for health care are geographical reasons for diseconomies of scale. It may be more expensive to provide an accessible service to the population of a larger geographical area, especially if accessibility is held constant or if patients' costs are included. In practice, there is assumed to be a trade-off between access and efficiency, with regional speciality services being accepted as being less accessible, and patient and social costs of care being ignored, by health authorities and providers.[15]

Availability of costly diagnostic and therapeutic resources within hospitals may increase costs if clinicians use them for patients that do not "require" them, that is, for patients for whom these interventions are relatively ineffective or inefficient. If these resources have excess capacity then the marginal cost of using them for lower priority patients may be low, but using up spare capacity in this way could in the long run lead to demands for further expansion, to accommodate more lower priority patients. Thus the long run average cost of treating patients with relatively simple conditions could increase in large hospitals.

Economies of scale may impair the efficiency of market mechanisms by promoting the growth of monopolies or oligopolies.[72] Thus if only one, or very few, hospitals in a country were able to treat certain cancers effectively and efficiently, there would be less competition to promote quality and efficiency, and providers of care would have an incentive to decrease the supply and to raise the price of care. It is however questionable whether monopolisation by hospitals would decrease supply and raise prices in a public sector service such as the National Health Service which, in contrast to private health systems, has mild competition or profit incentives for hospitals, and in which the internal market, to the extent that it exists, is managed according to government priorities.

The medical profession and its specialties do however operate as highly effective monopolies, limiting supply and raising prices of doctors. If the number of specialists able to provide a particular kind of cancer care is kept small, there is an incentive to reduce the supply of public care, because this increases demand and thus prices in the private sector. Agreements within specialities to li nit the supply of competitors mean that they act as cartels. Many National Health Service consultants work both for public and private sectors, which creates an economic incentive to behave in a monopolistic manner.

One reason for growing National Health Service waiting lists is thought to be consultants' incentive to redirect patients from the NHS to their own private practices by decreasing their supply of NHS service and driving NHS waiting lists up.[74] Yates has shown that in some surgical specialties, NHS surgeons do indeed reduce their NHS work below what they are contracted to provide, despite long waiting lists, and simultaneously increase their private work.[75]

### 2.2.1.2 Economies of scope

Economies of scope are closely related to, but a distinct concept from, economies of scale.[15, 71] Economies of scope occur when a firm, rather than producing a single product, produces several products with complementary resource requirements. For example, an oil refinery that produces plastics as well as petrol can exploit parts of the production process that are shared by the various products. Certain cancers may require a combination of advanced diagnostic, surgical, radiotherapeutic and oncological services, none of which would be fully utilised if used only for a single cancer. Some of these services may be more efficient if also used for non-cancer care. Thus general hospitals are invariably multi-product firms, exploiting economies of scope. Scale and scope are interrelated because a hospital may have to be large to exploit both the efficiency gains due to technology, specialisation and less reserve capacity, and economies of scope due to shared use of costly resources by different specialties.

In summary, despite the numerous arguments why economies of scale and scope may occur, there are also good reasons why their increase may be inefficient. It is thus necessary to examine empirical evidence.

## 2.2.2 Evidence of scale economies in health care

Despite numerous studies, high quality evidence for economies of scale is scarce, and evidence indicating the optimal scale of a hospital is even more elusive. This section will show that many studies of hospitals, using a variety of methods, have shown costs to vary with scale but that these findings are difficult to interpret. A leading problem with comparing hospitals or doctors is adjustment for patients' case mix and severity. Most studies use as units of analysis entire hospitals, which is of limited relevance to this thesis which examines the management of single diseases. Studies that examine specific

diseases, operations or specialities are more relevant, and some do show economies of scale, but have the disadvantages of excluding economies of scope or managerial diseconomies of scale for entire hospitals, as discussed below.

Two related studies have compared costs of pancreatic cancer patients treated in high, medium and low volume hospitals in the state of Maryland.[31, 34] These studies showed that for patients who had resections, hospital charges increased with decreasing hospital volume. For patient receiving bypasses or stents, however, there was no trend of increasing charges with changing hospital volumes. These comparisons adjusted for age, gender, race, comorbidity score and urgency of admission, but not for cancer stage. The studies did not examine relationships between hospital charges and surgeon volumes. None of the studies identified examined economies of scale in the investigation and treatment of gastric or oesophageal cancers. The rest of this section will review evidence obtained by examining entire hospitals, or single specialities within hospitals, as primary units of analysis.

The most recent and rigorous overview of the evidence is provided by a systematic review of the literature on economies of scale, conducted by Aletras *et al.*[71] A search of ten bibliographic databases identified 100 relevant studies published between 1967 and 1996. The review found that most studies showed constant returns to scale or diseconomies of scale. Where economies of scale existed they tended to be fully exploited up to 200 beds, larger hospitals showing diseconomies of, or constant returns to, scale. The studies were categorised methodologically as *ad hoc* econometric cost studies (36 studies), flexible econometric cost studies (23 studies), econometric production function studies (2 studies), data envelopment analyses (5 studies), survival analyses (8 studies), studies of multi-hospital arrangements (12 studies) and studies examining a hospital service in isolation (14 studies ).

### 2.2.2.1 Econometric studies

The econometric studies are essentially multiple regression analyses with hospitals as units of analysis, and examining various predictors of cost, with scale as one predictor variable. Inclusion of higher order terms permits non-linear cost-volume relationships to be examined. The main problem with the models i case mix adjustment, because larger hospitals may attract more costly patients and thus erroneously show diseconomies of scale, or vice versa. Adjustment for case mix was done with various degrees of

sophistication in these studies, but it is unlikely to be possible to control fully for the wide range of specialities, diseases and degrees of severity that varying between hospitals of different sizes. Of the numerous studies reviewed, only 5 appeared to achieve reasonable control for case mix differences. These studies showed that average costs per patient either decreased or stayed the same with increasing scale.[76-80]

### 2.2.2.2 Data envelopment analyses

Data envelopment analysis uses linear programming to examine the efficiency or productivity of units such as hospitals. The method entails comparing each unit's costs and outputs with those of the most efficient units. This allows hospitals to be ranked according to their relative efficiency. Several different outputs can be considered simultaneously. More recent developments of the method allow the assumption that average costs vary with varying scale. This enables one to identify the scale of those hospitals which are most efficient. The four data envelopment analyses reviewed varied widely in the number of beds associated with the greatest efficiency (i.e. around 350 beds,[81] 220-260 beds,[82, 83] and 500-520 beds).[84] A fifth study found that returns to scale decreased very gradually.[85] A leading problem, as with econometric studies, is adjustment for variations in case mix and quality of care.

### 2.2.2.3 Survival analyses

So-called survival analyses examined the relationship between how long hospitals survive before being closed down, assuming that, in a competitive health care market such as the United States, survival is an indicator of economic efficiency. Costs were ignored. Statistical analyses did not use survival analysis, but used linear or logistic regression analyses which allowed control for a limited number of confounding variables such as case mix or quality indicators. These studies found hospital sizes associated with a lower risk of closure to be between 100 and 600 or more in four studies using univariable analysis,[37, 86-88] and between 200 and 600 or more in four studies using multivariable analysis.[86, 88-90] Thus they show that small hospitals with fewer than 100 or 200 beds were more likely to close, but this does not prove that it was the small scale that caused the closure.

### 2.2.2.4 Single specialties

The last group of studies examined single specialties, with a limited range or service outputs, in contrast to all of the other studies, which included all hospital outputs. Aletras and colleagues question the value of such studies, because they necessarily exclude the economies of scope that may result from sharing resources between specialties, and the managerial diseconomies of scale in large hospitals.[71] This would be relevant in cancer care if, for example, only surgery was considered, and the cost advantages or disadvantages of having oncological services in the same hospital were ignored. A major advantage of such studies is that variation in case mix is greatly restricted, compared to studies including all specialties. Nevertheless, within specialties there is still room for considerable variation between hospitals in diagnostic and severity mix. The most straightforward of these studies were conducted by Munoz *et al*, who compared the average costs of treating patients managed by high and low volume surgeons, with some adjustment for case mix and severity.[91-93] Their separate studies compared urologists[93], neurosurgeons[92], and orthopaedic surgeons[91], and in each case found that average costs for high volume surgeons were significantly lower than for low volume surgeons. Once again, the authors acknowledge incomplete adjustment for case mix and severity. Another study of costs and surgeon volume found economies of scale for cholecystectomy, prostatectomy and intervertebral disk excision but not for hysterectomy[94]. Several studies examined hospital, ward or laboratory volume rather than doctor volume, and found economies of scale for neonatal care units[95], knee replacement surgery[96], maternity wards[97], heart surgery[98, 99], hospital pharmacies[100], nuclear medicine[101] and hospital dental care[102]. For the first four of these studies[95-98] there were U shaped cost-volume curves, with average costs increasing at the highest volumes.

In a more limited review of the literature, Harrison and Prentice[15] discussed additional limitations of research in this field. Firstly, outcomes are ignored - thus the studies are all cost analyses, rather than cost-effectiveness, cost-utility or cost-benefit analyses. Secondly, economies of scale and scope are not distinguished. Thirdly, different parts of the production process are likely to have different optimal scales, and within any hospital or specialty, different parts of the process are likely to be simultaneously below, above and at their optimal volumes. Research has so far b en unable to demonstrate these different optimal levels. Fourthly, these retrospective studies have limited predictive validity regarding new configurations of services, for example day surgery units or new

types of cancer centres. Fifthly, large and small hospitals may be complementary - for example small hospitals may be more efficient at treating minor or chronic conditions but unable to treat complex severe conditions - and average costs are a poor guide to the advantages of shifting patients from one to the other.

In summary, there is empirical evidence of a U shaped cost-volume curve, with the smallest hospitals, or the lowest volume surgeons, wards or units tending to be relatively inefficient in most studies and, in many studies, the largest units also being inefficient. However optimal scales cannot be precisely specified and confounding by case mix and severity is the leading problem. Where economies of scale exist they appear to be below about 200 beds, which means that most hospitals are operating at a scale at which average costs would increase with greater expansion. No studies were identified that explicitly examined relationships between costs and scope of services. Thus there is little empirical support for increasing the size of existing hospitals in order to reduce costs.

## 2.3 Effectiveness of investigations and treatments

Both the quality and the costs of care are determined largely by the types of investigations and treatments provided. Choice of interventions is in turn influenced by the expertise of health professionals, by the range of resources available, and by patients' health status and capacity to benefit. In order to judge the quality and efficiency of care provided, it is necessary to examine evidence of the effectiveness of the various interventions available, in relationship to patients health status and capacity to benefit. Explanation of observed volume-outcome relationships requires analyses of how clinical care, in addition to case mix and outcome, varies with doctor and hospital volumes. This section of the literature review will review the evidence on the effectiveness of the main investigations and treatments for oesophageal, gastric and pancreatic cancers.

Special investigations are necessary, in addition to clinical assessment by doctors, to confirm cancer diagnoses, and to assess the severity of disease in order to choose the most appropriate treatments. The main controversy is how intensively to investigate patients before deciding whether to operate or not to operate. Gastric and oesophageal cancers are anatomically more accessible to direct visualisation and biopsy than are pancreatic cancers. Pancreatic cancers tend to present with clinically more advanced disease, and may pose dilemmas as to whether invasive investigations justify the

consequent morbidity and cost. Evidence of the diagnostic validity of the main diagnostic tests for each cancer is reviewed.

High quality care can only improve survival if the treatments offered are effective. Additionally, poor quality care can impair survival iatrogenically, particularly as a result of surgical complications. This part of the review will examine the evidence of effectiveness of surgical and other treatments for each cancer. It will show that, except possibly for radical surgery for early gastric cancer, treatments do not unequivocally have large effects on survival. This raises the question of whether optimal choice of treatments would greatly affect survival in most patients, except perhaps by reducing the complications of treatment. A general controversy is what types of case should be operated on and how radical the surgery should be.

*Search strategy*

The electronic bibliographic databases Medline and Embase were searched for the periods 1980 to 1997. For each database, sets of search terms were used to detect a) evaluations of diagnostic and staging tests, b) evaluations of treatments and c) any studies of each of the three cancers. Studies detected by each of these searches were combined to find the evaluations of investigations and treatments relevant to each cancer. Additionally, references cited by studies detected in this way were also included.

In Medline a general 'maximally sensitive search strategy' for clinical trials was used,[103] and combined with the following search terms for each of the cancers (upper case denotes MESH heading, and lower case represents text in title, abstract or keywords):

- For oesophageal cancer: ("NEOPLASM, ESOPHAGEAL" or (("cancer" or "carcinoma" or "malignancy" or "neoplasm") and ("esophag$" or "oesophag$"))
- For gastric cancer: ("NEOPLASM,GASTRIC" or (("cancer" or "carcinoma" or "malignancy" or "neoplasm") and ("gastric" or "stomach"))
- For pancreatic cancer: ("NEOPLASM,PANCREATIC" or (("cancer" or "carcinoma" or "malignancy" or "neoplasm") and ("pancrea$")).

In Embase, the Thesaurus terms ("controlled study" or "randomised controlled trial") were combined with the following Thesaurus terms for each cancer:

- For oesophageal cancer: "esophageal carcinoma"

- For gastric cancer: "gastric carcinoma"
- For pancreatic cancer: "pancreatic carcinoma"

For evaluations of diagnostic tests the same cancer-specific terms were used, in combination with the names of each investigation being considered. The names of the respective investigations were obtained from review articles and recent text books.

*Assessment of study quality*

The aim of the search was to include the most valid evidence, from the most rigorous available evaluations, of the effectiveness each intervention. Evaluations of investigations were included if they compared tests with a gold standard test, which usually comprised pathological assessment of tumour presence and spread. The validity of studies of diagnostic tests was assessed using guidelines produced by the Evidence-Based Medicine Working Group.[104]

The validity of studies of therapeutic effectiveness was also assessed using guidelines produced by the Evidence-Based Medicine Working Group.[105] For evaluations of treatments most emphasis was given to randomised trials. However where no randomised trials were detected, other comparative studies were considered; these were given greater weight if they measured and adjusted for case mix differences between the groups being compared. Because of the relatively large numbers of randomised trials of chemotherapy and radiotherapy, comprising several hundred studies, and because few of these trials showed any effect on patient survival, not every trial was thoroughly examined and reported. Recent review articles, and reports of major clinical trials were examined in detail. For surgical trials, however, non-randomised trials were examined and reported in slightly more detail, because of the relative paucity of high quality randomised trials, and because surgery generally appears to be more effective in prolonging survival in patients with early stage disease.

## 2.3.1 Oesophageal cancer

### 2.3.1.1 Diagnosis and staging

There is limited scope for early diagnosis of oesophageal cancer. By the time the usual presenting symptom, dysphagia, is noticed, the oesophagus is usually two-thirds obstructed by the tumour, and has spread beyond the oesophageal epithelium.[106] Population screening, by means of blind exfoliative cytology, is used in areas where the cancer is endemic, but is not suitable in most parts of the world due to low disease prevalence and poor test validity.[106] In individuals at exceptionally high risk of disease (for example elderly heavy smokers and drinkers living in endemic areas) it may be appropriate to perform periodic endoscopic examinations with tissue staining, cytology and histology. However, there is little evidence of the effectiveness of early diagnosis in asymptomatic individuals.[106]

In making a diagnosis of oesophageal cancer, the mainstays of investigation are oesophagography using double contrast radiography (that is contrast swallow), and oesophagoscopy (that is endoscopy) with biopsy of suspected lesions. A leading textbook states that both investigations are "indispensable" in making a diagnosis.[106] They are relatively inexpensive, non-invasive and valid, and are complementary to each other, providing different views of the extent of tumour expansion into the oesophageal lumen.

There is more controversy over the most appropriate diagnostic tests, whether alone or in combination, for staging the cancer according to T (tumour invasion), N (lymph node involvement) and M (distant metastases) stages. The main purpose of staging is to identify patients who could benefit from potentially curative or palliative surgery, and those in whom surgery is not indicated. Generally only patients with Stage I disease, with no local invasion, nodal involvement or distant metastases, are eligible for potentially curative surgical resections.[107] The most commonly used investigation is computerised tomography, but endoscopic ultrasonography shows promise as a non-invasive test while laparoscopy and thoracoscopy allow direct visualisation of abdominal and thoracic metastases.

There is a substantial literature comparing the validity of staging investigations in detecting tumour invasion, nodal spread and distant metastases (summarised in Table 2.5), using as a 'gold standard' test pathological findings after surgery. In examining this

evidence, the comparison of different tests within studies is more valid than comparison between studies, owing to differences between studies in case mix, diagnostic thresholds, and methods of pathological examination which constitutes the gold standard test. Another problem of interpretation is that because of small sample sizes, estimates are imprecise for some studies. While there is considerable overlap between the performance of different tests, some general inferences are possible. It appears that computerised tomography (CT) is generally more sensitive than external ultrasonography, but endoscopic ultrasonography (EUS) is more sensitive than either. In detection of abdominal metastases, laparoscopy or laparoscopic ultrasound appears to be more sensitive and 'accurate' than computerised tomography. Unfortunately none of the studies reviewed compared laparoscopy or laparoscopic ultrasound with endoscopic ultrasound. A drawback of endoscopic ultrasonography is that it is impossible in between a sixth and a third of cases because of oesophageal obstruction.[106] Finally magnetic resonance imaging holds promise with, in one small study reviewed, a sensitivity of 100% in detecting nodal involvement, but with a low specificity of 60%.[108]

**Table 2.5. Oesophageal cancer. Sensitivity, specificity and accuracy* (%) of preoperative staging investigations compared to post operative pathology**

| Author | No. patients | Diagnosis | Lap Sensitivity | Lap Specificity | CT Sensitivity | CT Specificity | EUS Sensitivity | EUS Specificity | Ext US Sensitivity | Ext US Specificity | Other tests | Specificity | Sensitivity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Overhagen[109] | 113 | Distant metastases | | | 93 | 85 | | | 61 | 93 | US + CT | 83 | 81 |
| Greenberg[110] | 28 | No nodes (N0) | | | 67* | | 100* | | | | | | |
| | | Nodal spread | | | 50* | | 60* | | | | | | |
| Peters[111] | 42 | Wall penetration (T) | | | | | 77 | 75 | | | | | |
| | | Nodal spread | | | | | 92 | 55 | | | | | |
| | | Stage | | | | | 68 | 56 | | | | | |
| Krasna[108] | 49 | Nodal spread | | | 40 | 55 | 5 | 40 | | | Thoracoscopy | 40 | 100 |
| | | | | | | | | | | | MRI | 100 | 60 |
| Ziegler | 52 | T staging | | | 51* | | 89* | | | | | | |
| | | N staging | | | 51* | | 69* | | | | | | |
| Watt[112] | 90 | Hepatic metastases | 88 | 100 | 56 | 97 | | | 48 | 97 | | | |
| | | Peritoneal metastases | 89 | 100 | 0 | 100 | | | 22 | 100 | | | |
| | | Nodal metastases | 51 | 97 | 31 | 87 | | | 17 | 93 | | | |
| Matsubara[113] | 179 | Nodal involvement | | | | | | | | | CT+Ext US +palpation | <40 | >65 |
| Finch[114] | 36 | Resectability for potential cure | 100 | 73 | 75 | 60 | | | | | Lap. US | 100 | 91 |
| | | Distant metastases | 97 | 100 | 55 | 82 | | | | | Lap. US | 82 | 100 |
| O'Brien[115] | 110 | Distant metastases | 77 | | | | | | | | US + CT | 38 | |
| | | Peritoneal metastases | 96 | | | | | | | | US + CT | 21 | |
| | | Hepatic metastases | 60 | | | | | | | | US + CT | 47 | |
| Dittler[116] | 167 | Invasive tumour (>T1) | 86 | 96 | | | | | | | | | |
| Dittler[117] | 209 | Invasive tumour (>T1) | 78 | 93 | | | | | | | | | |
| Pooled data from 6 studies[118] | 256 | T stage | 88* | | 59* | | | | | | | | |
| | | N stage | 74* | | 54* | | | | | | | | |
| Tio[119] | 55 | Curative resectability | 83* | | 75* | | | | | | | | |
| | | Palliative resectability | 85* | | 44* | | | | | | | | |
| Giovannini[120] | 32 | Residual tumour after chemo+RXT | | | | | 91 | 78 | | | | | |

* Accuracy: ((true positives+true negatives)/total); EUS: endoscopic ultrasound; Lap: laparoscopy; CT: computerised tomography; Ext: external; MRI: magnetic resonance imaging

### 2.3.1.2 Treatment

Surgery or radiotherapy are the mainstays of treatment. Curative surgery is only possible in patients without metastases or lymphatic involvement[107]. Surgery or radiotherapy alone have limited effectiveness, and various combinations of surgery, radiotherapy, and chemotherapy have been used in attempts to prolong survival.[121] There is a wide range of palliative treatments, most of which aim to relieve oesophageal obstruction. This section will review the evidence on the effectiveness of the various treatments, used alone or in combination.

#### Potentially curative surgery

Surgery usually comprises oesophagectomy with regional lymphadenectomy. The main controversies in surgery are whether to replace thoracic with abdominal approaches, whether or not to perform extended lymphadenectomies and whether or not to perform extended oesophagectomies. Extended lymphadenectomies are relatively well supported by evidence, but the other innovations are not. As shown in this section, the first choice relies for evidence on a recent randomised trial, supplemented by non-randomised comparative studies. The second choice is aided by a recent randomised trial, supplemented by several non-randomised comparisons. The third choice has limited support, with evidence from two small non-randomised studies.

Transthoracic oesophagectomies were conventional until the introduction of transhiatal (that is abdominal) approaches, which were intended to avoid thoracotomies and other thoracic trauma. The only randomised trial showed no significance in four year survival, overall and in the subgroups with and without metastases.[122] It had limited statistical power, however, with only 67 patients. The largest non-randomised study comparing outcomes of transthoracic and transabdominal approaches was confined to patients without metastases, and found 5 year survival to be marginally (41% vs. 28%), but not statistically significantly, better in the transthoracic arm.[123] The only other high quality non-randomised studies, that accounted for case mix by stratifying by stage, found no significant difference in survival.[124-126] The only study that showed a significant difference between procedures (11% vs. 6%) did not take case mix into account in the analysis[127] and thus could be biased. Two further studies[128, 129] found no difference in outcomes. A small randomised trial, comparing anterior and posterior reconstructions

after transhiatal oesophagectomies, found lower hospital mortality (10% vs. 4%) and 30 day mortality (6% vs. 2%) in the latter group, but the differences were not significant.[130] In summary, there is still no convincing evidence that choice of surgical approach to the tumour affects mortality.

Extended lymphadenectomies are intended to increase the chance of resecting all affected nodes. Although extended 3 field lymph node dissections are not widely used in Britain, they are more commonly used in Japan. All studies cited here compared 5 year survival after 2 field and 3 field (i.e. extended) lymphadenecomies. Only one randomised controlled trial has been conducted, and found statistically significantly better survival in the 3 field group, overall (49% vs. 34%) and especially in the Stage III and IV subgroups.[131] However, because the 3 field arm had more patients with better prognoses, it is possible that randomisation may not have been effective, resulting in selection bias in this study.[132] Three non-randomised comparisons also found significantly better survival in the 3 field group, having stratified their analyses by stage or presence of metastases.[133-135]

Extended oesophagectomies were associated with significantly better 18 month[136] and 5 year survival[137] in two non-randomised studies. The second of these stratified analysis by stage, and found this survival difference was only significant in the Stage III and IV subgroup.[137] As these two studies were not randomised, were small and did not adequately adjust for case mix, better evidence is needed from randomised trials, or from large non-randomised trials that measure and adjust for case mix.

The role of pyloroplasty in oesophageal replacement by part of the stomach, in order to prevent gastric outlet obstruction, has been investigated in three randomised trials.[138-140]The largest trial randomised 200 patients to pyloroplasty or to no drainage, and found significantly faster gastric emptying, better tolerance of a solid diet and less frequent and severe symptoms in the pyloroplasty arm.[139] Two smaller trials found significantly faster gastric emptying[140] and significantly fewer symptoms of gastric stasis[138] in the pyloroplasty arms.

## Radiotherapy

Radical radiotherapy is an alternative to radical surgery for potentially curative treatment of oesophageal cancers. There has never been a randomised trial comparing surgery alone with radiotherapy alone.[107] In one non-randomised trial (n=102) from Australia, radical

oesophagectomy was compared with radical radiotherapy.[141] There was no difference in survival but strictures were more common after radiotherapy than after surgery. Hospital costs for surgical patients were 3.9 times as great as costs of radiotherapy patients. The cost and outcome differences are unlikely to be due to differences in case mix alone, as tumour length was greater in the radiotherapy group.

Adjuvant radiotherapy can be used in preparation for potentially curative surgery, so as to improve resectability rates. A 1995 review included six randomised trials comparing surgery alone with surgery plus radiotherapy.[142] None of the trials found significantly different resectability rates, postoperative mortality or survival, despite the relatively large sample sizes of some (n 360, 221, 208, 124, 89 and 60). The lack of effect of radiotherapy in these trials has been attributed to the low radiation doses used.[142] The review did not, however, include a small randomised trial published in the same year, that had different results.[143] That trial (n=72) found *no significant difference in 5 year* survival, but found significantly higher rates of postoperative anastomotic strictures and significantly delayed recovery in the radiation plus surgery arm than in the surgery alone arm.

In summary, there is still insufficient evidence to support radical or adjuvant radiation therapy as part of potentially curative treatment.

Immunotherapy and hyperthermia have also been investigated as adjuvant therapies but only immunotherapy shows promise at this stage. A trial of 66 patients randomised to receive hyperthermia with chemoradiotherapy or chemoradiotherapy alone, before surgery, found 5 year survival rates of 50% and 24% respectively.[144] The paper does not report on the statistical significance of this difference but the author of this thesis, using Pearson's $\chi^2$ test, found a p value of 0.03, that is significantly better 5 year survival in the hyperthermia arm. A trial of immunotherapy (protein-bound polysaccharide) randomised patients into four arms: radiotherapy with or without immunotherapy, and chemotherapy with or without immunotherapy.[145] There was no significant difference in 5 year survival.

## Chemotherapy

Chemotherapy can be used instead of, or in addition to, radiotherapy as adjuvant therapy for patients undergoing surgery. The best, althougl flawed, summary is provided by a meta-analysis of randomised trials and historical control studies that included chemotherapy with cisplatin, alone or with other agents.[146] Historical control studies

compared patients treated after chemotherapy became part of usual treatment, with patients treated in the same institutions before chemotherapy was used.

The meta-analysis included studies published between 1988 and 1995 and having chemotherapy in their intervention arms (with or without surgery and/or radiotherapy) and no chemotherapy in their control arms (but having surgery alone, or radiotherapy alone, or radiotherapy and surgery).[146] For most of the studies follow-up was for two years. Six of the eight historical control studies found significantly lower risk of death in their intervention arms, with a pooled odds ratio of 0.32 (95% CI 0.24-0.42). However only one of the 12 randomised trials found a significant difference in risk of death, favouring chemotherapy, and the pooled odds ratio showed no benefit of chemotherapy (OR 0.96; 95% CI 0.75-1.22). This difference in odds ratios between randomised trials and observational studies shows how observational studies, especially historical control studies, can produce biased results. The meta-analysis was impaired, however, by its pooling of studies that were markedly heterogeneous with regard to the treatments being compared. It excluded several relevant randomised trials, but their inclusion would not have affected the results.[147, 148]

A large (n 258) randomised trial comparing cisplatin-vindesine plus radiotherapy with radiotherapy alone, in patients undergoing surgery, found no significant difference in 5 year survival but significantly elevated blood urea and creatinine in the chemotherapy arm.[148] Another randomised trial comparing fluouracil-mitomycin plus radiotherapy versus radiotherapy alone found better two year survival in the former group.[147] A later progress report of the only statistically significant randomised trial included in the meta-analysis (n=123) reported that five year survival was significantly greater in the chemotherapy arm (27% vs. 0%).[149] A randomised cross-over trial (with patients receiving either radiotherapy or chemotherapy before surgery, and the other treatment after surgery) was unable, because of its design, to compare survival, but found no differences before surgery in tumour responses to treatment.[150] In summary, there is evidence from only two randomised trials that adjuvant chemotherapy contributes to survival, but there is evidence of no effect from twelve studies, several of which had greater statistical power.

## Palliation

Palliative treatments are mainly intended to reduce oesophageal obstruction and dysphagia, with intubation (stent insertion) the most common procedure, and laser therapy increasingly being used. A 1994 narrative literature review cited 29 non-comparative studies that reported reductions in obstruction after laser therapy.[151] Comparative studies, including several randomised trials, have compared laser recanalisation with stent intubation, injection, electrocoagulation and radiotherapy. Of four small randomised trials comparing laser therapy with intubation, three[152-154] found no difference in primary outcomes and one[155] found better outcomes after laser, as follows.

A small (n 40) randomised trial compared laser recanalisation with endoscopic intubation and found marginally longer survival (median 22 vs. 15 days; p=0.09) and significantly better swallowing grade in the laser arm.[155] A small (n=27) randomised trial comparing endoscopic laser with endoscopic intubation, and with intubation plus radiotherapy, found no significant difference in survival, but found significantly fewer complications of treatment in the laser arm.[152] Another randomised trial with 46 patients compared laser alone with laser plus intubation and found no difference in dysphagia, but complications were significantly more likely in intubated patients.[154] A small (n=40) non randomised comparison of laser recanalisation and endoscopic intubation, with similar patient characteristics in each group, found no significant differences in outcomes, although retreatment was much more likely to be needed in the laser group (16/17 vs. 2 18).[153] Several non-randomised comparisons of laser and intubation have found the two treatments to have similar effects on dysphagia.[151] One randomised trial (n=37) comparing laser and injection therapies found no differences in outcome.[156] Finally, a randomised trial (n–28) comparing laser to a BICAP tumour probe (i.e. electrocoagulation) found no difference in outcomes.[157]

A randomised comparison (n=23) of laser with endoluminal radiotherapy found no difference in dysphagia between trial arms, although dysphagia improved in both arms.[158] Another randomised trial (n=67) compared laser alone with laser plus external radiotherapy, and found significantly longer dysphagia controlled interval and treatment interval in the radiotherapy group.[159]

In summary, the before-after comparisons in almost all these trials suggest that palliative relief of dysphagia is possible, at least temporarily. However there is little evidence to support one method being best overall; this is partly attributable to the low power of the small trials. As different methods are more feasible for different tumour locations, choice of palliative method should probably be guided by the nature of the tumour and availability of treatments.[151]

## 2.3.2 Gastric cancer

### 2.3.2.1 Diagnosis and staging

Diagnostic and prognostic tests are useful in the early detection of cancer among asymptomatic populations, in investigation of symptomatic patients presenting to hospital for the first time, and in choice of surgical procedures or adjuvant therapy.

Mass population screening, using indirect contrast radiography, has been used throughout Japan since 1960.[160] This screening test was shown, in one prefecture of Japan, to have a sensitivity of 82% and a specificity of 77%.[160] A case-control study conducted in the same prefecture provides an estimate of the effectiveness of the screening programme.[161] The odds ratio of death from gastric cancer in people who had been screened at least once during the previous 5 years, compared to those who had not been screened, was 0.41. Current research on screening methods is increasingly focused on serum pepsinogens. A Japanese cohort study found the sensitivity and specificity of pepsinogen to be 67% and 82% respectively, using as a gold standard a battery of conventional diagnostic investigations conducted a year later.[162] As this thesis is concerned with patients who have been referred to hospital, and not with population screening, the literature on screening methods will not be discussed further.

Hospital investigations of patients presenting with dyspepsia are however an important part of secondary prevention of gastric cancer deaths. In the United Kingdom in the early 1970s it was estimated that gastric cancer was present in about 1 in every 53 cases presenting with dyspepsia to general practitioners.[163] The three main investigations to diagnose gastric cancer are contrast radiography, endoscopy and biopsy. Endoscopy has been shown, compared to a double contrast barium meal, to be both more sensitive (92% vs. 54%) and specific (100% vs. 91%). These estimates were obtained from a blinded

study of 100 patients that used as gold standard a review committee of endoscopists and radiologists.[164] With the rapid increase in endoscopy rates currently taking place,[165] it is predictable that more patients with a low prior prevalence of gastric cancer are being examined, resulting in a decreased positive predictive value and an increasing negative predictive value.[166] Histological confirmation of cases detected by endoscopy is necessary. Biopsies are usually done endoscopically and, in cases that undergo gastrectomy, are supplemented by histological examination of resected specimens.

Staging information is necessary for treatment choice, as discussed below, and is helpful in prognostication. To stage gastric cancers accurately, information on tumour invasion (T), lymph node involvement (N) and presence of distant metastases (M) is necessary. TNM staging is used by the American Joint Committee on Cancer and the Union Internationale Contre le Cancer (UICC). The most widely used staging system combines T, N and M information to allocate patients to stages 0, Ia, Ib, II, IIIa, IIIb, IV, and is based on a large prognostic study of Japanese and United States cases.[167] T and N status can only be fully assessed post-operatively, by removal and histological examination of the tumour and potentially affected nodes. M status, however, can be assessed without operation, by abdominal ultrasound or CT scan, and by chest X ray. Although the latter tests for metastases are not entirely sensitive or specific, identification of distant metastases is useful prognostically (denoting Stage IV disease regardless of T or N status) and for identifying patients in whom radical surgery is contra-indicated (as discussed under Treatment below).

The main tests used for pre-operative assessment of nodal and distant metastases are liver function tests, ultrasound, scintigraphy, computerised tomographic (CT) scan, and laparoscopy. The main value in detecting distant metastases is to prevent unnecessary laparotomies. Several studies have found laparoscopy and CT scans to be most sensitive in detection of distant metastasies.[168-170] Laparoscopy has added value when combined with CT scans so as to avoid unnecessary surgery. In one study laparoscopy found distant metastases in 23% of patients that had been considered to be eligible for curative resection after CT scan.[170] In only one of these cases was palliative surgery indicated. This suggests that CT scan is insensitive to metastases. A study of 360 patients, using a combination of tests as gold standard, quantified the sensitivity of laparoscopy (87%), scintigraphy (79%), and ultrasonography (79%).[169] Raised serum alkaline phosphatase, indicating liver metastases, was the least sensitive test. Another study compared pre-

operative (clinical, radiological and endoscopic), intra-operative and post-operative (pTNM) staging in 153 patients with gastric adenocarcinoma.[171] It showed that preoperative staging was not associated with postoperative staging or survival, whereas intra-operative staging was associated with both postoperative staging and survival. The authors conclude that all operable cases should undergo a laparotomy or laparoscopy to avoid suitable cases not receiving curative surgery due to inadequate preoperative assessment.[171] In future, laparoscopic ultrasonography may prove to be most valuable in preoperative staging, but experience of its use is still limited.

Variations between doctors and hospitals in the rigour with which patients are investigated hinders attempts to compare outcomes after adjustment for, or stratification by, case mix. In particular, surgeons who perform extended lymphadenectomies, meticulously remove all lymph nodes from excised specimens, and ensure that all nodes are examined histologically, are more likely to find evidence of distant node metastases than surgeons who do not.[29, 30] Therefore, for a given patient, they are more likely to designate the patient as having a more advanced stage of disease. Thus comparisons a patient classified, for example, as having stage II disease by a radical surgeon may in fact have less advanced disease than a patient classified as stage II by a conservative surgeon. For each stage of disease, and especially for stage I-III patients, radical surgeons would be expected to obtain better outcomes merely as an artefact of differential classification of stage. This potential problem is termed 'stage migration' and is widely recognised[29, 30] but has rarely been quantified.

The best evidence of the effect of stage migration comes from the Dutch randomized trial comparing R1 and R2 resections (discussed in the following section).[28] Of patients in the R2 arm of the trial, extended lymphadenectomy resulted in 30% being upstaged to N2 status. Five year survival was then compared, for each stage, according to whether or not the additional information from extended lyphadenectomy was taken into account in staging. Stage migration resulted in increased five year survival of 1% in stage Ia, 2% in stage II, and 15% in both stages IIIa and IIIb. Thus stage migration probably explains part of the difference in stage-specific survival rates when comparing R1 and R2 resections, or comparing Japanese and other countries.[28]

### 2.3.2.2 Treatments

Treatment guidelines have been produced by several authorities including, for example, the United States National Cancer Institute.[172] Recommended treatments are closely linked to patients' TNM staging. For patients with stages 0 to II, regional lymphadenectomy is recommended together with total or (if the lesion is localised) subtotal gastrectomy. For stage III patients, curative surgical resections, including regional lymphadenectomies, are recommended only for patients who do not have extensive nodal involvement. For stage IV patients, that is those with metastases, surgery is not recommended unless palliative resection is indicated to prevent bleeding or obstruction. Adjuvant chemotherapy or radiotherapy is not recommended except as part of clinical trials. The rest of this section will examine the evidence underlying these recommendations.

#### Potentially curative surgery

For patients with resectable tumours (i.e. stages 0-III - without metastases) the main choices are between total and subtotal gastrectomy, and between local or extended lymphadenectomy.

Total and subtotal (partial) gastrectomies have not been compared in randomised trials, and evidence of their relative effectiveness is limited to observational studies. A prospective multi-centre French study of 169 patients found no difference in 5 year survival between patients treated with either operation, whether or not nodal involvement or serosal extension was accounted for.[173] However a retrospective Italian study of 402 patients found that, among the subgroup of patients with lymph node involvement, subtotal gastrectomy was associated with a significantly better 5 year survival.[174] Total gastrectomy had double the operative mortality of subtotal gastrectomy in another case series.[175] Despite the lack of evidence of better outcomes with total gastrectomy, textbooks suggest that total gastrectomy is favoured for cancers of the upper half of the stomach, with controversy limited to the best procedure for cancer of the lower half of the stomach.[176] A 1987 survey of 18,365 patients across the United States found that, of patients with proximal tumours, 46% had total and 29% had subtotal gastrectomies, compared to 27% and 55%, respectively, of patients with lower third tumours.[177]

Probably the greatest controversy in gastric cancer surgery is whether or not to perform extended lympadenectomy at the time or gastrectomy, i.e. whether to perform a D1 (also called R1) lymph node resection, or more extensive D2 (i.e. R2) or D3 (i.e. R3) resections.[176] A D1 resection entails gastrectomy plus removal of all first tier, or peri-gastric, nodes. A D2 resection entails, additionally, resection of nodes located along the splenic and left gastric arteries and celiac axis. A D3 resection entails, additionally, removal of nodes on the hepatoduodenal ligament or mesenteric root.[132, 178-181] D2 and D3 resections are conventional in Japan but are performed relatively infrequently elsewhere. Several observational studies and four randomised trials have compared D1 with D2 and or D3 resections.[132]

The most definitive study comparing D1 and D2 resections was a Dutch randomised trial that randomly allocated 711 patients treated surgically with curative intent to either type of resection.[182] Patients in the D2 group had significantly higher rates of complications (43% versus 25%) and postoperative mortality (10% versus 4%), and significantly longer hospital stays. Five year survival rates did not differ significantly (47% versus 45%). This study shows that D2 resections should not be routinely used in patients with gastric cancer.

Results of a British MRC randomised trial comparing D2 and D1 resections, and with 200 patients in each arm, are still awaited. However an interim analysis found significantly worse postoperative hospital mortality (13% vs. 6.5%) and postoperative morbidity (46% vs. 28%) in the D2 arm than the D1 arm.[183] The worse outcomes in the D2 group were due to complications of splenectomy and pancreaticosplenectomy. A secondary analysis found that patients who had pancreaticosplenic resections had a 30% three year survival, compared to 50% in those who did not.[183] Survival differences between the two trials arms has not yet been reported.

A third randomised trial of only 55 patients found significantly longer mean survival in the D1 arm (1511 days) than in the D3 arm (922 days).[184] A fourth trial of only 43 patients found no significant difference in mortality, but significantly longer hospital stays in the D2 arm.[185]

The advantages of the observational studies identified are that they cover relatively large numbers of patients and have five year survival data. They have accounted for case mix differences by stratifying patients according to presence or absence of lymphatic

metastases[178, 179] or, more finely, according to disease stage.[180, 186] Both of the former studies show significantly better five year survival in the D2-D3 groups overall, and in the subgroups with lymphatic metastases, but not in the subgroups without metastases.[178, 179] Of the latter studies, one shows five year survival after D2 resection to be significantly better overall and in the stage III subgroup; survival was also better in the stage I and stage II subgroups, but not significantly so.[180] The fourth observational study found significantly better five year survival in the stage II and IIIa subgroups but not in the stage I, IIIb or IV subgroups.[186] Taken together, these studies suggest better outcomes after D2 resections in patients with nodal involvement. However this difference is likely to be confounded by stage migration.[28, 132, 178, 181] The differences between the results of observational studies and the Dutch trial suggest that the former may be biased or confounded.

In summary, randomised trial evidence shows that short term outcomes are worse after D2 resections than after less extensive resections. The longer term survival results of the British randomised trial is eagerly awaited. In the meantime the conclusions of the Dutch and British triallists, that D2 resections should not yet be advocated as standard surgery, are justified.[182, 184, 185, 187]

## Chemotherapy

Chemotherapy can be used post-operatively (adjuvant therapy), pre-operatively (neo-adjuvant therapy) or for treating metastatic disease.[176] A meta-analysis of postoperative chemotherapy found no significant decrease in deaths after chemotherapy combined with surgery with curative intent, compared to curative surgery only (odds ratio 0.88; 95% CI 0.78-1.08).[188] In only 2 of the 13 studies for which data were pooled was chemotherapy associated with a statistically significant survival advantage. The meta-analysis included studies published between 1980 and 1991. There was wide variation between the trials in factors that may have influenced outcomes, including chemotherapeutic agents, follow-up periods (ranging from 1.5 to 8 years), entry criteria, surgical procedures and follow-up policy, and thus the pooled odd ratio should be interpreted with caution. A more recent literature review included a wider range of studies, interventions (chemotherapy, immunotherapy, and/or radiotherapy), comparison groups (several did not have surgery-only arms) and surgical procedures (curative, palliative and unresectable), and wisely did not attempt to pool the outcomes.[189] Of the 43 trials reviewed, 9 showed significant

differences in survival between arms. Mitomycin and immunotherapy were most likely to be associated with better survival. Adverse side affects were commonly reported and led to several trials being discontinued or prolonged. More recently, two more randomised trials have been reported. They compare adjuvant intravenous[190] or intraperitoneal[191] mitomycin with surgery alone, and both showed significantly better survival in the mitomycin arms than in the surgery only arms. In summary, there is still scanty evidence that adjuvant chemotherapy improves survival, but adjuvant mitomycin and immunotherapy are promising.

Pre-operative chemotherapy could potentially improve survival by decreasing tumour size and micrometastases. However there is little evidence of its effectiveness, apart from two case series that have shown decreased tumour size or increased resectability after chemotherapy.[107, 192]

Chemotherapy, especially fluouracil, is most commonly used in treatment of advanced or metastatic disease. Although a leading text book states "There is no doubt that the use of cytotoxic chemotherapy in metastatic node disease can prolong survival,"[176] the supporting evidence is confined to two small randomised trials, one of which was ended prematurely. In one randomised trial, 17 patients receiving fluouracil, epirubicin and methotrexate had a median survival of 12.3 months, compared to 3.1 months in 19 patients who received best supportive care only ($p=0.0006$).[193] The second trial was stopped after only 10 patients had been randomized to the best supportive care arm, because of better outcomes in the chemotherapy arm. All subsequent patients, to a total of 30, were thereafter allocated to the chemotherapy (fluouracil, doxorubicin and methotrexate).[194] The respective median survivals were 10.0 and 3.0 months, respectively ($p<0.001$), but as this trial was stopped prematurely, its results cannot be regarded as conclusive.[195] Unfortunately it may consequently now be difficult to obtain ethical approval to conduct further trials.[195]

## Radiotherapy

There is little evidence to support the use of radiotherapy in either early or advanced gastric cancer.[107, 196] A recent narrative review identified eight phase III randomised trials in resected gastric cancers that including radiotherapy in at least one arm.[196] Unfortunately only two of the trials compared surgery plus radiotherapy with surgery alone. In one trial survival was better in the radiotherapy arm, and in the other trial

survival was better in the surgery only arm. The same review identified nine phase II trials in unresectable gastric cancers; most of these compared radiotherapy with radiochemotherapy, or chemotherapy with radiochemotherapy in various combinations. However there is no consistent survival advantage with radiotherapy alone or in combination.[196]

## 2.3.3 Pancreatic cancer

### 2.3.3.1 Diagnosis and staging

As with the other two cancers, the purpose of investigations is to establish a diagnosis and to guide choice of treatment. A key treatment decision is whether to attempt cure by resection of the tumour. Because of the late stage of presentation of most cases, only 10% to 20% are resectable.[197] Resectable tumours are those that have no evidence of pancreatic capsular invasion, nodal involvement or distant metastases. Obtaining preoperative evidence of any such spread avoids unnecessary surgery. This section reviews evidence of the validity and role of diagnostic and staging investigations.

A summary of validity estimates for selected tests is shown in Table 2.6, and these data are discussed below under the respective tests. In all studies cited in Table 2.6, the reference "gold" standard test was the full assessment of the patient after operation. The populations studied comprised patients deemed suitable for potentially curative surgery. The results may therefore not be generalisable to patients in whom the initial diagnosis of cancer has not yet been made. Caution in interpretation is also necessary because the small sample sizes reduce the precision of estimates.

**Table 2.6. Pancreatic cancer. Sensitivity, specificity and accuracy* (%) of diagnostic and preoperative staging investigations compared to post operative pathology**

| Author | No. patients | Diagnosis | Lap Sensitivity | Lap. Specificity | CT Sensitivity | CT Specificity | LUS Sensitivity | EUS Specificity | Ext US Sensitivity | Ext US Specificity | Other tests | Specificity | Sensitivity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Muller[198] | 24-49 | Tumour present | | | 69 | 64 | 94 | 100 | | | MRI | 83 | 100 |
| | | T stage | | | | | 45* | | 82* | | MRI | 50* | |
| | | N stage | | | 20 | 45 | 40 | 83 | | | MRI | 14 | 82 |
| Freeny[199] | 213 | Tumour present | | | 97* | | | | | | | | |
| | 71 | Resectable | | | 72 | | | | | | | | |
| Freeny[200] | 174 | Tumour present | | | 91* | | | | | | | | |
| | | Resectable | | | 100 | | | | | | | | |
| Friess[201] | 80 | Tumour present | | | | | | | | | PET | 94 | 88 |
| Snady[202] | 60 | Resectable tumour | | | | | 75 | | | | CT + ERCP | 38 | |
| John[203] | 40 | Resectable tumour | 50 | 100 | | | | | | | Laparoscopy + Lap US | 88 | 92 |
| Conlon[204] | 115 | Resectable tumour | 81 | 100 | | | | | | | | | |
| Rosch[205] | 60 | Portal venous invasion | | | 36 | 85 | 91 | 97 | 9 | 92 | | | |
| | | Nodes involved | | | 36* | | 72* | | 12* | | | | |

* Accuracy: ((true positives+true negatives)/total); EUS: endoscopic ultrasound; Lap: laparoscopy; CT: computerised tomography; Ext: external; MRI: magnetic resonance imaging; ERCP: endoscopic retrograde cholangiopancreatography; PET: positron emission tomography

Patient's clinical signs and symptoms provide some guidance as to choice of investigations. The characteristically late presentation of patients with pancreatic cancer is mainly due to the late development of symptoms. The most useful clinical sign is jaundice, which appears relatively early in tumours of the head of the pancreas, compared to tumours of the body and tail, and is thus positively associated with resectability. For example, two United States surgeons have reported that 45% of their patients with jaundice had resectable tumours, compared to 10% of those without jaundice.[197] This suggests that, other things being equal, patients with jaundice should be investigated more actively than if they did not have jaundice, firstly to establish an early diagnosis, and secondly to assess suitability for resection.

External ultrasonography is probably the least invasive and least expensive of the investigations that aim to visualise the tumour and its spread, and has the added advantage of not subjecting patients to ionising radiation. Depending on the skill of the ultrasonographer, one narrative review claims that its sensitivity and specificity in diagnosing pancreatic tumours is between 80% and 90%, and that it is accurate in detecting ascites and liver metastases, although no supporting evidence is cited.[197] Muller *et al* have shown external ultrasound to be relatively accurate in assessing tumour invasion,[198] but Rosch *et al* found poor sensitivity in detecting nodal involvement and venous invasion[205] (Table 2.6). These data suggest that external ultrasound is a suitable diagnostic test, to be used early in the diagnostic workup, but it has limited validity in assessing resectability.

In contrast, endoscopic ultrasonography, while being more invasive than external ultrasonography, has been shown in several studies to be relatively sensitive and specific in detection of tumour spread (Table 2.6), and more so than computerised tomography[198, 204, 205] This a relatively new procedure, and requires a specially trained operator familiar with both endoscopy and ultrasonography, but its promising results suggest that it should be used more frequently in future.[197] It has been recommended for confirmation of endoscopic retrograde cholangiopancreatography (ERCP) and computerised tomography findings.[206]

Dynamic computed tomography (CT) has been advocated as the best single modality for both diagnosis and staging together.[197] It has been sl own to have high sensitivity in diagnosing the presence of a tumour, and in predicting resectability,[198, 200] but has been found to have low sensitivity in detecting involved nodes or venous invasion.[198, 205]

Endoscopic retrograde cholangiopancreatography (ERCP) allows direct visualisation of duodenum and ampulla, and bile ducts stenosis, as well as permitting cytology.[197] ERCP results have been shown to be similar to those of computed tomography in diagnosing pancreatic tumours.[207, 208] However the latter two studies were conducted in groups of patients with a mixture of diagnoses and did not use surgical diagnoses as gold standards. One study that did found a combination of ERCP and computed tomography to have a low sensitivity in identifying resectable tumours.[202]

Magnetic resonance imaging was found in one study to be highly sensitive in diagnosing tumour presence, but less accurate or sensitive in identifying tumour invasion or nodal involvement.[198]

Finally, laparoscopy was shown in one study to have high sensitivity and specificity in identifying resectable tumours.[204] In another study laparoscopy alone was fairly insensitive in defining resectable tumours, but in combination with laparoscopic ultrasound the sensitivity increased markedly.[203]

## 2.3.3.2 Treatment

### Potentially curative surgery

As with the other two cancers, tumour resection is the only potentially curative treatment available, and is usually only appropriate in patients without local invasion, lymphatic involvement or distant metastases.[209] In the United States, such patients generally comprise less than 10% of all pancreatic cancers.[209] A view of surgical treatment patterns and outcomes in the UK is provided by a cancer registry study of 13,560 patients with pancreatic cancer in the West Midlands from 1957 to 1986, published in 1995.[210] The West Midlands population comprises about 10% of the total UK population.[211] Comparisons were made between patients registered from 1957 to 1976, and from 1977 to 1986. There was no change in the low resection rates (2.6%) for the two periods, but there were significant improvements in 30 day operative mortality (45% vs. 28% respectively) and 5 year survival following resections (2.6% vs. 9.7%). The proportions of patients having only laparotomies decreased from 20% to 15%, possibly reflecting improved preoperative workup, and 30 day mortality after only laparotomy decreased from 56% to 45%. These results show that, until two years ago, very few patients received potentially curative treatments and that, among those who did, operative

mortality was high and long-term survival was low. The results of the current study will indicate whether there has been any improvement to this discouraging pattern.

The main controversy regarding *treatment of patients eligible for potentially curative* surgery is the degree of radicality of resection, and in particular whether and when standard or radical resections are best. There are no randomized trials comparing the main resection procedures and thus one is reliant on evidence from non randomised comparisons and case series.

Standard resections generally entail partial, rather than total, pancreatectomy, and no retroperitoneal node dissection or portal vein resection.[212] However there are several options for different types of reconstruction, and whether or not to preserve the pylorus of the stomach. A case series of 201 patients treated in Johns Hopkins Hospital found a significantly higher five year survival following pylorus preserving pancreatico-duodenectomy than following classic pancreatico-duodenectomy.[213] Much of this apparent difference could be due to case mix differences, however. Multivariable survival analysis found tumour biology to be a much stronger predictor of long-term survival than type of resection or any other patient characteristic. Unfortunately the authors do not supply an adjusted hazard ratio comparing the two types of resection. Survival increased significantly for each successive decade of the series, independently of other prognostic factors.

A comparative case series of 1500 patients who had pancreatectomies in the United States, published in 1988, suggests that total pancreatectomy may be more hazardous than partial pancreatectomy.[214] It found an operative mortality rate of 3% after partial resections, compared with a rate of 18% after total pancreatectomies. This comparison did not adjust for case mix differences.

Radical resection entails pancreaticoduodenectomy or total gastrectomy, plus extensive retroperitoneal lymph node and soft tissue resection.[209] The main rationale for extended lymph node resection is that several case series have shown lymph node spread to be the most important prognostic factor for survival.[209] Thus it was assumed that removing regional nodes would improve survival. As with gastric cancer, Japanese surgeons have pioneered extended lympadenectomies as part of radical resections. A review of 10 reported Japanese case series following extended pancreatico-duodenectomies, and including 607 patients, showed variable operative mortality rates (median 5%, range 0%-

14%) and 5 year survival (median 20%, range 0%-28%).[209] One of these reports took stage into account, and included 57 patients with tumours under 2 cm in diameter.[215] Survival analysis was stratifed by stage and showed that in stage II patients, 5 year survival was significantly higher after extended resection (33%) than after standard resection (11%). There were no significant survival differences between the two procedures overall or in patients with other stages of disease.

A Norwegian prospective multi-centre study of 108 patients, followed up for five years and stratifed by stage, found no difference in mean survival after pancreatectomy with or without regional and nodal resection.[216] However survival was dramatically longer after either of these procedures than it was after palliative bypass alone, for each stage. Despite this attempt to account for case mix by stratifying by stage, it is plausible that the latter survival difference could reflect selection bias, due to surgeons avoiding radical surgery in patients with poorer prognosis due to operative risk factors.

Several randomized trials have assessed ways of improving outcomes after surgery, either by total parenteral nutrition, or by neutralising harmful pancreatic enzymes. Intravenous nutritional support seems justified after major gut surgery, but the evidence suggests otherwise. One trial randomised 117 patients to receive or not to receive total parenteral nutrition after pancreatic resections for malignancy.[217] Complications due to infections were significantly more common in the total parenteral nutrition arm (45% vs. 23%), but there were no other differences in outcome.

Pancreatic enzymes leaking onto wound sites after surgery can damage tissue. These enzymes can be neutralised by somatostatin and its analogues such as octreotide. Two multi-centre randomized trials conducted in Italy[218] and Germany[219] have all shown complications after pancreatic resections to be significantly and substantially less common in octreotide arms than in placebo arms. Both trials included patients with either pancreatic cancer or chronic pancreatitis. The respective complication rates overall were 16% vs. 29% ($p=0.01$)[218] and 32% vs. 55% ($p<0.005$)[219] and, for the pancreatic cancer subgroups, 22% vs. 35% ($p=0.08$) and 38% vs. 65% ($p<0.01$). In summary, complications after resection can be reduced by octreotide but may be increased by total parenteral nutrition.

## Palliative surgery

In patients who are not eligible for curative surgery it may be necessary to perform procedures to avoid jaundice, intestinal obstruction or pain.[220-222]

Jaundice due to bile duct obstruction can lead to liver failure and death, as well as causing severe symptoms. Jaundice can be palliated by surgically bypassing the tumour, by joining the bile duct to the duodenum or jejunum, to allow bile drainage. Alternatively, a stent can be inserted into the bile duct, either endoscopically[222] or percutaneously.

The best observational evidence comparing palliative treatments for jaundice comes from a meta-analysis of case series published between 1981 and 1990, covering 3484 cases.[223] Thirty day mortality rates for surgical bypass (12%) lay between those for percutaneous stent (9%) and endoscopic stent (14%). Early complications were more common after surgery than after percutaneous and endoscopic stents (31% vs. 16% and 21%), but the opposite was true for late complications (16% vs. 28% and 28%). Unfortunately this review did not provide confidence intervals for pooled data, or consider case mix variations.

Experimental evidence regarding relief of jaundice comes from four small randomized trials (n 50 for three trials, and n=127 for the other).[220] Relief of jaundice was obtained in most patients - between 76% and 96% of patients, depending on procedure and trial arm. Thirty day mortality was higher after surgery than after stent insertion in all trials, and median survival was shorter after surgery in three of the trials, but these differences were not statistically significant in any trial. These results suggest that non-operative stenting is preferable to surgical bypass, but they are not conclusive owing to the low power of the trials.

