An investigation into perioperative outcome following gastrointestinal resection in England

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Abstract

This thesis represents research from Hospital Episode Statistics data and provides an insight into gastrointestinal resectional surgery in England. It examines national outcomes following major colorectal resection, oesophagectomy and gastrectomy. Having established these outcomes, I ventured to investigate the commonly used mortality measures in the literature. I also studied the timing and causes of deaths following colorectal resection in English NHS Trust hospital. I was able to demonstrate that a significant number of adverse outcomes occur beyond the initial hospital stay. I evaluated the role of two key factors - minimally invasive surgery and surgeon volume in trying to mitigate these adverse outcomes.

I found that national outcome following elective or planned colorectal resection are comparable with other published cancer registry reports in England. For upper gastrointestinal resection for cancer, however, outcome are significantly worse than those from Far East, but superior to studies from the States. I derived 'medical morbidity' by studying secondary codes for medical complications. Surgical complications were quantified by using surrogates such as unplanned re-operation and re-intervention following the initial procedure.

I undertook a review of the literature for published outcomes following planned colorectal resection in the elderly. This demonstrated heterogeneity in studies with regards to sample size and type of study. The most commonly used measure of post-operative risk was in-hospital or 30-day mortality. In the elderly population, we demonstrated high mortality up to one year following emergency colorectal resection. To understand this excess mortality that is not taken into account by short term metrics, we studied the causes of deaths in these patients. Significant deaths occur in the young and elderly due to cardiac causes, up to one

year following major colorectal resection. This calls for further research to define a new intermediate term metric that accurately quantifies the mortality risk.

The uptake of minimally invasive gastrointestinal resection in England has been promising. During the study period there has been a steady rise in number of resections undertaken laparoscopically. In colorectal surgery, laparoscopic resection has been associated with shorter length of stay, reduced morbidity and mortality. Outcome following minimally invasive oesophagectomy and gastrectomy have shown this technique to be safe and potentially beneficial in reducing pulmonary complications and length of stay. However further research is needed into this. Oesophagectomy, gastrectomy and pancreatectomy for cancer have all demonstrated a positive volume-outcome relationship. With increasing surgeon caseload, risk of 30-day mortality is lower. These structure and process measures may be utilised by policy makers to improve outcome following gastrointestinal resection in England.

This thesis is dedicated to my grandmother

Mrs Rajarajeshwari Mamidanna

who is the inspiration behind me taking up Surgery as a career.

It was her dream to see the title 'Dr.' before my name.

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I do not have enough words to thank my family. My wife Prapoorna has been a constant source of energy and has made numerous sacrifices to see my thesis through. She has not only joined me in my moments of ecstasy whenever a research paper got published, but has also tolerated my moments of insanity. My darling daughter Saanvika has always brightened up my day with her smile, whether I came home after a tiring night shift or had an unproductive session of staring at the computer screen. I would also like to extend my gratitude towards my father, mother, brother and his family for providing me with the drive to achieve more with their words of encouragement and constantly keeping me focussed on my aspirations and goals. Without my family I would not have been able to complete this thesis. This one is for you all!

Declaration

I hereby declare that the work presented in this thesis is original and I confirm that I have performed this research myself. The findings in the research are from studies undertaken by me, except where it is referenced or carried out in collaboration with others who are appropriately credited. This thesis is a record of work which has not been previously submitted for a higher degree.

Ravikrishna Mamidanna *MBBS, MRCS* Dated: 5th September 2014

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List of Abbreviations

ACPGBI	Association of Coloproctology of Great Britain and Ireland
ACS	American College of Surgeons
AIHD	Acute Ischaemic Heart Disease
ARDS	Adult Respiratory Distress Syndrome
BMI	Body Mass Index
CABG	Coronary Artery Bypass Graft
CCF	Congestive Cardiac Failure
CIHD	Chronic Ischaemic Heart Disease
COPD	Chronic Obstructive Pulmonary Disease
CQC	Care Quality Commission
CUSUM	Cumulative Sum
DVT	Deep Vein Thrombosis
ERAS	Enhanced Recovery After Surgery
ERP	Enhanced Recovery Protocols
FCE	Finished Consultant Episode
HES	Hospital Episode Statistics
HQIP	Healthcare Quality Improvement Partnership
IBD	Inflammatory Bowel Disease
ICD	International Classification of Diseases
IQR	Inter-Quartile Range
ISD	Information Services Division
LADG	Laparoscopic (or laparoscopy assisted) Gastrectomy
LCS	Laparoscopic Colorectal Surgery

LG	Laparoscopic (or laparoscopy assisted) Gastrectomy
LOS	Length Of Stay
M&M	Mortality and Morbidity
MAS	Minimal Access Surgery
MEDPAR	Medicare Provider Analysis and Review
MIO	Minimally Invasive Oesophagectomy
NBOCAP	National Bowel Cancer Audit Programme
NBSR	National Bariatric Surgery Registry
NCEPOD	National Confidential Enquiry into Patient Outcome and Death
NEC	Not Elsewhere Classified
NHS	National Health Services
NOGCA	National Oesophago-Gastric Cancer Audit
NSQIP	National Surgical Quality Improvement Program
NTP	National Training Programme
NVASRS	National Veterans Affairs Surgical Risk Study
ODG	Open Distal Gastrectomy
OG	Open Gastrectomy
ONS	Office for National Statistics
OPCS	Office of Population, Censuses and Surveys
OR	Odds Ratio
PACE	Preoperative Assessment of Cancer in the Elderly
PE	Pulmonary Embolism
PEDW	Patient Episode Database for Wales
PIAG	Patient Information Advisory Group
ROC	Receiver Operating Characteristic

SCR	Surgical Clinical Reviewer
SCTS	Society for Cardiothoracic Surgery in Great Britain & Ireland
SHIP	ScottisH Informatics Programme
UCOD	Underlying Cause of Death
UK	United Kingdom
VA	Veterans Affairs
VTE	Venous Thrombo-Embolism
WHO	World Health Organization

Publications and presentations from the thesis

Publications

National outcomes and uptake of laparoscopic gastrectomy for cancer in England. Mamidanna R, Almoudaris AM, Bottle A, Aylin P, Faiz O, Hanna GB. *Surg Endosc. 2013 Apr 24. PMID:23612763*

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Reduced risk of medical morbidity and mortality in patients selected for laparoscopic colorectal resection in England: a population-based study. Mamidanna R, Burns EM, Bottle A, Aylin P, Stonell C, Hanna GB, Faiz O. *Arch Surg. 2012 Mar;147(3):219-27.*

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Journal correspondence

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Variability in length of stay after colorectal surgery: assessment of 182 hospitals in the national surgical quality improvement program. Mamidanna R, Almoudaris AM, Faiz O. Ann Surg. 2010 Nov;252(5):891-2; author reply 892.

Presentations

Title: Reduced mortality and morbidity in patients selected for laparoscopic colorectal resection in England: a population based study

Ravikrishna Mamidanna (Presented), Elaine Burns, Alex Bottle, Paul Aylin, George Hanna, Omar Faiz. 23rd September 2011, ESCP – Copenhagen, Denmark.

Title: Patients selected for laparoscopic colorectal resection are associated with lower mortality and morbidity – an English national study

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Chapter 1: INTRODUCTION

Healthcare providers today are faced with a challenge of constantly improving their services to satisfy the ever increasing demands and expectations of the general public. In the United Kingdom (UK) it is estimated that approximately £130 billion will be spent on healthcare in the year 2014 (Chantrill, 2013). The general population is exposed to a number of articles and reports in the media propagating innovative and improved care. Especially with regards to surgery, the needs of patients are diverse. Outcome reporting is central to establishing safety in surgery. Safe surgery must include acceptable postoperative mortality and complication rates. Provision of high quality care has been gaining increasing focus in the National Health Services (NHS).

Outcome reports provide objective numerical information for the patients to identify a provider that they feel would give them optimum treatment with maximum chances of a good outcome. Independent outcome measures, such as mortality, in most elective surgery fail to discriminate differing standards of safety between surgical providers as they are rarely occurring events and do not reflect significant morbidity that may have occurred throughout the perioperative period. To address the growing concerns of the public and the government regarding quality of healthcare, the Care Quality Commission (CQC), a health watchdog was setup in April 2009 under the Health and Social Care Act (2008). The (CQC) is an independent regulator of health and adult social care in England and has been setup to ensure better care for everyone in hospital, in a care home and at home (Care Quality Commission, 2009). In this context 'NHS Choices' is a website that has been setup to help the general population make choices about their healthcare and lifestyle and access information about various NHS services. This website is owned by the Department of Health and is an important part of their resource toolkit. Using this website performance of service providers can be displayed and patient feedback obtained in order to improve services.

1.1 Background

Patient safety poses a significant challenge to a modern health service. It is an essential component of high performance in healthcare. Every surgical procedure is inherently prone to complications. Perioperative complications are defined as unpredicted but preventable events that occur during surgery or in the postoperative period (de Cassia Braga Ribeiro and Kowalski, 2003). These adverse events not only raise treatment costs but delay adjuvant treatment, affect quality of life, and can even lead to mortality if not diagnosed and managed appropriately (Rhys Evans, 1989). Some of the variables that are established predictors of outcome following surgery include patient factors such as patient age and co-morbidity (Bowles et al., 2008, Hall and Hall, 1996). In addition to this, structural factors, such as achieving adequate annual operative caseload and adherence to evidence-based processes have also been demonstrated to affect outcome following major elective gastrointestinal resection (Birkmeyer et al., 2003, Ghaferi et al., 2009).

In the 1960s there was a large drive to improve quality in healthcare. Particularly influential were the concepts of Donabedian which described a three dimensional model for quality – combining structural and process factors to explain outcome (Donabedian, 1966). The concept of 'Clinical Governance' was introduced as a means of continuously improving the quality of patient care in the late 1990s (Scally and Donaldson, 1998). It is a framework that has been set up to constantly improve quality of care, maintain accountability and transparency and safeguard high standards of care, More recently, in 2008 the parliamentary under secretary of state Prof the Lord Darzi of Denham submitted a report to the government entitled *'High quality care for all: NHS Next Stage Review'* (Darzi, 2008). This was a review of the NHS in England which examined services across various 'pathways of care' engaging with patients, staff, stakeholders and the public. The report envisioned a healthcare system in the UK driven to raise standards of care. A proactive focus on public health, empowerment by patient involvement in healthcare decision making and finally improving patient experience were some of the strategies highlighted in this report. Similarly, the Chief Medical Officer, Sir Liam Donaldson emphasised the need for regular reporting of outcomes and analysis of adverse events in his report titled *'The challenge of quality and patient safety'* (Donaldson, 2008). Both the above reports highlighted the need for an NHS framework that monitors healthcare and ensures safe and effective care to all. This framework is essential not only to promote scientific and technical developments, but also to reassure the stakeholders that there are processes in place for protection against suboptimal practice.

1.2 Perioperative outcome

Outcome research revolves around identification of shortfalls in practice and development of strategies to improve care. Ultimately the idea is to prevent disease or mitigate its impact. Such research is increasingly being used not only by clinicians, but by allied groups such as policy makers, managers, politicians, insurance companies and legislative bodies. A wide variety of outcomes are measured ranging from ones proximal to interventions such as acute clinical events like mortality to ones distal from the patient experience measuring the performance of a system. Research targeted at preoperative outcome focuses on issues such as safety and effectiveness of an intervention, treatment or diagnostic test. The primary aim of such an undertaking is to measure tangible events experienced by the patient such as mortality and morbidity.

'*First do no harm*' – This was the maxim laid down by Hippocrates. The National Confidential Enquiry into Perioperative Deaths (NCEPOD) was established in 1988 to examine the quality of the delivery of care for surgical and anaesthetic patients (Campling EA, 1989). Since its inception, the NCEPOD has published various reports looking into different aspects of hospital care and is currently examining remediable factors in the perioperative care of patients aged 16 or over, who undergo inpatient surgery (both elective and emergency) (NCEPOD). This body persuades individuals and organisations to change how they deliver healthcare in an attempt to bridge the gap between 'current practice' and 'good practice'. Some of the problems traditionally associated with identifying or quantifying perioperative outcome have been variation in quality of data sources, lack of power in small reported series to identify variations in outcome, underrepresentation of certain groups such as the elderly, un-coordinated research in different healthcare systems and elements of bias. However perioperative outcome reporting is gaining worldwide attention and standardised outcome reporting systems will enable global comparisons between healthcare systems.

1.3 Outcome Reporting

Systems that are put in place to hold healthcare providers accountable for their services not only provide the public with a sense of security but also incentivise development of quality improvement programmes. If adverse event patterns can be identified, then action can be taken preemptively to prevent the repetition of similar events. Ernest Codman, a pioneering surgeon from Boston was the first to follow his patients' perioperative journey and kept 'End Results Cards' with demographic and outcome data (Hicks and Makary, 2013). Even in the early part of the twentieth century, he believed in maintaining logs of patient outcomes which could help in healthcare decision making regarding. He published a book *A Study in Hospital Efficiency* which included the outcomes from his own hospital. Although he was criticised for propagating public reporting of outcomes, in 1996 his work was recognised by the Joint Commission on Accreditation of Healthcare Organizations.

"We believe it is the duty of every hospital to establish a follow-up system, so that as far as possible the result of every case will be available at all times for investigation by members of the staff, the trustees, or administration, or by other authorized investigators or statisticians." - Ernest Codman.

Mandatory reporting can identify deviations from expected outcome, errors in care or near misses. The primary purpose of such reporting systems is to hold the healthcare providers accountable for any lapses in quality or safety of health provision. This has been explicitly highlighted by the Institute of Medicine in the report titled *'To Err is Human: Building a Safer Health System'* (Kohn et al., 2000). The report describes a threefold benefit of outcome reporting: a) to provide the public with a sense of security b) to incentivise the improvement in patient safety and c) to promote investment in patient safety initiatives. Along with mandatory reporting this report strongly recommended expanding voluntary reporting of adverse events and medical errors in order to improve outcomes. They suggested that voluntary reporting needs to be encouraged in order to identify infrequent lapses in healthcare.

Public reporting

Empowering the patients to choose the best available provider for their healthcare needs is an important initiative in the NHS. By publishing freely available and comprehensive outcome reports surgical teams are made accountable for improving the quality of perioperative care. In addition this will act as a motivation for providers to improve. The provision of such information to the consumers in a healthcare system i.e. patients could be justified on moral as well as legal grounds. It is well known that better informed and educated patients seek more preventative care and favour behaviours that improve health (Kenkel, 1991a). Hibbard extensively studied and reported on the influence of quality data in decision making by the consumers. Their group showed that presenting quality data in a more evaluable format and by making reports easier to use it were possible to engage the public in using these data for choosing an appropriate provider (Hibbard et al., 2001, Hibbard et al., 2002). In the United Kingdom as well as the United States of America more and more healthcare provider performance data are entering the public domain. Both private and public sectors are engaging in the contributing to these data. In 1999, Davies reported that most commonly cited reason for public reporting in the USA was for patients to be able to choose high performing providers, while in the UK it was mainly for accountability to the public (Davies and Marshall, 1999).

Cardiac surgery was one of the first specialist fields to undertake public reporting and also demonstrated an improvement in outcome following open reporting. The New York State Department of Health has been collecting data regarding risk factors, mortality, and complications of Coronary Artery Bypass Graft (*CABG)* surgery since 1989. One of the seminal papers by Hannan *et al* in 1994 analysed these data and demonstrated a 41% decrease in mortality after cardiac surgery following the introduction of such a quality improvement programme (Hannan et al., 1994). The Society for Cardiothoracic Surgery in Great Britain & Ireland (SCTS) pioneered data collection in the UK (Hickey et al., 2014). They have a register of all cardiothoracic operations since 1977 and are responsible for public release of outcomes. The SCTS have demonstrated a 25% reduction in mortality since 2003 following cardiac surgery.

This suggests that making performance information public stimulates quality improvement in the areas where performance is reported to be low. There is no doubt that patients' expectation from healthcare systems and their priorities are different to those of providers. Consumers may lack interest in the use of performance data due to difficulty in understanding the information, lack of trust in the data, or problems with access to the data. In the Sates, the Pennsylvania *Consumer Guide to Coronary Artery Bypass Graft [CABG] Surgery* provides mortality ratings of all cardiac surgeons and hospitals in the state. In 1998 a study was undertaken into the use of this report by Schneider and group who surveyed patients undergoing a CABG surgery (Schneider and Epstein, 1998). They found that only 12% of the patients were aware of the report and only 1% knew the correct mortality rating for their provider. Interestingly, although very few patients had used the *Consumer Guide*, a much larger number expressed an interest in seeing a copy when it was described to them.

One criticism of public reporting is that such an initiative may deter surgeons from undertaking operations on high-risk or co-morbid patients. This has paved way for risk-adjusted outcome reporting. However, the variable, and sometimes highly questionable, nature of the validity, reliability, and level of risk-adjustment of the published data raise concerns about the meaningfulness of the information that is publicly disclosed. This is certainly an important factor in acceptability and use of such data by physicians themselves.

Outcome reporting at local/institutional level

Morbidity and Mortality (M&M) meetings have become an integral part of audit/clinical governance. These weekly/monthly meetings have become a integral part of surgical education both in the UK and USA (Hamby et al., 2000). In 1988 Campbell described the various considerations in setting up M&M meetings and reiterated the importance of such an undertaking in training young surgeons (Campbell, 1988). There is an in-depth discussion of patients who died or suffered an adverse event. Rather than a blame game, such meetings encourage accountability and reflective practice. Various studies in the literature have showed that M&M meetings have been effective as an educational tool as well as effective in reducing errors (Gore, 2006, Harbison and Regehr, 1999, Murayama et al., 2002).

Outcome research encompasses a wide spectrum of studies: including the traditional clinical research (i.e. prospective randomised clinical trials, cohort studies, case-control studies, case-series) as well as health economics and health utility research. Administrative data have been shown to be useful for studying variation between surgical procedures, volume-outcome analyses, access to healthcare and trends analyses. Guller very succinctly described the role of prospective clinical trials and retrospective analyses in outcomes research and demonstrated that they have their respective strengths and limitations, but both deserve a place in surgical research (Guller, 2006). There has also been a recommendation for an electronic physician-reported event tracking system as part of a larger quality improvement programme (Bilimoria et al., 2009).

1.4 Data sources

The term 'data' refers to qualitative or quantitative attributes of a variable or set of variables and an organised collection of data for one or more uses is termed as a 'database'. Databases are increasingly used in healthcare research and for generating heath statistics. They are seen as a cost-effective way of storing vital data in a machine-readable form. Various high impact publications and reports have generated important results from analyses of databases (Stewart et al., 2004, Dimick et al., 2010, Finks et al., 2011, Murphy et al., 2004). Prospective case series and single centre studies have been criticised due the small sample size of these studies and their inherent predisposition to reporting and selection bias (Wallace, 2010). The advantage of using databases is the large sample size and the ability to apply the results to the general population. Broadly speaking databases can be classified into Clinical Registries and Routinely Collected Databases.

1.4.1 Clinical Registries

The primary aim of clinical registries or databases is to acquire and store data for the purpose of audit. These are usually prospectively collected data that include detailed patient demographic and clinical information. As the data are collected specifically for a research interest, there is an ownership on the part of the clinician. Various risk-adjustment strategies can be applied to these data in order to account for variation in surgeon case-mix. The pitfalls however of using such a registry is that submission is usually voluntary. Providers may choose not to submit, or submit only part of their data which can potentially skew the results (Karthikesalingam et al., 2013, Burns et al., 2013). Also, maintenance of such registries is resource intensive and requires specially trained staff. The Healthcare Quality Improvement Partnership (HQIP) was established in April 2008 with a view to promote quality in healthcare and improve health outcome by enabling those who commission, deliver and receive healthcare to measure and improve services (HQIP, 2008). On behalf of the Department of Health, HQIP also offers support in commissioning, compilation and maintenance of clinical registries. Currently a number of registries exist in the UK *[National bowel cancer audit programme (NBOCAP), Ileal Pouch Registry, National Bariatric Registry etc.]* (NBOCAP, NBSR, Ileal Pouch Registry). The HQIP mapped over 500 registries and databases and published the Directory of Clinical Databases and Registers in January 2014 (HQIP Directory, 2014).

National Bowel Cancer Audit Project (NBOCAP)

This audit was commissioned by the Health Quality Improvement Partnership under the clinical leadership and direction of the Association of Coloproctology of Great Britain and Ireland (ACPGBI). It is a comprehensive clinical dataset that is used to measure the process of care and clinical outcomes for patients treated for colorectal cancer, enabling comparisons between hospitals and bringing about improvements where necessary. Participating trusts submit their data via an online system or secure file transfer. Tekkis *et al*, previously demonstrated statistical models to derive predicted mortality from the ACPGBI data (Tekkis et al., 2003). Since then the dataset has been used in various studies to report outcomes and demonstrate variation. Tan and colleagues investigated the post-operative risk in the elderly group of patients undergoing surgery for colorectal cancer from the data submitted to the NBOCAP database (Tan et al., 2007). They studied demographics of patients undergoing colorectal cancer surgery and stratified outcomes based on age and gender. The same database has also been used to demonstrate variation in outcomes based on social deprivation (Tilney et al., 2009). Two important studies by Garout *et al,* and Almoudaris *et al,* compared the NBOCAP database with the national administrative Hospital Episode Statistics (HES) database (Garout et al., 2008, Almoudaris et al., 2011a). Garout and co-workers compared case volume and mortality for colorectal surgery and found that at a national level outcomes from NBOCAP and HES databases were comparable. However, when the data sets were compared at individual trust level, significant inconsistencies were observed. Interestingly, the study by Almoudaris and colleagues found a higher mortality rate in trusts that were not submitting data to the voluntary NBOCAP registry. Out of 152 trusts in England between 1st August 2007 and 31st July 2008, 15 trusts had not submitted any data and 5 had submitted less than 10% of their caseload. The 2013 NBOCAP Report has shown an increase in the rate of submission to the audit over the last few years, with 86% case ascertainment (cases reported to the audit versus those identified on HES) and 79% data completeness for patients undergoing major surgery. A qualitative study was undertaken by Cornish and co-workers to seek the surgeons' view of the National Bowel Cancer Audit (Cornish et al., 2011). From an e-survey results they found that the main reasons for non-submission of data were lack of technical support (23.6%), lack of funding (19.6%) and lack of dedicated audit time (18.9%). Overall however members of the ACPGBI felt that participation in this audit would improve the quality of care and surgical outcomes from treatment of colorectal cancer.

1.4.2 Routinely Collected Databases

Routinely collected data are primarily used for administrative purposes and policy making. These data represent the national population and are mandatory for providers to submit to. In addition to patient demographics some clinical parameters are collected based on which tangible outcomes can be derived. The results from such analyses can be safely applied to the general population. Although selection bias cannot be eliminated, these data are almost free from reporting bias due to the non-voluntary submission. Such datasets are currently widely being used on national and international levels for clinico-epidemiological research. The *Hospital Episode Statistics (HES)* is one such database which houses information on all patient episodes for NHS Trusts in England (NHS Information centre). HES is a data warehouse containing details of all admissions, outpatient appointments and A&E attendances at NHS hospitals in England. HES came into being in 1987 and since 2003 all out-patient records have been included. This database enables various national bodies and regulators, commissioning organisations and research institutions to monitor trends and patterns in NHS hospitals, assess effective delivery of care and support local planning. To some extent the published reports which are available online stand to inform patient choice. Each record in the database relates to one finished consultant episode, describing the time an individual spends under the care of one NHS consultant. The information held includes age, sex, area of usual residence, diagnosis or reason for admission to hospital, and procedure undertaken. This database is described in detail in Chapter 2.

Similar databases for Scotland and Wales include *Scottish Morbidity Database* and *Patient Episode Database for Wales (PEDW)* respectively (ISD Scotland, NHS Wales Informatics Service). The Information Services Division (ISD) is a part of ScottisH Informatics Programme (SHIP) and collects a wide range of health related administrative data in Scotland. The Scottish Morbidity Database is made up of various datasets e.g. SMR01 (acute hospital admissions), SMR04 (psychiatric admissions), SMR06 (cancer registrations) which are linked together. This database covers all patients in Scotland with a non-obstetric admission. This dataset currently holds data from 1980 onwards. The database has been extensively used for outcome reporting and McSorley *et al* recently published the rate of unplanned reoperation following surgery for colorectal cancer using the SMR (McSorley et al., 2013). Variations in outcome over a decade as well as seasonal variations for medical conditions such as asthma and atrial fibrillation have also been studied from this database

(Murphy et al., 2004, Roberts et al., 2013). The Patient Episode Database for Wales (PEDW) came into being in April 1991 and contains records of all episodes of inpatient and day case activity in NHS Wales hospitals. This includes planned and emergency admissions, minor and major operations, and hospital stays for giving birth. In addition the data warehouse also stores information on Welsh residents treated in English NHS Trusts. The data are used by the public health services for information regarding health service utilisation and also the incidence and prevalence of disease.

1.4.3 Databases in the United States of America

Various administrative datasets are maintained in the US, but there is no national database like the HES. In the 1980s, the US Congress felt that post-operative mortality rates in the Veterans Affairs (VA) hospitals were higher than the national norm. This led to the Department of Veterans Affairs to come under the public eye. A law was passed which made it mandatory for the VA to report its surgical outcomes on an annual basis. The idea was to publish risk adjusted outcomes to factor in severity of illness and then compare them to national averages. However there was no actual 'national average' that was available to compare outcomes to. This prompted the VA to establish the National VA Surgical Risk Study (NVASRS) in 44 VA medical centres using their expertise and infrastructure of advanced information systems (Daley et al., 1997, Gibbs et al., 1999). It was recognised that there was a need to build a statistically reliable database of patients' preoperative risk factors and postoperative outcomes in order to create methods for accurate risk adjustment and to account for random events. A dedicated nurse was assigned to collect data in each of the 44 medical centres. Data collected included preoperative, intra-operative and 30-day outcome variables on more than 117,000 major operations. The NVASRS was able to develop risk models for 30-day mortality and morbidity in nine surgical specialties. These risk-adjusted outcomes produced by the models matched the quality of systems and processes in the 44 hospitals thus allowing, for the first time, a comparative measurement of the quality of surgical care.

Following the success of this undertaking, in 1994, the National Surgical Quality Improvement Program (NSQIP) was established (Khuri et al., 1998). This would be an ongoing programme across all VA medical centres. In 2001 the American College of Surgeons launched a pilot programme to showcase the benefits of the NSQIP in improving outcomes and by 2004 ACS NSQIP became the first nationally validated, risk-adjusted, outcomes based programme to measure and improve surgical quality. The VA hospitals saw a 47 percent drop in postoperative mortality and a 43 percent drop in morbidity rates from 1991 to 2006. Under the NSQIP a trained Surgical Clinical Reviewer (SCR) is assigned the job of collecting preoperative data and further data through to 30 days postoperatively on randomly assigned patients. The number and types of variables collected differ from hospital to hospital, depending on the hospital's size, patient population and quality improvement focus. The American College of Surgeons provides SCR training, ongoing education opportunities and auditing to ensure data reliability. Data are entered online securely and can be accessed 24 hours a day. A Surgeon Champion assigned by each hospital leads and oversees program implementation and quality initiatives. Blinded, risk-adjusted information is shared with all hospitals, allowing them to nationally benchmark their complication rates and surgical outcomes. ACS also provides monthly conference calls, best practice guidelines and many other resources to help hospitals target problem areas and improve surgical outcomes. The ACS NSQIP collects data on 135 variables, including preoperative risk factors, intra-operative variables, and 30-day postoperative mortality and morbidity outcomes for patients undergoing major surgical procedures in both the inpatient and outpatient setting. Currently private sector hospitals have also been enrolled into the NSQIP.

A comprehensive report is prepared twice a year for administrators and surgical services staff to compare their risk-adjusted surgical outcomes to other participating sites. Risk-adjusted 30-day morbidity and mortality outcomes are computed for each participating hospital using hierarchical modeling and are reported as odds ratios (OR). Authorised users can view daily site-specific reports as well as those comparing their metrics to national averages. In this way they can monitor continuous improvement as desired between the more formal report cycles. Hall et al showed that among 118 ACS NSQIP hospitals, the programme helped prevent between 250 to 500 complications per year (Hall et al., 2009). In addition, 82 percent of those hospitals saw improvement in morbidity levels and 66 percent saw improvement in mortality levels.

The MEDPAR (Medicare Provider Analysis and Review) database contains data from claims for services provided to patients under the Medicare scheme. Medicare is a federal initiative which provides cover for hospital, physician and outpatient medical services to 97% of US citizens who are >= 65 years of age. This database allows researchers to track inpatient history and patterns/outcomes of care over time. Data of death information is appended up to three years after data of discharge. The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) is an authoritative source of information on cancer incidence and survival in the United States. This programme includes tumor registries in 18 geographic areas and coverage includes approximately 28% of the U.S. population. The database contains demographic information, primary site, histology, date of diagnosis, stage, treatment with surgery and radiation given in the first course of treatment, vital status, date and cause of death, and survival in months. SEER research data are released every Spring based on the previous November's submission of data. The current release includes data for cases diagnosed between 1973-2010, and is based on the November 2012 data submission from 18 SEER registries, who contribute cases from different years of diagnoses based on when they joined the SEER program. The SEER-Medicare database is a large warehouse of data from the two databases linked together. The linkage of the SEER-Medicare data is a collaborative effort of the NCI, the SEER registries, and the Centers for Medicare and Medicaid Services (CMS). This linkage of these two data sources results in a unique population-based source of information that can be used for an array of epidemiological and health services research (Du et al., 1999, Begg et al., 1998).

1.5 Gastrointestinal Surgery

Gastrointestinal surgery is a sub-specialty of general surgery involving operations on the alimentary tract or the digestive system. Typically gastrointestinal surgeons would have a special interest in a) Upper gastrointestinal surgery: oesophagus, stomach, proximal small bowel b) Hepatico-Pancreatico-Biliary surgery: liver, pancreas, gall bladder c) Lower gastrointestinal surgery: small bowel, colon, rectum, anus. Surgery on the gastrointestinal tract is indicated in a variety of benign and malignant conditions. Major resectional surgery is usually complex and associated with significant morbidity and mortality. It is estimated that there were approximately 1.8m gastrointestinal operations performed in NHS Trust hospitals between 2012-13 (Health & Social Care Information Centre, 2013). Of these over 55,000 were major resections.

Colorectal Resection

Colorectal resection is undertaken mainly for cancer. In 2012, over 1.3m cases of colorectal cancer were reported worldwide and this was responsible for just under 700,000 deaths (Ferlay J, 2012). Approximately 30,000 patients in the UK were diagnosed with colorectal cancer between April 2011 and March 2012 (NBOCAP, 2011). Of these, over 17000 patients underwent a major resection as part of the treatment. Benign conditions necessitating such resection are diverticular disease, inflammatory bowel disease (Crohn's disease and Ulcerative colitis) and polyposis. In the emergency setting the patients usually present with bowel obstruction, perforation or ischaemia. Although mortality is low with planned colorectal resection, such operations are associated with significant morbidity. For patients with colorectal cancer, surgery still remains the mainstay of treatment. Traditionally an open approach or a laparotomy was used to undertake colorectal resections. In 1991 Jacobs et al published their initial experience with laparoscopic colectomy as an alternative technique (Jacobs et al., 1991). After the successful application of laparoscopic surgery to cholecystectomy and appendicectomy, it was proposed as a better technique than traditional open colectomy in terms of post-operative recovery and shorter stay (Falk et al., 1993). Various trials have been undertaken to study differences in long term and short term outcomes between the two techniques. Laparoscopic surgery has been shown to be associated with lower intra-operative complications, quicker recovery and shorter hospital stay (Clinical Outcomes of Surgical Therapy Study Group, 2004). In terms of overall survival, disease-free survival, local or distant recurrence, and long-term quality of life for colon cancer, 5 year follow-up results from the CLASICC Trial did not however show any differences between the two groups (Jayne et al., 2010). Similarly a large meta-analysis of randomised controlled trials looking into long term survival following laparoscopic and open colectomy did not show any significant differences (Theophilus et al., 2013). From a cost effective point of view, initial criticism faced by proponents of laparoscopic colorectal surgery was that it incurred greater costs to the hospitals (Philipson et al., 1997, Bokey et al., 1996). Subsequent analyses however, taking into account the quicker recovery and shorter stay lead to higher postoperative care savings, have shown this technique to be cost effective (Ridgway et al., 2007).

In order to further enhance the benefits of minimally invasive surgery and add a better cosmetic result, Single Incision Laparoscopic Surgery (SILS) was developed initially to undertake appendicectomy and cholecystectomy (Navarra et al., 1997, Inoue et al., 1994). In order to obtain a virtually 'scarless' result, the camera and all instruments are inserted through the same incision via the umbilicus. Critics argue that the basic laparoscopic principles of triangulation are thus lost. This technique is still being evaluated for potential benefits in terms of post-operative pain and recovery. SILS has since been expanded to perform colectomy and Remzi in 2008 described SILS right hemicolectomy in humans (Remzi et al., 2008). Various systematic reviews have compared SILS to conventional multi-port laparoscopic colectomy and have demonstrated the technique to be safe in experienced hands (Yang and Chua, 2013, Fung and Aly, 2012). Although results are comparable, there is currently no definitive evidence of the relative benefits of one approach over the other. Results from good quality randomised controlled trials are awaited before judgments are passed.

Despite recent advances in anaesthesia and surgical practices such as pre-operative optimisation of physiology and post-operative intensive care and rehabilitative processes, patients are commonly faced with undesirable effects of surgery. These range from post-operative pain to more serious systemic complications. These deleterious effects of anaesthesia and surgery are seen even without any failures in the surgical technique. It has been suggested that the underlying aetiology for such morbidity is the surgical stress response (Kehlet, 1997). In order to reduce this stress response and improve post-operative outcome, Enhanced Recovery After Surgery (ERAS) or fast-track surgery has been designed, implemented and evaluated (Moiniche et al., 1995, Bradshaw et al., 1998). The overall aim of such a programme is to accelerate recovery, thus reducing hospital stay and preventing complications. ERAS or fast-track surgery as described by Kehlet *et al* is a multimodal recovery programme that targets pre-operative, intra-operative and post-operative aspects of care. Eskicioglu *et al* and Varadhan *et al* have undertaken meta-analyses of studies that compared outcome from ERAS versus traditional perioperative care (Eskicioglu et al., 2009, Varadhan et al., 2010). Both these studies reported shorter length of hospital stay in patients that underwent ERAS care. In addition, the same cohort of patients had a lower post-operative morbidity or complication rate. A recent Cochrane review has ratified the findings of these studies and in addition has demonstrated that the shorter length of stay in ERAS patients in not complicated by higher readmission rates (Navarra et al., 1997). Different studies have used various elements of the ERAS protocols and the compliance for each element is not constant. Hence, although the ERAS approach as a whole is shown to have beneficial effects on outcome, which elements from the programme actually impact on outcome is yet to be fully understood. The difference in approach to perioperative care in control groups also adds to the heterogeneity of available evidence. Compliance to protocols and impact of each element is currently being studied by various proponents of enhanced recovery and results from these studies are likely to shed light on the most important elements of fast track surgery and their contribution to reducing length of stay and/ or complications.

Robotic surgery has gained widespread acceptance in prostatectomy and is currently being increasingly used for colorectal surgery (Keller et al., 2013, Ramamoorthy and Obias, 2013). However it is still unclear whether the substantial increase in cost of care is associated with any short or long term advantages as compared to laparoscopic colorectal surgery (deSouza et al., 2010, Trastulli et al., 2012, Tyler et al., 2013). Currently the available data do not support the routine use of robotic surgery for colorectal resection as a cost-effective procedure. The argument in favour of robotic surgery is that it offers an advanced camera system with high magnification and that can be controlled by the operating surgeon. Despite various studies demonstrating the feasibility and safety profile of robotic colorectal surgery, operative times and total overall costs are greater with no difference in the length of postoperative stay compared with traditional laparoscopic surgery (Fung and Aly, 2013).

Upper Gastrointestinal Resection

Surgical resection is currently the mainstay of treatment for cancer of the oesophagus and stomach. The International Agency for Research on Cancer has estimated that in 2012 there were more than 1.4m cases of gastro-oesophageal cancer diagnosed worldwide (Ferlay J, 2012). This group of cancer was responsible for more than a million deaths in the same year. In the United Kingdom, more than 15,000 cases of gastro-oesophageal cancer were diagnosed in the same year. According to the Hospital Episode Statistics, between April 2012 and March 2013, there were about 1800 oesophageal and 3500 gastric resections undertaken in English NHS Trusts (for benign and malignant indications) (Health & Social Care Information Centre, 2013). Such major and complex surgery is associated with significant morbidity and mortality. However over the last decade there has been a significant improvement in mortality rates in the UK (Al-Sarira et al., 2007, Lazzarino et al., 2010). The various factors contributing to this fall in mortality include increasing surgeon experience, improvements in anaesthesia, intensive care and radiology and uptake of minimally invasive surgery. Centralisation of the oesophageal-gastric cancer services in the UK was undertaken due to the evidence of a strong volume-outcome relationship and this has probably had a large impact on the improvement in outcomes (Palser et al., 2009).

Various approaches and surgical techniques have been described for potential curative resection of oesophageal cancer. Considerable debate still exists as to the superiority of one technique over the other. Over the years various modifications and adaptations have been described and more recently minimally invasive oesophagectomy is being evaluated following the success of this approach in colorectal surgery. Transthoracic and transhiatal approaches to oesophagectomy have been practiced for many years, however, to date there is no conclusive evidence of the superiority of one over the other. Various systematic reviews and meta-analyses have failed to identify the better operative technique between the two (Hulscher et al., 2001, Rindani et al., 1999). More recently Boschier *et al* undertook an extensive literature search and concluded that the transhiatal approach was associated with shorter operative time, hospital stay and respiratory complications while transthoracic approach had fewer anastomotic leaks and strictures (Boshier et al., 2011). However there was no significant difference in survival rates. With the widespread use of minimally invasive techniques, laparoscopic or thoracoscopic or a combination of the two to perform an oesophagectomy has attracted attention. Various studies have demonstrated the safety and efficacy of minimally invasive oesophagectomy as compared to traditional surgery but there are surgeons who are not entirely convinced with the oncological results (Xu et al., 2013, Dolan et al., 2013). Meta-analyses comparing the open versus minimally invasive approaches have concluded that strong evidence from randomised controlled trials is needed before advocating the latter as the technique of choice (Verhage et al., 2009, Nagpal et al., 2010). Coker and colleagues have also described a robot assisted transhiatal oesophagectomy in selected patients and shown comparable outcomes to traditional surgery (Coker et al., 2014). This technique however needs further evaluation.

Gastric cancer is responsible for a significant number of cancer related deaths (Jemal et al., 2011). The highest incidence rates are in Eastern Asia, Eastern Europe, and South

America and the lowest rates are in North America and most parts of Africa (Jemal et al., 2011). Gastrectomy is usually undertaken with a curative intent. A recent study showed an association between gastrectomy performed in the Eastern countries and improved survival (Markar et al., 2013). The high prevalence, detection of early cancer and differences in chemotherapeutic and surgical strategies may account for this variation according to geography. Certainly there is not a lot of evidence suggesting differences in tumour biology or the genetic makeup to be responsible for this difference between the East and the West. Since Kitano first described laparoscopy assisted gastrectomy, the minimally invasive approach has become very popular, especially in the East (Kitano et al., 1994). However to achieve the same oncological resection laparoscopically is challenging and critics have raised questions regarding the lymph node yield between the two techniques. Until recent times, published literature included results from case series and restrospective studies showing that laparoscopic gastrectomy was feasible, safe and had comparable short term results to the open approach (Chen et al., 2009, Cho et al., 2009, Huscher et al., 2005). Long term results from clinical trials have now suggested that long term survival with laparoscopic gastrectomy is comparable to the traditional open surgery (Kim et al., 2014, Lee et al., 2013). Junfeng and colleagues reported outcomes from 120 cases of robotic gastrectomy and showed comparable results with laparoscopic surgery (Junfeng et al., 2014). However this technique currently remains accessible to only a few centres worldwide and the long term outcomes are yet to be evaluated.

1.6 Previous studies from HES Data

The Hospital Episode Statistics database has been used for studies as early as 1994 when Dixon *et al,* published regarding distribution of NHS funds by examining HES and other health agency records (Dixon et al., 1994). Since then numerous studies have been published examining the HES database to answer various clinical, managerial, policy making and resource allocation decisions.