If a surgical bypass is performed there is a choice between joining the intestine either to the gall bladder (cholecystoenterostomy) or to the bile duct (choledochoenterostomy). A small randomized trial (n=31), which included a minority of patients with obstruction due to chronic pancreatitis, found bypass failure to occur significantly more often if the gall bladder was used than if the bile duct was used.[224]

Duodenal obstruction, in which the tumour obstructs the passage of bowel contents, can be relieved surgically by joining the stomach to the jejunum (gastrojejunostomy).[220] The main controversy is whether the procedure should be performed prophylactically if a tumour is found to be unresectable at operation, but where there is no evidence of

obstruction yet.[220, 221] Three large reviews, covering a total of 10,550 patients, reported that between 13% and 21% of patients who did not undergo gastrojejunostomy at the time of their operation went on to require one before death.[220] There is thus a trade-off between the advantages of avoiding a second laparotomy later in a minority of patients, and the trauma and cost of preventive surgery which may have not benefit for the majority of patients.

Severe pain can relieved by chemical splanchnicectomy (also known as coeliac plexus block) in which coeliac nerves are killed by injecting alcohol at the time of laparotomy.[220, 221] Support for this procedure comes from a randomised trial of 139 patients in whom either alcohol or water (i.e. placebo) was injected.[225] It found significantly lower pain scores in the alcohol arm at 2, 4 and 6 months, and no difference in hospital mortality, postoperative complications or other outcomes. There was no difference in survival overall, but in the subgroup with severe preoperative pain, survival was significantly longer in the alcohol arm.

In summary, while stents may be marginally preferable to surgery in relieving jaundice, surgery has the advantage of allowing palliation of all three complications at the same time. The final decision on an individual's best course of treatment should however depend on their operative risk and severity of symptoms.

## Chemotherapy

Recent reviews agree that there is minimal evidence of chemotherapy alone having any effect on survival.[226, 227] There is however evidence from case series that tumours respond to 5-fluorouracil (5FU) in up to than 25% of cases,[226, 227] where response is defined as a 30% reduction in palpable hepatomegaly. In these trials there is no evidence that addition of any modulator to 5FU leads to a higher response rate.[226] A small case series found a 24% response to mitomycin.[227]

For patients having resections, the only evidence of the value of adjuvant chemotherapy comes from one small randomized trial.[228] Patients received either 5FU, doxorubicin and mitomycin plus surgery, or surgery alone. Median survival was significantly greater in the adjuvant therapy group than the surgery only group (23 vs. 11 months). However there was no significant difference in 5 year survival (4% vs. 8%). Definitive evidence is expected from a current randomized trial in which patients are randomized to surgery only, or with radiochemotherapy, chemotherapy only, or combination therapy.[229]

For patients with unresectable cancers, the strongest evidence of the superiority of combined radiotherapy and chemotherapy (5FU), compared to radiotherapy alone, comes from an early randomized trial of 194 patients.[230] One year survival was 10% in the radiation only group and 40% in the combined group, with no difference between high and low dose radiation.

Hormonal treatment with tamoxifen has been evaluated in two placebo-controlled randomised trials, but no significant difference in survival was found.[231, 232] A non-randomized trial found significantly longer survival in patients given tamoxifen than in matched controls (7 versus 3 months).[226]

### Radiotherapy

There is no experimental evidence that radiotherapy alone is effective in treating pancreatic cancers, or that radiation plus chemotherapy is superior to chemotherapy alone.[226, 227, 233] Evidence of the value or intra-operative radiotherapy is inconclusive. A case series of patients with locally advanced disease treated at the Mayo Clinic compared 122 patients who had external radiotherapy alone, with 22 patients who had external plus intra-operative radiotherapy.[234] There was no difference in survival but patients who had intra-operative radiotherapy were much more likely to have local control (66% vs. 20%). Another case series compared 35 patients who had surgery (resection or palliation) plus intra-operative radiotherapy, with 41 patients who had surgery only.[235] It found no difference in survival, and a higher rate of operative complications in the radiotherapy group.

## 2.3.4 Summary of evidence of the effectiveness of investigations and treatments

Investigations are performed to confirm diagnoses and to assess tumour spread, so as to provide prognostic information and guide treatment strategy. Diagnosis of oesophageal and gastric cancers is best achieved by endoscopy and biopsy. Pancreatic tumours are less accessible but may also be biopsied by endoscopy or ERCP; however in most cases pancreatic tumours cannot be accessed and thus diagnoses are reliant on CT. The main purpose of staging investigations is to identify patients with potentially curative disease, by excluding local invasion or spread to lymph nodes or other sites. Of the two most

commonly used staging tests, CT appears to be more sensitive and specific than external ultrasound, but the latter may be better for detecting liver metastases. Endoscopic ultrasound appears to be a highly sensitive and specific staging investigation with promise for the future. Magnetic resonance imaging is also promising but there have been few studies of its validity in staging. Laparoscopy may be most sensitive in identifying abdominal metastases, and could prevent unnecessary laparotomies. These generalisations are tentative, however, because of the highly variable results of individual studies, with overlaps in the sensitivities and specificities of the different tests. Most of these investigations are highly dependent on operators' manual and interpretative skills, and thus study results may have limited application to typical practice settings.

Potentially curative treatments entail tumour resection; the main controversies concern the radicality of resections. For gastric cancers extended lymphadenectomy appears to be harmful, and for pancreatic cancers there is no evidence to support extended lymphadenectomy. For pancreatic cancers, there is no evidence to support the more radical total pancreatectomies or pancreatico-duodenectomy instead of partial pancreatectomies, but choice of procedure should be guided by tumour size and location. For oesophageal cancers, extended lymphadenectomy in addition to tumour resection is supported by one randomised trial and several observational studies. Extended, rather than limited, oesophagectomies are also supported by several observational studies. There is no convincing evidence to support the use of adjuvant chemotherapy or radiotherapy together with potentially curative surgery for any of the cancers.

Palliative procedures aim to relieve gut obstruction for oesophageal or gastric cancers, and bile duct obstruction for pancreatic cancer. For gastric cancer, bypass surgery is the only option, for oesophageal cancer there is a choice of stent insertion or radiotherapy, and for pancreatic cancer there is a choice of stent insertion or bypass surgery. For pancreatic cancer, four small randomised trials suggest that stenting may be preferable to bypass surgery. Two small randomised trials suggest that chemotherapy may improve survival in advanced gastric cancer but there is no such evidence for advanced pancreatic or oesophageal cancers. None of the other main palliative options have been evaluated by randomised trials or by high quality observational studies.

The most striking finding of this part of the review is the paucity of evidence of effectiveness of the main treatment options. This suggests that even specialised upper gastrointestinal cancer care has a weak evidence base, and thus that experience,

judgement and skill, rather than scientific knowledge of treatment effectiveness, are key elements of specialisation. Given the scanty and often inconclusive evidence, clinical practice would be expected to vary widely.

## 2.4 Summary of literature review

This literature review has examined evidence of whether volumes of patients managed by individual hospitals or doctors are associated with patient outcomes and health care costs, and whether the health care interventions available are effective. Particular emphasis was placed on evidence about pancreatic, oesophageal and pancreatic cancers.

The volume-outcome literature shows that, for many diseases in many settings, hospitals and surgeons managing larger volumes of patients, or with other specialist attributes, appear to obtain better outcomes for their patients. However there are about as many studies showing no health outcome advantages. For oesophageal and gastric cancers specifically, there is little evidence to support the centralisation of care, but for pancreatic cancer the evidence is more convincing. Unmeasured and unadjusted case mix variation in most studies means that their results may be biased, while in many studies the short follow-up of survival, usually confined to hospital stays, limits their usefulness.

It is plausible that health care costs would vary with patient volumes, but the direction of effect is difficult to predict. More specialised units may do more for patients, at greater cost, and they may operate more or less efficiently. Most of the cost-volume literature examined entire hospitals, rather than specific conditions or specialties, and so its relevance to specialisation around specific cancer sites is limited. Three studies of other surgical specialties found average hospital costs to decrease with increasing surgeon volumes, and several studies of specific units within hospitals found costs to decrease, or have U-shaped relationships, with increasing volumes. These studies are almost all impaired by case mix variations which may have biased their results.

Specialist expertise is required for both sound clinical decisions and therapeutic skill. The evidence base for effective practice is limited, with few randomised trials comparing the main treatment options. It is critically important to identify patients who could benefit from potentially curative surgery – this largely entails looking for evidence of local or distant tumour spread so as to exclude those patients unlikely to benefit. Without

thorough investigation, patients with curable cancers could be missed or those with incurable cancers could be unnecessarily subjected to traumatic surgery.

In summary, little is known about the quality and cost of care for patients with pancreatic, oesophageal and gastric cancers, and how these vary with specialisation. The study reported in this thesis will attempt to add to the very limited knowledge in these areas.

# 3. METHODS

## 3.1 Aims

For patients with gastric, pancreatic and oesophageal cancers:

- To investigate the influences on survival and operative mortality of:
  - Hospital and doctor volumes
  - Treatments provided
  - Patients' personal characteristics and health status, and ecologic deprivation indices
- To investigate the influences on investigations and treatments of hospital and doctor volumes and of patients' personal health status
- To estimate the hospital costs of cancer care, and to examine the influences on total hospital costs, and costs per day of life, of patients health status, treatments provided, and doctor and hospital volumes.

## 3.2 Design

The study had a cohort design with a cost analysis. There were three separate cohorts and cost analyses - one for each cancer site. The same methods were used to study each cancer site. Some variables were however recorded for certain sites only.

## 3.3 Study population, inclusion criteria, power and duration of follow-up

The three cohort populations comprised all patients:

- newly diagnosed as having gastric, pancreatic or oesophageal cancer, and
- admitted or presenting to hospital between 1 July 1996 and 30 June 1997

- in any of the acute hospital trusts in the South and West region of England and (for pancreatic cancers only) six acute hospital trusts in South Wales, and
- having a diagnosis of one of the respective cancers recorded in hospital discharge, death or pathology records.

No sampling was used (statistical power is discussed below).

Eligible patients were identified from hospital data on discharge diagnoses, investigations, and pathology, and confirmed by examination of patients' hospital folders. The following ICD (versions 9 or 10) codes were used in identifying patients from discharge and death diagnoses: 150 for oesophageal cancer, 151 for gastric cancer and 157 for pancreatic cancer. Different hospitals used different methods for recording pathological diagnoses and for identifying eligible cases and so search methods were modified where necessary, in consultation with local hospital personnel. Multiple sources were used in each hospital, where possible, to maximise the sensitivity of case identification. Computerised databases, especially the Patient Administration System, were the primary data sources, but additional written records were used where appropriate. The specific patient lists examined in different hospitals included surgeons' lists, pathology lists, Clinical Audit department lists, and endoscopy lists; these were mainly from computerised databases. These were obtained through regular liaison with surgeons' and oncologists' secretaries, Clinical Audit departments, Medical Records departments, and endoscopy clerks. Patients with tumours of all histological types were included if the primary tumour occurred in the oesophagus, stomach or pancreas; in the statistical analysis patients with unusual histology were analysed separately or excluded from the analysis. Patients not admitted to hospital and with no pathological diagnosis were excluded from the study because of uncertainty about their diagnoses and because of logistical difficulties of identifying them. The researchers were in contact with each hospital approximately monthly, to identify the most recent admissions.

The study included patients having contact with any of the acute hospital trusts in the South and West region of England, as defined in June 1996. Patients managed at the following 23 hospital trusts were included in the study: Cheltenham District Hospital; Frenchay Hospital, Bristol; Gloucestershire Royal Hospital, Gloucester; North Devon District Hospital, Barnstable; North Hampshire Hospital, Basingstoke; Plymouth Hospitals Trust; Poole General Hospital, Poole; Princess Margaret Hospital, Swindon;

Queen Alexandra Hospital, Portsmouth; Royal Bournemouth Hospital; Royal Devon and Exeter Hospital; Royal Hampshire Hospital, Winchester; Royal United Hospital, Bath; Salisbury District Hospital; Southampton General Hospital; Southmead Hospital, Bristol; Musgrove Park Hospital, Taunton; Torbay Hospital, Torquay; Royal Cornwall Hospitals Trust, Truro; United Bristol Healthcare Trust; West Dorset Hospital, Dorchester; Yeovil Hospital; and Weston-Super-Mare General Hospital. In addition, for pancreatic cancers, the following six hospital trusts in south Wales were included in the study: Llandough Hospital, Penarth; Morriston Hospital, Swansea; Princess of Wales Hospital, Bridgend; Royal Gwent Hospital, Newport; Singleton Hospital, Swansea; and University Hospital, Cardiff.

South Wales pancreatic cancer patients were included in the study so as to increase the statistical power of the study to detect differences in survival between high and low volume hospitals and doctors. South Wales patients with gastric and oesophageal cancers were excluded because the Welsh Surgical Society was conducting a similar study at the same time, and therefore hospital personnel were reluctant to service two sets of researchers simultaneously.

A hospital trust was used as the basic unit of analysis, because hospital trusts are the basic organisational unit for National Health Service secondary care. Different hospitals within a trust may provide different services, but these are supposed to be functionally co-ordinated. For example, within the United Bristol Healthcare Trust, cancer care is provided both in the Bristol Royal Infirmary and in the Bristol Oncology Centre, with co-ordination between these sites. Iin order to characterise the degree of specialisation of services and access to multidisciplinary care, it therefore makes more sense to characterise trusts than to characterise hospitals. The main potential problem would be where trusts include more than one large acute general hospital, and these hospitals were functionally distinct. This was however not a problem in this study each trust included only one acute general hospital. Since the study Frenchay Hospital and Southmead Hospital have been amalgamated within the North Bristol Healthcare Trust, but that was not true at the time of the study. Another potential problem would be where small community hospitals as well as large district hospital with specialist cancer services were in the same trust but were not functiontionally co-ordinated. In these cases smaller hospitals may be erroneously ascribed specialist status. This problem was avoided by not

basing patient identification in smaller hospitals, which were thus under-represented in the study.

Several hospitals in the region, that were smaller than the hospitals listed above and were the main source of care for relatively few cancer patients, were excluded from the study to make it logistically feasible. Therefore, although the study included most cancer patients, the results of this study, and particularly evidence of volume-outcome relationships, may not be generalisable to the very lowest volume hospitals in the region. However, omitted patients and hospitals accounted for only a small proportion of patients in the region. Previous South and West cancer registry data, for the years 1988 to 1993 (supplied by Dr D Etherington, South and West Cancer Epidemiology Unit), showed that the 16 hospitals included in the study and from the area covered by that registry accounted for 86% of all registered oesophageal cancers, 75% of all registered gastric cancers and 72% of all registered pancreatic cancers. The proportions of all registered patients that ever passed through at least one of the hospitals included in the study are likely to be higher, however, as patients may have been registered by another hospital but still managed at some stage in a hospital included in the study.

The location of hospitals included in the study is shown in Figure 3.1. The regions included in the study were fairly representative of the United Kingdom (UK) as a whole, including urban, rural and remote areas, and affluent and deprived areas. The proportions of residents aged over 65 years in 1995 were higher in regions included in the study than in the United Kingdom as a whole (South Western: 17.4%; Wessex: 18.5%; Wales: 17.4%; UK: 15.8%).[255] The prevalence of long-standing illness, according to the General Household Survey, was higher in Wales (37%), and similar in the South and West (32%), compared to the UK (32%)[255] (the South and West region includes the former South Western and Wessex regionsCrude annual mortality rates in 1994 were higher in the Wessex region (11.4 per 1000) and Wales (11.6 per 1000) than in the UK (10.7 per 1000) but were similar in the South Western region (10.4 per 1000);[255] these differences partly reflect different age distributions. Patients included in the study came on average from more deprived areas than the UK population as a whole (mean Jarman deprivation index 1.9, standard deviation 13.9, where the national average Jarman index is 1.0). However study patients were drawn from areas with similar characteristics to the UK as a whole in terms of geography, deprivation and access to health care. Bristol, Plymouth and Southampton are large cities with deprived inner city areas; there are numerous medium

sized towns, and rural areas such as Somerset, Devon and Cornwall are inhabited both by middle class and poorer people and could be close to or distant from district hospitals.

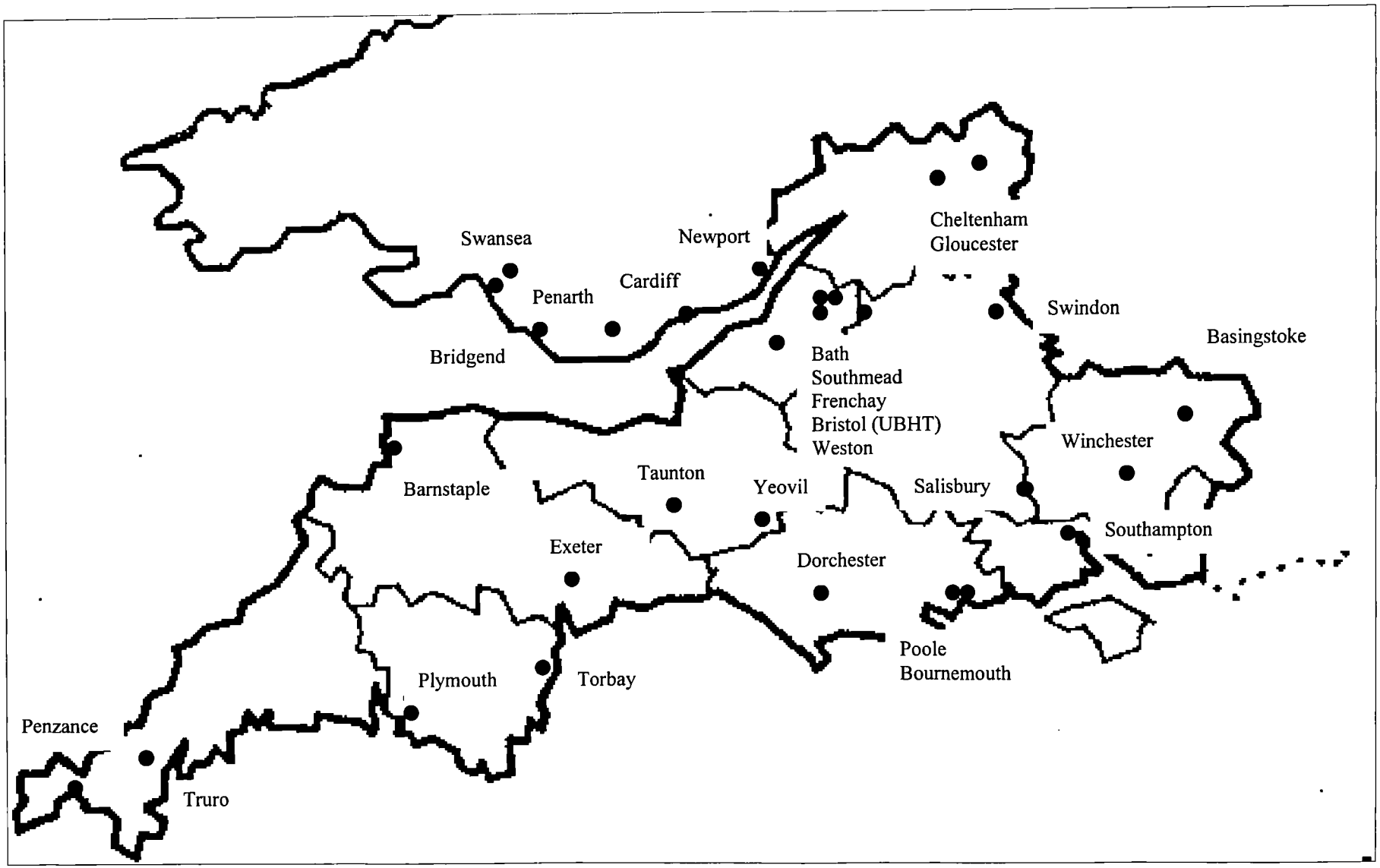



*Figure 3.1 Location of hospital trusts included in the study*

Statistical power was estimated in advance. The numbers of patients expected annually from the South West England hospitals included in the study were 670 oesophageal, 990 gastric, 640 pancreatic cancer cases, according to the author's estimates, based on registrations with the Wessex and the South West cancer registries' for the years 1988-1993. For a 5% significance level (two tailed) and 80% power, and assuming that 25% of cases were managed in high volume hospitals or by high volume doctors, these numbers would be sufficient to detect differences in one year survival of 10% (20% vs. 30%) for oesophageal cancer, 6% (5% vs. 11%) for pancreatic cancer, and 10% (30% vs. 40%) for stomach cancer.

The periods of observation were as follows. In tracking survival, the duration of follow-up after diagnosis ranged from 1 year 4 months (that is from 31 June 1997 to 31 October 1998) to 2 years 4 months (that is from 1 July 1996 to 31 October 1998). Cases still alive on 31 October 1998 were defined as censored in the survival analysis. In the cost analysis, to allow valid comparisons between patients despite different durations of follow-up, hospital costs of care were estimated for one year after the first presentation to the hospital or, if a patient died within a year of presentation, until the patient died.

## 3.4 Data collection

Data were obtained for each patient from two sources:

- Hospital records for clinical data (prognostic and hospital care variables)
- NHS Central Register for dates and causes of death

In addition, data on average costs of health care resources were obtained from a postal questionnaire survey of hospital managers.

All data collection was conducted under the direction of the author of this thesis.

### 3.4.1 Clinical data from hospital records

Most data for the study were extracted from patients' personal hospital records (that is files or folders), by one of three researcher associates. Each research associate was responsible for a set of specified hospitals in a d fined geographical area, including large and small hospitals, cancer centres and other hospitals, and teaching and other hospitals.

Data for each patient were recorded on two of four forms: one form was generic to all three cancers and three were specific to each cancer (Appendix). Forms were piloted by all three researchers in one hospital and amended before use. Forms were formatted for automatic scanning, using a Formic scanner and software.

Patient records were obtained as soon as possible after the researchers were notified of a case by the respective hospital, so as to minimise notes disappearing after patients' discharge or death. Patients' hospital records were examined for a second time, one year after first presentation to hospital, to capture all additional information recorded within a year of first presentation. To ensure comparability between patients despite differential periods of follow-up, information recorded in patients' notes more than one year after presentation was not recorded.

Ideally, all clinical data would have been coded and recorded by a single specialist surgeon. However this was not feasible or affordable given the amount of work required (over seven person-years of data collection). The main problem with data extraction from hospital records was potential misinterpretation of specialist clinical information by the research associates, who were not medically trained. This was avoided through training and careful supervision of the research associates by the author and the surgical collaborator (Professor D Alderson). Quality control of data collection was managed as follows.

First, research associates with experience of research using hospital clinical information were recruited. The research associates had higher degrees and substantial previous experience in health research. Second, familiarity with relevant disease-specific technical terms was promoted by studying surgical text books that detailed the respective operations, other treatments, and investigations, and by extensive reading and discussion of relevant medical journal articles. Third, during the pilot phase of the study the author examined the same hospital records as the research associates, and disagreements or different interpretations in data coding were discussed and clarified. Fourth, during routine data collection, when any researcher was uncertain about how to code a particular type of information, this was discussed collectively with the other researchers, the principal investigator and the surgical co-investigator. Decisions about coding, definitions and other rules were recorded in a log book so as to ensure consistent coding by the different researchers and over time. Meetings to discuss coding were held at least monthly during the first six months of data collection, and less frequently thereafter.

These meetings included the three research associates, the principal surgical collaborator, and the author of this thesis. If, in the light of these discussions, recoding of data already collected was necessary, data were recoded retrospectively, referring to additional patient information which the researchers had written on the backs of data forms. Fifth, to avoid coding errors, data were recorded in the most elementary form, with subsequent recoding performed by the author. For example, T, N and M staging was recorded by the research associates, but this was recoded into American Joint Committee on Cancer stages[172] by the author, using a algorithm specified in the data analysis programme (see section 3.4.1.2 below). Sixth, during preliminary data analysis patients with implausible patterns of investigation or treatment were identified, for example, patients with metastases who had resections. The data collection sheets of these patients were examined and, if no obvious coding errors were identified, their hospital records were re-examined.

The investigators had intended formally to assess data quality by comparing data recorded by the three research assoicates with data recorded by each other and with data recorded by the author, after examination of the same hospital records. Kappa statistics would have indicated the degree of agreement beyond that expected through chance. However the large sample sizes required for this exercise, and the early departure of the research associates to other jobs, made this unfeasible.

### 3.4.1.1 Variables obtained from hospital records

The following classes of variable were recorded for each patient:

- Demographic variables: age (calculated from date of birth), sex, address (including full postal code), occupation
- Presenting health status
  - Symptoms (for example, weight loss, dysphagia, gastrointestinal bleeding, abdominal pain, jaundice)
  - American Society of Anaesthetists (ASA) anaesthetic risk grade
  - Concurrent illness (especially ischaemic heart disease, hypertension, diabetes, chronic obstructive airway disease or asthma)
  - Concurrent medication
  - Smoking and drinking status

- Investigations performed (and whether pre- or post-operative)
  - Radiology and endoscopy (including abdominal ultrasound, endoscopic ultrasound, chest x ray, contrast swallow, computerised tomography (CT), angiography, magnetic resonance imaging (MRI), oesophageo-gastro-duodenoscopy (OGD), endoscopic retrograde cholangio-pancreatography (ERCP), laparoscopy, percutaneous transhepatic cholagiopancreatography (PTC), bronchoscopy)
  - Chemical pathology (including liver function tests, albumin levels, urea, creatinine, electrolytes, amylase, calcium, glucose, blood gases)
  - Histopathology and cytology
  - Haematology (first haemoglobin levels, and numbers of full blood counts)
  - Other diagnostic tests (electrocardiograms, pulmonary function tests)
- Treatments
  - Surgery (names of all procedures were recorded)
  - Stent insertion
  - Radiotherapy (pre- or post-operative, dose, internal or external, whether part of trial)
  - Chemotherapy (agents, doses, number of cycles, start and end dates)
  - Laser
  - Note that other treatments, including analgesia and nutritional supplementation, were not recorded, following a pilot study which found recording of complete drug information to be unfeasible because of its variety and quantity.
- Hospital attendance
  - Numbers of outpatient and day case visits, with corresponding hospital codes
  - Dates of admission and discharge, with corresponding hospital and consultant codes
  - Whether first admission, and main therapeutic intervention, were elective or as emergency

- Dates were recorded to measure time elapsed between the following points:
  - From referral to admission
  - From referral to first hospital attendance
  - From referral to diagnosis
  - From referral to first treatment
  - From first hospital attendance to first treatment

### 3.4.1.2 Defining and coding key variables

#### *Cancer staging*

Cancer stage was regarded as the most important prognostic variable. The research associates coded tumour, node and metastatic (T, N and M) grades, after examining all relevant and available information, including results of radiological and pathological investigations and surgeons' operation notes. The statistical analysis program, written by the author, then categorised patients according to American Joint Committee on Cancer staging, as specified in Table 3.1.[172] The stage coding algorithm was checked using a variety of cases. Because of the relatively small numbers of patients in several of the staging subgroups, in the final analysis stages were grouped into four categories: "Early" (stages I-III), "Incompletely staged" (T+ or N+ with other TNM data missing), "Advanced" (stage IV) or "Unstaged" (no T, NM data).

**Table 3.1 Cancer staging according to tumour, nodal and metastic involvement[172]**

| Pancreatic | Oesophageal | Gastric |
|---|---|---|
| Stage 0 | Stage 0 | Stage 0 |
| Tis, N0, M0 | Tis, N0, M0 | Tis, N0, M0 |
| Stage I | Stage I | Stage IA |
| T1, N0, M0 | T1, N0, M0 | T1, N0, M0 |
| T2, N0, M0 | Stage IIA | Stage IB |
| Stage II | T2, N0, M0 | T1, N1, M0 |
| T3, N0, M0 | T3, N0, M0 | T2, N0, M0 |
| Stage III | Stage IIB | Stage II |
| T1, N1, M0 | T1, N1, M0 | T1, N2, M0 |
| T2, N1, M0 | T2, N1, M0 | T2, N1, M0 |
| T3, N1, M0 | Stage III | T3, N0, M0 |
| Stage IVA | T3, N1, M0 | Stage IIIA |
| T4, Any N, M0 | T4, Any N, M0 | T2, N2, M0 |
| Stage IVB | Stage IV | T3, N1, M0 |
| Any T, Any N, M1 | Any T, Any N, M1 | T4, N0, M0 |
| | Stage IVA | Stage IIIB |
| | Any T, Any N, M1a | T3, N2, M0 |
| | Stage IVB | Stage IV |
| | Any T, Any N, M1b | T4, N1, M0 |
| | | T1, N3, M0 |
| | | T2, N3, M0 |
| | | T3, N3, M0 |
| | | T4, N2, M0 |
| | | T4, N3, M0 |
| | | Any T,Any N, M1 |

### *Social class*

In order to examine relationships between social class and presenting features, investigations, treatments and mortality, each patient was allocated three ecologic deprivation indicators. Townsend deprivation scores were derived from each patient's postal code, linked to enumeration district data from the 1991 census.[256] These data were obtained from the Manchester Information Datasets and Associated Services (MIDAS).

## Defining each patient's main hospital and doctor

Because a central aim of the study was to examine the influences of hospital and doctor characteristics on case mix, clinical practice, patient survival and hospital costs, it was necessary firstly to define each patient's main doctor and hospital. This was most straightforward where a patient was managed by only one consultant in one hospital. However, a quarter of all patients were managed in more than one hospital trust. In these cases a patient's main hospital was defined according to the following algorithm, which prioritises hospitals according to the therapy most likely to influence survival. If a patient underwent surgery in one hospital, then that hospital was designated as the patient's main hospital. If a patient underwent surgery in several hospitals then the hospital that

performed potentially curative surgery, or the most radical surgery, was designated as the main hospital. If a pancreatic or oesophageal patient did not have an operation but had a stent inserted, then the hospital in which the stent was inserted was designated as the main hospital. If the patient did not receive surgery nor a stent but received chemotherapy, then the hospital providing chemotherapy was designated as the main hospital. If the patient had neither surgery nor chemotherapy but had radiotherapy, then the hospital providing radiotherapy was the main hospital. If no surgery, chemotherapy or radiotherapy were provided then the first hospital that the patient attended for the cancer was designated as the main hospital.

A hospital was defined as a hospital trust. If several hospitals formed part of the same trust they were coded as a single hospital, on the assumption that a hospital trust comprises a functional unit regardless of its component buildings and departments.

A quarter of all patients were managed by more than one consultant. The patient's main doctor was defined as the consultant in whose care the patient was when receiving the main treatment. The algorithm for defining each patient's main consultant was the same as that used to define their main hospital.

Sensitivity analyses were conducted to examine whether possible misclassification of main hospital or doctor may have biased the principal results of the study. After each of the principal statistical analyses, patients managed by more than one hospital or doctor were excluded and the analyses repeated.

### Estimating hospital volume and doctor volume

The main hospital and doctor characteristics of interest were the numbers of newly diagnosed patients with each cancer managed by that hospital or doctor during the year of the study. These variables were termed the hospital volume and the doctor volume. Each patient was allotted a hospital volume and a doctor volume, which were the volumes for their main hospital and doctor. These variables were used to test the hypotheses that a patient's management, hospital resource use and survival were associated with their hospital's or their doctor's case load. The primary analyses were conducted using hospital and doctor volumes in the form of continuous variables, so as to make maximal use of available information. Additionally, the continuous volume variables were transformed into ordered categorical variables. Cutpoints were chosen so as to have roughly equal numbers of patients in each of three categories (that is low, medium and high volume) but

to have patients with the same doctor of hospital grouped together. The volume cutpoints used are reported separately as results. The purpose of using categorical volume variables was to examine the shape of volume-outcome and volume-process relationships and to make these relationships more easily interpretable.

In addition to the main doctor and hospital volume measures, doctor and hospital volumes were calculated specifically for surgery, radiotherapy and chemotherapy. For example, the surgical doctor volume for each patient who had surgery represented the number of patients with the same type of cancer who were operated on by the respective surgeon during the year. The robustness of the results to assumptions about patients' main hospitals or doctors is reported in the respective Results sections of this thesis.

### Data missing from patients' hospital records

Inevitably, some data were incompletely recorded in patients' hospital records. Missing data were most likely for variables recorded at the doctors' discretion, such as assessments of patients' clinical condition. Missing data were less likely for routinely recorded information, including outpatient attendance and dates of admission and discharge. Surgical procedures were likely to be recorded completely in case of future litigation, although the amount of detail in surgeons' operation notes varied. In all hospitals, test results were routinely filed in patients' notes, but it is possible that some pages of results may have gone missing. It was assumed that if there was no record of patients having received a test or treatment, then they had not received it.

However, for several key prognostic variables, data were missing because patients had not had the necessary investigations, partly because of their doctors' assessment of their prognosis. To avoid circularity in analysis of prognostic factors, if data on a prognostic variables were missing then they were recorded as missing and analysed as such. For example, if it was not known whether or not a patient had metastatic tumour spread, then their metastatic status was recorded as 'unknown'; the metastasis variable had three categories: 'present', 'absent' or 'unknown'.

If symptoms and co-existing disease were not recorded then patients were assumed not to have them. This is justified because these factors were usually recorded if present but were not recorded if absent, and non-recording was less likely to be due to doctors' assessment of a patient's prognosis than was non-recording of information that required a special investigation.

## 3.4.2 Mortality data from the NHS Central Register

Patients' survival was tracked with the NHS Central Register, which was able to track all but three patients and to identify them as dead or alive on the date of checking. For patients who had died, draft death certificates were obtained from the same source. The certificates specified dates of birth and death, causes of death, and occupation (or in the case of married women, husband's occupation). These occupational data were used to categorise patients' social class according to the Registrar General's classification. The first set of searching was completed on 31 October 1998, providing dates of death or censorship for the survival analysis.

## 3.4.3 Resource use and costs of hospital care

The cost analysis aimed to estimate the cost of hospital care provided to each patient in the cohort within a year of first presentation. These estimated costs were then compared between patients with more or less advanced disease, between those receiving or not receiving potentially curative treatment, and between those managed by hospitals or doctors with different patient volumes.

The cost analysis was restricted to health care provided by hospitals. The study excluded costs of health care provided outside hospital, and costs to patients, their families and wider society. Although the latter costs were of interest, their accurate estimation required major additional surveys which were beyond the capacity of the research team. Furthermore, because many patients had already died by the time the research team was notified of their diagnosis, it would not have been possible to interview them to obtain accurate cost estimates. Hospital costs were most directly relevant to the development of the NHS cancer programme, because reorganisation of hospital cancer care was its central and most costly aspect.[4]

A small proportion of patients included in the study was partly managed at hospitals excluded from the study; for those patients costs of care at the other hospitals were obtained by examining patients notes at the latter hospitals.

Each patient's cost of hospital care was estimated by multiplying the number of units of each resource item consumed by that patient with the respective unit cost, and summing these products for all types of resource item. The quantities of resources used by each

patient within one year of first presentation were obtained by examination of each patient's hospital records.

Unit costs of each resource item were obtained by a postal questionnaire survey of all participating hospitals. It was known in advance that many NHS hospitals did not calculate unit costs for each of type of resource item examined in this study. Furthermore it was known that hospitals varied widely in their costing methods, including their methods of allocating overhead costs to specific resource items.[236] It was thus not possible to obtain a unit cost for each resource item in each hospital that was valid and comparable between hospitals. Therefore for each resource item the same unit cost estimate was used for all hospitals. This unit cost estimate was the mean reported cost, obtained by the questionnaire survey. For two resource items – endoscopy and gastrectomy – the median unit cost was used instead of the mean unit cost, because the mean unit costs appeared to be implausibly high due to extremely high unit costs reported by one hospital in each case. Sensitivity analysis was used to examine the sensitivity of the estimated total cost of hospital care to the unit costs used, when the mean unit cost for each type of resource was replaced by the highest and then the lowest unit costs. For the most important resource item – inpatient days – first and third quartiles of unit cost were also used in the sensitivity analyses.

The main types of resources were days of ward care, outpatient and day case attendances, tests performed, surgical procedures, chemotherapy and radiotherapy. Each of these had several subheadings, as listed above under 'Variables obtained from hospital records'. Some of these variables, such as ward days or surgical procedures, represented complex mixes of resources. The cost of days in a ward included costs of accommodation, nursing, doctors, and drugs dispensed to inpatients but excluded costs of tests or surgical procedures, which were recorded separately, to avoid double counting. The cost of an operation included theatre costs but excluded intensive care or ward costs.

An additional variable - cost of hospital care per day of life - was calculated by dividing the total cost of hospital care by the survival time, up to a maximum survival time of 365 days. The reason for censoring survival time at one year was so as to make the cost and survival data equivalent, and comparable for all patients that had not died within a year. 31% of all patients survived for more than a year and thus had their costs censored in this way.

## 3.5 Statistical analysis

Raw data were stored in Access databases. Data were analysed using Stata (Release 5) statistical software.[237] Conventional statistical methods were used for summary description of variables.[237, 238] Proportions and their 95% confidence intervals were used to describe categorical variables. Normally distributed continuous variables were described using means and standard deviations, standard errors of means, and 95% confidence intervals of means. Continuous variables with skewed distributions were described using medians, ranges and inter-quartile ranges. Frequency distributions of continuous variables were examined by plotting histograms.

Similarly, conventional statistical tests were used to test hypotheses.[237, 238] Proportions were compared using Pearson's $\chi^2$ test or, if expected frequencies for any cell were 5 or less, using Fisher's exact test. For normally distributed continuous variables, means were compared using Student's t test. Correlation between normally distributed continuous variables was examined using Pearson's method. Correlation between continuous variables with non-normal distributions, or between a continuous variable and an ordered categorical variable, was examined using Spearman's method of rank correlation. A 5% significance level was used for testing hypotheses. However, statistical analysis emphasised estimation of differences and ratios, with 95% confidence intervals, rather than hypothesis testing. To examine the relationships between doctor or hospital volumes, and binary variables (such as symptoms or comorbidities, whether patients received specific tests or treatments, or operative mortality or one year survival), logistic regression was used.

To examine the independent relationships between one outcome variable and several explanatory variables, the following multivariable methods were used. Multiple logistic regression was used if the dependent variable was binary. Multiple linear regression was used if the dependent variable was continuous and normally distributed; this was mainly used for analysis of costs. If the continuous dependent variable had a positively skewed distribution, then the natural logarithm of each value was used in the multiple linear regression, provided that logarithmic transformation resulted improved the fit to a normal distribution. Cox's proportional hazards model was used for multivariable survival analysis after examining Kaplan-Meier survival curves and complementary log log plots

to ensure proportionality of hazards between categories of explanatory variables throughout the period of follow-up.[239]

In all multivariable models, explanatory variables were considered for insertion into the respective model if they were thought *a priori* to be potentially causally related to the outcome, or to be potential confounding factors. Automatic stepwise regression was not used – instead emphasis was placed on thoughtful prior model specification and model development based on examination of the main explanatory or confounding factors. A key aim was to control for case mix differences between different hospitals and different doctors so as to show the independent influences of hospital and doctor characteristics on clinical practices, health outcomes and costs. The change in the fit of a model after inclusion of each variable was assessed using likelihood ratio tests. Explanatory variables were removed from a model if they were found not to be independently associated with the respective outcome, and not to influence the magnitude of regression coefficients, odds ratios or hazard ratios for the putative causal factors of interest. Explanatory variables were only entered into models if they were likely to have occurred before the respective outcome, because causes must precede effects.

The following groups of explanatory variables were considered to be potential influences on the respective outcomes.

- Doctor and hospital volumes, and patients' age, sex, and Jarman and Townsend deprivation scores were examined in all models as potential influences on health care and prognosis.
- Influences on choice of diagnostic tests performed: symptoms and co-morbidity at presentation.
- Influences on choice of treatments given: symptoms, co-morbidity, preceding test results.
- Influences on mortality and survival: symptoms, co-morbidity, test results, treatments. Treatments were considered to be prognostic indicators because, for example, a surgeon's decision to perform a resection was based largely on their assessment of the degree of tumour spread and the patient's ability to survive major surgery.
- Influences on cost: patient's health status indicators, mode of admission, treatments provided.

In the regression analyses of predictors of cost, and cost per day of life, addition of the quadratic doctor volume terms significantly improved the respective models. In order to make the relationships between these cost and volume variables more easily interpretable, they were plotted graphically using Excel. The regression equations were used, with total cost, or cost per day of life, as the outcome variable. For each explanatory variable the coefficient from the regression model was multiplied by the mean value of the respective variable in the study population. These products were then summed and added to the regression constant to give an expected cost, or cost per day of life, for a range of doctor volumes, assuming that the other explanatory variables had the same distributions for all doctor volumes. The ranges of doctor volumes examined were those observed for the respective cancer.

The principal unit of analysis was a patient and the primary analyses assumed independence between patients. The potentially clustered nature of the data necessitated additional analysis, however. It was plausible that patients managed by the same doctor or the same hospital could be more similar to each other than would be expected if they were randomly sampled from the whole population. If substantial intra-doctor or intra-hospital correlation (that is, clustering) was present then the standard errors and confidence intervals obtained while assuming that patients were entirely independent of each other could be underestimated. Stata was used to examine the degree of intra-doctor and intra-hospital correlation for the main outcome measures, using the '11way' procedure. Adjusted standard errors and 95% confidence intervals were obtained by using the 'cluster' option in Stata's multiple logistic and Cox's proportional hazards procedures.[240]

# 4. PANCREATIC CANCER

## 4.1 Numbers of cases, hospital and doctor volumes

A total of 782 patients with pancreatic cancer were identified. Three quarters of all patients were managed in only one hospital trust (n=582), and the remaining quarter (n=200) were managed in at least two hospital trusts. 768 (98%) patients had received their main treatment in one of 31 acute hospital trusts in the area covered by the study. 28 hospitals were in South and West England and 8 were in south Wales. Another 14 patients received their main treatments in one of 9 hospital trusts outside the region. The hospital volumes of each trust are shown in Table 4.1. The number of patients per hospital ranged from 3 to 52 (median 23), and about a third (36%) of all patients were managed by the six hospitals with the largest patient volumes.

The corresponding doctor volumes (annual numbers of cases per doctor who provided the main treatment) are shown in Table 4.2, in less detail than hospital volumes because of the numerous doctors. A total of 224 main doctors were identified within the region: 19 were categorised as high volume doctors, 62 as medium volume doctors and 143 as low volume doctors. Volume cutpoints were chosen so as to have similar numbers in each category. The distribution of patients per doctor was highly skewed. The median number of patients per doctor was 2 (range 1-20; IQR 1-4) and the mean was 3.3 (SD 3.7). Twelve doctors managed at least one new patient every month, on average, and at the other end of the spectrum 102 doctors managed only one patient per year.

**Table 4.1. Hospital volumes: numbers of patients per hospital trust**

| Hospital code | No cases |
|---|---|
| **High volume hospitals** | **(n>35)** |
| A | 52 |
| B | 51 |
| C | 50 |
| D | 48 |
| E | 39 |
| F | 37 |
| All high volume | 277 |
| **Medium volume hospitals** | **(24≤n≤35)** |
| G | 33 |
| H | 33 |
| I | 30 |
| J | 29 |
| K | 28 |
| L | 28 |
| M | 25 |
| N | 24 |
| All medium volume | 230 |
| **Low volume hospitals** | **(n<24)** |
| O | 23 |
| P | 23 |
| Q | 22 |
| R | 21 |
| S | 21 |
| T | 19 |
| U | 17 |
| V | 17 |
| W | 16 |
| X | 14 |
| Y | 14 |
| Z | 13 |
| AA | 13 |
| BB | 11 |
| CC | 11 |
| DD | 3 |
| EE | 3 |
| All low volume | 261 |
| Out of region* | 14 |
| Total | 782 |

* One hospital had 4 cases, one had 3, and 7 had one each; hospital volumes not specified for these patients

**Table 4.2. Distribution of doctor volumes and patients**

| Doctor volume category | No. of doctors | Range of patients per doctor | No. of patients in category |
|---|---|---|---|
| Low volume | 143 | 1-3 | 242 |
| Medium volume | 62 | 4-9 | 245 |
| High volume | 19 | 10-20* | 255 |
| Doctor not identified** | - | - | 28 |
| Main treatment outside region** | - | - | 12 |
| Total | 224 | 1-20 | 782 |

* Median 12 ** Doctor volumes not specified for these patients

The relationship between hospital and doctor volume categories is shown in Table 4.3. Doctor volumes were significantly correlated with hospital volumes (Spearman's rho = 0.14; $p<0.0001$). However 23% of patients were managed by low volume doctors in high volume hospitals, or by high volume doctors in low volume hospitals ((86+85)/742).

**Table 4.3. Distribution of patients by doctor and hospital volume category**

| Hospital volume<br>Doctor volume | Low | Medium | High | Total |
|---|---|---|---|---|
| Low | 103 | 53 | 86 | 242 |
| Medium | 67 | 114 | 64 | 245 |
| High | 85 | 53 | 117 | 255 |
| Total | 255 | 220 | 267 | 742 |

## 4.2 Case mix: age, sex, comorbidity, symptoms, stage

The male:female ratio was 50%:50%. Most patients were elderly and the age distribution was slightly negatively skewed (mean age 72 years, median 73, range 23-96; IQR 65-80). About half (53%) of cases had some chronic comorbidity at the time of presentation, and 24% had more than one of the comorbid conditions considered. Between one tenth and one sixth of patients had ischaemic heart disease (IHD), chronic obstructive airway disease (COAD), diabetes or hypertension (Table 4.4). None of these factors, except for age, was significantly associated with either hospital or doctor volumes. Age was significantly and inversely associated with doctor volumes (Spearman's rank correlation coefficient = -0.08; P−0.029) but not with hospital volumes (Spearman's rank correlation coefficient − -0.060; P =0.098). Half of patients were initially admitted as emergency cases and this was more likely for patients of low volume doctors.

Slightly over half of patients were recorded as having jaundice, weight loss, or abdominal pain (Table 4.4). Patients of high volume doctors were significantly more likely to have jaundice and marginally less likely to present with vomiting. No other symptom was associated with doctor volume and no symptom was associated with hospital volume. Neither initial haemoglobin nor serum albumin levels were associated with doctor or hospital volumes (P>0.2 and Spearman's rank correlation coefficients <0.05 for all 4 comparisons, that is: for haemoglobin vs. doctor volume, for haemoglobin vs. hospital volume, for albumin vs. doctor volume and for albumin vs. hospital volume).

**Table 4.4. Age, sex, comorbidity and presenting symptoms**

| | Total | | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | | | 261 | 100 | 230 | 100 | 277 | 100 | | 242 | 100 | 245 | 100 | 255 | 100 | |
| Age (mean years) | 71.6 | | 72.6 | | 71.3 | | 71.2 | | 0.10 | 73.3 | | 70.4 | | 71.2 | | 0.03 |
| Sex (% female) | 394 | 50 | 132 | 51 | 129 | 56 | 127 | 49 | 0.37 | 126 | 52 | 128 | 52 | 116 | 45 | 0.11 |
| Elective first admission | 379 | 52 | 124 | 51 | 130 | 60 | 118 | 44 | 0.89 | 128 | 66 | 118 | 52 | 112 | 47 | 0.01 |
| **Comorbidity** | | | | | | | | | | | | | | | | |
| COAD | 74 | 10 | 25 | 10 | 22 | 10 | 27 | 10 | 0.52 | 26 | 11 | 22 | 9 | 24 | 9 | 0.73 |
| IHD | 100 | 13 | 40 | 15 | 20 | 9 | 40 | 14 | 0.80 | 31 | 13 | 32 | 13 | 36 | 14 | 0.52 |
| Hypertension | 134 | 17 | 45 | 17 | 42 | 18 | 47 | 17 | 0.92 | 38 | 16 | 43 | 18 | 48 | 19 | 0.36 |
| Diabetes | 114 | 15 | 39 | 15 | 39 | 17 | 35 | 13 | 0.42 | 36 | 15 | 31 | 13 | 42 | 16 | 0.50 |
| No. of chronic diseases (mean) | 0.93 | | 1.0 | | 0.85 | | 0.89 | | 0.20 | 0.92 | | 0.85 | | 1.0 | | 0.40 |
| **Symptoms** | | | | | | | | | | | | | | | | |
| Jaundice | 459 | 59 | 162 | 62 | 132 | 57 | 160 | 58 | 0.87 | 108 | 45 | 159 | 65 | 164 | 64 | <0.001 |
| Weight Loss | 443 | 57 | 144 | 55 | 124 | 59 | 155 | 56 | 0.83 | 132 | 55 | 138 | 56 | 151 | 59 | 0.25 |
| Abdominal Pain | 398 | 51 | 148 | 52 | 108 | 53 | 134 | 48 | 0.27 | 128 | 53 | 126 | 51 | 129 | 51 | 0.46 |
| Vomiting | 123 | 16 | 41 | 16 | 38 | 17 | 41 | 15 | 0.59 | 45 | 19 | 43 | 18 | 30 | 12 | 0.07 |

*# P value from logistic regression* with continuous explanatory volume variable, except Spearman's rank correlation for age and no. chronic diseases

Cancer staging, as judged by the end of the study period, provides a clearer view of the severity of the cancer, and how this varies according to doctor and hospital volume. It is apparent that few patients had early stage, and thus curable, disease (Table 4.5). Only 6% of cases were in stages I, II or III, and 31% had confirmed metastatic disease. Over half of cases had no T, N or M staging, and another 11% were partially staged. The overall P values from Pearson's $\chi^2$ tests show that staging varied significantly between hospital volumes but not between doctor volumes. In order to interpret this in more detail the staging categories were collapsed into various binary staging variables. This showed that early stage (I-III) disease was significantly more likely with increasing doctor volume and hospital volume. Confirmed metastatic disease was significantly more likely with decreasing doctor volume but was not associated with hospital volume. Completely unstaged disease was more likely with decreasing hospital volume, but not significantly so and was not associated with doctor volume. The respective P values should be regarded with caution as they were obtained by multiple comparison after recoding the staging variable and so they are not reported in detail here.

Other key prognostic variables were tumour location and histology. Two thirds of patients had tumours confined to the head or ampulla, in which resections are more likely to be possible (Table 4.6). However the validity of this localisation must be interpreted in the light of the investigations performed (see section 4.3 below). Forty percent of patients had a biopsy at some stage and, of these, 76% had adenocarcinoma, the rest having unspecified carcinoma, villous (n=1) or endocrine (n=4) tumours.

**Table 4.5. Pathological staging**

| | Total | | Hospital Volumes | | | | | | Doctor Volumes | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | | | 261 | | 230 | | 277 | | | 242 | | 245 | | 255 | | |
| **Detailed staging** | | | | | | | | | | | | | | | | |
| I | 24 | 3 | 3 | 1 | 7 | 3 | 14 | 5 | | 4 | 2 | 4 | 2 | 13 | 5 | |
| II | 5 | 1 | 1 | 0.4 | 2 | 1 | 2 | 1 | | 0 | 0 | 2 | 1 | 3 | 1 | |
| III | 18 | 2 | 3 | 1 | 5 | 2 | 10 | 4 | | 6 | 2 | 4 | 2 | 8 | 3 | |
| IV | 239 | 31 | 82 | 31 | 68 | 30 | 85 | 31 | | 94 | 39 | 74 | 30 | 65 | 25 | |
| Partially staged | | | | | | | | | | | | | | | | |
| T+orN+ | 44 | 6 | 15 | 6 | 8 | 3 | 18 | 7 | | 9 | 4 | 17 | 7 | 14 | 5 | |
| M0 | 45 | 6 | 14 | 5 | 13 | 6 | 17 | 6 | | 9 | 4 | 14 | 6 | 20 | 8 | |
| Unstaged* | 407 | 52 | 143 | 55 | 127 | 55 | 131 | 47 | 0.03 | 120 | 50 | 130 | 53 | 132 | 52 | 0.59 |
| **Combined stages** | | | | | | | | | | | | | | | | |
| "Early" (I-III) | 47 | 6 | 7 | 3 | 14 | 6 | 26 | 9 | | 10 | 4 | 10 | 4 | 24 | 9 | |
| "Intermediate" (T+ or N+ or M0) | 89 | 11 | 29 | 11 | 21 | 9 | 35 | 13 | | 18 | 7 | 31 | 19 | 34 | 13 | |
| "Late" (IV) | 239 | 31 | 82 | 31 | 68 | 30 | 85 | 31 | | 94 | 39 | 74 | 30 | 65 | 25 | |
| Unstaged* | 407 | 52 | 143 | 55 | 127 | 55 | 131 | 47 | 0.02 | 120 | 50 | 130 | 53 | 132 | 52 | 0.41 |

# P value from Pearson $\chi^2$ test. * No T, N or M pathological staging

**Table 4.6. Tumour location**

| Location | N | % |
|---|---|---|
| Head only | 465 | 59.5 |
| Body only | 43 | 5.5 |
| Tail only | 28 | 3.6 |
| Ampulla only | 61 | 7.8 |
| Combinations | 76 | 9.7 |
| Not specified | 109 | 13.9 |
| Total | 782 | 100.0 |

In summary, the overall case mix was severe: patients tended to be elderly, have at least one serious comorbid condition, have jaundice, and to have advanced or unknown stage cancer. Higher volume doctors tended to have patients with better prognoses. This was also true of hospitals but to a much lesser, and often statistically insignificant, extent.

# 4.3 Investigations performed

The investigations performed are shown in Table 4.7. Almost all patients had abdominal ultrasound, two thirds had ERCP and over half had CT scans. Laparoscopy was rarely performed. Only a third had a biopsy and fewer had any other imaging investigation. Patients who had abdominal ultrasound were more likely also to have a CT scan ($\chi^2$ test: P 0.03) and ERCP ($p<0.001$) but CT scan and ERCP were not associated with each other (P 0.19). Patients who had preoperative CT scans were more likely to have preoperative laparoscopy (6% vs. 2%; P−0.01).

Patients of higher volume doctors were significantly more likely to have ultrasound, ERCP, and cytology, and marginally more likely to have laparoscopy (P=0.07). CT scan and biopsy were not associated with doctor volume. CT scan and cytology were more likely with higher volume hospitals.

**Table 4.7 Investigations performed**

| | Total | | Hospital Volumes | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | | | 261 | | 230 | | 277 | | | 242 | | 245 | | 255 | | |
| Abdominal ultrasound | 661 | 86 | 230 | 88 | 196 | 85 | 245 | 88 | 0.89 | 202 | 83 | 212 | 87 | 236 | 92 | <0.001 |
| ERCP | 515 | 67 | 179 | 69 | 152 | 66 | 187 | 68 | 0.47 | 109 | 45 | 185 | 76 | 202 | 79 | <0.001 |
| CT | 438 | 57 | 149 | 57 | 136 | 59 | 170 | 61 | 0.05 | 148 | 61 | 147 | 60 | 151 | 59 | 0.78 |
| Biopsy | 277 | 36 | 103 | 39 | 90 | 39 | 116 | 42 | 0.25 | 103 | 43 | 102 | 42 | 101 | 40 | 0.86 |
| PTC | 125 | 16 | 40 | 15 | 35 | 15 | 56 | 20 | 0.07 | 25 | 10 | 55 | 22 | 48 | 19 | 0.19 |
| Cytology | 154 | 20 | 52 | 20 | 40 | 17 | 72 | 26 | 0.05 | 37 | 15 | 52 | 21 | 72 | 28 | 0.002 |
| OGD | 170 | 22 | 69 | 26 | 54 | 23 | 64 | 23 | 0.50 | 76 | 31 | 50 | 20 | 58 | 23 | 0.12 |
| Laparoscopy | 33 | 4 | 12 | 5 | 14 | 6 | 9 | 3 | 0.71 | 5 | 2 | 14 | 6 | 15 | 6 | 0.07 |

# P value from logistic regression with continuous explanatory volume variable

Choice of test is likely to be determined by patient characteristics, and in particular by potential suitability for curative or palliative surgery or stent insertion, as well as by doctor and hospital characteristics. As these are interrelated, logistic regression was used to investigate the independent influences of patient, hospital and doctor characteristics on the use of specific tests. As mentioned in the Methods chapter, variables that would be unlikely to be known to doctors at the time of ordering tests, such as T or N staging, were not included in the models. The following potential influences on test provision were examined: age, sex, Townsend deprivation score, presenting symptoms (jaundice, weight loss, abdominal pain, vomiting), comorbidity (COAD, ischaemic heart disease, diabetes or hypertension), mode of admission (elective or emergency), doctor volume and hospital volume. Further model specification aimed to provide the most parsimonious yet informative model. To make the results more readily interpretable, doctor and hospital volumes, which were primarily expressed as continuous variables, were also expressed as ordinal (low medium high) categorical variables.

The logistic regression models show that older patients were significantly and independently less likely to have CT, biopsy or laparoscopy (Table 4.8). Females were less likely than males to have OGD or biopsy. Patients with jaundice were more likely to have ERCP (OR 14.7), abdominal ultrasound and PTC, and less likely to have CT or biopsy. Patients with abdominal pain were more likely to have abdominal ultrasound. Patients with vomiting were more likely to have OGD and less likely to have ERCP. Patients with low albumin levels were less likely to have cytology.

Patients of higher volume doctors were more likely to have abdominal ultrasound, ERCP and cytology (Table 4.8). They were less likely to have OGD and marginally more likely to have laparoscopy. Patients of high volume hospitals were significantly more likely to have cytology when the continuous volume variable was used, but not when the categorical volume variable was used. There were minimal differences between crude and adjusted odds ratios, suggesting that confounding by case mix was not a serious problem in these comparisons. Of all the tests examined, the tests most strongly associated with doctor volumes were ERCP (OR for high vs. low: 4.7) and OGD (OR for high vs. low: 0.64).

The investigations with which deprivation scores were associated, independently of the variables shown in Table 4.8, were computed tomography and biopsy, which were

significantly less likely with increasing deprivation score. The adjusted odds ratios for computed tomograpy, for unit increases in Townsend deprivation score, 0.92 (0.86-0.98; P 0.006). The adjusted odds ratios for biopsy, for unit increases in Townsend deprivation score, was 0.91 (0.85-0.97; P 0.004).

**Table 4.8a. Predictors of test use: logistic regression models**

| Test | Doctor or hospital volume; as categorical or continuous | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI and P value | Other variables in full model** | OR | 95% CI | n/N ~ |
|---|---|---|---|---|---|---|---|---|---|
| Abdominal ultrasound | Doctor volume* | 1 09 | 1.04-1.14 | 1.07 | 1.02-1.12 | Jaundice | 2.7 | 1.7-4.4 | 683 742 |
| | | | | | *P 0 003* | Abdominal pain | 1.9 | 1.2-3.0 | |
| | Low | 1.0 | - | 1.0 | - | Chronic disease | 1.9 | 1.2-3.1 | |
| | Medium | 1.3 | 0.77-2.1 | 1.07 | 0 64-1 8 | | | | |
| | High | 2.5 | 1.4-4.4 | 2.1 | 1.1-3.7 | | | | |
| | | | | | *P 0 04* | | | | |
| ERCP | Doctor volume* | 1.11 | 1.08-1.15 | 1.10 | 1.07-1.15 | Jaundice | 14.8 | 9.8-22.1 | 522 742 |
| | | | | | *P<0 001* | Vomiting | 0.55 | 0.33-0.92 | |
| | Low | 1.0 | - | 1.0 | - | | | | |
| | Medium | 3.8 | 2.6-5.5 | 3.6 | 2.2-5.7 | | | | |
| | High | 4.7 | 3 1-6.9 | 4.7 | 2.9-7.8 | | | | |
| | | | | | *P<0.001* | | | | |
| CT | Hospital volume* | *1.01* | 1.00-1.02 | 1.01 | 1.00-1.02 | Age* | 0.91 | 0.89-0.93 | 465 767 |
| | | | | | *P 0.15* | Jaundice | 0.60 | 0.43-0.83 | |
| | Low | 1.0 | - | 1.0 | - | | | | |
| | Medium | 1.1 | 0.76-1.6 | 0.97 | 0.65-1.5 | | | | |
| | High | 1.2 | 0.85-1.7 | 1.1 | 0.72-1.5 | | | | |
| | | | | | *P 0 92* | | | | |
| Biopsy | Doctor volume* | 1.00 | 0.98-1.03 | 1.00 | 0.98-1.03 | Age* | 0.96 | 0.94-0.97 | 305 741 |
| | | | | | *P 0.75* | Sex (F vs. M) | 0.62 | 0.45-0.85 | |
| | Low | 1.0 | - | 1.0 | - | Jaundice | 0.39 | 0.28-0.53 | |
| | Medium | 1.0 | 0.67-1.4 | 1.0 | 0.69-1.51 | | | | |
| | High | 0.89 | 0.62-1.3 | 0.92 | *0.62-1.35* | | | | |
| | | | | | *P 0.84* | | | | |

Legend: * Continuous variable ** With continuous doctor or hospital variable in model No of events No. of patients in model

**Table 4.8b. Predictors of test use: logistic regression models (continued)**

| Test | Doctor or hospital volume | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI & and P ## | Other variables in full model * | OR | 95% CI | n N ~ |
|---|---|---|---|---|---|---|---|---|---|
| OGD | Doctor volume* | 0.98 | 0 95-1.01 | 0 98 | 0.95-1.01 | Sex (F vs. M) | 0.54 | 0.38-0.76 | 184 742 |
| | | | | | *P 0 12* | Vomiting | 2.0 | 1.3-3.1 | |
| | Low | 1 0 | - | 1.0 | - | | | | |
| | Medium | 0.56 | 0.37-0 85 | 0 56 | 0.37-0.84 | | | | |
| | High | 0 64 | 0 43-0.96 | 0 64 | 0.43-0.97 | | | | |
| | | | | | *P 0 01* | | | | |
| PTC | Hospital volume* | 1.01 | 1 00-1.03 | 1 01 | *1 00-1 03* | Jaundice | 4.0 | 2.4-6.7 | 128 717 |
| | | | | | *P 0 08* | Emergency admission | | | |
| | Low | 1.0 | - | 1.0 | - | (vs. elective) | 0.62 | 0.41-0.93 | |
| | Medium | 1 0 | 0.61-1.6 | 1 0 | 0.58-1.8 | | | | |
| | High | 1.4 | 0.90-2.2 | 1.4 | 0.90-2.3 | | | | |
| | | | | | *P 0 21* | | | | |
| Cytology | Doctor volume* | 1.05 | 1.02-1.08 | 1.04 | 1.00-1.07 | Albumin* | 1.04 | 1.00-1.07 | 151 702 |
| | | | | | *P 0 03* | Hospital volume* | 1.02 | 1.00-1.03 | |
| | Low | 1.0 | - | 1.0 | - | | | | |
| | Medium | 1.5 | 0.94-2.4 | 1.4 | 0.89-2.3 | | | | |
| | High | 2.2 | 1.4-3.4 | 2.0 | 1.2-3.1 | | | | |
| | | | | | *P 0.02* | | | | |
| Cytology | Hospital volume* | 1.01 | 1.00-1.03 | 1.02 | 1.00-1.03 | Albumin* | 1.04 | 1.00-1.07 | 151 683 |
| | | | | | *P 0 03* | Doctor volume* | 1.04 | 1.00-1.07 | |
| | Low | 1.0 | - | 1.0 | - | | | | |
| | Medium | 0.85 | 0.54-1.3 | 0.85 | 0.52-1.4 | | | | |
| | High | 1.4 | 0.94-2.1 | 1.4 | 0.87-2.1 | | | | |
| | | | | | *P 0.13* | | | | |
| Laparoscopy | Doctor volume* | 1.06 | 1.00-1.03 | 1.06 | 1.00-1.13 | Age* | 0.95 | 0.93-0.98 | 34 741 |
| | | | | | *P 0.08* | | | | |
| | Low | 1.0 | - | 1.0 | - | | | | |
| | Medium | 2.9 | 1.0-8.1 | 2.6 | 0.92-7.4 | | | | |
| | High | 3.0 | 1.1-8.3 | 2.8 | 1.0-8.0 | | | | |
| | | | | | *P 0.17* | | | | |

Legend: * Continuous variable ** With continuous doctor or hospital variable in model No. of events / No. of patients in model

# 4.4 Treatments provided

Few patients had potentially curative surgery, but the majority had some form of active palliative treatment (Table 4.10). 10% of patients had resections, 17% had bypass procedures, 58% had stents inserted, 12% had chemotherapy, 4% had radiotherapy and 24% had none of the treatments considered (that is, none of the above). The specific types of operative procedures are shown in Table 4.9.

**Table 4.9. Operations performed**

| Procedure | No. (N=782) | % |
|---|---|---|
| Resection | 77 | 9.8 |
| • Pancreaticoduodenectomy | 57 | 7.3 |
| • Pancreaticoduodenectomy (pylorus preserving) | 12 | 1.5 |
| • Total pancreatectomy | 1 | 0.1 |
| • Partial pancreatectomy | 4 | 0.5 |
| • Other or not specified | 3 | 0.4 |
| Bypass | 134 | 17.1 |
| • Biliary | 29 | 3.7 |
| • Gastroenterostomy | 28 | 3.6 |
| • Biliary and gastroenterostomy | 50 | 6.4 |
| • Triple | 16 | 2.0 |
| Coeliac plexus block | 18 | 2.3 |
| Laparotomy only* | 49 | 6.3 |
| Other operative procedures | 67 | 8.6 |
| Operation not specified | 11 | 1.4 |

* 17 had another procedure at another time

Table 4.10 shows the proportions of patients with each stage of disease who received each treatment. Almost all patients known to have early stage disease (I-III) had resections, and they were most likely to have any kind of treatment. They comprised only 6% of all patients, however. At the other end of the prognostic spectrum were patients with confirmed metastases (stage IV), who comprised 31% of patients. 39% of these patients had stents and 1% (n=22) had resections. 44% of Stage IV patients had none of the treatments considered, which was more likely than for any other stage. For patients with intermediate (partial) staging, the probabilities of all treatments were intermediate between those for early and advanced stages, except that this group was more likely than

any other to have a bypass procedure. The majority of patients (58%) were completely unstaged, and this group was most likely to have stents (66%); 5% had a resection, 15% had a bypass and 17% had none of the treatments considered.

Table 4.10 also shows how treatments were allocated to patients with different stages of disease (see percentages of row totals). Of resections, 54% were perf rmed in early stage patients and 29% in late stage patients. 61% of bypasses were perf rmed in unstaged patients and 27% in advanced stage patients, and 67% of stents were inserted in unstaged patients and 21% in advanced stage patients. Very few bypasses (1%) or stents (7% were performed in early stage patients.

The association between type of treatment and hospital and doctor volumes is shown in Table 4.11. Patients of higher volume hospitals were significantly m re likely to have resections and were significantly less likely to have bypass procedures r none of the treatments considered. Patients of higher volume doct rs were significantly more likely to have resections and stents and were significantly less likely t have n ne of the treatments considered. The percentages of row t tals sh w which kind f doctors or hospitals provided most of each treatment, bearing in mind that about a third of patients were in each hospital or doctor volume category. About half of all resections were done by the 19 high volume doctors, and in the 6 high volume h spitals In contrast, about half of all patients who were not actively treated were managed by low v lume doctors, who accounted for a fifth of all stents inserted. 46 % of stents were inserted in low volume hospitals.

**Table 4.10. Treatment provided by stage of disease**

| Treatment | Early (Stage I-III) | | | Intermediate (T+ or N+ or M0) | | | Advanced (Stage IV) | | | Unstaged | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Any treatment** | n | % row total | % column total | n | % row total | % column total | n | % row total | % column total | n | % row total | % column total | n | % column total |
| Resection | 42 | 54 | 89 | 10 | 13 | 23 | 3 | 4 | 1 | 22 | 29 | 5 | 77 | 10 |
| Bypass | 2 | 1 | 4 | 14 | 10 | 32 | 36 | 27 | 15 | 82 | 61 | 18 | 134 | 17 |
| Stent | 33 | 7 | 70 | 24 | 5 | 55 | 94 | 21 | 39 | 300 | 67 | 66 | 451 | 58 |
| Chemotherapy | 11 | 12 | 23 | 8 | 9 | 18 | 31 | 33 | 13 | 43 | 46 | 10 | 93 | 12 |
| Radiotherapy | 9 | 28 | 19 | 2 | 6 | 5 | 7 | 22 | 3 | 14 | 44 | 3 | 32 | 4 |
| **Combinations of treatments** | | | | | | | | | | | | | | |
| Resection & stent | 30 | 63 | 64 | 8 | 17 | 9 | 3 | 6 | 1 | 7 | 15 | 2 | 48 | 6 |
| Bypass & stent | 1 | 2 | 2 | 7 | 14 | 16 | 10 | 20 | 4 | 31 | 63 | 7 | 49 | 6 |
| Resection & chemotherapy | 9 | 69 | 19 | 2 | 15 | 5 | 1 | 8 | 0.4 | 1 | 8 | 0.2 | 13 | 2 |
| Resection & radiotherapy | 8 | 80 | 17 | 1 | 10 | 2 | 1 | 10 | 0.4 | 0 | 0 | 0 | 10 | 1 |
| Chemotherapy & radiotherapy | 6 | 29 | 13 | 1 | 5 | 2 | 3 | 14 | 1 | 11 | 52 | 2 | 21 | 3 |
| Resection & chemotherapy & radiotherapy | 6 | 86 | 13 | 0 | 0 | 0 | 1 | 14 | 0.4 | 0 | 0 | 0 | 7 | 1 |
| None of the above treatments | 0 | 0 | 0 | 8 | 4 | 18 | 105 | 55 | 44 | 78 | 41 | 17 | 191 | 24 |
| **Total** | 47 | 6 | 100 | 44 | 6 | 100 | 239 | 31 | 100 | 452 | 58 | 100 | 782 | 100 |

**Table 4.11. Treatment provided by hospital and doctor volumes**

| Treatment | Total | | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % column total | n | % column total | n | % column total | | n | % column total | n | %* | n | % column total | |
| Total | 782 | 100 | 261 | 100 | 230 | 100 | 277 | 100 | | 242 | 100 | 245 | 100 | 255 | 100 | |
| Resection | 77 | 10 | 13 | 5 | 21 | 9 | 44 | 16 | <0 001 | 16 | 7 | 21 | 9 | 36 | 14 | <0.001 |
| *% row total* | *100* | | | *16* | | *27* | | *57* | | | *22* | | *29* | | *49* | |
| By-pass | 130 | 17 | 59 | 23 | 37 | 16 | 33 | 12 | <0.001 | 43 | 18 | 43 | 18 | 39 | 15 | 0.72 |
| *% row total* | *100* | | | *46* | | *29* | | *26* | | *34* | | *34* | | *41* | | |
| Stent | 448 | 58 | 145 | 56 | 140 | 61 | 163 | 59 | 0.11 | 87 | 36 | 162 | 66 | 179 | 70 | <0.001 |
| *% row total* | *100* | | | *32* | | *31* | | *37* | | | *20* | | *38* | | *42* | |
| Radiotherapy | 31 | 4 | 12 | 5 | 7 | 3 | 12 | 4 | 0.57 | 8 | 3 | 14 | 6 | 8 | 3 | 0.89 |
| *% row total* | *100* | | | *38* | | *30* | | *36* | | | *27* | | *47* | | *27* | |
| Chemotherapy | 90 | 12 | 34 | 13 | 26 | 11 | 30 | 11 | 0.15 | 25 | 10 | 37 | 15 | 26 | 10 | 0.65 |
| *% row total* | *100* | | | *38* | | *29* | | *33* | | | *28* | | *42* | | *30* | |
| No active treatment | 191 | 24 | 79 | 30 | 53 | 23 | 55 | 20 | 0.014 | 95 | 39 | 41 | 17 | 46 | 18 | <0.001 |
| *% row total* | *100* | | | *42* | | *28* | | *29* | | | *52* | | *23* | | *25* | |

# P value from logistic regression with continuous explanatory volume variable

Logistic regression was used to assess the independent effect of each factor on each treatment provided. For each treatment, the following potential explanatory variables were examined: age, sex, deprivation scores (Townsend), emergency or elective admission, symptoms (jaundice, vomiting, abdominal pain, weight loss), comorbidity (ischaemic heart disease, COAD, diabetes or hypertension), test results (albumin, haemoglobin, presence of metastases) and doctor and hospital volumes. Tumour pathology was not considered as this would usually only be known at or after the time of treatment. Results of the regression analyses are shown in Table 4.12.

High volume doctors were twice as likely to provide resections, four times as likely to insert stents and half as likely to provide not active treatments, compared to low volume doctors, after adjusting for other explanatory variables. Doctor volume was however not associated with providing bypasses, radiotherapy or chemotherapy. High volume hospitals were four times as likely to provide resections and half as likely to provide bypasses or no treatment, compared with low volume hospitals. Hospital volumes were not associated with stents, radiotherapy or chemotherapy. The degree of confounding of hospital and doctor volumes by case mix and by each other can be assessed by comparing the crude and adjusted odds ratios for the volume variables. Adjustment had little effect on the magnitude of doctor or hospital volume effects, and did not make non-significant associations significant or vice versa. Use of continuous or categorical volume variables did not generally affect the significance of associations, except for associations between doctor volumes and resections, and between hospital volumes and no treatment.

Clinical factors associated with each treatment were as follows. Older patients were significantly less likely to have resections, bypasses, radiotherapy or chemotherapy and hence were more likely to have none of the treatments considered, independently of other clinical factors. Females were less likely to have chemotherapy. Jaundiced patients were nine times as likely to have a stent and were twice as likely to have chemotherapy. Compared to patients in whom metastases had been excluded, patients with metastases were less likely to have a resection (OR=0.03) or a stent. Vomiting patients were more likely to have a bypass. Patients with higher serum albumin levels were more likely to have resections and stents and were less likely to have no treatment. Emergency admissions were less likely to have chemotherapy. Coexisting chronic diseases did not appear to influence choice of treatment. Deprivation scores were not independently

associated with any treatment and their eclusion form the respective models did not influence the effects of doctor or hospital volumes.

**Table 4.12. Predictors of treatment provided: logistic regression models**

**4.12a. Influence of doctor volumes and other factors on treatment choice**

| Treatment | Doctor as categorical or continuous variable | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Resection | Doctor volume* | 1.08 | 1 04-1 12 | 1 06 | 1.01-1.11 | 0.03 | Age* | 0.93 | 0.90-0.95 | 69 683 |
| | Low | 1.0 | - | 1.0 | - | | Albumin* | 1.07 | 1.01-1 14 | |
| | Medium | 1.3 | 0.67-2.6 | 1.2 | 0.52-1.7 | 0.25 | M+ vs. M0 | 0.03 | 0.01-0.11 | |
| | High | 2.3 | 1.3-4.3 | 1.8 | 0.85-3.8 | | M? vs. M0 | 0.27 | 0 15-0 51 | |
| | | | | | | | Hospital volume* | 1.04 | 1.01-1.14 | |
| Bypass | Doctor volume* | 1.00 | 0.97 | 1.03 | 0.99-1.07 | 0.17 | Age* | 0.98 | 0.96-1.0 | 125 741 |
| | Low | 1.0 | - | 1.0 | - | | Vomiting | 2.3 | 1.4-3.6 | |
| | Medium | 0.99 | 0.62-1 6 | 0 97 | 0.60-1.6 | 0.97 | Hospital volume* | 0.97 | 0.95-0.98 | |
| | High | 0.84 | 0.52-1 3 | 0.94 | 0.58-1.5 | | | | | |
| Stent | Doctor volume* | 1.08 | 1.05-1.11 | 1.07 | 1.03-1.10 | <0.001 | Jaundice | 9.2 | 6.3-13.4 | 428 683 |
| | Low | 1.0 | 1.0 | - | - | | Albumin* | 1.05 | 1.01-1.08 | |
| | Medium | 3.5 | 2.4-5.0 | 3.0 | 1.9-4.8 | <0.001 | M+ vs. M0 | 0.46 | 0.28-0.75 | |
| | High | 4.2 | 2.9-6.1 | 3.9 | 2.5-6.2 | | M? vs. M0 | 1.06 | 0.63-1.6 | |
| Radiotherapy | Doctor volume* | 0.99 | 0.93-1.06 | 1.00 | 0.93-1.07 | 0.80 | Age* | 0.91 | 0.88-0.94 | 30 741 |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 1.8 | 0.73-4.3 | 1.6 | 0.61-4.1 | 0.41 | | | | |
| | High | 0.95 | 0.35-2.6 | 0.89 | 0.31-2.6 | | | | | |
| Chemo- | Doctor volume* | 0.99 | 0.95-1.03 | 0.96 | 0.92-1.01 | 0.11 | Age* | 0.91 | 0.89-0.93 | 88 693 |
| therapy | Low | 1.0 | - | 1.0 | - | | Sex (F vs. M) | 0.42 | 0.24-0.74 | |
| | Medium | 1.5 | 0.90-2.7 | 1.0 | 0.55-2.0 | 0.20 | Emergency | | | |
| | High | 0.99 | 0.55-1.8 | 0.61 | 0.31-1.2 | | admission | 0.44 | 0.24-0.78 | |
| | | | | | | | Jaundice | 2.4 | 1.4-4.2 | |
| No treatment | Doctor volume* | 0.92 | 0.89-0.95 | 0.95 | 0.92-0.99 | 0.02 | Age* | 1.02 | 1.00-1.05 | 164 702 |
| | Low | 1.0 | - | 1.0 | - | | Jaundice | 0.14 | 0.09-0.21 | |
| | Medium | 0.31 | 0.20-0.47 | 0.43 | 0.26-0.73 | 0.002 | Vomiting | 0.53 | 0.30-0.94 | |
| | High | 0.34 | 0.23-0.51 | 0.51 | 0.31-0.84 | | M+ vs. M0 | 5.9 | 3.1-11.0 | |
| | | | | | | | M? vs. M0 | 1.7 | 0.87-3.2 | |
| | | | | | | | Albumin* | 0.92 | 0.89-0.96 | |
| | | | | | | | Hospital volume* | 0.98 | 0.99-1.00 | |

## 4.12b. Influence of hospital volumes and other factors on treatment choice (continued)

| Treatment | Hospital volume as categorical or continuous variable | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Resection | Hospital volume* | 1.04 | 1.02-1 06 | 1.04 | 1 01-1.07 | <0.001 | Age* | 0.93 | 0.90-0.95 | 69 683 |
| | Low | 1 0 | - | 1.0 | - | | Albumin* | 1.07 | 1.01-1.14 | |
| | Medium | 2.1 | 1.0-4.3 | 1.5 | 0.6-3 5 | 0 007 | M+ vs. M0 | 0.03 | 0.01-0.11 | |
| | High | 3.9 | 2.0-7.6 | 3.2 | 1.4-7.1 | | M? vs. M0 | 0.27 | 0.15-0.51 | |
| | | | | | | | Doctor volume* | 1.08 | 1.04-1.12 | |
| Bypass | Hospital volume* | 0.97 | 0.95-0.98 | 0.97 | 0.95-0.98 | <0 001 | Age* | 0.98 | 0.96-0.99 | 125 767 |
| | Low | 1.0 | - | 1.0 | - | | Vomiting | 2.2 | 1.3-3.4 | |
| | Medium | 0.66 | 0.42-1.0 | 0.62 | 0.39-1.00 | 0.003 | | | | |
| | High | 0.46 | 0.29-0.74 | 0.45 | 0.27-0.71 | | | | | |
| Stent | Hospital volume* | 1.01 | 1.00-1.02 | 1.01 | 1.00-1.03 | 0.12 | Jaundice | 9.3 | 6.4-13.6 | 428 683 |
| | Low | 1.0 | - | 1.0 | - | | Albumin* | 1.05 | 1.01-1.08 | |
| | Medium | 1.2 | 0.87-1.8 | 1.5 | 0.97-2.4 | 0.19 | M+ vs. M0 | 0.47 | 0.29-0.76 | |
| | High | 1.1 | 0.81-1.6 | 1.2 | 0.75-1.8 | | M? vs. M0 | 1.1 | 0.70-1.8 | |
| | | | | | | | Doctor volume* | 1.06 | 1.03-1.10 | |
| Radiotherapy | Hospital volume* | 0.99 | 0.97-1.00 | 0.99 | 0.96-1.02 | 0.59 | Age* | 0.91 | 0.89-0.94 | 30 767 |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 0.65 | 0.25-1.7 | 0.54 | 0.19-1.5 | 0.45 | | | | |
| | High | 0.94 | 0.41-2.1 | 0.92 | 0.39-2.2 | | | | | |
| Chemotherapy | Hospital volume* | 0.99 | 0.97-1.01 | 0.99 | 0.97-1.00 | 0.32 | Age* | 0.92 | 0.90-0.95 | 79 664 |
| | Low | 1.0 | - | 1.0 | - | | Sex (F vs. M) | 0.37 | 0.21-0.67 | |
| | Medium | 0.85 | 0.49-1.5 | 0.73 | 0.36-1.5 | 0.56 | Emergency | 0.41 | 0.23-0.74 | |
| | High | 0.81 | 0.48-1.4 | 0.73 | 0.38-1.4 | | admission | 2.2 | 1.2-4.1 | |
| | | | | | | | Jaundice | 1.07 | 1.01-1.13 | |
| | | | | | | | Albumin* | 0.77 | 0.39-1.5 | |
| | | | | | | | M+ vs. M0 | 0.52 | 0.27-1.0 | |
| | | | | | | | M? vs. M0 | | | |

## 4.12c. Influence of hospital volumes and other factors on treatment choice (continued)

| Treatment | Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| None of the | Hospital volume* | 0.98 | 0.97-1.00 | 0.98 | 0.97-1.00 | 0.06 | Age* | 1.02 | 1.00-1.05 | 164 683 |
| above | Low | 1.0 | - | 1.0 | - | | Jaundice | 0.14 | 0.09-0.21 | |
| treatments | Medium | 0.69 | 0.46-1 0 | 0.60 | 0.35-1.00 | 0.03 | Vomiting | 0.53 | 0.30-0.94 | |
| | High | 0.57 | 0.38-0.85 | 0.52 | 0.31-0.86 | | M+ vs. M0 | 5.9 | 3.1-11.0 | |
| | | | | | | | M? vs. M0 | 1.7 | 0.87-3.2 | |
| | | | | | | | Albumin* | 0.92 | 0.89-0.96 | |
| | | | | | | | Doctor volume* | 0.95 | 0.92-0.99 | |

* *Continuous variable* ** *With continuous doctor or hospital variable in model* No of events No of patients in model M Metastatic status unknown

# 4.5 Survival

All patients but one were matched with the NHS Central Register. By 10 October 1998, 666 (85.2%) patients had died. The median duration of follow-up at that date was 4.5 months (range 3 days to 37.5 months) for all patients, 22.0 (range 16.4-34.4) months for survivors, and 3.4 months (range 3 days to 37.5 months) for patients that died.

## 4.5.1 Operative mortality

Operative mortality was defined as death within 30 days of the last operative procedure. The overall operative mortality rate was 16% (41/261) and did not differ significantly between patients having a resection (9 77; 12%), a bypass (23/133; 17%) or either a coeliac plexus block or laparotomy only (9 51; 18%) (P 0.51 from $\chi^2$ test). Operative mortality for these three types of procedure overall did not differ between low (16%), medium (12%) and high (18%) hospital volumes (logistic regression P=0.62). It also did not differ between low (19%), medium (12%) and high (17%) doctor volumes (P=0.94). When relationships between operative mortality and hospital and doctor volumes were examined separately for each of the three types of procedure, no associations were found (P values between 0.30 and 0.79).

Operative mortality was significantly more likely with the following patient characteristics: emergency admissions, high or no recorded ASA score, metastases, advanced cancer stage, older age, and lower albumin and haemoglobin levels. COAD and vomiting were marginally associated with operative mortality (P=0.053 and P=0.087 respectively). When the latter analyses were confined to patients having a resection, and patients who had a bypass, the associations were similar, although P values were generally larger because of smaller numbers of observations.

When the independent influences of each variable were examined in a multiple logistic regression model, most of these associations were no longer significant. With only 39 operative deaths, however, the analysis had limited statistical power. Only age, cancer stage and COAD were retained in the final model. Townsend deprivation score was not independently associated with operative mortality and its removal from the model did not influence the volumes effects. After adjusting for the latter variables there was still no

association between operative mortality and doctor or hospital volume (Table 4.13). The type of surgery was also not associated with operative mortality after adjustment for potential confounders. Table 4.13 shows that adjustment for confounders *had little* influence on the magnitude of volume-outcome effect estimates, except for the odds ratio for high volume doctors, which increased slightly from 0.86 to 1.2, but remained non-significant.

**Table 4.13. Predictors of operative mortality: logistic regression model**

| Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted OR | Adjusted 95%CI | n/N ~ |
|---|---|---|---|---|---|---|---|---|---|
| Doctor volume.* | 1.00 | 0.95-1.06 | 1.02 | 0.96-1.08 | 0.53 | Age* | 1.06 | 1.02-1.10 | 39 245 |
| | | | | | | COAD | 2.9 | 0.72-11.4 | |
| Low | 1.0 | - | 1.0 | - | 0.47 | Stage intermediate vs. I-III | 0.80 | 0.13-5.1 | |
| Medium | 0.61 | 0.26-1.5 | 0.65 | 0.25-1.7 | | Stage IV vs. I-III | 5.2 | 1.5-17.6 | |
| High | 0.86 | 0.39-1.9 | 1.2 | 0.47-2.8 | | Unstaged vs. I-III | 0.89 | 0.25-3.1 | |
| Hospital volume.* | 1.01 | 0.98-1.03 | 1.01 | 0.98-1.04 | 0.35 | | | | |
| Low | 1.0 | - | 1.0 | - | 0.30 | | | | |
| Medium | 0.72 | 0.29-1.8 | 0.52 | 0.17-1.4 | | | | | |
| High | 1.1 | 0.52-2.5 | 1.09 | 0.46-2.6 | | | | | |

* Continuous variable ** Adjusting for both doctor volume and hospital volume as continuous variables No. of events No. of patients in model

## 4.5.2 One year survival

All patients were followed for more than one year or until death. 182 patients (23% of total) survived for at least one year after first presentation to hospital. Survival to one year was significantly less likely for older patients, and patients with ischaemic heart disease, any chronic disease, weight loss, vomiting, emergency admission, metastases, nodal involvement, tumour invasion, advanced cancer stage, higher or no recorded ASA score, and lower initial haemoglobin and albumin levels. It was also significantly more likely with increasing hospital volume and with increasing doctor volume.

The independent influences of each of these factors was examined by logistic regression. This showed that most of the above explanatory variables were no longer associated with one year survival after adjustment for other covariates. The results of the final model are as shown in Table 4.14. Clinical factors independently associated with one year survival were younger age, elective admission, exclusion of metastases, and having a resection. ASA status was retained in the model because, although it was not a significant predictor, its inclusion affected the odds ratio for hospital volume, of which it was thus a confounder.

Hospital volume was strongly and significantly associated with one year survival, regardless of whether volume was expressed as a continuous or categorical variable, and regardless of adjustment for confounders. The odds ratio of 1.02 per extra patient corresponds to odds ratios of 1.1 (95% CI 1.0-1.2) for five extra patients, 1.2 (1.0-1.4) for 10 extra patients and 1.4 (1.1-1.9) for 20 extra patients. The analysis using categorical hospital volumes shows that patients of high volume hospitals were about twice as likely to survive for one year than patients of low volume hospitals, independently of other case mix variables. There was also a gradient of effect with patients of medium volume hospitals having an adjusted odds ratio that was intermediate between low and high volume hospitals. The crude odds ratios for hospital volume were slightly confounded, and decreased slightly when covariates were adjusted for, but remained significant predictors of survival. By contrast, the crude association between doctor volume and one year survival was not statistical significant. It was also strongly confounded, as seen by the reduction in odds ratios to around unity when covariates were adjusted for.

**Table 4.14. Predictors of one year survival: logistic regression model**

| Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted OR | Adjusted 95%CI | n N ~ |
|---|---|---|---|---|---|---|---|---|---|
| Doctor volume.* | 1.03 | 1.00-1.07 | 1.00 | 0.96-1.03 | 0.78 | Age* | 0.98 | 0.96-1.00 | 171 736 |
| | | | | | | Admission: emergency vs. elective | 1.8 | 1.2-2.6 | |
| Low | 1.0 | - | 1.0 | - | 0.94 | Admission: ? vs. elective | 1 6 | 0.73-3.7 | |
| Medium | 1.2 | 0.76-1.8 | 0.94 | 0.61-1.6 | | M+ vs. M0 | 0.21 | 0.12-0.37 | |
| High | 1.5 | 0.96-2.2 | 1.02 | 0.78-1.5 | | M? vs. M0 | 0.52 | 0.33-0.82 | |
| Hospital volume.* | 1.02 | 1.01-1.04 | 1.02 | 1.00-1.03 | 0.02 | ASA 3 vs. 1-2 | 1.0 | 0.47-2.3 | |
| | | | | | | ASA 4-5 vs. 1-2 | 0.58 | 0.15-2.3 | |
| Low | 1.0 | - | 1.0 | - | 0.04 | ASA? vs. 1-2 | 0.65 | 0.34-1.2 | |
| Medium | 1.4 | 0.92-2.3 | 1.2 | 0.71-2.0 | | Resection vs. no resection | 4.3 | 2.3-8.2 | |
| High | 2.2 | 1.5-3.4 | 1.8 | 1.1-2.8 | | | | | |

* Continuous variable ** Adjusting for both doctor volume and hospital volume as continuous variables ? Unknown mode of admission, or M status, or ASA status. ~ No. of events No of patients in model

## 4.5.3 Survival time

This section will firstly describe the relationships between survival time and key prognostic and treatment variables, primarily with regard to the proportionality of hazards for key prognostic variables. Thereafter the results of multivariable modelling, using Cox's proportional hazards model to estimate the independent effects of doctor and hospital volumes on survival, will be presented. Proportionality was assessed by examination of Kaplan-Meier survival curves and complementary log log plots. Figures 4.1-4.16 show that the proportionality assumption was valid for all explanatory variables except for chemotherapy and radiotherapy, for which the hazards appear to converge later in the period of follow-up. It was therefore necessary to stratify the analysis by radiotherapy and chemotherapy, which precluded obtaining valid hazard ratios for these two treatments, but did allow adjustment for their confounding.

*Figure 4.1. Survival curve for hospital volumes*

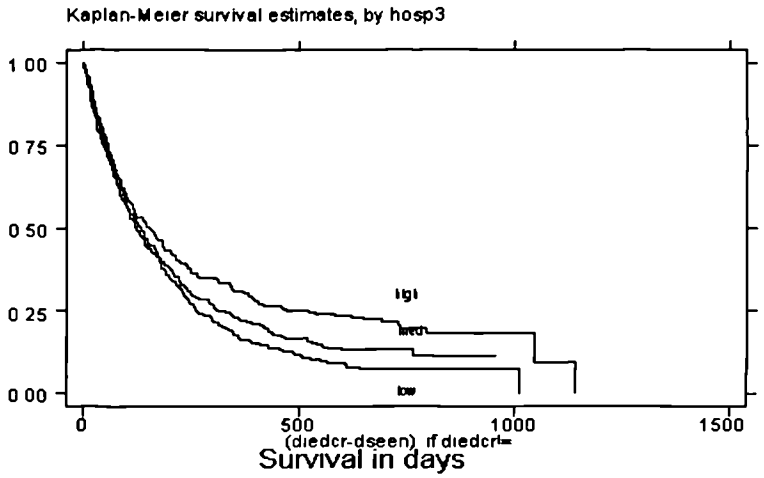


*Figure 4.2. Complementary log log plot for hospital volume*

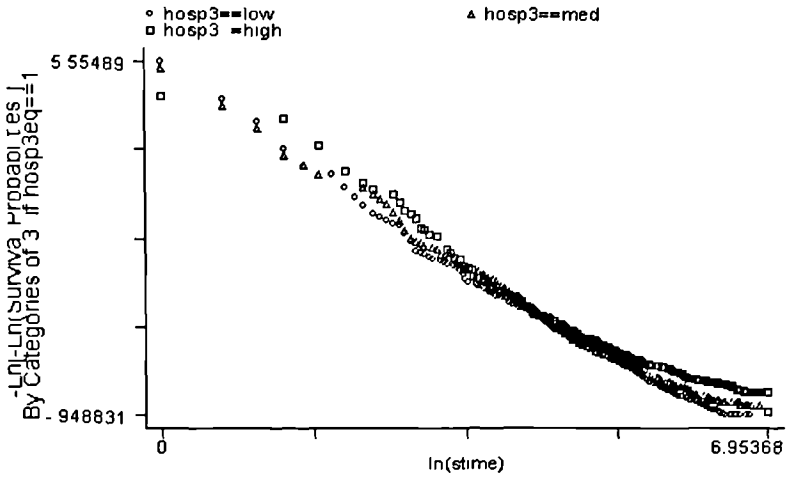



*Figure 4.3. Survival curve for doctor volumes*

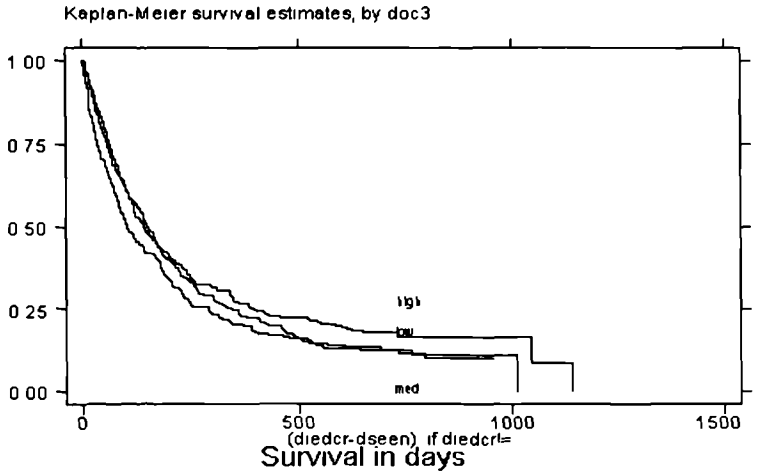



*Figure 4.4. Complementary log log plot for doctor volumes*

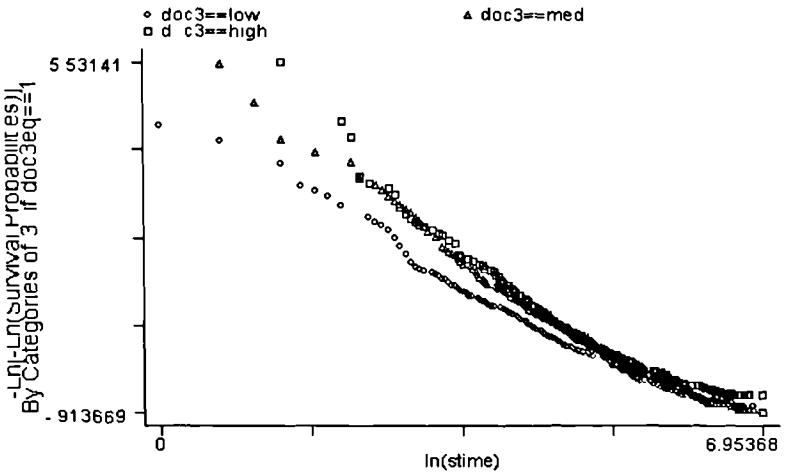


*Figure 4.5. Survival curve for cancer stage*

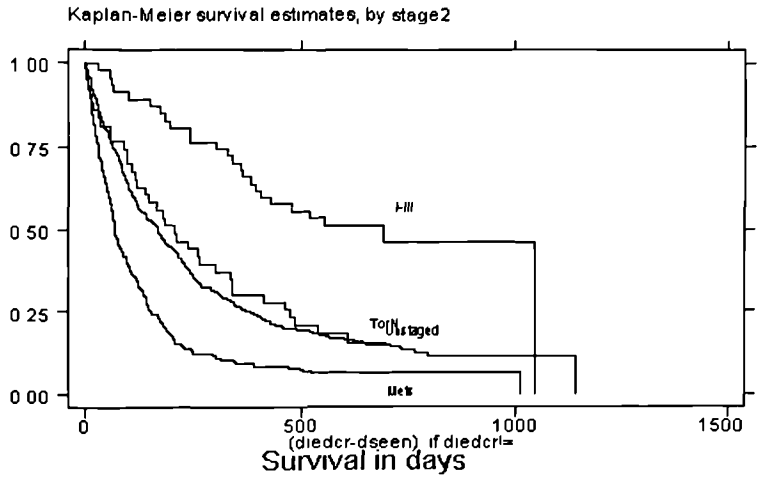



*Figure 4.6. Complementary log log plot for cancer stage*

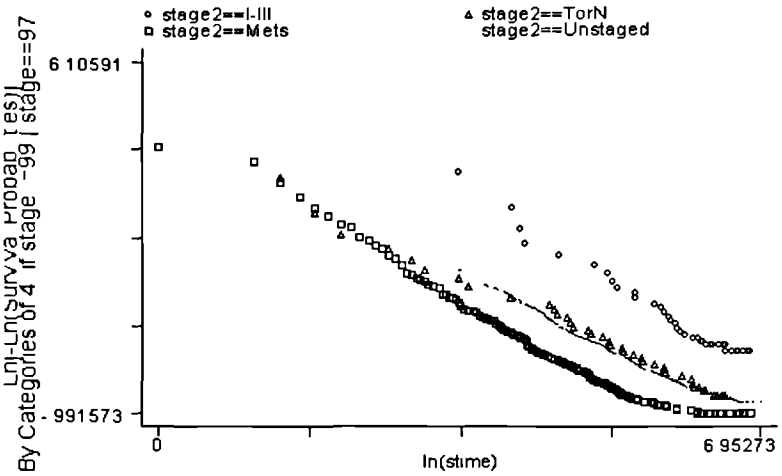



*Figure 4.7. Survival curve for resection vs. no resection*

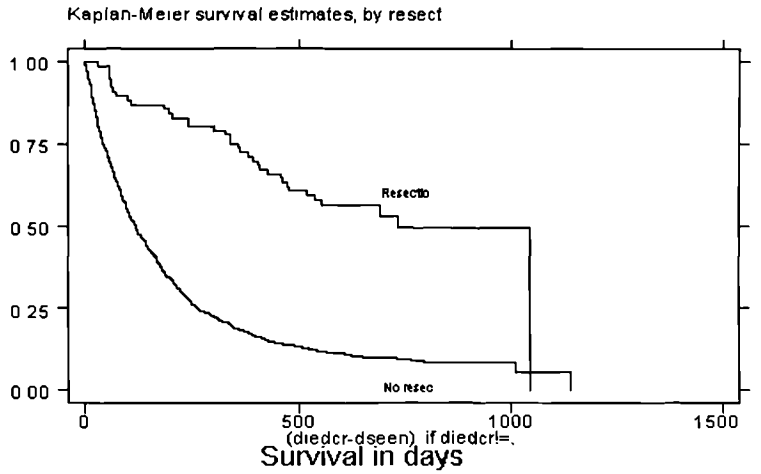


*Figure 4.8. Complementary log log plot for resection vs. no resection.*

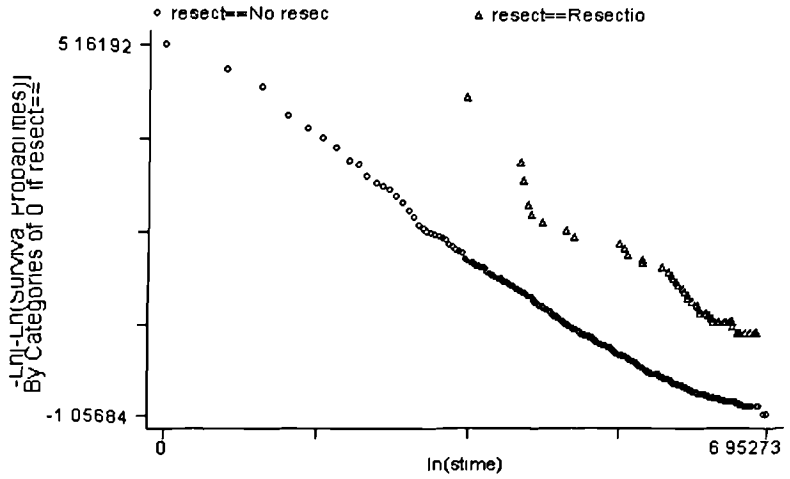



*Figure 4.9. Survival curve for age tertiles*

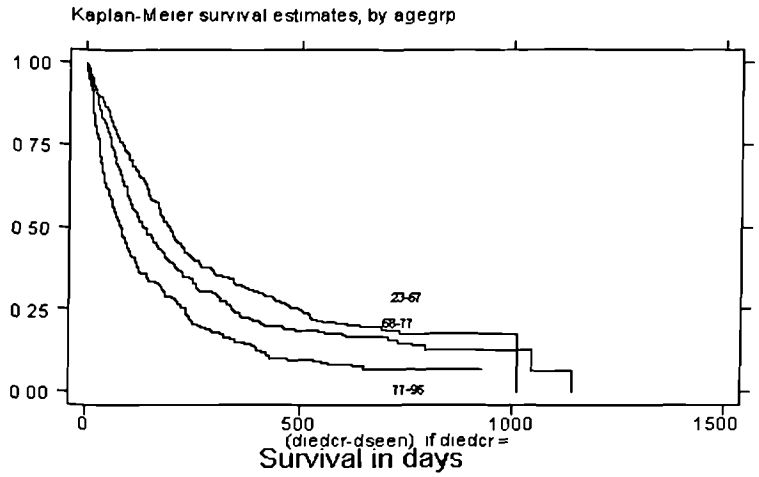



*Figure 4.10. Complementary log log plot for age tertiles*

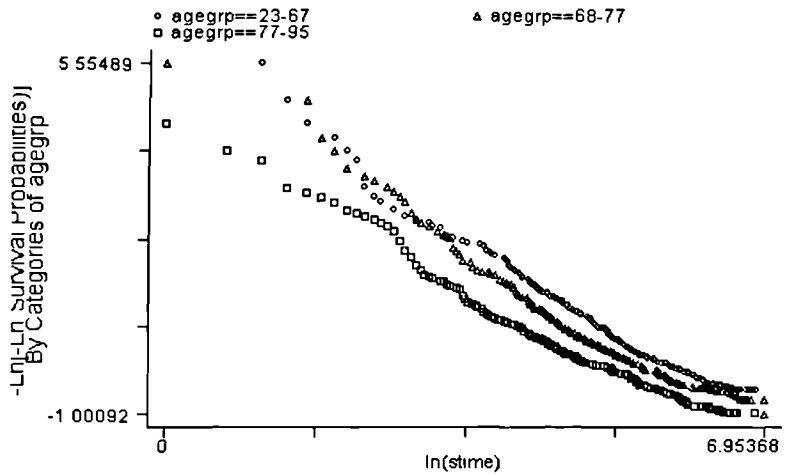


*Figure 4.11. Survival curve for chemotherapy*

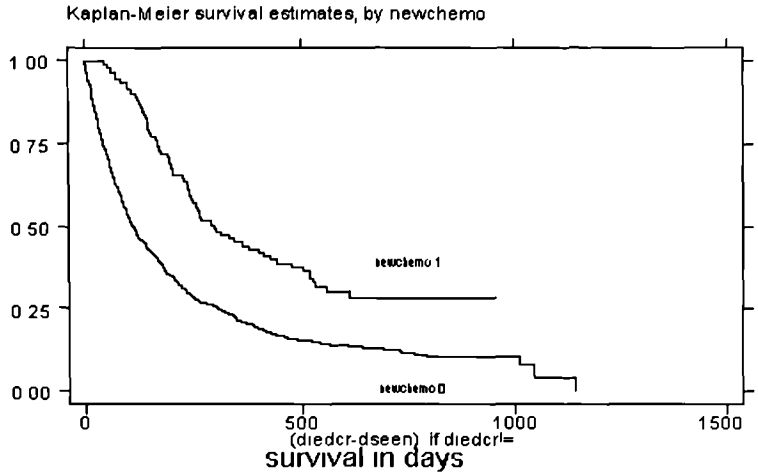



*Figure 4.12. Log log plot for chemotherapy*

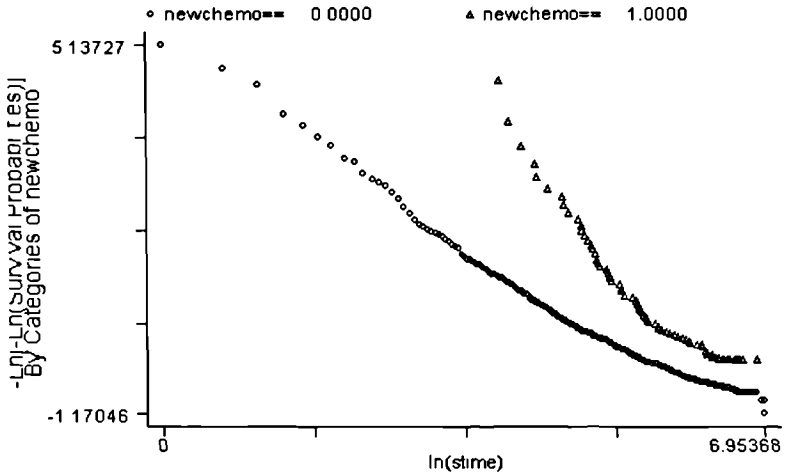



*Figure 4.13. Survival curve for radiotherapy*

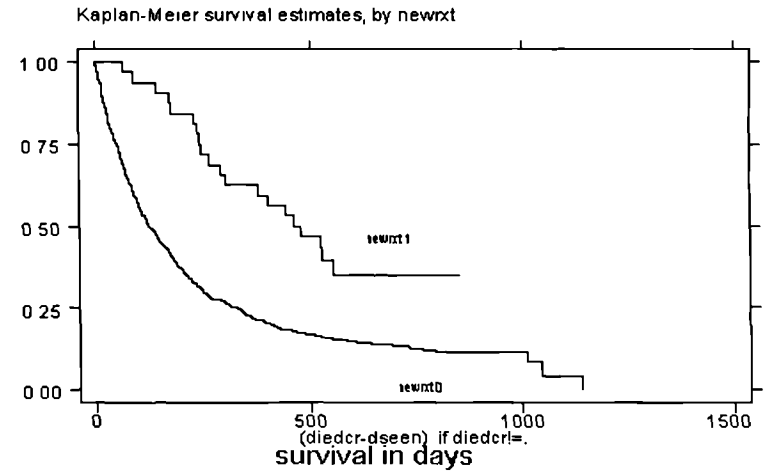
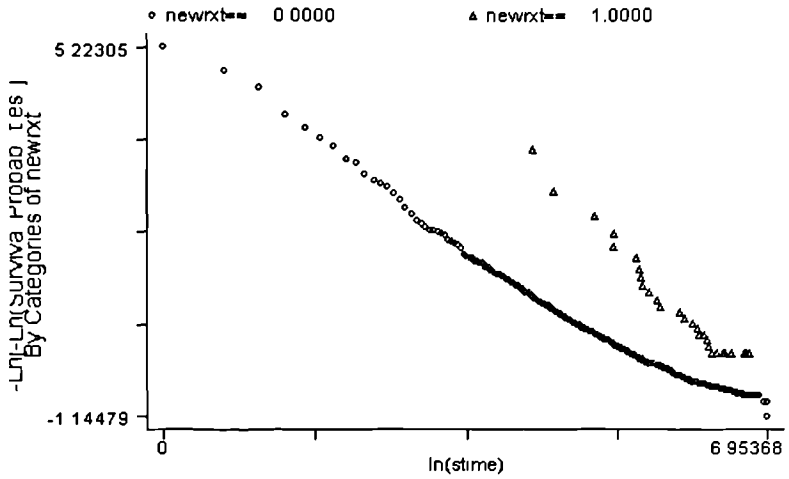


*Figure 4.14. Log log plot for radiotherapy*




The results of Cox's proportional hazards modelling are shown in Table 4.15. Hospital volume was independently and significantly associated with survival. This was true regardless of whether a continuous or a categorical volume variable was used, or whether covariates were adjusted for. The adjusted hazard ratio for continuous hospital volume of 0.99 per extra patient corresponds to hazard ratios of 0.95 (95% CI 0.92-0.98) for five extra patients, 0.89 (0.84-0.95) for 10 extra patients, 0.80 (0.70-0.90) for 20 extra patients and 0.64 (0.50-0.82) for 40 extra patients (Table 4.16). The latter figure would apply to a comparison of patients whose main hospital managed one new case per week, with patients whose main hospital managed one new case per month. The crude hazard ratio for hospital volume was not confounded, as shown by the very similar values for crude and adjusted hazard ratios. Townsend deprivation scores was not independently associated with survival time.

**Table 4.15. Predictors of survival time: Cox's proportional hazards model**

| Doctor or hospital volume as categorical or continuous variable | Crude HR | Crude 95%CI | Adjusted HR | Adjusted 95% CI | P# | Other variables in final model** | Adjusted HR | Adjusted 95%CI | n/N ~ |
|---|---|---|---|---|---|---|---|---|---|
| Hospital volume.* | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.001 | Emergency vs. elective | | | 584 701 |
| | | | | | | admission : | 1.2 | 1.0-1.5 | |
| Low | 1.0 | - | 1.0 | - | 0.005 | Admission: ? vs. elective | 0.85 | 0.58-1.3 | |
| Medium | 0.88 | 0.73-1.1 | 0.90 | 0.73-1.1 | | Albumin* | 0.97 | 0.96-0.99 | |
| High | 0.71 | 0.59-0.85 | 0.72 | 0.59-0.88 | | Ischaemic heart disease | 1.3 | 1.0-1.7 | |
| | | | | | | Diabetes | 1.3 | 1.0-1.6 | |
| Doctor volume.* | 0.98 | 0.97-0.99 | 0.99 | 0.98-1.01 | 0.46 | ASA 3 vs. 1-2 | 0.92 | 0.61-1.4 | |
| | | | | | | ASA 4-5 vs. 1-2 | 1.4 | 0.77-2.5 | |
| Low | 1.0 | - | 1.0 | - | 0.24 | ASA? vs. 1-2 | 1.3 | 0.91-1.7 | |
| Medium | 0.88 | 0.73-1.07 | 1.0 | 0.82-1.2 | | Stage T+/N+/M0 vs. I-III | 0.70 | 0.38-1.3 | |
| High | 0.78 | 0.65-1.95 | 0.93 | 0.76-1.1 | | Stage IV vs. III | 1.5 | 0.81-2.7 | |
| | | | | | | Stage ? vs. III | 0.72 | 0.40-1.3 | |
| | | | | | | Resection vs. none | 0.31 | 0.19-0.50 | |

* Continuous variable ** Adjusting for hospital volume as continuous variable, and stratified by chemotherapy and radiotherapy
~ No. of events / No. of patients in model ? Unknown mode of admission, cancer stage, or ASA status

**Table 4.16. Crude and adjusted hazard ratios for various differences in hospital volume**

| Difference in hospital volumes | Crude HR | | HR adjusted for case mix* and doctor volume | | HR adjusted for case mix*, doctor volume and treatments** | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| 1 | 0.990 | 0.984-0.996 | 0.988 | 0.982-0.995 | 0.989 | 0.982-0.995 |
| 10 | 0.906 | 0.855-0.961 | 0.887 | 0.831-0.947 | 0.894 | 0.837-0.956 |
| 40 | 0.675 | 0.534-0.853 | 0.619 | 0.477-0.803 | 0.639 | 0.490-0.834 |

* Emergency admission, albumin, ischaemic heart disease, diabetes, ASA score, stage. ** Chemotherapy, radiotherapy, resection.

By contrast, there was no evidence of an effect of doctor volumes on survival (Tables 4.15 and 4.17). The crude odds ratios for categorical doctor volume suggested slightly lower risk with higher volumes, but this was confounded because the hazard ratio approached unity with adjustment.

**Table 4.17. Crude and adjusted hazard ratios for various differences in doctor volume**

| Difference in doctor volumes | Crude HR | | HR adjusted for case mix* and hospital volume | | HR adjusted for case mix*, hospital volume and treatments** | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| 1 | 0.990 | 0.996-0.984 | 0.996 | 0.981-1.012 | 0.994 | 0.979-1.010 |
| 10 | 0.906 | 0.961-0.855 | 0.962 | 0.822-1.126 | 0.943 | 0.807-1.102 |

* Emergency admission, albumin, ischaemic heart disease, diabetes, ASA score, stage. ** Chemotherapy, radiotherapy, resection.

Patient factors independently predictive of worse survival were elective admission, ischaemic heart disease, diabetes, high or unrecorded ASA score, and stage IV disease, while having a resection, chemotherapy or radiotherapy was associated with better survival (Table 4.15). Although, for stage and ASA score, the confidence intervals of the odds ratio for each category included unity, the variables overall were significantly associated with survival (likelihood ratio test for addition to the model: $P<0.0001$ and $P=0.045$ respectively); their addition to the model influenced the magnitude of the odds ratio for hospital volume and they were therefore included in the final model.

The model was also extended to examine possible interactions between hospital volume, cancer stage and having a resection. The three respective hypotheses were specified in advance to avoid obtaining spurious associations through multiple testing. There were no significant interactions, as shown by the following P values for the respective interaction terms added separately to the above model: hospital volume and resection (P=0.26); hospital volume and stage (P=0.22); resection and stage (P=0.52).

The final model was also tested, adjusting for clustering on main hospital using the Stata Huber-White robust estimation procedure. This analysis resulted in slightly widened confidence intervals and higher P values compared to no adjustment for clustering, but the effect of hospital volume on survival remained statistically significant. The adjusted confidence intervals and P values were as follows. For the continuous categorical hospital volume variable, the adjusted odds ratio was 0.99 (95% CI 0.98-1.00, P=0.003). For the categorical hospital volume variable, the adjusted odds ratios were 0.90 (0.73-1.1) for the medium vs. low category and 0.72 (0.57-0.91) for the high vs. low category (P=0.02).