Cost analyses

The HES database has been used to estimate the cost of inpatient care for infectious intestinal diseases, oesophageal cancer, unintentional falls in elderly etc (Djuretic et al., 1996, Farndon et al., 1998, Scuffham et al., 2003). As it is representative of the national population, policy makers and clinicians are able to derive meaningful analyses by carefully studying the database. Beswick and co-workers used HES to study cardiac rehabilitation programmes and concluded that there was a need for more low-cost rehabilitation and also demonstrated the paucity of studies in this regard (Beswick et al., 2004). A study by Beynon looking at emergency admissions for falls during adverse weather significantly increased healthcare costs and suggested more responsibility to local councils to improve their public health measures (Beynon et al., 2011).

Sociodemographic analyses

In the late 90s, Gilthorpe demonstrated from HES that there was a strong correlation between social deprivation and access to oral surgery and suggested addition of a deprivation index to HES to study variation in service provision and utilisation amongst patients from different socio-economic groups (Gilthorpe and Bedi, 1997, Gilthorpe et al., 1997). Such ecological analyses were also undertaken using HES for cancers of colorectum, breast and lung, psychosis and surgery for hip replacement (Cookson et al., 2007, Croudace et al., 2000, Pollock and Vickers, 1998). More recently it was shown that patients with sickle cell disease from the most socio-economically deprived areas were at highest risk of readmissions and in-patient mortality (Aljuburi et al., 2013). HES has also been used to study the relationships between deprivation and duration of emergency admissions in paediatric patients (Kyle et al., 2012).

Outcomes analyses

One of the seminal papers published from HES was the comparison of paediatric cardiac surgery outcomes that found Bristol as an outlier for mortality as compared to the rest of the country(Aylin et al., 2001). Following a national enquiry and subsequent healthcare changes it was shown that mortality had improved not only in Bristol but nationally (Aylin et al., 2004). This not only prompted cardiac surgeons to make efforts to improve performance and quality of services but also to publish outcomes. Faiz *et al,* published outcomes following appendicectomy in adults and paediatric patients in a climate of increasing uptake of minimally invasive surgery (Faiz et al., 2008b, Faiz et al., 2008a). Similar studies on the comparison of outcomes following laparoscopic and open colorectal resections in an elective and non-elective setting have been undertaken (Faiz et al., 2011, Faiz et al., 2010b, Faiz et al., 2009). As with gastrointestinal surgery, HES has also been used to analyse outcomes from vascular procedures. Holt *et al,* used HES effectively and not only reported mortality and length of stay following aneurysm repair but also derived re-interventions as an outcome measure (Holt et al., 2010). Outcomes from urological surgeries, specifically the impact of case volume on mortality following cystectomy as well as post-procedural complications such as venous thrombo-embolism have also been undertaken from data obtained the from HES (McCabe et al., 2005, Mayer et al., 2010, Dyer et al., 2013).

Policy change

One of the most important policy decisions in recent times has been centralisation of complex surgery such as cancer resections. The Calman-Hine report, in 1995, outlined radical reform of the UK's cancer services with the aim of improving outcomes and reducing inequalities in NHS cancer care (Report, 1995). Since then numerous studies have examined the HES database for increasing sub-specialisation or re-organisation of various services, especially cancer surgery (Parry et al., 2004, Morris et al., 2006, Jolly et al., 2001) . Spurgeon in 2011 described how HES data can be analysed to evaluate and monitor organisational change (Spurgeon et al., 2011). This facilitated a more effective and intuitive exploration of HES in order to help healthcare professionals in monitoring change. In the context of payment by results, HES has also been used to identify cancellations of planned surgical procedures, factors underlying a high cancellation rate (both structural and patient related) and their impact on the healthcare resources (McIntosh et al., 2012).

Variation and Trends

As a database comprising of all NHS Trust hospitals, with mandatory reporting, HES is best placed to identify variation in the healthcare activities at a national level. Variation in the healthcare provision at geographical level, based on deprivation, seasonal variation and variation according to gender have been studied and reported from HES analyses (Bloor et al., 2008, Keenan et al., 2007, Sonnenberg, 2008). Similarly consultant activity, primary care admission rates and effect of policies and guidelines such as day case surgery have been evaluated using HES. Faiz *et al,* looked at trends in day-case surgery with respect to colorectal procedures and suggested resource savings may be possible by improving provision of day case colorectal surgery (Faiz et al., 2008c). Burns and colleagues proposed re-operation rate as a potential marker of surgical quality and their study of colorectal surgery in England showed a variation in re-operation rates amongst providers. In this study 22 out of 155 trusts had an adjusted re-operation rate above the upper 99.8% control limit.

Variation in surgical practice and outcomes have attracted a lot of press attention with the increasing awareness and demand for high quality services by patients. Differences in mode of admissions, staff to patient ratios, teaching hospital status and geographical variation have all been linked to differences in in-hospital mortality in England. Various outcome measures have been studied to describe such variation. Martin and Smith tried to explain the variation in inpatient length of stay in the NHS and identified factors such as access to NHS/private healthcare, waiting times for elective surgery and deprivation that contribute towards this variation (Martin and Smith, 1996). Morris *et al,* raised concerns over formation of permanent stomas in treatment of rectal cancer (Morris et al., 2008). This study showed that despite a fall in abdomino-perineal excision rates through the study period, there was significant variation in APE rates between surgeons and hospitals despite adjustment for case-mix.

1.7 Hypothesis and Aims

Hypothesis

There exists variation in outcome following gastrointestinal resection. Part of this is inevitable because of random variation; however variation in quality of healthcare services also contributes to variation in outcome. Poor outcome can be mitigated by structural and process changes to healthcare system in the UK.

Aims

The aims of this investigation are as follows:

1) To quantify perioperative outcome following gastrointestinal resection from a national English administrative database
2) To identify trends in reporting outcomes and describe the ideal metric to quantify mortality risk associated with gastrointestinal resection
3) To identify and describe factors [both structural (eg: volume or caseload) and process (eg: minimal access surgery)] that can be associated with an improvement in outcome following gastrointestinal resection

Chapter 2: METHODS

2.1 Data Sources

Studies undertaken in this thesis are retrospective analyses of prospectively maintained databases. Data sources for this investigation include Hospital Episode Statistics (HES) and Office for National Statistics (ONS).

2.1.1 Hospital Episode Statistics (HES)

HES are a data warehouse for routinely collected data from all NHS Trusts in England. The data are prospectively collected and entered by well-trained coders. The data include patient demographic details such as age, gender and post-code. At the heart of the data is a Finished Consultant Episode (FCE). FCEs are defined as episodes 'where a patient completed a period of care under a consultant and is either transferred to another consultant or discharged (Department of Health, 2000). Each patient episode is made up of diagnoses fields categorised according to the International Classification of Disease-10th revision (ICD-10) (World Health Organization, 1994) codes and procedure fields coded using the Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures-4th revision (OPCS-4) (Health, 2007). There are up to 20 diagnosis and 24 procedure fields for each patient episode. The diagnosis and procedure codes are made up of an alphabet and 3 or 4 numbers. The alphabet represents the area of body or organ system involved, with the codes becoming more specific towards the fourth digit. Information pertaining to the episode such as dates of admission and discharge, date of every procedure undertaken, mode of admission and destination following discharge are coded. Using the available data, variables such as the

Charlson's co-morbidity score (Charlson et al., 1987) and Carstairs index of social deprivation (Carstairs and Morris, 1989) can be derived. Outcome measure such as readmission and length of stay are available from the dataset. Linkage to the office for national statistics provides information on mortality at thirty days and one year.

2.1.2 Office for National Statistics (ONS)

The Office for National Statistics (ONS) is the UK Government's single largest statistical producer. ONS is the executive office of the UK Statistics Authority, a non-ministerial department which reports directly to Parliament. Linkage with the Hospital Episode Statistics data provides a range of information on economic, social and demographic statistics. In particular, we were interested in ONS data to overcome some of the limitations of HES data i.e. out-of-hospital mortality and causes of death. In order to explain some of the preliminary findings of our studies we wanted to investigate survival and cause of death following gastrointestinal resection. The patient records are matched using combinations of date of birth, gender, postcode and HES ID or NHS number and details pertaining to date and cause of death are available. Mr. Omar Faiz acquired the status of 'ONS approved researcher' and is the guardian for the HES data linked with ONS from the NHS Information Centre.

2.2 Ethics approval

We have permission from the Confidentiality Advisory Group under Section 251 of the NHS Act 2006 (formerly Section 60 approval from the Patient Information Advisory Group) to hold confidential data and analyse them for research purposes (PIAG 2-05(d)/2007). We have approval to use them for research and measuring quality of delivery of healthcare, from the South East Ethics Research Committee (10/H1102/25). Mr. Omar Faiz has been accredited as an 'Approved Researcher' by the ONS and hence we have been given mortality information using the HES-ONS linkage.

2.3 Disclosure

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2.4 Variable coding

For all studies, the index cases were identified using OPCS-4 procedure codes and the indication for surgical resection was ascertained from the WHO ICD-10 diagnosis codes.

2.4.1 Colorectal Resection

The specific OPCS-4 procedure codes that were used to identify patients undergoing major colorectal resectional surgery and their descriptions are enumerated below.

- **H04 Total excision of colon and rectum**

Excludes: Subtotal excision of colon (H29)
H04.1 Panproctocolectomy and ileostomy
Includes: Proctocolectomy NEC
H04.2 Panproctocolectomy and anastomosis of ileum to anus and creation of pouch HFQ
H04.3 Panproctocolectomy and anastomosis of ileum to anus NEC
H04.8 Other specified

H04.9 Unspecified

- **H05 Total excision of colon**

Excludes: Subtotal excision of colon (H29)

H05.1 Total colectomy and anastomosis of ileum to rectum

H05.2 Total colectomy and ileostomy and creation of rectal fistula HFQ

H05.3 Total colectomy and ileostomy NEC

H05.8 Other specified

H05.9 Unspecified

- **H06 Extended excision of right hemicolon**

Includes: Excision of right colon and other segment of ileum or colon and surrounding tissue

Caecum

H06.1 Extended right hemicolectomy and end to end anastomosis

H06.2 Extended right hemicolectomy and anastomosis of ileum to colon

H06.3 Extended right hemicolectomy and anastomosis NEC

H06.4 Extended right hemicolectomy and ileostomy HFQ

H06.8 Other specified

H06.9 Unspecified

- **H07 Other excision of right hemicolon**

Includes: Limited excision of caecum and terminal ileum caecum

H07.1 Right hemicolectomy and end to end anastomosis of ileum to colon

Includes: Ileocaecal resection

H07.2 Right hemicolectomy and side to side anastomosis of ileum to transverse colon

H07.3 Right hemicolectomy and anastomosis NEC

H07.4 Right hemicolectomy and ileostomy HFQ

H07.8 Other specified

H07.9 Unspecified

- **H08 Excision of transverse colon**

H08.1 Transverse colectomy and end to end anastomosis

H08.2 Transverse colectomy and anastomosis of ileum to colon

H08.3 Transverse colectomy and anastomosis NEC

H08.4 Transverse colectomy and ileostomy HFQ

H08.5 Transverse colectomy and exteriorisation of bowel NEC

Note: Use a secondary code for type of exteriorisation of bowel (H14, H15)

H08.8 Other specified

H08.9 Unspecified

- **H09 Excision of left hemicolon**

H09.1 Left hemicolectomy and end to end anastomosis of colon to rectum

H09.2 Left hemicolectomy and end to end anastomosis of colon to colon

H09.3 Left hemicolectomy and anastomosis NEC

H09.4 Left hemicolectomy and ileostomy HFQ

H09.5 Left hemicolectomy and exteriorisation of bowel NEC

Note: Use a secondary code for type of exteriorisation of bowel (H14, H15)

H09.8 Other specified

H09.9 Unspecified

- **H10 Excision of sigmoid colon**

H10.1 Sigmoid colectomy and end to end anastomosis of ileum to rectum

H10.2 Sigmoid colectomy and anastomosis of colon to rectum

H10.3 Sigmoid colectomy and anastomosis NEC

H10.4 Sigmoid colectomy and ileostomy HFQ

H10.5 Sigmoid colectomy and exteriorisation of bowel NEC

Note: Use a secondary code for type of exteriorisation of bowel (H14, H15)

H10.8 Other specified

H10.9 Unspecified

- **H11 Other excision of colon**

Includes: Excision of colon where segment removed is not stated

H11.1 Colectomy and end to end anastomosis of colon to colon NEC

H11.2 Colectomy and side to side anastomosis of ileum to colon NEC

H11.3 Colectomy and anastomosis NEC

H11.4 Colectomy and ileostomy NEC

H11.5 Colectomy and exteriorisation of bowel NEC

Note: Use a secondary code for type of exteriorisation of bowel (H14, H15)

H11.8 Other specified

H11.9 Unspecified

Includes: Colectomy NEC

Hemicolectomy NEC

- **H29 Subtotal excision of colon**

H29.1 Subtotal excision of colon and rectum and creation of colonic pouch and anastomosis of colon to anus

H29.2 Subtotal excision of colon and rectum and creation of colonic pouch NEC

H29.3 Subtotal excision of colon and creation of colonic pouch and anastomosis of colon to rectum

H29.4 Subtotal excision of colon and creation of colonic pouch NEC

H29.8 Other specified

H29.9 Unspecified

- **H33 Excision of rectum**

Includes: Excision of whole or part of rectum with or without part of sigmoid colon

H33.1 Abdominoperineal excision of rectum and end colostomy

H33.2 Proctectomy and anastomosis of colon to anus

H33.3 Anterior resection of rectum and anastomosis of colon to rectum using staples

Includes: Rectosigmoidectomy and anastomosis of colon to rectum

H33.4 Anterior resection of rectum and anastomosis NEC

H33.5 Rectosigmoidectomy and closure of rectal stump and exteriorisation of bowel

Note: Use a secondary code for type of exteriorisation of bowel (G74, H14–H15)

H33.6 Anterior resection of rectum and exteriorisation of bowel

Note: Use a secondary code for type of exteriorisation of bowel (G74, H14–H15)

H33.7 Perineal resection of rectum HFQ

H33.8 Other specified

H33.9 Unspecified

Includes: Rectosigmoidectomy NEC

Using the above procedure codes, the major resections were grouped as follows:

1. Subtotal/Total resection - panproctocolectomy or total colectomy (H04, H05), subtotal colectomy (H29)

2. Right sided resections - right hemicolectomy (H07), extended right hemicolectomy (H06) and transverse colectomy (H08)

3. Left sided resections - left hemicolectomy (H09), sigmoid colectomy (H10)

4. Rectal resections - anterior resection (H332-, H333, H334, H336, H338-, H339), abdomino-perineal resection (H331) and Hartmann's resection (H335) (Hartmann's resection for elective surgery was predominantly for rectal pathology)

The OPCS codes used to identify laparoscopic cases were Y50.8 and Y752. Y714 is the code for failed minimal access which has been in use since 2006. Patients undergoing procedures employing the latter code were included in the laparoscopic group. For patients who had more than one resection during the study period, their first resection was taken as the index resection. Based on the ICD-10 diagnosis codes, indications for surgery were categorised as malignancy (C18-C21), diverticulosis (K57), inflammatory bowel disease (IBD) (Crohn's K50, Ulcerative colitis K51) and other diagnoses.

2.4.2 Oesophagectomy

The OPCS-4 codes used to identify patients who underwent an oesophagectomy are G01, G02 and G03.

- **G01 Excision of oesophagus and stomach**

G01.1 Oesophagogastrectomy and anastomosis of oesophagus to stomach
G01.2 Oesophagogastrectomy and anastomosis of oesophagus to transposed jejunum
G01.3 Oesophagogastrectomy and anastomosis of oesophagus to jejunum NEC
G01.8 Other specified

G01.9 Unspecified

- **G02 Total excision of oesophagus**

G02.1 Total oesophagectomy and anastomosis of pharynx to stomach

G02.2 Total oesophagectomy and interposition of microvascularly attached jejunum

G02.3 Total oesophagectomy and interposition of jejunum NEC

G02.4 Total oesophagectomy and interposition of microvascularly attached colon

G02.5 Total oesophagectomy and interposition of colon NEC

G02.8 Other specified

G02.9 Unspecified

- **G03 Partial excision of oesophagus**

G03.1 Partial oesophagectomy and end to end anastomosis of oesophagus

Includes: Partial oesophagectomy and reanastomosis of oesophagus to stomach

G03.2 Partial oesophagectomy and interposition of microvascularly attached jejunum

G03.3 Partial oesophagectomy and anastomosis of oesophagus to transposed jejunum

G03.4 Partial oesophagectomy and anastomosis of oesophagus to jejunum NEC

G03.5 Partial oesophagectomy and interposition of microvascularly attached colon

G03.6 Partial oesophagectomy and interposition of colon NEC

G03.8 Other specified

G03.9 Unspecified

Includes: Oesophagectomy NEC

Patients with a benign indication were excluded and only those with a primary diagnosis of malignant neoplasm (ICD-10 code C15, C16.0) or carcinoma in situ of oesophagus (ICD-10 code D00.1) were included. Minimally invasive oesophagectomy (MIO) was defined by the use of laparoscopy and/or thoracoscopy. This was identified by the presence of a relevant procedure code in addition to the main oesophagectomy code. The OPCS-4 codes used to identify laparoscopy were Y50.8 (prior to April 2006) and Y75 (after April 2006) and those for thoracoscopy were Y49.8 (prior to April 2006) and Y74 (after April 2006). Total-MIO was defined as a procedure which included a code for both laparoscopy and thoracoscopy while the presence of any one of the above codes was termed as Hybrid-MIO.

2.4.3 Gastrectomy

Patients who underwent a gastric resection were coded as G27 (total) or G28 (partial).

- **G27 Total excision of stomach**

G27.1 Total gastrectomy and excision of surrounding tissue
G27.2 Total gastrectomy and anastomosis of oesophagus to duodenum
G27.3 Total gastrectomy and interposition of jejunum
G27.4 Total gastrectomy and anastomosis of oesophagus to transposed jejunum
G27.5 Total gastrectomy and anastomosis of oesophagus to jejunum NEC
G27.8 Other specified
G27.9 Unspecified

- **G28 Partial excision of stomach**

G28.1 Partial gastrectomy and anastomosis of stomach to duodenum
G28.2 Partial gastrectomy and anastomosis of stomach to transposed jejunum
G28.3 Partial gastrectomy and anastomosis of stomach to jejunum NEC
G28.4 Sleeve gastrectomy and duodenal switch
Excludes: Duodenal switch (G71.6)
G28.5 Sleeve gastrectomy NEC
G28.8 Other specified
G28.9 Unspecified
Includes: Gastrectomy NEC

Patients with a primary diagnosis of malignant neoplasm (ICD-10 code C16) or carcinoma in situ of stomach (ICD-10 code D00.2) were included. A laparoscopic procedure was identified by the following procedure codes: Y50.8 (prior to April 2006) and Y75 (after April 2006).

2.6 Outcome measures from HES

Primary outcome measures: Outcome variables available from the dataset include length of stay (LOS), readmission and mortality.

a) **Length of Stay (LOS):** Length of stay is the number of days in hospital since admission. This outcome is measured in days and described as a median with inter-quartile range (IQR). Post-operative length of stay (pLOS) can be calculated from the date of the index operation and subsequent discharge date.
b) **Readmission:** Unplanned or emergency admissions with any diagnosis within 28 days are termed as readmissions. These include readmission to a different hospital; or trust.
c) **Mortality** In-hospital mortality within 30 days is available and linkage with ONS provides 365-day in-and-out of hospital mortality (available only for resections undertaken prior to 2005). For data obtained directly from ONS, date of death is available and intermediate term mortality and long term survival can be calculated.

Secondary outcome measures: Secondary outcome measures are those not readily available from the database but ascertained using simple programming.

a) **Morbidity:** Medical complications or post-operative morbidity were identified by analyzing secondary diagnosis codes during the index admission and primary diagnosis codes for subsequent unplanned admissions using ICD-10 codes. The complications were grouped according to organ system involved (cardiac, respiratory, stroke, venous thrombo-embolism and renal failure). The relevant ICD-10 codes are enumerated in Table 1.

b) **Re-intervention:** Post-operative surgical morbidity was identified using surrogate markers such as re-operation and re-intervention. Re-operation was defined as any unplanned ‘return to theatre’ subsequent to the primary resection while re-intervention includes re-operation, radiology guided procedures and endoscopy.

Table 1: Co-morbidity and post-operative medical complications with ICD-10 diagnosis codes

Medical Condition	ICD-10 Codes
Venous Thrombo-embolism (VTE)	
Deep Vein Thrombosis (DVT)	I801, I802, I803
Pulmonary Embolism (PE)	I260, I269
Cardiac	
Angina	I20
Myocardial Infarction	I21, I22
Acute Ischaemic Heart Disease (AIHD)	I24
Chronic Ischaemic Heart Disease (CIHD)	I25
Congestive Cardiac Failure (CCF)	I50
Atrial Fibrillation or Flutter	I48
Hypertension	I10
Respiratory	
Pneumonia	J12-J16, J18, J22
Aspiration Pneumonia	J690, J691, J698
Pleural Effusion	J90, J91, J948
Adult Respiratory Distress Syndrome (ARDS)	J80
Acute Exacerbation of COPD^{+}	J44, J46
Chronic COPD	J40- J43, J448, J449, J45, J47
Atelectasis	J981
Respiratory Failure	J96
Pulmonary Oedema	J81
Stroke	
Acute Ischaemic Stroke	I63, I64
Sequelae of Stroke	I69
Renal	
Renal Failure	N17, N18, N990
Diabetes (Uncomplicated)	E109, E119, E149

2.6 Statistical Analyses

Statistical analyses were carried out using SPSS (Statistical Package for Social Sciences) version 18.0 (SPSS, Inc. an IBM company). Chi square test was used to compare categorical data. For tests of significance, p values <0.05 were considered significant. Medians and interquartile ranges (IQRs) have been presented for continuous, non-normal variables. Subgroup analyses were performed using the Chi square test and Mann-Whitney U test for categorical and continuous variables, respectively.

Risk adjusted analyses: Logistic regression models were created to identify independent predictors of binary outcomes such as mortality and morbidity. The covariates used to risk adjust for case-mix were:

Patient factors:

Age – age at the time of index operation was used as categorical data

Gender – Odds ratios were calculated for females with males as the reference group

Carstairs index – this is an index of social deprivation that uses four variables derived from the census:

- Proportion male unemployment
- Proportion overcrowded households
- Proportion no car/vans ownership
- Proportion low social class

This index has been shown to be a valid measure of deprivation (Morris and Carstairs, 1991) and has been extensively used in studies based on HES data (Lazzarino et al., 2011, Langford et al., 2012, Bagger et al., 2008).

Co-morbidity – All admissions up to five years prior to the index operation were analysed to identify pre-operative co-morbidity. Co-morbidity was further classified into cardiac, respiratory, venous thrombo-embolism, previous ischaemic stroke, renal failure and diabetes. Charlson score of co-morbidity was also available from HES data. This is a score calculated using secondary diagnoses. It is a weighted index with a range 0-37.

Mode of admission – elective or planned resection versus non-elective admission

Diagnosis – benign (inflammatory and non-inflammatory) versus malignant diagnoses

Structural factors:

Discharge year – especially for upper gastrointestinal resections, discharge year was used to understand the effects of centralisation

Volume – hospital volume and surgeon caseload

Process factors:

Type of resection – total or segmental colonic resection versus rectal resections; total versus partial gastrectomy

Minimal access surgery – use of laparoscopic or thoracoscopic approach

2.7 Limitations of HES

Accuracy: HES are administrative data collected by non-clinician coders who are trained to review case notes and code each episode into a set of diagnosis and procedure codes. Critics of HES complain about the accuracy of these data. Campbell and colleagues undertook a systematic review to assess the accuracy of United Kingdom hospital administrative data and found median accuracy rates of approximately 84% and 97% for diagnostic (ICD) and operation (OPCS) codes respectively (Campbell et al., 2001). More recently, a similar study by our team found an overall median accuracy rate of 83.2% with a significant improvement in accuracy over the years (Burns et al., 2012).

Bias: The strengths of these routinely collected datasets are that they capture all patients and thereby negate the potential reporting bias inherent in any carefully selected series of patients. However, this study is not immune to selection bias as regards to the surgical approach and evidence from randomised control trials with carefully constraining inclusion criteria is essential to draw firm conclusions.

Clinical or disease parameters: Limited variables are available from HES data giving rise to difficulty in case mix adjustment. For example, obesity is a known predictor of post-operative morbidity following colectomy. Although some recent studies have shown laparoscopic colectomy to be feasible in obese patients with comparable outcomes to non-obese many surgeons remain hesitant to offer a minimally invasive approach to this patient group. HES data do not include patient BMI and hence cannot account for this potential difference in patient selection. Similarly, a history of prior abdominal surgery cannot be ascertained from administrative data sources such as HES and may lead to unaccounted bias between patients selected for the conventional and laparoscopic approach. Similarly, intra-operative parameters such as blood loss, operative time and need for transfusion cannot be accounted for. In case of malignant diagnosis, stage of the disease is also not available.

Complications: Severity of complications cannot be ascertained from these data. Nevertheless, the large numbers of patients involved in such population based series mean that rarely occurring events can be detected in sufficient volume to permit comparative analyses. One further limitation that we recognise is that morbidity occurring outside of hospital i.e. managed on an outpatient basis will not find inclusion in our data. Thus, this study underestimates total complications occurring following surgery. Severe complications are, however, likely to require readmission and therefore find inclusion. As there are no specific diagnostic codes for some surgical complications such as 'anastomotic leak', surrogate codes such as those for re-operation are used to describe significant surgical morbidity.

CHAPTER 3: OUTCOMES FROM A ROUTINELY-COLLECTED ENGLISH NATIONAL DATABASE

Gastrointestinal resections are commonly undertaken for a variety of indications, benign and malignant, both in the elective and emergency setting. In 2012-2013, it has been estimated that more than 40,000 colorectal resections, 1700 oesophagectomies and 3000 gastrectomies were undertaken in English National Health Services Trust hospitals (Hospital Episode Statistics, 2013). Such complex surgery is associated with significant morbidity and mortality. I undertook a study to quantify the outcomes following major gastrointestinal resections, enumerated above, from a national dataset. Data were obtained from Hospital Episode Statistics and short-term and intermediate outcomes following major gastrointestinal resection were studied. Three specific types of surgery were studied viz. colorectal resection, oesophagectomy and gastrectomy. The HES database itself, along with variable coding and outcome measures derived have been explained in detail in Chapter 2.

3.1 Colorectal Resection

The National Bowel Cancer Audit is a clinical audit under the auspices of Association of Coloproctology of Great Britain and Ireland (ACPGBI). The annual report published in 2012, showed 29,445 new diagnoses of bowel cancer in England and Wales between April 2011 and March 2012 (NBOCAP, 2011). Of these patients 58.6% underwent a major resection. It has been estimated that the audit received data for approximately 85% of the total colorectal cancer burden in England and Wales. Considering this audit only included malignant diagnoses, if benign resections such as those for diverticulosis or inflammatory bowel disease are included, colorectal resection forms a large part of the major abdominal/pelvis surgery undertaken in the UK.

Colorectal resection is generally associated with a low mortality in an elective setting, but significant morbidity. Literature review has shown studies with up to 35-40% morbidity following major colorectal resection (Alves et al., 2005, Braga et al., 2002). More recently, various multi-modal approaches to improving perioperative outcome have been proposed. These include minimal-access surgery (MAS), use of short acting and regional anaesthesia, careful fluid monitoring, epidural analgesia etc. Post-operative mortality rates following planned colorectal resections have varied from 0 to 3.5% from reported case series (Alves et al., 2003, Jang et al., 2013, Senagore et al., 2003a, Van Arendonk et al., 2013). However, case series or single centre studies have historically been exposed to reporting bias and are usually underpowered to identify small differences in outcome associated with change in practice. Hence I aimed to study outcomes from a national database to be able to quantify mortality and morbidity from an English perspective.

3.1.1 Methods

HES data were obtained for all patients undergoing an elective or planned colorectal resection in an English NHS trust hospital between April 2001 and March 2008. If a patient had more than one resection during the study period, their first resection was taken as the index resection. Patients under the age of 18 and those who underwent an emergency surgery were excluded. Patients were divided into four age categories <55, 55-69, 70-79 and >79 years. The procedure codes used to identify the operations, co-morbidity and complications are as enumerated in Chapter 2. Benign and malignant diagnoses were included in the study. The indications for surgery were categorised as malignancy (C18, C19, C20, C21), diverticulosis (K57), inflammatory bowel disease (IBD) (Crohn's K50, Ulcerative colitis K51) and other diagnoses. Both unadjusted as well as risk-adjusted analyses were undertaken.

3.1.2 Outcome variables and statistical methodology

Length of stay (LOS) was taken as the duration (in days) spent in hospital during the primary admission. Median lengths of stay [+/- interquartile range (IQR)] are described. Post-operative medical morbidity was classified according to the presence of relevant ICD-10 diagnosis codes. In analysing complications according to an organ system, presence of any one complication pertaining to that system was considered. The medical complications that were considered in this study have been enumerated in Table 1 (Chapter 2). The presence of any of the above diagnosis codes (acute and chronic) in admissions up to 5 years preceding the resection was termed as preoperative co-morbidity. The presence of any of the acute codes post-operatively (i.e. after the index procedure) was termed as a morbidity or medical complication. For subsequent admissions, only the primary diagnosis code was used to identify medical morbidity. 30-day in-hospital mortality and 365-day in-and-out of hospital mortality were considered in our analysis. 365-day mortality was only available for resections performed until March 2005 and thus subsequent cases were excluded while analysing this particular outcome. Re-intervention was defined as any return to theatre on the index admission or on a subsequent admission within 28 days of the initial resection. This was either for laparotomy, intra-abdominal abscess drainage (image guided or open approach), stoma or wound complications requiring reoperation.

Statistical analyses were carried out using SPSS Version 18.0 (Statistical Package for Social Sciences, SPSS, Chicago, Illinois, USA). Categorical variables were investigated using the Chi-squared test. For tests of significance, p-values <0.05 were considered significant. Medians and interquartile ranges (IQR) have been presented for non-normal variables.

Multiple regression analyses were carried out to identify predictors of postoperative medical morbidity with these covariates: age, gender, diagnosis, type of resection, surgical approach (i.e. laparoscopic or open surgery), preoperative co-morbidity and re-intervention or return to theatre within 28 days. Subgroup analyses were performed using Chi squared test and Mann Whitney U test for categorical and continuous variables respectively.

3.1.2 Results

From the database, 212,248 patients were identified who underwent a colorectal resection during the study years. Of these, 73,513 (34.6%) of operations were undertaken in a non-elective setting and were hence excluded. Total number of elective resections in adult patients were 138,735 of which 128,840 (92.9%) were undertaken in a traditional or 'open' approach and 9,895 (7.1%) were undertaken using a laparoscopic approach. The different types of resections undertaken have been enumerated in detail in Table 2.

Demographics

Median patient age was 69 years (IQR 59-77). Around 1 in 6 patients was aged 80 years or above. There was a slight male dominance (52.9%) as compared to female patients (47.1%). Majority of the patients (70.1%) underwent surgery for a malignant cause. Just under half of the operations were rectal resections. Cardiorespiratory co-morbidity and Diabetes were the most commonly coded secondary diagnoses. One in five patients had a pre-operative cardiac co-morbidity. The detailed demographics and descriptive characteristics of the patients are shown in Table 3.

Table 2: Frequency of colorectal resections carried out in English NHS Trusts

Resection	Elective				Non-Elective	
	Open		Laparoscopic			
	n	(%)	n	(%)	n	(%)
Total Colectomy+	5888	(4.57)	260	(2.63)	4920	(6.70)
Right Hemicolectomy	31451	(24.41)	3278	(33.13)	25383	(34.53)
Extended Right Hemicolectomy*	6601	(5.12)	319	(3.22)	6537	(8.89)
Left Hemicolectomy	7923	(6.15)	486	(4.91)	3479	(4.73)
Sigmoid Colectomy	16035	(12.45)	1470	(14.86)	8337	(11.34)
Abdomino-Perineal Resection	9910	(7.69)	503	(5.08)	569	(0.77)
Anterior Resection	43575	(33.82)	3331	(33.66)	3425	(4.66)
Hartmann's Resection	7466	(5.79)	248	(2.51)	20863	(28.38)
Total	**128840**	**(100)**	**9895**	**(100)**	**73513**	**(100)**

n=sample size, %=percentage; +includes subtotal and panproctocolectomy; *includes transverse colectomy

Table 3: Descriptive characteristics of patients undergoing elective colorectal resection
(April 2001 - March 2008)

	n	(%)
Age		
<55 years	23944	(17.3)
55-69 years	48101	(34.7)
70-79 years	44523	(32.1)
>79 years	22167	(16.0)
Gender		
Male	73379	(52.9)
Female	65356	(47.1)
Diagnosis		
Malignancy	97303	(70.1)
Diverticulosis	12035	(8.7)
IBD	9847	(7.1)
Other	19550	(14.1)
Resection		
Subtotal/Total	6160	(4.4)
Right sided	41650	(30.0)
Left Sided	25914	(18.7)
Rectal	65011	(46.9)
Preoperative Co-morbidity		
Cardiac	27542	(19.9)
Respiratory	8252	(5.9)
VTE	712	(0.5)
Stroke	451	(0.3)
Renal	921	(0.7)
Diabetes	7322	(5.3)

Length of Stay and Readmission

Overall median length of stay was 11 days with an inter-quartile range of 9-16 days. The median LOS for patients who had no medical complication during their index admission was 11 days (IQR 8-15), while that for patients that had at least one medical complication postoperatively was 15 days (IQR 11-25). Twelve thousand nine hundred and forty eight patients (9.3%) had an unplanned readmission within 28-days.

Mortality and morbidity

30-day in-hospital mortality was 3.3% (4,515). 14.6% (n=20,319) patients had at least one medical complication within thirty days. Frequencies of specific medical complications following elective colorectal resection have been shown in Table 4. Majority of the complications were cardiac (n=12,270, 8.9%) and respiratory (n=8,439, 6.2%). Overall 6.1% of the patients underwent a re-operation within 28 days of surgery. Mortality and morbidity in patients with a pre-operative co-morbidity (5.3% and 24.9% respectively) were significantly higher than patients with no co-morbidity (2.6% and 11.2% respectively, $p<0.001$). One year mortality was only available for patients who underwent their surgery prior to 2005. Out of 95,742 patients for whom these data were available, 10,585 (11.1%) died within one year of surgery.

Table 4: Short term outcomes following elective colorectal resection

Outcome	n	(%)
Length of Stay	11 days	IQR (9-16)
Readmission	12,948	(9.3)
Mortality	4,515	(3.3)
Morbidity	20,319	(14.6)
Cardiac	12,307	(8.9)
Respiratory	8,538	(6.2)
VTE	918	(0.7)
Stroke	356	(0.3)
Renal Failure	1,992	(1.4)
Angina	5,488	(4.0)
Myocardial Infarction	1,339	(1.0)
Congestive Cardiac Failure	2,470	(1.8)
Atrial Flutter/Fibrillation	4,587	(3.3)
Pneumonia	6,064	(4.4)
Pleural Effusion	2,119	(1.5)
Respiratory Failure	989	(0.7)
Other Respiratory*	1,235	(0.9)
Deep Vein Thrombosis	352	(0.3)
Pulmonary Embolism	615	(0.4)

**Other Respiratory=Acute Exacerbation of COPD, Pulmonary Oedema, Post-procedural respiratory complications*

Risk-adjusted outcomes

Univariate analysis was undertaken and covariates with a $p<0.05$ were included in a multiple regression model. Case-mix adjustment for surgical approach, age, gender, diagnosis, type of resection and re-intervention was undertaken. Advancing age, male gender and pre-operative cardiac (OR 1.3) and respiratory (OR 1.5) co-morbidity and diabetes (OR 1.24) were independent determinants of both 30-day and 365-day mortality ($p<0.001$) (Table 5). Interestingly, laparoscopic approach was associated with a significant lower risk of mortality as compared to the traditional open approach after case-mix adjustment. The risk of death within 30 days of surgery was doubled in the presence of pre-operative renal failure ($p<0.001$) and previous stroke ($p<0.001$). Similar risk-adjusted models were created for medical complications which showed that advancing age, use of laparoscopic approach, pre-operative co-morbidity and re-intervention significantly increased the risk of post-operative morbidity (Tables 6 and 7). Patients with previous thrombo-embolic complications demonstrated a significantly elevated risk of developing DVT or PE up to one year following surgery (OR 9.79; 95% CI 7.06-13.56 95% CI; $p<0.001$). The risk of developing DVT or PE was higher in patients with malignant disease as compared with IBD or diverticulosis. The presence of a preoperative diagnosis of diabetes predisposes to postoperative cardiac complications and renal failure.