Secondary analysis examined the influences of surgical volume on survival. The above analysis was repeated but confined to the 259 patients who had some type of surgery, replacing hospital volume with hospital surgical volume (numbers of patients with pancreatic cancer receiving a surgical procedure in that hospital over a year), and using the same explanatory variables as shown in Table 4.15. This analysis found survival to be unrelated to hospital surgical volume (HR 1.00, 95% CI 0.97-1.02, P=0.74). Similar analyses were conducted using chemotherapy and radiotherapy volumes, and confined to patients who received only these treatments, but none of these measures was independently associated with survival time.

Survival was also compared between patients who were mainly managed by a doctor who only managed one patient per year, and all other patients. Survival appeared to be slightly worse in the former patients, with a hazard ratio of 1.3 (95% CI 1.0-1.6, P=0.02). However, after adjustment for the other variables listed in Table 4.15, except for doctor volume, there was no significant independent association (HR 1.2, 95% CI 0.96-1.6, P=0.10).

# 5. OESOPHAGEAL CANCER

## 5.1 Numbers of cases, hospital and doctor volumes

A total of 781 patients with oesophageal cancer were identified. Two thirds of all patients were managed in only one hospital trust (n=522), and the remaining third (n=259) were managed in at least two hospital trusts. 766 (98%) patients had received their main treatment in one of 23 acute hospital trusts in the region. Another 15 patients received their main treatments in one of 10 hospital trusts outside the region. The hospital volumes of each trust are shown in Table 5.1.

The corresponding doctor volumes (annual numbers of cases per doctor who provided the main treatment) are shown in Table 5.2. Less detail is provided than for hospital volumes because of the numerous doctors. A total of 152 main doctors were identified within the region: 10 were categorised as high volume doctors, 26 as medium volume doctors and 116 as low volume doctors. Volume cutpoints were chosen so as to have similar numbers in each category. The distribution of patients per doctor was highly skewed. The median number of patients per doctor was 2 (range 1-47; IQR 1-6) and the mean was 4.9 (SD 6.8). Four doctors managed more than one new patient every two weeks, on average, and at the other end of the spectrum 63 doctors managed only one patient per year. Doctor volumes were significantly correlated with hospital volumes (Spearman's rho = 0.32; $p<0.0001$).

## Table 5.1. Hospital volumes: numbers of patients per hospital trust in which patients received their main treatments

| Hospital code | No. cases |
|---|---|
| **High volume hospitals (n>55)** | |
| A | 83 |
| B | 70 |
| C | 66 |
| D | 60 |
| *All high volume* | *279* |
| **Medium volume hospitals (33≤n≤55)** | |
| E | 53 |
| F | 46 |
| G | 42 |
| H | 42 |
| I | 35 |
| *All medium volume* | *218* |
| **Low volume hospitals (n<33)** | |
| J | 32 |
| K | 27 |
| L | 24 |
| M | 23 |
| N | 22 |
| O | 21 |
| P | 19 |
| Q | 17 |
| R | 17 |
| S | *16* |
| T | 16 |
| U | 15 |
| V | 13 |
| W | 7 |
| *All low volume* | *269* |
| Out of region* | 15 |
| **Total** | **781** |

* One hospital had 6 cases, 9 had one each; hospital volumes not specified for these patients.

## Table 5.2. Distribution of doctor volumes and patients

| Doctor volume category | No. of patients in category | No. of doctors | Range of patients per doctor |
|---|---|---|---|
| High volume | 254 | 10 | 17-47* |
| Medium volume | 252 | 26 | 7-15 |
| Low volume | 240 | 116 | 1-6 |
| Doctor not identified** | 20 | - | - |
| Main treatment outside region** | 15 | - | - |
| Total | 781 | 152 | 1-47 |

* Median 22. ** Doctor volumes not specified for these patients.

The distribution of patients in hospital and doctor volume categories are shown in Table 5.3. The table suggests some specialisation by doctors within medium volume hospitals. In both medium and high volume hospitals, patients were most likely to have high volume doctors. Eighteen percent ((85+46)/746) of patients had a high volume hospital but a low volume doctor, or a low volume hospital but a high volume doctor.

**Table 5.3. Distribution of patients by doctor and hospital volume category**

| Hospital volume / Doctor volume | Low | Medium | High | Total |
|---|---|---|---|---|
| Low | 105 | 50 | 85 | 240 |
| Medium | 111 | 60 | 81 | 252 |
| High | 46 | 104 | 104 | 254 |
| Total | 262 | 214 | 270 | 746 |

## 5.2 Case mix: age, sex, comorbidity, symptoms, stage

The distributions of patients' demographic characteristics, mode of admission, comorbidities and symptoms, and their relationships with doctor and hospital volumes, are shown in Table 5.4. The male:female ratio was 61%:39%. Most patients were elderly and the age distribution was slightly negatively skewed (mean age 71 years, median 72, range 19-100; IQR 65-80). Accordingly, about half (53%) of cases had some comorbidity at the time of presentation.

Age was significantly and inversely associated with doctor volumes (Spearman's correlation coefficient = -0.23; P <0.0001) but not with hospital volumes (Spearman's correlation coefficient = -0.067; P =0.07) (Table 5.4). Sex was not significantly associated with doctor or hospital volumes. Patients of higher volume hospitals and doctors were significantly less likely to be admitted as emergencies. Patients of higher volume hospitals and doctors had significantly fewer comorbidities, although there were no associations with specific conditions.

Most patients were recorded as having dysphagia or weight loss, with a quarter or less recorded as having other gastrointestinal or systemic symptoms (Table 5.4). None of the symptoms considered was associated with doctor or hospital volumes. Albumin levels were significantly and negatively associated with hospital volumes (Spearman's correlation coefficient = -0.16; P<0.0001) but were not associated with doctor volumes (Spearman's correlation coefficient = 0.032 ; P=0.42).

Cancer staging, as judged by the end of the study period, provides a clearer view of the severity of the cancer, and how this varies according to doctor and hospital volume. It is apparent that few patients had early stage, and thus curable, disease (Table 5.5). The distribution of cancer staging differed significantly between doctor volume categories but not between hospital volume categories. Patients of higher volume doctors were more likely to have early stage disease and less likely to have metastases or completely unstaged disease.

**Table 5.4. Age, sex, comorbidity and presenting symptoms**

| | Total | | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | 781 | 100 | 269 | | 218 | | 279 | | | 240 | | 252 | | 254 | | |
| Age (mean years) | 71 | | 72.4 | | 70.6 | | 70.7 | | 0.07 | 75.6 | | 69.2 | | 68.6 | | <0.0001 |
| Sex (% female) | 308 | 39 | 106 | 39 | 82 | 38 | 111 | 40 | 0.65 | 105 | 44 | 93 | 37 | 91 | 36 | 0.49 |
| Emergency first admission | 175 | 23 | 68 | 25 | 49 | 22 | 57 | 20 | 0.03 | 75 | 31 | 44 | 17 | 46 | 18 | 0.001 |
| **Comorbidity** | | | | | | | | | | | | | | | | |
| COAD | 80 | 10 | 28 | 10 | 24 | 11 | 28 | 10 | 0.40 | 30 | 13 | 26 | 10 | 21 | 8 | 0.21 |
| IHD | 116 | 15 | 48 | 18 | 28 | 13 | 39 | 14 | 0.28 | 35 | 15 | 41 | 16 | 35 | 14 | 0.99 |
| Hypertension | 137 | 18 | 47 | 17 | 44 | 20 | 43 | 15 | 0.53 | 43 | 18 | 44 | 17 | 44 | 17 | 0.25 |
| Diabetes | 57 | 7 | 19 | 7 | 9 | 4 | 29 | 10 | 0.13 | 16 | 7 | 23 | 9 | 18 | 7 | 0.68 |
| No. chronic diseases (mean) | 0.87 | | 0.94 | | 0.81 | | 0.86 | | 0.46 | 0.99 | | 0.88 | | 0.75 | | 0.002 |
| **Symptoms** | | | | | | | | | | | | | | | | |
| Dysphagia | 644 | 83 | 216 | 80 | 183 | 84 | 231 | 83 | 0.69 | 195 | 81 | 203 | 81 | 213 | 84 | 0.66 |
| Vomiting | 130 | 17 | 44 | 16 | 34 | 16 | 46 | 16 | 0.76 | 45 | 19 | 35 | 14 | 40 | 16 | 0.73 |
| GI bleeding | 13 | 2 | 63 | 1 | 4 | 2 | 6 | 2 | 0.46 | 4 | 2 | 6 | 2 | 3 | 1 | 0.96 |
| Abdominal Pain | 204 | 26 | 69 | 26 | 63 | 29 | 37 | 24 | 0.54 | 62 | 26 | 77 | 31 | 57 | 22 | 0.21 |
| Weight Loss | 434 | 56 | 148 | 55 | 119 | 55 | 158 | 57 | 0.85 | 130 | 54 | 143 | 57 | 140 | 55 | 0.98 |

# P value from logistic regression with continuous explanatory volume variable, except Spearman's rank correlation for age and number of chronic diseases

## Table 5.5. Pathological staging

| Stage | Total | | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | | | 269 | | 218 | | 279 | | | | | | | | | |
| **Detailed staging** | | | | | | | | | | | | | | | | |
| I | 11 | 1 | 2 | 1 | 4 | 2 | 5 | 2 | | 0 | 0 | 1 | 1 | 10 | 4 | |
| II | 87 | 11 | 27 | 10 | 27 | 12 | 33 | 12 | | 12 | 5 | 22 | 10 | 53 | 21 | |
| III | 73 | 9 | 22 | 8 | 17 | 8 | 33 | 12 | | 10 | 4 | 25 | 10 | 37 | 14 | |
| IV | 105 | 13 | 35 | 13 | 29 | 13 | 37 | 13 | | 22 | 9 | 29 | 12 | 14 | 6 | |
| **Partially staged** | | | | | | | | | | | | | | | | |
| T+orN+ | 95 | 12 | 29 | 11 | 28 | 13 | 36 | 13 | | 20 | 8 | 34 | 13 | 38 | 15 | |
| M0 | 70 | 9 | 26 | 9 | 22 | 10 | 18 | 6 | | 22 | 9 | 29 | 12 | 14 | 6 | |
| Unstaged* | 340 | 43 | 128 | 48 | 91 | 42 | 117 | 42 | 0.77 | 144 | 60 | 103 | 41 | 72 | 28 | <0.001 |
| **Combined stages** | | | | | | | | | | | | | | | | |
| "Early" (I-III) | 171 | 22 | 51 | 19 | 48 | 22 | 71 | 25 | | 22 | 9 | 48 | 19 | 100 | 39 | |
| "Intermediate" | 165 | 21 | 55 | 20 | 50 | 23 | 54 | 19 | | 42 | 18 | 63 | 25 | 52 | 20 | |
| (T+ or N+ or M0) | | | | | | | | | | | | | | | | |
| "Late" (IV) | 105 | 13 | 35 | 13 | 29 | 13 | 37 | 13 | | 32 | 13 | 38 | 15 | 30 | 12 | |
| Unstaged* | 340 | 44 | 128 | 48 | 91 | 42 | 117 | 42 | 0.58 | 144 | 60 | 103 | 41 | 72 | 28 | <0.001 |

# P value from Pearson $\chi^2$ test. * No T, N or M pathological staging

Other key descriptive and prognostic variables were tumour location and histology. Most cases occurred in the lower half of the oesophagus (Table 5.6). Of all 781 cases, 201 (26%) were junctional adenocarcinomas, having been either classified as such at or after operation, or being located more than 35 cm. from the incisors, and having a histological diagnosis of adenocarcinoma. The significance of junctional tumours is that some of them would have started as gastric cancers and spread into the oesophagus, and would thus be expected to behave more like gastric tumours. Patients of higher volume doctors cancers were significantly more likely to have junctional tumours (logistic regression P value = 0.01) but there was no association with hospital volumes (P=0.33).

**Table 5.6. Location: distance of tumour from incisors**

| | n | % |
|---|---|---|
| 0-18 cm | 20 | 2 |
| 19-24 cm | 40 | 5 |
| 25-32 cm | 272 | 35 |
| 33-40 cm | 241 | 31 |
| >41 cm | 42 | 5 |
| Not specified | 166 | 21 |
| Total | 781 | 100 |

Half of all cancers were adenocarcinomas. About a third were squamous carcinomas (Table 5.7). 95 cases (12% of total) were reported to have had Barrett's oesophagus in the past or as a comorbidity. Cases with previous Barrett's oesophagus were more likely to have early stage cancer (32% were of stages I-III, compared to 21% of all other cases), and were less likely to have metastases (5% vs. 15%).

**Table 5.7. Histology**

| | n | % |
|---|---|---|
| Adenocarcinoma | 412 | 53% |
| Squamous | 234 | 30% |
| Small Cell | 9 | 1% |
| Other | 4 | 1% |
| Carcinoma (not specified) | 58 | 7% |
| No histology | 64 | 8% |
| Total | 781 | 100% |

In summary, the overall case mix was severe: patients tended to be elderly, have serious comorbidities, have symptoms of obstruction and weight loss, and to have advanced stage cancer. Higher volume doctors tended to have patients with better prognoses. This was also true of hospitals but to a lesser, and often statistically insignificant, extent.

# 5.3 Investigations performed

Diagnostic and staging investigations varied widely between patients (Table 5.8). Almost all patients (96%) had oesophago-gastro-duodenoscopy (OGD) and 89% had biopsies. Over half of patients had CT scans, and a fifth had abdominal ultrasounds. Endoscopic ultrasound (EUS) and laparoscopy were rarely used. Use of CT scan, contrast swallow and endoscopic ultrasound was associated with doctor volumes but not with hospital volumes, suggesting that doctors' preferences rather than availability of equipment determined choice of test. CT scans and abdominal ultrasounds appeared partly to be substitutes for each other, and they were inversely associated with each other ($\chi^2$=10.8; df 1; P 0.001). CT scans were used most often by high volume doctors. Endoscopic ultrasound was used most often by high volume doctors in medium volume hospitals.

**Table 5.8. Investigations performed**

| | Total | | Hospital Volumes | | | | | | Doctor Volumes | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | | | 261 | | 230 | | 277 | | | 242 | | 245 | | 255 | | |
| CT | 416 | 53 | 138 | 51 | 119 | 55 | 146 | 52 | 0.51 | 95 | 40 | 135 | 54 | 167 | 66 | <0.001 |
| Abdominal ultrasound | 167 | 21 | 57 | 21 | 36 | 16 | 72 | 26 | 0.17 | 58 | 24 | 65 | 26 | 39 | 15 | 0.57 |
| OGD | 749 | 96 | 261 | 97 | 206 | 94 | 286 | 96 | 0.86 | 225 | 91 | 249 | 99 | 242 | 95 | 0.13 |
| Contrast swallow | 397 | 51 | 146 | 54 | 109 | 50 | 135 | 48 | 0.25 | 125 | 52 | 134 | 53 | 122 | 48 | 0.12 |
| Biopsy | 696 | 89 | 238 | 88 | 198 | 91 | 245 | 88 | 0.97 | 204 | 85 | 234 | 93 | 225 | 8 | 0.45 |
| Laparoscopy | 50 | 6 | 15 | 6 | 18 | 8 | 16 | 6 | 0.77 | 7 | 3 | 28 | 11 | 14 | 6 | 0.36 |
| EUS | 42 | 5 | 8 | 3 | 34 | 16 | 0 | 0 | 0.02 | 3 | 1 | 12 | 5 | 26 | 10 | 0.02 |

# P value from logistic regression with continuous explanatory volume variable

Patients with junctional tumours were slightly but significantly more likely than other patients to have a CT scan (61% vs. 50%, P−0.005), abdominal ultrasound (26% vs. 20%, P 0.05) or laparoscopy (93% vs. 87%, P=0.04), but were no more likely to have any of the other investigations.

Choice of test is likely to be determined by patient characteristics, and in particular by potential suitability for curative surgery, as well as by doctor and hospital characteristics. Thus regression analyses were used to investigate the independent influences of patient, hospital and doctor characteristics on the use of specific tests. As mentioned in the Methods chapter, explanatory variables such as T or N staging that would be unlikely to be known to doctors at the time of ordering tests were not included in the models.

The logistic regression analyses showed that the only patient characteristic that influenced use of preoperative CT scan, EUS or laparoscopy was age, with older patients being significantly less likely to receive any of these tests, regardless of other presenting features (Table 5.9). Higher doctor volumes were associated with significantly increased probability of having CT, adjusted for age. The probabilities of laparoscopy and EUS were highest for patients of medium volume doctors and so the apparent influence of doctor volumes depended on whether a continuous or categorical volume variable was used. Contrast swallow was more likely in patients with dysphagia, and with lower doctor volumes, but odds ratios for the categorical doctor volume variable show that there was no clear trend with doctor volume. Given the non-linear and non-exponential nature of the volume-test relationship for contrast swallow, laparoscopy and EUS, the analyses using volume categories, instead of continuous measures, are most readily interpretable. Abdominal ultrasound was not associated with age, doctor or hospital volumes, but was significantly more likely in the presence of weight loss (adjusted OR=1.6; 1.2-2.2) and less likely in the presence of dysphagia (adjusted OR=0.36; 0.24-0.55).

The investigations with which deprivation scores were associated, independently of the variables shown in Table 5.9, were computed tomography and contrast swallow, which were, respectively, significantly less likely and more likely with increasing deprivation score. The adjusted odds ratios for computed tomograpy, for unit increases in Townsend deprivation scores, was 0.92 (0.85-0.99; P=0.02). The adjusted odds ratio for contrast swallow, for a unit increase in Townsend score, was 1.08 (95% CI 1.01-1.16; P<0.02).

**Table 5.9. Predictors of test use: logistic regression models**

| Test | Doctor or hospital volume; as categorical or continuous | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P# | Other variables in full model** | OR | 95%CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| CT | Doctor volume* | 1.03 | 1.02-1.05 | 1.02 | 1.01-1.04 | 0.001 | Age* | 0.93 | 0.91-0.94 | 417 743 |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 2.0 | 1.4-2.9 | 1.4 | 0.92-2.0 | 0.0003 | | | | |
| | High | 3.2 | 2.2-4.6 | 2.2 | 1.5-3.4 | | | | | |
| EUS | Doctor volume* | 1.02 | 1.00 | 1.07 | 1.03-1.11 | 0.001 | Age* | 0.96 | 0.94-0.99 | 41 743 |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 4.0 | 1.1-14.2 | 3.1 | 0.84-11.3 | 0.0001 | | | | |
| | High | 9.0 | 2.7-30.2 | 13.5 | 3.8-48.6 | | | | | |
| | Hospital volume* | 0.98 | 0.97-1.00 | 0.96 | 0.93-0.98 | 0.001 | | | | |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 6.0 | 2.7-13.3 | 4.6 | 1.9-11.0 | 0.001 | | | | |
| | High | ## | - | ## | - | | | | | |
| Contrast swallow | Doctor volume* | 0.99 | 0.73-1.5 | 0.99 | 0.97-1.00 | 0.02 | Dysphagia | 3.4 | 2.3-5.2 | 380 746 |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 1.0 | 0.73-1.5 | 1.1 | 0.74-1.5 | 0.33 | | | | |
| | High | 0.85 | 0.60-1.2 | 0.82 | 0.57-1.2 | | | | | |
| Laparoscopy | Doctor volume* | 0.99 | 0.96-1.01 | 0.98 | 0.95-1.00 | 0.08 | Age* | 0.94 | 0.92-0.96 | 49 743 |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 4.2 | 1.8-9.7 | 3.0 | 1.3-7.1 | 0.008 | | | | |
| | High | 1.9 | 0.77-4.9 | 1.3 | 0.49-3.3 | | | | | |

* Continuous variable. ** With continuous doctor volume variable in model. ~ No. events / No. with complete data in model. ## Empty cell so cannot compute OR.

# 5.3 Treatment provided

Patients were most likely to have stents inserted or to receive radiotherapy (Table 5.10). Tumour resection was attempted only in one patient in nine; similar proportions of patients had chemotherapy, or had none of the treatments considered. Cancer stage was a major influence on treatment provided. Resections were most likely in patients with early (92%) or intermediate (57%) stage. Of all resections, 64% were performed in patients with early or intermediate stage, who comprised a quarter of all patients. In contrast, stents were most likely in patient with advanced or unstaged disease, who accounted for about half of all stents inserted. Chemotherapy and radiotherapy did not appear to be as strongly influenced by stage. Chemotherapy was most likely for patients with advanced stage, whereas radiotherapy was most likely for patient with unstaged or partially staged disease. 10% of all patients received none of the treatments considered, which was most likely in patients with advanced (18%) or unstaged (14%) disease. Relatively few patients received combinations of treatments, and the most likely combination was stent and radiotherapy.

Resections, chemotherapy and radiotherapy were significantly more likely with increasing hospital and doctor volumes (Table 5.11). In contrast, stenting, and none of the treatments considered, were significantly less likely with higher volumes. In order to assess whether these associations were artefacts of the way in which the main doctor or main hospital was defined, the analyses were repeated with the subgroup of patients (67% of total) who were managed only in one hospital and by only one doctor. The same trends were present in this subgroup.

Patients with junctional tumours were significantly more likely than other patients to have a resection (47% vs. 26%, $P<0.001$) and were significantly less likely to have a radiotherapy (12% vs. 27%, $P<0.001$), but were not significantly different with regard to stents, chemotherapy, or receiving none of the treatments considered.

Logistic regression was used to investigate the independent influences of doctor and hospital volumes, and patient characteristics, on choice of treatment (Table 5.12). Explanatory variables were only included in the models if they were likely to have been known before treatment was chosen. Thus M stage was considered as a potential explanatory variable but T and N stages, which require surgery for accurate assessment,

were not included. Other explanatory variables considered were age, sex, emergency or elective first admission, symptoms (weight loss and dysphagia), comorbidity (ischaemic heart disease, chronic obstructive airways disease, diabetes and hypertension), initial blood albumin and haemoglobin levels, and junctional tumours.

Patients of higher volume doctors were significantly more likely to have resections and chemotherapy, and were significantly less likely to have radiotherapy or no treatment, independently of other confounding variables including hospital volume (Table 5.12). Patients of higher volume hospitals were significantly and independently more likely to have radiotherapy. Hospital volume was not independently associated with any other treatment. These associations with doctor and hospital volumes were partly confounded, as shown by the odds ratios for these variables becoming closer to unity once other variables were controlled for (Table 5.12). Stenting was not independently associated with either hospital or doctor volumes.

It is possible that for patients having radiotherapy or chemotherapy, the patient's main doctor or hospital, and thus doctor and hospital volumes, were misclassified (see Methods). To examine whether such misclassification could have affected the apparent relationships between volumes, radiotherapy and chemotherapy, the relevant analyses were therefore repeated, but confined to patients treated in only one hospital and by one consultant, in whom volumes could not be thus misclassified. The associations between volumes, radiotherapy and chemotherapy persisted in this subgroup, supporting the results of the main analyses. However the odds ratios for doctor and hospital volumes in the subgroup were of larger magnitude than in the total population, suggesting that misclassification of main doctor or hospital may have attenuated the estimated strength of association with chemotherapy and radiotherapy.

Several patient characteristics were independently associated with the respective treatments (Table 5.12). Most treatments were less likely with older age, lower albumin or haemoglobin levels, or metastases, while stents and chemotherapy were more common with dysphagia. Resections were more likely with younger age, no reported weight loss, higher haemoglobin levels, junctional tumours and no metastases. Stenting was more likely with older age, reported weight loss, reported dysphagia, and metastases. Chemotherapy was more likely with younger age, dysphagia, higher albumin levels, and metastases. Radiotherapy was more likely with younger age, higher albumin levels and

non-junctional tumours. None of the treatments considered was more likely with older age, emergency admission, no dysphagia, lower albumin levels, and metastases.

Only dilatation was associated with deprivation scores, independently of the variables shown in Table 5.11. The adjusted odds ratios for dilatation, for unit increases in Townsend deprivation scores was 0.93 (0.86-1.008; P=0.08).

Each the above treatments was associated with each of the others, suggesting that some treatments complemented each other, while others were substitutes for each other. Patients who had resections were more likely, compared to those who did not, to have chemotherapy (16% vs. 9%; p 0.004) and were less likely to have radiotherapy (13% vs. 28%; p<0.001) or stents (6% vs. 53%; p<0.001). Patients who had radiotherapy were more likely to have chemotherapy than patients who did not (18% vs. 9%; p=0.001). Patients who had stents were less likely to have radiotherapy (18% vs. 27%; p=0.008) or chemotherapy (7% vs. 14%; p=0.007).

## Table 5.10. Treatment provided, by stage of disease

| Treatment | Early (Stage I-III) | | | Intermediate (T+ or N+ or M0) | | | Advanced (Stage IV) | | | Unstaged | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Any treatment** | n | % row | % column | n | % row | % column | n | % row | % column | n | % row | % column | n | % column |
| Resection | 157 | 64 | 92 | 54 | 22 | 57 | 16 | 7 | 15 | 15 | 6 | 4 | 242 | 31 |
| Any surgery (excluding stents) | 162 | 58 | 94 | 58 | 21 | 61 | 27 | 10 | 26 | 32 | 11 | 8 | 279 | 36 |
| Stent | 13 | 4 | 8 | 24 | 8 | 25 | 47 | 16 | 44 | 214 | 72 | 52 | 298 | 38 |
| Dilatation | 68 | 24 | 40 | 57 | 20 | 35 | 32 | 11 | 14 | 131 | 45 | 39 | 288 | 37 |
| Chemotherapy | 25 | 28 | 15 | 12 | 14 | 13 | 23 | 26 | 22 | 28 | 32 | 7 | 88 | 11 |
| Radiotherapy | 14 | 13 | 14 | 22 | 12 | 23 | 18 | 10 | 17 | 120 | 65 | 29 | 184 | 24 |
| **Treatment combinations** | | | | | | | | | | | | | | |
| Resection & stent | 9 | 60 | 5 | 1 | 7 | 1 | 1 | 7 | 1 | 4 | 27 | 1 | 15 | 2 |
| Resection & chemotherapy | 24 | 62 | 14 | 8 | 21 | 8 | 5 | 13 | 5 | 2 | 5 | 1 | 39 | 5 |
| Resection & radiotherapy | 21 | 66 | 12 | 5 | 16 | 5 | 2 | 6 | 2 | 4 | 13 | 1 | 32 | 4 |
| Stent and radiotherapy | 3 | 5 | 2 | 21 | 38 | 13 | 6 | 11 | 6 | 25 | 45 | 7 | 55 | 7 |
| Chemotherapy & radiotherapy | 5 | 15 | 3 | 6 | 18 | 6 | 10 | 30 | 10 | 12 | 36 | 3 | 33 | 4 |
| Resection & chemotherapy & radiotherapy | 5 | 55 | 3 | 2 | 22 | 2 | 2 | 22 | 2 | 0 | 0 | 0 | 9 | 1 |
| None of the above | 1 | 1 | 1 | 2 | 2 | 2 | 19 | 23 | 18 | 59 | 72 | 14 | 81 | 10 |

**Table 5.11. Treatments provided, by doctor and hospital volumes**

| Treatment | Total | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n (%) | n | % | n | % | n | % | | n | % | n | % | n | % | |
| Resection | 242 (31%) | 69 | 26 | 65 | 30 | 107 | 38 | <0.001 | 26 | 11 | 74 | 29 | 141 | 56 | <0.001 |
| Stent | 298 (38%) | 119 | 44 | 78 | 36 | 98 | 35 | 0.03 | 100 | 42 | 103 | 41 | 82 | 32 | 0.04 |
| Chemotherapy* | 88 (11%) | 15 | 5 | 34 | 15 | 32 | 13 | 0.17 | 12 | 5 | 87 | 15 | 33 | 13 | 0.007 |
| Radiotherapy** | 184 (24%) | 25 | 14 | 56 | 32 | 92 | 36 | <0.001 | 61 | 25 | 81 | 32 | 24 | 9 | <0.001 |
| None of the above treatments | 81 (10%) | 40 | 15 | 22 | 10 | 18 | 6 | <0.001 | 54 | 22 | 15 | 6 | 11 | 4 | <0.001 |

# P value from logistic regression

**Table 5.12a. Influences on treatment provided: logistic regression models (legend at foot of 5.12b)**

| Treatment | Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted OR | Adjusted 95%CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Resection | Doctor volume* | 1.07 | 1.06-1.09 | 1.07 | 1.05-1.09 | <0.001 | Age* | 0.93 | 0.91-0.95 | 452 |
| | Low | 1.0 | - | 1.0 | - | | Weight loss | 0.51 | 0.33-0.79 | 689 |
| | Medium | 3.4 | 2.1-5.6 | 2.4 | 1.3-4.3 | <0.0001 | Haemoglobin* | 1.2 | 1.03-1.28 | |
| | High | 10.3 | 6.4-16.5 | 7.7 | 4.3-13.8 | | M+ vs. M0 | 0.07 | 0.04-0.15 | |
| | | | | | | | M? vs. M0 | 0.15 | 0.10-0.24 | |
| | | | | | | | Junctional tumours | 2.0 | 1.3-3.3 | |
| | Hospital volume* | 1.01 | 1.01-1.02 | 0.99 | 0.98-1.00 | 0.10 | | | | |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 1.2 | 0.82-1.8 | 0.99 | 0.58-1.7 | 0.89 | | | | |
| | High | 1.8 | 1.3-2.6 | 0.88 | 0.51-1.5 | | | | | |
| Stent | Doctor volume* | 0 99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.90 | Age* | 1.04 | 1.02-1.06 | 284 |
| | Low | 1.0 | - | 1.0 | - | | Weight loss | 1.5 | 1.1-2.1 | 742 |
| | Medium | 0.97 | 0.68-1.4 | 1.4 | 0.93-2.1 | 0.18 | Dysphagia | 4.5 | 1.9-5.6 | |
| | High | 0.67 | 0.46-0.96 | 1.1 | 0.66-1.5 | | M+ vs. M0 | 3.3 | 1.6-3.4 | |
| | | | | | | | M? vs. M0 | 2.3 | 2.7-7.9 | |
| | Hospital volume* | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.00 | 0.18 | | | | |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 0.70 | 0.49-1.01 | 0.71 | 0.47-1.1 | 0.16 | | | | |
| | High | 0.68 | 0.48-0.96 | 0.71 | 0.48-1.1 | | | | | |
| Chemotherapy | Doctor volume* | 1.02 | 1.01-1.04 | 1.01 | 1.00-1.04 | 0.09 | Age* | 0.94 | 0.92-0.96 | 73 |
| | Low | 1.0 | - | 1.0 | - | | Dysphagia | 2.5 | 1.1-5.9 | 618 |
| | Medium | 3.2 | 1.7-6.4 | 2.4 | 1.1-5.3 | 0.02 | Albumin* | 1.07 | 1.02-1.12 | |
| | High | 2.8 | 1.4-5.6 | 2.0 | 0.90-4.5 | | M+ vs. M0 | 2.6 | 1.3-5.1 | |
| | | | | | | | M? vs. M0 | 1.2 | 0.62-2.2 | |
| | Hospital volume* | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.01 | 0.63 | | | | |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 2.1 | 1.2-3.9 | 1.9 | 0.97-3.7 | 0.17 | | | | |
| | High | 1.6 | 0.86-2.8 | 1.4 | 0.67-2.8 | | | | | |

## Table 5.12b. Influences on treatment provided: logistic regression models (continued)

| Treatment | Doctor or hospital *volume* as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Radiotherapy | Doctor volume* | 0.97 | 0.95-0.98 | 0.95 | 0.93-0.97 | <0.001 | Age* | 0.98 | 0.96-1.00 | 129 |
| | Low | 1.0 | - | 1.0 | - | | Albumin* | 1.07 | 1.03-1.11 | 616 |
| | Medium | 1.4 | 0.94-2.1 | 1.4 | 0.83-2.2 | <0.0001 | Junctional tumours | 0.39 | 0.22-0.67 | |
| | High | 0.31 | 0.18-0.51 | 0.19 | 0.10-0.36 | | | | | |
| | Hospital volume* | 1.02 | 1.01-1.03 | 1.03 | 1.02-1.04 | <0.001 | | | | |
| | Low | 1.0 | - | 1.0 | - | | | | | |
| | Medium | 2.4 | 1.5-3.8 | 2.6 | 1.4-4.6 | <0.001 | | | | |
| | High | 3.4 | 2.2-5.3 | 5.2 | 3.0-9.0 | | | | | |
| None of the bove treatments | Doctor volume* | 0.89 | 0.85-0.92 | 0.91 | 0.86-0.95 | <0.001 | Admission: | | | 58 |
| | Low | 1.0 | - | 1.0 | | | - emergency vs. | | | 621 |
| | Medium | 0.22 | 0.12-0.40 | 0.20 | 0.09-0.45 | <0.0001 | elective | 3.8 | 1.9-7.3 | |
| | High | 0.16 | 0.08-0.31 | 0.23 | 0.10-0.55 | | - unknown vs. elective | 3.6 | 1.2-10.6 | |
| | Hospital volume* | 0.97 | 0.97-0.99 | 0.99 | 097-1.00 | 0.17 | Dysphagia | 0.21 | 0.11-0.42 | |
| | Low | 1.0 | - | 1.0 | - | | Albumin* | 0.91 | 0.86-0.96 | |
| | Medium | 0.64 | 0.37-1.1 | 1.4 | 0.62-2.9 | 0.06 | M+ vs. M0 | 6.1 | 2.0-18.5 | |
| | High | 0.39 | 0.22-0.71 | 0.47 | 0.26-1.1 | | M? vs. M0 | 4.0 | 1.5-10.5 | |

* Continuous variable ** Adjusted for continuous doctor volumes (for resection, stent, and chemotherapy) or for continuous doctor and hospital volumes (for radiotherapy and no treatment). M? M status unknown. ~ No. events / No with complete data in model

# 5.5 Survival

All patients but one were matched with the NHS Central Register. By 10 October 1998, 580 (75%) patients had died. The median duration of follow-up at that time was 8.1 months (range 7 days to 33.7 months) for all patients, 22.0 (range 16.4-33.7) months for survivors, and 4.9 months (range 6 days to 26.9 months) for patients that died.
Three outcome measures were examined: operative mortality (i.e. death within 30 days of last surgery), one-year survival, and survival time. Influences on the first two outcomes were examined using multiple logistic regression, and influences on survival were examined using Cox's proportional hazards model. Potential explanatory variables examined in the models were as defined in the Methods. They included hospital and doctor volumes, age, sex, Townsend deprivation scores, symptoms (weight loss and dysphagia), comorbidities (ischaemic heart disease, chronic obstructive airways disease, diabetes and hypertension), initial haemoglobin and albumin levels, tumour histology, T stage, N stage, M stage, emergency or elective admission, and treatments given. T, N and M stages were firstly examined as separate variables and then, in order to obtain a statistically more powerful variable with larger cell sizes, as a composite staging variables with the following four categories: stage I-III; incompletely staged but with nodes or tumour invasion; with metastases; or unstaged. For operative mortality, the American Society of Anesthetists (ASA) score was also examined as a potentially explanatory variable.

## 5.5.1 Operative mortality

Operative mortality was significantly lower among patients of high volume doctors than among patients of low and medium volume doctors combined (8% vs. 15%, p=0.046), and was the same in the low and medium doctor volume categories. Patient factors significantly or marginally associated with operative mortality were older age (P=0.05), ischaemic heart disease (P=0.02), advanced stage (P=0.009) and higher ASA score (P=0.08). Junctional adenocarcinoma was not associated with operative mortality.

In the logistic regression model, operative mortality was less likely with increasing doctor volume (OR=0.97; 95% CI 0.94-1.00, P=0.03, for each extra patient treated by one's doctor), after adjusting for age, stage, ASA score, and ischaemic heart disease (Table

5.13). This result implies that one's risk of operative mortality decreases by about 3% with each extra patient that one's doctor manages per year. This corresponds to an odds ratio of 0.83 (95% CI 0.72-0.98) for an increase in doctor volumes of 5, an odds ratio of 0.68 (0.52-0.96) for an increase in doctor volumes of 10, and an odds ratio of 0.47 (0.27-0.93) for an increase in doctor volumes of 20. A similar pattern was observed when the categorical doctor volume variable was used in the model, although the association was not significant. Hospital volume and Townsend deprivation score were not independently associated with operative mortality. None of the other factors included in the full model was independently significantly associated with operative mortality, and thus none are shown in the Table. However these variables were included in the model because they were considered *a priori* to be important prognostic factors, and they were found to be confounders because their inclusion influenced the magnitude of the odds ratio for doctor volumes.

**Table 5.13. Operative mortality and doctor volumes: logistic regression model**

| Doctor volume as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted* OR | Adjusted* 95% CI | P | n/N~ |
|---|---|---|---|---|---|---|
| Doctor volume* | 0.96 | 0.94-0.99 | 0.97 | 0.94-1.0 | 0.03 | 36/ 322 |
| Low | 1.0 | - | 1.0 | - | | |
| Medium | 0.98 | 0.37-2.63 | 1.1 | 0.39-3.3 | 0.33 | |
| High | 0.48 | 0.18-1.3 | 0.59 | 0.21-1.7 | | |

* adjusted for age, stage, ASA score, resection and ischaemic heart disease ~ No. events No. with complete data in model

A secondary analysis repeated the above but instead of hospital volume used hospital surgical volume, that is, the number of cases receiving an operative procedure for pancreatic cancer during the year. The adjusted odds ratio suggested a survival advantage of higher hospital surgical volume, but this was not significant (OR 0.98, 95% CI 0.95-1.00, P=0.09, n=322).

## 5.5.2 One year survival

287 patients (37% of total) survived at least one year after first presenting to hospital. Before case mix was considered, one year survival increased significantly (P<0.001) with increasing doctor volume, but was not associated with hospital volume. However the crude association with doctor volume appeared to be due to confounding by case mix, and was no longer significant after adjustment (Table 5.14). Patients were significantly and independently more likely to survive at least a year if they were younger, were admitted as elective cases, had higher albumin levels, did not report dysphagia, or did have a resection. Junctional adenocarcinoma was associated with one year survival (OR 1.5; 95% CI 1.1-2.1) before adjustment, but this association disappeared after adjustment for other factors in the model. The odds ratio for survival, for each increasing patient managed by one's doctor, was 1.01 (95% CI 0.99-1.02), adjusted for age, mode of admission, dysphagia, albumin, having a resection, and hospital volume. Hospital volume was not associated with one year survival (crude P=0.12, adjusted P=0.86). Adjustment for clustering on main hospital did not affect these conclusions.

**Table 5.14. One year survival and doctor volumes: logistic regression model**

| Doctor volume as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|
| Doctor volume* | 1.03 | 1.02-1.05 | 1.01 | 0 99-1.02 | 0.37 | Age* | 0.98 | 0.97-1.00 | 235 616 |
| | | | | | | Emergency admission vs. elective | 0.60 | 0.37-0.98 | |
| Low | 1.0 | - | 1.0 | - | | Mode of admission unknown vs. | | | |
| Medium | 1.7 | 1.2-2.5 | 0.93 | 0.57-1.5 | 0.12 | elective | 1.3 | 0.68-2.7 | |
| High | 2.8 | 1.9-4.1 | 1.1 | 0.67-1.8 | | Dysphagia | 0.56 | 0.34-0.91 | |
| | | | | | | Albumin* | 1.04 | 1.02-1.08 | |
| | | | | | | Resection | 5.1 | 3.4-7.9 | |

* Continuous variable ** Adjusted for continuous doctor volumes No events No with complete data in model

## 5.5.3 Survival time

Survival time was better with higher doctor volumes, higher hospital volumes, younger age, no reported weight loss, no reported dysphagia, higher albumin levels, early stage cancer, junctional adenocarcinoma (OR 0.81, 95% CI 0.67-0.98), any adenocarcinoma, Barretts oesophagus and in patients who had a resection or chemotherapy or did not have a stent. There was no association with radiotherapy. In order to assess the appropriateness of including these variables in a multivariable Cox's proportional hazards model, that is, the proportionality of hazards throughout the follow-up period, the Kaplan Meier survival curves and complementary log log plots for each variable were examined (Figures 5.1 to 5.16).

*Figure 5.1. Survival curves for doctor volume*

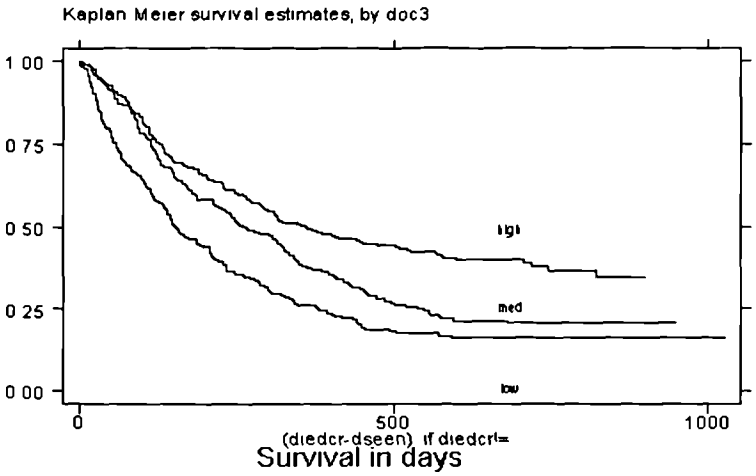



*Figure 5.2. Complementary log log plot for doctor volume*

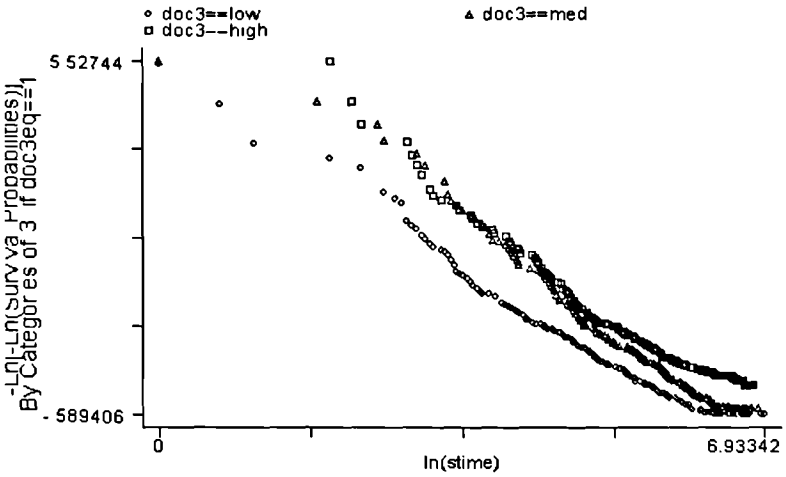


*Figure 5.3. Survival curve for hospital volume*

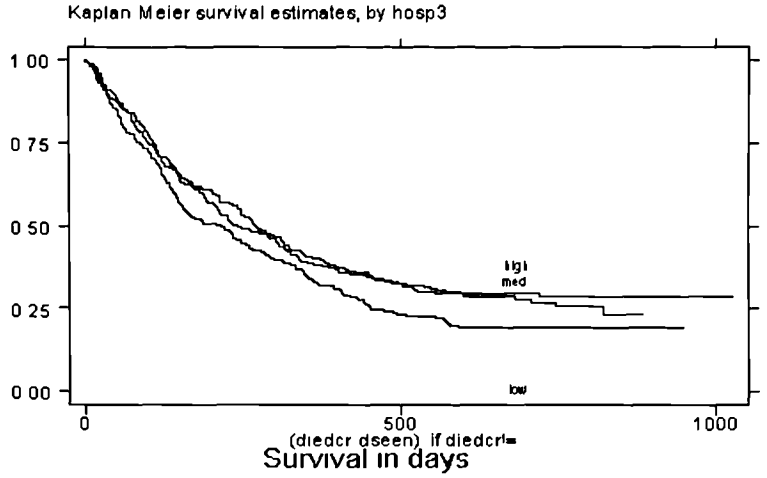



*Figure 5.4. Complementary log log plot for hospital volume*

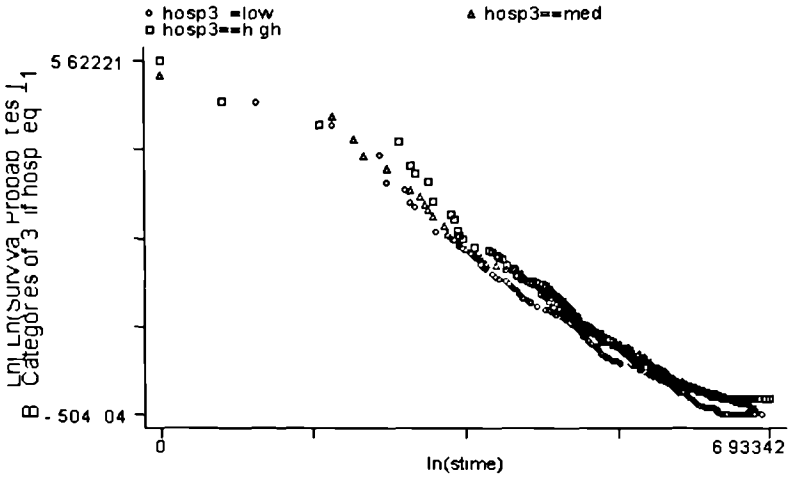



*Figure 5.5. Survival curves for cancer stage*

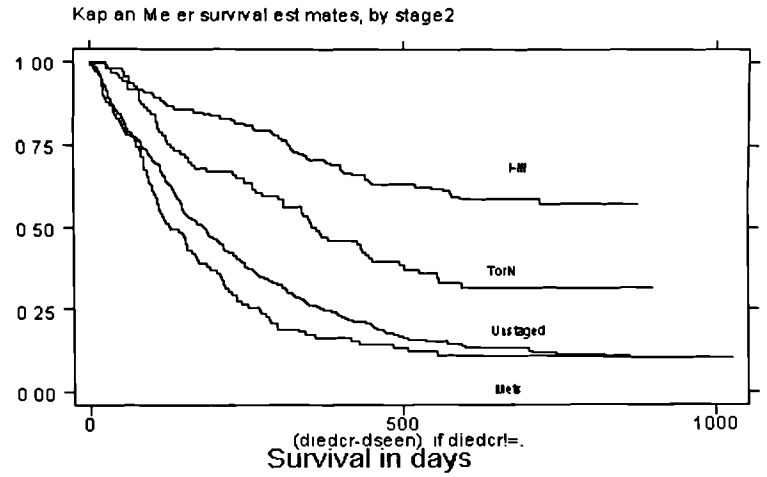


*Figure 5.6. Complementary log log plot for cancer stage*

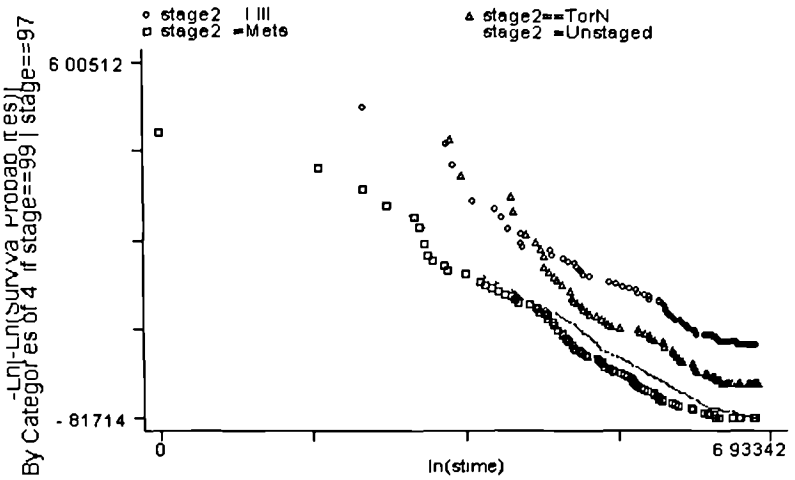



*Figure 5.7. Survival curves for age tertiles*

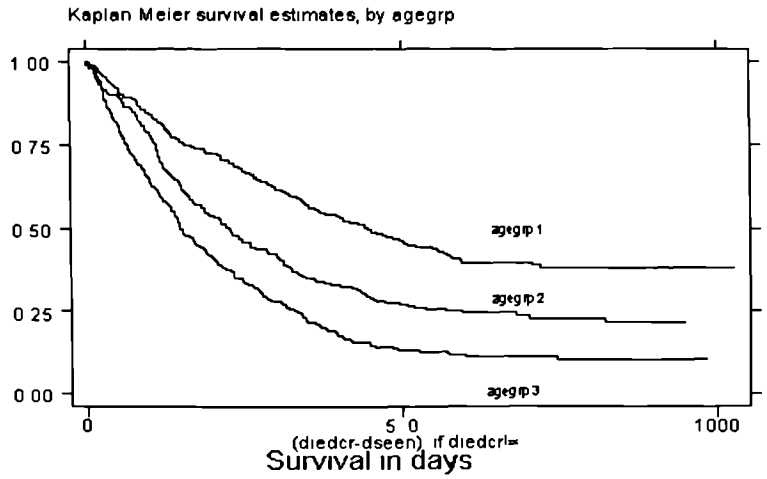



*Figure 5.8. Complementary log log plot for age tertiles*

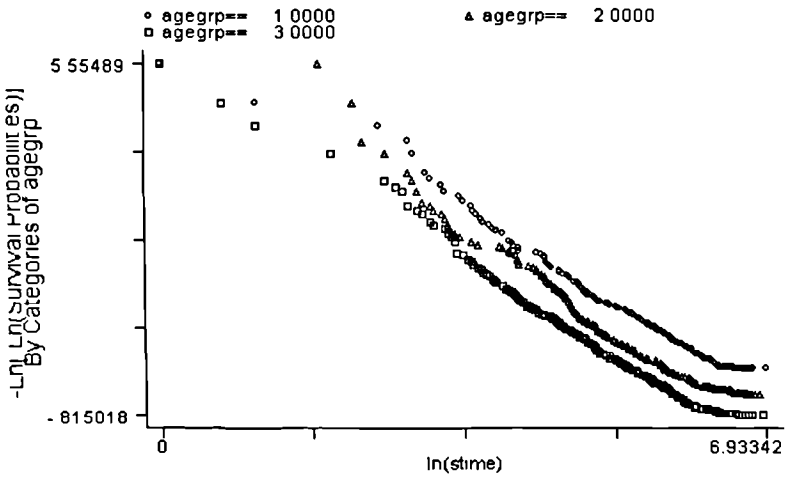


*Figure 5.9. Survival curve for resection*

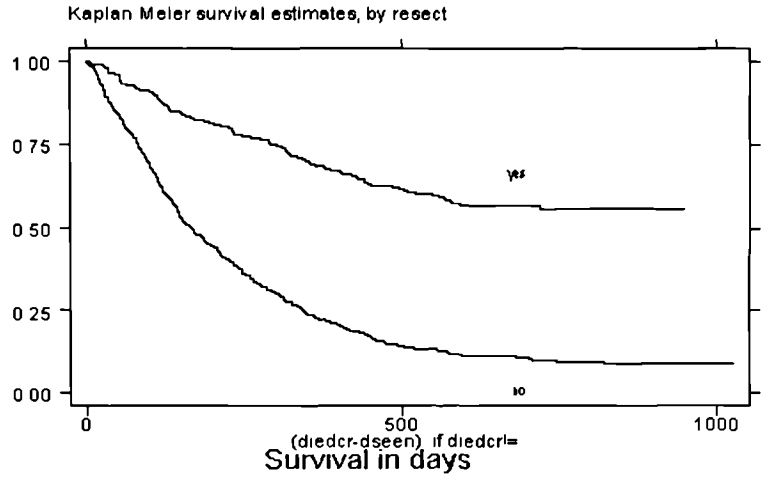



*Figure 5.10. Complementary log log plot for resection*

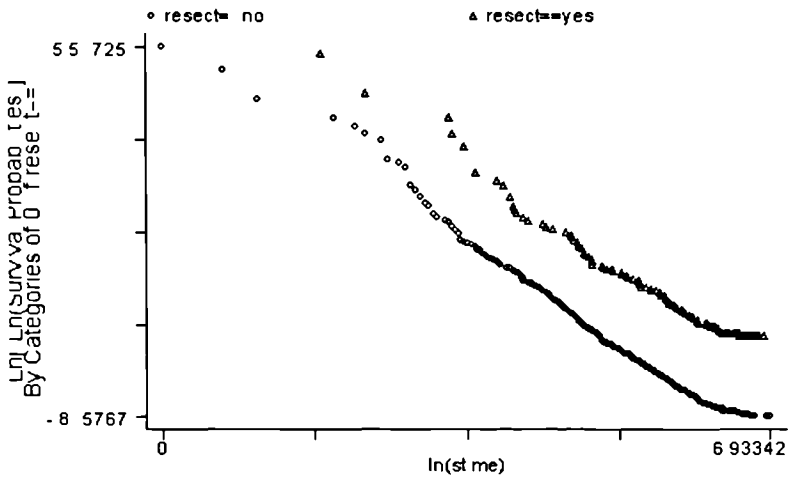



*Figure 5.11. Survival curve for chemotherapy*

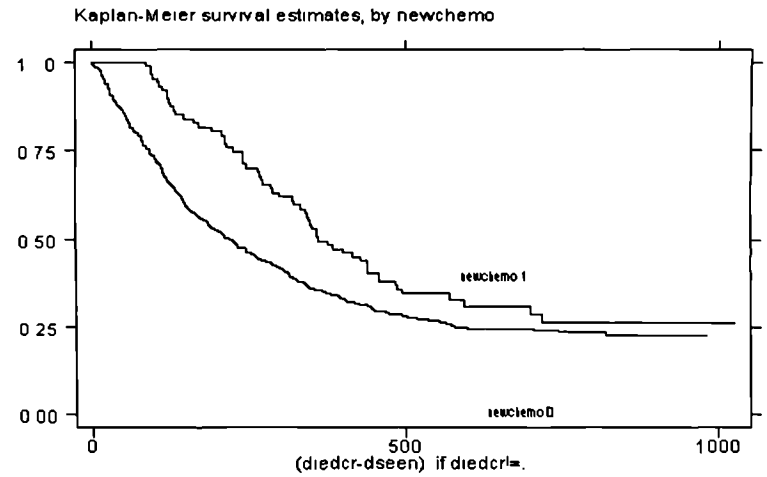


*Figure 5.12. Complementary log log plot for chemotherapy*

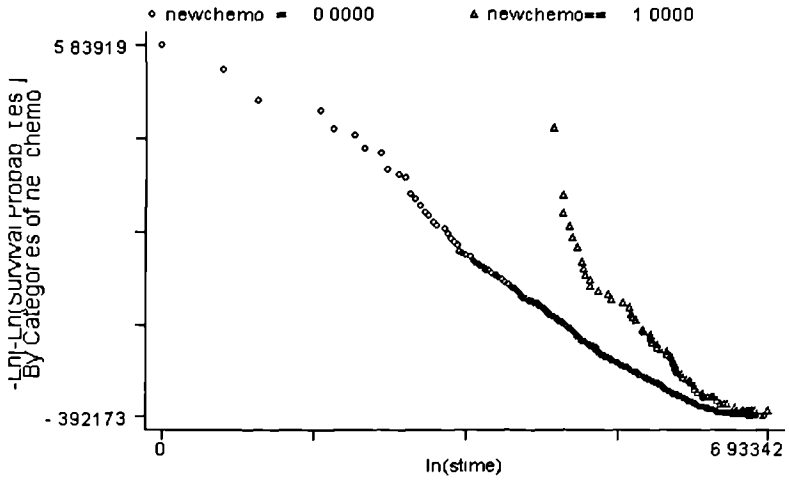



*Figure 5.13. Survival curves for radiotherapy*

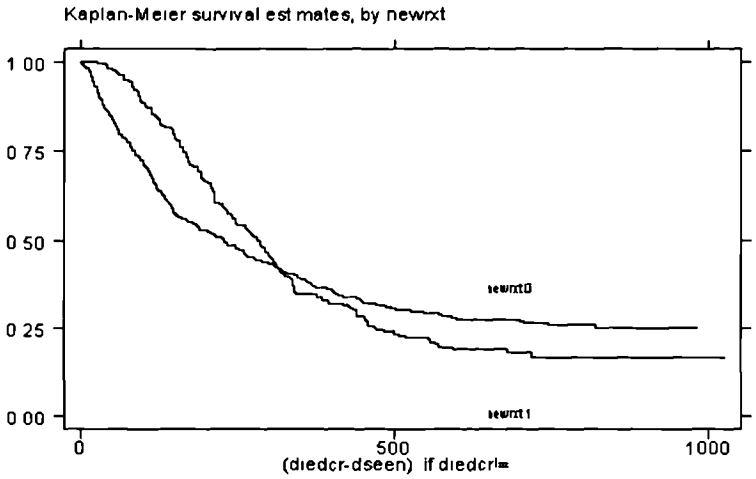



*Figure 5.14. Complementary log log plot for radiotherapy*

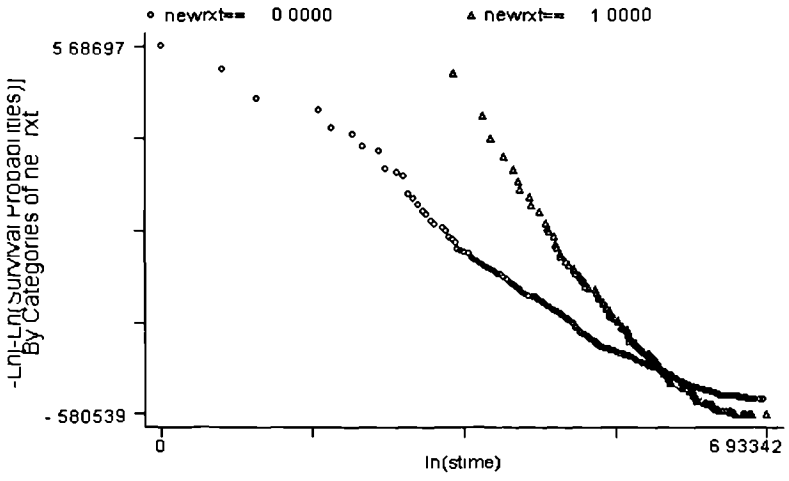


*Figure 5.15 Survival curves for stent*

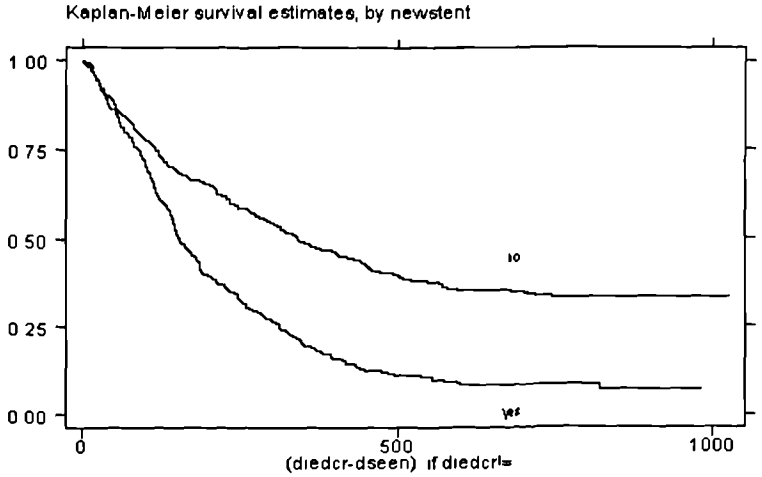
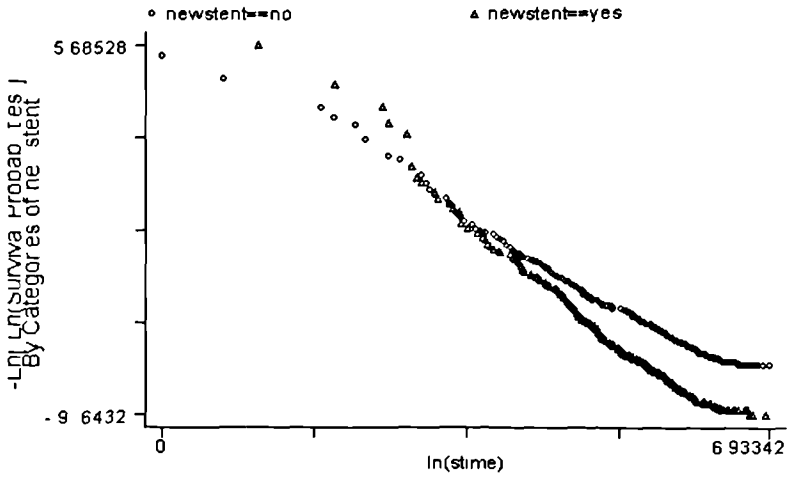



*Figure 5.16. Complementary log log plot for stent*




The above curves show that all of the variables, except for chemotherapy, radiotherapy and stent, show approximately proportional hazards throughout the period of follow-up and were appropriate for inclusion in the proportional hazards model. For chemotherapy, however, the relative survival advantage appeared to decrease over time in both the survival and complementary log log plots. For stents, the log log plots intersected, also suggesting non-proportionality. It was thus necessary to stratify the analysis by chemotherapy and stenting, precluding obtaining independent hazard ratios for these variables. For radiotherapy, survival curves crossed after about a year of follow-up, with patients receiving radiotherapy having better survival earlier and worse survival later.

Results of the final proportional hazards model are shown in Table 5.15.

**Table 5.15. Predictors of survival time: Cox's proportional hazards model**

| Doctor or hospital volume as categorical or continuous variable | Crude HR | Crude 95%CI | Adjusted HR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted HR | Adjusted 95%CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|
| Doctor volume.* | 0.98 | 0.97-0.98 | 0.99 | 0.98-1.00 | 0.038 | Age* | 1.01 | 1.00-1 02 | 452 616 |
| Low | 1.0 | - | 1.0 | - | | Weight loss | 1.4 | 1.2-1.7 | |
| Medium | 0.73 | 0.60-0.89 | 0.98 | 0.78-1.2 | 0.23 | Albumin* | 0.97 | 0.96-0.99 | |
| High | 0.50 | 0.40-0.61 | 0.82 | 0.64-1.1 | | Resection vs. none | 0.43 | 0.31-0.62 | |
| Hospital volume.* | 0.99 | 0.99-1.00 | 1.00 | 1.00-1.00 | 0.97 | Stage T+/N+/M0 vs. I-III | 1.1 | 0.78-1.7 | |
| Low | 1.0 | - | 1.0 | - | | Stage IV vs. I-III | 2.2 | 1.5-3.4 | |
| Medium | 0.80 | 0.65-0.99 | 0.85 | 0.67-1.1 | 0.34 | Unstaged vs. I-III | 1.2 | 0.78-1.8 | |
| High | 0.79 | 0.65-0.96 | 0.98 | 0.78-1.2 | | | | | |

* Continuous variable ** Adjusting for both doctor volume as continuous variables, and stratified by chemotherapy and stent. ~ No. events No with complete data in model

In the final model, survival was significantly better with increasing doctor volume, after adjusting for age, reported weight loss, albumin level, stage and whether or not patients had a resection, stent, or chemotherapy (Table 5.15). Dysphagia, histological adenocarcinoma, junctional adenocarcinoma and Barrett's oesophagus were no longer significant or influential independent prognostic factors and were excluded from the model. Additional stratification by radiotherapy did not affect the magnitude of the odds ratio for doctor volumes and thus radiotherapy was not a confounder and was excluded from the final model. Townsend deprivation score was not independently associated with survival time and its removal from the model did not influence the volume effects.

The hazard ratio of 0.991 for each unit increase in doctor volume corresponds to hazard ratios of 0.956 (95% CI 0.915-0.997) for every extra 5 patients managed mainly by one's doctor, and 0.913 (0.838-0.995) for every extra 10 patients (Table 5.16). Compared to patients of doctors who managed one new case per month, patients of doctors who managed one new case per week – a difference of 40 new cases per year - would have a hazard ratio of 0.694 (0.493-0.980). Comparison of crude and adjusted odds ratios shows that the crude odds ratio was strongly confounded by case mix and treatment mix (Table 5.16)

**Table 5.16. Crude and adjusted hazard ratios for various doctor volume differences**

| Difference in doctor volumes | Crude HR | | HR adjusted for case mix* and hospital volume | | HR adjusted for case mix*, hospital volume and treatments** | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| 1 | 0.974 | 0.966-0.830 | 0.986 | 0.977-0.995 | 0.991 | 0.982-1.000 |
| 10 | 0.768 | 0.711-0.830 | 0.868 | 0.793-0.950 | 0.913 | 0.838-0.995 |
| 40 | 0.348 | 0.255-0.575 | 0.568 | 0.395-0.815 | 0.694 | 0.493-0.980 |

* Age, weight loss, albumin, stage. ** Chemotherapy, stent.

In a secondary analysis, hazard ratios were compared across deciles of doctor volumes, showing a particularly poor survival for the lowest decile. When patients with doctor volumes of one were compared with all other patients, they had an adjusted hazards ratio of 1.57 (95% CI 1.2-2.1, P=0.005). This finding must be interpreted with caution, however, as the cutpoint was chosen after examining the results and not *a priori*. Hospital volume was not associated with survival.

There was no independent association between hospital volume and survival (Tables 5.15 and 5.17). Comparison of crude and adjusted hazard ratios shows that the crude hazard ratio was confounded by both case mix and treatment mix (Table 5.17).

**Table 5.17. Crude and adjusted hazard ratios for various hospital volume differences**

| Difference in hospital volumes | Crude HR | | HR adjusted for case mix* and doctor volume | | HR adjusted for case mix*, doctor volume and treatments** | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| 1 | 0.995 | 0.991-0.998 | 1.000 | 0.995-1.004 | 1.001 | 0.997-1.005 |
| 10 | 0.948 | 0.914-0.985 | 0.996 | 0.955-1.038 | 1.011 | 0.968-1.056 |
| 40 | 0.809 | 0.696-0.940 | 0.983 | 0.832-1.160 | 1.045 | 0.878-1.243 |

* Age, weight loss, albumin, stage ** Chemotherapy, stent.

Secondary analyses examined the influences of surgical, radiotherapy and chemotherapy volumes on survival time, in patients who received only these respective treatments. None of these volume measures was independently associated with survival time.

A secondary analysis using the same variables shown in Table 5.15, but adjusting for clustering on patients' main hospital, produced marginally wider confidence intervals for the hazard ratio associated with a unit increase in doctor volume but did not influence the magnitude of the hazard ratio (0.991, 95% CI 0.981-1.000; P=0.062).

# 6. GASTRIC CANCER

## 6.1 Numbers of cases, hospital and doctor volumes

A total of 731 patients with gastric cancer were identified. Of all patients, 82% were each managed in only one hospital trust (n 599), and the remaining 18% (n=132) were each managed in at least two hospital trusts. 722 (99%) patients had received their main treatment in one of the 23 acute hospital trusts in the region. Another 9 patients received their main treatments in one of hospital trusts outside the region; no hospital volumes were allocated to these patients. Table 6.1 shows the hospital volumes of each trust.

The corresponding doctor volumes are shown in Table 6.2, in less detail than hospital volumes because of the numerous doctors. A total of 213 main doctors were identified within the region: 18 were categorised as high volume doctors, 31 as medium volume doctors and 157 as low volume doctors. Volume cutpoints were chosen so as to have similar numbers in each category. The distribution of patients per doctor was highly skewed. The median number of patients per doctor was 7 (range 1-33; IQR 3-12) and the mean was 8.3 (SD 6.2). Ten doctors managed more than one new patient every month, on average, and at the other end of the spectrum 97 doctors managed only one patient per year.

## Table 6.1. Patient volumes per hospital trust

| Hospital code | No. cases | |
|---|---|---|
| **High volume hospitals (n>40)** | | |
| A | | 67 |
| B | | 62 |
| C | | 60 |
| D | | 44 |
| *All high volume* | *233* | |
| **Medium volume hospitals (26<n<39)** | | |
| E | | 40 |
| F | | 40 |
| G | | 38 |
| H | | 38 |
| I | | 36 |
| J | | 33 |
| K | | 31 |
| *All medium volume* | *256* | |
| **Low volume hospitals (n<25)** | | |
| L | | 26 |
| M | | 25 |
| N | | 25 |
| O | | 24 |
| P | | 24 |
| Q | | 23 |
| R | | 22 |
| S | | 15 |
| T | | 15 |
| U | | 14 |
| V | | 11 |
| W | | 9 |
| *All low volume* | *233* | |
| Out of region | | 9 |
| **Total** | | **731** |

## Table 6.2. Distribution of doctor volumes and patients

| Doctor volume category | No. of patients in category | No. of doctors | Range of patients per doctor |
|---|---|---|---|
| High volume | 255 | 18 | 10-22 |
| Medium volume | 207 | 31 | 5-9 |
| Low volume | 251 | 157 | 1-4 |
| Doctor not identified* | 9 | - | - |
| Main treatment outside region* | 9 | 7 | - |
| Total | 731 | 213 | - |

* Doctor volumes not specified for these patients

Doctor volumes were significantly and negatively correlated with hospital volumes (Spearman's rank correlation = -0.13; $p<0.0008$). The distribution of patients in the

hospital and doctor volume categories are shown in Table 6.3, which shows lack of correspondence between the specialisation of doctors and the specialisation of hospitals. A quarter of patients were mainly managed by high volume doctors in low volume hospitals, or by low volume doctors in high volume hospitals.

**Table 6.3. Distribution of patients by doctor and hospital volume category**

| Hospital volume<br>Doctor volume | Low | Medium | High | Total |
|---|---|---|---|---|
| Low | 75 | 82 | 94 | 251 |
| Medium | 75 | 50 | 82 | 207 |
| High | 80 | 121 | 54 | 255 |
| Total | 230 | 253 | 230 | 713 |

## 6.2 Case mix: age, sex, comorbidity, symptoms, stage

The distributions of demographic characteristics, mode of admission, comorbidities and symptoms, in relation to doctor and hospital volumes, are shown in Table 6.4. The male:female ratio was 65%:35%. Most patients were elderly and the age distribution was slightly negatively skewed (mean age 73 years, median 74, range 40-94; IQR 67-82). About half (45%) of cases had some comorbidity at the time of presentation.

Patients of higher volume doctors were significantly more likely to be younger, male and to have ischaemic heart disease and were significantly less likely to be admitted as emergencies. Hospital volumes were not significantly associated with any of the prognostic factors tabulated. However initial serum albumin levels were significantly lower with increasing hospital volume (Spearman's rank correlation coefficient = -0.16, P<0.0001), and were significantly higher with increasing doctor volume (Spearman's rank correlation coefficient – 0.19, P<0.0001).

Most patients were recorded as having weight loss, half had abdominal pain, and a quarter or less were recorded as having other gastrointestinal or systemic symptoms (Table 6.4). None of the symptoms was associated with doctor or hospital volumes.

Cancer staging, as judged by the end of the study period, provides a clearer view of the severity of the cancer, and how this varies according to doctor and hospital volume. Few patients had early stage, and thus potentially curable, disease (Table 6.5). The distribution of cancer staging differed significantly between doctor volume categories but not between hospital volume categories. Patients of higher volume doctors were more likely to have early stage disease and less likely to have metastases or completely unstaged disease. Patients of higher volume hospitals were significantly more likely to have metastases (P 0.02).

**Table 6.4. Age, sex, comorbidity and presenting symptoms**

| | Total | | Hospital Volumes | | | | | | Doctor Volumes | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | 731 | 100 | 233 | 100 | 256 | 100 | 233 | 100 | | 251 | 100 | 207 | 100 | 255 | 100 | |
| Age (mean years) | 73.4 | | 72.5 | | 73.1 | | 74.5 | | 0.38 | 75.3 | | 72.7 | | 71.9 | | <0.0001 |
| Sex (% female) | 257 | 35 | 76 | 33 | 92 | 36 | 85 | 36 | | 101 | 40 | 67 | 32 | 83 | 33 | 0.02 |
| Emergency first admission | 289 | 40 | 97 | 42 | 100 | 39 | 89 | 38 | 0.36 | 131 | 52 | 69 | 33 | 80 | 31 | <0.001 |
| **Comorbidity** | | | | | | | | | | | | | | | | |
| COAD | 81 | 11 | 24 | 10 | 24 | 9 | 33 | 14 | 0.18 | 32 | 13 | 21 | 10 | 26 | 10 | 0.24 |
| IHD | 133 | 18 | 42 | 18 | 49 | 19 | 40 | 17 | 0.80 | 36 | 14 | 36 | 17 | 57 | 22 | 0.02 |
| Hypertension | 131 | 18 | 45 | 19 | 47 | 14 | 47 | 20 | 0.69 | 44 | 18 | 34 | 16 | 50 | 20 | 0.56 |
| Diabetes | 68 | 9 | 25 | 11 | 19 | 7 | 24 | 10 | 0.97 | 21 | 8 | 14 | 7 | 33 | 13 | 0.13 |
| No. chronic diseases (mean) | 0.98 | | 0.99 | | 0.87 | | 1.1 | | 0.54 | 0.96 | | 0.91 | | 1.0 | | 0.88 |
| **Symptoms** | | | | | | | | | | | | | | | | |
| Dysphagia | 184 | 25 | 68 | 29 | 60 | 23 | 53 | 23 | 0.16 | 54 | 22 | 56 | 27 | 68 | 27 | 0.59 |
| Vomiting | 186 | 25 | 60 | 26 | 60 | 23 | 63 | 27 | 0.96 | 63 | 25 | 44 | 21 | 74 | 29 | 0.41 |
| GI bleeding | 61 | 8 | 18 | 8 | 21 | 8 | 21 | 9 | 0.70 | 21 | 8 | 19 | 9 | 20 | 8 | 0.93 |
| Abdominal Pain | 364 | 50 | 112 | 48 | 123 | 48 | 125 | 54 | 0.50 | 118 | 47 | 111 | 54 | 131 | 51 | 0.20 |
| Weight Loss | 414 | 75 | 138 | 59 | 140 | 55 | 133 | 57 | 0.94 | 135 | 54 | 112 | 54 | 159 | 63 | 0.17 |

# P value from logistic regression with continuous explanatory volume variable, except Spearman's rank correlation for age and no. chronic disease

## Table 6.5. Stage of disease

| | Total | | Hospital Volumes | | | | | | Doctor Volumes | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | 731 | 100 | 233 | 100 | 256 | 100 | 233 | 100 | | 251 | 100 | 207 | 100 | 255 | 100 | |
| **Detailed staging** | | | | | | | | | | | | | | | | |
| I | 41 | 6 | 13 | 6 | 13 | 5 | 14 | 6 | | 9 | 4 | 10 | 5 | 21 | 8 | |
| II | 78 | 11 | 34 | 15 | 25 | 10 | 18 | 8 | | 9 | 4 | 23 | 11 | 45 | 18 | |
| III | 49 | 7 | 19 | 8 | 17 | 7 | 13 | 6 | | 11 | 4 | 13 | 3 | 25 | 10 | |
| IV | 194 | 27 | 54 | 23 | 71 | 28 | 67 | 29 | | 77 | 31 | 54 | 26 | 59 | 23 | |
| Partially staged | | | | | | | | | | | | | | | | |
| M0 | 41 | 6 | 10 | 4 | 13 | 5 | 16 | 7 | | 17 | 7 | 12 | 6 | 9 | 4 | |
| T+ or N+ | 108 | 15 | 35 | 15 | 37 | 14 | 35 | 15 | | 23 | 9 | 30 | 14 | 53 | 21 | |
| Unstaged* | 220 | 30 | 68 | 29 | 80 | 31 | 70 | 30 | 0.61 | 105 | 42 | 65 | 31 | 43 | 17 | <0.001 |
| **Combined stages** | | | | | | | | | | | | | | | | |
| "Early" (I-III) | 168 | 23 | 66 | 28 | 55 | 21 | 45 | 19 | | 29 | 12 | 46 | 22 | 91 | 36 | |
| "Intermediate" (T+ or N+ or M0) | 149 | 20 | 45 | 19 | 50 | 20 | 51 | 22 | | 40 | 16 | 42 | 20 | 62 | 24 | |
| "Late" (IV) | 194 | 27 | 54 | 23 | 71 | 28 | 67 | 29 | | 77 | 31 | 54 | 26 | 59 | 23 | |
| Unstaged* | 220 | 30 | 68 | 29 | 80 | 31 | 70 | 30 | 0.35 | 105 | 42 | 65 | 31 | 43 | 17 | <0.001 |

# P value from Pearson $\chi^2$ test. * No T, N or M staging

Other key descriptive and prognostic variables were tumour location and histology. A third of cases occurred in the body of the stomach and another quarter were located in the cardia or fundus (Table 6.6).

**Table 6.6. Location of tumours**

| | n | % |
|---|---|---|
| Body | 233 | 32 |
| Antrum | 155 | 21 |
| Cardia | 123 | 17 |
| Fundus | 72 | 10 |
| Stump | 18 | 2 |
| Junction | 43 | 6 |
| Not stated | 87 | 12 |
| Total | 731 | 100 |

Almost all cases (91%) had histological reports. Three quarters of all cancers were confirmed adenocarcinomas (Table 6.7). Four were squamous carcinomas.

**Table 6.7. Histology**

| | n | % |
|---|---|---|
| Adenocarcinoma | 558 | 76 |
| Carcinoma (type not specified) | 63 | 9 |
| Other | 45 | 6 |
| No histology | 65 | 9 |
| **Total** | 731 | 100 |

For the purposes of this study, adenocarcinomas of the cardia or fundus were defined as junctional cancers, and comprised 30% of all 731 cancers. Patients with junctional tumours were significantly more likely than other patients to be male and to report dysphagia, and probability of having a junctional tumours was not associated with doctor volumes or hospital volumes (P=0.68 and P=0.55 respectively).

In summary, the overall case mix was severe, although less so than for pancreatic or oesophageal cancers. Patients tended to be elderly, have serious comorbidities, have symptoms of obstruction and weight loss, and to have advanced stage cancer. Patients of higher volume doctors tended to have better prognostic features, whereas patients of higher volume hospitals were more likely to have metastases and low albumin levels.

# 6.3 Investigations performed

Diagnostic and staging investigations varied widely between patients (Table 6.8). Almost all patients (90%) had oesophago-gastro-duodenoscopy (OGD) and 80% had biopsies. About forty percent had CT scans, the same proportion had abdominal ultrasounds and a quarter had contrast swallows. Endoscopic ultrasound (EUS) and laparoscopy are potentially the two most valid methods of identifying tumour spread before attempted resections, but were rarely used. OGD, biopsy, laparoscopy and EUS were significantly more likely with increasing doctor volume, and no test was associated with hospital volume (Table 6.8).

Patients with junctional tumours were significantly more likely than other patients to have a CT scan (52% vs. 35%, P<0.001), biopsy (93% vs. 85%, P=0.003) or EUS (3% vs. 1%, P 0.02), but were no more likely to have any of the other investigations.

The logistic regression analysis (Table 6.9) showed that patients of higher volume doctors were significantly more likely to have an OGD, biopsy, laparoscopy or EUS, independently of presenting features. Increasing hospital volume was associated only with abdominal ultrasound. For abdominal ultrasound the relationships with doctor volumes was U-shaped, as shown by the odds ratios for the volume categories; with the continuous volume variable the model was improved by addition of a quadratic doctor volume term (P 0.001). In general this suggests that doctors' preferences rather than availability of equipment determined choice of test.

The logistic regression analysis also showed that patients admitted as emergencies were more likely to have abdominal ultrasound and less likely to have a biopsy or laparoscopy. Patients with junctional adenocarcinomas were more likely to have biopsy, laparoscopy or EUS (OR 0.78). Patients with gastrointestinal bleeding were more likely to have laparoscopy or EUS. Vomiting reduced the likelihood of biopsy while dysphagia reduced the likelihood of abdominal ultrasound. Older patients were less likely to have EUS.

The investigations with which deprivation scores were associated, independently of the variables shown in Table 6.9, were contrast swallow, biopsy, and endoscopic ultrasound. Townsend score was not independently associated with contrast swallow. Townsend score was not independently associated with biopsy. The adjusted odds ratios for

endoscopic ultrasound, for unit increases in Townsend deprivation score, was 1.74 (1.28-2.37; P<0.001).

**Table 6.8. Investigations performed overall and by hospital and doctor volumes**

| Investigation | Total | | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| | 731 | 100 | 233 | 100 | 256 | 100 | 233 | 100 | | 251 | 100 | 207 | 100 | 255 | 100 | |
| OGD | 657 | 90 | 208 | 99 | 238 | 93 | 203 | 87 | 0.81 | 212 | 84 | 195 | 94 | 234 | 92 | 0.02 |
| Biopsy | 637 | 87 | 203 | 87 | 226 | 88 | 200 | 86 | 0.90 | 203 | 81 | 190 | 92 | 228 | 89 | 0.05 |
| Abdominal ultrasound | 307 | 42 | 81 | 35 | 129 | 50 | 94 | 40 | 0.12 | 117 | 47 | 69 | 33 | 115 | 45 | 0.10 |
| CT | 292 | 40 | 95 | 41 | 87 | 34 | 106 | 45 | 0.47 | 90 | 36 | 90 | 43 | 104 | 41 | 0.63 |
| Swallow | 181 | 25 | 69 | 30 | 46 | 18 | 65 | 28 | 0.95 | 54 | 22 | 59 | 29 | 65 | 25 | 0.75 |
| Laparoscopy | 85 | 12 | 23 | 10 | 43 | 17 | 18 | 8 | 0.73 | 15 | 6 | 18 | 9 | 51 | 20 | <0.001 |
| EUS | 11 | 2 | 3 | 1 | 8 | 3 | 0 | 0 | 0.34 | 2 | 1 | 0 | 0 | 9 | 4 | 0.001 |

# P value from logistic regression with continuous explanatory volume variable

## Table 6.9. Predictors of test use: logistic regression models

| Test | Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | OR | 95% CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| OGD | Doctor volume* | 1 06 | 1 01 | 1 05 | 1 01-1 10 | 0 02 | Sex F vs. M | 0 68 | 0.41-1.1 | 641 710 |
| | Low | 1 0 | - | 1 0 | - | | Junctional vs other | 1 5 | 0 84-2 8 | |
| | *Medium* | 3 0 | 1 5-5 9 | 2 8 | 1 4-5 5 | 0 004 | | | | |
| | High | 2 0 | 1 2-3 6 | 2 0 | 1 1-3 5 | | | | | |
| Biopsy | Doctor volume* | 1 04 | 1.00-1 08 | 1 03 | 0 99-1 07 | 0 10 | Admission: emergency | | | 637 713 |
| | Low | 1 0 | - | 1.0 | - | | vs elective | 0.62 | 0 38-0 98 | |
| | Medium | 2 6 | 1 5-4 8 | 2 3 | 1.3-4 2 | 0 007 | Admission: ? vs. elective | 1.8 | 0.52-6.1 | |
| | High | 2 0 | 1 2-3 3 | 1 9 | 1 1-3.3 | | Vomiting | 0.56 | 0.35-0.89 | |
| | | | | | | | Junctional vs. other | 2 0 | 1.2-3.6 | |
| *Abdominal* ultrasound | *Doctor volume** | *1 02* | *1.00-1 04* | 1 03 | 1 00-1.05 | 0 03 | Admission emergency | | | 304 713 |
| | Low | 1.0 | - | 1.0 | - | | vs. elective | 1.6 | *1.2-2.3* | |
| | Medium | 0.57 | 0.39-0 84 | 0.61 | 0.41-0.91 | 0.02 | Admission: ? vs. elective | 0.36 | 0 16-0.80 | |
| | High | 0.94 | 0.66-1.3 | 0.99 | 0.68-1.4 | | Dysphagia | 0.69 | 0.48-1.0 | |
| | | | | | | | Weight loss | 1.4 | 1.0-1.9 | |
| | | | | | | | Hospital volume* | 1.01 | 1.00-1.02 | |
| Laparoscopy | Doctor volume* | 1.11 | 1.08-1.15 | 1.10 | 1.06-1.15 | <0.001 | Age* | 0.97 | 0.95-0.99 | 85 710 |
| | Low | 1.0 | - | 1.0 | - | | GI bleed | 2.3 | 1.01-5.3 | |
| | *Medium* | 1 5 | 0 74-3 1 | 1.1 | 0.53-2.3 | <0.0001 | Admission: emergency | | | |
| | High | 3.9 | 2.1-7.2 | 3.0 | 1.6-5.6 | | vs. elective | 0.51 | 0.29-0.90 | |
| | | | | | | | *Admission: ? vs. elective* | 0.15 | 0.02-1.2 | |
| | | | | | | | Junctional vs. other | 1.7 | 1.1-2.9 | |
| EUS | Doctor volume* | 1.19 | 1.08-1.32 | 1.24 | 1.09-1.41 | 0.001 | Age* | 0.94 | 0.89-0.99 | 11 710 |
| | Low | 1.0 | - | 1.0 | - | | GI bleed | 9.9 | 2.1-47.5 | |
| | Medium | ## | ## | ## | ## | 0.08 | Junctional vs. other | 7.8 | 1.9-31.7 | |
| | High | 4.6 | 0.97-21.3 | 4.2 | 0.85-21.1 | | | | | |

* Continuous variable. ~ No. events / No with complete data in model. ## empty cell so cannot compute OR.

# 6.4 Treatment provided

Resections were performed in slightly over a third of patients (Table 6.10). Few patients had any of the other treatments considered, the most common of which was chemotherapy. Resections were significantly more likely with increasing doctor volume and less likely with increasing hospital volume. Bypasses were also more likely with increasing doctor volume. The likelihood of receiving none of the treatments decreased significantly with increasing doctor volume, and increased slightly but non-significantly with increasing hospital volume.

Cancer stage had a major influence on treatment provided (Table 6.11). Resections were most likely in patients with early (95%) or intermediate (45%) stage cancer. Of all resections, 60% were performed in patients with early stage disease, who comprised a quarter of all patients. Chemotherapy and radiotherapy did not appear to be as strongly influenced by stage. Chemotherapy was slightly more likely for patients with advanced stage. Half of all patients received none of the treatments considered, which was most likely in patients with advanced (56%) or unstaged (81%) disease.

Patients with junctional tumours were significantly more likely than other patients to have a stent (6% vs. 1%, P<0.001) and were significantly less likely to have a resection (31% vs. 39%, P 0.05) or bypass (1% vs. 7%, P=0.002), but were no different with regard to the other treatments.

**Table 6.10. Treatments provided**

| Treatment | Total | | Hospital Volumes | | | | | | | Doctor Volumes | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Low | | Medium | | High | | P# | Low | | Medium | | High | | P# |
| | n | % | n | % | n | % | n | % | | n | % | n | % | n | % | |
| Resection | 267 | 37 | 97 | 42 | 92 | 36 | 73 | 31 | 0.01 | 44 | 18 | 71 | 34 | 146 | 57 | <0.001 |
| Bypass | 37 | 5 | 13 | 6 | 12 | 5 | 12 | 5 | 0.83 | 7 | 3 | 10 | 5 | 19 | 7 | 0.01 |
| Stent | 19 | 3 | 11 | 5 | 1 | 0.4 | 11 | 5 | 0.80 | 3 | 1 | 13 | 6 | 7 | 3 | 0.87 |
| Chemotherapy* | 83 | 11 | 19 | 8 | 43 | 17 | 20 | 9 | 0.91 | 5 | 2 | 9 | 4 | 4 | 2 | 0.85 |
| Radiotherapy** | 18 | 2 | 5 | 2 | 9 | 4 | 4 | 2 | 0.94 | 5 | 2 | 8 | 4 | 5 | 2 | 0.57 |
| None of the above | 348 | 48 | 103 | 44 | 118 | 46 | 124 | 53 | 0.09 | 172 | 69 | 87 | 42 | 80 | 31 | <0.001 |

# P value from logistic regression model

**Table 6.11. Treatment provided by stage of disease**

| Treatment | Early (Stage I-III) | | | Intermediate (T+ or N+ or M0) | | | Advanced (Stage IV) | | | Unstaged | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % row | % col. | n | % row | % col. | n | % row | % col. | n | % row | % col. | n | % col. |
| Resection | 159 | 60 | 95 | 67 | 25 | 45 | 30 | 11 | 15 | 11 | 4 | 5 | 267 | 37 |
| Bypass | 2 | 5 | 1 | 10 | 27 | 7 | 20 | 54 | 10 | 5 | 14 | 2 | 37 | 5 |
| Stent | 1 | 5 | 1 | 5 | 26 | 3 | 7 | 37 | 4 | 6 | 32 | 3 | 19 | 2 |
| Chemotherapy | 17 | 20 | 10 | 15 | 18 | 10 | 34 | 41 | 18 | 17 | 20 | 8 | 83 | 11 |
| Radiotherapy | 3 | 17 | 2 | 1 | 6 | 1 | 7 | 39 | 4 | 7 | 39 | 3 | 18 | 2 |
| **Combinations** | | | | | | | | | | | | | | |
| Resection & stent | 0 | 0 | 0 | 1 | 17 | 1 | 3 | 50 | 2 | 2 | 33 | 1 | 6 | 1 |
| Resection & chemotherapy | 14 | 64 | 8 | 5 | 23 | 3 | 2 | 9 | 1 | 1 | 5 | 0.5 | 22 | 3 |
| Resection & radiotherapy | 2 | 67 | 1 | 0 | 0 | 0 | 1 | 33 | 0.5 | 0 | 0 | 0 | 3 | 0.4 |
| Chemotherapy & radiotherapy | 2 | 29 | 1 | 1 | 41 | 1 | 2 | 29 | 1 | 2 | 29 | 1 | 7 | 1 |
| None of the above | 3 | 1 | 2 | 58 | 17 | 39 | 108 | 31 | 56 | 179 | 51 | 81 | 348 | 48 |
| TOTAL | 168 | 23 | 100 | 149 | 20 | 100 | 194 | 27 | 100 | 220 | 30 | 100 | 731 | 100 |

Logistic regression was used to investigate the independent influences of doctor and hospital volumes, and patient characteristics, on choice of treatment (Table 6.12). Explanatory variables were only included in the models if they were likely to have been known before treatment was chosen. For example, M stage was considered as a potential explanatory variable but T and N stages, which require surgery for accurate assessment, were not. Other explanatory variables considered were age, sex, emergency or elective first admission, symptoms (especially weight loss and dysphagia), comorbidity (ischaemic heart disease, chronic obstructive airways disease, diabetes and hypertension), initial blood albumin and haemoglobin levels, and junctional tumours.

Patients of higher volume doctors were significantly more likely to have a resection or bypass and significantly less likely to have chemotherapy, or none of the treatments considered. Radiotherapy was not associated with doctor volume. The relationship between stents and doctor volume had a non-linear inverted U shape, as shown by the odds ratios for doctor volume categories; the model with continuous doctor volume was significantly improved by addition of a quadratic doctor volume term (P=0.04). Hospital volume was not independently associated with any treatment.

It is possible that for patients having radiotherapy or chemotherapy, each patient's main doctor or hospital, and thus doctor and hospital volumes, were misclassified (see Methods). To investigate whether such misclassification could have affected the apparent relationships between volumes, radiotherapy and chemotherapy, the relevant analyses were repeated, but confined to patients treated in only one hospital and by one consultant. This subgroup analysis found the same relationship between chemotherapy and doctor volumes as was found when all patients were included. Radiotherapy was less likely for high than for low doctor volumes (OR 0 43, 95% CI 0.19-0.98, P=0.05) but there was no association with continuous doctor volumes (P=0.22).

The following patient characteristics were independently associated with the respective treatments, controlling for doctor volumes. Older patients were less likely to have a resection, stent or chemotherapy. Patients with high albumin levels were more likely to have resections and less likely to have chemotherapy. Patients with metastases were less likely to have a resection or bypass. Patients with junctional adenocarcinomas were less likely to have a resection or bypass and more likely to have a stent. Emergency admissions were less likely to have a resection or stent.

The treatments with which deprivation scores were associated, independently of the variables shown in Table 6.12, were bypass and chemotherapy, which were significantly less likely with increasing deprivation score. The adjusted odds ratio for bypass, for unit increases in Jarman deprivation scores, was 0.97 (95% CI 0.94-1.00; P=0.04). The adjusted odds ratio for chemotherapy for unit increases in Townsend deprivation score, was 0.89 (95% CI 0.80-1.00; P<0.001). Other deprivation scores were not independently associated with these nor any other treatments and their removal from the models did not influence volume effects.

**Table 6.12a. Influences on treatment provided (logistic regression models)**

| Treatment | Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Resection | Doctor volume* | 1.02 | 1.10-1.16 | 1.11 | 1.07-1.14 | 0.001 | Age* | 0.98 | 0.96-1.0 | 246 622 |
| | Low | 1.0 | 1.0 | 1.0 | - | | Weight loss | 0.42 | 0.28-6.5 | |
| | Medium | 2.5 | 1.6-3.8 | 1.8 | 1.0-3.1 | 0.0001 | Emergency | | | |
| | High | 6.3 | 4.2-9.5 | 5.1 | 3.0-8.5 | | admission | 0.62 | 0.41-0.96 | |
| | | | | | | | Albumin* | 1.04 | 1.00-1.08 | |
| | | | | | | | M+ vs. M0 | 0.16 | 0.10-0.25 | |
| | | | | | | | M? vs. M0 | 0.08 | 0.05-0.14 | |
| | | | | | | | Junctional vs. other | 0.54 | 0.35-0.85 | |
| Bypass | Doctor volume* | 1.07 | 1.02-1.13 | 1.07 | 1.02-1.13 | 0.01 | Vomiting | 3.0 | 1.5-6.2 | 37 713 |
| | Low | 1.0 | - | 1.0 | - | | M+ vs. M0 | 4.5 | 1.9-10.9 | |
| | Medium | 1.8 | 0.66-4.7 | 2.3 | 0.85-6.5 | 0.05 | M? vs. M0 | 1.0 | 0.37-2.8 | |
| | High | 2.8 | 1.2-6.8 | 3.1 | 1.2-7.8 | | Junctional vs. other | 0.24 | 0.07-0.81 | |
| Stent | Doctor volume* | 1.00 | 0.93-1.08 | 0.97 | 0.89-1.06 | 0.52 | Age* | 0.97 | 0.93-1.00 | 19 691 |
| | Low | 1.0 | - | 1.0 | - | | Emergency | | | |
| | Medium | 7.7 | 1.7-34.6 | 4.8 | 1.0-23.0 | 0.002 | admission | 0.12 | 0.02-0.92 | |
| | High | 2.5 | 0.47-13.0 | 1.6 | 0.79-8.7 | | Dysphagia | 5.3 | 1.8-15.5 | |
| | | | | | | | Junctional vs. other | 4.2 | 1.4-12.5 | |

**Table 6.12b. Influences on treatment provided (logistic regression model) (continued)**

| Treatment | Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95%CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | Adjusted OR | Adjusted 95%CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Chemotherapy | Doctor volume* | 1.00 | 0.97-1.04 | 0.96 | 0.92-1 00 | 0.09 | Age* | 0.93 | 0.91-0.95 | 77 622 |
| | Low | 1.0 | - | 1.0 | - | | Weight loss | 2.4 | 1.3-4.3 | |
| | Medium | 1.2 | 0.72-2.2 | 0.87 | 0.47-1.6 | 0.02 | Vomiting | 0.28 | 0.13-0.62 | |
| | High | 0.78 | 0.43-1.4 | 0.40 | 0.20-0.78 | | Albumin* | 0.96 | 1.01-1.11 | |
| Radiotherapy | Doctor volume* | 0.98 | 0.90-1.05 | 0.95 | 0.87-1.04 | 0.25 | Age* | 0.93 | 0.89-0.96 | 18 710 |
| | Low | 1.0 | - | 1.0 | 1.0 | | Abdominal pain | 0.37 | 0.13-1.0 | |
| | Medium | 2.0 | 0.64-6.1 | 1.6 | 0.49-5.1 | 0.38 | | | | |
| | High | 0.98 | 0.28-3.4 | 0.69 | 0.19-2.5 | | | | | |
| None of the above treatments | Doctor volume* | 0.89 | 0.87-0.92 | 0.94 | 0.11-0.97 | <0.001 | Age* | 1.04 | 1.03-1.07 | 351 622 |
| | Low | 1.0 | - | 1.0 | - | | Emergency admission | 2.0 | 1.3-2.9 | |
| | Medium | .33 | 0.23-0.49 | 0.42 | 0.26-0.68 | <0.000 1 | Albumin* | 0.94 | 0.90-0.97 | |
| | High | .21 | 0.14-0.31 | 0.37 | 0.23-0.58 | | M+ vs. M0 | 4.9 | 3.0-8.1 | |
| | | | | | | | M? vs. M0 | 4.9 | 3.0-7.8 | |
| | | | | | | | Junctional vs. other | 1.6 | 1.0-2.4 | |

* Continuous variable ** Adjusted for continuous doctor volumes No. events / No. with complete data in model

## 6.5 Survival

All patients but one were matched with the NHS Central Register. By 10 October 1998, 557 (76%) patients had died. The median duration of follow-up at that time was 6.0 months (range 3 days to 30.2 months) for all patients, 22.8 (range 15.9-30.2) months for survivors, and 3.7 months (range 2 days to 25.0 months) for patients that died.
Three outcome measures were examined: operative mortality (i.e. death within 30 days of last surgery), one-year survival, and survival time. Influences on the first two outcomes were examined using multiple logistic regression, and influences on survival were examined using Cox's proportional hazards model. Possible explanatory variables considered for inclusion in the models were as defined in the Methods. They included hospital and doctor volumes, age, sex, symptoms (especially weight loss and dysphagia), comorbidities (ischaemic heart disease, chronic obstructive airways disease, diabetes and hypertension), initial haemoglobin and albumin levels, tumour histology, T stage, N stage, M stage, emergency or elective admission, and treatments given. T, N and M stages were firstly examined as separate variables and then as a composite staging variables with the following four categories: stage I-III; incompletely staged but with nodes or tumour invasion; with metastases; or unstaged. For operative mortality, the American Society of Anesthetists (ASA) score was also examined as a potentially explanatory variable.

## 6.5.1 Operative mortality

Of the 404 patients who had a surgical procedure, 55 (14%) died within 30 days. When prognostic variables were not taken into account, there was no association between operative mortality and doctor or hospital volumes. In the logistic regression model, however, operative mortality decreased significantly with increasing hospital volume (Table 6.13). The odds ratio of 0.95 for continuous doctor volume indicates that operative mortality decreased by about 5% for each extra patient managed by one's doctor per year. This corresponds to an odds ratio of 0.77 (95% CI 0.62-1.0) for a difference in doctor volumes of 5, and an odds ratio of 0.60 (95% CI 0.39-1.0) for a difference in doctor volumes of 10. Townsend deprivation scores was not independently associated with operative mortality.

Type of surgical procedure was not associated with operative mortality. The doctor volume effect on operative mortality was slightly but not significantly smaller in patients who had resections than in patients who had other procedures (P value for interaction between procedure and doctor volume terms = 0.08). Hospital volume was not associated with operative mortality. Secondary analysis using doctor's surgical volume instead of total doctor volume produced similar results. Secondary analysis using hospital surgical volume instead of hospital total volume found no association between operative mortality and hospital surgical volume.

**Table 6.13. Operative mortality and doctor volumes: logistic regression model**

| Doctor volume as categorical or continuous variable | Crude OR | Crude 95% CI | Adjusted OR | Adjusted 95% CI | P | Other variables in full model** | Adjusted OR | Adjusted 95% CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|
| Doctor volume* | 0.95 | 0.91-1..00 | 0.95 | 0.90-1 00 | 0 05 | Age* | 1.04 | 1.01-1.08 | 54 370 |
| Low | 1 0 | - | 1.0 | - | | Albumin* | 0.95 | 0.90-1.00 | |
| Medium | 0.52 | 0.23-1.2 | 0.50 | 0.21-1 2 | 0.17 | ASA score: | | | |
| High | 0 55 | 0.27-1 1 | 0.52 | 0.24-1.1 | | • 3 vs. 1-2 | 0.89 | 0.35-2.2 | |
| | | | | | | • 4-5 vs. 1-2 | 3.2 | 0.64-15.8 | |
| Hospital volume* | 1.01 | 0.99-1.03 | 1.00 | 0.98-1.02 | 0.81 | • Unknown vs. 1-2 | 0.89 | 0.40-2.0 | |
| Low | 1.0 | - | 1.0 | - | | | | | |
| Medium | 0.73 | 0.35-1.5 | 0.70 | 0.30-1.7 | 0.69 | | | | |
| High | 1.2 | 0.60-2.3 | 0.81 | 0.39-1.7 | | | | | |

* Continuous variable ** Adjusted for continuous doctor volumes No events No with complete data in model

## 6.5.2 One year survival

246 patients (34% total) survived at least one year after first presenting to hospital. One year survival appeared to increase with increasing doctor and doctor volumes but the association was marginally significant (P 0.07) for hospital volume only (Table 6.14). The odds ratio of 1.01 indicates an increased probability of surviving a year of about 1% for each extra patient managed by one's doctor or hospital annually. This corresponds to an odds ratio of 1.1 (95%CI 0.99-1.3) for a difference in hospital volumes of 10, an odds ratio of 1.3 (95% CI 0.98-1.6) for a difference in hospital volumes of 20, and an odds ratio of 1.6 (95% CI 0.97-2.7) for a difference in hospital volumes of 40. The latter figure suggests that patients were about 60% more likely to survive a year if managed in hospitals managing one new case per week compared to hospitals managing one new case per month. The odds ratios for doctor volumes were of similar magnitude but had much wider confidence intervals and did not approach significance.

One year survival was more likely with higher albumin levels, in patients having a resection or chemotherapy, and was less likely in patients reporting weight loss or vomiting, having junctional adenocarcinomas, or with advanced stages of disease.

**Table 6.14. Predictors of one year survival: logistic regression model**

| Doctor volume as categorical or continuous variable | Crude OR | Crude 95°oCI | Adjusted OR | Adjusted 95°o CI | P | Other variables in full model** | Adjusted OR | Adjusted 95°o CI | n/N~ |
|---|---|---|---|---|---|---|---|---|---|
| Doctor volume* | 1.06 | 1.03-1.09 | 1.01 | 0.97-1.05 | 0.55 | Albumin* | 1.11 | 1 06-1.16 | 215 614 |
| Low | 1.0 | - | 1.0 | - | | Weight loss | 0.62 | 0.41-0.94 | |
| Medium | 2.0 | 1.4-3.1 | 1.5 | 0.86-2.1 | 0.38 | Vomiting | 0.57 | 0.34-0.93 | |
| High | 2.3 | 1.5-3.4 | 1.2 | 0.7-2.1 | | Junctional vs. other | 0.52 | 0.33-0.83 | |
| | | | | | | Stage T+N+ or M0 vs. I-III | 0.43 | 0.24-0.79 | |
| Hospital volume* | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.03 | 0.07 | Stage IV vs. I-III | 0.19 | 0.10-0.37 | |
| Low | 1.0 | - | 1.0 | 1.0 | | Stage unknown vs. I-III | 0.52 | 0.25-1.08 | |
| Medium | 1.25 | 0.66-1.8 | 1.7 | 0.99-2.8 | 0.15 | Resection vs. none | 3.9 | 2.2-6.9 | |
| High | 0.84 | 0.57-1.3 | 1.4 | 0.82-2.3 | | Chemotherapy vs. none | 3.1 | 1.7-5.8 | |

Legend: * Continuous variable ** Adjusted for continuous hospital volumes No events No with complete data in model

## 6.5.3 Survival time

The same explanatory variables were examined for possible associations with survival time as were examined for one year survival. Kaplan Meier survival curves, and complementary log log plots were examined for explanatory variables were examined to assess proportionality of hazards throughout the period of follow-up, and thus suitability for inclusion in the proportional hazards model. Figures 6.1 to 6.20 show that hazards were proportional throughout the period of follow-up for all relevant explanatory variables, except for chemotherapy and radiotherapy. The initial survival advantage of chemotherapy disappeared during the latter period of follow-up, and the initial survival advantage of radiotherapy appeared to be reversed during the latter period of follow-up. It was thus necessary to stratify by chemotherapy and radiotherapy in the proportional hazards analysis, precluding obtaining hazard ratios for these two variables.