Table 5: Multiple logistic regression analysis for 30-day and 365-day mortality

	30-Day Mortality (n=4515/138735)			365-Day Mortality (n=8958/75101)*		
	Odds Ratio	95% CI for OR	p value	Odds Ratio	95% CI for OR	p value
Surgical Approach			<0.001			<0.001
Open	1.00			1.00		
Laparoscopic	0.46	(0.39, 0.53)	<0.001	0.43	(0.34, 0.54)	<0.001
Age			<0.001			<0.001
<55 years	1.00			1.00		
56-69 years	2.44	(2.02, 2.93)	<0.001	1.74	(1.57, 1.93)	<0.001
70-79 years	6.44	(5.38, 7.70)	<0.001	3.09	(2.79, 3.42)	<0.001
>79 years	14.66	(12.23, 17.57)	<0.001	5.37	(4.84, 5.97)	<0.001
Gender			<0.001			<0.001
Male	1.00			1.00		
Female	0.66	(0.62, 0.70)	<0.001	0.83	(0.79, 0.87)	<0.001
Diagnosis			<0.001			<0.001
Malignancy	1.00			1.00		
Diverticulosis	1.16	(1.02, 1.32)	0.025	0.56	(0.50, 0.62)	<0.001
IBD	0.48	(0.36, 0.64)	<0.001	0.24	(0.20, 0.30)	<0.001
Other	2.21	(2.04, 2.39)	<0.001	1.30	(1.21, 1.38)	<0.001
Resection			<0.001			<0.001
Total/Subtotal	1.00			1.00		
Right Sided	0.52	(0.44, 0.62)	<0.001	0.90	(0.78, 1.05)	0.173
Left Sided	0.44	(0.37, 0.53)	<0.001	0.69	(0.59, 0.81)	<0.001
Rectal	0.49	(0.41, 0.58)	<0.001	0.74	(0.64, 0.86)	<0.001
Preoperative Co-morbidity						
Absence of co-morbidity for each organ system	1.00					
Cardiac	1.30	(1.22, 1.40)	<0.001	1.16	(1.09, 1.23)	<0.001
Respiratory	1.59	(1.44, 1.77)	<0.001	1.39	(1.26, 1.52)	<0.001
VTE	1.02	(0.71, 1.46)	0.918	1.46	(1.09, 1.94)	0.010
Stroke	2.07	(1.50, 2.85)	<0.001	1.86	(1.37, 2.52)	<0.001
Renal Failure	2.46	(1.99, 3.04)	<0.001	3.33	(2.68, 4.14)	<0.001
Diabetes	1.24	(1.10, 1.39)	<0.001	1.27	(1.15, 1.41)	<0.001
Surgical Complications						
Re-intervention	3.84	(3.53, 4.18)	<0.001	2.83	(2.62, 3.06)	<0.001

**365-Day mortality data only available prior to 2005.*

Table 6: Multiple regression model for 30-day medical complications in patients undergoing elective colorectal resection

	Cardiac			Respiratory			VTE			Stroke			Renal Failure		
	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value
Surgical Approach			<0.001			<0.001			0.001			0.008			0.001
Open	1.00			1.00			1.00			1.00			1.00		
Laparoscopic	0.79	(0.73, 0.85)	<0.001	0.78	(0.71, 0.86)	<0.001	0.55	(0.40, 0.77)	0.001	0.46	(0.26, 0.82)	0.008	0.72	(0.59, 0.88)	0.001
Age			<0.001			<0.001			<0.001			<0.001			<0.001
<55 years	1.00			1.00			1.00			1.00			1.00		
56-69 years	5.37	(4.63, 6.24)	<0.001	1.45	(1.32, 1.58)	<0.001	1.51	(1.18, 1.92)	0.001	2.65	(1.35, 5.22)	0.005	2.22	(1.78, 2.76)	<0.001
70-79 years	11.36	(9.80, 13.17)	<0.001	2.21	(2.02, 2.42)	<0.001	1.81	(1.41, 2.32)	<0.001	6.81	(3.53, 13.13)	<0.001	3.71	(2.99, 4.60)	<0.001
>79 years	18.26	(15.72, 21.21)	<0.001	3.41	(3.10, 3.74)	<0.001	1.86	(1.41, 2.44)	<0.001	9.09	(4.65, 17.76)	<0.001	5.71	(4.57, 7.14)	<0.001
Gender			<0.001			<0.001			0.491			0.600			<0.001
Male	1.00			1.00			1.00			1.00			1.00		
Female	0.76	(0.73, 0.79)	<0.001	0.70	(0.67, 0.74)	<0.001	1.05	(0.92, 1.20)	0.491	1.06	(0.85, 1.32)	0.600	0.53	(0.48, 0.59)	<0.001
Diagnosis			<0.001			<0.001			0.088			0.015			<0.001
Malignancy	1.00			1.00			1.00			1.00			1.00		
Diverticulosis	1.26	(1.17, 1.36)	<0.001	1.26	(1.15, 1.37)	<0.001	0.80	(0.61, 1.07)	0.131	0.92	(0.59, 1.44)	0.729	1.55	(1.29, 1.85)	<0.001
IBD	0.72	(0.61, 0.85)	<0.001	0.79	(0.69, 0.91)	0.001	0.91	(0.64, 1.30)	0.614	0.29	(0.09, 0.98)	0.045	0.73	(0.52, 1.01)	0.060
Other	1.08	(1.02, 1.15)	0.009	1.51	(1.41, 1.60)	<0.001	1.18	(0.98, 1.42)	0.091	1.41	(1.05, 1.89)	0.022	2.38	(2.13, 2.67)	<0.001
Resection			0.049			<0.001			0.238			0.245			<0.001
Total/Subtotal	1.00			1.00			1.00			1.00			1.00		
Right Sided	0.90	(0.78, 1.03)	0.112	0.75	(0.66, 0.85)	<0.001	0.84	(0.58, 1.20)	0.332	0.57	(0.30, 1.10)	0.094	0.56	(0.44, 0.71)	<0.001
Left Sided	0.89	(0.78, 1.03)	0.112	0.67	(0.59, 0.77)	<0.001	0.75	(0.51, 1.11)	0.153	0.55	(0.28, 1.07)	0.079	0.44	(0.34, 0.57)	<0.001
Rectal	0.86	(0.75, 0.98)	0.026	0.74	(0.65, 0.84)	<0.001	0.90	(0.63, 1.29)	0.573	0.65	(0.35, 1.23)	0.187	0.62	(0.49, 0.78)	<0.001
Preoperative Comorbidity															
Absence of comorbidity for each organ system	1.00			1.00			1.00			1.00			1.00		
Cardiac	2.85	(2.73, 2.97)	<0.001	1.12	(1.06, 1.19)	<0.001	0.88	(0.73, 1.04)	0.139	1.35	(1.06, 1.73)	0.016	1.47	(1.33, 1.64)	<0.001
Respiratory	1.28	(1.19, 1.37)	<0.001	1.87	(1.73, 2.02)	<0.001	1.07	(0.82, 1.40)	0.625	1.08	(0.73, 1.62)	0.691	1.30	(1.11, 1.53)	0.001
VTE	0.78	(0.60, 1.00)	0.049	1.03	(0.78, 1.37)	0.835	9.79	(7.06, 13.56)	<0.001	0.79	(0.20, 3.20)	0.741	1.04	(0.61, 1.76)	0.900
Stroke	1.01	(0.78, 1.29)	0.966	1.39	(1.02, 1.88)	0.035	1.12	(0.41, 3.03)	0.829	9.15	(5.23, 16.01)	<0.001	1.57	(0.95, 2.62)	0.082
Renal Failure	1.16	(0.97, 1.38)	0.099	1.31	(1.05, 1.62)	0.015	0.58	(0.22, 1.57)	0.287	1.09	(0.40, 2.96)	0.870	4.29	(3.37, 5.47)	<0.001
Diabetes	1.14	(1.06, 1.22)	<0.001	1.09	(1.00, 1.20)	0.064	1.11	(0.83, 1.49)	0.469	1.06	(0.70, 1.60)	0.778	1.71	(1.47, 1.98)	<0.001
Surgical Complications															
Re-intervention	1.68	(1.57, 1.81)	<0.001	4.27	(4.01, 4.54)	<0.001	2.24	(1.83, 2.74)	<0.001	2.51	(1.83, 3.43)	<0.001	6.61	(5.96, 7.33)	<0.001

Table 7: Multiple regression model for 365-day medical complications in patients undergoing elective colorectal resection

	Cardiac			Respiratory			VTE			Stroke			Renal Failure		
	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value
Surgical Approach			0.001			0.025			0.049			0.144			0.315
Open	1.00			1.00			1.00			1.00			1.00		
Laparoscopic	0.68	(0.55, 0.85)	0.001	0.75	(0.59, 0.96)	0.025	0.41	(0.17, 1.00)	0.049	0.23	(0.03, 1.65)	0.144	0.78	(0.48, 1.27)	0.315
Age			<0.001			<0.001			0.045			<0.001			<0.001
<55 years	1.00			1.00			1.00			1.00			1.00		
56-69 years	5.60	(4.54, 6.90)	<0.001	1.46	(1.29, 1.66)	<0.001	1.28	(0.96, 1.70)	0.091	3.31	(1.28, 8.57)	0.014	2.04	(1.54, 2.70)	<0.001
70-79 years	12.12	(9.86, 14.91)	<0.001	2.28	(2.01, 2.58)	<0.001	1.47	(1.10, 1.97)	0.009	9.19	(3.64, 23.19)	<0.001	2.92	(2.21, 3.86)	<0.001
>79 years	19.71	(15.98, 24.30)	<0.001	3.46	(3.04, 3.94)	<0.001	1.48	(1.07, 2.05)	0.018	13.16	(5.15, 33.68)	<0.001	4.68	(3.50, 6.26)	<0.001
Gender			<0.001			<0.001			0.836			0.639			<0.001
Male	1.00			1.00			1.00			1.00			1.00		
Female	0.76	(0.72, 0.81)	<0.001	0.70	(0.66, 0.75)	<0.001	1.02	(0.86, 1.20)	0.836	1.07	(0.81, 1.40)	0.639	0.56	(0.49, 0.64)	<0.001
Diagnosis			<0.001			<0.001			0.328			0.522			<0.001
Malignancy	1.00			1.00			1.00			1.00			1.00		
Diverticulosis	1.33	(1.2, 1.46)	<0.001	1.18	(1.05, 1.33)	0.006	0.82	(0.59, 1.14)	0.227	1.13	(0.68, 1.89)	0.637	1.29	(1.01, 1.66)	0.042
IBD	0.78	(0.62, 0.97)	0.025	0.83	(0.69, 1.00)	0.053	0.76	(0.49, 1.18)	0.222	0.43	(0.12, 1.48)	0.179	0.59	(0.37, 0.95)	0.029
Other	1.12	(1.03, 1.22)	0.006	1.44	(1.32, 1.58)	<0.001	0.86	(0.67, 1.11)	0.253	1.08	(0.72, 1.62)	0.721	2.30	(1.97, 2.69)	<0.001
Resection			0.417			0.012			0.013			0.212			<0.001
Total/Subtotal	1.00			1.00			1.00			1.00			1.00		
Right Sided	0.94	(0.78, 1.14)	0.552	0.80	(0.67, 0.96)	0.017	0.84	(0.53, 1.33)	0.451	0.48	(0.23, 1.01)	0.053	0.59	(0.42, 0.82)	0.002
Left Sided	0.95	(0.78, 1.15)	0.575	0.77	(0.64, 0.93)	0.006	0.78	(0.48, 1.27)	0.32	0.44	(0.20, 0.95)	0.036	0.51	(0.36, 0.72)	<0.001
Rectal	0.91	(0.75, 1.09)	0.303	0.85	(0.71, 1.02)	0.074	1.08	(0.69, 1.69)	0.748	0.49	(0.23, 1.00)	0.051	0.74	(0.54, 1.03)	0.073
Preoperative Co-morbidity															
Absence of co-morbidity for each organ system	1.00			1.00			1.00			1.00			1.00		
Cardiac	3.02	(2.84, 3.20)	<0.001	1.16	(1.07, 1.26)	<0.001	0.89	(0.7, 1.12)	0.304	1.18	(0.85, 1.65)	0.319	1.65	(1.43, 1.92)	<0.001
Respiratory	1.34	(1.21, 1.48)	<0.001	2.01	(1.79, 2.24)	<0.001	1.11	(0.78, 1.58)	0.567	1.26	(0.75, 2.10)	0.379	1.19	(0.94, 1.51)	0.148
VTE	0.82	(0.57, 1.18)	0.277	0.87	(0.56, 1.35)	0.522	7.81	(4.84, 12.6)	<0.001	1.49	(0.37, 6.12)	0.577	1.41	(0.71, 2.80)	0.322
Stroke	1.04	(0.73, 1.48)	0.819	1.20	(0.76, 1.90)	0.439	0.00	(0,0)	0.995	5.10	(2.04, 12.73)	<0.001	1.38	(0.64, 2.99)	0.411
Renal Failure	1.30	(1.00, 1.68)	0.052	1.41	(1.02, 1.94)	0.039	0.57	(0.14, 2.3)	0.429	1.64	(0.51, 5.24)	0.406	4.13	(2.86, 5.96)	<0.001
Diabetes	1.17	(1.05, 1.30)	0.003	0.99	(0.86, 1.15)	0.914	1.14	(0.77, 1.68)	0.517	1.61	(0.98, 2.64)	0.062	1.63	(1.30, 2.05)	<0.001
Surgical Complications															
Re-intervention	1.62	(1.46, 1.79)	<0.001	4.00	(3.66, 4.37)	<0.001	2.51	(1.98, 3.19)	<0.001	2.50	(1.66, 3.77)	<0.001	6.01	(5.19, 6.95)	<0.001

3.2 Oesophagectomy

Oesophageal cancer is associated with significant mortality and its incidence has increased in the UK, especially in men (Cancer Research UK, 2013a). In the year 2011 there were around 7,600 deaths due to oesophageal cancer in the UK. The mainstay of potentially curative treatment remains surgery i.e. oesophagectomy. Various techniques and approaches to oesophagectomy have been described in the literature (Lewis, 1946, McKeown, 1976, Orringer et al., 2007, Orringer et al., 1999). Broadly speaking however, this is a complex surgical resection associated with high morbidity and significant mortality. Since Luft *et al* proposed the concept of volume and outcome relationship in 1979, various studies have shown that high volume centres performing upper gastrointestinal resection are associated with better outcomes (Gordon et al., 1999, Lauder et al., 2010, Lin et al., 2006, Luft et al., 1979, Matthews et al., 1986). The English National Health Service Executive Guidance recommended the process of centralisation of upper gastrointestinal cancer services in the UK (Palser et al., 2009). This study aimed to quantify national outcomes following oesophagectomy in the post-centralisation era.

3.2.1. Methods

HES data were analysed for patients who underwent an elective or planned oesophagectomy in an English NHS Trust hospital for a malignant diagnosis. Adult patients who underwent a surgical resection of the oesophagus between April 2005 and March 2010 were included. The detailed methodology including the procedure codes used to identify patients that underwent an oesophagectomy has been explained in Chapter 2. Patients with a benign indication were excluded and only those with a primary diagnosis of malignant neoplasm (ICD-10 code C15, C16.0) or carcinoma in situ of oesophagus (ICD-10 code

D00.1) were included. The Carstairs index was used by linking the HES data to patient postcode to determine the social deprivation index (Carstairs and Morris, 1989).

3.2.2 Outcome variables and statistical methodology

Length of stay (LOS) was taken as the duration (in days) spent in hospital during the primary admission; an LOS of 0 means the patient was admitted and discharged on the same day. We report median lengths of stay with inter-quartile ranges (IQR). Unplanned admissions within 28 days were termed as readmission. 30-day in-hospital mortality has been reported. Post-operative medical morbidity was taken from the secondary diagnosis fields of the index admission and the primary diagnosis codes from any subsequent unplanned admissions within 30 days of surgery. Complications were grouped according to involvement of an organ system and presence of any one complication pertaining to that system was considered. The medical complications that were considered in this study and the corresponding ICD-10 codes are described in Table 1 (Chapter 2). The presence of any of the diagnostic codes (acute and chronic) in admissions up to 5 years preceding the surgery was termed as pre-operative co-morbidity. HES data do not have present-on-admission flags for the secondary diagnoses.

Any unplanned procedure such as endoscopy, radiology guided procedure or return to theatre during the index admission or within 30 days of initial surgery was termed as re-intervention (HES records the dates of all procedures). Laparotomy, thoracotomy or use of minimally invasive approach subsequent to the index surgery was defined as re-operation or return to theatre. Both re-intervention and re-operation were determined by analysing procedure codes. Return to theatre or re-intervention on the same day as the index surgery could not be identified due to limitations of the dataset. Statistical analyses were carried out using SPSS Version 18.0 (Statistical Package for Social Sciences, SPSS, Chicago, Illinois, USA). A p-value <0.05 was considered significant. Unadjusted analyses were done and variables with a p value <0.1 were included in the subsequent multiple regression models. Risk-adjustment was performed for surgical approach, age, gender, social deprivation index, pre-operative co-morbidities and year of discharge. Subgroup analyses were carried out using Chi squared test and Mann Whitney U test for categorical and continuous variables respectively.

3.2.3. Results

During the study period 7,502 patients underwent an oesophagectomy for cancer. Non-elective operations and patients under the age of 18 years were excluded.

Demographics

Three quarters of the patients were male (n=5762, 76.8%). Carstairs index was used to determine the degree of social deprivation using the patients' postcode. Only 0.4% of the patients were missing this information. 20.9% of patients belonged to least deprived areas. Overall 3,392 (45.2%) patients had at least one pre-operative co-morbidity, the majority of these being cardiorespiratory. Demographic details have been enumerated in Table 8.

Short term outcomes

Median length of stay was 15 days (IQR 12-22 days). 1,036 (13.8%) patients had an unplanned admission within 28 days. Overall 30-day in-hospital mortality was 4.3% (320/7502). 30-day medical morbidity rate was 39.0%. The majority of the complications were pertaining to the respiratory system (Tables 9 and 10). Any procedure which was surgical, endoscopic or radiological, undertaken within 30 days of oesophagectomy was classified as a re-intervention. This includes laparotomy/thoracotomy, wound debridement, drainage of abscess, pleural drainage etc. 18.1% patients had a re-intervention and 457 (6.1%) of patients underwent a re-operation. Details of the various re-interventions have been enumerated in Table 10.

Table 8: Descriptive characteristics of patients undergoing oesophagectomy for cancer
(April 2005 - March 2010)

	n=7502	(%)
Age		
<60 years	2250	(30.0)
60-70 years	3226	(43.0)
>70 years	2026	(27.0)
Gender		
Male	5762	(76.8)
Female	1740	(23.2)
Carstairs Index		
(least deprived) 1	1571	(20.9)
2	1763	(23.5)
3	1688	(22.5)
4	1388	(18.5)
(most deprived) 5	1060	(14.1)
Unclassified	32	(0.4)
Co-morbidities		
Cardiac	2634	(35.1)
Respiratory	923	(12.3)
VTE	196	(2.6)
Stroke	43	(0.6)
Renal Failure	68	(0.9)
Diabetes	688	(9.2)

Table 9: Unadjusted short term outcomes, within 30 days of oesophagectomy

Outcomes	n=7502	(%)
Mortality		
30-day, in-hospital	320	(4.3)
Medical Morbidity		
Cardiac	979	(13.0)
Respiratory	2339	(31.2)
VTE	149	(2.0)
Stroke	16	(0.2)
Renal Failure	143	(1.9)
Surgical Complications		
Re-intervention	1359	(18.1)
Re-operation	457	(6.1)
Readmission		
Within 28 days	1036	(13.8)
Length Of Stay, median (IQR)	15 days	(12-22)

Table 10: Frequencies of complications after oesophagectomy for cancer

Complication	n=7502	(%)
Morbidity		
Angina	215	(2.9)
Myocardial Infarction	49	(0.7)
Congestive Cardiac Failure	68	(0.9)
Atrial Fibrillation	713	(9.5)
Pneumonia	1411	(18.8)
Pleural Effusion	1174	(15.6)
Respiratory Failure	284	(3.8)
Other Respiratory Complications[@]	247	(3.3)
Deep Vein Thrombosis (DVT)	45	(0.6)
Pulmonary Embolism (PE)	111	(1.5)
Stroke	16	(0.2)
Renal Failure	143	(1.9)
Re-intervention		
Laparotomy	181	(2.4)
Thoracotomy	351	(4.7)
Minimally invasive surgery	30	(0.4)
Endoscopy	479	(6.4)
Radiology guided procedure	338	(4.5)

**Other Respiratory=Acute Exacerbation of COPD, Pulmonary Oedema, Post-procedural respiratory complications*

Risk-adjusted outcomes

Univariate analyses showed that surgical approach, gender, social deprivation and year of discharge (financial year) were not significant determinants of 30-day mortality. Risk-adjusted multiple regression analyses were undertaken for 30-day mortality and morbidity. Advancing age (>70 years: OR 2.55, 95%CI 1.86-3.50, p<0.001), cardiac co-morbidity (OR 1.38, 95%CI 1.09-1.74, p=0.007) and re-intervention (OR 3.05, 95%CI 2.42-3.86, p<0.001) were independent determinants of mortality. Patients with previous cardiac morbidity had a 38% higher risk of mortality while those who underwent a re-intervention had three times the risk of 30-day mortality. Advancing age was an independent determinant for post-operative cardiac complications and renal failure. Patients with pre-operative venous thrombo-embolism had twelve times higher risk of having a post-operative venous thrombo-embolism. A re-intervention was associated with higher risk of post-operative medical complications, especially respiratory (OR 6.87, 95% CI 6.03-7.82, p<0.001) and renal failure (OR 6.63, 95% CI 4.70-9.34, p<0.001).

Table 11: Logistic regression analysis for 30-day in-hospital mortality following oesophagectomy

Variable	Unadjusted analysis			Multiple regression analysis		
	OR	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Surgical Approach						
Open	1.00					
MIO	0.92	(0.67, 1.27)	0.605			
Age			***<0.001***			<0.001
<60 years	1.00			1.00		
60-70 years	1.41	(1.03, 1.94)	0.034	1.30	(0.94, 1.79)	0.111
>70 years	2.82	(2.07, 3.84)	<0.001	2.55	(1.86, 3.50)	<0.001
Gender						
Male	1.00					
Female	1.03	(0.79, 1.34)	0.810			
Carstairs Index			0.354			
1	1.00					
2	1.26	(0.88, 1.81)	0.208			
3	1.42	(0.99, 2.02)	0.057			
4	1.41	(0.97, 2.05)	0.070			
5	1.48	(1.00, 2.19)	0.053			
Unclassified	1.95	(0.45, 8.37)	0.370			
Pre-operative Co-morbidities						
Absence of comorbidity	1.00					
Cardiac	1.60	(1.28, 2.01)	***<0.001***	1.38	(1.09, 1.74)	0.007
Respiratory	1.27	(0.93, 1.74)	0.134			
VTE	0.83	(0.39, 1.77)	0.627			
Stroke	0.53	(0.07, 3.88)	0.535			
RenalFailure	1.79	(0.72, 4.49)	0.212			
Diabetes	1.35	(0.96, 1.92)	0.088			
Re-intervention	3.09	(2.45, 3.90)	***<0.001***	3.05	(2.42, 3.86)	<0.001
Discharge Year			0.267			
2005	1.00					
2006	0.82	(0.57, 1.18)	0.284			
2007	1.00	(0.70, 1.42)	0.996			
2008	1.20	(0.86, 1.69)	0.285			
2009	0.91	(0.63, 1.31)	0.594			

Table 12: Multiple regression analysis for 30-day medical morbidity according to organ system involvement

Variables	Cardiac			Respiratory			VTE			Stroke			Renal Failure		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Surgical Approach			0.089			0.049			0.815			0.714			0.123
Open	1.00			1.00			1.00			1.00			1.00		
MIO	0.84	(0.69, 1.03)	0.089	0.86	(0.74, 1.00)	0.049	0.95	(0.60, 1.49)	0.815	0.76	(0.17, 3.36)	0.714	0.66	(0.40, 1.12)	0.123
Age			<0.001			0.226			0.117			0.185			<0.001
<60 years	1.00			1.00			1.00			1.00			1.00		
60-70 years	2.02	(1.65, 2.46)	<0.001	1.09	(0.96, 1.24)	0.206	1.44	(0.94, 2.21)	0.093	6.95	(0.88, 55.10)	0.066	1.60	(0.95, 2.67)	0.075
>70 years	2.91	(2.37, 3.58)	<0.001	1.13	(0.98, 1.31)	0.093	1.61	(1.01, 2.56)	0.045	5.68	(0.65, 49.80)	0.117	2.89	(1.73, 4.82)	<0.001
Gender			0.543			0.033			0.711			0.129			0.112
Male	1.00			1.00			1.00			1.00			1.00		
Female	0.95	(0.81, 1.12)	0.543	1.15	(1.01, 1.30)	0.033	1.07	(0.74, 1.57)	0.711	0.21	(0.03, 1.58)	0.129	0.71	(0.46, 1.08)	0.112
Carstairs Index			0.090			0.004			0.963			0.525			0.432
1	1.00			1.00			1.00			1.00			1.00		
2	0.91	(0.74, 1.13)	0.404	0.85	(0.72, 1.00)	0.046	0.84	(0.51, 1.37)	0.474	1.28	(0.28, 5.77)	0.751	1.46	(0.86, 2.47)	0.161
3	1.11	(0.90, 1.37)	0.316	0.87	(0.74, 1.02)	0.085	0.89	(0.54, 1.46)	0.639	0.62	(0.10, 3.71)	0.598	1.24	(0.73, 2.13)	0.425
4	1.17	(0.94, 1.45)	0.168	1.04	(0.88, 1.22)	0.683	0.99	(0.59, 1.65)	0.969	0.79	(0.13, 4.78)	0.798	1.02	(0.56, 1.86)	0.940
5	1.21	(0.96, 1.53)	0.114	1.17	(0.98, 1.39)	0.094	0.80	(0.45, 1.45)	0.469	2.61	(0.61, 11.11)	0.194	1.68	(0.95, 2.95)	0.075
Unclassified	0.54	(0.16, 1.82)	0.317	1.10	(0.50, 2.41)	0.822	0.00	(0, 0)	0.998	0.00	(0, 0)	0.998	1.01	(0.13, 7.98)	0.994
Pre-operative Co-morbidities															
Cardiac	1.75	(1.52, 2.02)	<0.001	1.02	(0.91, 1.15)	0.714	0.81	(0.56, 1.17)	0.253	0.96	(0.34, 2.73)	0.938	1.75	(1.22, 2.50)	0.002
Respiratory	1.09	(0.89, 1.33)	0.399	1.38	(1.18, 1.61)	<0.001	1.07	(0.66, 1.72)	0.783	1.40	(0.39, 5.03)	0.605	1.13	(0.71, 1.80)	0.595
VTE	0.77	(0.48, 1.22)	0.261	0.97	(0.69, 1.35)	0.832	12.63	(8.26, 19.32)	<0.001	0.00	(0, 0)	0.996	0.50	(0.12, 2.07)	0.339
Stroke	0.68	(0.26, 1.76)	0.428	1.59	(0.82, 3.08)	0.175	2.60	(0.61, 11.12)	0.199	0.00	(0, 0)	0.998	2.78	(0.81, 9.53)	0.105
Renal Failure	1.29	(0.69, 2.41)	0.428	0.98	(0.56, 1.71)	0.945	0.57	(0.08, 4.28)	0.581	0.00	(0, 0)	0.997	4.09	(1.52, 10.98)	0.005
Diabetes	0.85	(0.67, 1.07)	0.167	1.07	(0.89, 1.29)	0.500	0.89	(0.48, 1.65)	0.710	1.82	(0.49, 6.85)	0.374	1.23	(0.74, 2.03)	0.434
Re-intervention	2.22	(1.90, 2.60)	<0.001	6.87	(6.03, 7.82)	<0.001	1.67	(1.15, 2.44)	0.008	2.81	(1.01, 7.79)	0.048	6.63	(4.70, 9.34)	<0.001

3.3 Gastrectomy

Recent years have seen a decline in the incidence of gastric cancer, but it is still responsible for around 3% of cancer deaths in the UK (Cancer Research UK, 2013b). Improvements in lifestyle and management of Helicobacter pylori colonisation have contributed to the decrease in the incidence of stomach cancer, especially in the West (Ferlay et al., 2010). Several strategies such as extended lymphadenectomy (Birkmeyer et al., 2006, Chang and Birkmeyer, 2006, Hanna et al., 2012) the use of perioperative chemotherapy/ chemoradiotherapy (Birkmeyer et al., 2003, Macdonald et al., 2001) and centralisation of surgical services for upper gastrointestinal cancer (Anderson et al., 2011) have improved the outcomes after gastric cancer resection. However outcomes have been demonstrated to be better in the Far East such as Japan and Korea as compared to the West (Strong et al., 2010). Possible explanation may be the variations in tumour site/stage, chemo-radiotherapeutic strategies, aggressive/extensive surgery and caseload. To date there have been no published papers on national outcomes in England following gastric resection for cancer. This study aimed to quantify the medical and surgical morbidity following elective gastrectomy and also examine the introduction of minimally invasive gastrectomy in England.

3.3.1. Methods

All patients that underwent an elective or planned gastrectomy (partial and total) in English NHS Trust hospitals between April 2000 and March 2010 were included. Data were obtained from Hospital Episode Statistics (HES) and retrospectively analysed. Admissions up to five years prior to surgery were examined and organ system specific co-morbidity status was determined using appropriate ICD-10 diagnosis codes (Table 1, Chapter 2). Various codes representing chronic conditions were used to distinguish co-morbidity from complications. Following discharge, unplanned admissions were studied to identify post-operative morbidity.

3.3.2 Outcome variables and statistical methodology

Length of Stay (LOS) and readmission rate were derived for each patient from the HES database. Median LOS in days with interquartile range (IQR) is reported. Unplanned admissions within twenty-eight days of discharge were classified as a readmission. Linkage to the Office for National Statistics provides 30-day in-hospital mortality. Morbidity and re-intervention have been used as markers to represent medical and surgical complications. Post-operative medical morbidity was identified from the secondary diagnosis fields of the index admissions and the primary diagnosis codes from any subsequent unplanned admissions within thirty days of surgery (Table 1, Chapter 2). Complications were grouped according to involvement of an organ system. ICD-10 codes which represent acute conditions were used to identify medical morbidity and those that are used to code chronic conditions were considered as co-morbidities. Re-intervention was defined as any unplanned return to theatre (re-operation) or procedure such as an endoscopy or radiology guided procedure (e.g. drain) during the index admission or within 30 days of initial surgery (HES records the dates of all procedures). Re-intervention on the same day as the index surgery could not be identified due to limitations of the dataset.

A p-value <0.05 was considered significant. Chi squared test was used to determine significance for non-normally distributed, categorical data in unadjusted analyses. Regression modelling used the following variables: surgical approach, age, gender, social deprivation, pre-operative co-morbidities and year of discharge. Variables with a significance of p<0.1 on unadjusted analyses were entered into a multiple regression model. Mann Whitney U test was used for comparing Length of Stay (LOS).

3.3.3. Results

From the database, 10,713 patients were identified who underwent an elective gastrectomy, of which two in three patients were male. Majority of the patients were elderly and aged >70 years (Table 13). Cardiorespiratory conditions and diabetes were the most common co-morbidity coded.

Short term outcomes

Overall 30-day in-hospital mortality was 5.5% (594/10,713). Median length of stay was 14 days (IQR 11-19 days). Respiratory complications were most common after a gastrectomy (13.5%) and almost a quarter of the patients had at least one complication post-operatively. Detailed descriptions of complications and short term outcomes have been shown in Table 14. Eight hundred and thirty-two (7.8%) patients underwent a re-intervention within thirty days of surgery. Of these, 431 (4.0%) patients had a re-operation (laparotomy or a subsequent procedure for wound related complications).

Risk-adjusted outcomes

Multiple regression analyses showed that advancing age and male gender were associated with a higher risk of mortality (Table 15). Similarly patients with a pre-operative cardiac (OR 1.30, 95%CI 1.04-1.86, p=0.028) and respiratory (OR 1.62, 95%CI 1.14-2.29, p=0.007) co-morbidity were associated with a significantly higher risk of 30-day mortality. The presence of a re-intervention increased the risk of mortality by fivefold (OR 5.35, 95%CI 3.90-7.33, p <0.001).

Table 13: Descriptive characteristics of patients undergoing gastrectomy for cancer *(April 2000 - March 2010)*

	n=10,713	(%)
Age		
<60 years	1,784	(16.7)
60-70 years	3,319	(31.0)
71-80 years	4,338	(40.5)
>80 years	1,272	(11.9)
Gender		
Male	7,007	(65.4)
Female	3,706	(34.6)
Carstairs Index		
(least deprived) 1	1,450	(13.5)
2	2,141	(20.0)
3	2,304	(21.5)
4	2,356	(22.0)
(most deprived) 5	2,447	(22.8)
Unclassified		
Co-morbidities	3,628	(33.9)
Cardiac	1,237	(11.5)
Respiratory	183	(1.7)
VTE	116	(1.1)
Stroke	119	(1.1)
Renal Failure	996	(9.3)
Diabetes	1,784	(16.7)

VTE = venous thrombo-embolism

Table 14: Unadjusted short term outcomes, within 30 days of gastrectomy

Outcomes	**n=10,713**	**(%)**
Mortality		
30-day, in-hospital	594	(5.5)
Medical Morbidity	2,431	(22.7)
Cardiac	1,172	(10.9)
Respiratory	1,442	(13.5)
VTE	101	(0.9)
Stroke	37	(0.3)
Renal Failure	155	(1.4)
Surgical Complications		
Re-intervention	832	(7.8)
Re-operation	431	(4.0)
Readmission		
Within 28 days	1,098	(10.2)
Length Of Stay, median (IQR)	14 days	(11-19)

Table 15: Unadjusted and multiple logistic regression analyses for 30-day medical mortality following elective gastrectomy

Variable	Unadjusted analysis			Multiple regression analysis		
	OR	95% CI	p value	OR	95% CI	p value
Surgical Approach			0.461			
OG	(Ref)					
LG	0.85	(0.56-1.31)	0.461			
Age			<0.001			<0.001
<60 years	(Ref)			(Ref)		
60-70 years	2.25	(1.52-3.33)	<0.001	2.01	(1.36-2.99)	<0.001
71-80 years	4.13	(2.84-5.97)	<0.001	3.67	(2.52-5.31)	<0.001
>80 years	6.07	(4.09-9.01)	<0.001	5.42	(3.64-8.08)	<0.001
Gender			0.007			0.007
Male	(Ref)			(Ref)		
Female	0.78	(0.65-0.93)	0.007	0.84	(0.76-0.93)	0.001
Carstairs Index			0.224			
1 (least deprived)	(Ref)					
2	0.75	(0.56-1.02)	0.064			
3	0.81	(0.60-1.08)	0.144			
4	1.11	(0.84-1.46)	0.465			
5 (most deprived)	1.06	(0.80-1.39)	0.696			
Pre-operative Comorbidities						
Absence of specific comorbidity	(Ref)					
Cardiac	1.48	(1.25-1.75)	<0.001	1.21	(1.01-1.45)	0.038
Respiratory	1.77	(1.42-2.20)	<0.001	1.57	(1.25-1.97)	<0.001
VTE	1.40	(0.74-2.32)	0.354			
Stroke	2.98	(1.77-5.02)	<0.001	2.41	(1.41-4.12)	0.001
Renal Failure	2.69	(1.58-4.59)	<0.001	2.07	(1.19-3.58)	0.010
Diabetes	1.24	(0.86-1.48)	0.401			
Discharge Year			<0.001			<0.001
2000-2003	(Ref)			(Ref)		
2004-2006	0.69	(0.56-0.85)	<0.001	0.65	(0.53-0.)	<0.001
2007-2009	0.64	(0.51-0.79)	<0.001	0.59	(0.47-0.73)	<0.001

Table 16: Frequencies of complications after gastrectomy for cancer

Complication	n=10,713	(%)
Morbidity		
Angina	535	(5.0)
Myocardial Infarction	119	(1.1)
Congestive Cardiac Failure	194	(1.8)
Atrial Fibrillation	445	(4.2)
Pneumonia	905	(8.4)
Pleural Effusion	525	(4.9)
Respiratory Failure	250	(2.3)
Other Respiratory Complications[@]	190	(1.8)
Deep Vein Thrombosis (DVT)	43	(0.4)
Pulmonary Embolism (PE)	66	(0.6)
Stroke	37	(0.3)
Renal Failure	155	(1.4)
Re-intervention		
Laparotomy	408	(3.8)
Wound complications	194	(1.8)
Endoscopy	229	(2.1)
Radiology guided procedure	291	(2.7)

3.4 Discussion

This population based study has examined, from a national database, outcome following three major gastrointestinal resections: colorectal resection, oesophagectomy and gastrectomy. I was able to identify medical and surgical morbidity or complications and quantify perioperative outcomes following planned gastrointestinal resection in England. Broadly speaking, the outcomes are comparable to those previously reported in literature.

Traditionally, following colorectal surgery, studies have reported morbidity rates in the range of 24-30% (Stratton et al., 2006, Tan et al., 2011). Studies from large databases, such as the NSQIP database from the United States have shown overall morbidity rates of 24-25% (Matthews et al., 2006, Fowke et al., 2006). Our study has shown an overall medical morbidity rate of 14.6%. Although one has to bear in mind that the NSQIP database is maintained by trained nurses and a large number of variables pertaining to complications of all levels of severity are input as compared to an administrative database such as HES. Recent advances such as use of laparoscopic colorectal surgery and increasing use of enhanced recovery pathways would have contributed to an improvement in perioperative outcomes, but to discern this is beyond the scope of this study. Further detailed scrutiny of variation in outcomes between open and laparoscopic surgery has been undertaken and reported in Chapter 6.

Outcomes following upper-gastrointestinal resection from HES data are comparable to the National Oesophago-Gastric Cancer Audit report from 2009 (NHS Information centre, 2009). This report quoted 30-day mortality rates of 3.2% and 4.2% for oesophagectomy and gastrectomy respectively. The mortality figures from the current study (4.3% for oesophagectomy and 5.5% for gastrectomy) include data which are not restricted to voluntary submission by units. The mortality following oesophagectomy in 2002-2003 was 7.6% and the same in 1997-1999 was 11.7% (Al-Sarira et al., 2007). Thus this study has shown an improvement in outcomes following oesophagectomy, reflecting increasing experience of surgeons and improvement in post-operative care setup such as intensive care units. This bears evidence to the success of the process of centralisation of upper gastrointestinal services in the UK. Outcomes from the East, following gastrectomy have traditionally been superior as compared to the UK and the current study ratifies this. Literature review has shown studies from Japanese and Korean centres reporting short term mortality rates of 0-1.6% and complication rates of 13-19% (Hwang et al., 2009, Jeong et al., 2009, Kim et al., 2010, Kim et al., 2008, Kuwabara et al., 2011). Alternatively reports from United States have demonstrated mortality rates of 6-7.6% and morbidity rates as high as 33.3%. The results from England, as shown in this study, are intermediate, with a mortality rate of 4.6% and morbidity rate of 25.6%. One must however tread cautiously while comparing outcomes from national databases to those from case series. There is increasing evidence demonstrating the safety of minimally invasive oesophagectomy and gastrectomy. Although the UK has limited experience, we have reported outcomes following minimally invasive upper gastrointestinal resection (oesophagectomy and gastrectomy) in Chapter 6.

CHAPTER 4: WHAT IS THE IDEAL MORTALITY MEASURE?

Understanding endpoints of health services, taking into account patients' experiences, preferences and values with a view to provide scientific evidence relating to decision making in the healthcare system is vital for any improvement in quality of health services. This has collectively been termed as 'Outcomes Research' (Clancy and Eisenberg, 1998). However there is a wide variation in the choice of outcome measures that units/professionals choose to report and a wide variation in the propensity for individuals to report outcomes. This makes it difficult for policy makers to compare service providers in a healthcare system or to generate meaningful global comparisons between different heath systems. Almoudaris and colleagues demonstrated that in England, those units that voluntarily submitted data to a colorectal cancer registry had better outcomes that those that did not submit (Almoudaris et al., 2011a). Although it is easy to assume that units with better outcomes would normally choose to submit data or report their outcome, it may well follow on that if outcome reporting were made compulsory, there may be an improvement in quality of service provision in order for units to be comparable to peers.

Traditionally, mortality within thirty days of surgery, either in-hospital or in & out of hospital, is reported as a short term outcome measure. Studies looking at long term survival commonly report three or five year survival rates. More recently there has been a call to consider intermediate mortality outcomes as it has been perceived that significant mortality exits beyond the initial perioperative period and there may be an association with the surgical insult (Dekker et al., 2011, Visser et al., 2009). We proposed to study the published literature and analyse commonly reported outcome measures to ascertain any variation(/homogeneity) that is present. For this purpose we chose to study colorectal resection in the older population as a homogenous group of patients and undertook a literature review.

4a Which mortality measure is widely used in colorectal literature?

4a.1 Introduction

Why elderly and why colorectal resection?

The lack of consensus on definitions of outcome measures poses a challenge in assessing outcome, especially in a discreet cohort of patients such as the 'elderly'. Traditionally, patients over the age of 65 years have been termed 'elderly', however different studies have arbitrarily chosen the cut-off to be >70, >75 or even >80 years. The older patients pose a challenge to surgeons as they are not only physiologically different to the general younger population, but differ in their mode of presentation and stage of disease at presentation (Pofahl and Pories, 2003, Rosenthal and Kavic, 2004). An improvement in quality of healthcare and lifestyle changes over the years has resulted in greater life expectancy. Thus the number of elderly patients likely to present to a hospital is on the rise. In the UK, the population aged 75 years and over is nearly set to double from around 4.9 million in 2010 to 8.9 million in 2035 (Office for National Statistics, 2011).

Colorectal cancer is the fourth most commonly occurring cancer in the United Kingdom (Cancer Research UK, 2014). It accounted for 40,700 (12.5%) of all new cancers in 2010 and was responsible for over 15,000 deaths in the same year. Radical surgery with a curative intent is often the treatment of choice in the majority of colon cancers. More than eight out of ten cases of colorectal cancer are diagnosed in people over the age of 60 years

(Cancer Research UK, 2013a). Colorectal resections in the elderly are mostly performed for malignant diagnoses. Colorectal resections for benign causes however, such as diverticulosis or inflammatory bowel disease, are also accompanied by significant mortality and morbidity in older patients (Faiz et al., 2011). Currently there seems to be no definite consensus in the literature on whether age is an independent determinant of outcome following colorectal resection in the elderly. We undertook this study to define the postoperative mortality risk amongst elderly patients (aged 70 years or over) undergoing elective colorectal resection and to demonstrate at what time period post-operatively, measuring mortality is likely to be most meaningful.

4a.2 Methods

Two reviewers (RM and AA) undertook an electronic search of the EMBASE, MEDLINE and PUBMED databases for studies that reported mortality outcome in the elderly following elective or planned colorectal resection. All titles and abstracts of the studies returned by the search were assessed for relevance to the study question. Full text articles of included abstracts were then retrieved electronically and manually and all relevant data were extracted into a Microsoft Excel spreadsheet. The references from all included studies were reviewed. Studies that were not included in the primary search, but were relevant to the study question and fulfilled the inclusion and exclusion criteria were subsequently included as cross references. In any case of disagreement, arbitration was performed by a third author (OF). The detailed search terms have been described in Table 17. For the purpose of the literature search, limits were set for human subjects, English language and studies published in the year

2000 or later. The list of studies returned by the search was catalogued using EndnoteX3. Duplicates were removed at every level.

Inclusion and exclusion criteria

Studies were only included if they were published in or after the year 2000 and reported on mortality in the patients aged 70 years or above. Studies that did not explicitly state whether they included emergency admissions were included in the review. Articles in press and published online in English were also considered. Studies were excluded if they did not report mortality data. Those studies which included data from patients operated prior to 1995 were also excluded irrespective of when published. Articles that targeted the general population and did not target the elderly primarily were not included in the study, unless they reported mortality figures specific to an elderly subgroup. Journal correspondence and studies that included patients undergoing emergency surgery were excluded, unless they analysed emergency and elective patients separately. Studies with a sample size of less than thirty patients were also excluded.

Study outcome

Postoperative mortality rate was the principal outcome measure. This included 30-day mortality, ‘in-hospital mortality’, ’30-day in-hospital mortality’, and ’30-day in-and-out-of hospital mortality’. Mortality arising beyond the initial perioperative period (up to 1 year following surgery) was also reviewed. If studies did not report a mortality rate, but quoted numbers of deaths, the corresponding mortality rate (percentage) was calculated using the sample size.