*Figure 6.1. Survival curve for doctor volume categories*

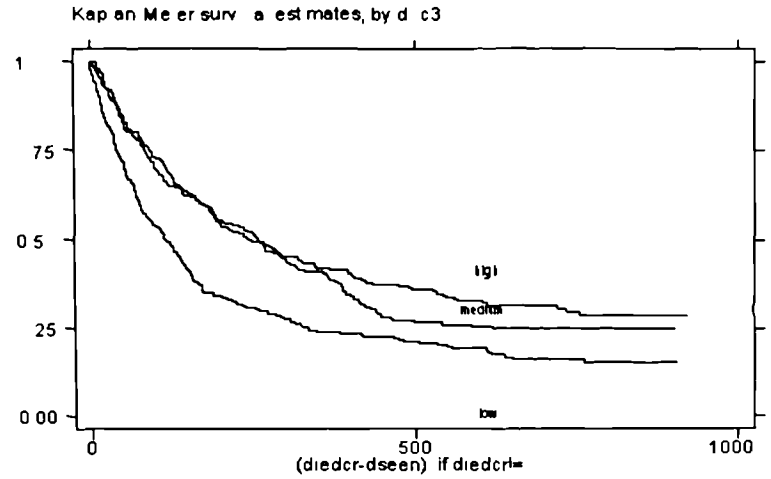


*Figure 6.2. Complementary log log plot for doctor volume categories*

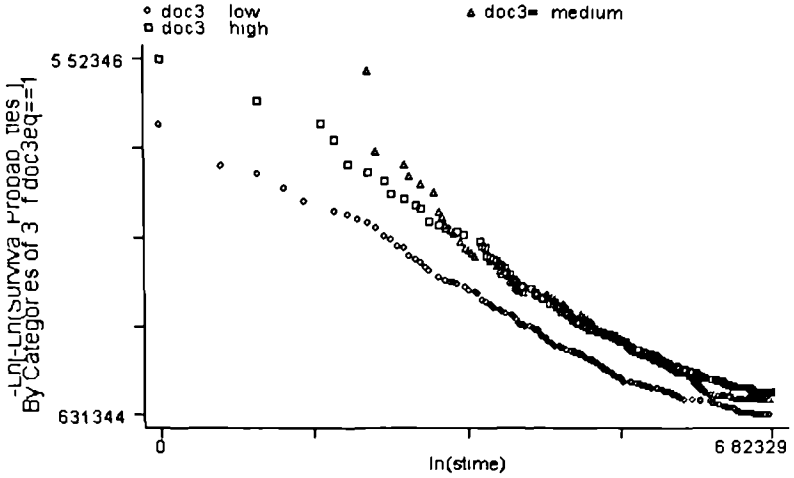



*Figure 6.3. Survival curves for hospital volume categories*

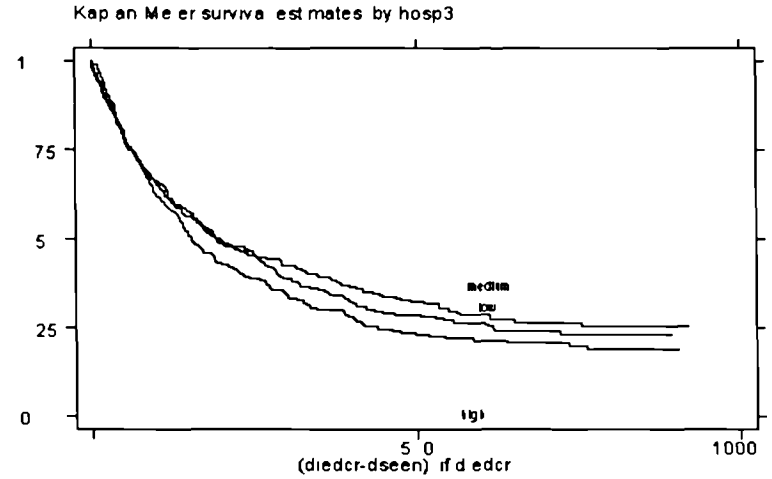



*Figure 6.4. Complementary log log plot for hospital volume categories*

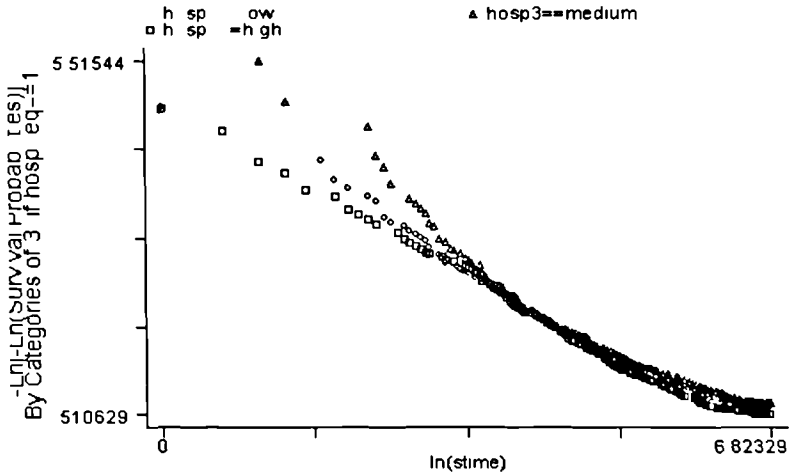


*Figure 6.5. Survival curves for age tertiles*

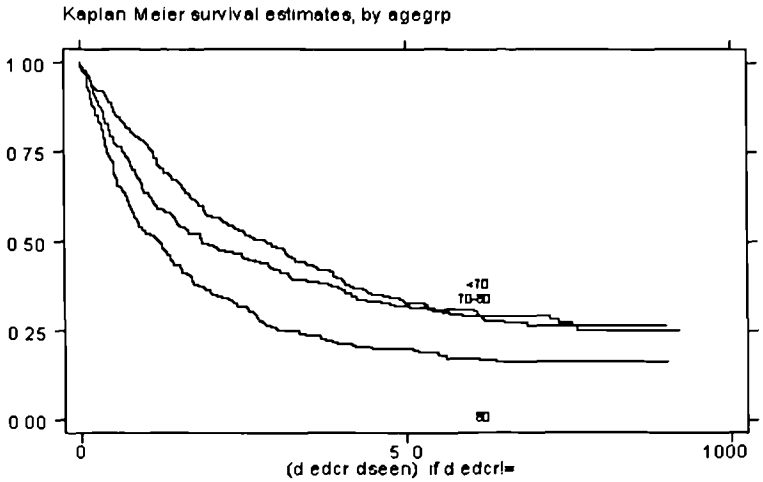



*Figure 6.6. Complementary log log plot for age tertiles*

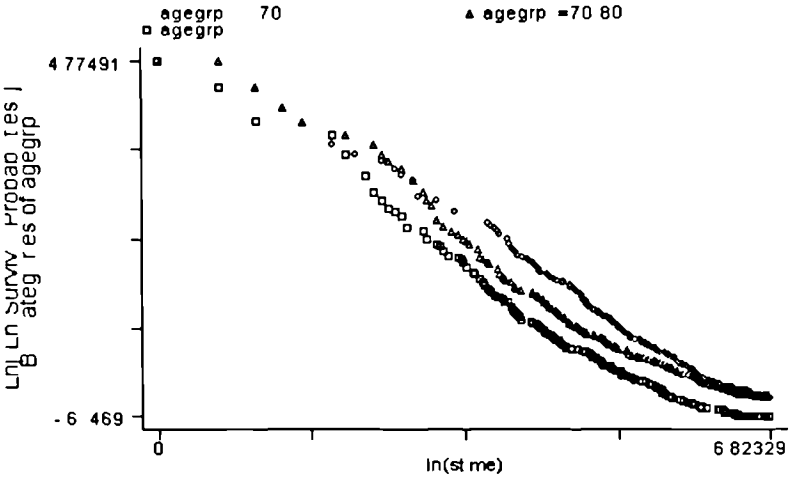



*Figure 6.7. Survival curve for vomiting*

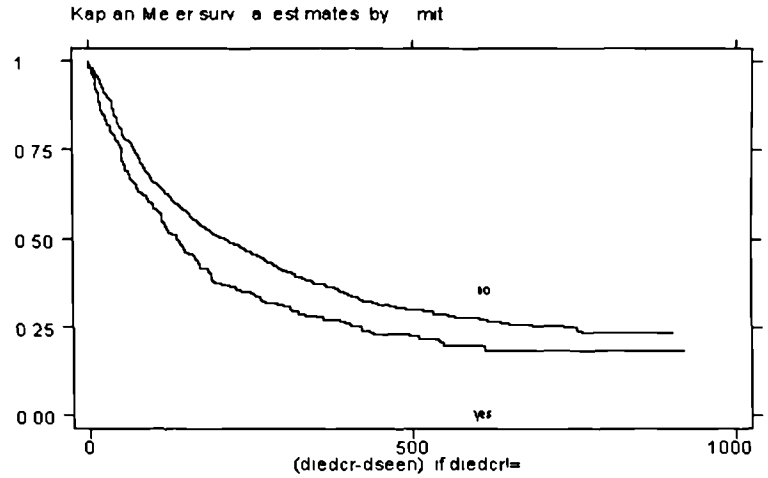


*Figure 6.8. Complementary log log plot for vomiting*

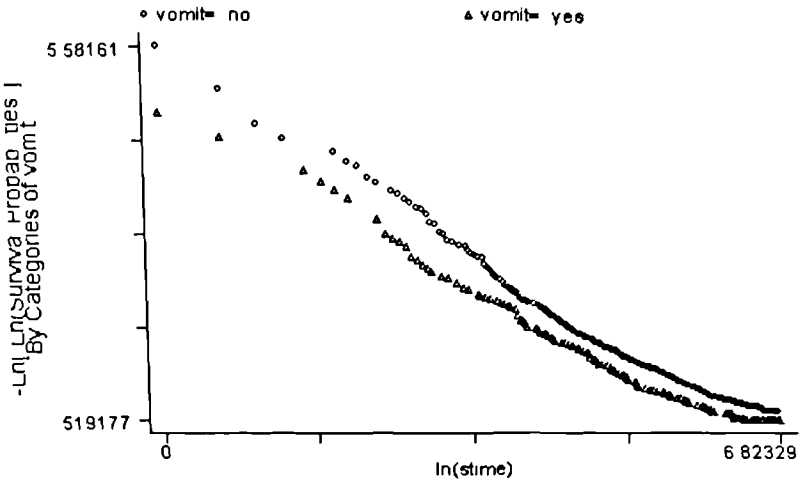



*Figure 6.9. Survival curve for serum albumin tertiles*

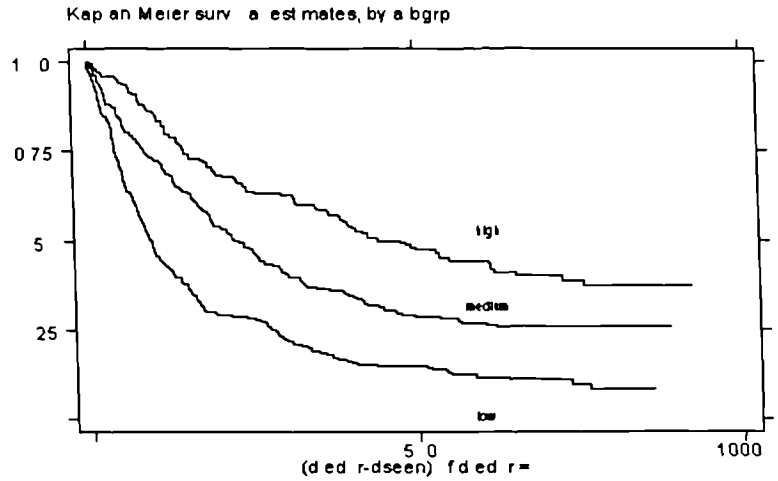



*Figure 6.10. Complementary log log plot for serum albumin tertiles*

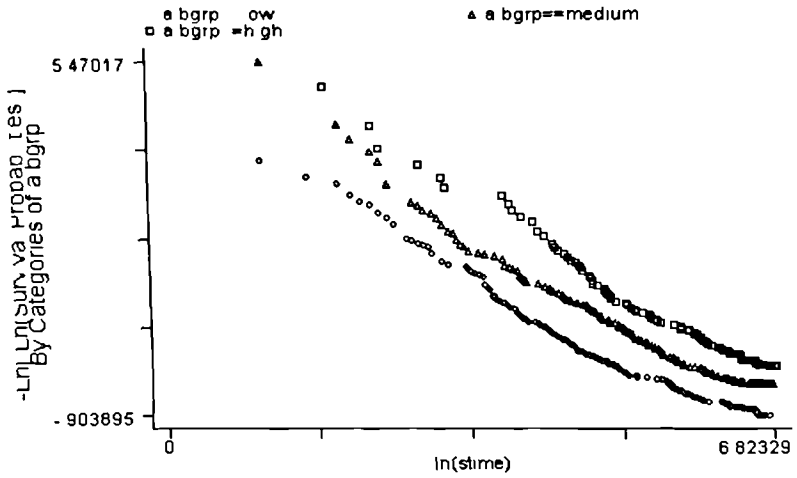


*Figure 6.11. Survival curves for junctional tumours*

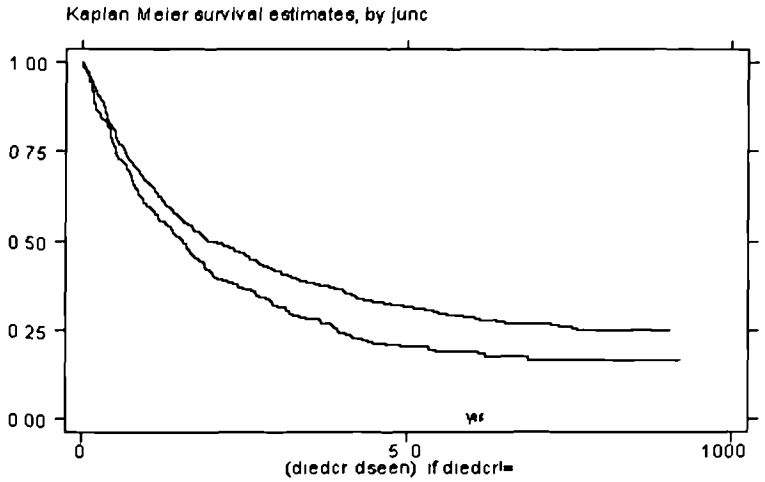



*Figure.6.12. Complementary log log plot for junctional tumours*

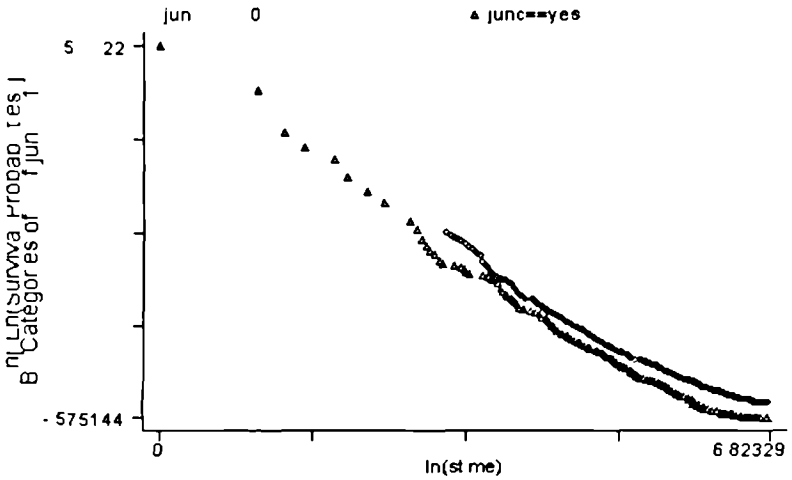



*Figure 6.13. Survival curves for cancer stages*

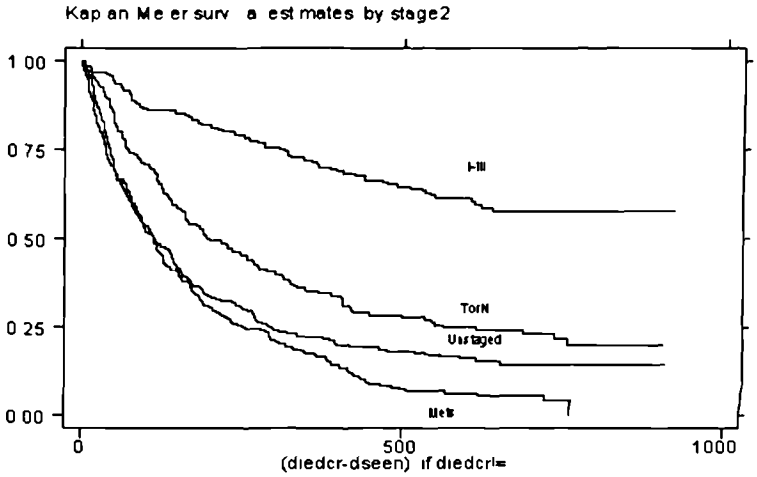


*Figure 6.14. Complementary log log plot for cancer stages*

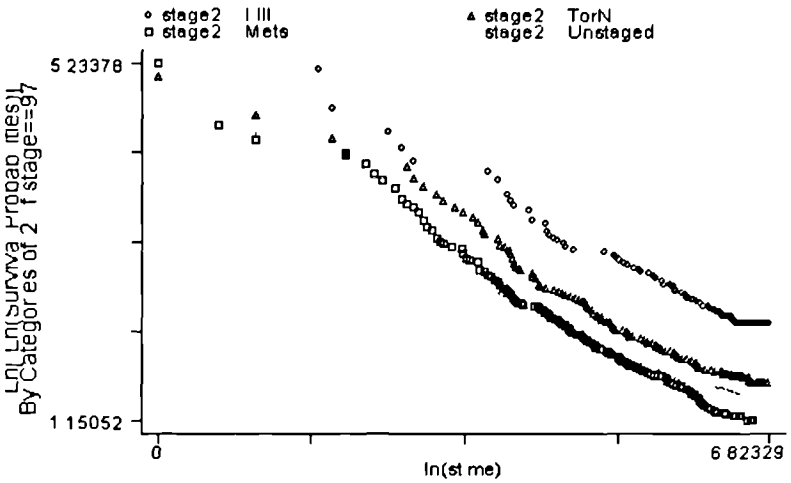



*Figure 6.15. Survival curve for resections*

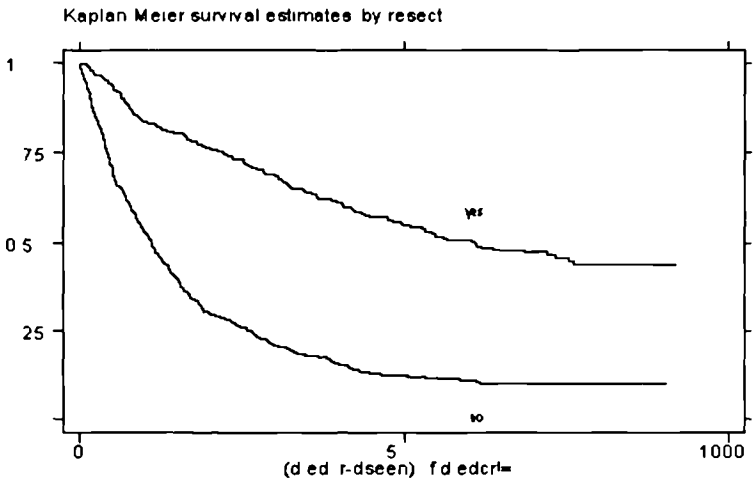



*Figure 6.16. Complementary log log plot for resections*

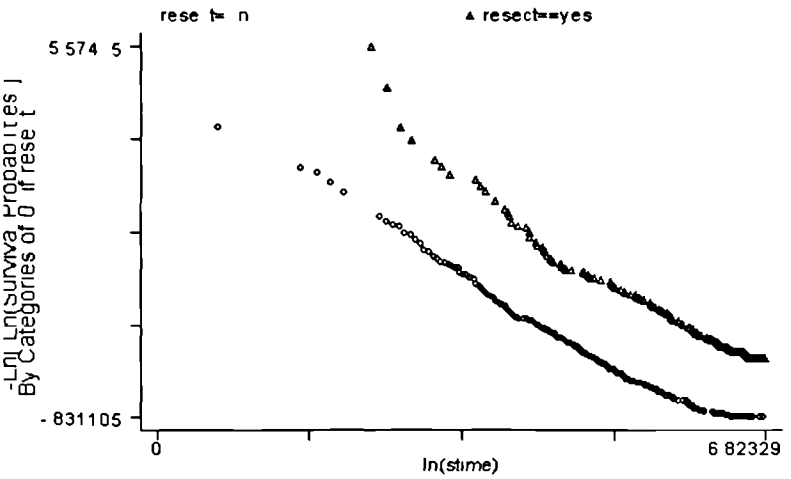


*Figure 6.17. Survival curve for chemotherapy*

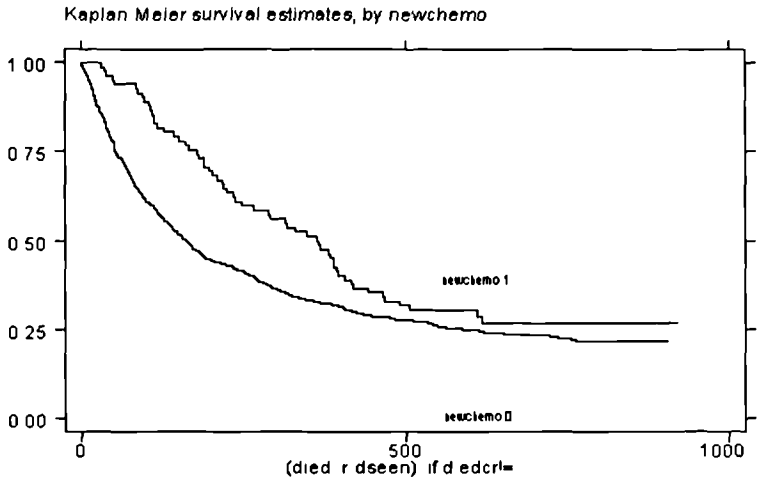



*Figure 6.18. Complementary log log plot for chemotherapy*

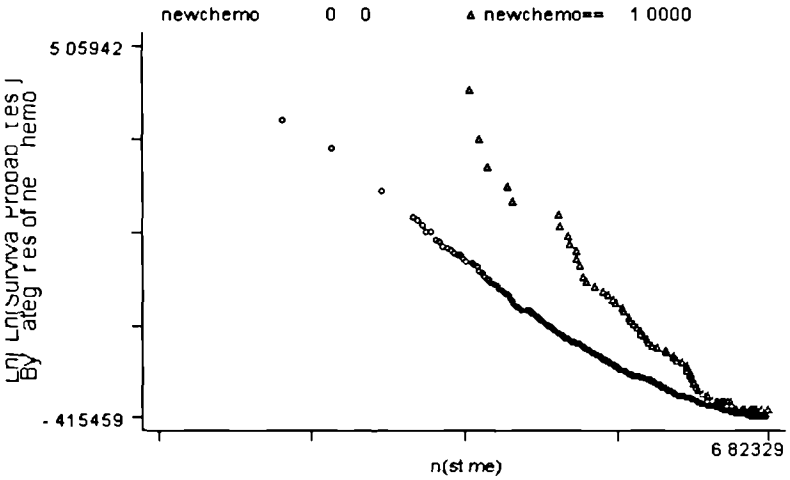



*Figure 6.19. Survival curve for radiotherapy*

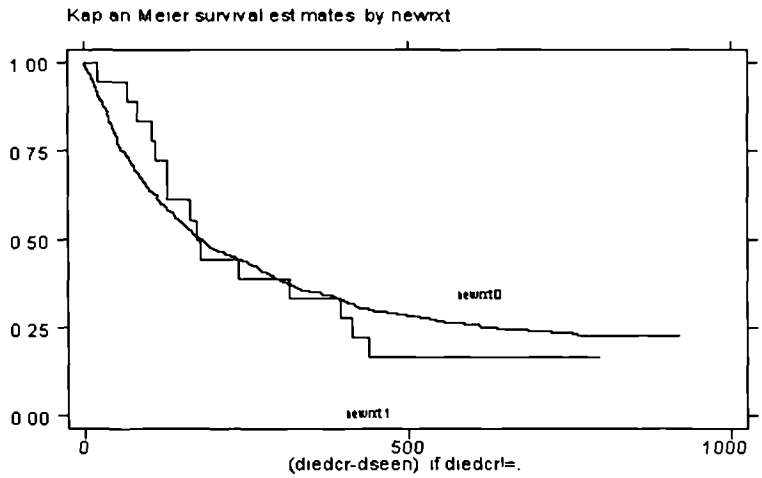
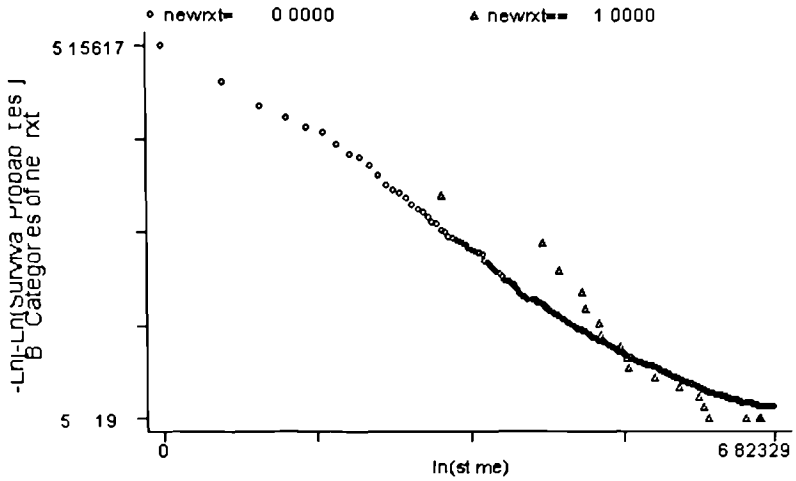


*Figure 6.20. Complementary log log plot for radiotherapy*




Before adjustment for prognostic and treatment variables, it appeared that survival time was significantly longer with increasing doctor volumes, and that there was no association with hospital volumes (Table 6.15). With adjustment, however, a different pattern emerged. Survival time was significantly better with increasing hospital volume but was no longer associated with doctor volume. Townsend deprivation score was not independently associated with survival time and its removal from the model did not influence volume effects.

**Table 6.15. Predictors of survival time: Cox's proportional hazards model**

| Doctor or hospital volume as categorical or continuous variable | Crude OR | Crude 95%CI | P# | Adjust-ed OR | Adjusted 95% CI | P# | Other variables in full model** | Adjusted OR | Adjusted 95%CI | n N~ |
|---|---|---|---|---|---|---|---|---|---|---|
| Doctor volume.* | 0.96 | 0.95-0.98 | <0.001 | 0.99 | 0.98-1.01 | 0.51 | Age* | 1.01 | 1.00-1.02 | 478 622 |
| Low | 1.0 | - | | 1.0 | - | | Vomiting | 1.4 | 1.1-1.7 | |
| Medium | 0.67 | 0.55-0.83 | | 0.87 | 0.68-1.1 | | Albumin* | 0.94 | 0.93-1.7 | |
| High | 0.60 | 0.49-0.74 | <0.0001 | 0.95 | 0.75-1.2 | 0.48 | Junctional vs. other | 1.4 | 1.1-1.7 | |
| | | | | | | | Stage T+N+ or M0 vs. I-III | 1.9 | 1.4-2.8 | |
| Hospital volume.* | 1.00 | 1.00-1.01 | 0.38 | 0.99 | 0.99-1.00 | 0.03 | Stage IV vs. I-III | 3.2 | 2.2-4.6 | |
| Low | 1.0 | - | | 1.0 | - | | Stage unknown vs. I-III | 1.8 | 1.2-2.7 | |
| Medium | 0.93 | 0.76-1.2 | | 0.83 | 0.66-1.0 | | Resection vs. none | 0.46 | 0.35-0.61 | |
| High | 1.12 | 0.91-1.4 | 0.20 | 0.82 | 0.65-1.0 | 0.15 | | | | |

* Continuous variable ** Adjusted for both doctor and hospital volume as continuous variables, and stratified by chemotherapy and radiotherapy No events No with complete data in model

The hazard ratio of 0.99 for hospital volume suggests that one's risk of death at any time after presentation was 1% lower for every extra patient that one's hospital managed annually. This corresponds to a hazard ratio of 0.94 (95% CI 0.89-0.99) for a difference in hospital volumes of 10, a hazard ratio of 0.89 (95% CI 0.79-0.99) for a difference in hospital volumes of 20, and a hazard ratio of 0.78 (95% CI 0.62-0.97) for a difference in hospital volumes of 40 (Table 6.16). The latter figure suggests that patients were about 20% less likely to die at any time after presentation if managed in hospitals managing one new case per week compared to hospitals managing one new case per month.

**Table 6.16. Crude and adjusted hazard ratios for various differences in hospital volume**

| Difference in hospital volumes | Crude HR | | HR adjusted for case mix* and doctor volume | | HR adjusted for case mix*, doctor volume and treatments** | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| 1 | 1.002 | 0.997-1.007 | 0.995 | 0.989-1.001 | 0.994 | 0.988-0.999 |
| 10 | 1.023 | 0.972-1.076 | 0.951 | 0.899-1.006 | 0.938 | 0.886-0.993 |
| 40 | 1.094 | 0.894-1.338 | 0.819 | 0.654-1.025 | 0.775 | 0.616-0.974 |

* Age, vomiting, albumin, junctional tumour, stage ** Chemotherapy, radiotherapy, resection

Table 6.17 shows how the crude hazard ratio for doctor volume was confounded by both case mix and treatment mix.

**Table 6.17. Crude and adjusted hazard ratios for various doctor volume differences**

| Difference in doctor volume | Crude HR | | HR adjusted for case mix* and hospital volume | | HR adjusted for case mix*, hospital volume and treatments** | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| 1 | 0.961 | 0.947-0.976 | 0.989 | 0.973-1.005 | 0.994 | 0.978-1.011 |
| 10 | 0.675 | 0.583-0.782 | 0.892 | 0.758-1.050 | 0.946 | 0.800-1.118 |

* Age, vomiting, albumin, junctional tumour, stage ** Chemotherapy, radiotherapy, resection.

The reason that adjustment for prognostic and treatment factors reversed the apparent associations with doctor and hospital volumes is that higher volume hospitals were more likely to have patients with worse prognoses, whereas higher volume doctors were more likely to have patients with better prognoses (as shown in section 6.2).

To assess whether the effect of hospital volume on survival differed in patients who had resections from patients who did not, a hospital volume and resection interaction term was added to the model. The P value for the addition of the interaction term was of marginal statistical significance (P=0.054). The analysis was thus conducted separately

for patients who did and did not have a resection. This suggested that the survival advantage in higher volume hospitals was mainly among patients who did not have a resection (odds ratio for hospital volume 0.99, 95% CI 0.98-1.00; P=0.005) and was absent among patients who did have a resection (odds ratio for hospital volume 1.00, 95% CI 0.99-1.01; P 0.77). There was no interaction between cancer stage and hospital volume (P 0.67).

Adjustment for clustering of survival on main hospital produced similar results to those shown in Table 6.15. The odds ratio for the continuous hospital volume variable remained 0.99 (95% CI 0.99-1.00; P 0.03).

A secondary analysis was confined to patients who had surgery, and used hospital and doctor surgical volumes instead of total hospital and doctor volume as explanatory variables, together with the other variables shown in Table 6.15. There was no association between hospital or doctor surgical volume and survival. Similar analyses of chemotherapy and radiotherapy volumes found no associations with survival time.

# 7. COST OF HOSPITAL CARE

This chapter reports the estimated cost of all hospital care provided, and the hospital cost per day of life, for a period up to one year after first presentation or to time of death. Additionally, it reports the relationships between these two cost measures, prognostic factors, treatments provided and doctor and hospital volumes.

## 7.1 Hospital unit costs per resource item

11 of 23 (48%) hospitals in the South and West region responded to the questionnaire. Non-respondents were telephoned and stated that they were unable to provide the information requested. Response rates were higher for high hospital volume hospitals (75%) than for medium (57%) or low (25%) volume hospitals.

The results of the survey of hospital unit costs are shown in Table 7.1. Most hospitals that responded to the questionnaire were unable to provide unit costs for each type of resource, and some of these were supplied by fewer than five hospitals. However 9 of the 11 respondents were able to provide unit costs for the most important resource item, namely unit cost per day in a surgical ward. For most resources, median and mean unit costs were similar, suggesting that the mean unit costs were fairly robust. For half of the resource items, the median unit cost differed from the mean unit cost by less than 8% of the mean. Highest and lowest reported unit costs are shown in Table 7.1. For most resources the maximum unit cost was several times higher than the minimum unit cost, suggesting that different costing methods were used at the extremes. There were no trends of lower or higher unit costs in higher or lower volume hospitals; Figure 7.1 shows this statement to be true for the most important resource item - surgical in-patient day.

*Figure 7.1. Reported costs (£) per day in a surgical ward, excluding tests and treatments, and hospital volume (total number of all three cancers managed by the respective hospital in one year)*

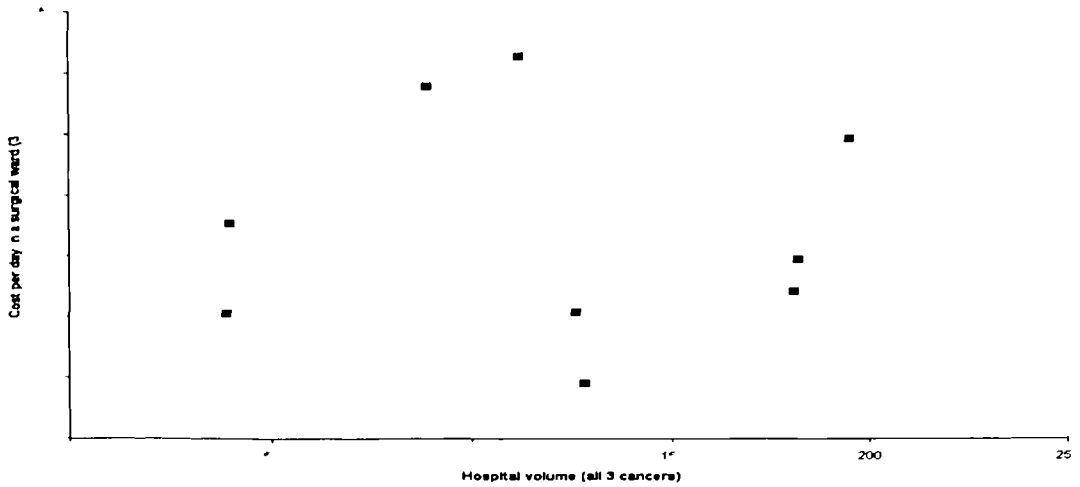



**Table 7.1a. Unit costs of resource items**

| Resource item | Median unit cost | Mean unit cost | No of respondents |
|---|---|---|---|
| **Hospital stays and visits** | | | |
| Day in surgical ward | 147.00 | 180.59 | 9 |
| Day in ITU | 1217.00 | 1246.08 | 8 |
| Surgical OPD visit | 68.00 | 67.92 | 10 |
| Oncology OPD visit | 79 00 | 86.78 | 9 |
| **Pathology tests** | | | |
| Whole blood count | 2.50 | 3.67 | 9 |
| Coagulation | 4.50 | 9.54 | 8 |
| Urine MCS | 3.19 | 3.58 | 8 |
| Cytology | 25.67 | 23.69 | 9 |
| Histology | 33.52 | 29.39 | 9 |
| Electrolytes | 4.74 | 4.43 | 9 |
| Liver function | 4.85 | 4.60 | 9 |
| Amylase | 3.27 | 3.74 | 9 |
| Calcium | 3.13 | 3.30 | 9 |
| Glucose | 3.27 | 3.54 | 9 |
| Blood gases | 3.38 | 8.01 | 8 |
| **Radiology & imaging** | | | |
| Chest X ray | 14.00 | 13.67 | 10 |
| Contrast swallow | 79.82 | 90.93 | 10 |
| Bronchoscopy | 121.97 | 264.32 | 8 |
| Abdominal CT | 79.82 | 95.71 | 10 |
| MRI | 303.60 | 405.96 | 8 |
| Angiography | 303.60 | 428.67 | 9 |
| Abdominal ultrasound | 33.90 | 53.08 | 10 |
| EUS | 414.50 | 414.50 | 2 |

*Continued on next page*

## Table 7.1b. Unit costs of resource items (continued)

| Resource item | Median unit cost | Mean unit cost | No of respondents |
|---|---|---|---|
| OGD* | 238.00 | 709.13 | 9 |
| Laparoscopy | 575.00 | 575.00 | 3 |
| PTC | 529.89 | 546.98 | 6 |
| ERCP | 489.50 | 492.83 | 8 |
| **Miscellaneous** | | | |
| ECG | 37.00 | 45.56 | 9 |
| Pulmonary function | 42.00 | 52.50 | 4 |
| Blood transfusion (per unit) | 33.02 | 35.62 | 5 |
| **Pancreatic cancer treatments** | | | |
| Dilatation of bile duct | 800.00 | 763.00 | 4 |
| Pancreatic stent | 800.00 | 763.00 | 5 |
| Laser of pancreas | 548.50 | 548.50 | 2 |
| Pancreatico-duodenectomy | 1726.00 | 1834.33 | 4 |
| Pancreatectomy | 1535.00 | 1945.67 | 4 |
| Bypass | 1024.00 | 975.67 | 3 |
| Laser | 390.00 | 418.67 | 4 |
| Radiotherapy | 1460.00 | 1422.33 | 3 |
| Chemotherapy** | | 1046.32 | |
| **Gastric cancer treatments** | | | |
| Gastrectomy | 1180.50 | 1099.75 | 5 |
| Bypass* | 896.00 | 2868.00 | 3 |
| Laparotomy only | 735.50 | 751.75 | 4 |
| Laser | 541.00 | 541.00 | 2 |
| Radiotherapy | 1460.00 | 1422.33 | 3 |
| Chemotherapy** | | 615.38 | |
| **Oesophageal cancer treatments** | | | |
| Oesophagectomy | 2390.00 | 2028.40 | 5 |
| Bypass | 1521.00 | 1671.80 | 4 |
| Dilatation | 1417.00 | 1251.50 | 5 |
| Stent | 1711.00 | 1547.75 | 6 |
| Laparotomy only | 1280.00 | 1379.33 | 3 |
| Thoracotomy only | 2390.00 | 1930.40 | 4 |
| Laser | 740.00 | 970.67 | 3 |
| Radiotherapy | 2190.00 | 1838.40 | 4 |
| Chemotherapy** | | 432.28 | |

Legend * Median used instead of mean unit cost in base estimates ** Mean chemotherapy costs per treated patient obtained from types and quantities of agents recorded in hospital notes, and unit costs from British National Formulary

# 7.2 Pancreatic cancer

## 7.2.1 Components and distribution of total cost

Table 7.2 shows that the mean cost of hospital care per patient, including all care received within a year of presentation, was £7240. Ward care, represented by bed days, accounted for 64% of the total cost. Specific treatments, of which resections were most important, accounted for a quarter of total costs. Investigations accounted for 19% of total costs.

**Table 7.2. Mean hospital cost per pancreatic cancer patient**

| Resource | Mean | % of Total |
|---|---|---|
| Ward bed days | 4629 | 63.9 |
| Outpatient attendances | 227 | 3.1 |
| Investigations | 1032 | 14.3 |
| All specific treatments | 1353 | 18.7 |
| *Resection* | *182* | 2.5 |
| *Bypass surgery* | *167* | 2.3 |
| *Stent insertion* | *441* | 6.1 |
| *ERCP & dilatation* | *331* | 4.6 |
| *Laparotomy only* | *35* | 0.5 |
| *Radiotherapy* | *58* | 0.8 |
| *Chemotherapy* | *125* | 1.7 |
| *Blood transfusion* | *13* | 0.2 |
| Total | 7240 | 100.0 |

The distribution of total costs was positively skewed (Figure 7.2). However only four patients cost more than £30 000 each. Logarithmic transformation of cost did not improve the symmetry of the distribution (Figure 7.3). Comparisons of costs between different categories of patients, and linear regression analyses of total costs, used the untransformed total cost.

*Figure 7.2. Distribution of total cost*

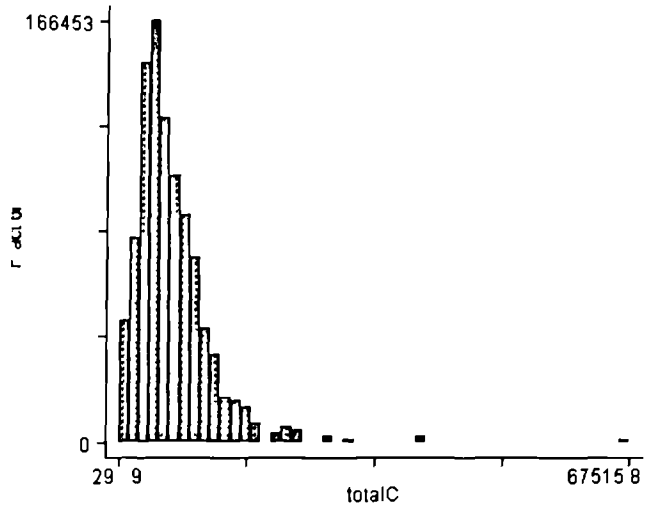
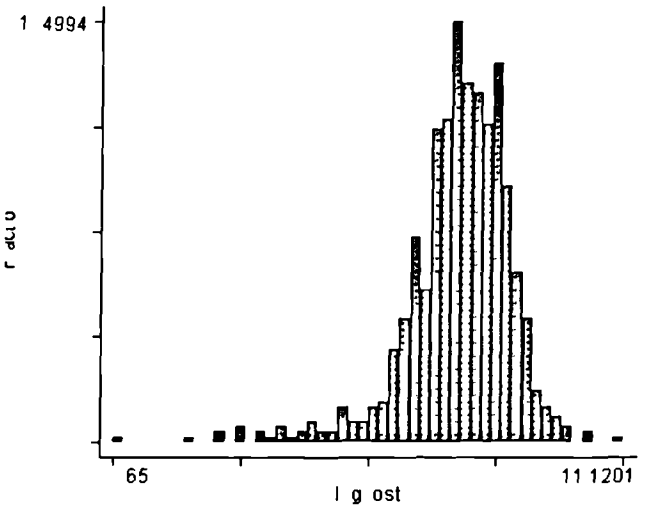



*Figure 7.3. Distribution of natural log of total cost*




A major determinant of total cost was bed days. A high proportion of patients had multiple admissions. Table 7.3 shows that half of patients were admitted to hospital at least twice within a year of presentation, and almost a quarter three or more times.

**Table 7.3. Frequency distribution of number of admissions per patient**

| No of admissions | No of patients | % of patients (N=781) |
|---|---|---|
| 1 or more | 759 | 97.2 |
| 2 or more | 409 | 52.4 |
| 3 or more | 179 | 22.9 |
| 4 or more | 113 | 14.5 |
| 5 or more | 88 | 11.3 |
| 6 or more | 35 | 4.5 |
| 7 or more | 12 | 1.5 |
| 8 or more | 6 | 0.8 |

## 7.2.2 Sensitivity analysis

The sensitivity of total cost to assumptions about the unit costs of each resource item was examined by replacing the mean unit cost reported by each responding hospital with, firstly, the lowest reported unit cost and then with the highest reported unit cost. The results of the sensitivity analysis are shown in Table 7.4. The total cost estimate was highly sensitive to assumptions about the unit cost of a day in a hospital bed. If the mean unit cost per bed day was replaced by the first (£104) and third (£246) quartiles of reported unit costs, instead of the lowest and highest unit costs, the changes in total cost were 27% and +23% respectively. Total cost was increased or decreased by more than 5% if the mean unit costs of OGD, ERCP, stent or resection were replaced by the highest or lowest respective unit costs. Total cost was moderately sensitive to assumptions about the unit costs of outpatient attendances, coagulation screening, electrolyte assays, liver function tests, abdominal CT, and PTC, increasing or decreasing by between 1% and 5% of the base estimate. Total cost was insensitive to the assumed unit cost of the other 22 resource items, varying by less than 1% when the respective highest and lowest unit costs were substituted.

**Table 7.4. Sensitivity analysis: percentage change in total cost when mean reported unit cost was replaced by lowest and highest respective unit costs**

| Resource item | Mean unit cost (£) | Lowest unit cost (£) | Highest unit cost (£) | Decrease when *substituting* lowest unit cost (%) | Increase when *substituting* highest unit cost (%) |
|---|---|---|---|---|---|
| Bed days | 181 | 45 | 313 | 48.2 | 46.9 |
| Outpatient visits | 68 | 40 | 90 | 1.3 | 1.0 |
| **Investigations** | | | | | |
| Whole blood count | 4 | 1 | 10 | 0.3 | 0.9 |
| Coagulation | 10 | 2 | 31 | 0.6 | 1.5 |
| Urine MCS | 4 | 2 | 7 | 0.1 | 0.1 |
| Cytology | 24 | 3 | 46 | 0.1 | 0.1 |
| Histology | 29 | 10 | 42 | 0.2 | 0.1 |
| Electrolytes | 4 | 1 | 13 | 0.5 | 1.2 |
| Liver function | 5 | 1 | 15 | 0.4 | 1.3 |
| Amylase | 4 | 1 | 7 | 0.1 | 0.1 |
| Calcium | 3 | 1 | 7 | 0.1 | 0.2 |
| Glucose | 4 | 1 | 7 | 0.1 | 0.2 |
| Blood gases | 8 | 1 | 23 | 0.1 | 0.1 |
| Chest X ray | 14 | 5 | 22 | 0.1 | 0.1 |
| Contrast swallow | 91 | 30 | 198 | 0.2 | 0.3 |
| Abdominal CT | 96 | 30 | 198 | 0.8 | 1.2 |
| MRI | 406 | 62 | 844 | 0.1 | 0.1 |
| Angiography | 429 | 51 | 869 | 0.1 | 0.1 |
| Abdominal ultrasound | 53 | 13 | 51 | 0.7 | 0.0 |
| EUS | 415 | 161 | 668 | 0.0 | 0.0 |
| OGD* | 238 | 30 | 1889 | 1.0 | 7.6 |
| Laparoscopy | 575 | 283 | 867 | 0.0 | 0.0 |
| Bronchoscopy | 264 | 50 | 938 | 0.0 | 0.0 |
| PTC | 547 | 241 | 1029 | 1.1 | 1.7 |
| ERCP | 493 | 152 | 1205 | 3.1 | 6.6 |
| Pulmonary function | 53 | 11 | 135 | 0.0 | 0.0 |
| ECG | 46 | 5 | 105 | 0.5 | 0.8 |
| **Treatments** | | | | | |
| Resection | 1946 | 707 | 3595 | 7.5 | 10.0 |
| Bypass | 976 | 707 | 1196 | 0.6 | 0.5 |
| Laparotomy | 752 | 256 | 1081 | 0.2 | 0.2 |
| Stent | 763 | 297 | 1715 | 3.7 | 7.6 |
| Radiotherapy | 1422 | 69 | 2738 | 0.8 | 0.7 |
| Transfusion | 36 | 30 | 46 | 0.0 | 0.1 |

* Median unit cost used in base estimate

## 7.2.3 Predictors of total cost

Patients' total costs were compared according to age, mode of admission, stage of disease, types of treatment provided, and doctor and hospital volumes. Significant differences were found for all of these comparisons but, because all of these patient factors were interrelated, only the results of multiple linear regression analyses are reported.

Total costs increased significantly with increasing doctor volume, but this was no longer significant after adjusting for hospital volume, age, emergency admission, and stage (Table 7.5). However the explanatory variables included in the model only accounted for 8% of the variation in cost. Hospital volume was not associated with total cost, with or without adjustment for doctor volume, age, emergency admission, and stage (Table 7.5).

**Table 7.5. Relationships between cost and doctor and hospital volumes: linear regression models.**

| Explanatory variable | Other explanatory variables in model | Coefficient for volume | 95% CL | P | $R^2$ |
|---|---|---|---|---|---|
| Doctor volume | None | 86* | 19, 152 | 0.012 | 0.0085 |
| | Hospital volume | 77* | 9, 145 | 0.026 | 0.011 |
| | Hospital volume, age, emergency admission, stage, weight loss | 53* | -14, 120 | 0.12 | 0.083 |
| Hospital volume | None | 23** | -5, 51 | 0.10 | 0.0034 |
| | Doctor volume | 18** | -10, 47 | 0.22 | 0.011 |
| | Doctor volume, age, emergency admission, stage, weight loss | 12** | -16, 40 | 0.41 | 0.083 |

* Coefficient for doctor volume ** Coefficient for hospital volume

When treatments provided were added to the full model specified in Table 7.5, doctor volume alone was no longer independently associated with total cost. However addition of a quadratic doctor volume term significantly improved the model ($P<0.03$). The $R^2$ for the full model, including treatments, was 0.22. The independent effects of types of treatment and emergency admission on total cost, as indicated by the regression coefficients, are shown in Table 7.6. These values reflect not only the cost of the specific treatments, but also the associated bed days, outpatient attendances and investigations.

**Table 7.6. Factors contributing to total hospital cost of care***

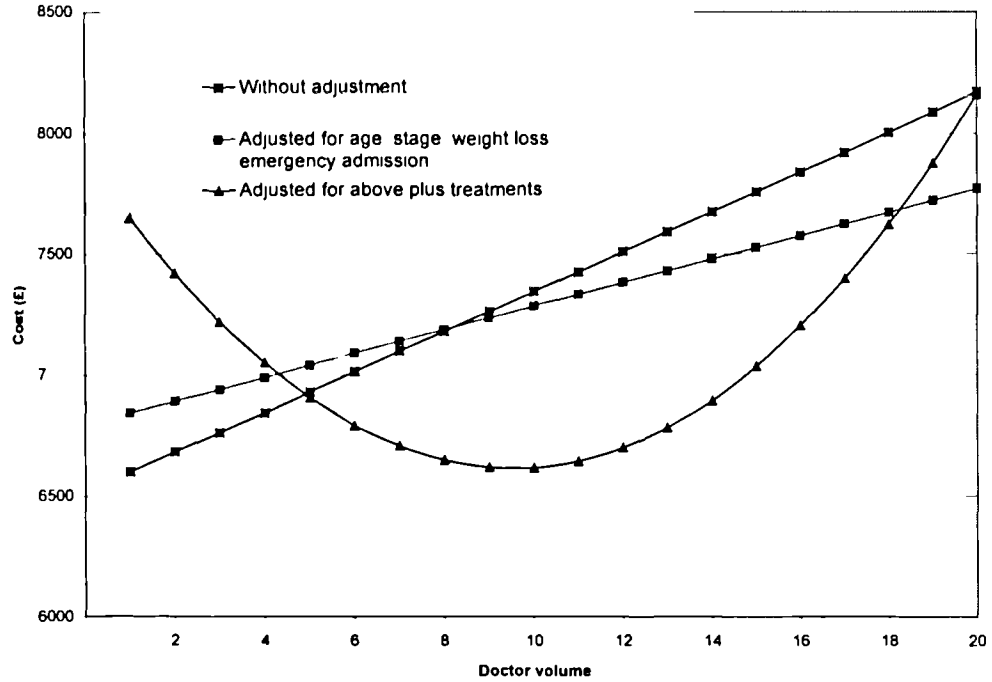
| Variable | Coefficient (£) | 95% CI | P |
|---|---|---|---|
| Surgery | 3178 | 2369, 3987 | <0.001 |
| ERCP | 2148 | 1105, 3191 | <0.001 |
| Stent | 1350 | 349, 2351 | 0.008 |
| Chemotherapy | 1039 | -124, 2204 | 0.08 |
| Radiotherapy | 3435 | 1586, 5284 | <0.001 |
| Emergency admission | 772 | 91, 1454 | 0.03 |
| Constant | 5093 | 1740, 8445 | 0.003 |

* Adjusted for age, sex, weight loss and hospital and doctor volume

To help interpretation of the respective coefficients, the relationship between doctor volume and total cost was plotted on a spreadsheet, using the coefficients from the various regression models and the mean values or probabilities of each explanatory variable observed in the study population (Figure 7.4). The assumes an average distribution of each variable for all doctor volumes. Figure 7.4 shows that total cost increases with increasing doctor volume. However after adjustment for treatments there is a U shaped cost-volume relationship, with the lowest cost occurring at a doctor volume of about 10. The other two curves are linear because addition of a quadratic doctor volume term did not improve the respective models.

The largest component of costs was days of inpatient stay. In order to examine whether variation in days of stay explained the above pattern, the above regression analyses were repeated but using days of stay instead of total cost as outcome variables. In these analysis, days of stay had a similar U shaped relationship with doctor volume, but only once the case mix and treatment variables were included in the model.

*Figure 7.4. Effect on total cost according to doctor volume (from linear regression model, with or without adjustment for hospital volume, age, weight loss, stage, emergency admission, resection, stent, ERCP, chemotherapy and radiotherapy, and assuming average distribution of patients for these variables).*




## 7.2.4 Cost of hospital care per day of life

Cost of hospital care within a year of presentation depended on survival time. An additional cost variable we created by dividing the total cost by survival time in days, censored at 365 days. This survival cutpoint was chosen to correspond to the duration of follow-up of cost data. Cost per day was positively skewed (Figure 7.5), but the natural log of this variable (called "log cost per day") was more symmetrically distributed (Figure 7.6). The latter variable was therefore used in subsequent linear regression analyses.

*Figure 7.5. Frequency distribution of cost per day of life (up to one year)*

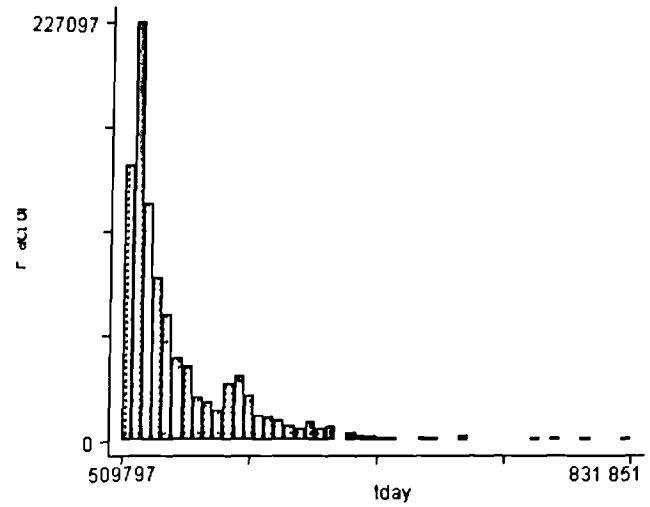
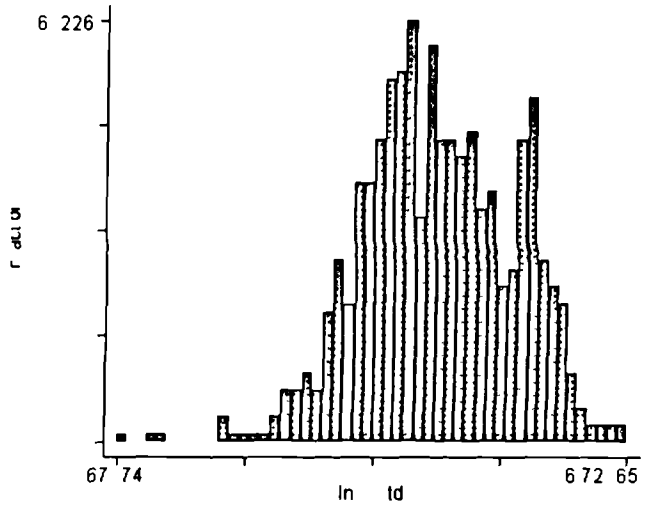



*Figure 7.6. Frequency distribution of natural log of cost per day of life*

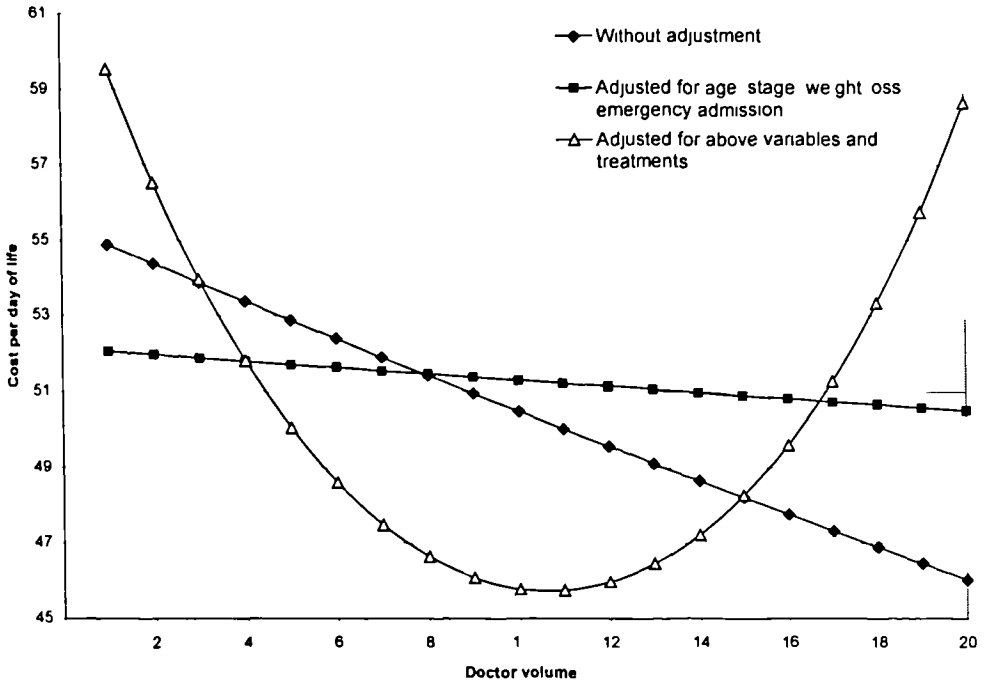



In crude regression analyses, neither hospital volume nor doctor volume was associated with log of cost per day of life. In multiple regression models, addition of age, stage and emergency admission did not change this finding. After addition of treatments to the model, doctor volume and its square were significantly associated with the cost per day of life.

The effect of doctor volume on cost per day of life is shown in Figure 7.7. These curves are derived from the respective regression analyses, with or without adjustment for hospital volume, age, emergency admission, stage, resection, stent, ERCP, chemotherapy and radiotherapy, and assuming average distribution of these variables. After adjustment for treatments, there was a U shaped relationship which was symmetrical for the observed range of doctor volumes, and with patients in the mid range costing about £15 per day

less than patients at the extremes. For the analyses not adjusting for treatments the curves were not significantly different from horizontal.

*Figure 7.7. Variation in cost per day of life with doctor volume (from linear regression model, with or without adjustment for hospital volume, age, emergency admission, stage, resection, stent, ERCP, chemotherapy and radiotherapy, and assuming average distribution of these variables).*



# 7.3 Oesophageal cancer

## 7.3.1 Components and distribution of total cost

The mean hospital cost for patients with oesophageal cancer was £8117, of which 56% was accounted for by ward bed days (Table 7.7). Specific treatments - of which resection, stent, dilatation and radiotherapy were most important accounted for 28% of costs, with investigations contributing a further 11% and outpatient visits 5%.

**Table 7.7. Mean cost per oesophageal cancer patient: total and contributory costs**

| Resource | Mean | SD | % of Total |
|---|---|---|---|
| Ward bed days | 4542 | 5373 | 55.8 |
| Outpatient attendances | 367 | 509 | 4.5 |
| Investigations | 924 | 593 | 11.4 |
| All specific treatments | 2302 | 1391 | 28.3 |
| • *Resection* | *408* | *813* | *5.0* |
| • *Stent insertion* | *593* | *752* | *7.3* |
| • *Dilatation* | *521* | *617* | *6.4* |
| • *Laparotomy only* | *247* | *529* | *3.0* |
| • *Laser* | *33* | *175* | *0.4* |
| • *Radiotherapy* | *435* | *782* | *5.3* |
| • *Chemotherapy* | *48* | *192* | *0.6* |
| • *Blood transfusion* | *17* | *36* | *0.2* |
| Total | 8137 | 3903 | 100.0 |

Total cost was skewed to the right, with six patients costing over £30000 each (Figure 7.8). Aside from these six cases, the distribution of total cost was however fairly symmetrically distributed, and logarithmic transformation did not improve the symmetry of the distribution (Figure 7.9). Regression analyses were therefore performed with total cost as outcome variable.

*Figure 7.8. Distribution of total cost of hospital care (excluding 6 cases each costing more than £30000)*

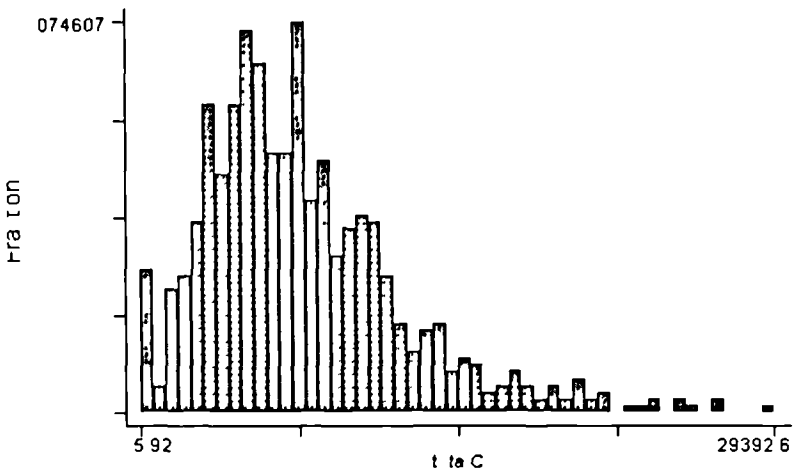
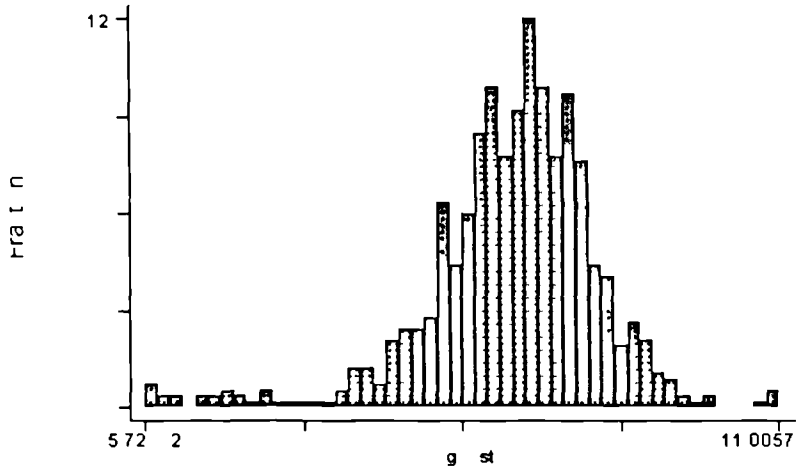



*Figure 7 9. Distribution of natural log of total cost*




As shown below, the major determinant of total cost was bed days. A high proportion of patients had multiple admissions. Table 7.8 shows that half of patients were admitted to hospital at least twice within a year of presentation.

**Table 7.8. Frequency distribution of number of admissions per patient**

| No of admissions | No of patients | % of patients (N=776) |
|---|---|---|
| 1 or more | 692 | 89.2 |
| 2 or more | 400 | 51.5 |
| 3 or more | 206 | 26.5 |
| 4 or more | 136 | 17.5 |
| 5 or more | 106 | 13.7 |
| 6 or more | 69 | 8.9 |
| 7 or more | 31 | 4.0 |
| 8 or more | 23 | 3.0 |

## 7.3.2 Sensitivity analysis

The sensitivity of the total cost estimate to assumed unit costs was assessed by replacing the mean reported unit cost of each unit with the lowest and then the highest unit costs (Table 7.9). Total cost was most sensitive to unit costs of bed days (42% lower to 41% higher) and OGD (3% lower to 20% higher), followed by outpatient visits, stents, dilatation and radiotherapy (variation 5-10%) and by resection, laparotomy (variation 1-4%). It was insensitive to the unit costs of the other 26 resources, with total cost varying by less than 1%. If the mean unit cost per bed day was replaced by the first (£104) and third (£246) centiles of reported unit costs, instead of the lowest and highest unit costs, the changes in total cost were -24% and +20% respectively.