4a.3 Results

The initial electronic search yielded 236 studies. The titles and abstracts were downloaded into EndNote and both reviewers (RM and AA) assessed them against the inclusion and exclusion criteria. At this stage 149 studies were excluded from the review. Of the exclusions, fifty-four studies included operations performed prior to 1995, eighteen studies included emergency resections and five studies had a sample size smaller than thirty. Other reasons for exclusion were as follows: twenty-three studies did not comment on mortality in the elderly patients and twelve studies included other types of surgery such as repair of rectal prolapse, formation or closure of stoma and concomitant gynaecological procedures. Thirty-two studies were not relevant to the study topic and 5 were letters/correspondence.

Full-text articles were retrieved electronically and manually for the remaining 87 abstracts. The two reviewers (RM and AA) agreed on all but 3 abstracts. Following a review by (OF), 2 abstracts were excluded and 1 was included into the study. Thirty of these studies did not report mortality specifically in the elderly cohort. Eight studies included other surgical procedures such as cholecystectomy and hernia repairs, seven studies included data prior to 1995 and five studies did not involve colorectal resection at all. Patients presenting as an emergency had been included in twenty three studies and these did not report separate outcome for emergency and elective surgery. The latter studies were consequently rejected.
Fourteen studies were included in the review. All the references of considered articles were reviewed and cross referenced and a further 35 potentially relevant studies were identified. Of these studies 32 were subsequently excluded because 21 referred to data collected prior to 1995, 7 included emergencies, 2 articles were not available in English and 2 studies were

reviews of papers excluded from the current study. Following cross referencing three studies were added to the previous inclusions and 17 articles were finally included in the review (see Figure 1). An in-depth description of the included studies, inclusion of patients, outcome measures investigated and mortality rate can be found in Table 18.

Studies included in the review

Two out of seventeen studies included in the review represented retrospective analyses of prospectively maintained databases (Faiz et al., 2011, Tan et al., 2007), one was a multicentre prospective study (Marusch et al., 2005) and two were case-matched series (Feng et al., 2006, Senagore et al., 2003b). Only one study included randomised patients (Frasson et al., 2008). Seven prospective studies reported outcome from a single centre (Araujo et al., 2007, Ceulemans et al., 2004, Kruschewski et al., 2007, Law et al., 2002, Kirchgatterer et al., 2005, Cheung et al., 2007, Fiscon et al., 2010) while the remaining four were retrospective studies (Basili et al., 2008, De Santis and Frigo, 2005, Gurevitch et al., 2009, Tei et al., 2009). All the patients included in the studies were ≥ 70 years of age. There were no randomised-control trials identified in this review.

The study by Faiz and colleagues had the largest sample size of 28,746 patients aged >75 years (Faiz et al., 2011). This was a population based study of elective colonic resections carried out in English NHS trust hospitals. They reported an overall 30-day in-hospital mortality rate of 5.4%. They also reported an intermediate mortality outcome measure in different age groups. 365-day mortality was 15.6% (75-79 years), 18.8% (80-84 years) and 23.3% (85-89 years) in the respective age groups.. A subgroup analysis was also reported in the over 90-year old patients. The 30-day and 365-day mortality for these patients were 10.1% and 26.2% for proximal and 12.9% and 36.1% for distal resections respectively. Another interesting finding in this study was the significantly lower mortality among the 865 patients who underwent laparoscopic surgery (3.1%, p<0.001). Tan and colleagues reported outcomes from the National Bowel Cancer Audit Project, a voluntary national clinical cancer registry serving England and Wales (Tan et al., 2007). This audit collects data from hospitals in the UK and aims to improve surgical outcomes and quality of care for patients. Their study included 11,494 patients aged 75 years or above. Overall 30-day in-and-out of hospital mortality in this study for colon and rectal resections was 7.2%. Similar mortality rates were demonstrated in octogenarians undergoing resection for colorectal cancer in a multicentre German study (Marusch et al., 2005). Postoperative in-hospital mortality in the latter study was 6.3% for elective cases.

Ten studies reported outcomes following laparoscopic colorectal resection in the elderly (Ceulemans et al., 2004, De Santis and Frigo, 2005, Faiz et al., 2011, Feng et al., 2006, Frasson et al., 2008, Law et al., 2002, Senagore et al., 2003b, Cheung et al., 2007, Fiscon et al., 2010, Tei et al., 2009), of which six studies compared the minimally invasive approach to traditional open surgery (Faiz et al., 2011, Feng et al., 2006, Frasson et al., 2008, Law et al., 2002, Senagore et al., 2003b, Tei et al., 2009). All of these patients were aged 70 years or above. Ceulemans *et al,* (2004, n=41), De Santis *et al*, (2005, n=81) and Fiscon *et al*, (2010, n=81) reported no deaths in their respective series of elderly patients (age ≥75 years) undergoing laparoscopic colorectal resections (Ceulemans et al., 2004, De Santis and Frigo, 2005, Fiscon et al., 2010). Similarly Feng and Senagore, in their respective case-matched studies, reported no mortality in the elderly group that underwent minimal access surgery (sample sizes n=51 and n=50 respectively) (Feng et al., 2006, Senagore et al., 2003b). Law and colleagues (2002) observed lower mortality in their laparoscopic patient group while Frasson and co-workers (2008) reported a higher mortality amongst patients treated using laparoscopy when compared with elderly patients that underwent open resection (Frasson et al., 2008, Law et al., 2002) Overall, however the mortality recorded by Frasson and colleagues, even within the laparoscopic group, was low (2.2%). A study evaluating surgery for primary rectal cancer by Kruchewski and co-workers investigated 276 patients, of which 53 were aged above 75 years (Kruschewski et al., 2007). Postoperative mortality in this group was 3.8%. They identified nicotine abuse and coronary heart disease to be associated with poor outcome such as anastomotic leak and mortality. Basili and co-workers studied a series of patients who underwent elective and emergency colorectal resection for cancer (Basili et al., 2008). The patients were classified into two age groups and results of elective and emergency surgery were presented separately. The outcome measure was perioperative death or death within 30 days of surgery. For elective surgery, 30-day mortality rate was 3.1% for patients aged 75 years and above. In subgroup analysis they reported mortality rates of 4.4% (n=4/90) in patients aged 75-84 years and 12.5% (n=3/24) in patients aged 85 years or above. There was no mortality in the 66-74 age group. Araujo and colleagues (Araujo et al., 2007) examined outcome in a cohort of 90 patients aged 75 and above, the operative mortality was 13.3%. Single centre studies by Tei *et al* (Tei et al., 2009), Gurevitch (2009) (Gurevitch et al., 2009), Kirchgatterer (2005) (Kirchgatterer et al., 2005) and Cheung (2007) (Cheung et al., 2007) reported 0-3% mortality in octogenarians undergoing planned surgery for colorectal cancer.

Table 17: Search terms used for literature review

1	general surgery
2	surgery
3	colorectal surgery
4	**1 OR 2 OR 3**
5	colectomy
6	hemicolectomy
7	anterior resection
8	pouch
9	perineal excision
10	abdominoperineal excision
11	abdominoperineal resection
12	**5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11**
13	elective
14	scheduled
15	planned
16	**13 OR 14 OR 15**
17	elderly
18	geriatric
19	aged
20	**17 OR 18 OR 19**
21	mortality
22	death
23	**21 OR 22**
24	**4 AND 12 AND 16 AND 20 AND 23**

Table 18: Description and results of studies included in the review

First Author (Year)	Type of study		Study Dates	Diagnosis	Approach	Sample Size	Age	Mortality (%)	
Faiz (2010)(Faiz et al., 2010a)	Population database	national	April 1996 - March 2007	M	Lap	865	>75	3.1	30-day in-hospital mortality
					Open	27881	>75	5.4	
Tan (2007)(Tan et al., 2007)	Clinical registry	national	March 2000 - April 2005	M	NS	11494	>=75	7.2	30-day in and out of hospital mortality
Marusch (2005)(Marusch et al., 2005)	Prospective	multicentre	January 2000 - December 2001	M	NS	2374	>=80	6.3	post-operative, in-hospital mortality
Frasson (2008)(Frasson et al., 2008)	Prospective, randomised	single centre	NR	B,M	Lap	89	>=70	2.2	post-operative mortality
					Open	112	>=70	0.9	
Senagore (2003)(Senagore et al., 2003b)	Case-matched	single centre	March 1999 - December 2001	B,M	Lap	50	>=70	0.0	operative mortality
					Open	123	>=70	1.6	
Feng (2006)(Feng et al., 2006)	Case-matched	single centre	January 2003 - October 2004	M	Lap	51	>70	0.0	post-operative mortality
					Open	102	>70	2.0	
Law (2002)(Law et al., 2002)	Prospective, cohort	single centre	June 2000 - December 2001	B,M	Lap	65	>=70	1.5	30-day mortality
					Open	89	>=70	5.6	
Cheung (2007)(Cheung et al., 2007)	Prospective, cohort	single centre	July 1996 - June 2006	M	Lap	101	>=80	3.0	30-day mortality
Araujo (2007)(Araujo et al., 2007)	Prospective, cohort	single centre	January 1995 - January 2002	M	Open	90	>=75	13.3	in-hospital or 30-day mortality
Fiscon (2010)(Fiscon et al., 2010)	Prospective, cohort	single centre	June 2005 - January 2009	M	Lap	81	>=75	0.0	
Kirchgatterer (2005)(Kirchgatterer et al., 2005)	Prospective	single centre	January 1995 - December 2002	M	NS	54	>80	2.0	in-hospital mortality
Kruchewski (2007)(Kruschewski et al., 2007)	Prospective	single centre	January 1995 - December 2004	M	Open	53	>75	3.8	post-operative mortality
Ceulemans (2004)(Ceulemans et al., 2004)	Prospective, cohort	single centre	January 2000- June 2001	B,M	Lap	41	>=75	0.0	30-day mortality
Basili (2008)(Basili et al., 2008)	Retrospective	single centre	July 2003- December 2005	M	NS	134	75-84	4.4	30-day mortality
							>=85	12.5	
Tei (2009)(Tei et al., 2009)	Retrospective	single centre	January 2004 - December 2007	M	Lap	51	>70	2.0	perioperative mortality
					Open	78	>70	0.0	
DeSantis (2005)(De Santis and Frigo, 2005)	Retrospective	single centre	June 2002 - May 2005	B,M	Lap	81	>75	0.0	
Gurevitch (2009)(Gurevitch et al., 2009)	Retrospective	single centre	January 2001 - December 2006	M	NS	28	>=80	0.0	in-hospital or 30-day mortality

Diagnosis: M=Malignant, B=Benign ; Approach: Lap=Laparoscopic; NR=Not recorded; NS=Not specified

Table 19: Description of study types and patient selection criteria.

First Author	Reference	Type of study		Patient Inclusion
Faiz	(Faiz et al., 2010a)	Population database	national	Compulsory routinely collected national administrative database-no selection used
Tan	(Tan et al., 2007)	Clinical registry	national	Voluntary submission of cases to registry
Marusch	(Marusch et al., 2005)	Prospective	multicentre	Voluntary submission to prospective database
Frasson	(Frasson et al., 2008)	Prospective, randomised	single centre	Selected series on basis of clinical and pathological criteria
Senagore	(Senagore et al., 2003b)	Case-matched	single centre	Selected series on basis of BMI and previous abdominal surgery
Feng	(Feng et al., 2006)	Case-matched	single centre	Selected and matched series on basis of clinical and pathological criteria
Law	(Law et al., 2002)	Prospective, cohort	single centre	Selected series on basis of operative intent and previous colorectal cancer
Cheung	(Cheung et al., 2007)	Prospective, cohort	single centre	Selected series from prospective database on basis of clinical and pathological criteria
Araujo	(Araujo et al., 2007)	Prospective, cohort	single centre	Selected series based on age
Fiscon	(Fiscon et al., 2010)	Prospective, cohort	single centre	Selected series
Kirchgatterer	(Kirchgatterer et al., 2005)	Prospective	single centre	Series from prospective database (selection criteria not specific)
Kruchewski	(Kruschewski et al., 2007)	Prospective	single centre	Selected series (reoperations excluded)
Ceulemans	(Ceulemans et al., 2004)	Prospective, cohort	single centre	Consecutive series selected based on co-morbidity and previous surgery
Basili	(Basili et al., 2008)	Retrospective	single centre	Case series unselected
Tei	(Tei et al., 2009)	Retrospective	single centre	Consecutive series (T4 tumours excluded from laparoscopy arm)
DeSantis	(De Santis and Frigo, 2005)	Retrospective	single centre	Selected series
Gurevitch	(Gurevitch et al., 2009)	Retrospective	single centre	Case series (selection criteria not explicit)

4a.4 Discussion

This review identified significant variation in reported mortality rates among studies published in the first decade of this century investigating the impact of elective colorectal resection on the elderly. At a glance, the results appear reassuring when considering surgery in this potentially vulnerable group, however most studies represented single centre series with small patient numbers. The latter studies mostly reported lower mortality rates in the perioperative period than national audits derived from national administrative or registry sources. Moreover, the largest study in this analysis that utilised routinely-collected data from England identified that a large number of deaths occurred in the elderly cohort undergoing elective colonic surgery beyond the immediate perioperative period. Under such circumstances short term postoperative mortality measures may be falsely reassuring.

Variation in mortality rates

An obvious explanation for the variation seen in this review would be differences in case-mix, operative techniques, chemotherapeutic strategies, cancer staging and time to presentation. In spite of the above, one cannot ignore the differences in sample sizes between single centre case series and database analyses. Two national English outcome audits; a population based study by Faiz and colleagues (Faiz et al., 2011) (sample size 28,746) and a registry analysis by Tan and co-workers (Tan et al., 2007) (sample size 11,494) were the largest studies included and quoted 30-day mortality rates of 5.4% and 7.2% respectively. On the other hand, studies that reported no mortality in their elderly groups comprised fewer than hundred patients (Ceulemans et al., 2004, De Santis and Frigo, 2005, Feng et al., 2006, Fiscon et al., 2010, Gurevitch et al., 2009, Senagore et al., 2003b). This leads to heterogeneity amongst the included studies, making it impossible to undertake a meta-analysis. Hence caution should be exercised when interpreting results from small case series as these may not be truly representative of the general population. Variability has also been noticed in the definition of the 'elderly', but >= 70 years has generally been used to define this cohort of patients.

Is 30-day mortality an appropriate measure of risk?

Almost all of the studies included in this review reported 30-day mortality or post-operative mortality. Modern post-operative care including high dependency and intensive care may see the patient through the initial surgical insult, only to succumb at a later stage. Faiz *et al* showed a doubling of mortality in the eleven months that followed surgery as compared to the 30-day mortality (Faiz et al., 2011). Similarly Kirchgatterer reported survival rates of 88%, 49% and 44% at 1, 3 and 5 years respectively in elderly patients operated for colorectal cancer (Kirchgatterer et al., 2005). Thus a low 30-day or post-operative mortality, although seemingly acceptable, is not a true reflection of the post-operative journey of the elderly patient. In 2009, Visser and colleagues demonstrated from American data that mortality almost doubled at 90 days following colorectal surgery (Visser et al., 2009). Dekker and colleagues in their analysis of a Dutch cancer registry highlight this further by showing a 16% excess mortality at one year when compared to 30 days(Dekker et al., 2011). There is no doubt that the 30-day mortality metric vastly underestimates true mortality. The deleterious effects of anaesthesia, surgery and post-operative morbidity are not limited to the immediate post-operative period, especially in the elderly. This calls for an intermediate term outcome measure of mortality as a true measure of risk.

Limitations of the study

As only literature published in English has been analysed, this gives rise to the possibility of bias. Furthermore it is not possible to account for cohorts that are unpublished due to 'poor results'. A desire to publish good results when institutional case series are submitted may underlie the extremely low mortality reported in most of the smaller studies. Highly competent clinicians may also be more predisposed to disseminating their results and therefore the literature that relates to institutional audits of outcome may not be representative of the broader context.

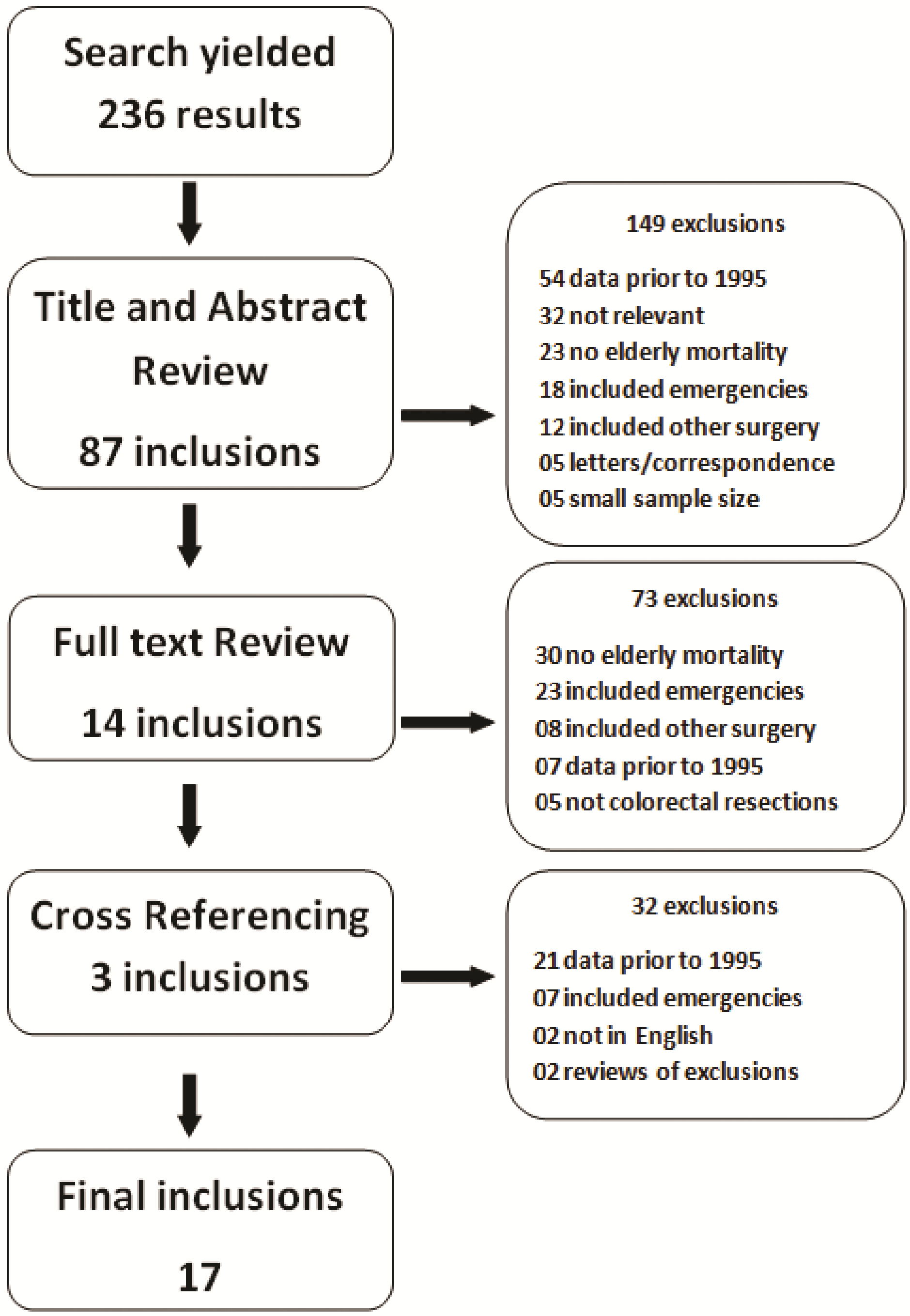


Figure 1: Schematic representation of included studies following literature search

4b Which mortality measure truly reflects perioperative risk following colorectal resection?

4b.1 Introduction

Postoperative mortality in colorectal surgery has been reported widely in the literature (Faiz et al., 2011, Panis et al., 2011, Visser et al., 2009). A thorough review of the published literature shows that by convention death is reported as a postoperative mortality when it occurs within thirty days of surgery (Charlson et al., 1987, Merkow et al., 2013, Morris et al., 2011b, Tekkis et al., 2004). There is increasing evidence that significant mortality occurs beyond the initial thirty day period in malignant as well as benign resections, both in the elective and emergency settings (Faiz et al., 2011, Mamidanna et al., 2012b). This finding appears to be more pronounced in certain vulnerable groups of patients. These include elderly patients and those patients with several, or severe, pre-existing medical co-morbidities that compromise the circulatory, respiratory or renal physiology (Mamidanna et al., 2012b, van Gestel et al., 2013).

It is difficult to ascertain whether mortality following surgery is directly attributable to the surgical or anaesthetic insult. As time passes by, mortality due to malignancy itself is expected. However immediate post-operative deaths are usually due to acute conditions such as cardiorespiratory failure. When studying intermediate term outcomes, especially deaths occurring beyond the initial thirty day period but within one year of surgery, it is important to understand what the patients are dying from. Generally speaking it would be considered a failure of surgery or decision making if planned surgery is not expected to improve survival beyond a few months. This study aimed to look at the timing of deaths following colorectal resection and the reported underlying cause of death in these patients.

The World Health Organization (WHO) defines the underlying cause of death as “the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury” (World Health Organization, 1994). Since 1st January 2001 the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10, WHO 1992–1994) has been used to classify cause of death in England and Wales (World Health Organization, Office for National Statistics, 2012b). In majority of the cases the cause of death is ascertained from the medical certificate of cause of death (MCCD). In a small number of cases, the cause of death is issued following a coroner’s inquest or a post mortem. The 'General Principle' followed while coding the underlying cause of death is that it is the lowest (last) of the causes of death entered into Part I of the certificate. For example, if the direct cause of death was 'Myocardial infarction' but the patient was known to have Ischaemic Heart Disease then in this simple case Myocardial infarction would be entered on line I(a) and Ischaemic heart disease on line I(b) and it would be Ischaemic heart disease which would be taken as the 'Underlying cause of death'. There are strict criteria laid down for labeling a particular condition as the underlying cause of death. In short the following rules are considered while coding the cause of death from a death certificate:

- *General Principle*

Select the condition entered alone on the lowest used line of Part I of the Death Certificate only if it could have given rise to all the conditions mentioned above it.

- *Rule 1*

If the general principle does not apply; is there a sequence terminating in the first condition entered? If so the originating cause of the sequence is selected as the UCD. If there is more than one sequence then the originating cause of the first named sequence is selected.

- *Rule 2*

If there is no reported sequence leading to the first named condition then the first named condition is selected as the UCD.

- *Rule 3*

If the condition selected by any of the General Principle, Rule 1, or Rule 2 is clearly a direct consequence of another reported condition, whether stated in Part I or Part II of the certificate, then this primary condition should be selected as the UCD.

Our study aims to analyse causes and timing of death in the immediate and intermediate postoperative period. This might facilitate objective preoperative patient stratification and selection, enable targeted optimisation and proactive postoperative management of 'at-risk' patient groups.

4b.2 Methods

Data were obtained from the Hospital Episode Statistics (HES) database. Patients undergoing colorectal resections in an English National Health Services (NHS) hospital between April 2001 and February 2007 were included. Linkage with Office for National Statistics (ONS) provided date and cause of death details. The

Office for National Statistics (ONS) is the United Kingdom (UK) Government's single largest statistical provider. ONS is the executive office of the UK Statistics Authority, a non-ministerial department which reports directly to Parliament. Linkage with the Hospital Episode Statistics data provides a range of information on economic, social and demographic statistics. In particular, we were interested in postoperative mortality data, both in-hospital and out-of-hospital mortality. Pre-operative co-morbidities were ascertained by grouping diagnosis codes from International Classification of Disease-10th revision (ICD-10)(World Health Organization, 1994) and the Charlson co-morbidity index was derived from these codes (Charlson et al., 1987).

Database inclusions and variable coding

Index cases were identified using the OPCS-4 codes for major colorectal resections. The procedures were grouped as **A) Subtotal/Total resection** - panproctocolectomy or total colectomy (H04, H05), subtotal colectomy (H29); **B) Right sided resections** - right hemicolectomy (H07), extended right hemicolectomy (H06) and transverse colectomy (H08); **C) Left sided resections** - left hemicolectomy (H09), sigmoid colectomy (H10) and **D) Rectal resections** - anterior resection (H332, H333, H334, H336, H338, H339), abdomino-perineal resection (H331) and Hartmann's resection (H335) (Hartmann's resection for elective surgery was predominantly for rectal pathology)

If a patient had more than one resection during the study period, their first resection was taken as the index resection. The indications for surgery were categorised as **A) malignant** (C18, C19, C20, C21) and **B) benign** [diverticulosis

(K57), inflammatory bowel disease (IBD) (Crohn's K50, Ulcerative colitis K51) and other diagnoses]. Age was subcategorised into <= 65 years, 66-75 years, 76-85 years and >85 years. Patients <18 years of age have been excluded from analyses.

Outcome variables

Mortality rates (in- and out-of-hospital) were calculated at 30 days, 60 days, 90 days, 6 months, 9 months, 1 year from date of surgery. Underlying cause of death diagnosis codes (ICD-10) obtained from linkage with ONS were grouped into the following categories: colorectal cancer (CRC), other malignancy, cardiac, respiratory, gastrointestinal, neurological and other causes.

Statistical methodology

Statistical analyses were carried out using SPSS Version 18.0 (Statistical Package for Social Sciences, SPSS, Chicago, Illinois, USA). For tests of significance, p-values <0.05 were considered significant. Categorical variables were investigated using the Chi-squared test.

4b.3 Results

During the study period (between April 2001 and February 2007), 171,791 patients were identified who underwent a colorectal resection in an NHS Trust hospital in England. Majority of these resections were undertaken as a planned (elective) surgery [112,639 (65.6%)] and 59,152 (34.4%) patients underwent a non-elective resection.

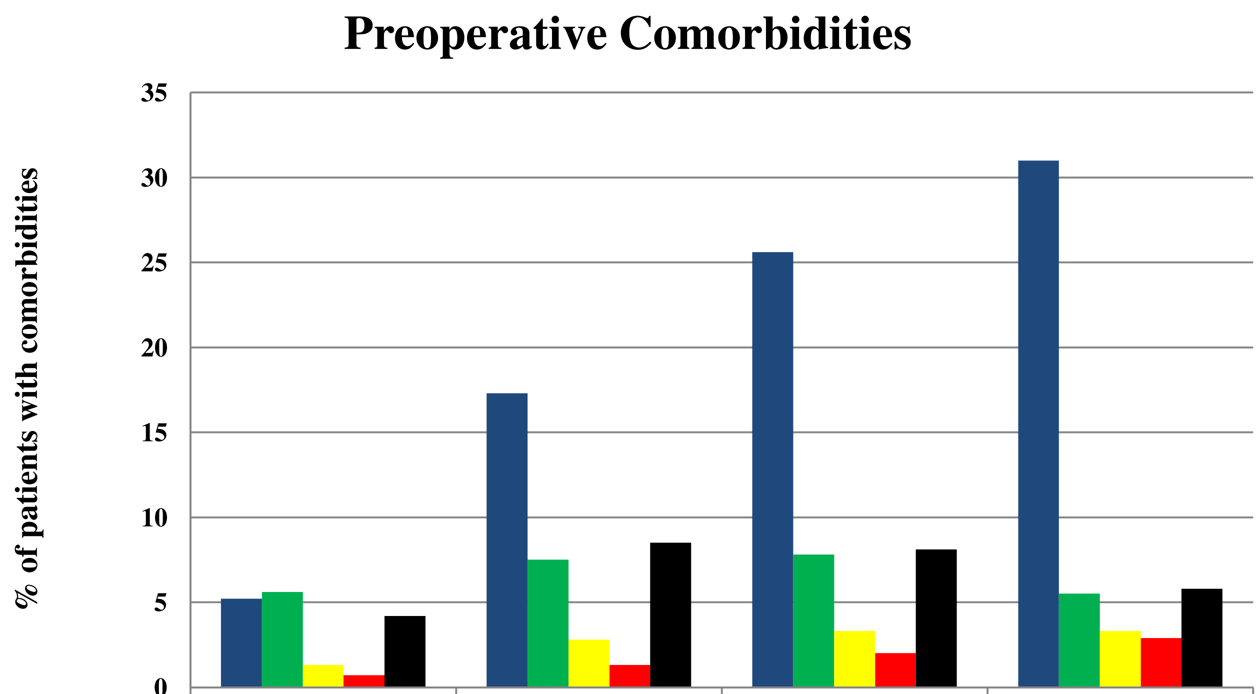
Patient demographics

The median age of the patients included in the study was 69 years (Inter-quartile Range 58-77 years). Five percent of the patients included in the study (8,586/171,791) were over the age of 85 years. There was an equal distribution of both sexes. The detailed demographic characteristics of the patients undergoing colorectal resection between the study dates are described in Table 20. Almost two thirds of the resections were undertaken for a malignant diagnosis (107,820, 62.8%). Rectal resections were undertaken in 42.6% of the patients (73,172/171,791).

Pre-operative co-morbidity was summarised according to the organ system involved. The most frequently occurring co-morbidities were those assigned cardiac (26,318, 15.3%) and respiratory (11,533, 6.7%) diagnosis codes. 11,231 (6.5%) patients were coded for diabetes. Other co-morbidities included prior history of venous thrombo-embolism (3,992, 2.3%) and renal failure (2,248, 1.3%) (Figure 2). Using the ICD-10 diagnosis codes Charlson's co-morbidity score was derived and patients were grouped into Charlson 0 (30.2%), 1-2 (44.9%) and >= 3 (24.9%).

Table 20: Demographic details of patients undergoing colorectal resection

		N=171,791	(%)
Age	<=65 years	68,440	(39.8)
	66-75 years	50,349	(29.3)
	76-85 years	44,416	(25.9)
	>85 years	8,586	(5.0)
Gender	Male	87,000	(50.6)
	Female	84,791	(49.4)
Diagnosis	Malignant	107,820	(62.8)
	Benign	63,971	(37.2)
Resection Type	Total/Subtotal	8,311	(4.8)
	Right sided	59,120	(34.4)
	Left sided	31,188	(18.2)
	Rectal	73,172	(42.6)
Charlson Score	0	51894	(30.2)
	1-3	77096	(44.9)
	>3	42802	(24.9)
Mode of admission	Non-elective	59,152	(34.4)
	Elective	112,639	(65.6)



	<=65 years	66-75 years	76-85 years	>85 years
Cardiac	5.2	17.3	25.6	31
Respiratory	5.6	7.5	7.8	5.5
VTE	1.3	2.8	3.3	3.3
Renal	0.7	1.3	2	2.9
Diabetes	4.2	8.5	8.1	5.8

Figure 2: Preoperative comorbidities in patients undergoing colorectal resection

Mortality

The overall 30-day mortality rate was 8.5%. Mortality was significantly high in patients undergoing an emergency resection (17.4%) as compared to those who had a planned surgery (3.8%) ($p<0.001$). Overall one year mortality was 18.5% (11.7% for elective and 31.6% ($p<0.001$) for non-elective resections). For patients aged >85 years 30-day mortality for elective resections was 12.1% and for non-elective resection this was significantly higher at 37.1%. Mortality rates following elective and non-elective colorectal resection at various intervals post-operatively have been shown in Table 21.

Cause of death

The underlying cause of death was analysed for those patients who died following a colorectal resection. Following elective surgery, 38.6% of patients that died within 30 days had an underlying cause of death cited as colorectal cancer while 25.4% patients died of cardiac causes. At 90 days the corresponding proportions were 40.7% and 22.1% respectively. The deaths attributed to colorectal cancer increased over time and almost half of the patients that died at one year or later had a primary cause of death coded as colorectal cancer. Deaths due to cardiac causes were high until 1 year (22.1% at 90 days and 15.3% at one year). Amongst patients who died after non-elective colorectal resections, the most common cause of death were classed as gastrointestinal causes, such as perforation, obstruction or ischaemia of bowel. A quarter of the patients had an underlying cause of death as colorectal cancer. Figures 5 (elective) & 6 (non-elective) describe the trend of patients dying due to various causes at different intervals following colorectal resections.

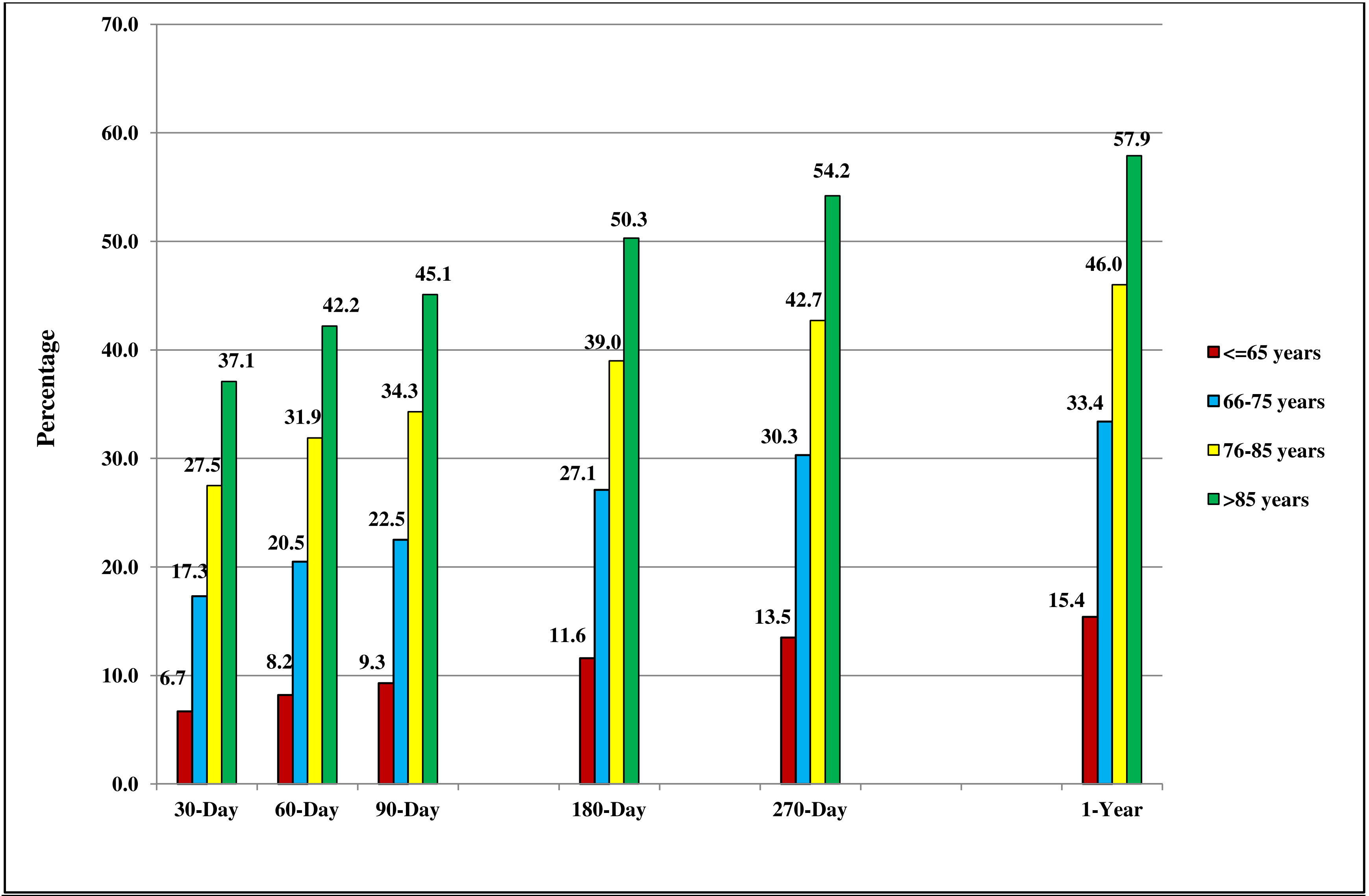


Figure 3: Mortality Rate following Non-elective Colorectal resection

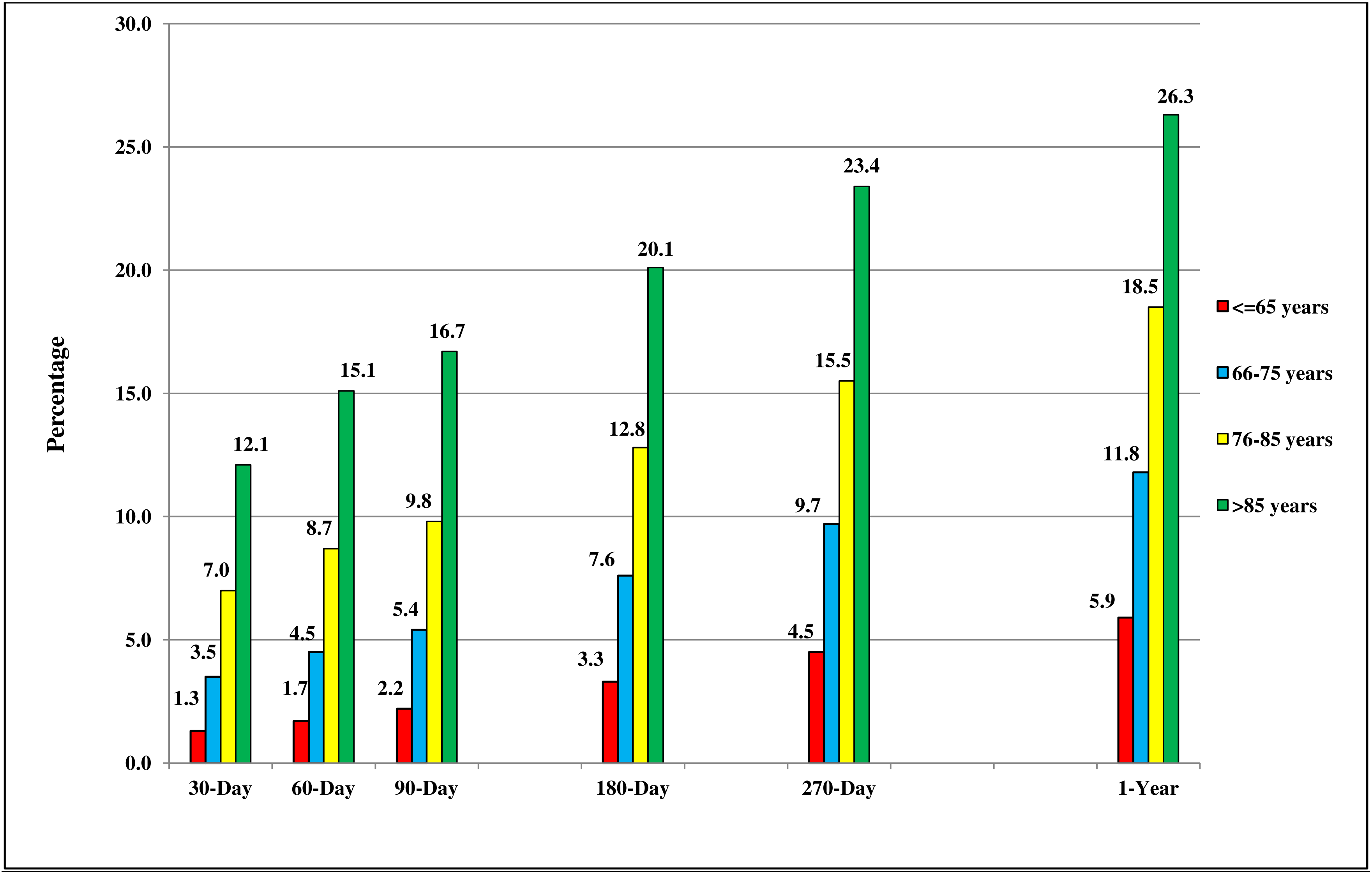


Figure 4: Mortality Rate following Elective Colorectal resection

Table 21: Age-specific mortality rates and population average mortality and life expectancy

Age groups	30 Day		60 Day		90 Day		1 Year		Average age-specific mortality rate*	Average Life expectancy between 2005 and 2007	% increase in mortality for elective patients (30-90 days)
	EL	**NE**	**EL**	**NE**	**EL**	**NE**	**EL**	**NE**			
</=65	1.3	6.7	1.7	8.2	2.2	9.3	5.9	15.4	0.3	39.8	69.2
66-75	3.5	17.3	4.5	20.5	5.4	22.5	11.8	33.4	1.9	14.5	54.2
76-85	7.0	27.5	8.7	31.9	9.8	34.3	18.5	46.0	6.1	8.2	40.0
>85	12.1	37.1	15.1	42.2	16.7	45.1	26.3	57.9	15.4	3.6	38.0

EL: Elective surgery, NE: Non-elective surgery. All rates in percentage.
**: Population-specific mortality rates for year 2007.*

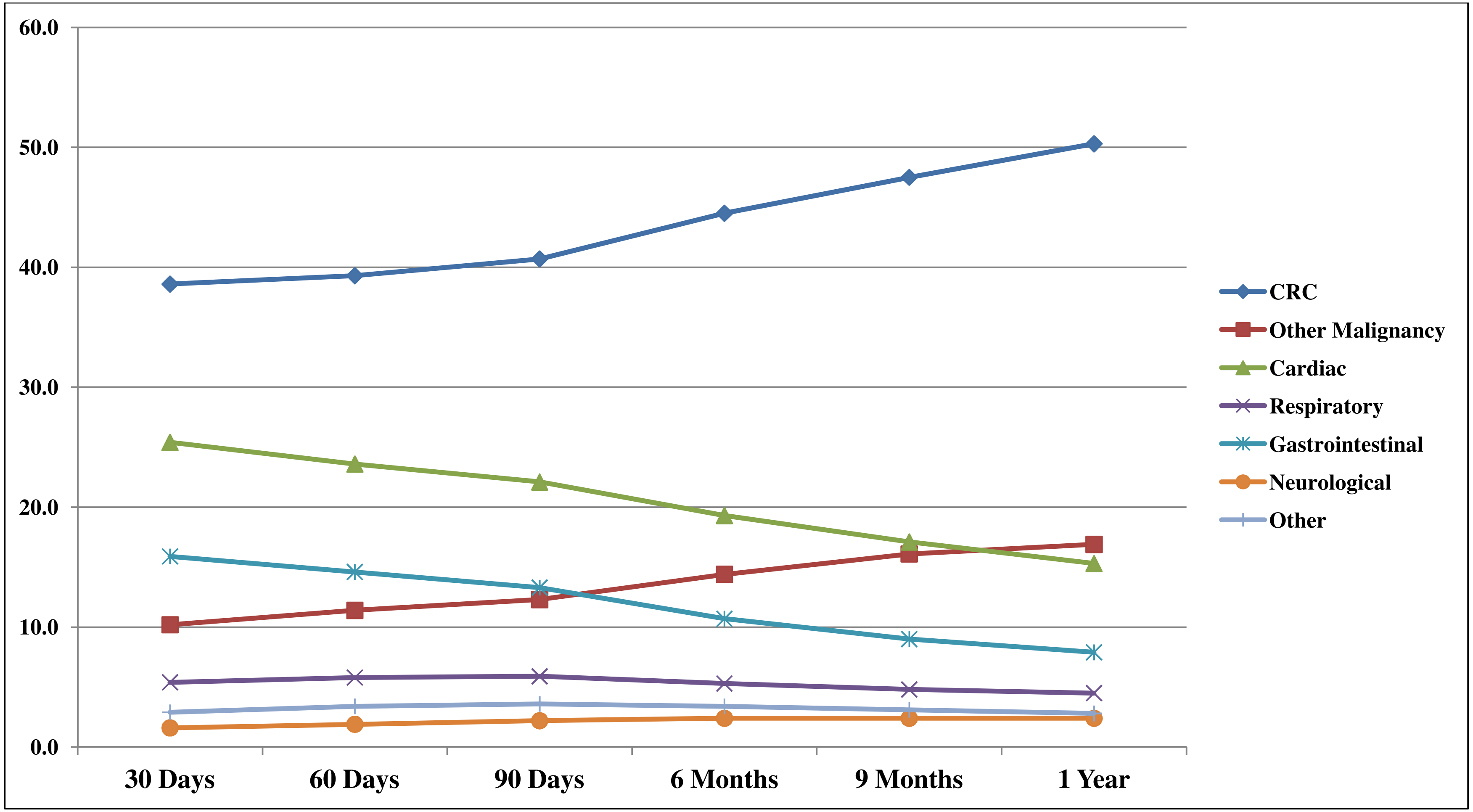


Figure 5: Cause of death at different intervals following elective colorectal resection

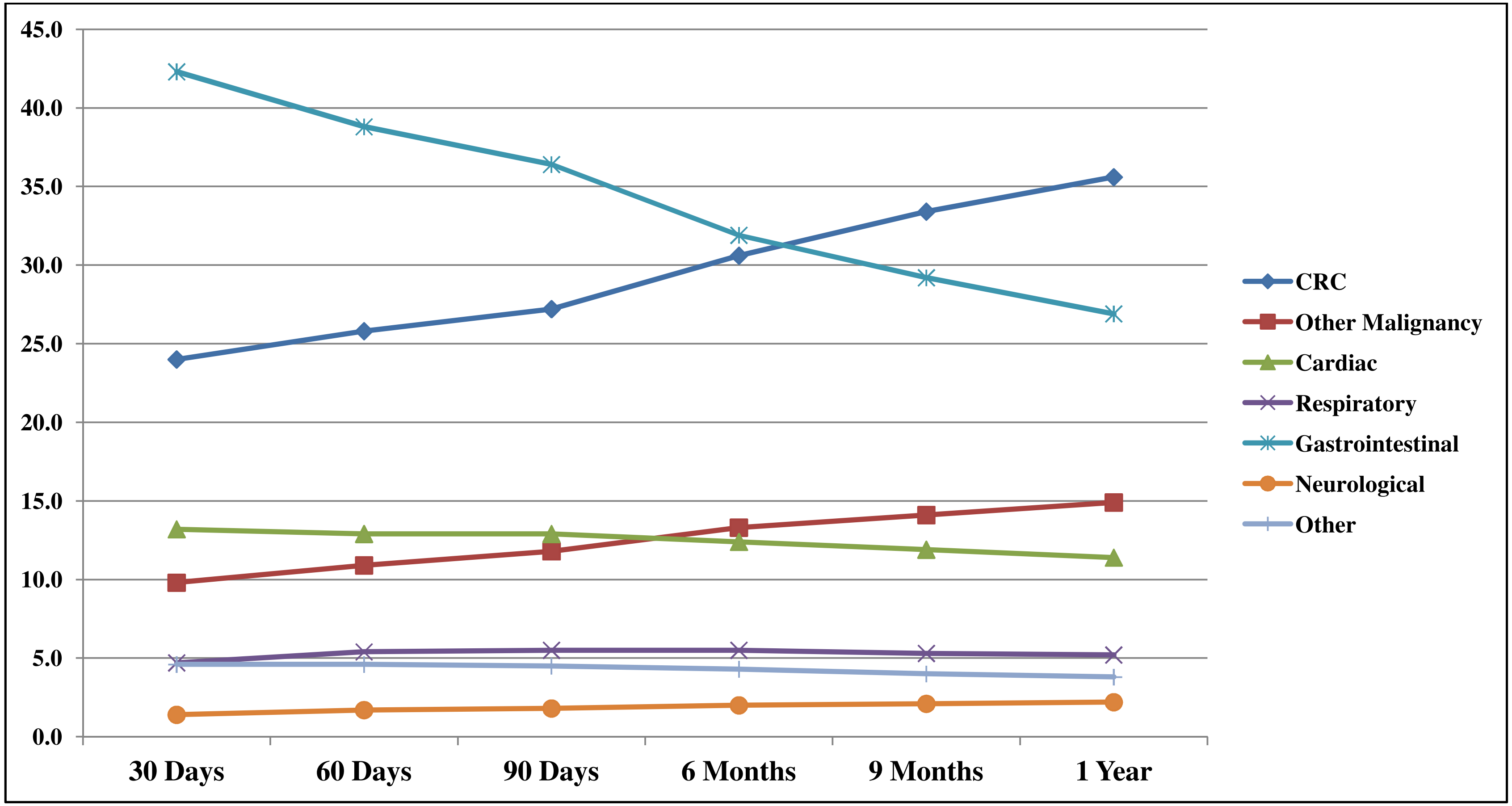


Figure 6: Cause of Death at different intervals following non-elective colorectal resection

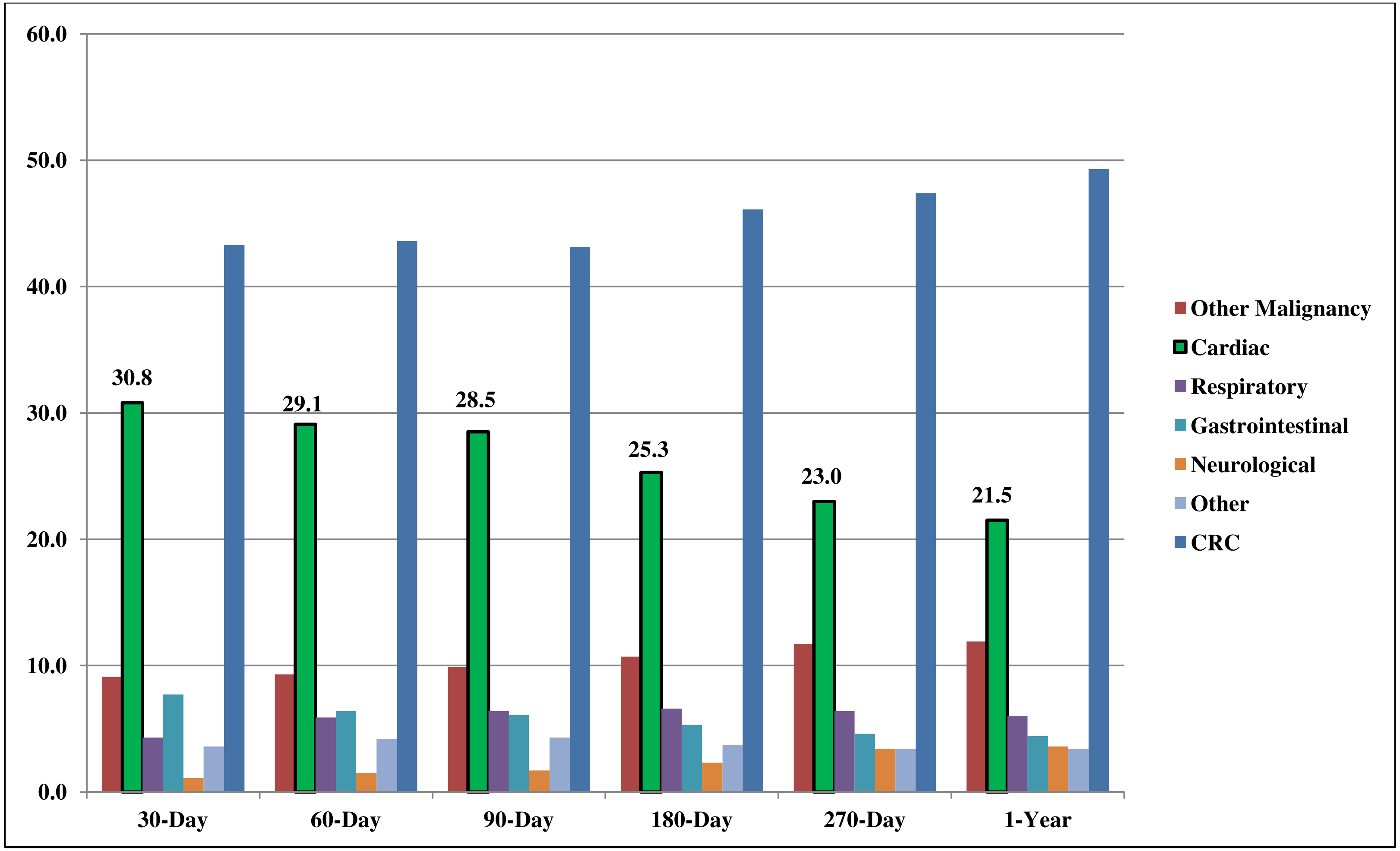


Figure 7: Causes of Death in Elective Cancer patients >85 years

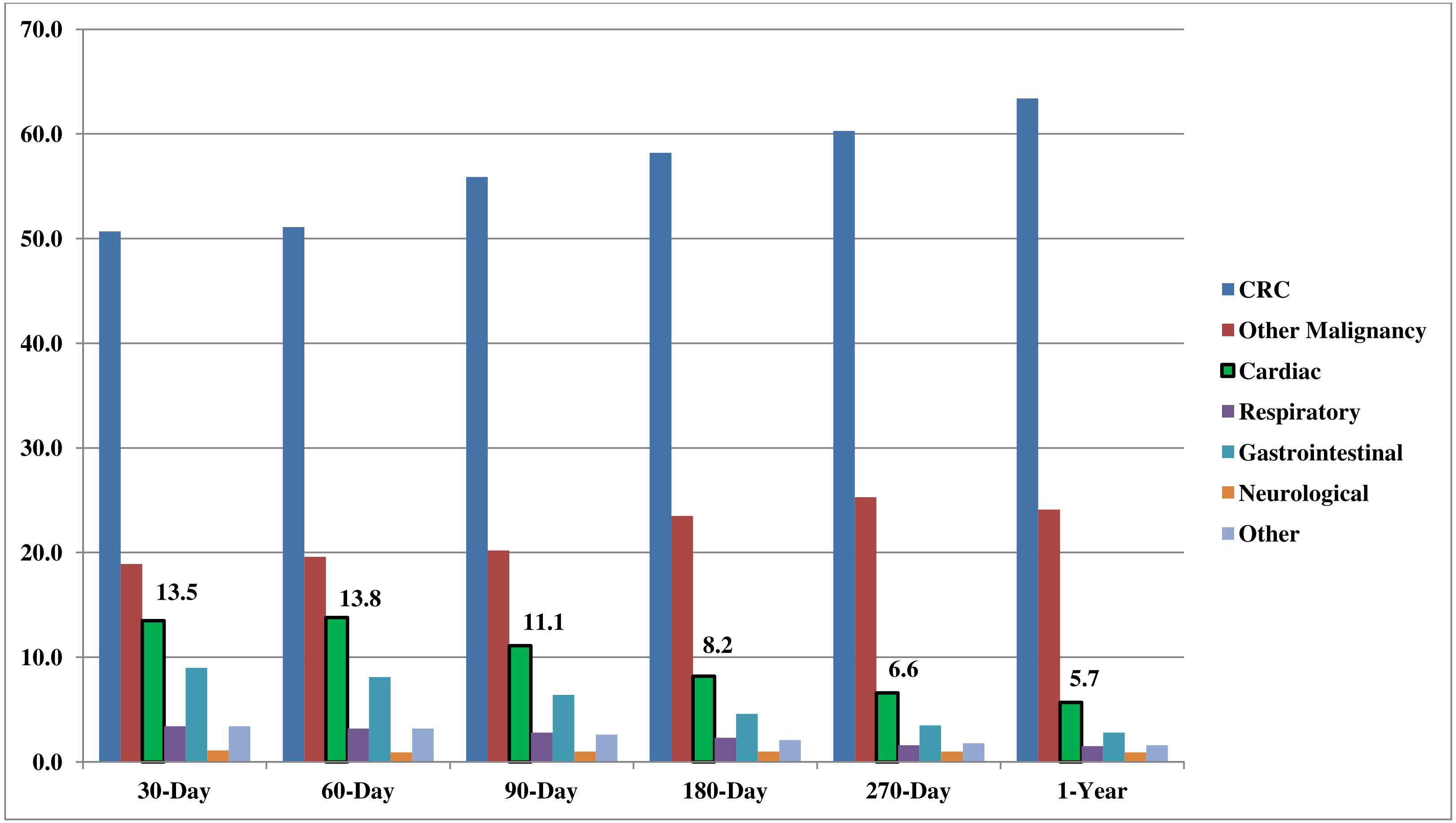


Figure 8: Causes of Death in Elective Cancer patients <=65 years

4b.4 Discussion

This chapter examines the causes and timing of death following colorectal surgery from a national routinely collated database. A significant proportion of deaths due to cardiac causes occur beyond the initial thirty days, up to one year following surgery. The percentage of deaths due to cardiac causes even at one year is higher than those seen in the general population. This may be attributable to the effects of surgery and/or anaesthesia. This observational study undertaken using a national database shows that mortality that may be attributable to the effects of the primary operation are not fully captured in outcome measurements when a 30-day benchmark is used. This has important implications regarding the information that is presented to patients as well as providing avenues for potential mortality risk reduction.

Mortality rates measured at 90 days were substantially higher than those at 30 days. Of note, in elective patients, there was a significant increase in mortality, and the proportional increase between the two timeframes was greatest in the <=65 years cohort (69.2% increase vs 38% increase in >85 year cohort) (Table 21). The higher 90-day mortality may suggest that the effects of surgery and anaesthesia have a lasting effect beyond 30 days. Certainly, when compared with national age-specific mortality data (Office for National Statistics, 2012a, Office for National Statistics, 2008), those that underwent a colorectal resection have a higher mortality rate at 90 days and 1 year following surgery (Table 21). Specifically, in the elderly age group (>85 years) the life expectancy of the general population during 2005-2007 was 3.6 years. However, within the first year following surgery, a quarter of these patients died in the elective setting, and less than half of those presenting as an emergency survived the first year. This increased mortality beyond the first month may potentially reflect enhanced physiological stress attributable to surgery itself or the stress of an anaesthetic.

In the elective setting, surgeons are duty-bound to adequately counsel patients on relevant risks and complications of surgery. Postoperative mortality would be one of the pertinent risks which would be discussed. The most frequently cited statistics in these consultations almost always use 30 days as the benchmark for postoperative death (Khuri et al., 1998, Panis et al., 2011, Tekkis et al., 2004). Our study demonstrates that mortality risk is probably underestimated when 30-day statistics are conveyed. A recent population-based study by Damhius and coworkers (Damhuis et al., 2012) reviewed timings of postoperative mortality in eight cancer types. They noted that a 90-day timeframe would capture both death directly linked to the index operation as well as other causes, which may be of less significance to the surgeon, but may be important to the patient preoperatively when deciding on whether or not to have the surgery. It would seem important that patients be informed of the likelihood of death from any cause up to one year of surgery, certainly within three months of surgery. Under such circumstances some high risk candidates may opt to avoid surgical intervention altogether.

Thirty day postoperative mortality is also used as a quality indicator for measuring performance of surgeons and surgical units. As such, underestimation of postoperative mortality has important implications regarding quality assessment. This could result in erroneous judgements regarding clinical governance and commissioning of services (Fink et al., 2002, Ingraham et al., 2010a, Merkow et al., 2013). Given the importance of mortality as an outcome both to patients and health providers, it is essential that surgeons (and physicians) accurately describe and quantify the risk of death attributable to surgery. This study, amongst others (Visser et al., 2009, van Gestel et al., 2013, Mamidanna et al., 2012a), suggests that a substantial proportion of postoperative mortality in elective colorectal surgery occurs beyond the 30-day period. The latter deaths are, however, not currently being attributed to the surgical insult or perioperative care. Similar variations in mortality rates were noted when extending the benchmark in other fields such as pulmonary resection surgery (Bryant et al., 2010). Variation in causes of death over differing postoperative timescales was observed. Postoperative mortality is often an acute event that results from organ failure. This may include surgical complications or cardiorespiratory conditions such as myocardial infarction or respiratory infection amongst others. In elective resections, colorectal cancer was the most common underlying cause of death, followed by cardiac causes. In-hospital deaths, especially following elective resections for cancer, are more likely to have an underlying cause of death attributed to colorectal cancer, whilst the direct mode of death may be respiratory or cardiac in origin.

Our study demonstrates that following colorectal resection the risk of death due to cardiac causes remains elevated beyond the commonly used 30-day benchmark. Overall there were 8,586 patients >85 years who underwent colorectal resection. Of these, 1176 (13.7%) died of an underlying cardiac cause of death. In the sub-group of elective colorectal resections for cancer, we observed that cardiac causes of death accounted for a high proportion of death up to one year after surgery. This was most evident in the elderly where amongst patients aged 85 years or older, where cardiac causes of death were reported in 28.5% cases (Figure 7). On closer scrutiny, most of these deaths are occurring in patients with pre-existing cardiac co-morbidities. There is a case for arguing that a high proportion of deaths in the elderly could be attributable to pre-existing cardiac conditions or even senescence alone. However, in patients > 85 years, with no pre-existing cardiac conditions, there were 10% deaths due to cardiac causes at one year following surgery. In addition, according to published statistics from the Office for National Statistics, in the age group 85 years and above, the death rate from heart disease was 7.1% in England in 2007 (Office for National Statistics, 2008). Thus there is clearly an excess cardiac mortality in these patients following a major surgical intervention, and this risk extends beyond the first thirty days. The same national report estimated a 0.4-0.5% death rate due to heart disease in the population aged <65 years. In our study there were 68,440 patients belonging to this age group, of which 1,060 (1.5%) died from cardiac causes. The trends in causes of deaths in the younger population also shows significant deaths attributable to cardiac causes up to one year (Figure 8). Furthermore, amongst the patients with underlying causes of death being coded as 'colorectal cancer' there may be a significant proportion that may have had acute or sub-acute postoperative medical complication which resulted in their deaths.

Recent research has identified a link between early elevated post-operative troponin levels and 30-day mortality (Devereaux et al., 2012). A global scientific collaboration has observed an asosciation between increased post-operative troponin assays and risk of 30-day mortality. Our study from routinely collected data potentially supports a hypothesis that subclinical myocardial ischaemia may occur. Moreover any perioperative insult may manifest beyond 30 days. We postulate that cardiac function may be adversely affected by perioperative events in some subjects leading to cardiovascular compromise within the months that follow surgery. Further research will be required to identify patient groups at particular risk of late mortality secondary to preventable cardiac causes.

The limitations of our study include the administrative nature of the data thus raising concerns about accuracy and the absence of certain clinical parameters such as stage of cancer and body mass index which would affect outcome following surgery. Yin *et al* reported on inaccurate coding of patients' Underlying Cancer Cause of Death (UCOD) and how this altered the survival estimates of colon and rectal cancer patients in the California Cancer Registry (many rectal cancers were coded as colonic cancers) (Yin et al., 2011). As such, there may be inaccuracies in documentation of causes of death. Nevertheless, taking into account the possible inaccuracy in coding, we still observed significant trends following colorectal surgery. In non-elective operations, causes of death coded as 'colorectal cancer' increased over the one-year period postoperatively, gastrointestinal causes decreased after a peak in the first 30 days and cardiac causes remained stable at about 13% of total deaths though the first year (Figure 6). It is possible that a significant percentage of the patients coded as dying from a 'gastrointestinal' cause i.e. perforation or obstruction may have had an underlying colorectal malignancy diagnosed subsequently on histopathological examination or post mortem.

CHAPTER 5: COLORECTAL RESECTION IN HIGH RISK PATIENT GROUPS: THE ELDERLY

The ageing population of the UK mirrors that in many other European countries. Increased longevity has however not been accompanied by a rise in 'healthy' life expectancy. This has resulted in a proportionally greater demands on public services such as healthcare. By 2050 one in five of the global population aged 60 years or older is forecast to be an octogenarian. This represents a five-fold increase in the size of the extreme elderly population since 2000 (United Nations. Dept. of Economic and Social Affairs. Population Division., 2002). A significant proportion of the public spending on benefits is focussed on the elderly people. It is estimated that about 65% of Department for Work and Pensions benefit expenditure goes to those over the working age (Cracknell, 2010). This was equivalent to £100 billion in 2010/11 or one-seventh of the entire public expenditure. The ageing of the population will have a major impact on the organisation and delivery of health care. Old people often have limited regenerative abilities and are more prone to disease, syndromes, and sickness than younger adults. Of particular importance will be the shift from acute to chronic illnesses.

The incidence of benign and malignant colonic disease increases with age (Basili et al., 2008, Poon et al., 1998, Pavlidis et al., 2006). Colorectal cancer is the third most common cancer in the United Kingdom (UK) with eight out of ten cases occurring in people aged over 60 years (Cancer Research UK, 2014). Hence, as life expectancy increases there is likely to be a concomitant increase in the number of colorectal procedures offered to elderly patients. In an elective setting, elderly patients that present to the outpatient clinics with a colorectal pathology requiring a surgical intervention can be counseled regarding the risks and benefits associated with surgical management. In most hospitals such patients are pre-assessed to ascertain their pre-operative fitness. This gives the opportunity to undertake pre-operative physiological and nutritional optimisation. In contrast, emergency presentation mandates prompt intervention. Patients who present as an emergency have higher morbidity and mortality than elective management across all age groups (Ingraham et al., 2010b, Irvin, 1988). It is well-known that older patients present more frequently with advanced disease requiring emergency surgery(McGillicuddy et al., 2009). To make matters worse, this patient cohort is associated with higher incidence of comorbities such as cardiorespiratory, metabolic or renal disease. It has been shown that such co-morbidity is also independently related to poor outcome following colorectal resection (Boyd et al., 1980). Several studies have examined outcome in elderly subjects following both elective and emergency surgery (Walton et al., 2006) looking specifically at colorectal procedures (Basili et al., 2008, Ingraham et al., 2010b, Pavlidis et al., 2006). Such studies report worse postoperative outcome in the elderly when compared with younger cohorts. Whether this represents the impact of as age *per se,* or, the increased likelihood of concomitant co-morbidities is unclear. Survival rates amongst UK patients with colorectal cancer are inferior to counterparts in many European countries(Brenner et al., 2011). Recent comparison between English and Scandinavian populations suggests that poor outcome in England relates to an excess of deaths that occur amongst the elderly in the three months that follow a diagnosis of colorectal cancer (Morris et al., 2011a). The latter study did not however specify whether operative or non-operative candidates were at high risk of mortality. Understanding the cause of poor outcome in elderly subjects with surgical disease may guide future improvement in health care delivery to this population.

This chapter examines a cohort of elderly patients who have undergone non-elective colorectal resection over a seven year period in English NHS hospitals. The aims of the study are to quantify the risks associated with emergency colorectal surgery in the elderly and thereby evaluate the relationship between age and postoperative outcome.

5.1 Methods

HES data were obtained for elderly patients who underwent a non-elective colorectal resection between April 2001 and March 2008 in an English NHS Trust. Elderly patients were defined as patients aged 70 years or above. Age was further sub-categorised into three groups: group A (70-75 years), group B (76-80 years) and group C (>80 years). Admissions with medical complaints up to five years prior to the surgery were studied to ascertain the co-morbidity status. The diagnosis codes from these admissions were grouped according to the organ system involved (Table 1, Chapter 2). HES data do not have a 'present on admission' flag and some medical conditions (e.g. atrial fibrillation etc.) were coded as co-morbidity if present in previous admissions, but categorised as complications if present on the index admission but not previously coded. The OPCS codes used to identify various resections have been described in detail in Chapter 2.

Outcome variables

The primary outcome measures were 'in-hospital' mortality within 30 days and 'in and out of hospital' mortality within one year of surgery. Secondary end-points were length of stay (LOS), readmission and post-operative medical morbidity. Duration of hospital stay in days, from date of surgery to date of discharge/ in-hospital death was termed as p-LOS. Unplanned admissions within 28 days of discharge were termed readmissions. Post-operative medical complications (morbidity) have been categorised as cardiac, respiratory, venous thrombo-embolism (VTE), ischaemic stroke and renal failure. All secondary diagnosis fields on the index admission and primary diagnosis fields on subsequent unplanned admissions up to one year were considered for this purpose. OPCS-4 codes for laparotomy, intra-abdominal abscess drainage, and stoma or wound complications requiring re-operation were used to determine re-operation on the index admission or on a subsequent admission within 28 days.

5.2 Results

Patient characteristics

From April 2001 to March 2008, 36,767 non-elective colorectal resections were performed on patients aged 70 years or older in English NHS Trust hospitals. There were more females than males in the study population (58.3% females versus 41.7% males). Patients >80 years of age represented 38.0% (13,964/36,767) of the study population. The demographic characteristics have been shown in Table 21. Overall, 17,437 (47.4%) patients had a malignant diagnosis. Other causes for resections included volvulus, ischaemic bowel, non-traumatic perforation of intestine and adhesional obstruction. Left sided colonic resections were performed in 16,978 (46.2%) patients. Left and right sided resections were almost equal in age group C (44.4% and 44.5% respectively), but left sided resections predominated in the younger cohorts.

Table 22: Descriptive characteristics of elderly patients undergoing non-elective colorectal

(April 2001 - March 2008)

		n=36,767	**(%)**
Age	70-75 years	11,982	(32.6)
	76-80 years	10,821	(29.4)
	>80 years	13,964	(38.0)
Gender	Male	15,321	(41.7)
	Female	21,446	(58.3)
Diagnosis	Malignancy	17,437	(47.4)
	Diverticulosis	7,920	(21.5)
	IBD	782	(2.2)
	Other	10,628	(28.9)
Type of Resection	Total/Subtotal	1,762	(4.8)
	Right Sided	15,227	(41.4)
	Left Sided	16,978	(46.2)
	Rectal	2,800	(7.6)
Preoperative Co-morbidity	Cardiac	7,967	(21.7)
	Respiratory	2,517	(6.8)
	VTE	247	(0.7)
	Stroke	222	(0.6)
	Renal	444	(1.2)
	Diabetes	1,710	(4.7)

IBD=Inflammatory Bowel Disease, VTE=venous thrombo-embolism

Outcome measures

***Length of stay*:**

Overall median LOS was 21 days [IQR 13-35 days]. The median length of stay in patients over 80 years (22 days [13-38 IQR]) was significantly longer than the younger groups (20 days [13-24 IQR], p<0.001). As compared with patients in group A, there was a 39% higher risk of having a LOS beyond the 75th percentile in patients >80 years (Odds Ratio 1.39, 95%CI 1.31-1.47, p<0.001).

Specifically, length of stay from the surgery to discharge or in-hospital death was also analysed. This was termed p-LOS (Post-operative LOS). Overall median p-LOS was 15 days (9-26 IQR). P-LOS for the three age groups was as follows: 70-75 years [14 days (9-24 IQR)], 76-80 years [15 days (9-27 IQR)] and >80 years [16 days (8-28 IQR)], p<0.001. As compared with patients in group A, there was a 29% higher risk of having a p-LOS beyond the 75th percentile in patients >80 years (Odds Ratio 1.29, 95%CI 1.22-1.37, p<0.001).

***Readmission*:**

Readmission rate amongst the study patients was 7.3% (n=2,690). More patients in group A (i.e. younger) were readmitted as compared with the octogenarians (Table 22). On univariate as well as risk adjusted analyses, increasing age was associated with lower readmission rates (Table 23). Multiple regression analyses showed that pre-operative cardiac co-morbidity (OR 1.24, 95%CI 1.13-1.37, p<0.001) and diabetes (OR 1.28, 95%CI 1.08-1.51, p=0.004) were also independent determinants of readmission (Table 23).

Re-operation:

Overall re-operation rate was 6.3%. 2,209 patients were returned to theatre for a surgical complication on the index admission or within 28 days. Re-operation rate was significantly lower in group C (4.7%) when compared to groups A and B (7.9% and 6.5% respectively, p<0.001). Re-operation was an independent determinant of 30-day mortality (OR 1.40, 95%CI 1.27-1.55, p<0.001). Patients who underwent a re-operation had a 66% higher risk of mortality at one year (OR 1.66, 95%CI 1.48-1.87, p<0.001).

***Mortality*:**

The overall 30-day in-hospital mortality rate was 24.1% (8,874 patients). This was significantly higher in group C (31%) when compared with groups A and B (17% and 23.3% respectively, p<0.001). On unadjusted analyses, age, gender, diagnosis, type of resection and cardiorespiratory and renal co-morbidity were found to be predictors of mortality (Table 24). These variables were entered in a risk adjusted multiple regression model. Patients in group C demonstrated more than twice the odds of 30-day mortality when compared with those in group A (OR 2.36, 95%CI 2.22-2.51, p<0.001).

Mortality rate at one year was 42.9% (9,056/21,097). With advancing age, one year mortality increased significantly. In group C, 51.2% of patients died within one year of surgery (n=4,035). Advancing age, diagnosis and type of resection were significant predictors of 365-day mortality. The odds of one year mortality doubled in group C when compared with group A (OR 1.99, 95%CI 1.86-2.13, p<0.001).

Medical morbidity:

Overall 30-day morbidity rate was 33.7% (12,394/36,767). Complications pertaining to cardiac and respiratory systems were most frequently coded (Table 25). One in five patients in group C had a cardiac complication post-operatively. When compared with group A, patients over the age of 80 years had a significantly higher incidence of angina (7.1% versus 5.7%), myocardial infarction (2.7% versus 1.9%), heart failure (8.6% versus 4.1%) and new onset atrial fibrillation (8.1% versus 4.6%) [all $p<0.001$]. Pneumonia occurred in 1,780 (12.7%) elderly patients aged >80 years.

Table 23: Outcomes (unadjusted) in elderly patients undergoing non-elective colorectal resection

Outcome	Overall 36,767		70-75 years 11,982		76-80 years 10,821		>80 years 13,964		p value[@]
	n	(%)	n	(%)	n	(%)	n	(%)	
Length of Stay Median (IQR)	21	(1(3-35)	19	(12-24)	21	(13-35)	22	(13-38)	p<0.001[#]
Length of Stay (p-LOS) Median (IQR)	15	(9-26)	14	(9-24)	15	(9-27)	16	(8-28)	p<0.001[#]
Readmissions (within 28 days)	2,690	(7.3)	1,028	(8.6)	804	(7.4)	858	(6.1)	p<0.001
Re-operation (within 28 days)	2,209	(6.3)	905	(7.9)	675	(6.5)	629	(4.7)	P<0.001
30-day Mortality (in-hospital)	8,874	(24.1)	2,033	(17.0)	2,517	(23.3)	4,324	(31.0)	p<0.001
	Overall 21,079		**70-75 years 6,944**		**76-80 years 6,267**		**>80 years 7,886**		
365-day Mortality* (in and out of hospital)	9,056	(42.9)	2,413	(34.7)	2,608	(41.6)	4,035	(51.2)	p<0.001

*IQR = Inter-Quartile Range, [@]=Chi squared Test, [#]=Mann Whitney U Test, *= available only prior to 2005*

Table 24: Logistic regression analyses for readmission after non-elective colorectal resection in the elderly

	Unadjusted Analysis			**Adjusted Analysis**		
	OR	95% CI	p value	OR	95% CI	p value
Age			<0.001			<0.001
70-75 years	1.00			1.00		
76-80 years	0.86	(0.78, 0.94)	0.001	0.87	(0.79, 0.96)	0.007
>80 years	0.70	(0.64, 0.77)	<0.001	0.72	(0.66, 0.80)	<0.001
Gender			0.038			0.412
Male	1.00			1.00		
Female	0.92	(0.85, 0.99)	0.038	0.97	(0.89, 1.05)	0.412
Diagnosis			0.144			
Malignancy	1.00			-		
Diverticulosis	1.12	(1.02, 1.24)	0.022	-		
IBD	1.09	(0.83, 1.43)	0.522	-		
Other	1.03	(0.94, 1.13)	0.524	-		
Resection			0.110			
Total/Subtotal	1.00			-		
Right Sided	1.11	(0.92, 1.35)	0.280	-		
Left Sided	0.97	(0.80, 1.18)	0.774	-		
Rectal	1.13	(0.90, 1.42)	0.308	-		
Preoperative Co-morbidity						
Absence of Co-morbidity	1.00					
Cardiac	1.29	(1.18, 1.41)	<0.001	1.25	(1.13, 1.37)	<0.001
Respiratory	1.11	(0.96, 1.29)	0.157	-		
VTE	1.56	(1.04, 2.33)	0.030	1.44	(0.95, 2.17)	0.085
Stroke	1.40	(0.90, 2.17)	0.138	-		
Renal Failure	1.44	(1.05, 1.96)	0.022	1.24	(0.90, 1.70)	0.188
Diabetes	1.49	(1.26, 1.75)	<0.001	1.32	(1.12, 1.57)	0.001
Re-operation	1.63	(1.42, 1.87)	<0.001	1.57	(1.36, 1.81)	<0.001

OR = Odds Ratio, CI=Confidence Interval

Table 25: Logistic regression analyses for mortality following non-elective colorectal resection in the elderly

	30-Day Mortality				365-Day Mortality			
	Unadjusted Analysis		Adjusted Analysis		Unadjusted Analysis		Adjusted Analysis	
	OR 95% CI	p value	OR 95% CI	p value	OR 95% CI	p value	OR 95% CI	p value
Age		<0.001		<0.001		<0.001		<0.001
70-75 years	1.00		1.00		1.00		1.00	
76-80 years	1.48 (1.39, 1.58)	<0.001	1.52 (1.42, 1.63)	<0.001	1.39(1.28, 1.51)	<0.001	1.34(1.25, 1.45)	<0.001
>80 years	2.20 (2.10, 2.33)	<0.001	2.40 (2.26, 2.56)	<0.001	2.11(1.95, 2.28)	<0.001	2.05(1.91, 2.19)	<0.001
Gender		0.016		0.501		0.291		
Male	1.00		1.00		1.00		-	
Female	1.06 (1.01, 1.12)	0.016	0.98 (0.93, 1.04)	0.501	1.04(0.97, 1.10)	0.291	-	
Diagnosis		<0.001		<0.001		<0.001		<0.001
Malignancy	1.00		1.00		1.00		1.00	
Diverticulosis	1.58 (1.48, 1.68)	<0.001	1.47 (1.37, 1.58)	<0.001	1.60(1.47, 1.74)	<0.001	0.88(0.81, 0.95)	0.001
IBD	1.46 (1.24, 1.73)	<0.001	1.31 (1.08, 1.57)	0.005	1.29(1.03, 1.62)	0.030	0.75(0.60, 0.93)	0.008
Other	2.21 (2.09, 2.34)	<0.001	2.13 (2.01, 2.26)	<0.001	2.21(2.05, 2.37)	<0.001	1.37(1.28, 1.47)	<0.001
Resection		<0.001				<0.001		<0.001
Total/Subtotal	1.00		1.00	<0.001	1.00		1.00	
Right Sided	0.48 (0.44, 0.54)	<0.001	0.51 (0.45, 0.58)	<0.001	0.59(0.50, 0.69)	<0.001	0.74(0.63, 0.86)	<0.001
Left Sided	0.65 (0.58, 0.72)	<0.001	0.64 (0.57, 0.73)	<0.001	0.78(0.67, 0.91)	0.001	0.73(0.62, 0.85)	<0.001
Rectal	0.37 (0.32, 0.43)	<0.001	0.40 (0.34, 0.46)	<0.001	0.46(0.38, 0.56)	<0.001	0.55(0.46, 0.66)	<0.001
Preoperative Co-morbidity								
Absence of Co-morbidity	1.00				1.00		1.00	
Cardiac	1.23 (1.16, 1.30)	<0.001	1.06 (1.00, 1.13)	0.076	1.23(1.14, 1.34)	<0.001	1.13(1.04, 1.22)	0.002
Respiratory	1.39 (1.27, 1.52)	<0.001	1.31 (1.19, 1.45)	<0.001	1.37(1.21, 1.56)	<0.001	1.30(1.15, 1.47)	<0.001
VTE	1.20 (0.90, 1.58)	0.212	-		1.14(0.79, 1.64)	0.498	-	
Stroke	1.28 (0.95, 1.71)	0.102	-		1.09(0.71, 1.68)	0.695	-	
Renal Failure	2.29 (1.90, 2.78)	<0.001	1.90 (1.55, 2.33)	<0.001	2.11(1.59, 2.81)	<0.001	2.08(1.54, 2.81)	<0.001
Diabetes	1.10 (0.98, 1.23)	0.102	-		1.20(1.02, 1.41)	0.027	0.09(0.94, 1.27)	0.274
Re-operation	1.35 (1.23, 1.48)	<0.001	1.40 (1.27, 1.55)	<0.001	1.55(1.38, 1.74)	<0.001	1.66(1.48, 1.87)	<0.001

OR = Odds Ratio, CI=Confidence Interval

Table 26: Post-operative medical morbidity following emergency colorectal resection

Organ System	Overall 36,767		70-75 years 11,982		76-80 years 10,821		>80 years 13,964		p value[@]
	n	(%)	n	(%)	n	(%)	n	(%)	
30-Day Morbidity									
Cardiac	6739	(18.3)	1736	(14.5)	1901	(17.6)	3102	(22.2)	<0.001
Respiratory	6126	(16.7)	1736	(14.5)	1850	(17.1)	2540	(18.2)	<0.001
VTE	523	(1.4)	158	(1.3)	182	(1.7)	183	(1.3)	0.025
Stroke	362	(1.0)	101	(0.8)	101	(0.9)	160	(1.0)	0.039
Renal Failure	2213	(6.0)	684	(5.7)	642	(5.9)	887	(6.4)	0.085

[@]=*Chi squared Test*

Table 27: Cardiorespiratory complications in the elderly

	70-75 years		>80 years		p value
	n	(%)	n	(%)	
Angina	680/11,982	**(5.7)**	990/13,964	**(7.1)**	<0.001
Myocardial Infarction	232/11,982	**(1.9)**	383/13,964	**(2.7)**	<0.001
Congestive Cardiac Failure	492/11,982	**(4.1)**	1,196/13,964	**(8.6)**	<0.001
New onset AF	554/11,982	**(4.6)**	1,125/13,964	**(8.1)**	<0.001
Pneumonia	1,124/11,982	**(9.4)**	1,780/13,964	**(12.7)**	<0.001

5.3 Discussion

This chapter examines non-elective colorectal resection in the elderly population in English NHS trusts and quantifies the morbidity and mortality in this high risk patient cohort. One in four patients aged over 70 years died within 30 days of surgery. Half of all patients operated upon aged >80 years died within a year of surgery. These results provide an important insight into the short term and intermediate term consequences of unplanned colorectal resection in elderly patients.