**Table 7.9. Sensitivity analysis: effect on total cost of replacing mean unit cost of each resource with lowest and highest reported unit costs.**

| Resource item | Mean unit cost (£) | Lowest unit cost (£) | Highest unit cost (£) | Decrease when substituting lowest unit cost (%) | Increase when substituting highest unit cost (%) |
|---|---|---|---|---|---|
| Bed days | 180.59 | 44.58 | 313.00 | 41.8 | 40.7 |
| Outpatient visits | 67.92 | 39.56 | 90 00 | 1.9 | 1.5 |
| **Investigations** | | | | | |
| Whole blood count | 3.67 | 1.38 | 10.14 | 0.2 | 0.6 |
| Coagulation | 9.54 | 1.72 | 31.00 | 0.2 | 0.7 |
| Urine MCS | 3.58 | 1.98 | 6.68 | 0.1 | 0.1 |
| Cytology | 23 69 | 3.38 | 45.96 | 0.0 | 0.0 |
| Histology | 29.39 | 10.14 | 42.00 | 0.0 | 0.0 |
| Electrolytes | 4.43 | 1.23 | 12.75 | 0.3 | 0.8 |
| Liver function | 4.60 | 1.23 | 15.30 | 0.2 | 0.7 |
| Amylase | 3.74 | 1.34 | 7.00 | 0.0 | 0.0 |
| Calcium | 3 30 | 1.23 | 7.00 | 0.1 | 0.1 |
| Glucose | 3 54 | 1.23 | 7.00 | 0.0 | 0.1 |
| Blood gases | 8 01 | 1.23 | 22.60 | 0.1 | 0.3 |
| Chest X ray | 13 67 | 5.00 | 22.00 | 0.1 | 0.1 |
| Contrast swallow | 90 93 | 30.36 | 198.00 | 0.7 | 1.2 |
| Abdominal CT | 95 71 | 30.36 | 198.00 | 0.5 | 0.9 |
| MRI | 405.96 | 62.00 | 843.60 | 0.1 | 0.1 |
| Angiography | 428 67 | 51.00 | 869.36 | 0.0 | 0.0 |
| Abdominal ultrasound | 53 08 | 12 65 | 51.00 | 0.2 | 0.0 |
| EUS | 414 50 | 161.00 | 668.00 | 0.0 | 0.0 |
| OGD* | 238 00* | 30.36 | 1889.00 | 2.6 | 20.3 |
| Laparoscopy | 575 00 | 283.00 | 867.00 | 0.0 | 0.0 |
| PTC | 546.98 | 241 00 | 1029.00 | 0.0 | 0.1 |
| ERCP | 492 83 | 151 80 | 1205.00 | 0.0 | 0.1 |
| Bronchoscopy | 264.32 | 50.00 | 938.00 | 0.1 | 0.2 |
| Pulmonary function | 52.50 | 10.5 | 135 | 0.1 | 0.1 |
| ECG | 45.56 | 5 | 105 | 0.5 | 0.8 |
| **Treatments** | | | | | |
| Laser | 970.67 | 54 | 2118 | 0.4 | 0.5 |
| Dilatation | 1251.50 | 54 | 2118 | 6.1 | 4.4 |
| Stent | 1547.75 | 54 | 2715 | 7.0 | 5.5 |
| Resection | 2028.40 | 1584 | 2867 | 1.1 | 2.1 |
| Laparotomy | 1379.33 | 390 | 2468 | 2.2 | 2.4 |
| Radiotherapy | 1838.40 | 69 | 2738 | 5.1 | 2.6 |
| Transfusion | 35.62 | 30 | 46.42 | 0.0 | 0.1 |

* Median unit cost used in base analysis

## 7.4.3 Predictors of total cost

Several case mix and treatment variables, and hospital and doctor volumes, were associated with total cost. Multiple logistic regression was used to assess the independent contribution of each type of variable. Table 7.10 shows that the total cost of hospital care increased significantly with increasing doctor volume even after adjustment for hospital volume, age, emergency admission, weight loss and stage. This suggests that the cost of a patient's hospital care increased by about £50 for every extra patient managed annually by one's main doctor. Hospital volume was weakly associated with total cost in the simplest model, but adjustment for doctor volume and case mix variables rendered the apparent association small and non-significant. The full model explained 6% of the variation in total cost. The cost of junctional cancers was not significantly different from the cost of other cancers.

**Table 7.10. Effects on total cost of doctor volume and hospital volume: linear regression models (N=737).**

| Explanatory variable | Other explanatory variables in model | Coefficient for volume | 95% CL | P | $R^2$ |
|---|---|---|---|---|---|
| Doctor volume | None | 69.7* | 36 2, 103 | <0.001 | 0.022 |
| | Hospital volume | 67.9* | 30.5, 105 | <0.001 | 0.022 |
| | Hospital volume, age, weight loss, dysphagia, stage, emergency admission | 50.6* | 11.5, 89.6 | 0.011 | 0.064 |
| Hospital volume | None | 19.4** | 0.54, 38.4 | 0.044 | 0.005 |
| | Doctor volume | 2.14** | -19.1, 23.4 | 0.84 | 0.022 |
| | Doctor volume, age, weight loss, dysphagia, stage, emergency admission | 6.00** | -15.0, 27.0 | 0.57 | 0.064 |

* Coefficient for doctor volume ** Coefficient for hospital volume

After further adjustment for treatments in the logistic regression models, doctor volume was associated with total cost only if a quadratic doctor volume term was added to the model. Hospital volume was not associated with total cost.

Table 7.11 shows the independent effects of treatments on total costs, as indicated by the coefficients of the latter model. Patients receiving surgery cost £3581 more than patients who did not, which is considerably more than the cost of the operation alone, and is presumably mainly due to extra bed days. Similarly, patients receiving radiotherapy cost

considerably more than patients receiving stents or chemotherapy. Patients admitted as emergencies cost about £1600 more than elective admissions.

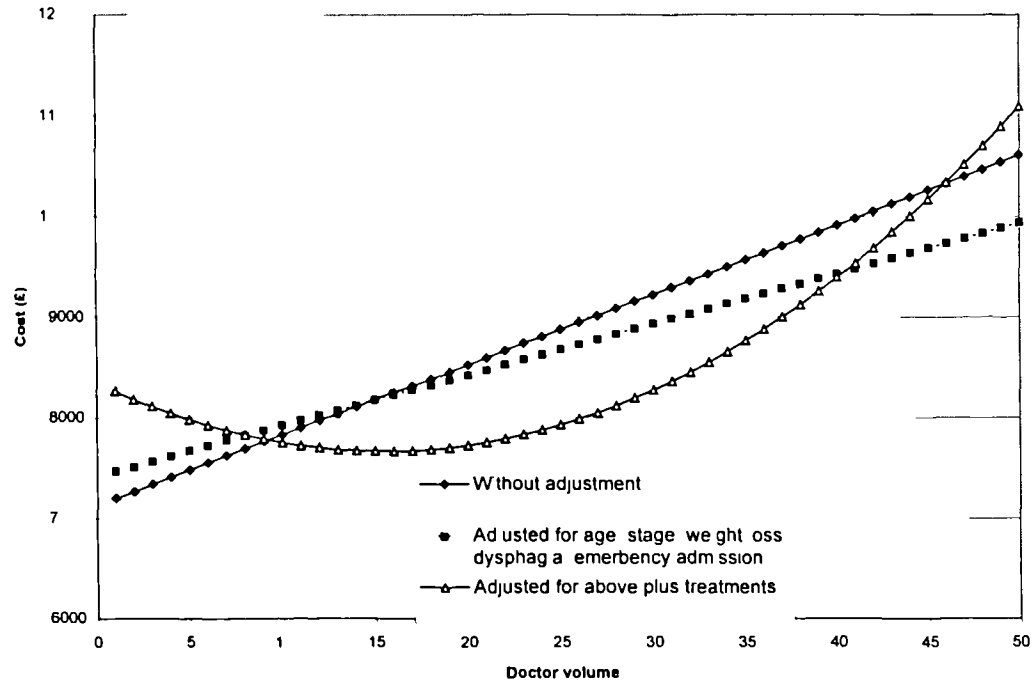
**Table 7.11. Independent effects of treatments and emergency admission on total hospital cost of care***

| Variable | Coefficient (£) | 95% CL | P |
|---|---|---|---|
| Surgery | 3581 | 2401, 4761 | <0.001 |
| Stent | 1877 | 984, 2769 | <0.001 |
| Chemotherapy | 1545 | 207, 2882 | 0.024 |
| Radiotherapy | 3278 | 2242, 4713 | <0.001 |
| Emergency admission | 1614 | 628, 2600 | 0.001 |

* adjusting for doctor volume hospital volume age stage dysphagia and weight loss N 736

The effect of doctor volume on total cost, with and without adjustments, and assuming average distributions of variables for all doctor volumes, is illustrated in Figure 7.10. For all analyses cost per patient increased substantially with increasing doctor volume. The trends for analyses without adjustment for treatments are linear because addition of the quadratic doctor volume term did not significantly improve these models.

*Figure 7.10 Effect of doctor volume on total cost (with and without adjustment for age, stage, weight loss, dysphagia, emergency admission, surgery, stent, chemotherapy, and radiotherapy, and assuming average distribution of these variables)*




The largest component of costs was days of stay. In order to examine whether variation in days of stay explained the above pattern, the above regression analyses were repeated but using days of stay instead of total cost as outcome variables. In these analysis, doctor

volume had a similar J shaped relationship with doctor volume, once the case mix and treatment variables were included in the model.

## 7.4.4 Cost per day of life

Total cost of hospital care within a year of first presentation was divided by survival time within a year of presentation. This variable was called "cost per day of life", and had a positively skewed distribution (Figure 7.11). The natural logarithm of this variable was however approximately normally distributed, permitting linear regression analyses (Figure 7.12)

*Figure 7.11. Distribution of cost per day of life*

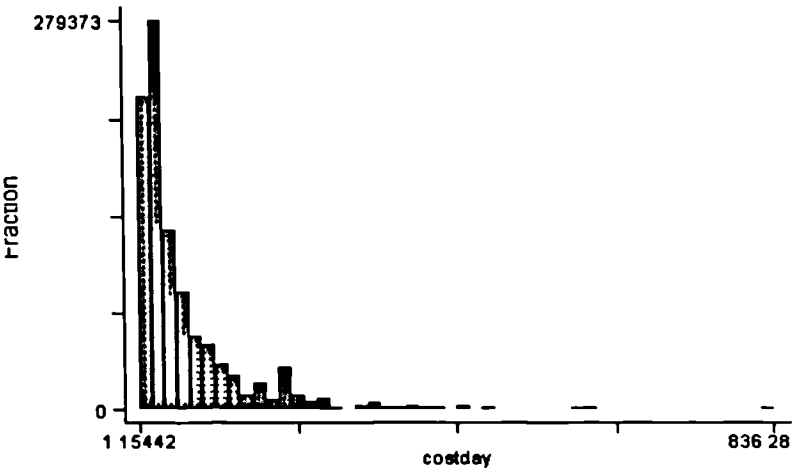
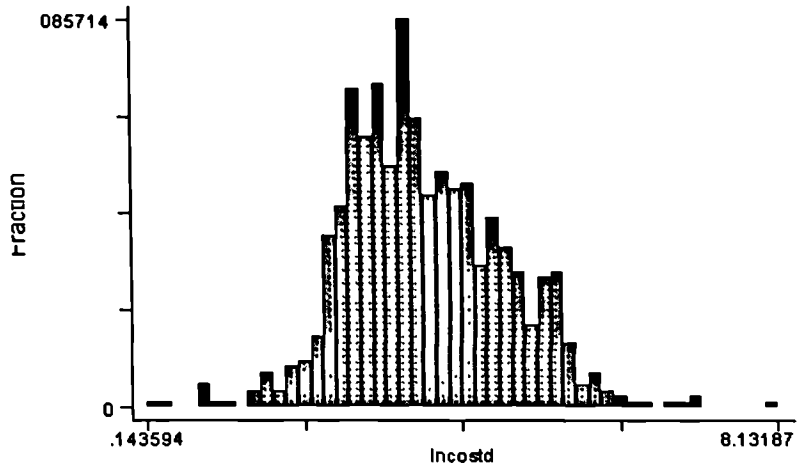



*Figure 7.12. Distribution of log of cost per day of life*




Doctor volume was significantly associated with the log of cost per day of life. This association remained significant after addition of case mix variables – age, weight loss, dysphagia, stage – to the model. Further addition of a quadratic doctor volume term

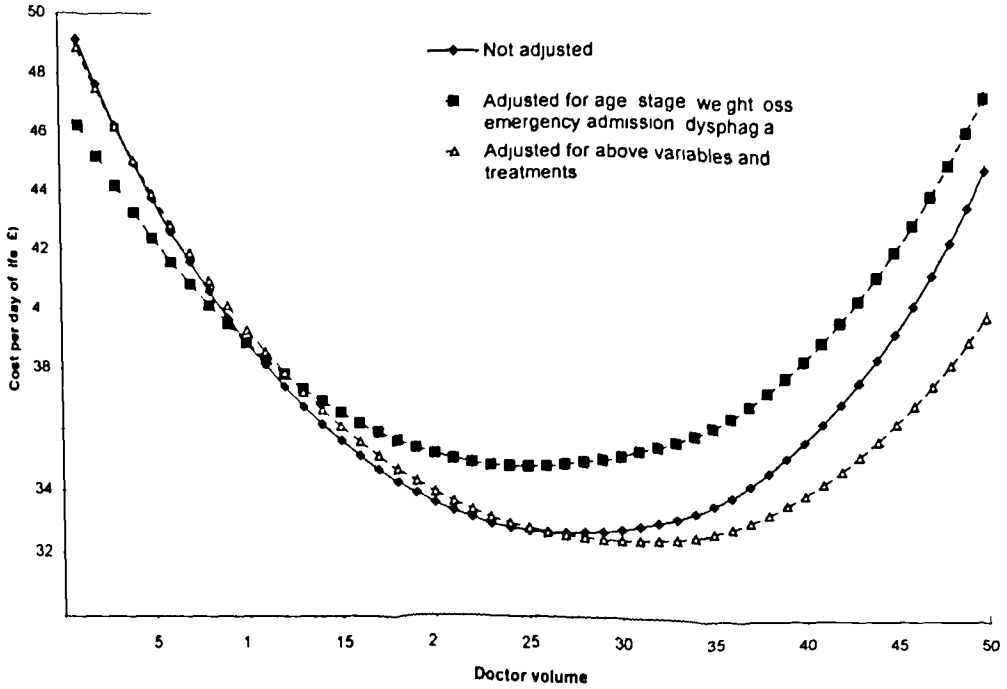
significantly improved the model (P 0.004). Addition of treatment variables surgery, stent, chemotherapy and radiotherapy improved the model further but did not greatly influence the independent effect of doctor volume. The regression coefficients for doctor volume and its square are shown in Table 7.12.

**Table 7.12. Effect of doctor volume on log of cost per day: regression coefficients and $R^2$ values from linear regression models (n=736).**

| Adjusted for | Coefficient for doctor volume (95% CL) | Coefficient for doctor volume$^2$ (95% CL) | $R^2$ for model |
|---|---|---|---|
| Nothing | -0 032 (-0 052, -0.013) | 0.00061 (0.00019, 0.0010) | 0.02 |
| Age, wei ht loss, junctional tumour, emergency admission | -0 025 (-0.013, 0.0056) | 0.00049 (0.000079, 0.00091) | 0.12 |
| Above variables and ur ery, chemotherapy and radiotherapy | -0 030 (-0.049, -0.011) | 0.00051 (0 000099, 0.00091) | 0.17 |

Figure 7.13 shows the relationship between cost per day of life and doctor volume expressed by the above coefficients together with the respective coefficients for other variables in models, and assuming average distributions of variables at all doctor volumes. The curves for the models with or without adjustments are similar, with higher costs at the extremes of doctor volume. However adjustment for treatments suggests that doctor volume independently increases costs more at the lower volume end of the spectrum than at the higher volume end.

*Figure 7.13. Effect of doctor volume on cost per day of life (with and without adjustment for age, stage, weight loss, dysphagia, emergency admission, surgery, stent, chemotherapy and radiotherapy and assuming average distribution of these variables)*



# 7.4 Gastric cancer

## 7.5.1 Components and distribution of total cost

Table 7.13 shows that the mean cost of hospital care per patient, including all care received within a year of presentation, was £5702. Ward care, represented by bed days, accounted for 71% of the total cost. Specific treatments, of which resections were most important, accounted for 11% total costs, which was less than the cost of investigations (13%).

**Table 7.13. Mean cost per patient: total and contributory costs**

| Resource item | Mean | SD | % of Total |
|---|---|---|---|
| Ward bed days | 4066 | 4319 | 71.3 |
| Outpatient attendances | 283 | 396 | 5.0 |
| Investigations | 712 | 493 | 12.5 |
| All specific treatments | 642 | 627 | 11.3 |
| • *Resection* | *399* | *529* | *7.0* |
| • *Bypass* | *46* | *197* | *0.8* |
| • *Laser* | *3* | *40* | *0.1* |
| • *Laparotomy only* | *76* | *226* | *1.3* |
| • *Radiotherapy* | *24* | *181* | *0.4* |
| • *Chemotherapy* | *70* | *278* | *1.2* |
| • *Blood transfusion* | *24* | *41* | *0.4* |
| Total | 5702 | 4775 | 100.0 |

The distribution of total costs was positively skewed (Figure 7.14). Four patients cost more than £30 000 each. Logarithmic transformation resulted in a slightly negatively skewed distribution (7.15). Linear regression analyses of total costs, reported below, used the untransformed total cost.

*Figure 7.14. Distribution of total cost*

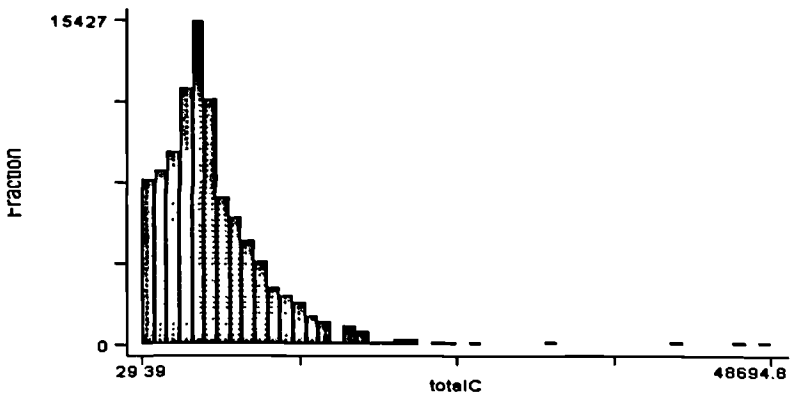
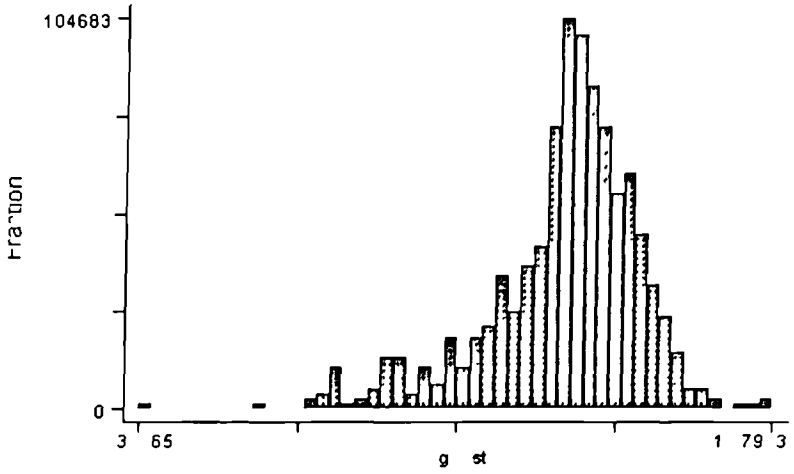


*Figure 7.15. Distribution of natural log of total cost*




As shown below, the major determinant of total cost was bed days. A high proportion of patients had multiple admissions. Table 7.14 shows that 42% of patients were admitted to hospital at least twice within a year of presentation.

**Table 7.14. Frequency distribution of number of admissions per patient**

| No of admissions | No of patients | % of patients (N=726) |
|---|---|---|
| 1 or more | 678 | 93.4 |
| 2 or more | 305 | 42.0 |
| 3 or more | 139 | 19 1 |
| 4 or more | 62 | 8.5 |
| 5 or more | 57 | 7.9 |
| 6 or more | 23 | 3.2 |
| 7 or more | 14 | 1.9 |
| 8 or more | 9 | 1.2 |

## 7.5.2 Sensitivity analysis

The sensitivity of total cost to assumptions about the unit costs of each resource item was examined by replacing the mean unit cost reported by each responding hospital with, firstly, the lowest reported unit cost and then with the highest reported unit cost. The results of the sensitivity analysis are shown in Table 7.14. The total cost estimate was highly sensitive to assumptions about the unit cost of a day in a hospital bed. If the mean unit cost per bed day was replaced by the first (£104) and third (£246) centiles of reported unit costs, instead of the lowest and highest unit costs, the changes in total cost were –30% and +26% respectively. Total cost was increased or decreased by more than 5% if the mean unit costs of OGD, resection or bypass were replaced by the highest or lowest respective unit costs. Total cost was moderately sensitive to assumptions about the unit costs of outpatient attendances, whole blood count, coagulation screening, electrolyte assays, ECG and abdominal CT, increasing or decreasing by between 1% and 5% of the base estimate. Total cost was insensitive to the assumed unit cost of the other 23 resource items, varying by less than 1% when the respective highest and lowest unit costs were substituted.

**Table 7.14. Sensitivity analysis: percentage change in total cost when mean reported unit cost was replaced by lowest and highest respective unit costs**

| Resource item | Mean unit cost (£) | Lowest unit cost (£) | Highest unit cost (£) | Decrease when substituting lowest unit cost (%) | Increase when substituting highest unit cost (%) |
|---|---|---|---|---|---|
| Bed days | 180.59 | 44.58 | 313.00 | 53.7 | 52.3 |
| Outpatient visits | 67 92 | 39.56 | 90.00 | 1.6 | 1.2 |
| Investigations | | | | | |
| Whole blood count | 3.67 | 1.38 | 10.14 | 0.4 | 1.0 |
| Coagulation | 9 54 | 1.72 | 31.00 | 0.4 | 1.0 |
| Urine MCS | 3 58 | 1.98 | 6.68 | 0.1 | 0.2 |
| Cytology | 23 69 | 3.38 | 45.96 | 0.0 | 0.1 |
| Histology | 29 39 | 10 14 | 42.00 | 0.1 | 0.0 |
| Electrolytes | 4.45 | 1.23 | 12.75 | 0.5 | 1.3 |
| Liver function | 4 60 | 1.23 | 15.30 | 0.3 | 1.1 |
| Amylase | 3 74 | 1.34 | 7.00 | 0.0 | 0.0 |
| Calcium | 3.30 | 1.23 | 7.00 | 0.1 | 0.2 |
| Glucose | 3 54 | 1.23 | 7.00 | 0.1 | 0.1 |
| Blood gases | 8 01 | 1.23 | 22.60 | 0.1 | 0.1 |
| Chest X ray | 13 67 | 5.00 | 22.00 | 0.1 | 0.1 |
| Contrast swallow | 90.93 | 30.36 | 198.00 | 0.5 | 0.9 |
| Abdominal CT | 95 71 | 30.36 | 198.00 | 0.6 | 1.0 |
| MRI | 405 96 | 62 00 | 843.60 | 0.0 | 0.1 |
| Angiography | 428 67 | 51.00 | 869.36 | 0.0 | 0.0 |
| Abdominal ultrasound | 53 08 | 12 65 | 51.00 | 0.4 | 0.0 |
| EUS | 414.50 | 161.00 | 668.00 | 0.0 | 0.0 |
| OGD* | 238.00 | 30 36 | 1889.00 | 5.0 | 39.8 |
| Laparoscopy | 575.00 | 283 00 | 867.00 | 0.0 | 0.0 |
| PTC | 546.98 | 241.0 | 1029.00 | 0.0 | 0.1 |
| ERCP | 492.83 | 151.80 | 1205.00 | 0.1 | 0.3 |
| Bronchoscopy | 264.32 | 50.00 | 938.00 | 0.0 | 0.0 |
| Pulmonary function | 52 50 | 10.50 | 135.00 | 0.1 | 0.1 |
| ECG | 45.56 | 5.00 | 105.00 | 0.8 | 1.2 |
| Treatments | | | | | |
| Gastrectomy | 1099.75 | 503.00 | 2520.00 | 3.8 | 9.1 |
| Bypass* | 896 00 | 503 00 | 9177.00 | 0.4 | 7.4 |
| Laparotomy | 751.75 | 256.00 | 1081.00 | 0.9 | 0.6 |
| Laser | 541.00 | 171.00 | 911.00 | 0.0 | 0.0 |
| Transfusion | 35.62 | 30.00 | 46.42 | 0.1 | 0.1 |
| Radiotherapy | 1422.33 | 69.00 | 2738.00 | 0.4 | 0.4 |

* Median unit cost used in base estimate

## 7.5.3 Predictors of total cost

Patients' total costs were compared according to age, mode of admission, stage of disease, types of treatment provided, and doctor and hospital volumes. Significant differences were found for all of these comparisons but, because all of these patient factors were interrelated, only the results of multiple linear regression analyses are reported.

Total costs increased significantly with increasing doctor volume. However this association was no longer significant (P 0.07) after adjusting for hospital volume, age, weight loss, stage, junctional tumours and emergency admission. Table 7.15 shows that total costs of hospital care increased by about £54 (95% £-5.1-£113) with each extra patient managed annually by one's main doctor. The explanatory variables included in the model only accounted for 10% of the variation in cost. Hospital volume was not associated with total cost, with or without adjustment for doctor volume, age, emergency admission, and stage (Table).

**Table 7.15. Relationships between cost and doctor and hospital volumes: linear regression models.**

| Explanatory variable | Other explanatory variables in model | Co-efficient | 95% CL | P | $R^2$ |
|---|---|---|---|---|---|
| Doctor volume | None | 104* | 47.8, 160 | <0.001 | 0.018 |
| Doctor volume | Hospital volume | 111* | 53.5, 168 | <0.001 | 0.021 |
| Doctor volume | Hospital volume, age, stage, junctional tumours and emergency admission | 53.9* | -5.32, 113 | 0.074 | 0.10 |
| Hospital volume | None | 10.4** | -10.8, 36.5 | 0.34 | 0.0013 |
| Hospital volume | Doctor volume | 15.0** | -6.54, 36.5 | 0.17 | 0.021 |
| Hospital volume | Doctor volume, age, stage, junctional tumours and emergency admission | 16.1** | -4.76, 37.0 | 0.13 | 0.10 |

* Coefficient for doctor volume ** Coefficient for hospital volume

When treatments provided were added to the full model shown in Table 7.15, doctor volume alone was no longer independently associated with total cost. Addition of a quadratic doctor volume term did not significantly improve the model. The independent contributions of doctor volume and of specific treatments, after adjusting for hospital volume, age, stage, weight loss, junctional tumours and emergency admission, are shown in Table 7.16. The coefficients for treatments indicate the difference in total costs between those who did and did not have the treatments, adjusting for all other variables in the model. These differences in total cost reflect not only the cost of the specific

treatments, but also the associated bed days, outpatient attendances and investigations. The $R^2$ value for the full model, including treatments, was 0.17.

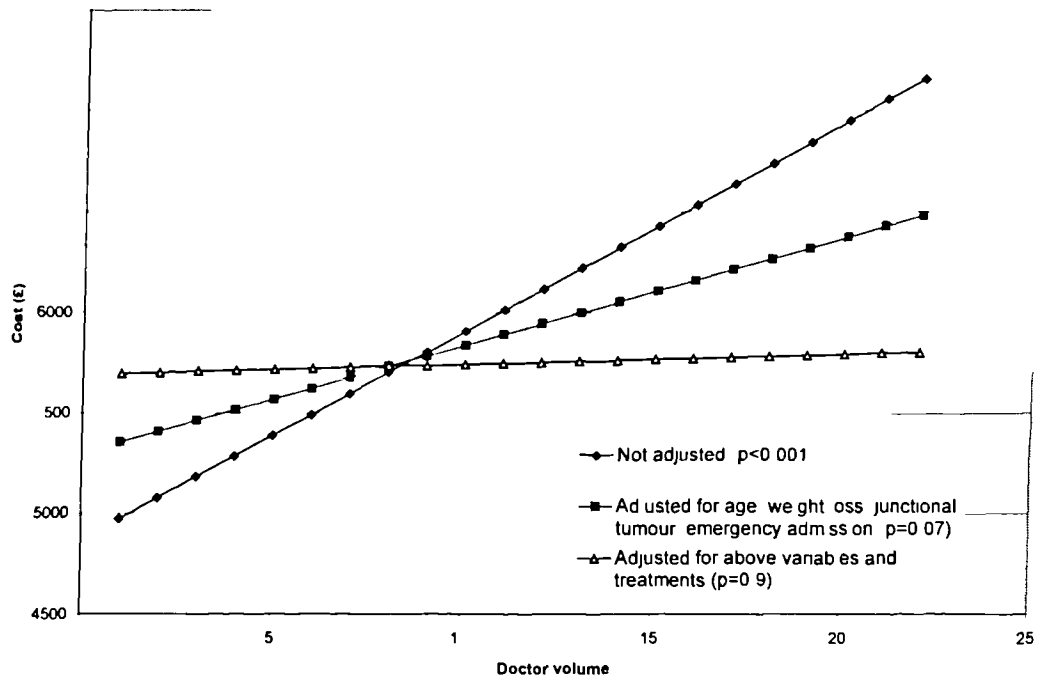
**Table 7.16. Independent effect of treatments and mode of admission on total hospital cost of care**

| Variable | Coefficient* (£) | 95% CL | P |
|---|---|---|---|
| Surgery | 2819 | 1944, 3694 | <0.001 |
| Chemotherapy | 1788 | 696, 2880 | 0.001 |
| Radiotherapy | 2592 | 473, 4712 | 0.02 |
| Emergency admission | 662 | -34, 1358 | 0.06 |

* Adjusted for age, weight loss, stage, hospital volume and doctor volume. N=705, $R^2$=0.17

Figure 7.16 shows the effect of doctor volume on total cost, with and without adjustment for case mix and treatment variables. It shows that adjustment for case mix variables reduced the apparent effect, and further adjustment for treatments eliminated the effect. Thus most of the effect of doctor volume and cost could be attributed to case mix and types of treatment.

*Figure 7.16 Effect of doctor volume on total cost (with and without adjustment for age, weight loss, stage, emergency admission, surgery, chemotherapy and radiotherapy, and assuming average distributions of these variables)*




The above analysis was repeated using the log of total cost as dependent variable and all of the explanatory variables specified in Table 7.16. In this analysis, hospital volume was independently but weakly associated with the log of total cost (coefficient=0.0038, 95% CI 0.00055-0.0071; P 0.02). This corresponds to a 4% increase in mean cost of care for

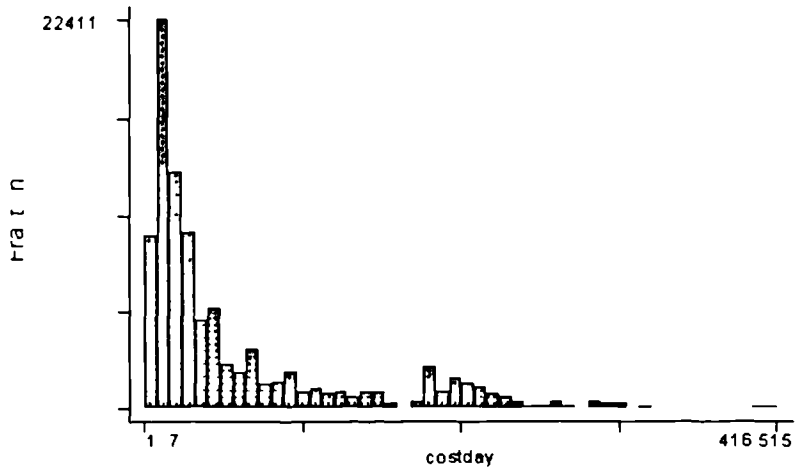
every extra 10 patients managed by one's hospital, or a 21% increase for every extra 50 patients.

Most of the variation in total cost was explained by variation in days of stay. When total cost was regressed on days of stay, the $R^2$ value was 0.94, although days of stay only accounted for 71% of the total cost (Table 7.13). Addition of hospital and doctor volumes, age, stage, weight loss and emergency admission added little ($R^2$ 0.97) and further addition of treatment variables increased the $R^2$ value to 0.98.

## 7.5.4 Cost of hospital care per day of life

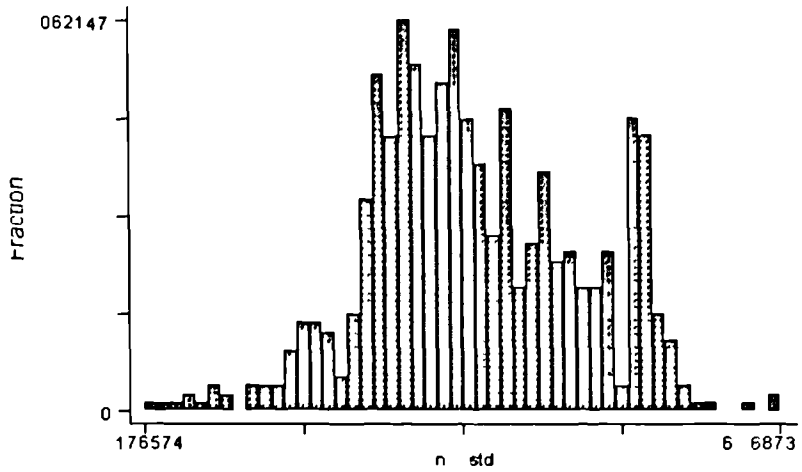
Cost of hospital care within a year of presentation would clearly depend on survival time. An additional cost variable we created by dividing the total cost by survival time, censored at 365 days. This survival cutpoint was chosen to correspond to the duration of follow-up of cost data. Cost per day was positively skewed (Figure 7.17), but the natural log of this variable (called "log cost per day") was more symmetrically distributed (Figure 7.18). The latter variable was therefore used in subsequent regression analyses.

*Figure 7.17 Frequency distribution of cost per day of life (up to one year)**




* excluding 3 patients costing £500 per day

*Figure 7.18. Frequency distribution of natural log of cost per day of life*



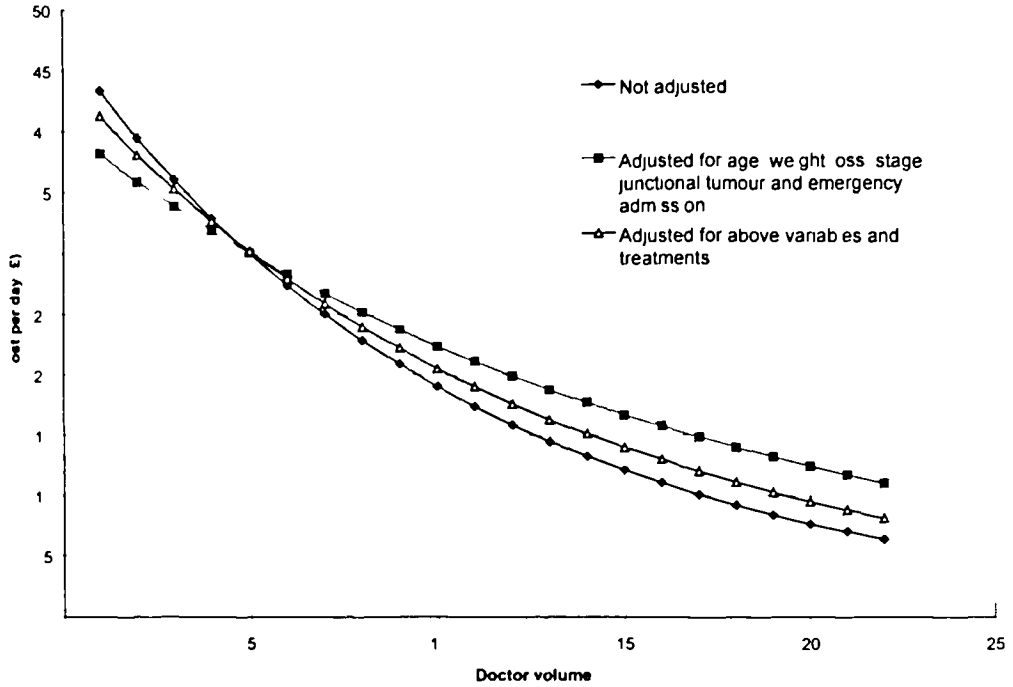

In crude regression analyses, doctor volume was positively associated with log of cost per day of life. Addition of a quadratic doctor volume term improved the model (P–0.004). This association remained after adjustment for hospital volume age, weight loss, stage, emergency admission and junctional tumour; addition of these case mix variable significantly improved the model (P<0.0001). Addition of treatment variables – surgery, chemotherapy and radiotherapy improved the model further (P 0.0002) but had only a slight effect on the coefficients for doctor volume and its square. The respective coefficients for doctor volume and its square are shown in Table 7.17.

**Table 7.17. Effect of doctor volume on log of cost per day: regression coefficients and $R^2$ values from linear regression models (n=693).**

| Adjusted for | Coefficient for doctor volume (95% CI) | Coefficient for doctor volume$^2$ (95% CI) | $R^2$ for model |
|---|---|---|---|
| Nothing | -0 89 (-0.14, -0.038) | 0.0037 (0.0012, 0.0062) | 0.02 |
| Age, weight loss, junctional tumour, emergency admission | -0.059 (-0.11, -0.0077) | 0.0027 (0.00053, 0.0051) | 0.16 |
| Above variables and surgery, chemotherapy and radiotherapy | -0.077 (-0.13, -0.026) | 0.0032 (0.00083, 0.0055) | 0.18 |

Figure 7.19 shows the effect of doctor volume on cost per day of life with or without adjusting for hospital volume, age, emergency admission, stage, junctional tumour, surgery, chemotherapy and radiotherapy, and assuming average distribution of these variables. It shows that costs per day decreased dramatically with increasing doctor volume, and this relationship persisted after adjustment for case mix and treatment variables.

*Figure 7.19. Effect of doctor volume on cost per day of life (with or without adjusting for hospital volume, age, emergency admission, stage, junctional tumour, surgery, chemotherapy and radiotherapy and assuming average distribution of these variables).*




# 7.5 Summary of cost analysis

The cost analysis suggests that patients of higher volume doctors were managed at greater cost. This was partly due to higher volume doctors' higher probability of ordering costly investigations and of providing curative or other active treatments. However, once case mix and treatments were controlled, it appeared that care by low volume doctors was also associated with higher costs than average, largely due to longer inpatient stays. When costs per day of life were examined, care by low volume doctors appeared particularly costly, for all three cancers. The interpretation of these findings is discussed in greater detail in section 8.4.

# 8. DISCUSSION

This study shows that specialisation of cancer care, as indicated by hospitals' and doctors' annual volumes of patients, influences the distribution of patients by disease severity, the choice of tests and treatments, survival and operative mortality, and costs. These results are summarised in Table 8. The study supports the specialisation of cancer care for patients with pancreatic, oesophageal and gastric cancers. It suggests that there may be considerable survival benefits of specialisation even for cancers that have relatively poor prognoses, and that there may be survival advantages even among patients who do not receive potentially curative treatment.

The study found that costs of hospital care increased with increasing doctor volumes, mainly because of more intensive management, with consequently longer inpatient stays. More complex patterns of cost and volume emerged, however, when case mix, types of treatment, and survival time were taken into account, with patients of low volume doctors appearing also to receive relatively costly care. Thus increasing specialisation is likely to increase the costs of hospital care, but could also increase its efficiency.

As with most observational epidemiological studies, the results are likely to have some degree of bias, because of systematic difference between patients of higher and lower volume doctors and hospitals, and because imperfect information about patients' health status prevented optimal adjustment for these factors. However the study has carefully measured and adjusted for an exceptionally wide range of the most important prognostic variables, greatly reducing bias and increasing confidence in the results.

The study has implications for health policy in the United Kingdom and internationally, for health services research methodology, and for theory about health services. This chapter will discuss all of the above points in detail.

**Table 8. Summary of significant independent* associations with increasing doctor and hospital volumes**

| Cancer site & volume measure | Stage | Investigations | Treatments | Outcomes | Cost |
|---|---|---|---|---|---|
| **PANCREAS** | | | | | |
| **Doctor volume** | More I-III<br>Much less IV<br>Same unstaged | More US, ERCP, cytology | More resections, stents, less untreated | No associations | Increased total cost (J-shaped relationship on adjusting for treatments)<br>U shaped relationship with cost per day of life |
| **Hospital volume** | More I-III<br>Same IV<br>Less unstaged | More cytology | More resections, bypasses, less untreated | Longer survival time | No associations |
| **OESOPHAGUS** | | | | | |
| **Doctor volume** | Much more I-III<br>Same IV<br>Less unstaged | More CT, EUS;<br>less contrast swallow, less laparoscopy | More resections;<br>less radiotherapy, less untreated | Lower operative mortality<br>Longer survival time | Increased total cost (J-shaped relationship on adjusting for treatments)<br>U shaped relationship with cost per day of life |
| **Hospital volume** | More I-III<br>Same IV<br>Same unstaged | More EUS | More radiotherapy | No associations | No associations |
| **GASTRIC** | | | | | |
| **Doctor volume** | Much more I-III<br>Less IV<br>Less unstaged | More OGD, US, laparoscopy, EUS | More resection, bypass;<br>less chemotherapy,<br>less untreated | Lower operative mortality | Increased total cost (disappears on adjusting for treatments)<br>Decreased cost per day of life |
| **Hospital volume** | Less I-III<br>More IV<br>Same unstaged | No associations | No associations | Longer survival time | No associations |

* All results, except Stage column, adjusted for case mix. US abdominal ultrasound, EUS endoscopic ultrasound, OGD oesophagogastroduodenoscopy (endoscopy), CT computerised tomography

# 8.1 Case mix, clinical practice and patient volumes

This study sheds light on how specialists in pancreatic, oesophageal or gastric cancers differ from other doctors and hospitals managing these cancers, in the types of patients they see and in what they do for them.

Doctor and hospital volumes were used as the primary indicators of specialisation. Greater numbers of patients indicate greater current clinical experience with one disease.[20-22] Although patient volumes do not capture other dimensions of specialisation such as knowledge, interests qualifications, duration of experience, or facilities, they have the advantage of being objective, and do not depend on doctors' or hospitals' reports on their own specialist status, which might be biased. This study suggests that, in terms of patient volumes for these three cancers, hospitals and doctors follow a continuum of specialisation, rather being clearly demarcated as either specialists or non-specialists. Use of a simple specialist/non-specialist dichotomy, instead of continuous volume variables, might therefore have obscured more subtle trends.[21] For most of the variables studied, including case mix, tests, treatments, outcomes and costs, there were consistent trends with increasing volumes rather than obvious discontinuities.

Medical consultants and hospitals were the principal health service units for measuring patient volumes, but they did not themselves necessarily embody all aspects of specialisation. Consultants and hospitals, while being important entities in their own right, were also foci of specialisation within complex systems of health care.[21] Consultant volumes, while directly reflecting doctors' experience, were also proxy indicators of the experience of their associated teams, including nursing, paramedical, theatre and junior medical staff. Hospital volumes for one type of cancer were also proxy indicators of the experience of nurses, anaesthetists, radiotherapists or oncologists who managed patients with different diseases but similar problems. Hospital and doctor volumes were highly correlated with each other. Fortunately, simultaneous statistical adjustment, and the substantial numbers of patients with both higher volume doctors and lower volume hospitals, or vice versa, allowed the effects of doctor-related factors and hospital-related factors to be distinguished.

An advantage of this study, compared to most other studies of volume-outcome relationships,[10, 20-22, 25] is the detailed analysis of how both clinical practice and case mix

vary with increasing patient volumes. This helps to shed light on what specialisation comprises in practice. Higher volume doctors and hospitals were more likely to manage patients with less severe disease. In contrast, patients of low volume doctors and hospitals were more likely to have metastases; the only exception was that higher volume hospitals were more likely to manage gastric cancer patients with metastatic disease. Thus patients with potentially curable disease tended to be referred to more specialised doctors and hospitals. Another explanation may be that higher volume doctors were more likely to investigate, and were thus able to identify those patients with early stage disease, by excluding tumour spread. However more thorough investigation would also have increased the proportions of patients found to have advanced disease,[28-30] which were shown to be less frequent with higher volumes.

Lower volume doctors and hospitals were less likely to know the cancer stage of their patients. The health care needs of these "unstaged" patients for treatment are not clear, and so it is difficult to judge the quality of their care. It is however plausible that, if they had been more thoroughly investigated, then more of them might have benefited from potentially curative, or active palliative, treatments. There appeared to be large numbers of doctors each managing very few patients and doing little for them, either diagnostically or therapeutically. It may be true that general practitioners selectively refer apparently terminally ill patients to such doctors, and it may be appropriate to do very little for such patients other than to offer supportive care. However it could be argued that, given the difficulty of assessing patients with these cancers, expert assessment is justified in all patients even if they subsequently receive no active treatment. Alternatively, minimal standards for investigations could be specified, for wherever patients are managed. This question of the minimum standard of assessment required for all patients is important for cancer policy because of the large proportions of patients presenting with advanced disease.[1]

Patients of higher volume doctors were more likely to receive a range of diagnostic and staging investigations, independently of their initial clinical presentation. In contrast, few investigations were associated with hospital volumes. This suggests that it was doctors' inclination to investigate, rather than the availability of hospital facilities, that primarily influenced whether investigations are ordered. The types of investigation that were more likely with higher doctor volumes were in general those shown in the scientific literature to be most effective for diagnosis and staging, as discussed in section 3.3 of the literature

review. Examples include ultrasound and ERCP for pancreatic cancer, CT and endoscopic ultrasound for oesophageal cancer, and laparoscopy and endoscopic ultrasound for gastric cancer. It should be noted of endoscopic ultrasound, however, that it was available in only two hospitals in the region, and that because it is a relatively new technology that is dependent on operator skill, its performance in practice may differ from its performance under research conditions. More thorough preoperative investigations may have prevented unnecessary operations in some patients. For example, 73 gastric patients had "open and close" laparotomies with no other surgical procedure performed, presumably owing to tumour spread found at the time of operation. Among gastric cancer patients who had surgery, such laparotomy-only cases were significantly less likely with increasing doctor volume (P 0.05), which may reflect more thorough pre-operative investigation.

Patients of higher volume doctors were more likely to receive several treatments, independently of their measured health status. Most importantly, resections were more likely with higher volume doctors for all three cancers, independently of prognostic factors. This reflects a combination of two processes. Firstly, patients with potentially curable disease were more likely to be referred to specialist surgeons to be assessed for tumour resectability. This is supported by the finding that, for all three cancers, higher volume doctors were significantly more likely to manage patients with early stage disease. Secondly, higher volume doctors may be more likely to do resections independently of their patients' clinical status. This is supported by the finding that resections remained significantly more likely with higher doctor volumes, even after adjusting for important prognostic variables such as the presence of metastases. Similar considerations apply to pancreatic stents and gastric bypass procedures, both of which were independently associated with doctor volumes. It is also noteworthy that the likelihood of resections for oesophageal and gastric cancers was not associated with hospital volumes. This suggests that, as with investigations, it is doctor's characteristics rather than hospital facilities that determine whether patients receive potentially curative surgery. Pancreatic cancer was different in that resections were independently associated with increasing hospital volume as well as with increasing doctor volumes.

Equally striking was the increasing probability of no active treatment with decreasing doctor volumes, and the lack of association of no active treatment with hospital volumes. This suggests that doctor's characteristics rather than hospital facilities determine

whether patients receive treatment at all, other than basic supportive care. It may be appropriate that less specialised doctors manage terminally ill patients, given the reduced scope for intervention. It is however plausible that some patients with potentially treatable disease were not offered treatment, either because their low volume doctors had not adequately investigated them in order to identify those who could benefit from treatment, or because their doctors were unable to provide the treatments themselves but were disinclined to refer such patients.

Analyses of doctor and hospital volumes in relation to provision of chemotherapy and radiotherapy should be interpreted with caution, because of the assumptions made in defining patients' main doctors and main hospitals. Patients who had surgery or stents in addition to radiotherapy or chemotherapy were added to the volumes of the doctors and hospitals who provided the surgery or stents, and not to the volumes of the radiotherapists or oncologists and their hospitals. Thus the patient volumes of radiotherapists and oncologists and their hospitals tended to be underestimated. Doctor and hospital volumes specifically for radiotherapy and chemotherapy were calculated, in addition to the primary doctor and hospital volumes, but these could not be used to explain patients' probability of receiving these treatments because of the circularity in the analysis: patients who did not receive the treatments would have radiotherapy and chemotherapy volumes of zero and therefore the volume measures would necessarily be associated with the respective treatments.

In summary, higher volume doctors were more likely to work in higher volume hospitals, but substantial numbers worked in medium and lower volume hospitals. Higher volume doctors managed higher proportions of patients with early stage disease, and were more inclined to investigate and to offer active treatments. In contrast, lower volume doctors were more likely to manage patients with metastatic disease, were less inclined to investigate their patients and thus had higher proportions of patients whose cancer stage was unknown, and were less likely to provide active treatments. Higher volume hospitals managed higher proportions of pancreatic and oesophageal cancer patients with early stage disease, but managed higher proportions of gastric cancer patients with metastatic disease. Patients in higher volume hospitals were not more likely to be investigated more thoroughly, and were not more likely to receive most kinds of treatment (except for pancreatic surgery and oesophageal radiotherapy).

## 8.2 Operative mortality and survival time

Surgery was performed on about a quarter of pancreatic cancer patients and about a third of oesophageal and gastric cancer patients. Operative mortality was substantially lower for oesophageal and gastric patients of higher volume doctors. The magnitudes of effect were large, with differences in doctor volumes of 10 patients per year associated with reductions in risk of about a third. This finding is most likely to be due to experienced surgeons' greater operative skill, but other factors such as their clinical judgement and the specialist expertise of their support staff may also have contributed. For pancreatic cancers, operative mortality was not associated with doctor volumes. This finding may be partly due to the small number of operative deaths (n 44) which resulted in an imprecise estimate of the odds ratio (0.96-1.08, for a unit increase in doctor volume). It may also reflect inadequate specialisation of pancreatic cancer surgery. Only 21% of resections were done by surgeons who did 5 or more resections per year, and only 13% of all pancreatic operations were done by surgeons who did 10 or more operations on pancreatic cancer cases per year; thus the number of patients who could have benefited from their surgeon's expertise might have been too small for any benefit to be detected.

The substantial survival advantages of higher doctor or hospital volumes among the full spectrum of patients, including the majority who did not receive surgery, is an important and original finding. For these cancers, similar results have only been found in the recent United States study showing lower hospital mortality with higher hospital volumes in the full spectrum of pancreatic cancer patients, and not only in those having resections.[31] However in that study high volumes existed in only one hospital and its generalisability was thus limited. These results are somewhat more surprising than the lower operative mortality associated with higher doctor volumes among surgical patients alone, because in surgery the relationship between experience and skill seems most obvious. These results suggest that, even among patients with apparently incurable cancer, specialisation may prolong survival. It was apparent that, in the full range of patients, both pancreatic and gastric cancer patients had substantially better survival with increasing hospital volumes, but that survival was unrelated to doctor volumes. This finding may reflect the quality of care other than that provided by their doctors. For example, nursing care, nutrition, physiotherapy or other services may be better in more specialised hospitals. It is

not clear why hospital volume had no apparent effect on survival in oesophageal cancer patients whereas it did for pancreatic and gastric cancer patients.

The strong association of doctor volume with survival in the full range of oesophageal cancer patients is likely to be due to therapeutic skill as well as to expert judgement in selecting appropriate treatments. Although for pancreatic and gastric cancer patients survival advantages were not significantly associated with doctor volumes, the respective hazard ratios were not greatly different from those for oesophageal cancer patients (hazard ratios for a doctor volume difference of 10: 0.94 and 0.95 versus 0.91 respectively) and the direction of effect was the same. Thus there may be some advantage in concentrating pancreatic and gastric cancer care among fewer doctors, but this study had insufficient power to show that these apparent advantages were not due to chance.

The true magnitude of the effects of higher volumes on mortality and survival time may be different from the estimates obtained by this study. That is, some bias may have persisted despite meticulous efforts to eliminate it. Examination of the consequences of adjustment for confounding on the magnitudes of volume effects provides some insight into the adequacy of adjustment. Without adjustment for case mix or treatments, for all three cancers survival was longer with higher doctor and hospital volumes. The only exception was gastric cancer, for which crude survival was worse with increasing hospital volumes. With adjustment for case mix and treatments, the estimated effects of larger volumes were reduced or disappeared, or were reversed in the case of gastric cancer and hospital volume. Extrapolation from this trend suggests that with better prognostic information and adjustment the advantages of higher volumes would decrease further; for gastric cancer however the advantage of higher hospital volumes would increase. This need not be the case however, and better adjustment for prognosis could have unpredictable effects on hazard ratios. Whatever the true magnitudes of effect of doctor or hospital volume, however, it is striking that no multivariable analyses indicated that higher volumes were associated with worse outcomes.

The magnitudes of effect found in this study are substantial when compared to well conducted studies of other cancers in the United Kingdom, as discussed in the literature review (section 3.1.2.5). In this study, hazard ratios associated with a hospital or doctor volume difference of 40 patients per year were 0.64, 0.69 and 0.77 for pancreatic, oesophageal and gastric cancers respectively. In the Yorkshire study of survival after breast cancer surgery, the adjusted risk of death among patients of surgeons treating more

than 30 patients per year was 0.85 relative to patients of surgeons treating fewer than 10 patients per year.[8] In that study there was no additional survival advantage with surgeon volumes above 30 patients per year. In the Scottish study of survival after breast cancer surgery, the adjusted relative risk of death for patients of specialist breast surgeons compared to patients of other surgeons was 0.83.[9] Two studies have shown benefits of specialist care that are at least as large as those found in this study. In the Scottish study of survival with ovarian cancer, the adjusted hazard ratio for patients who attended a combined gynaecological oncological clinic was 0.66 compared to other patients.[6] The Scottish study of survival in malignant teratoma patients found an adjusted hazards ratio for death of 2.8 in the patients of four small units compared to the patients of one large unit.[7] The Northern Irish study of survival in patients with colorectal cancer found no advantage of higher doctor or hospital volumes.[43] There is clearly a need for rigorous similar studies of other cancers in the United Kingdom, if specialisation of services is to be tailored according to anatomical cancer site.

## 8.3 Effectiveness of specific treatments

The effectiveness of the various treatments cannot validly be assessed without random allocation of patients either to each of the treatments or to control groups not receiving the respective treatments.[241] This observational study provides some indication of the effectiveness of specific treatments in prolonging survival, because of its ability to compare treated and untreated patients while adjusting for numerous prognostic factors. However confounding was certainly present, in that patients were allocated to treatments or to no treatment according to prior assessment of their prognosis, and prior prognoses were likely to influence outcomes independently of the effectiveness of treatment.

Tumour resection was associated with the largest survival differences between treated and untreated patients. The crude hazard ratios for patients who had pancreatic, oesophageal and gastric cancer resections, compared to those who did not, were 0.25, 0.26 and 0.29, respectively. These figures reflect a combination of the effects on mortality of two types of medical intervention: the selection of patients for resection, and the surgical removal of tumours. The adjusted hazard ratios were 0.31, 0.43 and 0.46, respectively. Thus tumour resections were associated with a reduced risk of death of between about a half and two thirds, independently of measured confounders. The

relative influences of these two interventions could not entirely be distinguished, but adjustment for prognostic variables considerably reduced the magnitude of bias.

Patients who received radiotherapy or chemotherapy were more likely to survive during the first few months after presentation, compared to patients who did not. However, for all three cancers, and for both radiotherapy and chemotherapy, this initial survival advantage decreased over time, as shown by the respective Kaplan-Meier survival curves. For both gastric and oesophageal cancers, patients receiving radiotherapy had poorer survival after about, respectively, six months and a year of follow-up. These results reflect the combination of both treatment and selection effects, as with resections. It may be that patients were selected for radiotherapy or chemotherapy because they were fit enough to withstand the adverse effects of these treatments, but this relative fitness was short-lived. Alternatively it may be that the treatments were beneficial in the short term but ineffective or harmful in the longer term. Unfortunately Cox's proportional hazards model could not be used to obtain hazard ratios for these treatments, adjusted for baseline prognoses, because the hazards of treated and untreated patients were not proportional over time. It was however possible to control for confounding by radiotherapy and chemotherapy by stratified analysis. Logistic regression, using death before a given period as outcome, would be misleading because the magnitudes of the odds ratios would depend primarily on the time points chosen.

## 8.4 Costs of care

This study investigated how costs of hospital care varied with doctor and hospital volumes, so as to provide an indication of current resource use and of how costs to the National Health Service may change with an increased concentration of cancer care. It was not possible to obtain valid hospital-specific and doctor-specific unit costs for each resource item, and so it was not possible clearly to identify economies or diseconomies of scale. However it was possible to examine the quantities of resource items used, with unit costs providing a relative weighting that allowed the costs of different resource items to be combined.

Costs of hospital care were significantly associated with doctor volumes but not with hospital volumes. The lack of association of costs with hospital volumes may be partly due to the lack of hospital-specific unit costs. Another likely explanation is that hospital

volumes were shown not to be associated with the likelihood of patients receiving most tests and treatments. It was to be expected that crude costs would increase with increasing doctor volumes, as it had already been shown that several investigations and treatments were more likely with increasing doctor volumes. However case mix and treatments were not the only determinants of cost variations, as shown by the multiple linear regression analyses that adjusted for case mix and treatments.

For pancreatic cancer patients the relationship between cost and doctor volume was complex. In the crude analysis, costs increased with increasing doctor volume. After adjustment for case mix and treatments, however, a significant U shaped cost-volume relationship emerged, that is, adjusted costs were higher for patients of low volume doctors than for patients of medium volume doctors, but were not as high as for patients of high volume doctors. This pattern was caused by variations in lengths of stay that were independent of measured case mix and treatments, as shown by regressions with days of stay as outcome variable and with the same explanatory variables as were used in the cost analyses. These analyses found the same U shaped relationship between days of stay and doctor volumes. Thus, compared to medium volume doctors, both high and low volume doctors kept their patients in hospital for longer periods, for reasons that were not due to the measured case mix factors or treatments provided.