Colorectal cancer is a disease of later life, the incidence doubling with every decade after the age of 40 years with a median age of diagnosis of 70 years (Basili et al., 2008, Cress et al., 2006, Mulcahy et al., 1994). Unsurprisingly, just under half of the study population had a diagnosis code pertaining to colorectal malignancy. Traditionally, it has been shown that elderly patients have poorer outcomes following surgery for colorectal cancer with a large number of them presenting as an emergency with obstruction or perforation(Basili et al., 2008, Pavlidis et al., 2006). The decision to undertake emergency surgery in an elderly patient must factor the risks and benefits of surgery, anaesthesia and intensive therapy, current and expected quality of life as well as the patient's desires. Interestingly, in our study the risk of short and intermediate term mortality following surgery for benign conditions was greater than that posed by malignancy. One could explain this by the fact that benign conditions are generally inflammatory in nature, drawing a greater physiological stress response. This, especially in the elderly with already depleting physiological reserves, could pose a greater challenge for recovery. This may also suggest that the mortality risk associated with surgery may be of greater relevance than the natural course of the disease process itself i.e. malignancy..

Various case series that have reported short term mortality outcome following elective colorectal resection in the elderly cite rates between 0% and 3.1%(Basili et al., 2008, De Santis and Frigo, 2005, Frasson et al., 2008). Literature review would, however, suggest that these figures are potentially falsely reassuring when everyday surgical practice is examined. Observational studies carried out using clinical registry data and national administrative data sources have reported that short-term mortality is in fact in the range of 5.4% - 7.18% (Faiz et al., 2010a, Tan et al., 2007). Faiz and colleagues demonstrated in the elective setting however that 30-day mortality measures overestimate survival as many patient deaths occur beyond the initial 30-day period but within the first year of surgery. There is indeed a large variation in the mortality rates reported within case series and observational studies from registry data. This has been clearly demonstrated in the systematic review of such studies (see Chapter 4). Visser and co-workers in the United States found that mortality following colorectal surgery doubled from 4.3% at thirty days to 9.1% at ninety days(Visser et al., 2009). They found similar trends for elective as well as emergency surgery. Their group has suggested 90-day mortality as a potential measure of outcome as they also observed that a large proportion of the deleterious effects of surgery occur beyond the primary admission. The current study supports a similar observation in patients undergoing non-elective surgery. An ongoing postoperative stress response coupled with associated patient frailty could potentially account for these extra deaths in the intermediate term. The current study demonstrated that one in six elderly patients develop a postoperative cardiopulmonary complication following emergency large bowel resection. This is consistent with the literature(McGillicuddy et al., 2009, Mulcahy et al., 1994). General anaesthesia, coupled with the presenting surgical disease and consequent surgical insult, is associated with detrimental cardiorespiratory effects, especially in high risk patients(Daganou et al., 1998). These factors could potentially contribute towards the late deaths observed in this population based study.

Whether this mortality is a direct result of the surgical insult or natural senescence can only be ascertained from survival analyses comparing these patients with normal elderly subjects. Using national population projections from the Office for National Statistics, we compared the mortality rates in the patients undergoing non-elective colorectal resection and general population of the same age group (Table 27). These figures show that death rates, even at one year following surgery, are significantly higher than the general population and worse that the life expectancy, even in the extreme elderly. According to ONS, for the general male population older than 80 years, death rate (for the year 2010) was 14.8% with a life expectancy of 4.7 years (in females this was 12% and 5.4 years). However in our study half of the over 80 population died within one year of surgery.

The term 'non-elective' or ‘emergency’ surgery in the context of this study describes the mode of admission. The urgency of the operation cannot be ascertained from HES data. In the current study 42.1% of patients were operated on within 2 days of admission (Figure 9). In addition, the mortality figures correspond to other studies in literature which have reported outcomes following emergency colorectal surgery in the elderly (Kenkel, 1991d, Wagner and Kenkel, 1991, Kenkel, 1991b, Kenkel, 1991c). This suggests that in such scenarios, there is no time for pre-operative optimisation of the cardiorespiratory physiology in order to improve outcome and potentially increase survival. This is a liberty that is limited to planned or elective surgery, whereby pre-assessment can be undertaken and there is time to undertake interventions to improve the physiological status of the patient. The patients themselves do not have the opportunity to consider the various risks and benefits of the operation, thus furthermore increasing the importance of the conveying to them and relatives, not only immediate, but intermediate outcomes as well.

Table 28: One year mortality rates of study population and projected life expectancy for age-matched general English population

Age groups	Male					Female				
	Study population		**General population**			**Study population**		**General population**		
	Number of deaths	(%)	Number of deaths per 1000,000 population	(%)	**LE**	Number of deaths	(%)	Number of deaths per 1000,000 population	(%)	**LE**
70-75	1148/3251	(35.3)	2766	(2.8)	11.8	1265/3693	(34.3)	1811	(1.8)	14.0
76-80	1159/2689	(43.1)	4916	(4.9)	8.6	1449/3578	(40.5)	3434	(3.4)	10.3
>80	1497/2856	(52.0)	14798	(14.8)	4.7	2538/5030	(50.5)	12609	(12.0)	5.4

LE = projected life expectancy in years

Source: 2010-based National Population Projections. Office for National Statistics (Published 26 October 2011) (http://www.ons.gov.uk/ons/taxonomy/index.html?nscl=Population)

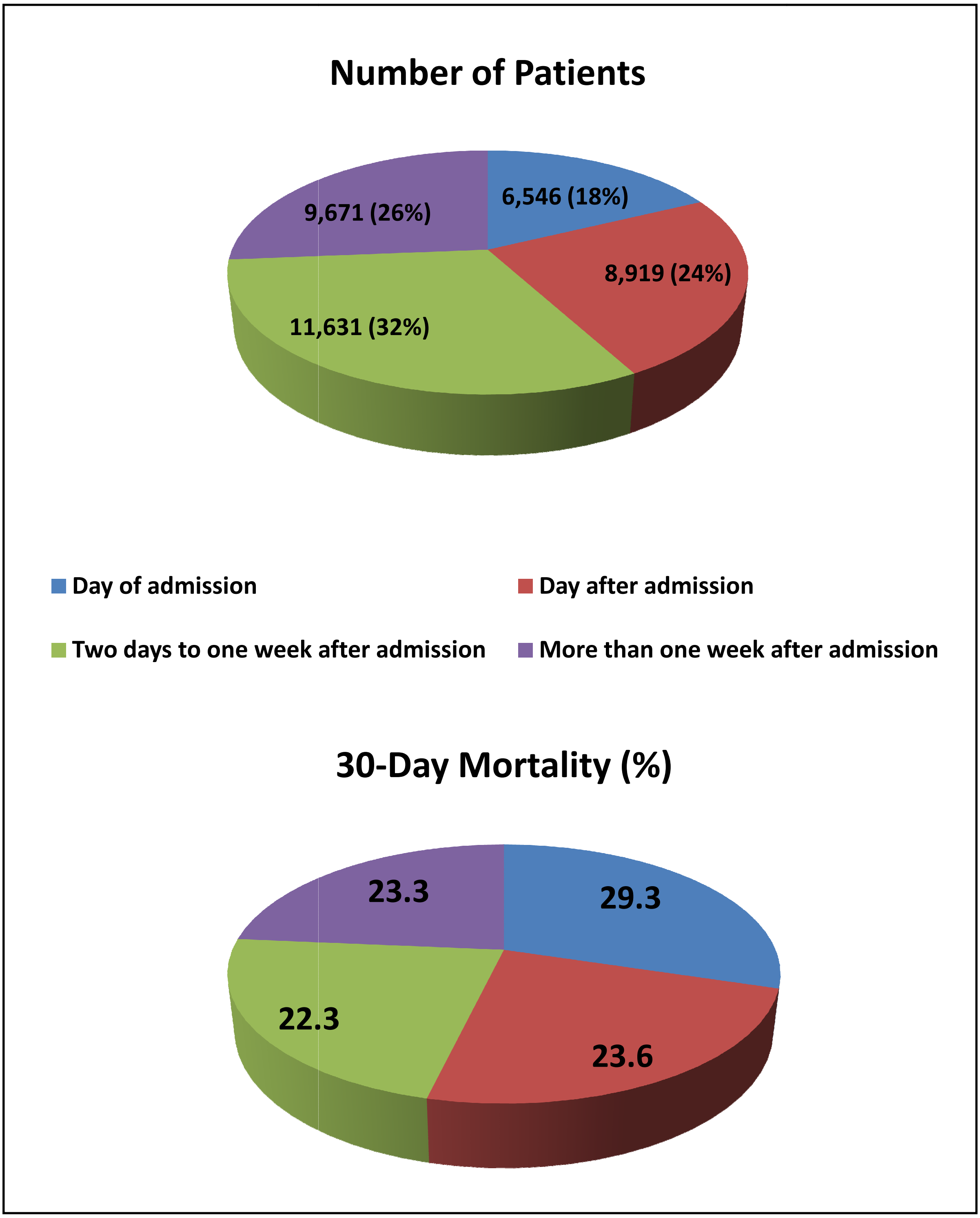


Figure 9: Time interval between admission and surgery and 30-day mortality

Age and mortality

Fewer octogenarians in this study underwent a re-operation as compared to the younger age groups. This may suggest that elderly patients may have a poor outcome following surgical complications. Lower re-operation rate may also reflect the reluctance of surgeons to subject these patients to further surgical and anaesthetic insult. The presence of an independent and causal relationship between advancing patient age and mortality following bowel resection has been debated. Some investigators have demonstrated the absence of such an association (Catena et al., 2002, Hermans et al., 2010, Pavlidis et al., 2006). In contrast, analysis of the Rotterdam Cancer Registry has suggested that outcome is age-dependent in a colorectal cancer population(Damhuis et al., 1996). The current study also observed that advanced age is an independent determinant of 30-day as well as 365-day mortality following emergency colorectal surgery. Octogenarians have twice the short term risk of death as compared with those aged 70-75 years. Improvements in pre-operative assessment may facilitate identification of elderly patients that can withstand major resectional surgery. Physiological, in addition to functional, patient assessment as is being conducted in the Preoperative Assessment of Cancer in the Elderly (PACE) study could rationalise pre-operative decision-making through improved stratification of patients into surgical and non-surgical management groups (Audisio et al., 2008). Although it is desirable to offer curative resection to all patients, application of alternative strategies (such as diverting stoma for obstruction) may represent, in patients with an extremely poor perioperative outlook, a more appropriate management path. Obviously, the patients' views are central to such decisions but offering full information regarding the likely outcome in the immediate term is essential for autonomous decision-making.

This study informs upon the delayed effects of emergency colorectal resection in the elderly population. Denial of operations to patients who are elderly is not appropriate. Rationalisation of decision-making is, however, warranted. In addition, improved perioperative care, including greater access to intensive care facilities and in-hospital physiotherapy may be essential components to enhancing outcome in this patient group. A multidisciplinary approach involving physicians has been successfully implemented, and shown to improve outcome, amongst elderly patients admitted with fractured neck of femur(Adunsky et al., 2005). A similar in-hospital and community approach involving elderly care services in the management of patients presenting with emergency colorectal conditions could prove invaluable. There is a paucity of studies that have sought to investigate the post-operative / post-discharge changes that occur in quality of life following colorectal resection among elderly patients. Some studies have however demonstrated a decline in physical functioning and a consequent increase in dependence among the elderly following surgery for colorectal cancer (Mastracci et al., 2006). Similar functional loss has been observed in elderly patients discharged from surgical intensive care (Udekwu et al., 2001). Improvement in intermediate outcome following gastrointestinal resection in elderly patients may only be achievable by an approach that involves intensive community support and ongoing rehabilitation following hospital discharge. General practitioners, community nurses, occupational therapists and physiotherapists need to be aware of the late morbidity and mortality that often ensues major emergency colorectal surgery in this vulnerable patient group.

CHAPTER 6: REDUCING RISK IN GASTROINTESTINAL RESECTION – THE ROLE AND IMPACT OF MINIMAL ACCESS SURGERY

Minimal access surgery (MAS) or laparoscopic surgery has been widely promoted as a minimally invasive approach to the abdominal cavity. Since it was first described, this approach has been widely used by gynaecologists and subsequently found its way into general surgical practice. Muhe performed the first laparoscopic cholecystectomy in 1985 and this procedure has now become the gold standard treatment for symptomatic gallstones (Reynolds, 2001). Laparoscopic cholecystectomy has been shown to be superior to the open approach, with reduced postoperative pain, shortened hospital stay, faster recuperation and earlier return to normal function (Keus et al., 2006). Although the evidence is equivocal, laparoscopic approach has also been widely publicised for performing an appendicectomy. The attenuated surgical stress response following laparoscopic surgery may be responsible for improved outcome. Moreover, biochemical markers of surgical stress such as C-Reactive Protein, Tumor Necrosis Factor and Endothelin have been shown to be higher following open surgery when compared with the laparoscopic approach (Madbouly et al., 2010).

6a Reduced risk of mortality and morbidity in patients selected for elective colorectal resection

After being accepted as the gold standard for cholecystectomy, laparoscopic surgery has been widely undertaken to perform colorectal resections. This uptake of laparoscopic colorectal surgery has been ratified by various large randomized trials (UK MRC, CLASICC, COST, COLOR) that have demonstrated the safety and feasibility of this technique in routine practice (Braga et al., 2002, Jayne et al., 2007, Liang et al., 2007, Champault et al., 2002, Hazebroek, 2002, Lacy et al., 2002). In addition, benefits over open surgery such as decreased post-operative pain, earlier mobilisation, quicker recovery and reduced length of stay have been demonstrated in various studies. Specifically, two large population based studies, one from the United States using the National Surgical Quality Improvement Program (NSQIP) (Kennedy et al., 2009) data and the second from the UK using Hospital Episode Statistics (Faiz et al., 2009) data have shown a significant reduction in short-term morbidity and mortality in patients undergoing laparoscopic colorectal resection. The latter study by Faiz and colleagues also demonstrated that the lower risk of mortality following laparoscopic colorectal resection was evident even at one year following surgery. However the study was unable to provide an explanation for the same. To examine these findings the current study analysed HES data to compare short term and intermediate term outcomes following laparoscopic and open elective colorectal resection.

6a.1 Methods

The dataset used for this study, variable coding and outcome measures have been described in detail in sections 2.4.1 and 3.2.1 of this report. Patients undergoing elective colorectal resections between April 2001 and March 2008 were included. Patients were labeled as ‘Lap’ or ‘Open’ groups depending on the surgical approach. The OPCS codes used to identify laparoscopic cases were Y50.8 and Y752. Y714 is the code for failed minimal access which has been in use since 2006. Patients undergoing procedures employing the latter code were included in the laparoscopic group. Patients were tracked for a period of 365 days following surgery for subsequent unplanned admissions with specific problems related to cardiac, respiratory and renal systems along with venous thrombo-embolism (VTE) and stroke. Pre-operative co-morbidity status was ascertained by recording admissions with medical complaints for a 5-year period prior to the index operation.

6a.2 Results

Of the 138,735 patients identified from the database 128,840 (92.9%) underwent an 'open' colorectal resection while 9,895 (7.1%) underwent a 'lap' procedure. The percentage of laparoscopic procedure significantly increased from 2000-2001 (0.8%) to 2007-2008 (19.6%) (Figure 10).

Demographics

Patients were divided into the following age groups: <55 years, 55-69 years, 70-79 years and >79 years. Majority of the patients were aged between 55 and 79 years (92,624/138,735). There were more females as compared to males in the lap group (51.4% females and 48.6% males) while in the open group there were 46.8% females and 53.2% males. The majority of patients in both the groups had a malignant diagnosis (70.4% in the open group and 66.7% in the lap group). There were more right sided resections in the lap group and more rectal resections in the open group. The demographic details of both groups are shown in Table 28. Cardiac co-morbidity was most common in both groups. More patients in the open group had a previous DVT/PE (0.5% versus 0.3%, p<0.001) while more patients in the lap group had a diagnosis of diabetes (6.0% versus 5.2%, p=0.001). 2,259 (22.8%) patients in the lap group had a pre-existing cardiac co-morbidity while only 19.6% (25,283) in the open group had a cardiac co-morbidity (p<0.001).

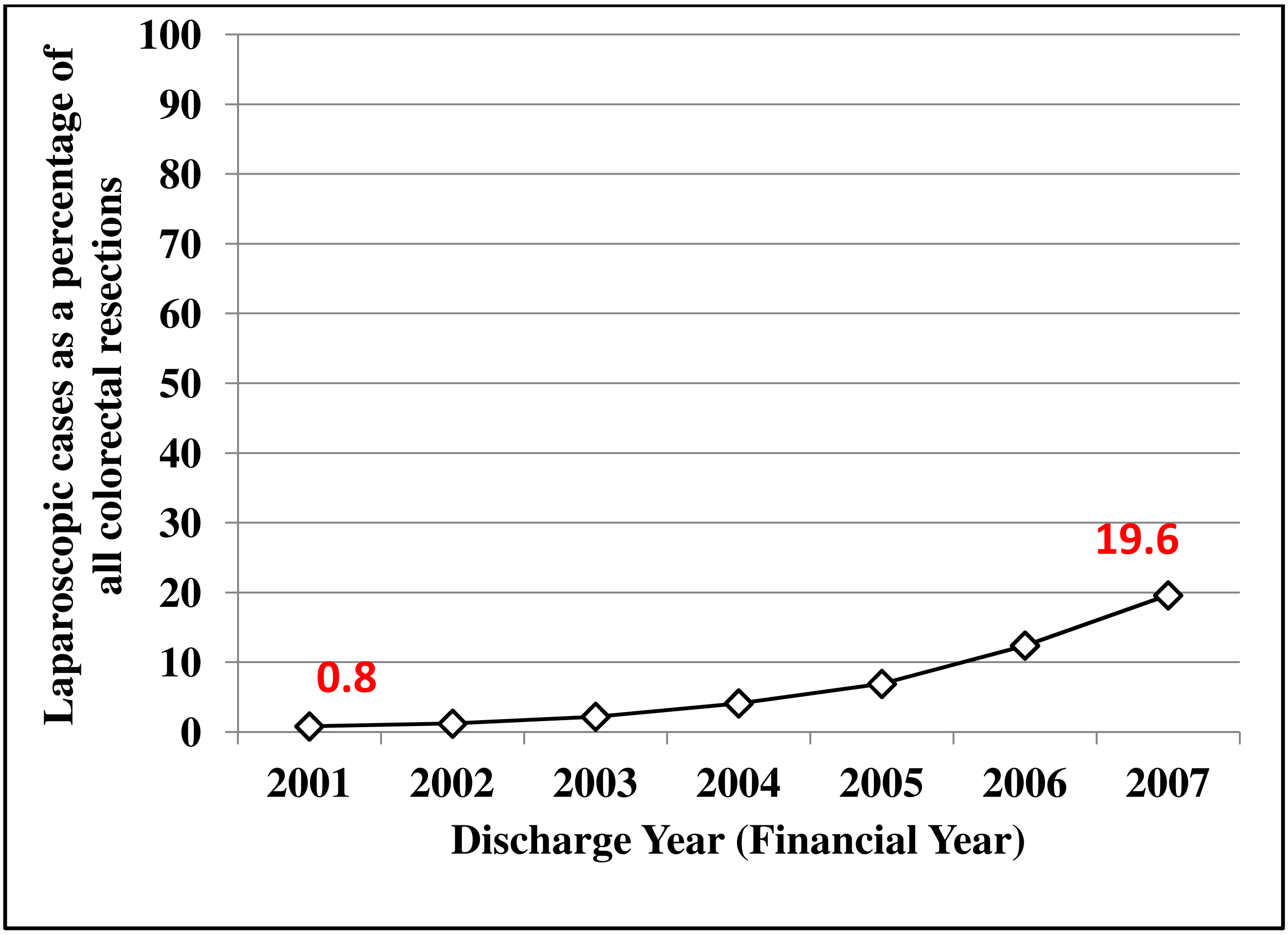


Figure 10: Uptake of laparoscopic colorectal resection in English NHS Trusts

Table 29: Descriptive characteristics of patients undergoing elective colorectal resection *(April 2001- March 2008)*

	Open N=12,8840		Laparoscopic N=9,895		
	n	(%)	n	(%)	p value [¥]
Age					<0.001
<55 years	22,079	(17.1)	1,865	(18.8)	
55-69 years	44,755	(34.8)	3,346	(33.9)	
70-79 years	41,476	(32.2)	3,047	(30.8)	
>79 years	20,530	(15.9)	1,637	(16.5)	
Gender					<0.001
Male	68,567	(53.2)	4,812	(48.6)	
Female	60,273	(46.8)	5,083	(51.4)	
Diagnosis					<0.001
Malignancy	90,707	(70.4)	6,596	(66.7)	
Diverticulosis	11,033	(8.6)	1,002	(10.1)	
IBD	9,149	(7.1)	698	(7.1)	
Other	17,951	(13.9)	1,599	(16.1)	
Resection					<0.001
Subtotal/Total	5,900	(4.6)	260	(2.6)	
Right sided	38,053	(29.5)	3,597	(36.4)	
Left Sided	23,958	(18.6)	1,956	(19.7)	
Rectal	60,929	(47.3)	4,082	(41.3)	
Preoperative Co-morbidity					
Cardiac	25,283	(19.6)	2,259	(22.8)	<0.001
Respiratory	7,622	(5.9)	630	(6.4)	0.068
VTE	684	(0.5)	28	(0.3)	0.001
Stroke	423	(0.3)	28	(0.3)	0.445
Renal	861	(0.7)	60	(0.6)	0.465
Diabetes	6,729	(5.2)	593	(6.0)	0.001

[¥] = *Chi Squared Test*

Short term outcomes

30-day mortality following open colorectal surgery was 3.4% (n=4,351) and 1.7% (n=164) after a laparoscopic procedure (p<0.001). Length of stay was significantly lower in the lap group [7 days (IQR 5-11 days)] as compared to the open group [12 days (IQR 9-17 days)] (p<0.001). 12.4% of patients from the lap group (1,227/9,895) had a post-operative medical complication as compared to 14.8% (19,092/12,8840) from the open group (p<0.001). Specifically, myocardial infarction, congestive heart failure, pneumonia, respiratory failure and venous thrombo-embolism occurred less frequently in the lap group (Table 30).

Intermediate outcomes

For patients operated prior to 2005, one year mortality was available via linkage with the ONS. 365-day mortality was 12.1% (8875/73540) in the open group which was significantly higher than the lap group (5.3% 83/1561) (p<0.001). Similarly medical morbidity coded from subsequent admissions up to one year was significantly higher in the open group as compared to the lap group (15.8% and 13.6% respectively, p<0.001).

Risk adjusted outcomes

Multiple logistic regression models were created with risk-adjustment for age, gender, diagnosis, type of resection, co-morbidity and re-intervention. Patients in the lap group had a lower risk of 30-day mortality (OR 0.46, 95%CI 0.39-0.53, p<0.001) and 365-day mortality (OR 0.43, 95%CI 0.34-0.54, p<0.001) as compared to those who underwent conventional open surgery. The laparoscopic approach was also associated with a lower risk of cardiorespiratory complications, venous thrombo-embolism and renal failure in the short term. (Table 31. Also see Tables 5 and 6, Chapter 3).

Table 30: Outcomes following elective open and laparoscopic colorectal resection

Outcomes	**Open**		**Lap**		
	n=12,8840	**(%)**	**n=9,895**	**(%)**	**p value***
Mortality					
30-day, in-hospital	4,351	(3.4)	164	(1.7)	<0.001
365-day, in & out of hospital#	8,875/73,540	(12.1)	83/1,561	(5.3)	<0.001
Medical Morbidity	19,092	(14.8)	1,227	(12.4)	<0.001
Readmission	12,368	(9.6)	998	(10.1)	0.069
Length Of Stay, median (IQR)	12 days	(9-17)	7 days	(5-11)	<0.001@

* = Chi squared test; # = only prior to 2005 @ = Mann-Whitney U test; IQR= Inter Quartile Range

Table 31: Post-operative medical morbidity occurring within 30 days of elective colorectal resection

	30-day Medical Morbidity							
	Open (n=128,840)		Lap (n=9,895)		p value[¥]	Total (n=138,735)	
	n	(%)	n	(%)		N	(%)
Cardiac	11,550	(9.0)	757	(7.7)	<0.001	12307	(8.9)
Respiratory	8,038	(6.2)	500	(5.1)	<0.001	8538	(6.2)
VTE	882	(0.7)	36	(0.4)	<0.001	918	(0.7)
Stroke	344	(0.3)	12	(0.1)	0.006	356	(0.3)
Renal Failure	1,886	(1.5)	106	(1.1)	0.002	1992	(1.4)
Angina	5,127	(4.0)	361	(3.6)	0.104	5488	(4.0)
Myocardial Infarction	1,271	(1.0)	68	(0.7)	0.003	1339	(1.0)
Congestive Cardiac Failure	2,365	(1.8)	105	(1.1)	<0.001	2470	(1.8)
Atrial Flutter/Fibrillation	4,283	(3.3)	304	(3.1)	0.177	4587	(3.3)
Pneumonia	5,719	(4.4)	345	(3.5)	<0.001	6064	(4.4)
Pleural Effusion	1,993	(1.5)	126	(1.3)	0.033	2119	(1.5)
Respiratory Failure	944	(0.7)	45	(0.5)	0.002	989	(0.7)
Other Respiratory*	1,159	(0.9)	76	(0.8)	0.180	1235	(0.9)
Deep Vein Thrombosis	343	(0.3)	9	(0.1)	0.001	352	(0.3)
Pulmonary Embolism	584	(0.5)	31	(0.3)	0.043	615	(0.4)

[¥] *=Chi squared test; *Other Respiratory=Acute Exacerbation of COPD, Pulmonary Oedema, Post-procedural respiratory complications*

Table 32: Lower risk of medical morbidity following laparoscopic colorectal resection

	Cardiac			Respiratory			VTE			Stroke			Renal Failure		
	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value	OR	95% CI for OR	p value
Surgical Approach			<0.001			<0.001			0.001			0.008			0.001
Open	1.00			1.00			1.00			1.00			1.00		
Laparoscopic	0.79	(0.73, 0.85)	<0.001	0.78	(0.71, 0.86)	<0.001	0.55	(0.40, 0.77)	0.001	0.46	(0.26, 0.82)	0.008	0.72	(0.59, 0.88)	0.001

Odds Ratios from a multiple regression model including risk adjustment for Age, Gender, Diagnosis, Type of resection and Pre-operative co-morbidity.

6a.3 Discussion

This national observational study has demonstrated lower mortality and medical morbidity risk to patients selected for the laparoscopic approach to colorectal resection. The physiological impact of the pneumoperitoneum incurred at the time of laparoscopy includes an increase in cardiac afterload with an associated decrease in venous return(Kashtan et al., 1981, Joris et al., 1993). Our findings suggest, however, that such intra-operative physiological changes do not translate into increased post-operative complications. In the present investigation patients undergoing laparoscopic surgery demonstrated a lower incidence of acute myocardial infarction, congestive cardiac failure, pneumonia and acute respiratory failure. An explanation for these findings might be accounted for by the reduced surgical stress inflicted by laparoscopic surgery when compared with traditional care.

Patients selected to undergo a laparoscopic approach were at nearly half the risk of developing VTE at 30 days when compared with those undergoing open surgery. Routine inpatient data (as relates to our findings) are unlikely to identify a significant proportion of cases of DVT which are treated on an outpatient basis if occurring beyond discharge. On analysis of DVT cases on the index admission, however, a statistically significant increase in the incidence of DVT following open surgery was still identified. This may in part be explained by higher number of patients with a prior history of VTE in the open group. Risk-adjustment including pre-operative co-morbidity demonstrated a ten-fold risk in developing VTE within 30 days of surgery amongst patients with a prior history of VTE. Certainly, laparoscopy is associated with early ambulation which may limit postoperative venous stasis. The surgical stress response is a recognised pro-coagulant state. The reduced stress response following laparoscopic surgery may therefore explain the study findings.

Covariate interaction

I tested for an interaction between surgical approach and age with patients <55 years of age and undergoing open surgery as the reference group. This showed that patients aged 55 to 80 years and undergoing laparoscopic surgery had lower risk of mortality (p<0.001). Only the elderly aged >80 years showed a higher risk of death when compared with those <55 years of age (OR 1.26, 05% CI 1.00-1.59, p=0.049). Similar analysis for co-morbidity and surgical approach demonstrated that patients with pre-operative co-morbidity who underwent laparoscopic surgery had a 44% lower risk of mortality when compared with those in the open group but with no co-morbidity (OR 0.56; 95% CI 0.44-0.79; ,p<0.001).

Co-morbidity and laparoscopy

A subset analysis was undertaken to study the outcomes in patients with pre-existing co-morbidity and those who were fit and healthy pre-operatively. There is an arguement that during the initial learning curve of laparoscopic surgery, there is a tendency for case selection. Patients those who are fit and healthy, with early disease may be favoured for laparoscopic surgery. On the other hand, complex patients such as advanced disease, high BMI or significant cardiorespiratory compromise would be offered tradition open surgery as an easier surgical approach and also to try and minimise operative time. However with the advancement of minimally invasive surgery and anaesthethesia, operative times are comparable and in fact laparoscopy may have an added advantage of smaller incisions, minimal tissue injury and lesser physiological stress response. In our study, outcomes were better in patients that underwent laparoscopic surgery as compared to the traditional open approach in the presence and absence of pre-operative co-morbidity (Table 32).

Table 33: Comparison of outcomes in patients with and without preoperative co-morbidity

	Open					Laparoscopic				
	Preoperative co-morbidity **Absent** 96,993		Preoperative co-morbidity **Present** 31,847			Preoperative co-morbidity **Absent** 7104		Preoperative co-morbidity **Present** 2791		
	n	(%)	n	(%)	p value ¥	n	(%)	n	(%)	p value ¥
30-day Mortality	2598	(2.7)	1753	(5.5)	<0.001	95	(1.3)	69	(2.5)	<0.001
30-day Morbidity	11,016	(11.4)	8,078	(25.4)	<0.001	677	(9.5)	548	(19.6)	<0.001
365-day Mortality*	6296	(10.8)	2579	(16.8)	<0.001	53	(4.3)	30	(9.1)	0.001
Length of Stay *Days (IQR)*	11	(9-16)	13	(9-19)	<0.001@	7	(5-11)	8	(6-12)	<0.001@

¥ = Chi squared test; * = only available prior to 2005; @ = Mann-Whitney U test; IQR = Inter-Quartile Range

However, these benefits are dually associated with Enhanced Recovery Protocols (ERPs) also. In the United Kingdom many enthusiasts for laparoscopy are also proponents of enhanced recovery. In our study an excess of patients receiving enhanced recovery care in the laparoscopic group could potentially have contributed, to some extent, to the reduced morbidity identified in this group. Another weakness of this study is that this study is not immune to selection bias as regards to the surgical approach and evidence from randomised control trials with carefully constraining inclusion criteria is essential to draw firm conclusions. Morbidity occurring outside of hospital i.e. managed on an outpatient basis will not find inclusion in our data. Thus, this study underestimates total complications occurring following surgery. Severe complications are, however, likely to require readmission and therefore find inclusion. For the reasons above as well as the exclusion of surgical morbidity we accept that total actual postoperative morbidity is likely to be higher than our recorded figures.

6b Short-term outcomes following open and minimally invasive oesophagectomy

In an attempt to mirror the success achieved in colorectal resection, recently minimally invasive oesophagectomy (MIO) has been increasingly performed (Lazzarino et al., 2010). However, in spite of studies showing this technique to be safe and feasible, there has been no conclusive evidence of any benefits over the 'open' technique (Hamouda et al., 2010, Luketich et al., 2003, Verhage et al., 2009). Systematic reviews and meta-analyses form the main body of evidence in the absence of large randomised controlled trials. Although some studies have reported improvement in morbidity following MIO, there is no significant reduction in mortality proven (Gemmill and McCulloch, 2007, Law, 2006). To date no population based study has been undertaken to evaluate the morbidity following MIO and open surgery. Our team has previously demonstrated the increasing uptake of MIO in English NHS Trusts and described the mortality, length of stay and emergency readmissions following open and MIO between 1996 and 2008 (Lazzarino et al., 2010). The current study aims to identify and quantify morbidity and re-interventions following open and MIO for cancer in England over 5 years (2005-2009). This recent period was selected because it is more representative of established techniques as the MIO to open oesophagectomy ratio was very small (0.6% - 3.8%) between 1996-2004 (Lazzarino et al., 2010) and represented the learning curve of introducing MIO.

6b.1 Methods

The HES database used for this study has been described in detail in Chapters 2 and 3 of this report. We report outcome for patients operated between April 2005 and March 2010. This period was chosen to exclude the learning curve of surgeons and take into account the process of centralisation of services in England. Minimally invasive oesophagectomy (MIO) was defined by the use of laparoscopy and/or thoracoscopy. This was identified by the presence of a relevant procedure code in addition to the main oesophagectomy code. The OPCS-4 codes used to identify laparoscopy were Y50.8 (prior to April 2006) and Y75 (after April 2006) and those for thoracoscopy were Y49.8 (prior to April 2006) and Y74 (after April 2006). Total-MIO was defined as a procedure which included a code for both laparoscopy and thoracoscopy while the presence of any one of the above codes was termed as Hybrid-MIO.

Outcome variables

Mortality and Length of Stay (LOS):

We used in-hospital mortality within 30 days of the procedure. Length of stay (LOS) was taken as the duration (in days) spent in hospital during the primary admission and we report median lengths of stay with inter-quartile ranges (IQR).

Medical morbidity:

Post-operative medical morbidity was taken from the secondary diagnosis fields of the index admission and the primary diagnosis codes from any subsequent unplanned admissions within 30 days of surgery. Complications were grouped according to involvement of an organ system and presence of any one complication pertaining to that system was considered.

Re-intervention and Re-operation:

Any unplanned procedure such as endoscopy, radiology guided procedure or return to theatre during the index admission or within 30 days of initial surgery was termed as re-intervention (HES records the dates of all procedures). Laparotomy, thoracotomy or use of minimally invasive approach subsequent to the index surgery was defined as re-operation or return to theatre. Both re-intervention and re-operation were determined by analysing procedure codes. Return to theatre or re-intervention on the same day as the index surgery could not be identified due to limitations of the dataset.

6b.2 Results

During the five year period we identified 7,502 patients who underwent an oesophagectomy for cancer in an English NHS Trust hospital. Of these 6,347 (84.6%) were open and 1,155 (15.4%) underwent an MIO. Figure 11 shows the increasing use of MAS over the study period. Descriptive characteristics of the patients in the two groups have been shown in Table 33. Age and gender distribution between the two patient groups (MIO and Open surgery) were similar. More patients in the MIO group resided in affluent areas. Pre-operative co-morbidity profile was also similar in both the groups, with majority of the patients having cardiac co-morbidity.

Short term outcomes

There was no statistical difference in the 30-day in-hospital mortality between the MIO (4.0%) and open (4.3%) groups (p=0.605) (Table 34). Median LOS in the both the groups was 15 days. The significant p value held true even after log transformation and may be attributable to the large sample size. Readmission rates were similar in both groups. Similarly, medical morbidity rates were not statistically different between the two groups (38.0% and 39.2% in the MIO and open groups respectively, p=0.457). Unadjusted analyses showed similar incidence of respiratory complications in the two groups, but a lower rate of pleural effusion in the MIO group as compared to the open group (12.8% and 16.2% respectively, p=0.004). There were however significant differences in the re-operation and re-intervention rates between the two groups. More patients in the MIO group underwent a re-operation or a procedure such as endoscopy or radiology guided procedure.

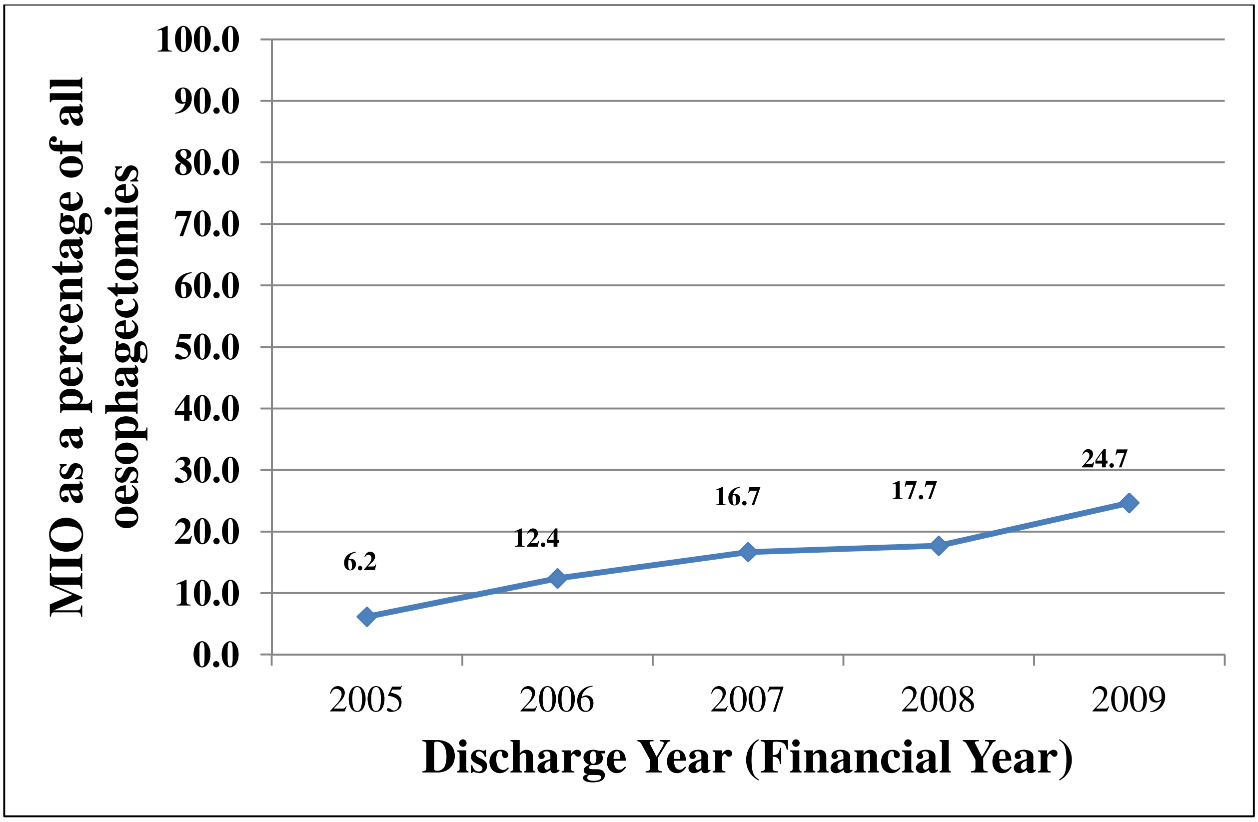


Figure 11: Uptake of Minimally Invasive Oesophagectomy (MIO) in English NHS Trusts

Table 34: Descriptive characteristics of patients undergoing oesophagectomy for cancer *(April 2005 - March 2010)*

	Oesophagectomy				
	Open		MIO		
	n=6347	(%)	n=1155	(%)	p value*
Age					0.218
<60 years	1,916	(30.2)	334	(28.9)	
60-70 years	2,741	(43.2)	485	(42.0)	
>70 years	1,690	(26.6)	336	(29.1)	
Gender					0.711
Male	4,870	(76.7)	892	(77.2)	
Female	1,477	(23.3)	263	(22.8)	
Carstairs Index					0.003
(least deprived) 1	1,283	(20.2)	288	(24.9)	
2	1,498	(23.6)	264	(22.9)	
3	1,424	(22.4)	264	(22.9)	
4	1,192	(18.8)	196	(17.0)	
(most deprived) 5	920	(14.5)	140	(12.1)	
Unclassified	30	(0.5)	2	(0.2)	
Co-morbidities					
Cardiac	2,234	(35.2)	400	(34.6)	0.711
Respiratory	782	(12.3)	141	(12.2)	0.914
VTE	158	(2.5)	38	(3.3)	0.117
Stroke	37	(0.6)	6	(0.5)	0.793
Renal Failure	57	(0.9)	11	(1.0)	0.858
Diabetes	598	(9.4)	90	(7.8)	0.078

** = Chi squared test; VTE = venous thrombo-embolism*

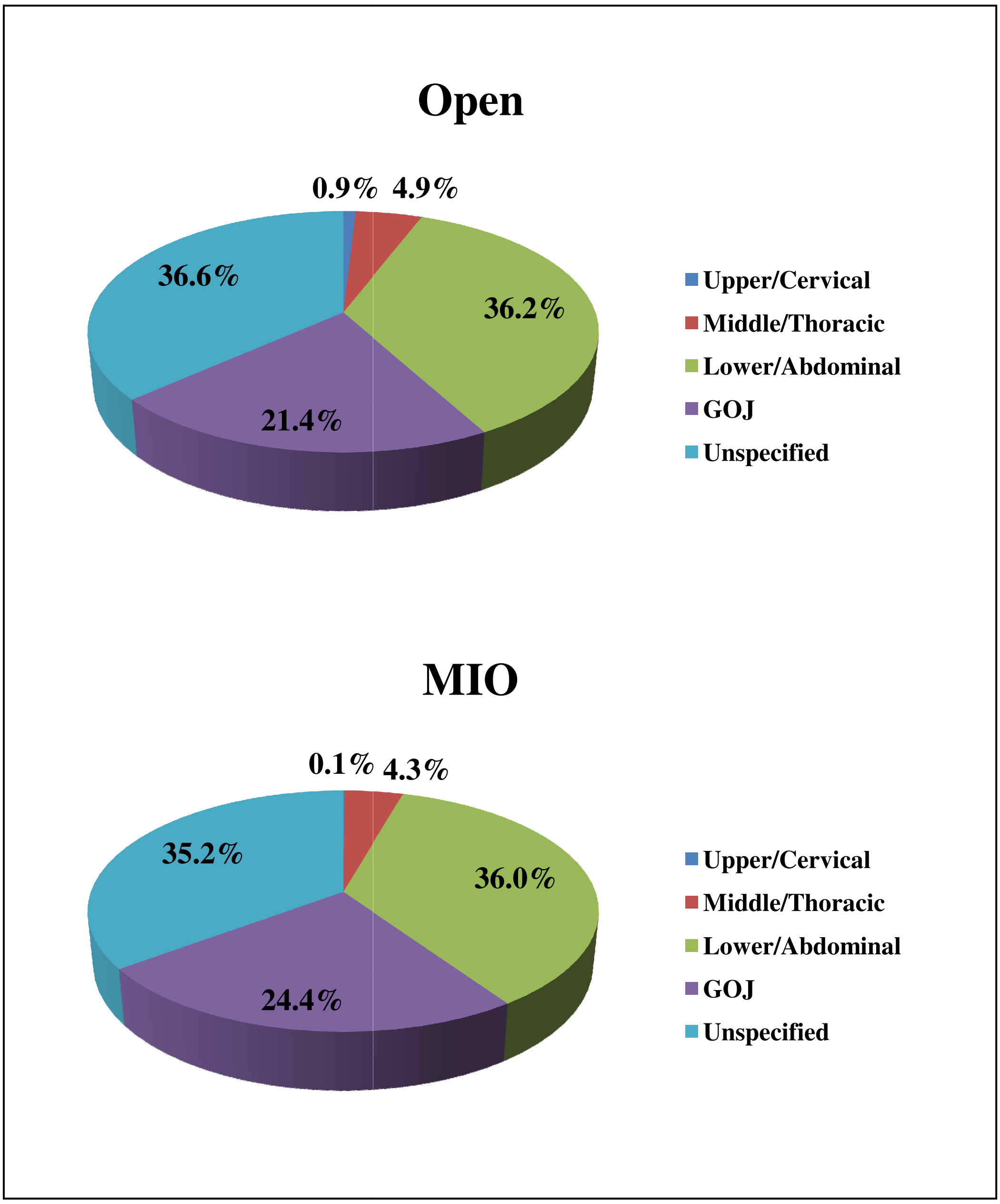


Figure 12: Site of oesophageal cancer according to ICD-10 diagnosis codes

Table 35: Unadjusted short term outcomes, within 30 days of oesophagectomy

Outcomes		Oesophagectomy				
		Open		MIO		
		n=6347	(%)	n=1155	(%)	p value*
Mortality						
	30-day, in-hospital	274	(4.3)	46	(4.0)	0.605
Medical Morbidity						
	Cardiac	841	(13.3)	138	(11.9)	0.227
	Respiratory	1992	(31.4)	347	(30.0)	0.365
	VTE	125	(2.0)	24	(2.1)	0.808
	Stroke	14	(0.2)	2	(0.2)	0.748
	Renal Failure	126	(2.0)	17	(1.5)	0.241
Surgical Complications						
	Re-intervention	1117	(17.6)	242	(21.0)	0.006
	Re-operation	355	(5.6)	102	(8.8)	<0.001
Readmission						
	Within 28 days	885	(13.9)	151	(13.1)	0.431
Length Of Stay, median (IQR)		15 days	(12-23)	15 days	(12-22)	<0.001[@]

** = Chi squared test; [@] = Mann-Whitney U test; IQR= Inter Quartile Range*

Table 36: Frequencies of short term medical complications after oesophagectomy

Medical Complication	**Oesophagectomy**				
	Open		**MIO**		
	n=6347	**(%)**	**n=1155**	**(%)**	**p value***
Angina	187	(2.9)	28	(2.4)	0.328
Myocardial Infarction	45	(0.7)	4	(0.3)	0.159
Congestive Cardiac Failure	61	(1.0)	7	(0.6)	0.242
Atrial Fibrillation	611	(9.6)	102	(8.8)	0.397
Pneumonia	1181	(18.6)	230	(19.9)	0.296
Pleural Effusion	**1026**	**(16.2)**	**148**	**(12.8)**	**0.004**
Respiratory Failure	238	(3.7)	46	(4.0)	0.703
Other Respiratory Complications[@]	219	(3.5)	28	(2.4)	0.072
Deep Vein Thrombosis (DVT)	39	(0.6)	6	(0.5)	0.701
Pulmonary Embolism (PE)	92	(1.4)	19	(1.6)	0.613
Stroke	14	(0.2)	2	(0.2)	0.748
Renal Failure	126	(2.0)	17	(1.5)	0.241

* = Chi squared test; [@] = Exacerbation of COPD, Pulmonary oedema, Post-procedural respiratory complications

Risk adjusted outcomes

Univariate analyses showed that surgical approach was not a determinant of mortality (OR 0.92, 95% CI 0.67-1.27, p=0.605). Multiple regression models were created for predicting post-operative medical morbidity. MIO was associated with a 14% lower risk of respiratory complications as compared to the open approach (OR 0.86, 95%CI 0.74-1.00, p=0.049). This may reflect the lower incidence of pleural effusion in this group of patients. However the surgical approach was not a significant determinant for other morbidity.

Subgroup analyses

On further dividing the MIO group into Total-MIO and Hybrid-MIO, subsequent endoscopic procedures after the initial surgery were more frequently coded in the patients undergoing a Total-MIO procedure (16.2% versus 6.4%, p<0.001). Post-operative medical morbidity was also similar between these two sub-groups (overall morbidity 39.2% in Hybrid-MIO and 34.2% in Total-MIO groups, p=0.131). The comparison between the two groups has been shown in detail in Table 37.

Table 37: Short term surgical complications (re-interventions) after oesophagectomy

Re-intervention	Open n=6347	(%)	MIO n=1155	(%)	p value*
Laparotomy	146	(2.3)	35	(3.0)	0.137
Thoracotomy	268	(4.2)	83	(7.2)	<0.001
Minimally invasive surgery	12	(0.2)	18	(1.6)	<0.001
Endoscopy	378	(6.0)	101	(8.7)	<0.001
Radiology guided procedure	291	(4.6)	47	(4.1)	0.437

* = Chi squared test

Table 38: Comparison of medical complications between Hybrid-MIO and Total-MIO

Complication	Hybrid-MIO n=877	(%)	Total-MIO n=278	(%)	p value*
Re-intervention					
Laparotomy	22	(2.5)	13	(4.7)	0.066
Thoracotomy	59	(6.7)	24	(8.6)	0.284
Minimally invasive surgery	12	(1.4)	6	(2.2)	0.354
Endoscopy	56	(6.4)	45	(16.2)	<0.001
Radiology guided procedure	33	(3.8)	14	(5.0)	0.349
Medical Morbidity					
Overall Morbidity	344	(39.2)	95	(34.2)	0.131
Cardiac	102	(11.6)	36	(12.9)	0.555
Respiratory	274	(31.2)	73	(26.3)	0.114
VTE	22	(2.5)	2	(0.7)	0.068
Stroke	1	(0.1)	1	(0.4)	0.391
Renal Failure	9	(1.0)	8	(2.9)	0.025

* = *Chi squared test*

6b.3. Discussion

The study has shown a steady increase the use of MIO in England. However no significant benefit over the open approach in terms of reduction in risk of mortality, length of stay or morbidity was demonstrated, albeit there is a small improvement in rates of pleural effusion. On the contrary, MIO was associated with a higher re-intervention rate, in the setting where the two groups are matched evenly in terms of age, gender and co-morbidity. With every progressive study year, the odds ratio for re-intervention increased. A re-intervention was associated with an increased post-operative morbidity with a three-fold increase in the risk of mortality. There was a six times higher risk of respiratory complications and renal failure in the presence of a re-intervention. We cannot determine from the data whether this is a causal association or a treatment for encountered complications. One would expect surgeons to have a lower threshold to perform an endoscopy in patients undergoing MIO because of the risk of gastric tube ischaemia.

The study has its own limitations. It is difficult to reliably identify patients who have undergone conversion to the open approach. Also, the data does not include stage of disease. Lazzarino and colleagues previously demonstrated from HES data that patients undergoing MIO had a lower mortality at one year following MIO, but this study was unable to examine whether there was a propensity to perform MIO in patients with early disease(Lazzarino et al., 2010). Surrogate markers such as re-operation have been used to identify major surgical morbidity as there is no specific code for identifying anastomotic leak. MIO appears to be a safe procedure with outcomes comparable to the open approach, but the study failed to demonstrate any added advantages of this method. Evidence from randomised trials will be needed to draw definitive conclusions. There is a need for studies to examine the long term / oncological outcomes following the two surgical approaches.

6c Introduction of laparoscopic gastrectomy in England

Newer advances in gastrointestinal resection surgery include Minimal Access Surgery (MAS), such as laparoscopy. Gastrectomy is in itself a technically challenging operation giving rise to apprehension amongst surgeons regarding oncological value of laparoscopic stomach resection. A significant change in surgical practice can only be brought about by robust evidence from large prospective studies or randomised trials. The relatively lower incidence of gastric cancer as compared to colorectal malignancy in the West, is a limiting factor to this effect.

Since Kitano described laparoscopy assisted partial gastrectomy in the early nineties, this procedure has gained popularity in Japan (Kitano et al., 1994). A number of randomised trials have been undertaken in Japan and Korea and Ohtani *et al* conducted a meta-analysis of four such trials comparing laparoscopy-assisted distal gastrectomy (LADG) and open distal gastrectomy (ODG) (Ohtani et al., 2010). They concluded that LADG was associated with lesser intra-operative blood loss, analgesia requirement and post-operative complications in the LADG group, along with increased operative time and lower lymph node yield. This study only included 267 patients. Another meta-analysis by Chen and colleagues included six randomised controlled trials comprising of 629 patients and found similar results(Chen et al., 2009). Both the above meta-analyses could not comment on the oncological value of LADG when compared to ODG. Smaller studies from the West have also concluded that laparoscopic gastrectomy is feasible and safe in selected patients(Varela et al., 2006, Weber et al., 2003, Strong et al., 2009, Huscher et al., 2005). An explanation for paucity of literature pertaining to laparoscopic gastrectomy from the West could be the lower detection of early gastric cancer. This study aims to examine the uptake of laparoscopic gastrectomy in England and compare outcomes with the traditional open approach.

6c.1 Methods

All patients who underwent an elective gastrectomy (partial and total) in an English NHS Trust hospital between April 2001 and March 2010 were included. Data were obtained from Hospital Episode Statistics (HES) database and retrospectively analysed (as described in Chapters 2 and 3 of this report). A laparoscopic procedure was identified by the following procedure codes: Y50.8 (prior to April 2006) and Y75 (after April 2006). 30-day in-hospital mortality, length of stay (LOS) and readmission were the primary outcome measures. Post-operative medical morbidity and re-interventions were used to identify medical and surgical complications following the procedures. Re-intervention was defined as any unplanned return to theatre (re-operation) or procedure such as an endoscopy or radiology guided procedure (e.g. drain) during the index admission or within 30 days of initial surgery (HES records the dates of all procedures). Re-intervention on the same day as the index surgery could not be identified due to limitations of the dataset.

5c.2 Results

Between April 2000 and March 2010 10,713 patients underwent an elective gastrectomy for cancer. Of these 10,233 (95.5%) were undertaken using the traditional open approach (OG) while 480 (4.5%) patients underwent a laparoscopic or laparoscopy-assisted gastrectomy (LG). Figure 13 shows the trends in the uptake of LG in England over the ten year period. There has been an increasing number and relative proportion of laparoscopic gastrectomy procedures performed over the study years, reaching 16.1% for cancer in 2009. The procedure code for conversion to open surgery was only introduced in 2006 and hence all patients who had a code for laparoscopy were included in the LG group.

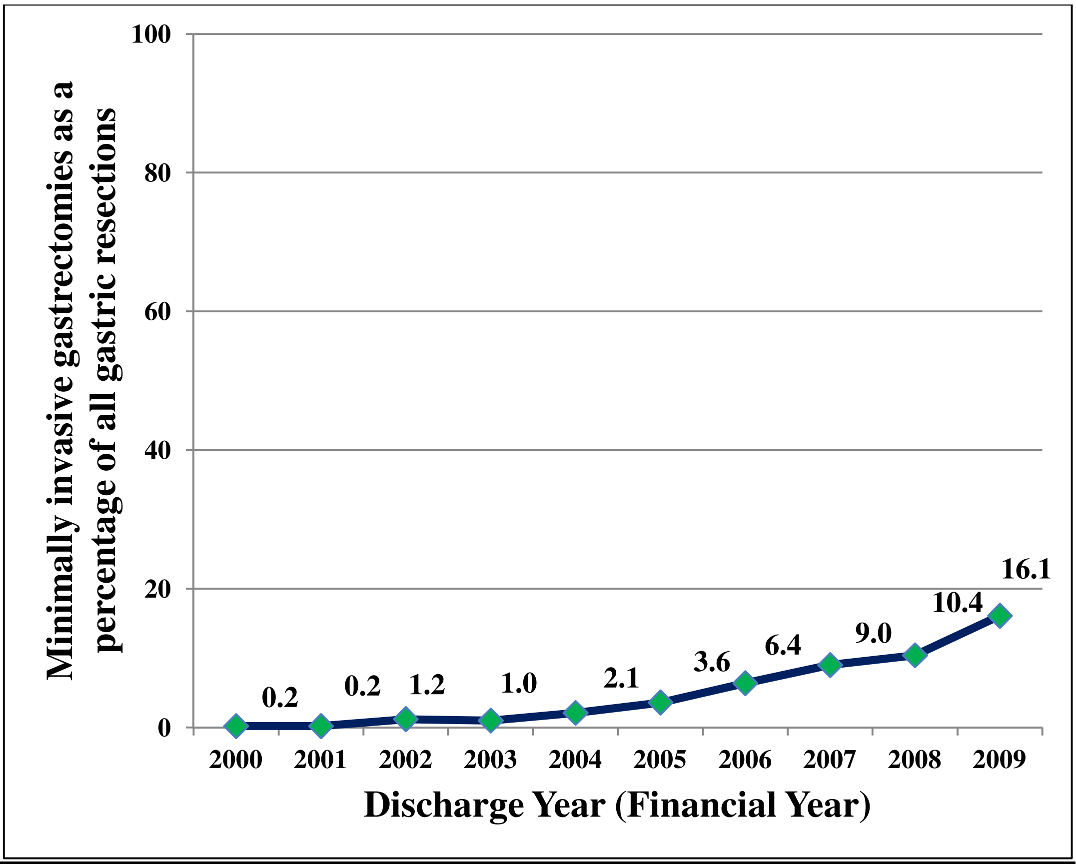


Figure 13: Uptake of laparoscopic gastrectomy in English NHS Trusts

Demographics

Patients were divided into four age-groups (<60, 60-70, 71-80 and >80 years). The majority of the patients were aged between 60-80 years. There was a high number of males in the study population (1:2 female to male ratio) . There were no statistical differences between the OG and LG groups with respect to social deprivation as ascertained by the Carstairs index. Majority of the patients in both the groups had cardiac co-morbidity. In the patients who underwent LG, there was higher cardiac and respiratory co-morbidity and diabetes as compared to those in OG group. Patient demographics have been detailed in Table 38.

Short term outcomes

LG group was associated with a shorter length of stay. Median LOS for the OG and LG groups was 13 days (IQR 10-18 days) and 11 days (IQR 8-16 days) respectively ($p<0.001$). 30-day mortality rate for the OG group was 5.6% while the same for patients in the LG group was 4.8% ($p=0.461$). Patients who underwent LG had a readmission rate of 12.1% and overall morbidity rate of 29%. There were no statistical differences between the OG and LG groups with respect to mortality, morbidity, re-intervention or readmission. Respiratory complications were the most common in both the groups. Details of short term outcomes have been shown in Table 39. We studied in detail the re-interventions between the two groups (Table 40). There was no significant difference between the LG and OG groups during the study period, and also in the latter 5 years. In the LG group, 4.6% of patients had a laparotomy following the index operation and 1.5% had wound related complications requiring further procedures. Overall, 2.7% patients that underwent a gastrectomy had a subsequent endoscopic procedure. However it is beyond the current data to identify the indications for these procedures.

Table 39: Descriptive characteristics of patients undergoing open and laparoscopic gastrectomy

	Gastrectomy				
	OG		LG		
	n=10,233	(%)	n=480	(%)	p value*
Age					<0.001
<60 years	1716	(16.8)	68	(14.2)	
60-70 years	3208	(31.3)	111	(31.0)	
71-80 years	4131	(40.4)	207	(43.1)	
>80 years	1178	(11.5)	94	(19.6)	
Gender					<0.001
Male	6781	(65.8)	276	(57.5)	
Female	3502	(34.2)	204	(42.5)	
Carstairs Index					0.906
(least deprived) 1	1379	(13.5)	71	(14.8)	
2	2049	(20.0)	93	(19.4)	
3	2199	(21.5)	105	(21.9)	
4	2248	(22.0)	108	(22.5)	
(most deprived) 5	2345	(22.9)	102	(21.3)	
Co-morbidities					
Cardiac	3421	(33.4)	207	(43.1)	<0.001
Respiratory	1162	(11.4)	75	(15.6)	0.004
VTE	173	(1.7)	10	(2.1)	0.516
Stroke	109	(1.1)	7	(1.5)	0.416
Renal Failure	110	(1.1)	9	(1.9)	0.102
Diabetes	937	(9.2)	59	(12.3)	0.021

** = Chi squared test; VTE = venous thrombo-embolism*

Table 40: Unadjusted short term outcomes after gastrectomy

Outcomes	OG		LG		
	n=10,233	(%)	n=480	(%)	p value*
Mortality					
30-day, in-hospital	571	(5.6)	23	(4.8)	0.461
Overall Morbidity	2661	(26.0)	139	(29.0)	0.150
Medical Morbidity					
Cardiac	1109	(10.8)	63	(13.1)	0.117
Respiratory	1376	(13.4)	66	(13.8)	0.849
VTE	97	(0.9)	4	(0.8)	0.800
Stroke	36	(0.4)	1	(0.2)	0.601
Renal Failure	146	(1.4)	9	(1.9)	0.422
Surgical Complications					
Re-intervention	789	(7.7)	43	(9.0)	0.318
Re-operation	409	(4.0)	22	(4.6)	0.523
Readmission					
Within 28 days	1040	(10.2)	58	(12.1)	0.175
Length Of Stay, median (IQR)	14 days	(11-19)	11 days	(08-17)	<0.001[@]
Specific Medical Complications					
Angina	512	(5.0)	23	(4.8)	0.835
Myocardial Infarction	115	(1.1)	4	(0.8)	0.553
Congestive Cardiac Failure	187	(1.8)	7	(1.5)	0.553
Atrial Fibrillation	421	(4.1)	24	(5.0)	0.059
Pneumonia	858	(8.4)	47	(9.8)	0.279
Pleural Effusion	495	(4.8)	30	(6.3)	0.161
Respiratory Failure	237	(2.3)	13	(2.7)	0.578
Other Respiratory Complications[#]	184	(1.8)	6	(1.3)	0.374
Deep Vein Thrombosis (DVT)	42	(0.4)	1	(0.2)	0.494
Pulmonary Embolism (PE)	63	(0.6)	3	(0.6)	0.980
Stroke	36	(0.4)	1	(0.2)	0.601
Renal Failure	146	(1.4)	9	(1.9)	0.422

** = Chi squared test; [@] = Mann-Whitney U test; IQR= Inter Quartile Range; [#] = Exacerbation of COPD, Pulmonary oedema, Post-procedural respiratory complications*

Table 41: Short term surgical complications (re-interventions) after gastrectomy

Re-intervention	OG		LG			Total	
	2000-2009 (10 years)						
	n=10,233	**(%)**	**n=480**	**(%)**	**p value***	**n=10,713**	**(%)**
Laparotomy	386	(3.8)	22	(4.6)	0.364	408	(3.8)
Wound complications	187	(1.8)	7	(1.5)	0.553	194	(1.8)
Endoscopy	215	(2.1)	14	(2.9)	0.227	229	(2.1)
Radiology guided procedure	276	(2.7)	15	(3.1)	0.573	291	(2.7)
	2005-2009 (5 years)						
	n=4329	**(%)**	**n=427**	**(%)**	**p value***	**n=4756**	**(%)**
Laparotomy	179	(4.1)	19	(4.4)	0.756	198	(4.2)
Wound complications	88	(2.0)	6	(1.4)	0.374	94	(2.0)
Endoscopy	95	(2.2)	14	(3.3)	0.153	109	(2.3)
Radiology guided procedure	167	(3.9)	15	(3.5)	0.723	182	(3.8)

* = Chi squared test

Risk adjusted outcomes

On univariate analysis, surgical approach was not found to be a determinant of mortality (OR 0.85, 95%CI 0.56-1.31, p=0.900). Multiple regression models for medical complications also did not show the use of laparoscopy to be independently associated with lower risk of morbidity (See Chapter 3).

Subgroup analysis

A subgroup analysis for patients undergoing partial and total gastrectomy was also undertaken for the latter 5 years of the study. In both the subgroups, outcomes for LG and OG were compared. A significant difference was seen in length of stay. Patients in the LG group had a shorter length of stay in both subgroups i.e. partial and total gastrectomy. Median LOS was 10 days (IQR 8-15) and 12 days (IQR 10-16) ($p<0.001$) for LG and OG groups that underwent partial gastrectomy respectively. There was no difference seen the groups with respect to mortality or morbidity. Details of the comparison are shown in Table 41.

Table 42: Short term outcomes following elective partial and total gastrectomy for cancer

Outcomes	Partial Gastrectomy					Total Gastrectomy				
	OG		LG			OG		LG		
	n=2,437	(%)	n=304	(%)	p value*	n=1,892	(%)	n=123	(%)	p value*
Mortality										
30-day, in-hospital	88	(3.6)	8	(2.6)	0.381	109	(5.8)	12	(9.8)	0.071
Medical Morbidity										
Cardiac	264	(10.8)	37	(12.2)	0.482	242	(12.8)	17	(13.8)	0.741
Respiratory	303	(12.4)	36	(11.8)	0.768	402	(21.2)	25	(20.3)	0.808
VTE	27	(1.1)	2	(0.7)	0.470	27	(1.4)	2	(1.6)	0.858
Stroke	8	(0.3)	1	(0.3)	0.998	6	(0.3)	0	(0)	0.532
Renal Failure	29	(1.2)	6	(2)	0.251	41	(2.2)	1	(0.8)	0.308
Surgical Complications										
Re-intervention	156	(6.4)	25	(8.2)	0.228	231	(12.2)	15	(12.2)	0.996
Re-operation	94	(3.9)	12	(3.9)	0.939	100	(5.3)	7	(5.7)	0.846
Readmission										
Within 28 days	213	(8.7)	30	(9.9)	0.514	281	(14.9)	23	(18.7)	0.248
Length Of Stay, median (IQR)	**12**	**(10-16)**	**10**	**(8-15)**	**<0.001@**	**14**	**(11-21)**	**13**	**(10-18)**	**0.008@**

** = Chi squared test; @ = Mann-Whitney U test; IQR= Inter Quartile Range*

6c.3 Discussion

This is the first national study in England that describes the outcomes following gastrectomy and also the uptake of laparoscopic gastrectomy in England over a period of ten years. Laparoscopic or laparoscopy-assisted gastrectomy has been safely introduced in England. Although this technique is not yet widely used, the number of cases has steadily increased over the last 10 years. The results from our population-based study corroborate the findings of other randomised controlled trials(Huscher et al., 2005), meta-analyses (Chen et al., 2009, Ohtani et al., 2010) and the interim analysis from the Korea Laparoscopic Gastrointestinal Surgery Study Group (KLASS) trial (Kim et al., 2010) showing no significant differences in mortality and key morbidity outcomes between laparoscopic and open gastrectomy. Importantly, LG is not associated with worse outcomes as compared to the open approach. However, this study did demonstrate a decrease in length of stay in patients undergoing LG. Intra-operative factors such as duration of surgery, blood loss and need for transfusion and analgesic requirements are beyond the scope of this study. Similarly, stage of disease was not available. Large prospective studies or trials may be able to demonstrate benefits of the laparoscopic approach, if any. More importantly, oncological value and long term survival data are needed before this technique is widely accepted. In the UK, due to the low incidence / pick-up of early gastric cancer as compared to the East, gaining proficiency in this complex technique is challenging.

This population based study has demonstrated the potential advantages of minimally invasive colorectal resection. The patients in our study who were selected for laparoscopic colorectal resection were associated a significantly lower risk of mortality and morbidity, with a shorter duration of hospital stay. These findings echo the results from various prospective studies and case series. Although the long term survival and oncological value needs further research, it is probably safe to assume that minimally invasive colorectal surgery, in well trained hands, can potentially improve outcome. The benefits of laparoscopic surgery are not limited to the younger population. Studies have suggested that it is safe and beneficial amongst high-risk groups such as morbidly obese patients and those with high ASA grades (Nguyen et al., 2001, Sugerman et al., 1992, Marks et al., 2008). Studies have also ratified its safety in elderly cohorts (Lian et al., 2010, Person et al., 2008). This has prompted an increase in use of minimally invasive techniques in the elderly. Age related reduction in physiological reserves and presence of co-morbidities make the elderly susceptible to complications. From the covariate interaction analyses in our study, it is possible to suggest that laparoscopy is safe and possibly advantageous among elderly patients and those with associated co-morbidity.

The success of MAS in colorectal resection has not been mirrored in upper gastrointestinal resection surgery. . This may be due to the proficiency gain curve observed on the uptake of new procedures or because of the trauma incurred from the extent of lymphadenectomy required for gastro-oesophageal cancer resection exceeds the benefits obtained from minimising trauma of the access. The current study has shown that MIO and LG are safe, with comparable outcomes to open surgery, but no reduction in risk of mortality or serious morbidity. However it remains to be seen whether increasing uptake of MAS and surgeon experience would contribute towards improving outcome following MIO and LG, as reported in studies from the East. Data from randomised controlled trials evaluating long term survival and patients' reported outcomes are essential before the final judgement on the value of MAS in the management of upper gastrointestinal cancer.

CHAPTER 7: ROLE OF VOLUME IN IMPROVING OUTCOME: IS THERE SUCH A THING AS 'TOO MUCH' OR 'TOO LITTLE' IN SURGERY?

In the late 1980s, it was shown that there existed an inverse relationship between the number of patients treated in a centre (for specific diagnoses) and the outcomes (Hughes et al., 1988, Maerki et al., 1986). However it was unclear whether this volume-outcome relationship reflected certain characteristics of the high volume centres or was primarily as a result of the individual physician or surgeon experience at centres with a high flux of patients (Kelly and Hellinger, 1986). Broadly speaking, it has been shown that hospitals that perform small numbers of certain surgical procedures have higher operative mortality rates (Birkmeyer et al., 2002). This inverse relationship between hospital volume and operative mortality might be due to a variety of factors. Some of the proposed explanations include the availability of greater resources for non-operative diagnosis and treatment at larger, higher-volume hospitals (Chang and Birkmeyer, 2006). However, the majority of the hospital volume effect can be attributed to the surgeon experience or caseload (Birkmeyer et al., 2003). It may be safe to say that the lives of many patients could potentially be saved if all surgeons undertaking complex procedures performed a minimum number of procedures each year to maintain their skills. As part of quality and safety improvement initiatives, healthcare organisations have sought to centralise certain cancer services in an effort to increase both hospital and surgeon volumes and improve patient outcome. However, the relationship between surgeon volume and operative mortality cannot be indefinitely extrapolated. A point must be reached when a surgeon is performing enough procedures and any more would be of no further advantage to the patient. A proficiency curve relationship of this kind has yet to be demonstrated for surgeon volume and operative mortality.

To date, no studies have reported evidence-based thresholds for classifying surgeons either as low or high volume practitioners. Suggested thresholds are arbitrary and do not describe a logical method of determining a recommended minimum surgeon volume. This would prove valuable for health service quality benchmarking. The previously established volume-outcome relationship has prompted centralisation of services such as upper gastrointestinal cancer, hepato-pancreatico-biliary surgery and vascular surgery. Previous studies are now out of date and might not be applicable to modern practice, and future studies may be compounded by the fact that centralisation would have eliminated low volume practice. Case series and registry data may be underpowered to measure surgeon volume with the precision required, control for confounding or generalise their results. To address these issues, we analyzed the surgeon volume and operative mortality associated with three different cancer resections using Hospital Episodes and Statistics (HES) database. We had two primary aims: to assess whether there was a proficiency curve-like relationship between surgeon volume and operative mortality and to determine the minimum surgeon volume that produced an operative mortality insignificantly different from that at the plateau or optimum of the curve.

6.1 Methods

HES data were obtained for patients undergoing oesophagectomy, gastrectomy and pancreatectomy in English NHS Trust hospitals. Patients who underwent elective resections for a malignant diagnosis were selected over a 10-year period (April 2000- March 2010). We used the first resection as the index operation if a patient had more than one resection during the study period. We excluded all patients that were less than 18 years old and we also excluded emergency procedures. We ascertained each patient's pre-operative co-morbidity and social deprivation statuses using the Charlson and Carstairs indices respectively.

Outcome

The primary outcome measure was operative mortality, which we defined as in-hospital mortality within 30 days of surgery. We derived 95% confidence interval of the mortality rate based on odds ratios and standard error estimated from a logistic regression model where 30-day mortality served as the dependent variable and surgeon volume served as the factorial independent variable.

Surgeon volume

We defined surgeon volume for each patient’s record as the average annual number of operations carried out by that patient's surgeon. We defined surgeon experience as the number of years in which a surgeon had operated on at least one case.

Mixed-effects logistic regression models were used to analyse the relationship between surgeon volume and mortality. Surgeon volume was included as a continuous predictor with adjustment for surgeon experience and patient characteristics (age, gender, co-morbidity, social deprivation indices). Clustering of patients within surgeons as well as clustering of surgeons within hospitals (NHS Trusts) was incorporated. Odds ratios for surgeon volume were derived from the mixed-effects models. We also divided volumes into tertiles in order to demonstrate the impact of covariates. Patient characteristics, surgeon experience, raw and risk-adjusted mortality rates for low, medium and high volumes were compared using the analysis of variance test.

CUmulative SUM (CUSUM) analysis (Grigg et al., 2003) was used to determine both the existence and the value of volume threshold, if any. Volume threshold was defined as the minimum annual caseload for an alteration in mortality-volume relationships. The CUSUM curve plots the cumulative difference between the observed and the expected mortality (i.e. O-E, y-axis) against the surgeon volume (x-axis). We derived the expected mortality from the mixed-effects model as above, but excluded surgeon volume as a predictor. Based on our definition, the CUSUM curve goes upward every time the observed mortality exceeds the expected mortality and vice versa. As an inverse relationship between volume and mortality was expected, we hypothesised that the volume threshold would coincide where the CUSUM curve peaked.

To determine the reliability of a threshold, we analysed the likelihood that the CUSUM curve would peak at the same magnitude in randomly ordered operative cases derived from 1000 bootstrapping samples with replacement. In each iteration, we recorded the peak magnitude of the simulated CUSUM curve. The confidence level of a change in volume-mortality relationship is defined as the proportion of the simulated peak magnitudes that are less than the one observed in the original CUSUM. A 95% confidence level or above is considered as indicating a reliable change.

In addition to CUSUM analysis, we also tried the change point model analysis which is commonly applied to time series data (Park, 2011) and the threshold searching by binary comparison reported in previous studies (Birkmeyer et al., 2006, Birkmeyer et al., 2002). We finally decided to use the CUSUM approach for its ability to demonstrate visually the change in relationship between surgeon mortality and surgeon volume and for the possibility of using bootstrapping to determine whether or not a suggested threshold actually existed. We analysed each operation separately using SPSS version 19 (an IBM company) and the open source statistical package R (version 3.0.1).

I would like to acknowledge the invaluable help and advice from Ms Zhifang Ni (PhD Research Associate, Imperial College) and Sir David Spielgelhalter (Statistical Laboratory, Cambridge University) in undertaking the statistical analyses in this study.

6.2 Results

I retrieved data on 16,572 oesophagectomies, 12,622 gastrectomies and 9,116 pancreatectomies that had all been performed in patients diagnosed to treat cancer. The oesophagectomies had been performed by 305 consultants, the gastrectomies by 452 consultants and the pancreatectomies by 187 consultants. Surgeon volume ranged from 2-29 oesophagectomies, 1-14 gastrectomies and 2-31 pancreatectomies per surgeon per year.

After controlling for surgeon experience, patient age, sex, co-morbidity and social deprivation, as well as clustering of mortality within hospitals and within surgeons, higher surgeon volume as a continuous variable was a significant predictor of lower mortality in oesophagectomies (OR=0.966, 95% CI=(0.945, 0.988)), gastrectomies (OR=0.928, 95% CI=(0.891, 0.967)) and pancreatectomies (OR=0.959, 95% CI=(0.933, 0.986)). In other words, each additional case of oesophagectomy, gastrectomy and pancreatectomy would reduce mortality odds by 3.4%, 7.2% and 4.1% respectively. Figure 14 shows raw mortality as a function of surgeon annual case loads.

I also fitted surgeon volume into three categories by including a similar proportion of data in the low, medium and high volume categories. The cut-offs between each volume category were 8 and 12 oesophagectomies, 5 and 7 gastrectomies and 7 and 11 pancreatectomies per surgeon per year. Surgeons in the high volume category had on average 3-4 more years of experience than surgeons in the low volume category. Patients who had oesophagectomies by surgeons in the high volume category were more likely to be elderly and from socially deprived areas. Patients who had oesophagectomies by surgeons in the high volume category had a significantly lower mortality rate compared with the low volume category ($OR_{low-high}$=1.50, CI=(1.11,2.03)), which was also true for gastrectomies ($OR_{low-high}$=1.74, CI=(1.33,2.28)). Patients who had pancreatectomies by surgeons in either the high or medium volume categories had a significantly lower mortality rate compared with the low volume category ($OR_{low-med}$=1.45, CI=(1.07, 1.98); $OR_{low-high}$=1.73, CI=(1.23,2.43)). Figure 15 shows risk adjusted mortality rates and raw mortality rates for the three cancer resections. Table 43 shows the patient characteristics, surgeon experience raw and risk adjusted mortality rates in each surgeon volume category.

CUSUM analysis for the three resections showed that possible changes in the surgeon volume-mortality relationship occurred around 10 cases per year for oesophagectomies, gastrectomies and pancreatectomies (Figure 16). However, none of these changes were reliable. Bootstrapping sampling (n=1000) found that the confidence levels were respectively 11.5% for oesophagectomies, 34% for gastrectomies and 8% for pancreatectomies. We were therefore unable to recommend definitive minimum surgeon volumes for achieving lower mortalities. This reflects a monotonous negative relationship between surgeon volume and mortality and that mortality rates had not plateaued within the current volume ranges.

Table 43: Patient characteristics, surgeon experience, raw and risk adjusted mortality

	Low volume surgeon	Medium volume surgeon	High volume surgeon	p value
Oesophagectomy	**1-8 cases**	**9-12 cases**	**13-29 cases**	
% of male	77.2%	76.1%	75.7%	0.152
% of age>70	26.7%	26.2%	30.4%	0.000
% of Charlson scores>5	29.6%	28.4%	30.0%	0.105
% of Carstairs score<=3	65.3%	66.3%	68.6%	0.001
mean years of experience	8	10	12	<0.001
mean risk adjusted mortality rate	0.0519	0.0431	0.0296	<0.001
mean raw mortality rate	0.0538	0.0437	0.0298	<0.001
Gastrectomy	**2-5 cases**	**6-7 cases**	**8-14 cases**	
% of male	63.9%	65.3%	65.2%	0.316
% of age>70	51.7%	50.8%	50.4%	0.428
% of Charlson score>5	32.6%	36.0%	31.3%	0.000
% of Carstairs score<=3	59.2%	56.7%	53.0%	0.000
mean years of experience	7	9	11	<0.001
mean risk adjusted mortality rate	0.0520	0.0448	0.0336	<0.001
mean raw mortality rate	0.0561	0.0457	0.0332	<0.001
Pancreatectomy	**2-7 cases**	**8-11 cases**	**12-31 cases**	
% of male	54.0%	51.5%	51.7%	0.080
% of age>70	28.5%	28.5%	29.9%	0.409
% of Charlson score>5	28.7%	27.4%	25.1%	0.001
% of Carstairs score<=3	67.3%	67.8%	67.6%	0.913
mean years of experience	8	10	11	<0.001
mean risk adjusted mortality rate	0.0440	0.0346	0.0294	<0.001
mean raw mortality rate	0.0469	0.0336	0.0299	<0.001

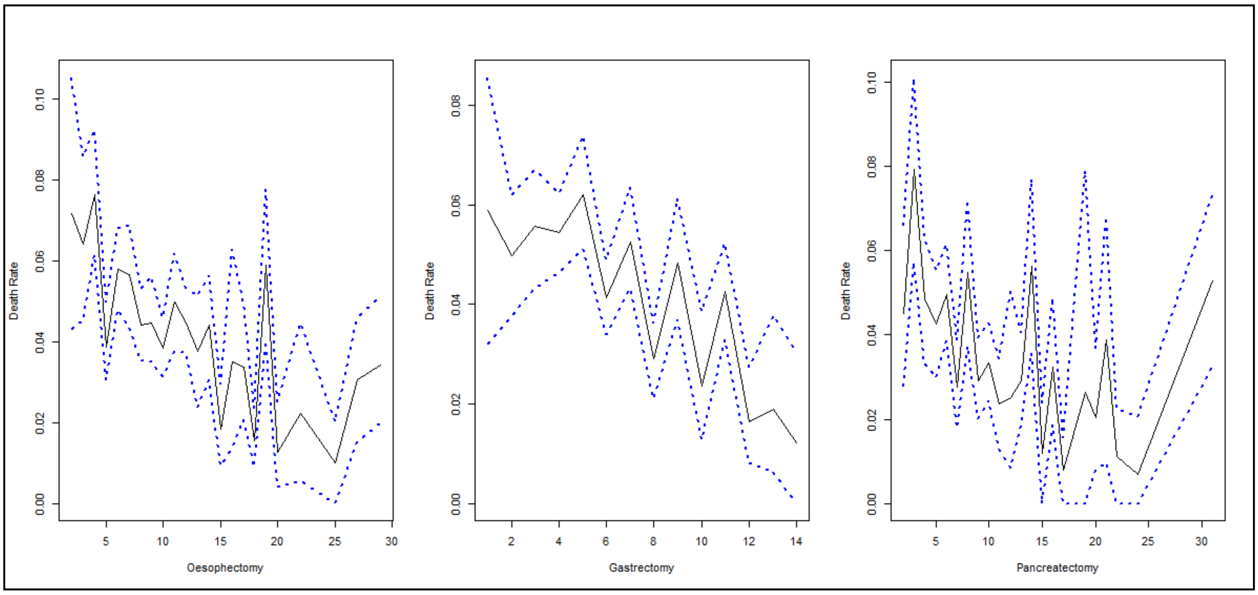


Figure 14: Raw mortality as a function of caseload per year.