For oesophageal cancer, the relationship between costs and doctor volumes was similar to the relationship for pancreatic cancer, but the higher adjusted cost for low volume doctors was not as dramatic. In the crude analysis, costs increased with increasing doctor volume. When case mix and treatments were included in the regression model, there was a J shaped relationship between cost and doctor volume. As for pancreatic cancer patients, this pattern was explained by variations in length of stay that were independent of measured case mix factors and treatments.

For gastric cancers, case mix and choice of treatments accounted for all of the higher cost with higher doctor volumes, as shown by the disappearance of the cost-volume relationship once these factors were adjusted for.

Patients who lived longer might be expected to cost hospitals more than patients who died earlier. This is because few patients would be unequivocally cured and survivors would be likely to continue to use hospital care for some time, as indicated by the numerous admissions per patient. On the other hand, terminally ill patients could also be

# SPOC STUDY

G1 : **Reference Number** G2 : **Date of Birth** (D D M M Y Y)

G3 : **Gender** Male ☐ Female ☐

G4 **Smoker** Yes ☐ No ☐ NS ☐ Ex ☐

G5 **Alcohol** Yes ☐ No ☐ NS ☐

**Occupation** (1 2 3 4 5 6 7 8 9 10 11 12)

G7 **Ethnic Origin** (1 2 3 4 5 6 7 8 9 10 11 12)

## PRESENTING SYMPTOMS

G8 (a) **Dysphagia** (1 2 3 4 5 6)

1 = Total 4 Solids
2 = Liquids 5 = Normal
3 – Semi Solids 6 – Not Specified

(b) (c) (d) (e)

1 = GI Bleed
2 = Abdominal Mass
3 = Cough
4 = Jaundice
5 = Lymphadenopathy
6 = Weight Loss
7 = Hoarseness
7 = Reflux / Heartburn
8 = Perforation
9 = Vomiting
10 = Anaemia
11 = Abdominal Pain
12 = Odynophagia

## CO-MORBIDITY

G9 (a) **ASA Status** (1 2 3 4 5 6)

1 ASA I 4 – ASA IV
2 = ASA II 5 – ASA V
3 – ASA III 6 Not Specified

(b) (c) (d) (e)

1 = Acute Pancreatitis
2 = Dementia
3 = COAD/ Asthma
4 = MI
5 = Heart Failure
6 = Chronic Pancreatitis
7 = Barretts Oesphagus
8 = Arthritis
9 = Deformities
10 = Hypertension
11 = Stroke
12 = IHD / Angina
13 =Diabetes

G10 **Previous GI Surgery**

Biliary = 1 Pancreatic = 3
Colonic 2 Gastroduodenal = 4

## DRUG HISTORY

G11 (a) (b) (c) (d) (e) (f)

0 = None
1 = Diuretics
2 = Cardiac
3 = Diabetes(Insulin)
4 = Diabetes (Oral)
5 = Bronchodilators
6 = Proton Pump Inhibitors
7 = H2 receptor antagonists
8 = NSAIDS
9 = Steroids
10 = Antihypertensives
11 = Not Stated

## MANAGEMENT

**Hospital Number**

G13 **Hospital**

G14 **Consultant**

(a) Date of presentation (D D M M Y Y)

(b) Date Referred (D D M M Y Y)

(c) Date first seen at this hospital (D D M M Y Y)

(d) Outpatient visits at this hospital

(e) No of Day case visits

(f) No of admissions

(a) Date admitted (First) (D D M M Y Y)

(b) Date of treatment (D D M M Y Y)

(c) Date of discharge (D D M M Y Y)

(d) Date admitted (Second) (D D M M Y Y)

(e) Date of treatment (D D M M Y Y)

(f) Date of discharge (D D M M Y Y)



R&D Support Unit, Bristol Royal Infirmary

## 8.5 Deprivation, care and mortality

Townsend deprivation score was not independently associated with operative mortality or survival time and its removal from the respective models did not influence the volume estimated effects of doctor or hospital volumes. Thus ecological deprivation score was not a confounder. Deprivation score was independently associated with the probability of receiving several tests or treatments, but there were no consistent patterns. Most importantly, more deprived patients were no less likely to receive resections, and were no more likely to receive no active treatments, independently of clinical presentation. However, for both oesophageal and pancreatic cancers, more deprived patients were significantly less likely to have computed tomography. These largely negative findings might be partly an artifact of misclassification of individuals' socioeconomic status by use of ecologic (enumeration district-level) deprivation indicators. They are however reassuring that inequity in management are unlikely to be serious problems once patients reach hospital.

For gastric and pancreatic cancers, greater deprivation was associated with greater hospital volumes, probably reflecting the concentration of poverty and large hospitals in the larger cities. This suggests that, for these cancers, patients from more deprived areas had access to more specialised hospitals. However this correlation was weak ($R^2 = 0.01$ for pancreatic cancer and $R^2 = 0.02$ for gastric cancer). There was no association between Townsend deprivation score and hospital volume for oesophageal cancer, or with doctor volume for any cancer. Thus the effects of hospital and doctor volumes, and ecological deprivation scores, can be distinguished from each other with some confidence. Individual-level deprivation measures may have permitted these relationships to be examined with greater validity.

## 8.6 Strengths and weaknesses of the study

The key strengths of the study were the inclusion of all acute hospital trusts in the region, the large sample sizes, the prospective cohort design, the prospective identification of cases which allowed almost all of the patients' hospital records to be traced and examined, the inclusion of a wide range of clinical information so as to allow thorough adjustment for prognostic case mix variables, the use of patient volumes as a robust and

objective measure of specialisation, the tracking of survival of virtually all cases, and the careful multivariable data analyses. The inclusion in the study of patients' prognostic and outcome measures, doctors' and hospitals' characteristics, health care processes and costs provides an unusually rich picture of a highly complex system, allowing the various mechanisms operating to be distinguished while permitting their interrelationships to be analysed. The study thus exemplifies the kind of research needed for a thorough understanding of hospitals and health care systems,[18, 19] as discussed at the end of the Introduction. However research of this nature also has inherent restrictions.

The key limitations of the epidemiological part of the study were the exclusion from the study of patients not admitted to participating hospitals, the reliance on diverse hospital sources to identify cases, imperfect information on patient prognosis at the time of presentation to hospital, and variable quality of clinical information recorded in hospital records. The exclusion of patients who did not attend acute hospitals means that the study results cannot be generalised to them. As mentioned in Methods, cancer registry data showed that in recent years the hospitals included in the study accounted for 72% of pancreatic, 86% of oesophageal, and 75% of gastric cancer registrations. It is highly plausible that patients in excluded, smaller, hospitals would have characteristics similar to study patients of low volume hospitals, but this is not certain.

The reliance on hospital sources rather than on cancer registries for identification of cases means that some eligible cases may not have been identified. It is also possible that some consultants or hospitals may have withheld notification of certain cases that reflected badly on their quality of care.[242] However the latter bias was unlikely as patient identification and notification were usually done by administrative and not by clinical staff. The numbers of patients included comprised high proportions of the numbers projected from previous cancer registrations from the same hospitals. The numbers of patients included in the study from the South and West region, as proportions of the numbers expected, were 87% (583/670) for pancreatic cancers, and 93% (1512/1630) for oesophageal and gastric cancers together. The number of oesophageal cancers was less (79%) than expected and the number of gastric cancers was more (114%) than expected, probably reflecting differences in classification of junctional adenocarcinomas between this study and cancer registries. The investigators' ability rapidly to identify patients and to access their hospital records arguably outweighed the advantages of relying on cancer

registries for case identification and attempting to trace their records years after first presentation.

Imperfect information on illness severity is an inherent problem in observational studies of the quality of care, in which confounding is likely.[27] This problem was aggravated by the fact that for these cancers accurate staging requires costly and potentially traumatic investigations, which were often not done. There were two partial solutions to the problem of inaccurate or missing prognostic information. Firstly, an exceptionally large number of important prognostic factors – including age, mode of admission, symptoms, co-morbidities and biochemical measures, as well as tumour-specific factors - were measured and included in the analyses. All patients had some prognostic information available. Biochemical measures such as serum albumin levels were available for almost all patients and were strongly associated with survival. Secondly, where important factors such as T, N or M staging were not known, this fact was coded as a separate category of the respective staging variable. Missing data thereby conveyed prognostic information, because unstaged patients generally had prognoses that were worse than patients with early stage disease, but were better than patients with metastatic disease. The influence of adjustment for prognostic variables on the magnitude and even direction of hazard ratios further suggests that the study was able substantially to control for confounding of volume effects by case mix. Adjustment had the least effect on hazard ratios for pancreatic cancers, suggesting that the study was less able to account for case mix differences among pancreatic cancers than among oesophageal cancers. In contrast, adjustment had marked effects on hazard ratios for gastric cancers. For oesophageal cancers, the effect of adjustment on hazard ratios was intermediate between that found for the other two cancers. These observations are in keeping with the observation that the proportions of patients who were at least partly staged were 48% of pancreatic cancers, 57% of oesophageal cancers, and 70% of gastric cancers.

Designation of each patient's main doctor and main hospital was not always clear, and may have resulted in incorrect estimates of the two key explanatory variables, namely hospital volume and doctor volume. This was especially a problem for patients managed in more than one hospital or specialty. However the various sensitivity analyses used – excluding patients managed by more than one doctor or hospital, and using patient volumes specific to surgery, chemotherapy and radiotherapy – showed the primary analyses to be robust to assumptions about the main doctor and main hospital in such

patients. A related cause of concern was the surprisingly numerous doctors who appeared to manage only one case of the respective cancer during a year. Unfortunately the specialties of these doctors were not recorded; the research workers reported that many were geriatricians and other physicians. It is plausible that the patient volumes for these lowest volume doctors may have been incorrectly estimated, but it is unlikely that doctors with volumes of one or two patients were in fact medium or high volume doctors. It is difficult to conceive how misclassification of doctor and hospital volumes would be differential with regard to survival: this would occur if those higher volume doctors who tended to have poorer survival were more likely than other higher volume doctors to be misclassified as lower volume doctors. Non-differential misclassification of doctor and hospital volumes would tend to bias associations with these variables toward the null; if it had occurred then the true hazard ratios would be further from unity than the estimated hazard ratios.[27]

A more fundamental limitation of the study was its exclusion of quality of life from the outcome assessment. For large proportions of patients, cure was not possible. For these patients the outcomes of palliation of symptoms and of emotional and social support would probably be more important than survival time.[243] Quality of life assessment was beyond the scope of a study of this size. It would have required interviews with, or completion of questionnaires by, the patients and/or their carers. The high mortality rate would have meant that many patients, and especially those with the worst prognoses, would not have been able to provide information by the time they were contacted. As discussed under research priorities, other study designs are necessary to assess quality of life outcomes.

The main strength of the cost analyses was the detailed estimation of resource use for each patient, which allowed statistically powerful analyses of the various influences on costs of care. The main limitations of the cost analyses were the absence of valid hospital-specific unit cost estimates, the inability of many hospitals to provide unit cost estimates, imperfect control of confounding by case mix, and consideration only of hospital costs.

The lack of hospital-specific unit costs meant that the study could not examine the relative efficiency with which different hospitals produced specific resource units, and thus potential economies of scale. Estimates of unit costs for each resource item in each hospital are generally not available, and where they do exist costing methods vary widely,

severely impairing comparability.[236] The most recent and sophisticated attempt by the National Health Service to apply standard costing methods to all surgical healthcare resource groups (HRGs) resulted in widely variable results, with variations largely due to differences in costing methods between hospitals, rather than solely due to than differences in efficiency.[244]

The sensitivity analyses in this study showed, however, that the total cost estimates were fairly insensitive to assumptions about the costs of individual resource items, and were most sensitive to assumptions about costs per day in a hospital ward. The cost per day in a ward used in this study was £180, or 80% of the average cost per inpatient per day in a surgical ward in England in 1994/5 (that is, £223) reported by the Office for Health Economics.[245] Substitution of the latter figure for the former figure would have increased the estimated hospital costs. It would also have strengthened the associations observed between costs and doctor volumes, because doctor volumes were associated with lengths of stay for all three cancers. However it was considered most appropriate to use the unit costs for bed days derived from the same source as the unit costs for the other resource items.

Confounding of cost estimates is likely to have occurred, as discussed above with reference to survival and mortality; the same caveats therefore apply to the cost analyses. It would have been desirable to estimate health care costs incurred outside the hospital, and costs of travel, visiting, home care, lost productivity and social services, but these were beyond the scope of the study, as they would have required information to be obtained directly from patients or their carers. Exclusion of patients' and households' costs is relevant to the context of this study because concentration of services into fewer hospitals would mean that some patients and their families would have to travel further to hospital, which may also mean longer admissions. This study found hospital costs to depend largely on lengths of stay; shorter admissions would reduce costs to the National Health Service but would probably increase the costs of home care and social services. Thus part of the apparent efficiency gains with increasing doctor volumes could be due to cost shifting from health services to households and to other agencies.

## 8.7 Implications for health services

The study provides evidence supporting the concentration of care of oesophageal, gastric and pancreatic cancers into fewer hospital trusts and under the supervision of fewer consultants. It does not provide evidence to help identify volume thresholds for defining specialists, however, because the health benefits of increasing volumes appeared to increase along a continuum, rather than increasing noticeably at any particular volume. Concentration and specialisation of cancer care entails various inter-related processes, which were beyond the scope of the study to assess. These include education and training of specialist doctors; development of sub-specialties within surgery, medicine, radiotherapy and oncology; education and training and specialisation of allied professionals; concentration of appliances and other technologies; development of clinical practice guidelines for different types of patients in different settings; and the development of referral patterns.[1, 12, 13, 98, 242] Assuring the quality of cancer care has implications for evaluation and surveillance, which will be discussed below under implications for health services research methods (section 8.7).

Improving the quality of cancer care will require more resources and more money.[4] This study suggests that greater specialisation will result in patients being investigated and treated more intensively. If funding increases are small or non-existent it will be necessary to look for cost savings in some areas to finance quality improvements in others. This study provides unique evidence of the cost of cancer care in the National Health Service, and of factors contributing most to costs. It appears that costs associated with care of patients in wards account for most of hospital costs, that specific treatments such as operations, radiotherapy and chemotherapy account for between 20% and 30% of hospital costs, and that investigations cost only slightly less than specific treatments. These results are not surprising considering that most patients do not have curable disease but are likely to be severely ill and incapacitated. As more intensive investigation and (at least surgical) treatment appear indirectly to be associated with lower mortality, the main remaining area for possible cost savings is therefore by reducing lengths of inpatient admissions. This would be appropriate if shorter admissions represented true efficiency gains – for example due to more rapid diagnostic work-up, fewer operative complications, and better discharge planning – and not simply cost shifting from the health service to households or Social Services budgets, or neglect of terminally ill

patients. This study suggests that if fewer patients were managed by very low volume doctors, shorter admissions could result in hospital cost savings that could help offset the increased costs of specialised care. If greater specialisation were to lead to more intensive management combined with shorter hospital admissions, it would be in keeping with general trends in the hospitals in the United Kingdom and internationally.[15]

Identification of cancer units and cancer centres is already underway in the National Health Service, in many regions on the basis of specific cancer sites. The Calman-Hine proposals focus on the identification of specialist hospitals – cancer centres and cancer units - rather than specialist doctors.[1] This study shows that both should be considered simultaneously.[12]

The results of this study, together with results of studies of other cancer sites discussed in the literature review, suggest that the benefits of specialisation apply to some cancers, but not necessarily to others.[10, 20, 242] However it should be recognised that, in the various studies, some positive results as well as some negative results could be attributed to flaws in study design and data quality. In general there are more studies that have failed convincingly to demonstrate advantages of specialisation because of flawed design and flawed data than there are studies that have convincingly shown no benefits of specialisation.[10, 20, 242] This study's finding of substantial benefits of specialisation even for these three cancer sites that tend to have poor prognoses, and even for patients with advanced disease, may have implications for other cancers. These results suggest that specialisation may be beneficial for other cancer sites for which few patients have curable disease and for which similar evaluation research has not yet been carried out, and may be beneficial for palliative as well as curative care. This speculation however clearly depends on further evidence for confirmation or refutation.

# 8.8 Implications for health services research methods

This study exemplifies observational epidemiology[24] and economic analysis[246] applied to the evaluation of health care. As discussed earlier, it illustrates the key strengths and weaknesses of this kind of research. Patients are unlikely to agree to be randomly allocated to inexperienced doctors or to smaller hospitals, and their doctors too are unlikely to agree to such randomisation, and so experimental evidence of the relative effectiveness and efficiency of specialised care will remain elusive.[24] Therefore observational studies, with comparison of similar types of patients managed in different settings, or measurement and adjustment for systematic differences between patients managed in different settings, remain necessary. Two recent reviews comparing results of observational and experimental studies of effectiveness, for a limited range of health care interventions, concluded that observational studies are not necessarily biased, in comparison with experimental studies, provided that confounding factors are adequately measured and controlled for.[247, 248]

Confounding is a particularly acute problem when observational epidemiology is used to evaluate treatments.[27] Because treatments are often chosen on the basis of expected prognoses, one would expect outcomes to differ, and one would therefore be less confident of having controlled for all systematic differences between comparison groups. However this would be less of a problem if one were able to control for those same prognostic factors that influenced decisions about where or how to treat. In other words, this "confounding by indication"[249] would be diminished if one could control for the indications. At least two such variables – age and cancer stage - were extensively used in this study. In contrast, a prognostic variable like serum albumin was a confounder and was extensively controlled for but probably did not directly influence referral decisions.

An advantage of observational studies such as this is the relative ease of recruiting large numbers of patients, enhancing statistical power. This is especially valuable when estimating small effects. Another advantage is that inclusion of most relevant patients from a large geographical area enhances the generalisability of the findings.[24] Thus, compared to randomised trials, the loss of internal validity is partly compensated for by the gain in power and external validity. However generalisation of health services research findings may be difficult, as the following discussion shows.

A central aim of scientific research is to be able to make inferences that apply beyond the immediate scope of a specific study.[27] The generalisability of the study's findings to other regions of the United Kingdom and to other countries should therefore be considered. It is most likely that the findings do apply to other regions of the United Kingdom because of similarities in the organisation of the National Health Service, in its resource constraints, in the training and registration of professionals, and because of the large amount of inter-regional migration of health professionals. Thus specialisation and corresponding distributions of patients, resources, clinical practice and expertise are unlikely to differ greatly between the regions. The geographical area covered by the study includes 13% of the total population of England, and most of the population of Wales.[245] It is also fairly representative of the country socially and demographically, as it includes moderately large cities, relatively remote rural areas and small towns, and affluent and deprived areas: factors which would be expected to influence access to specialised care. The main limitation to generalisability within the United Kingdom is the exclusion of patients never admitted to acute, or district general, hospitals, who were estimated to comprise between about 15% to 25% of all patients with these cancers.

It is less clear to what extent the results can be generalised to other countries. This depends on how cancer care is organised, how much variation there is in the quality of care, and how much scope there is for improvement. All developed countries would be able to obtain the main treatments, but differ in the finance available to pay for them. The United Kingdom's health care expenditure per capita is lower than most countries with similar incomes,[250] but this is partly due to relatively low labour costs. Thus other European countries may or may not be better resourced, but more resources need not necessarily mean better quality care. In the United States cancer care would tend to be better resourced than in the United Kingdom, but there would be greater inequalities in the quality of care, with substantial scope for improvement in some areas. Other developed countries may have less scope for improvement than the United Kingdom, as it is well recognised that cancer survival in the United Kingdom is relatively poor compared to other developed countries, especially for gastric cancer.[251] Low income countries would have much greater scope for improving the quality of cancer care through specialisation but it is questionable whether this would be affordable or a priority.[250] Whatever the differences between countries, however, it is likely that professionals caring for patients with pancreatic, oesophageal and gastric cancers would be interested in the

results of this study and would be better placed than the author to consider its relevance to their own settings, taking into account the patterns of disease and clinical practice described here.

The only way to increase the geographical generalisability of studies such as this would be to include patients from other regions or other countries. This would be logistically arduous if data were to be collected in the same way as in this study, but may be feasible if routine data were collected and included the relevant prognostic, process and outcome variables. Efforts to compare cancer survival in diverse European countries suggest that this may be possible in future.[251]

This raises the question of whether it would be feasible routinely to collect such data for surveillance of the quality of cancer care. The main problem is while the most important prognostic variable for cancers is cancer stage, staging may require costly and traumatic investigations that may be inappropriate for patients with apparently terminal illness. It may be reasonable however for all patients to have an ultrasound or CT scan to look for metastases, and for the finding to be coded as metastases included, excluded or unknown. This study has also shown the prognostic value of serum albumin levels, which could be obtained relatively inexpensively on all patients, with no risk of harm. Both of these tests, and especially identification or exclusion of metastases, should be of value in choosing treatments and their costs might then be justified. If these two variables, together with age and treatments provided, were recorded for all patients, and if these data were linked to centrally registered mortality data, then relatively valid comparisons of the quality of cancer care could continually be made between doctors and hospitals and over time. The critical problems then would be ethical concerns about the confidentiality of patient, doctor and hospital identities, and political and managerial problems of dealing with poor performance.

## 8.9 Future research priorities

This study represents a major attempt to answer the question of whether and how the quality and costs of cancer care varied with doctor and hospital volumes. Clearly this study does not provide complete answers. Future research priorities should be considered.

First, an extension of the present study will investigate the influences of patients' social class and geographical location, as indicated by their address postal codes, on access to care, as indicated by delays from referral to admission and treatment, proportions of patients admitted as emergencies, and their doctors' and hospitals' patient volumes. This will allow further examination of the trade-offs between quality, cost and access.[15]

Second, it is necessary to extend the current body of evidence to consider other cancer sites. The present state of knowledge is too heterogeneous to conclude that increasing doctor or hospital volumes will increase the quality of care for all cancer sites.

Third, implementation of the National Health Service's cancer policy framework should be evaluated. Its uneven application in different regions may allow comparisons between rapidly and slowly changing processes. On a national scale, it would be possible to use routinely collected Hospital Episode Statistics to describe, for each cancer site, changes in the degree of concentration of patients onto fewer sites. The same data would allow hospital mortality to be monitored, and for hospital volumes to be estimated.[252] Case mix data are limited but include age and comorbidity. These data could be combined to examine whether greater concentration of cancer care is associated with improved hospital mortality, after specific surgical procedures and in patients who do not receive surgery.

Fourth, influences on survival times could be analysed on a larger scale.[253] Cancer registry data linked to death registrations would allow survival times to be examined using routine data. The key limitation is the paucity of staging data for many cancer sites in most cancer registries. In future, routine recording of prognostic factors would allow more valid comparisons.

Fifth, quality of life outcomes should be examined, in patients receiving either potentially curative or palliative care. This research would require direct contact with patients, and would thus probably need to be conducted on a smaller scale, and to include qualitative methods so as to enhance understanding of outcomes from patients' perspective.

Final, randomised trials comparing the main treatment options are required. As shown in the literature review, there are very few randomised trials to inform the choices of the patients and practitioners, especially for surgery. This study illustrates the limited value of using observational studies of this kind to evaluate the effectiveness of tumour resections and other specific treatments.

## 8.10 Observations and theory

The relationship between the results of this study and the underlying theory can be briefly summarised. The observations were largely determined by the theory of volume-outcome relationships, and support it. The theory, as discussed by Luft,[21] Harrison[15] and others, is that specialisation of health care, as indicated by patient volumes, may be associated with better health outcomes, for two main reasons. First, selective referral to specialists of patients with better prognoses may result in better outcomes for specialists' patients, independently of the effectiveness of health care. This study has shown such selective referral to have occurred for all three cancers (with the exception of gastric cancers patients and their hospitals). Second, "practice makes perfect". "Practice" refers not only to clinicians' therapeutic skills but also to their diagnostic skills and decision-making, and refers not only to the lead clinicians but also to the other services and professionals on which they depend.

This study suggests that practice does improve effectiveness, that is, higher doctor or hospital volumes were associated with better outcomes. The relationship between surgical skill and surgical experience is most clearly interpretable: for patients having gastric or oesophageal surgery, operative mortality was inversely related to doctor volume. Among the broad spectrum of patients who received a variety of treatments, or received no active treatment, the mechanisms whereby specialisation influenced outcomes was more complex and less amenable to clear observation. The greater propensity of higher volume doctors to use tests and treatments, independently of patients' presenting clinical features, may have contributed to better outcomes. Thus analysis of health care processes helped elucidate mechanisms linking structural and outcome variables.[15, 18] Additionally, the skill with which tests and treatments were provided, and judgements about whom not to treat aggressively, may also have contributed to better outcomes, but were not readily observable.

Economic theory predicts that economies of scale may exist in health care,[70, 71] as in any kind of firm or production unit.[72] Average costs would tend to decrease with increasing scale, but would increase above the most efficient scale, resulting in a U shaped cost-volume curve.[71, 72] The U-shaped relationships between doctor volumes and costs of care for pancreatic and oesophageal cancers, and the decreasing cost per day of life with increasing doctor volumes for gastric cancers, appear superficially to support this model. However this evidence of scale economies in cancer care is questionable for several reasons: valid hospital-specific and doctor-specific unit cost estimates were not available, hospital volumes were not associated with costs, and doctor volumes for one disease are qualitatively different from the scale of firms. The cost analysis thus provided original evidence of the cost implications of the combination of case mix, clinical practice and survival, in relation to doctor and hospital volumes, but should not be considered to support the theory of economies of scale in this context.

The relevant theory could be broadened to include inter-relationships between the effectiveness, efficiency, equity and humanity of cancer care.[15, 254] However such theory would extend beyond the evidence reported in this thesis and will not be discussed further.

This study suggests that more specialised cancer care can reduce mortality and influence hospital costs. These findings may apply beyond the geographical and temporal limitations of the study, and to other types of cancer, but such generalisations require caution. Despite its limitations, the study supports the concentration of cancer care into fewer hospitals and to fewer doctors. Such developments in the United Kingdom should continue for pancreatic, oesophageal and gastric cancers.

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# APPENDIX 1. PRESENTATIONS OF RESULTS

Preliminary results of the study were presented at the Association of Surgeons' Annual Conference, Southampton, April 1999:

M Bachmann, D Alderson, D Edwards, C Bedford, S Wotton, T Peters, I Harvey. Case mix, clinical practice, survival & specialisation for pancreatic, oesophageal and gastric cancers

# APPENDIX 2. DATA COLLECTION FORMS

- General (SPOC) form for all patients
- Form for pancreatic cancer patients
- Form for oesophageal cancer patients
- Form for gastric cancer patients

# SPOC STUDY

G1 : **Reference Number** G2 : **Date of Birth** (D D M M Y Y)

G3 : **Gender** Male ☐ Female ☐

G4 **Smoker** Yes ☐ No ☐ NS ☐ Ex ☐

G5 **Alcohol** Yes ☐ No ☐ NS ☐

G6 **Occupation** (1 2 3 4 5 6 7 8 9 10 11 12)

G7 **Ethnic Origin** (1 2 3 4 5 6 7 8 9 10 11 12)

## PRESENTING SYMPTOMS

G8 (a) **Dysphagia** (1 2 3 4 5 6)

1 = Total
2 = Liquids
3 = Semi Solids
4 = Solids
5 = Normal
6 = Not Specified

(b) (c) (d) (e)

1 = GI Bleed
2 = Abdominal Mass
3 = Cough
4 = Jaundice
5 = Lymphadenopathy
6 = Weight Loss
7 = Hoarseness
7 = Reflux / Heartburn
8 = Perforation
9 = Vomiting
10 = Anaemia
11 = Abdominal Pain
12 Odynophagia

## CO-MORBIDITY

G9 (a) **ASA Status** (1 2 3 4 5 6)

1 = ASA I
2 = ASA II
3 = ASA III
4 = ASA IV
5 = ASA V
6 = Not Specified

(b) (c) (d) (e)

1 = Acute Pancreatitis
2 = Dementia
3 = COAD/ Asthma
4 = MI
5 = Heart Failure
6 = Chronic Pancreatitis
7 = Barretts Oesphagus
8 = Arthritis
9 = Deformities
10 = Hypertension
11 = Stroke
12 = IHD / Angina
13 =Diabetes

G10 **Previous GI Surgery**

Biliary = 1 Pancreatic = 3
Colonic = 2 Gastroduodenal = 4

## DRUG HISTORY

G11 (a) (b) (c) (d) (e) (f)

0 = None
1 = Diuretics
2 = Cardiac
3 = Diabetes(Insulin)
4 = Diabetes (Oral)
5 = Bronchodilators
6 = Proton Pump Inhibitors
7 = H2 receptor antagonists
8 = NSAIDS
9 = Steroids
10 = Antihypertensives
11 = Not Stated

## MANAGEMENT

G12 **Hospital Number**

G13 **Hospital**

G14 **Consultant**

G15 (a) Date of presentation (D D M M Y Y)

(b) Date Referred (D D M M Y Y)

(c) Date first seen at this hospital (D D M M Y Y)

(d) No Outpatient visits at this hospital

(e) No of Day case visits

(f) No of admissions

G16 (a) Date admitted (First) (D D M M Y Y)

(b) Date of treatment (D D M M Y Y)

(c) Date of discharge (D D M M Y Y)

(d) Date admitted (Second) (D D M M Y Y)

(e) Date of treatment (D D M M Y Y)

(f) Date of discharge (D D M M Y Y)

(g) Date admitted (Third) D D M M Y Y

(h) Date of treatment D D M M Y Y

(i) Date of discharge D D M M Y Y

(j) Date admitted (Forth) D D M M Y Y

(k) Date of treatment D D M M Y Y

(l) Date of discharge D D M M Y Y

G17 **Admission** Emergency 1 Elective 2

G18 **Intervention** Emergency 1 Elective 2

G19 **Referral from**

1 - 39 Other Hospital
40 GP
41 Open Access Endoscopy
42 Other Specialty
43 Other Non coded hospital

G20 **Patient managed at more than one site** Yes ☐ No ☐

G21 **Hospital Number**

G22 **Hospital**

G23 **Consultant**

G24 (a) Date Referred D D M M Y Y

(b) Date first seen at this hospital D D M M Y Y

G25 **No of admissions**

G26 (a) Date admitted (First) D D M M Y Y

(b) Date of treatment D D M M Y Y

(c) Date of discharge D D M M Y Y

(d) Date admitted (Second) D D M M Y Y

(e) Date of treatment D D M M Y Y

(f) Date of discharge D D M M Y Y

(g) Date admitted (Third) D D M M Y Y

(h) Date of treatment D D M M Y Y

(i) Date of discharge D D M M Y Y

(j) Date admitted (Forth) D D M M Y Y

(k) Date of treatment D D M M Y Y

(l) Date of discharge D D M M Y Y

G27 No Outpatient visits

G28 No of Day case visits

G29 **Referral from**

1 - 39 Other Hospital
40 GP
41 Open Access Endoscopy
42 Other Specialty
43 Other Non coded hospital

G30 Date first seen by GI Specialist / Endoscopist D D M M Y Y

G31 Date of Diagnosis D D M M Y Y

## INVESTIGATIONS

G32 (a) **Blood Count**

(b) Hb

(c) MCV

(d) Hct /PCV

G33 (a) **Blood Transfusions** Pre Op

(b) Total

(c) Total no of units

G34 (a) **Coagulation** | (b) One Stage Prothrombin Time | (c) INR

G35 (a) **Electrolytes** | (b) Urea | (c) Creatinine

G36 (a) **LFT** | (b) Albumin | (c) Globulin | (d) Bilirubin | (e) Gamma GT | (f) AST | (g) ALT | (h) Alkaline Phosphatase

G37 **Amylase** G38 **Calcium** G39 **Glucose** G40 **Microbiology** G41 (a) **Blood Gases** (b) pO2 (c) pCO2

G42 (a) other (b) G43 (a) other (b) G44 (a) other (b) G45 (a) other (b)

## RADIOLOGY AND ENDSCOPY

| | Pre Op | Post Op | | Pre Op | Post Op | | Pre Op | Post Op | |
|---|---|---|---|---|---|---|---|---|---|
| G46 (a) Abdominal Ultrasound | | | (b) | G47 (a) Angiography | | | (b) | G48 (a) ECG | | | (b) |
| G49 (a) Contrast Swallow | | | (b) | G50 (a) Biopsy | | | (b) | G51 (a) MRI | | | (b) |
| G52 (a) Bronchoscopy | | | (b) | G53 (a) Chest Xray | | | (b) | G54 (a) Laparoscopy | | | (b) |
| G55 (a) CT Scan | | | (b) | G56 (a) Cytology | | | (b) | G57 (a) EUS | | | (b) |
| G58 (a) OGD | | | (b) | G59 (a) Dilatation | | | (b) | G60 (a) Pulmonary Function Tests | | | (b) |
| G61 (a) ERCP | | | (b) | G62 (a) PTC | | | (b) | G63 (a) Other Endoscopy | | | (b) |
| G64 (a) Other Xrays | | | (b) | G65 (a) CTAP | | | (b) | | | | |

G66 **Pre treatment histological confirmation**
Yes ☐
No ☐

G67 **If yes Biopsy**
1 Endoscopically
2 Percutaneous
3 Other ☐

G68 **If yes Cytology**
1 Endoscopically
2 Percutaneous
3 Other ☐

**Type of US**

| G69 (a) Intraluminal | (b) Laparoscopic | (c) Intraoperative | (d) Abdominal |
|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ |

G70 **Complications of investigations** ☐☐

1 Bleeding
2 T - O Fistula
3 Pneumonia
4 Pancreatitis
5 Oesophageal Perforation
6 Duodenal Perforation



R&D Support Unit, Bristol Royal Infirmary

# PANCREATIC CANCER

P1 (a) **Location**

1 Head
2 Body
3 Tail
4 Ampulla
5 Head Body
6 Head Ampulla
7 Body Tail
8 Head Ampulla Body
9 Head Body Tail
10 Head Body Tail Ampulla
11 Not Specified

(b) **Diameter**

P2 **Treatment**

1 Yes
2 Patient unfit
3 Cancer too advanced
4 Incidental finding at PM
5 Died prior to treatment
6 Patient refused consent

P3 **Reference number**

P4 (a) **Dilatation**

1 No
2 Dilatation only
3 Dilatation & Laser
4 Dilatation & Alcohol

(b) **Consultant** (c) **Hospital Code**

P5 (a) **Stent**

1 No
2 Conventional (Plastic)
3 Covered (Metal)
4 Uncovered (Metal)
5 Pulsion
6 Not Specified
7 Unsucessful attempt

(b) **Consultant** (c) **Hospital Code**

(d) **Inserted by**

1 Surgeon
2 Physician
3 Radiologist
4 – Endoscopist
5 – Not Specified

(e) **Procedure**

1 ERCP alone
2 PTC alone
3 Combined

(f) **Complications**

1 Bleeding
2 Pneumonia
3 Duodenal Perforation
4 Infection
5 Pancreatitis

P6 (a) **Laser** Yes ☐ No ☐

(b) **Consultant** (c) **Hospital Code**

P7 (a) **Radiotherapy**

1 No
2 Pre Op
3 Post Op
4 Pre & Post Op

(b) **Trial** Yes ☐ No ☐

(c) **Consultant** (d) **Hospital Code**

(e) **How**

1 External
2 Brachy Intraluminal
3 Not Specified

(f) **Dose** cGy (g) **Fraction**

P8 (a) **Chemotherapy**

1 No
2 Pre Op
3 Post Op
4 Pre & Post Op

(b) **Trial** Yes ☐ No ☐

(c) **Consultant** (d) **Hospital Code**

P9 **Start Date** D D M M Y Y

P10 **Finish Date** D D M M Y Y

P11 **Cycles**

**Chemotherapy Agents**

P12 (a) (b) mg/m2 (c) Total Dose

P13 (a) (b) mg/m2 (c) Total Dose

P14 (a) (b) mg/m2 (c) Total Dose

P15 (a) (b) mg/m2 (c) Total Dose

1 5 Fluorouracil
2 Cisplatin
3 Carboplatin
4 Epirubicin
5 Doxorubicin

# SURGICAL TREATMENT

P16 **Grade of Surgeon**

1 Consultant
2 Clinical Assistant
3 Staff Grade
4 Specialist Reg (HST)
5 SHO (BST)
6 Other

P17 **Grade of anaesthestist**

1 Consultant
2 Associate Specialist
3 Staff Grade
4 Specialist Reg (HST)
5 SHO (BST)
6 Other

P18 **Supervision** Yes ☐ NK ☐ No ☐

P19 **Hospital Code**

19 **Surgery**
Yes ☐
No ☐

P20 **Type of surgery** ☐
1 Absolute
2 Relative
3 Non Curative
4 Not Specified

P21 **Bypass** ☐
1 Biliary alone
2 Gastroenterostomy alone
3 Biliary & Gastro
4 Triple

P22 **Procedure** ☐☐
1 Pan duodenectomy
2 Laparotomy only
3 Total Pancreatomy
4 Pan duodenectomy (pylorus)
5 Coeliac plexus block

P23 **Reconstruction** ☐
1 P1 S2 B3
2 P1 B2 S3
3 P2 S1 B3
4 P2 B1 S3
5 P3 S1 B2
6 P3 B1 S2

**Anastomosis**

P24 **Biliary** D J
G ☐ ☐
B ☐ ☐

P25 **Pancreatic** ☐

P26 **Jejunal** ☐

G Gall Bladder
B Bile Duct

1 D Duodenum
2 J Jejunum
3 S Stomach

P27 (a) **Type**
Sutured ☐
Stapled ☐

(b) **Stitch**

| | S | D | I | C |
|---|---|---|---|---|
| B | ☐ | ☐ | ☐ | ☐ |
| P | ☐ | ☐ | ☐ | ☐ |
| J | ☐ | ☐ | ☐ | ☐ |

P28 **Biliary** ☐☐

P29 **Jejunum** ☐☐

P30 **Pancreas** ☐☐

1 C
2 V
3 D
4 M
5 PDS
6 S
7 P
8 N
9 Other

P31 **Site of Tumour at operation**
Head ☐ Tail ☐
Body ☐ Ampulla ☐

P32 **Length of Procedure** H H M M ☐☐☐☐

P33 **Other organs removed** ☐☐

1 Pericardium
2 Stomach
3 Spleen
4 Crura
5 Omentum
6 Oesophagus
7 Liver
8 Lung
9 Gallbladder
10 Colon

P34 (a) **Intraoperative complications** ☐☐
0 None
1 Tracheal or bronchial injury
2 Bleeding
3 Cardiac event

(b) **Did this lead to a change of procedure**
Yes ☐ No ☐

## Post Operative Care

P35 **Time in ITU** H H M M ☐☐☐☐

P36 **Time in HDU** H H M M ☐☐☐☐

P37 **Ventilation**
Yes ☐
No ☐
NK ☐

P38 **Time on ventilator** H H M M ☐☐☐☐

**Pain Relief**
P39 (a) ☐ (b) ☐ (c) ☐
1 Epidural
2 Intercostal Block
3 Paraverterbral Block
4 Opiates (Continous)
5 - Opiates (IM)
6 NSAIDS
7 PCA

**DVT Prophylaxis**
P40 (a) ☐ (b) ☐ (c) ☐
0 None
1 LMW heparin / Clexane
2 TEDS
3 Minihep
4 Mechanical

P41 **Prophylactic Antibiotics**
Yes ☐ No ☐ NS ☐

## POST OPERATIVE COMPLICATIONS

P42 **Pulmonary Problems** ☐☐
1 Effusion
2 Chylothorax
3 Aspiration
4 Haemothorax
5 Bronchopneumonia
6 ARDS
7 Pneumothorax

P43 (a) **Bleeding** ☐
1 Chest
2 Adbomen
3 Both

(b) **Further operation required**
Yes ☐ No ☐

P44 (a) **Anastomosis** ☐
1 Leak
2 Haemorrhage
3 Both

(b) **If leak then where** ☐
1 Pancreatic (P)
2 Biliary (B)
3 GI (G)
4 P & B
5 P & G
6 B & G
7 P & B & G
8 Not Specified

P45 **Sepsis** ☐
1 Wound
2 Central Line
3 Abcess requiring drainage
4 Intra abdominal

P46 **Organ Failure** ☐☐
1 CVA
2 MI
3 DVT
4 PE
5 Hoarseness due to RI N damage

P47 **Other** ☐☐
1 Pulmonary
2 Renal
3 DIC
4 Cardiac
5 Hepatic

## PATHOLOGY

P47 **Histology**

1 Adenocarcinoma
2 Not Stated / Carcinoma

P48 **Differentiation**

1 Well 4 – Undifferentiated
2 Moderate 5 Not Stated
3 Poor

**Lymph nodes**

P49 (a) **No.examined**

(b) **No. Positive**

(c) **+ve nodes no. unspecified** Yes ☐ No ☐

**Staging**

P50 (a) **T**

1 TX 5 T1b
2 T0 6 T2
3 T1 7 T3
4 T1a 8 invasive

(b) **N** NX ☐ N0 ☐ N1 ☐

(c) **M** MX ☐ M0 ☐ M1 ☐

## DEATH

P51 Date of Death

D D M M Y Y

P52 **Immediate Cause of Death**

1 Directly due to cancer
2 Directly due to operative complications
3 Directl y due to investigative complications
4 Directly due to stent insertion
5 Not related to either operation or tumour (tumour present)
6 Not related to either operation or tumour (tumour absent)
7 Indirectly related to operation (CVA, MI, Gross respiratory probs

# OESOPHAGEAL CANCER

O1 (a) **Location** Yes ☐ No ☐ (b) **Length** ☐☐ cm (c) **Distance from incisor teeth** ☐☐ cm

O2 **Treatment** ☐☐
1 Yes
2 Patient unfit
3 Cancer too advanced
4 Incidental finding at PM
5 Died prior to treatment
6 Patient refused consent

O3 **Reference Number** ☐☐☐☐

O4 (a) **Dilatation** ☐
1 No
2 Dilatation only
3 Dilatation & Laser
4 Dilatation & Alcohol
(b) **Consultant** ☐☐☐ (c) **Hospital Code** ☐☐

O5 (a) **Stent** ☐
1 No
2 Conventional (Plastic)
3 Covered (Metal)
4 Uncovered (Metal)
5 Pulsion
6 Not Specified
7 Unsucessful attempt
(b) **Consultant** ☐☐☐ (c) **Hospital Code** ☐☐

O6 (a) **Inserted By** ☐
1 Surgeon
2 Physician
3 Radiologist
4 Endoscopist
5 Not Specified
(b) **Complications** ☐☐
1 Bleeding
2 Pneumonia
3 Duodenal Perforation
4 Infection
5 Pancreatitis

O7 (a) **Laser** Yes ☐ No ☐ (b) **Consultant** ☐☐☐ (c) **Hospital Code** ☐☐

O8 (a) **Radiotherapy** ☐
1 No
2 Pre Op
3 Post Op
4 Pre & Post Op
(b) **Trial** Yes ☐ No ☐ (c) **Consultant** ☐☐☐ (d) **Hospital Code** ☐☐

(e) **How** ☐
1 External
2 Brachy Intraluminal
3 Not Specified
(f) **Dose** ☐☐☐☐ cGy (g) **Fraction** ☐☐☐☐

O9 (a) **Chemotherapy** ☐
1 No
2 Pre Op
3 Post Op
4 Pre & Post Op
(b) **Trial** Yes ☐ No ☐ (c) **Consultant** ☐☐☐ (d) **Hospital Code** ☐☐

O10 **Start Date** D D M M Y Y ☐☐☐☐☐☐

O11 **Finish Date** D D M M Y Y ☐☐☐☐☐☐

O12 **Cycles** ☐☐☐

**Chemotherapy Agents**

O13 (a) ☐☐ (b) mg/m2 ☐☐☐ (c) Total Dose ☐☐☐☐

O14 (a) ☐☐ (b) mg/m2 ☐☐☐ (c) Total Dose ☐☐☐☐

1 5 - Fluorouracil
2 Cisplatin
3 Carboplatin
4 Epirubicin
5 Doxorubicin

O15 (a) ☐☐ (b) mg/m2 ☐☐☐ (c) Total Dose ☐☐☐☐

O16 (a) ☐☐ (b) mg/m2 ☐☐☐ (c) Total Dose ☐☐☐☐

# SURGICAL TREATMENT

O17 **Grade of Surgeon** ☐
1 Consultant
2 – Clinical Assistant
3 – Staff Grade
4 Specialist Reg (HST)
5 SHO (BST)
6 Other

O18 **Grade of anaesthestist** ☐
1 Consultant
2 Associate Specialist
3 Staff Grade
4 Specialist Reg (HST)
5 SHO (BST)
6 Other

O19 **Supervision**
Yes ☐
No ☐
NK ☐

O20 **Hospital Code** ☐☐

O20 **Surgery** Yes ☐ No ☐

O21 **Type of surgery** ☐ 1 = Absolute 2 = Relative 3 = Non Curative 4 = Not Specified

O22 **Procedure** ☐☐ 1 = THO 2 = Ivor Lewis 3 = L Thoraco abdominal 4 = Mc Keown 3 Stage 5 = By Pass 6 = Laparotomy only 7 = Thoractomy only

## Incisions

O23 (a) **Neck** ☐ (b) **Chest** ☐ 1 = Left 2 = Right (c) **Abdomen** ☐ 1 = Midline 2 = Rooftop 3 = Other

## Reconstruction

(a) **Colon** ☐ 1 = Left 2 – Right 3 – Transverse 4 Unspecified

O24 (b) **Jejunum** ☐ 1 = Microvascular 2 = Pouch 3 = Roux en Y 4 = Unspecified

(c) **Stomach** Yes ☐ No ☐

O25 **Route** ☐ 1 = Oesophageal Bed 2 = Retrosternal 3 = Subcutaneous 4 = Unspecified

## Anastomosis

O26 (a) **Type** Sutured ☐ Stapled ☐

(b) **Stitch** S ☐ D ☐ I ☐ C ☐

O27 **Material** ☐☐ 1 = C 2 = V 3 = D 4 = M 5 = PDS 6 = S 7 = P 8 = N 9 = Other

O28 **Site of tumour** Upper 1/3 ☐ Lower 1/3 ☐ Middle 1/3 ☐ Junctional ☐

O29 **Length of Procedure** H H M M ☐☐☐☐

O30 **Other Organs Removed** ☐☐ 1 = Pericardium 2 = Stomach 3 = Spleen 4 = Crura 5 = Omentum 6 = Pancreas 7 = Liver 8 = Lung 9 = Gallbladder 10 = Colon

O31 (a) **Intraoperative Complications** ☐☐ 0 = None 1 = Tracheal or bronchial injury 2 = Bleeding 3 = Cardiac event

(b) **Did this lead to a change of procedure** Yes ☐ No ☐

## POST OPERATIVE CARE

O32 **Time in ITU** H H M M ☐☐☐☐

O33 **Time in HDU** H H M M ☐☐☐☐

O34 **Ventilation** Yes ☐ No ☐ NK ☐

O35 **Time on ventilator** H H M M ☐☐:☐☐

**Pain Relief**

O36 (a) ☐ 1 = Epidural 2 = Intercostal Block 3 = Paraverterbral Block 4 = Opiates (Continous)

(b) ☐ 5 – Opiates (IM) 6 = NSAIDS 7 = PCA

(c) ☐

**DVT Prophylaxis**

O37 (a) ☐ 0 = None 1 = MMW Heparin / Clexane 2 = TEDS

(b) ☐ 3 = Minihep 4 = Mechanical 5 = Not Stated

(c) ☐

**Prophylactic Antibiotics**

O38 Yes ☐ No ☐ Not Stated ☐

## POST OPERATIVE COMPLICATIONS

O39 **Pulmonary Problems** ☐☐ 1 = Effusion 2 = Chylothorax 3 =Aspiration 4 = Haemothorax 5 = Bronchopneumonia 6 = ARDS 7 = Pneumothorax

O40 (a) **Bleeding** ☐ 1 = Chest 2 = Abdomen 3 = Both

(b) **Further operation required** Yes ☐ No ☐

041 (a) **Anastomosis** ☐ 1 = Leak 2 = Haemorrhage 3 = Both

(b) **If leak where** ☐ 1 – Neck 2 = Chest 3 = Adbomen 4 = Neck and Abdomen 5 = Neck and Chest 6 = Chest and Adbomen

O42 **Sepsis** ☐ 1 = Wound 2 = Central Line 3 = Abcess requiring drainage 4 = Intra Abdominal

O43 **Organ Failure** ☐☐ 1 = CVA 2 = MI 3 = DVT 4 = PE 5 = Hoarseness due to RLN

O44 **Other** ☐☐ 1 = Pulmonary 2 = Renal 3 = DIC 4 = Cardiac 5 = Hepatic

## PATHOLOGY

O45 **Histology**
1 Adenocarcinoma
2 Small Cell
3 Squamous
4 – Not Stated Carcinoma

O46 **Gross Appearance**
1 Ulcerative
2 Protuberant
3 Flat
4 Other
5 Not Stated

O47 **Differentiation**
1 Well
2 Moderate
3 Poor
4 Undifferentiated
5 Not Stated

**Lymph nodes**

O48 (a) **No.examined**

(b) **No. Positive**

(c) **+ve nodes, no. unspecified**
Yes ☐ No ☐

**Staging**

O49 (a) **T**
1 TX 5 – T2
2 T0 6 T3
3 Tis 7 T4
4 T1 8 invasive

**N** (b) NX ☐ N0 ☐ N1 ☐

**M** (c) MX ☐ M0 ☐ M1 ☐

## DEATH

050 Date of Death

| D | D | M | M | Y | Y |
|---|---|---|---|---|---|
| | | | | | |

O51 **Immediate Cause of Death**

1 Directly due to cancer
2 Directly due to operative complications
3 Directl y due to investigative complications
4 Directly due to stent insertion
5 Not related to either operation or tumour (tumour present)
6 Not related to either operation or tumour (tumour absent)
7 Indirectly related to operation (CVA, MI, Gross respiratory probs

# GASTRIC CANCER

S1 (a) **Location**

1 Cardia (C) 2 Body (B) 3 Fundus (F) 4 Antrum (A) 5 C/F 6 C/B 7 B/F 8 B/A 9 C/F/B 10 F/B/A 11 C/F/B/A 12 Not Specified

(b) **Diameter**

S2 **Treatment**

1 Yes 2 Patient unfit 3 Cancer too advanced 4 Incidental finding at PM 5 Died prior to treatment 6 Patient refused consent

S3 **Reference Number**

S4 (a) **Laser** Yes ☐ No ☐

(b) **Consultant**

(c) **Hospital Code**

S5 (a) **Radiotherapy**

1 No 2 Pre Op 3 Post Op 4 Pre & Post Op

(b) **Trial** Yes ☐ No ☐

(c) **Consultant**

(d) **Hospital Code**

(e) **How**

1 External 2 Brachy Intraluminal 3 Not Specified

(f) **Dose** cGy

(g) **Fraction**

S6 (a) **Chemotherapy**

1 No 2 Pre Op 3 Post Op 4 Pre & Post Op

(b) **Trial** Yes ☐ No ☐

(c) **Consultant**

(d) **Hospital Code**

S7 **Start Date** D D M M Y Y

S8 **Finish Date** D D M M Y Y

S9 **Cycles**

**Chemotherapy Agents**

S10 (a) (b) mg/m2 (c) Total Dose S11 (a) (b) mg/m2 (c) Total Dose

S12 (a) (b) mg/m2 (c) Total Dose S13 (a) (b) mg/m2 (c) Total Dose

1 = 5 - Fluorouracil
2 = Cisplatin
3 = Carboplatin
4 = Epirubicin
5 = Doxorubicin

# SURGICAL TREATMENT

S14 **Grade of Surgeon**

1 Consultant 2 Clinical Assistant 3 Staff Grade 4 Specialist Reg (HST) 5 SHO (BST) 6 Other

S15 **Grade of anaesthestist**

1 Consultant 2 Associate Specialist 3 Staff Grade 4 Specialist Reg (HST) 5 SHO (BST) 6 Other

S16 **Supervision** Yes ☐ No ☐ NK ☐

S17 **Hospital Code**

S18 **Surgery** Yes ☐ No ☐

S19 **Type of Surgery** 1 Absolute 2 Relative 3 Curative 4 Not Specified

S20 **Procedure** 1 Sub Total Gastrectom 2 Total Gastrectomy 3 Distal Gastrectomy 4 Proximal Gastrectomy 5 = Laparotomy (open & close) 6 – Bypass 7 Local excision

S21 **Lymph Nodes** 1 D1 2 D2 3 D3

S22 **Incisions** 1 Midline 2 Rooftop 3 Other

S23 **Reconstruction** 1 =Billroth 1 2 Billroth 2 Polya 3 = Roux en Y 4 = Pouch

**Anastomosis**

S24 (a) Sutured ☐ Stapled ☐

(b) **Stitch** S ☐ D ☐ I ☐ C ☐

S25 **Material** 1 C 2 V 3 D 4 M 5 – PDS 6 – S 7 = P 8 = N 9 = Other

S25 **Site of Tumour at operation**

Cardia ☐ Antrum ☐

Body ☐ Fundus ☐

S26 **Length of Procedure** H H M M

S27 **Other Organs removed**

1 = Pericardium 6 = Oesophagus
2 = Pancreas 7 = Liver
3= Spleen 8 = Lung
4 = Crura 9 = Gallbladder
5 = Omentum 10 = Colon

S28 (a) **Intra Operative Complications**

1 None
2 Tracheal or bronchial injury
3 Bleeding
4 Cardiac event

(b) **Did this lead to a change of procedure**

Yes ☐ No ☐

## POST OPERATIVE CARE

S29 **Time in ITU** H H M M

S30 **Time in HDU** H H M M

S31 **Ventilation**

Yes ☐ No ☐ NK ☐

S32 **Time on ventilator** H H : M M

**Pain Relief**

S33 (a) ☐ (b) ☐ (c) ☐

1 Epidural
2 Intercostal Block
3 Paraverterbral Block
4 Opiates (Continuous)
5 Opiates (IM)
6 NSAIDS
7 PCA

**DVT Prophylaxis**

S34 (a) ☐ (b) ☐ (c) ☐

0 None
1 LMW Heparin / Clexane
2 TEDS
3 = Minihep
4 = Mechanical
5 Not Stated

S35 **Prophylactic Antibiotics**

Yes ☐ Not Stated ☐ No ☐

## POST OPERATIVE COMPLICATIONS

36 **Pulmonary Problems** ☐

1 Effusion
2 Chylothorax
3 Aspiration
4 Haemorthorax
5 Bronchopneumonia
6 ARDS
7 Pneuothorax

S37 (a) **Bleeding** ☐

1 = Chest
2 = Abdomen
3 = Both

(b) **Further operation required**

Yes ☐ No ☐

S38 (a) **Anastomosis** ☐

1 Leak
2 Haemorrhage
3 Both

(b) **If leak then where** ☐

1 Pancreatic (P)
2 Biliary (B)
3 GI (G)
4 P & B
5 P & G
6 B & G
7 B & P & G
8 Not Specified

S39 **Sepsis** ☐

1 = Wound
2 = Central Line
3 = Abcess requiring drainage
4 Intra abdominal

S40 **Organ Failure** ☐

1 = CVA
2 = MI
3 = DVT
4 = PE
5 = Hoarsness due to RLN

S41 **Other** ☐

1 = Pulmonary
2 = Renal
3 = DIC
4 = Cardiac
5 = Hepatic

## PATHOLOGY

S42 **Histology** ☐

1 Adenocarcinoma
2 Lymphomal
3 Stromal
4 Not Stated Carcinoma

S43 **Gross Appearance** ☐

1 = Ulcerative
2 = Protuberant
3 = Flat
4 = Not Stated
5 Other

S44 **Differentiation** ☐

1 = Well
2 = Moderate
3 = Poor
4 = Undifferentiated
5 = Not Stated

**Lymph nodes**

S45 (a) **No.examined** ☐

(b) **No. Positive** ☐

(c) **+ve nodes, no. unspecified**

Yes ☐ No ☐

**Staging**

S46 (a) **T** ☐

1 TX
2 T0
3 Tis
4 T1
5 T2
6 T3
7 T4
8 invasive

(b) **N** NX ☐ N1 ☐ N0 ☐ N2 ☐

(c) **M** MX ☐ M0 ☐ M1 ☐

## DEATH

S47 **Date of Death** D D M M Y Y

S48 **Immediate Cause of Death** ☐

1 = Directly due to cancer
2 = Directly due to operative complications
3 = Directl y due to investigative complications
4 = Directly due to stent insertion
5 = Not related to either operation or tumour (tumour present)
6 = Not related to either operation or tumour (tumour absent)
7 = Indirectly related to operation (CVA, MI, Gross respiratory probs)