Solid lines: observed mortality; dashed lines: 95% confidence interval from bootstrap sampling (n=500)

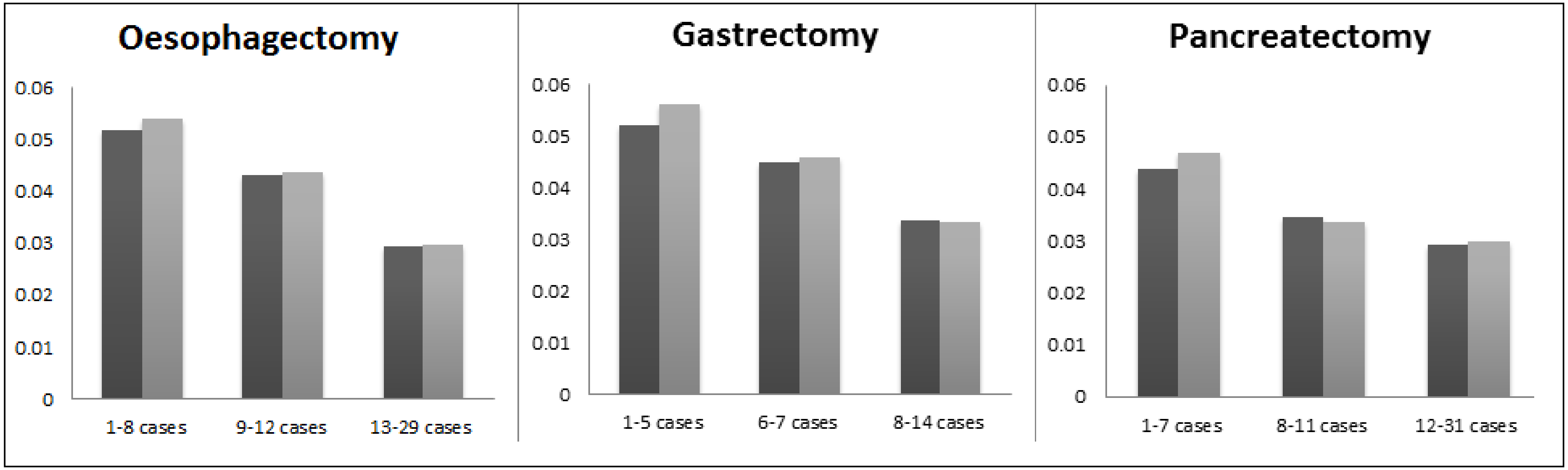


Figure 15: Raw and risk adjusted cancer mortality in low, medium and high surgeon volume categories.
Dark-coloured bars: risk-adjusted mortality rates; light-coloured bars: raw mortality rates.

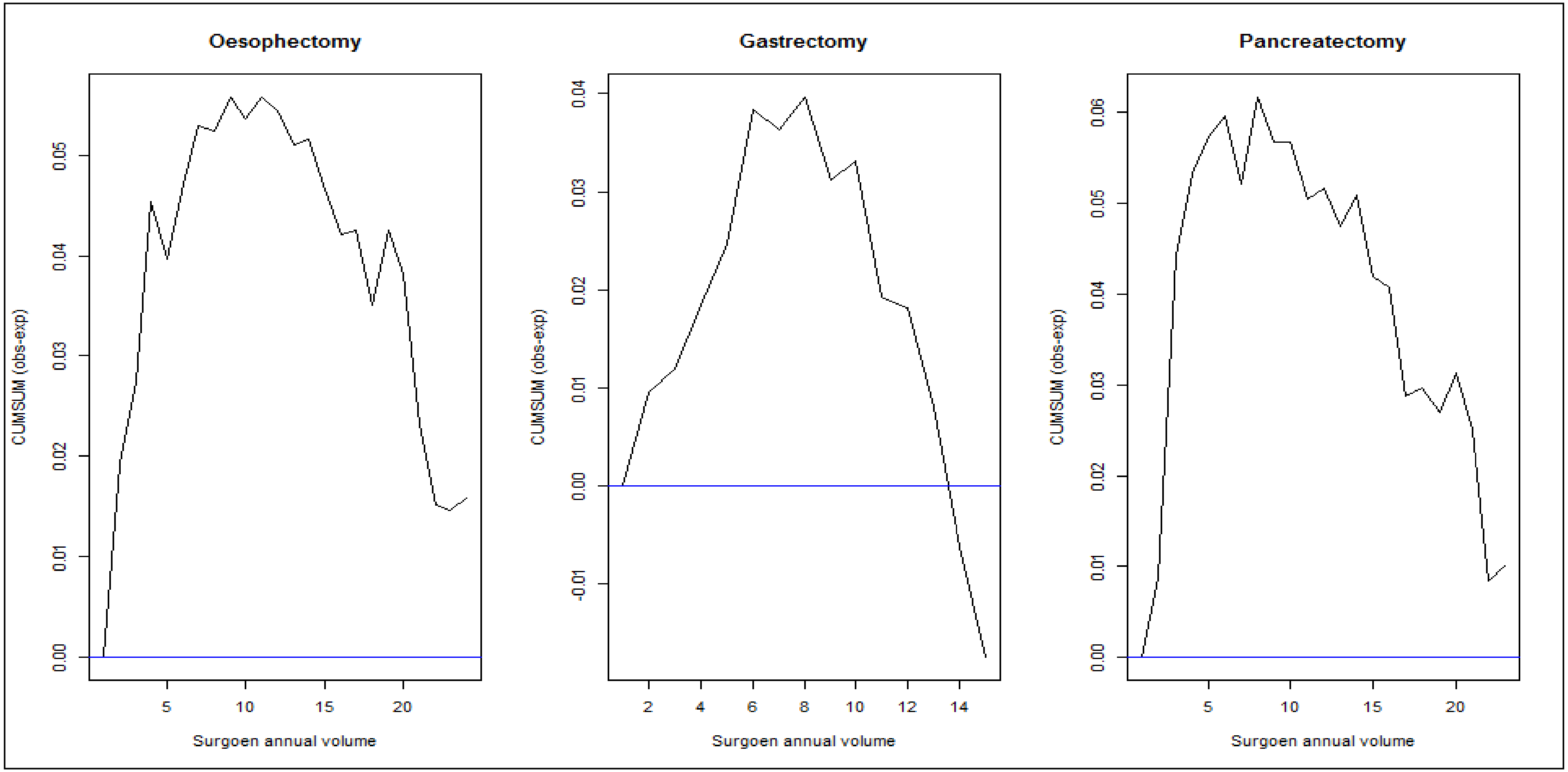


Figure 16: CUSUM curves of observed versus expected mortality rates

6.2 Discussion

In this population-based cohort study, I demonstrated that annual surgeon volume and 30-day postoperative mortality had a proficiency relationship in oesophagectomy, gastrectomy and pancreatectomy for cancer. The effect of surgeon volumes on postoperative mortality rates was independent of patient age, gender, socioeconomic and co-morbidities indices. I intended to determine a minimum surgeon volume above which no further significant reduction in operative mortality was achieved. However, there was no plateau in the proficiency curves and therefore no limit to the surgeon volume and operative mortality relationship was demonstrated. As surgeons performed more operations their results continued to improve and no plateau was demonstrated. I could not recommend a minimum surgeon volume and higher surgeon volumes than those included in our data could yield even better mortality rates.

The need for centralisation of services, in particular major surgery and cancer resections, has been demonstrated well in the past, both in the UK and USA (Finlayson et al., 2003, Finlayson and Birkmeyer, 2003, Birkmeyer et al., 2002, Palser et al., 2009, Moxey et al., 2012, Karthikesalingam et al., 2010). The two main principles behind this paradigm shift are a) practice makes one better i.e. experienced surgeons are likely to have better outcomes b) centres with good outcomes are likely to have more referrals, in turn increasing their volume. Traditionally the definition of 'low' and 'high' volume centres for various complex surgery have been arbitrarily chosen according to the data distribution in various studies. Various reports have suggested minimum annual surgeon volumes of 5-17 oesophagectomies (Bachmann et al., 2002, Birkmeyer et al., 2003, Dimick et al., 2005, Miller et al., 1997, Urbach and Austin, 2005), 10 gastrectomies (Bachmann et al., 2002) and 3-5 pancreatectomies (Birkmeyer et al., 2003, Ho et al., 2006, Urbach and Austin, 2005). Some patient, surgeon and healthcare organisations have targets of minimum annual surgeon volumes of 5 oesophagectomies and 5 pancreatectomies per surgeon per year in Germany (Geraedts et al., 2008) and 2 oesophagectomies and 2 pancreatectomies in the USA from the Leapfrog group (Birkmeyer and Dimick, 2004). However, none of these recommendations are based on robust methodology. Ross *et al* published a statistical method of determining a recommended minimum volume that a hospital should receive in order to achieve a mortality rate insignificantly different to the optimum in patients with heart attacks, heart failure and pneumonia (Ross et al., 2010). We employed a similar approach to investigate the recommended practitioner volumes for surgical procedures.

The strength of our study was the large data set from an entire population that covered periods before, during and after the process of centralisation and accounted for important patient variables including age, gender, socioeconomic status and co-morbidities that are known to influence postoperative mortality rate (Palser et al., 2009). We used multiple logistic regressions to adjust for the effects of these variables. The weakness of our study was the lack of information on cancer staging and operative approach, which can influence mortality rate (Boshier et al., 2011). The implication of this work is that many lives could potentially be saved if oesophageal, gastric and pancreatic surgeons performed even more operations and treated all patients.

CHAPTER 8: DISCUSSION OF STUDY FINDINGS

The primary aim of this thesis was to provide a comprehensive outlook of gastrointestinal resectional surgery in England. To this effect, a national database was thoroughly studied, analysed and various outcome measures were derived to assess the quality of gastrointestinal resection in England. In particular, the following key issues were aimed to be addressed:

1) To quantify perioperative outcome following gastrointestinal resection from a national English administrative database

After securing required ethical and information governance approvals, Hospital Episode Statistics data were obtained and analysed as part of this research. The rationale behind using a national, administrative database was to be able to understand outcomes in England while limiting reporting bias that would be inherent to case series or voluntary registry analyses. Data submission to HES is mandatory and would be invaluable in understanding the trends in gastrointestinal surgery in English NHS hospitals. The data were cleaned and analysed and we were able to determine important outcomes such as mortality, length of stay and readmission following colorectal, oesophageal and gastric resections. In addition, we derived medical morbidity, an outcome measure that has not been previously reported from HES. Any surgery that involves an anastomosis, is exposed to risk of an anastomotic leak - which is a significant surgical complication and is associated with high morbidity and possibly mortality. As there is currently no code to identify a leak from ICD-10 or OPCS coding systems, we used a HES derived metric 're-operation' as a surrogate to identify significant surgical morbidity that would otherwise be missed from administrative databases. This metric was derived and described in detail from HES data and attracted a lot of interest from the surgical community (Burns et al., 2011). With recent advances in radiological procedures, a significant patient cohort with surgical complications can avoid major re-operation and their pathology can be dealt with minimally invasive radiologically guided procedures. This prompted us to derive another outcome measure 're-intervention' which would encompass a whole spectrum of procedures using radiology, endoscopy or surgery to deal with complications.

2) To identify trends in reporting outcomes and describe the ideal metric to quantify risk associated with gastrointestinal resection

A systematic review of the available literature was undertaken to study the trends in reporting outcomes in colorectal surgery. In particular, we wanted to examine what was perceived as an adequate measure of risk of mortality. Elective or planned surgery gives the surgical and anesthetic team to adequately assess a patient's physiology and ability to withstand a major stress such as surgery or general anaesthetic. There is evidence that the elderly have a significant risk of mortality following major surgery such as colorectal resection. For these reasons we chose planned colorectal resection in elderly population as our target cohort. The systematic review identified a large variation the mortality risk reported in the literature, mostly depending on the size of the study. Almost all studies chose 30-day mortality (in-hospital or post discharge) as their primary risk measure. However, from a previous study on the elderly from HES data, it was evident that significant mortality occurs beyond the initial thirty day period (Faiz et al., 2011). Other studies ratified this finding and expressed concerns that thirty day metrics may underestimate the risk associated with major colorectal surgery (Visser et al., 2009, Dekker et al., 2011). It is however difficult to attribute mortality in the intermediate period to surgery or anesthesia. To understand this intermediate mortality (between 30 days and 1 year), we undertook a study to identify the causes of death in such patients. Data from Office for National Statistics were obtained, linked to HES data, and we derived the underlying cause of death for patients undergoing colorectal resection. There was significant number deaths attributable to cardiac causes up to one year following surgery. One could argue that elderly patients, with significant pre-existing co-morbidities would be at higher risk of deaths from cardiac causes. However, this risk could be enhanced by the fact that their physiology is subjected to severe stress during a major operation. We propose that this risk exists beyond the initial hospital stay, certainly beyond the first thirty days. Of interest, there was significant mortality due to cardiac causes even in fit, young population, which further supports our arguement. We have answered the question whether thirty day mortality is an ideal risk measure - and the answer is no - however further research is needed into whether we can stratify risk better using a 90-day mortality metric.

3) **To identify and describe factors [both structural (eg: volume or caseload) and process (eg: minimal access surgery)] that can be associated with an improvement in outcome following gastrointestinal resection**

Although outcomes measurement cannot distinguish efficacy from effectiveness: (outcomes may be poor because the right treatment is badly applied or the wrong treatment is carried out well), outcomes measurement must always take into account factors other than the intervention that may be very important in determining outcomes. It is well known that the most important outcomes may be the least easy to measure, so easily-measured but irrelevant outcomes are chosen (e.g. mortality instead of disability). Currently, following any major surgery, mortality is the widely accepted outcome metric that is reported by healthcare professionals. We wanted to explore any structural or process factors that might in turn have bearing on the outcome, thus aiding in the measurement of quality of healthcare. For this purpose, we chose to study the role of Minimal-Access Surgery (MAS) in gastrointestinal surgery and evaluate this technique against the traditional open surgery. Laparoscopy is now widely accepted as the gold standard for cholecystectomy and commonly used surgical approach to appendicectomy and various gynaecological operations. Numerous trials have already shown laparoscopic colorectal resection to be safe, with added benefits of shorter length of stay. Faiz *et al* demonstrated using HES data that patients undergoing laparoscopic colorectal resection in England had lower mortality rates even at one year following surgery (Faiz et al., 2009). Carrying on from this work, we were able to demonstrate that this mortality benefit, could at least partly, be explained by a lower medical complication or morbidity rate in these patients. Smaller scars, lesser pain, quicker recovery and improved outcomes prompted the application of MAS to upper gastrointestinal resections as well. Laparoscopic / thoracoscopic or a combination of both has been described in the literature as safe approaches to oesophageal resection, but there is no concrete evidence of a significant improvement in outcome or survival as compared to open surgery. Similarly, studies from the East have shown laparoscopic or laparoscopy-assisted gastrectomy to be feasible with potential benefits in early gastric cancer. From HES, we have shown that MAS for oesophagectomy and gastrectomy is increasingly being used in England. Although we haven't been able to demonstrate a significant benefit in terms of morbidity or mortality over the open approach, LG has been shown to be associated with a shorter length of stay. Looking beyond mortality alone as an outcome measure - there is scope for further research to demonstrate cost-effectiveness, patient satisfaction and long-term survival benefits of MAS in upper gastrointestinal surgery. One of the important structural factors that healthcare policy makes consider is the throughput of an institution/department/surgeon. This is termed as hospital 'volume' or surgeon 'caseload'. This concept follows the dictum of '*practice makes one perfect*'. There is an abundance of evidence showing an inverse relationship between provider volume and outcome in upper gastrointestinal surgery. However, there is no consistency amongst reported studies as to what would be defined as 'high volume' or 'low volume'. We attempted to understand better the volume-outcome relationship following upper gastrointestinal resections for cancer. Our aim was to identify and define whether there exists an optimum/ideal volume threshold around which one would expect the best outcome. We could demonstrate a positive relationship between surgeon caseload and lower mortality for oesophagectomy, gastrectomy and pancreatectomy. However, no reliable volume thresholds were identified for any of the above three surgeries (confidence level from CUSUM analyses was <95%).

8.1 The Data

This report shows the feasibility of using Hospital Episode Statistics database to derive national trends and outcomes following gastrointestinal resection. Within the limitations of the data, outcomes such as mortality, length of stay and readmission are some of the available variables. Age, gender, social deprivation, diagnosis, types of resection and surgical approach have been used in multiple regression models to adjust for differences in case-mix across the practice at a national level. Understanding the data also enables derivation of other meaningful outcome measures or performance indicators. Medical morbidity or complications have not been described in detail previously using HES data. A thorough review of the ICD-10 coding system and the clinical coding practices in England enabled us to identify pre-operative co-morbidity and post-operative complications. HES has previously been used to derive markers of quality such as re-operation and failure to rescue (Burns et al., 2011, Almoudaris et al., 2013, Almoudaris et al., 2011b). Burns *et al* reported the re-operation rate following colorectal resection which could potentially be used for benchmarking purposes alongside other metrics such as mortality (Burns et al., 2011). The use of OPCS codes to identify return to theatre and subsequent risk adjustment using other HES variables has demonstrated a significant variation in the re-operation rates across England. A reliable and reusable measure which can demonstrate variation in practice or performance could have potential as a valid quality metric. Of course further studies are required to establish the accuracy and reliability of this metric from HES. Almoudaris and colleagues used the re-operation variable and derived 'failure to rescue' - a marker of quality defined as the percentage of patients that die following a serious complication after colorectal resection (Almoudaris et al., 2011b). Thus we have successfully shown that despite being an administrative database, it is feasible to use HES for studying surgical practice and performance in England.

8.2 National outcomes

This report has quantified the outcomes following three major gastrointestinal resectional surgeries: colorectal resection, oesophagectomy and gastrectomy in English NHS Trust hospitals.

Colorectal resection

Between April 2001 and March 2008, we identified 138,735 patients who underwent an elective colorectal resection. The 30-day in-hospital mortality rate was 3.3%. According to the 2013 NBOCAP report, thirty day mortality following major resection has improved steadily from 4% (2008-09) to 2.9% (2011-12) over the last five years (NBOCAP, 2011). In particular, for the period 2011-12, the 30-day mortality following planned resections has dropped to 2.3%. Although the NBOCAP started as a voluntary registry with only 8,000 cases in the year 2000, currently it is estimated to have a case ascertainment of 85%. A large multi-national public health comparison of survival of patients with colorectal cancer showed that in England, survival from colorectal cancer is lower than in Australia, Canada and most Nordic and western European countries (Coleman et al., 2011). However this study does not specify patients that had a surgical resection. The aim of the study was to show significant variation in survival across countries and thus help in formulation of strategies for cancer control. A positive outcome from this study was the finding that during the study period of 1995-2007, the survival from colorectal cancer significantly improved, not only in England, but worldwide. A recent comparison of survival amongst patients diagnosed with CRC in the United Kingdom and Scandinavian countries has offered a partial explanation for this finding (Morris et al., 2011a). The study determined that an excess of elderly patients died in the UK within three months of their diagnosis of CRC accounting for survival differences between countries. Unfortunately the study was not able to inform upon whether elderly patients died following surgical intervention. It seems likely that either case-mix differences between countries, or under- or over-treatment of elderly patients in England, underlie this finding. To further understand the reason behind this geographical variation, it is important to understand the colorectal practice in England. To this effect Morris and colleagues analysed data from the National Cancer Data Repository and demonstrated significant variation the risk-adjusted thirty-day mortality rates across England (Morris et al., 2011b). Between 1998 and 2006, they identified 160,920 patients and studied 30-day institutional mortality rates across the country. The advantage of this repository is that it is HES data linked with cancer registry data, thus providing additional information on stage of tumor and other clinical parameters missing from HES. Reporting national outcomes and demonstrating variation (within the country and worldwide) are the first step towards assessing the quality of services provided. Hence we further delved into the depths of the available resources to try and identify other factors that directly or indirectly contribute towards mortality (or survival) to provide a framework for further research in order to improve the quality of surgical care for colorectal pathology.

An important difference between this thesis and NBOCAP and other national studies from repository data is that we have included resections for benign conditions such as inflammatory bowel disease, diverticulosis and other non-cancer causes. Out of 40,046 patients in the benign category, 1,386 (3.3%) died within thirty days. This shows that the risk of mortality following resection, between benign conditions and cancer, is similar. On risk-adjustment, diverticulosis was associated with a 16% higher risk of thirty day mortality (OR 1.16, 95% CI 1.02-1.32, p=0.025) as compared to cancer. One explanation of this could be that such benign conditions may already cause an inflammatory response which accentuates the physiological stress of surgery. Another interesting finding of the study was the increasing use of laparoscopic approach to colorectal resections over the study period.

Upper gastrointestinal resection

In a ten year period from April 2000 to March 2010, 14,959 patients were identified from HES who underwent an oesophagectomy as a planned operation for cancer. A minimally invasive approach was used in 1,297 (8.7%) of these. In order to be able to quantify the mortality and morbidity outcomes post-centralisation of services, we only analysed the latter five years. Between April 2005 and March 2010, 7,502 oesophagectomies were undertaken of which 1,155 (15.4%) were coded as minimally invasive. Short term outcomes included 30-day in-hospital mortality of 4.3% (320/7,502), readmission rate of

13.8% (1,036/7,502) and a median length of stay of 15 days (12-22 IQR). The results are overall comparable to various studies in the literature reporting a wide range of mortality rates between 5.5% to 13.1% (Bailey et al., 2003, Chang et al., 2008, Lai et al., 2007) and high morbidity rates ranging from 40-60% (Bailey et al., 2003, Altorki and Skinner, 2001, Boyle et al., 1999) following oesophagectomy. Within England, the study has shown a significant improvement in mortality from 1997 (11.7%) to 2010 (4.3%) reflecting improvements in surgery and post-operative care, centralisation of services and perhaps advances in adjuvant and neo-adjuvant therapies. Patients undergoing a gastrectomy for cancer had a 30-day mortality rate of 4.6% and morbidity rates of 25.6%. We only selected elective surgery for a malignant diagnosis, as the results would be skewed by emergency gastrectomy performed by non-specialists in patients presenting with acute haemorrhage or perforation. Studies from the Far East have reported significantly better outcomes than England (short term mortality rates of 0-1.6% and complication rates of 13-19%) (Hwang et al., 2009, Jeong et al., 2009, Kim et al., 2010, Kim et al., 2008, Kuwabara et al., 2011) while reports from United States have demonstrated mortality rates of 6-7.6% and morbidity rates as high as 33.3% (Smith et al., 2007, Grossmann et al., 2002). The outcomes from our study are comparable to the results from the West and this may indicate the differences in disease prevalence, tumour charcteristics and surgical practice between the East and the West.

The results from these studies are similar to the National Oesophago-Gastric Cancer Audit report of 2009 which showed a 3.2% 30-day mortaility rate following oesophagectomy and 4.2% following gastrectomy (NHS Information centre, 2009). However, the report estimates a case ascertainment of 73% for patients undergoing surgical treatment. The morbidity rates ranged from 22-35%. To the best of our knowledge, this is the only English national study that has quantified morbidity and re-operations following oesophago-gastric resections for cancer.

8.3 The ideal metric that reflects true perioperative risk

Mortality is one of the key metric that belongs to the 'outcome' category of the Donabedian model and is most commonly used as a marker of quality of healthcare. Having described the national outcomes following gastrointestinal resection, we attempted to seek from literature which mortality measure was most commonly being reported. A systematic review of contemporary literature pertaining to elective colorectal resection in elderly population was undertaken. Out of 236 studies found from the initial search, 17 studies fit the inclusion and exclusion criteria and were chosen for the review. There was a large variation in the reported mortality rates following elective colorectal resection in the older population (0 to 7.2%). Interestingly almost all the studies had reported on 30-day mortality or post-operative mortality. There is an increasing body of evidence that there exists significant mortality that occurs beyond thirty days, which may be attributable to the delayed effects of surgery and anaesthesia. Recent advances in the intra-operative monitoring, post-operative high dependency and intensive care have a big role in seeing patients through the initial operative insult. This has certainly improved in-hospital mortality following major surgery. Depending on the pre-assessment findings, most centres now have a policy of a planned high dependency stay overnight, or longer, for patients who are classified as high risk. High one year mortality rates reported in various studies capture this excess mortality that is missed when reporting short term measures such as 30-day mortality (Kirchgatterer et al., 2005, Faiz et al., 2011). These findings raise the important of question of whether 30-day mortality outcomes underestimate the true risk associated with major surgery such as colorectal resection? If indeed the excess mortality between thirty days and one year is purely related to the disease progression rather than surgery, this questions the judgement and decision making of the surgical team. Especially when major resection is undertaken for cancer, is surgery really indicated if the expected prognosis is less than one year? In an emergency setting, one does not always have the luxury of knowing the diagnosis or prognosis, but in cases of planned resection one would expect a significant chance of survival beyond one year. We postulated that analysing the cause of death in patients dying within one year of surgery may shed light on these issues.

Anlaysis of the underlying cause of death in patients that died within one year of undergoing a colorectal resection was undertaken. This study helped understand the timing and causes of death, in English patients undergoing colorectal resections. Important findings of this study were a significant proportion of deaths up to one year. As one would expect, in patients with colorectal cancer, as the time passed, increasing number of deaths were coded as due to the cancer itself. However, in both young patients (<= 65 years) and in the elderly (>85 years) there were high number of deaths due to cardiac causes, significantly more than those reported in the general population of similar age groups. Of course senescence accounts for a large proportion of deaths in the extreme elderly, but our study showed that even in those without previous history of cardiac illnesses, there is a high proportion that died from cardiac causes. This is more pronounced in the younger population, all the more supporting our argument.

While more detailed research is required into which mortality metric would most accurately represent the post-operative risk, there is an increasing body of evidence suggesting 90-day mortality as an outcome measure that may provide a better estimate of the risk of death and also be used as a quality indicator. The National Bowel Cancer Audit also recognised the importance of intermediate outcome measures and started reporting 90-day mortality in its Annual Report 2011 (NBOCAP, 2011). A recent study using HES-ONS linked data looked at outlier status for units in England for case-mix adjusted mortality at 30, 90, 180 and 365 days (Byrne et al., 2013). This study reported a 11.3% 90-day mortality rate following elective and non-elective colorectal resections between 2001-2007. The authors found that 90-day mortality reporting not only identified all the outliers shown in a 30-day mortality model, but also identified more outliers when compared to the traditional outcome measure. They concluded that this metric may provide a better reflection of perioperative outcome by allowing more time for the effects of surgical care to become manifest.

8.4 Outcome in high risk patient cohorts

A healthcare framework cannot be generalised to be applicable to all patients. The clinical pathways have to be catered to different patient groups, depending on their special needs. Despite following the current best evidence in decision making and newer advances in surgical techniques, on occasions, outcomes will be worse than the national average. Such patient groups would be labelled as 'high risk'. Patients presenting to the hospital as an emergency, patients with high body mass index (obesity), severe co-morbidities such as poorly controlled diabetes, dialysis dependent or past history of severe cardiac disease are some of the examples in this cohort. An important subset of this group would be the 'elderly' patients. No doubt surgeons will at some point in their career be faced with an elderly patient who on one hand is unlikely to survive without an operation and on the other is deemed high-risk with a likely poor outcome following major surgery. Lengthy discussions, within the multi-disciplinary team involving anaesthetists, intensivists and physicians as also the family and relatives of the patient is of paramount importance. One cannot overemphasise the importance of taking into account the wishes of the patient. However, these discussions are only meaningful when one can communicate the true perioperative risk with the patient and relatives. Clearly, quoting a 30-day mortality in these circumstances would not convey the true risk attached to a major surgery such as colorectal resection, in the elderly. In order to quantify these risks we undertook a study of non-elective (or emergency) colorectal resection in patients aged 70 years or older. Of the 36,767 patients in the study, 8,874 (24.1%) died within thirty days of an unplanned colorectal resection. More importantly, the one year mortality rate was 42.9%. Of the patients aged more than 80 years, only a half of those operated made it to one year. These figures were significantly higher than the death rate amongst the general population of similar age, suggesting that these deaths cannot be explained by senescence alone. The mortality rates from our study corroborate the postoperative risk in the elderly as reported in other studies (Racz et al., 2012, Oliphant et al., 2014, Kolfschoten et al., 2012).

Frailty has been shown to be one of the predictors of short-term mortality in the elderly following colorectal resection (Neuman et al., 2013). Frailty is characterised by a reduced physiological reserve and resistance to stressors, which occurs as a result of physiologic multisystem decline (Fried et al., 2001). Surgeons aim to undertake a thorough assessment of patients' overall well-being at the time of a preoperative evaluation, relying on assessment of co-morbidity through review of the medical records and conversations with primary care doctors. However, this is not always possible when a patient presents as an emergency. Sometimes surgeons have to rely on their clinical judgment to provide an overall gestalt of their patients' wellness and ability to undergo surgery, rather than a formal assessment of fitness (or frailty). Studies have shown that elective or planned colorectal resection, even in the elderly, is feasible, safe and worthwhile and should be offered for the same indications as in younger population (Guo et al., 2014, Ahmed et al., 2014). Some studies have even demonstrated that laparoscopic colorectal resection should be offered to elderly patients as it has been shown to be associated with shorter length of stay, less intra-operative blood loss and fewer cardiorespiratory complications (She et al., 2013, Grailey et al., 2013). However, in the emergency setting, elderly patients have significant risk of mortality, both in the short term and up to one year (Racz et al., 2012, Oliphant et al., 2014, Kolfschoten et al., 2012). These findings do not preclude emergency surgery in the elderly. The main aim of this study was to generate awareness about the high mortality in this patient cohort up to one year, which we feel should be explicitly mentioned as part of the consent process. Despite there being limited scope for any pre-operative optimisation of these patients, there is scope for a multi-disciplinary approach in their post-operative care. Early input from intensivists, geriatric physicians and allied departments such as occupational and physiotherapy can go a long way in improving outcome in the elderly. The ortho-geriatric model for post-operative care of elderly patients with hip fractures has been shown to improve outcomes and even lower mortality rates (Wakeman et al., 2004, Thwaites et al., 2005). Such a model of care for elderly patients undergoing emergency surgery, especially major abdominal surgery, would prove invaluable in not only improving survival, but also quality of life. Care does not end at the hospital for the elderly. A large proportion of these patients need an intermediate rehabilitation programme before discharge to the community. Even in the community, primary care framework should be tailored for strict monitoring of the needs of these patients. Our study showed that with advancing age, risk of readmission and re-operation is reduced, suggesting reluctance on the part of the surgical team to re-intervene given the already compromised physiology. The outcome following a major complication in this age-group is poor as shown by the high 'failure-to-rescue' rates in two American studies (Sheetz et al., 2014, Matsushima et al., 2014). We do not advocate denying all elderly patients an emergency operation. It is, however, of paramount importance to convey the significant risk of mortality (and morbidity), in the immediate post-operative period and extending up to one year, to the patients, relatives and also the primary care team.

8.5 Strategies to improve outcome - Process and Structure

Avedis Donabedian in his seminal paper on evaluating healthcare, described structure, process and outcome as the three distinct domains of assessing the quality of healthcare (Donabedian, 1966). This theory remains as the dominant paradigm for underscoring the quality of care today. These three domains are complementary and should be used collectively to monitor quality of healthcare. According to this model, quality of care is represented by an integration from structure to process and to outcome, but not by one or the other independently. Health services researchers have applied this model to examine the relationship between structure and outcome, between process and outcome, and between structure and process. In order to provide an accurate assessment of the quality of care a framework consisting of these three elements is essential, rather than considering them separately.

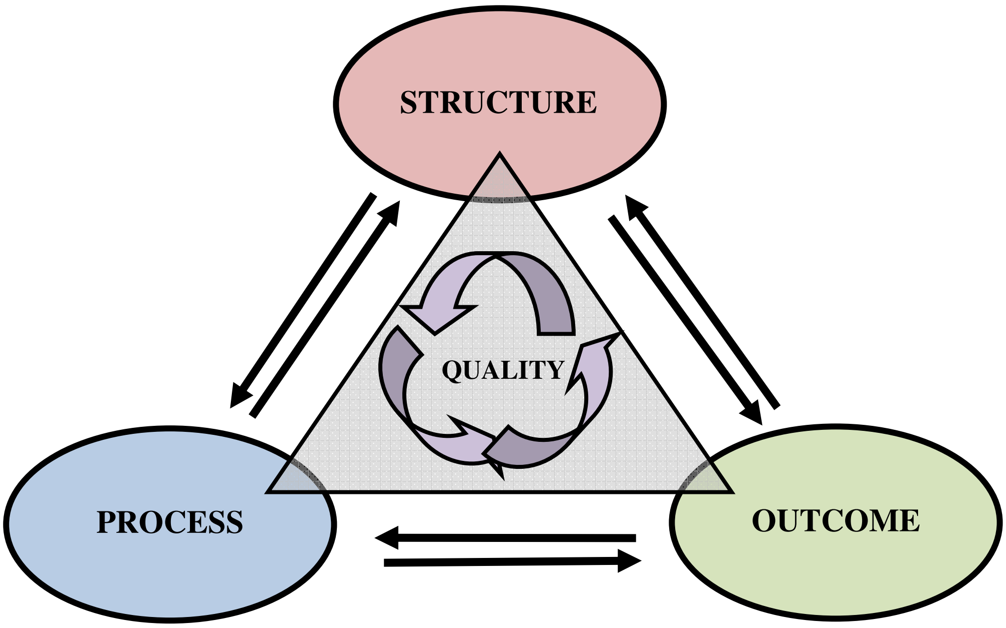


Figure 17: Schematic of the Donabedian Model

Minimal Access Surgery (MAS)

Donabedian defined process as a transactional nature of providing and receiving care involving both the providers and recipients of care. Within the domain of 'process' are included a) the roles of a provider eg. diagnosing, recommending, and implementing treatment, and b) the roles of the consumer (patient) eg. seeking care and adhering to treatment recommendations. In addition, technical aspects of care such as use of evidence based recent advances eg. MAS such as laparoscopy are also included within this group. We analysed HES data to underpin this aspect of quality measurement and study the use of MAS in gastrointestinal resection in England and its role in improving outcomes.

Laparoscopic colorectal resection

Laparoscopic colorectal resection is being performed worldwide for cancer as well as various benign conditions. Our study from HES data has shown an exponential rise in the use of this approach from 2001 to 2007 (Fig 6a.1). Since this procedure was described, various trials have established the safety and efficacy of laparoscopic colorectal resection when compared with the traditional open approach (Braga et al., 2002, Champault et al., 2002, Hazebroek, 2002, Jayne et al., 2007, Liang et al., 2007). In addition, this approach has been shown to be associated with reduced requirement of opioid analgesia, shorter length of stay and reduced intra-operative blood loss. Faiz *et al* used HES data to demonstrate a significant reduction in post-operative mortality (both at thirty days and at one year) following laparoscopic colorectal resection in English NHS hospitals (Faiz et al., 2009). In order to understand these results and explain the differences in mortality at one year, we undertook a similar analyses, with more contemporary data and compared medical morbidity between open and laparoscopic approaches. In addition to shorter length of stay and reduced mortality risk, we have shown that patients selected for laparoscopic colorectal resection were at reduced risk of medical complications (cardiorespiratory, renal and thrombo-embolic) (Tables 29 and 30).

Major surgery and anaesthesia have deterrent effects on the body physiology leading to aberrations in the lung expansion, gas exchange, cardiac pre-load and various other factors disrupting the body equilibrium (Daganou et al., 1998, Mathias, 2005). This coupled with a stress response mounted by the body to the tissue trauma associated with surgery contribute towards various post-operative medical complications such as pneumonia, myocardial infarction, DVT/PE and stroke. In particular, patients undergoing laparoscopic surgery demonstrated a lower incidence of acute myocardial infarction, congestive cardiac failure, pneumonia and acute respiratory failure. This may partially explain why there were mortality differences between the two groups even at one year. Stress response to tissue trauma is a pro-coagulant state. This coupled with increased operative times with laparoscopy as shown in some studies poses an enhanced risk of venous thrombo-embolism (Buunen et al., 2009, Fleshman et al., 2007). Conversely, laparoscopy has been shown to be associated with lesser post-operative pain and thus early ambulation. This reduces venous stasis. Thus there is a theoretical benefit of reduced risk of venous thrombo-embolism. Certainly in our study, patients selected to undergo a laparoscopic approach were at nearly half the risk of developing VTE at 30 days when compared with those undergoing open surgery. Admittedly, there were more patients in the open group with a previous history of DVT/PE.

Some of the benefits observed in our study, in patients in the laparoscopic group, are similar to the advantages of multi-modal approaches such as Enhanced Recovery After Surgery (ERAS). ERAS or fast-track surgery as described by Kehlet et al is a multimodal recovery programme that targets pre-operative, intra-operative and post-operative aspects of care (Kehlet, 2009, Kehlet and Wilmore, 2002, Health & Social Care Information Centre, 2013, Jacobs et al., 1991). The pathway includes pre-operative counselling, epidural /

regional anaesthesia and analgesia, minimally invasive surgery, optimal fluid management, early feeding and mobilisation – a combination of these approaches is proposed to reduce hypoxaemia, hypercoagulability and other metabolic states associated with a stress response. The idea is to mitigate factors that are responsible for extended hospital stay such as paralytic ileus, suboptimal analgesic control and identify and manage complications at an early stage. Overall aim of an ERAS programme is to accelerate recovery, thus reducing hospital stay and preventing complications. Large meta-analyses of studies that have reported on outcomes from ERAS pathways have demonstrated a shorter length of stay with an added reduction in risk of post-operative morbidity (Eskicioglu et al., 2009, Varadhan et al., 2010). A Cochrane review of the evidence has in addition reported that the shorter length of stay in these patients is not complicated by higher readmission rates (Spanjersberg et al., 2011). Figures 19 and 20 describe the rationale behind ERAS and the various components of this programme.

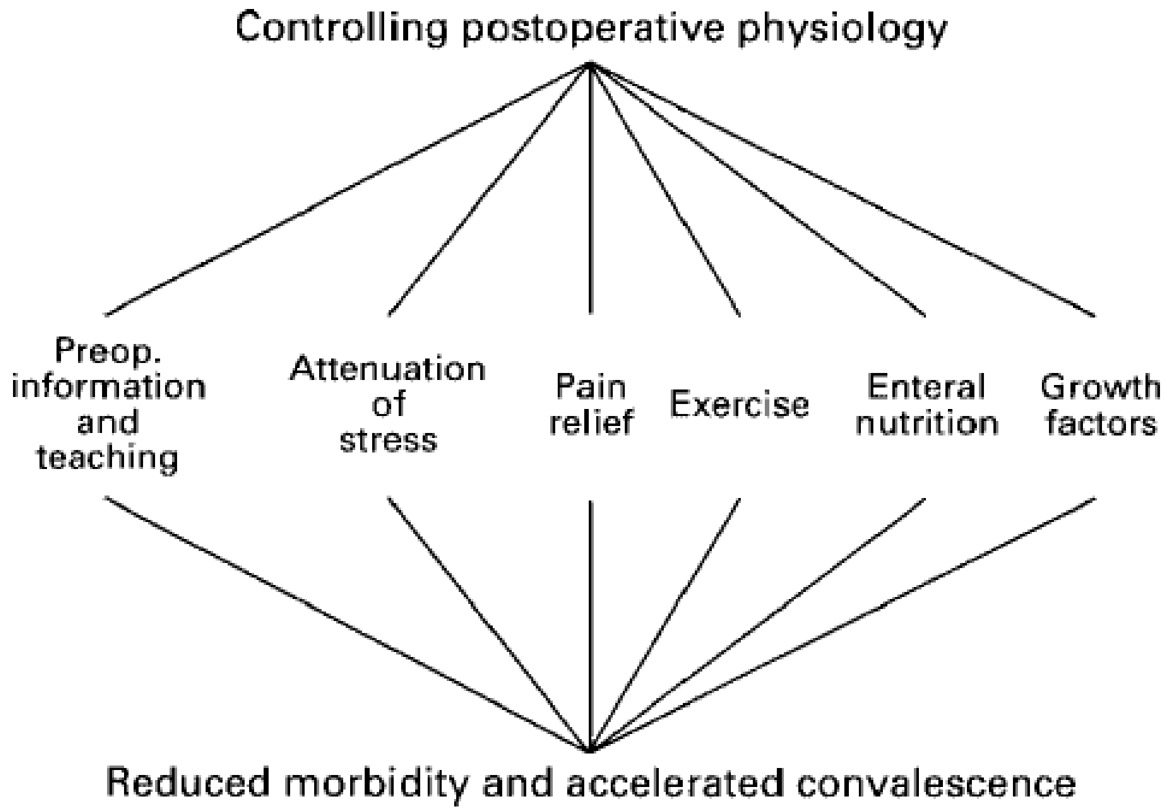


Figure 18: Multimodal interventions towards control of the postoperative period (1997)
(from British Journal of Anaesthesia 1997;78:606-617)

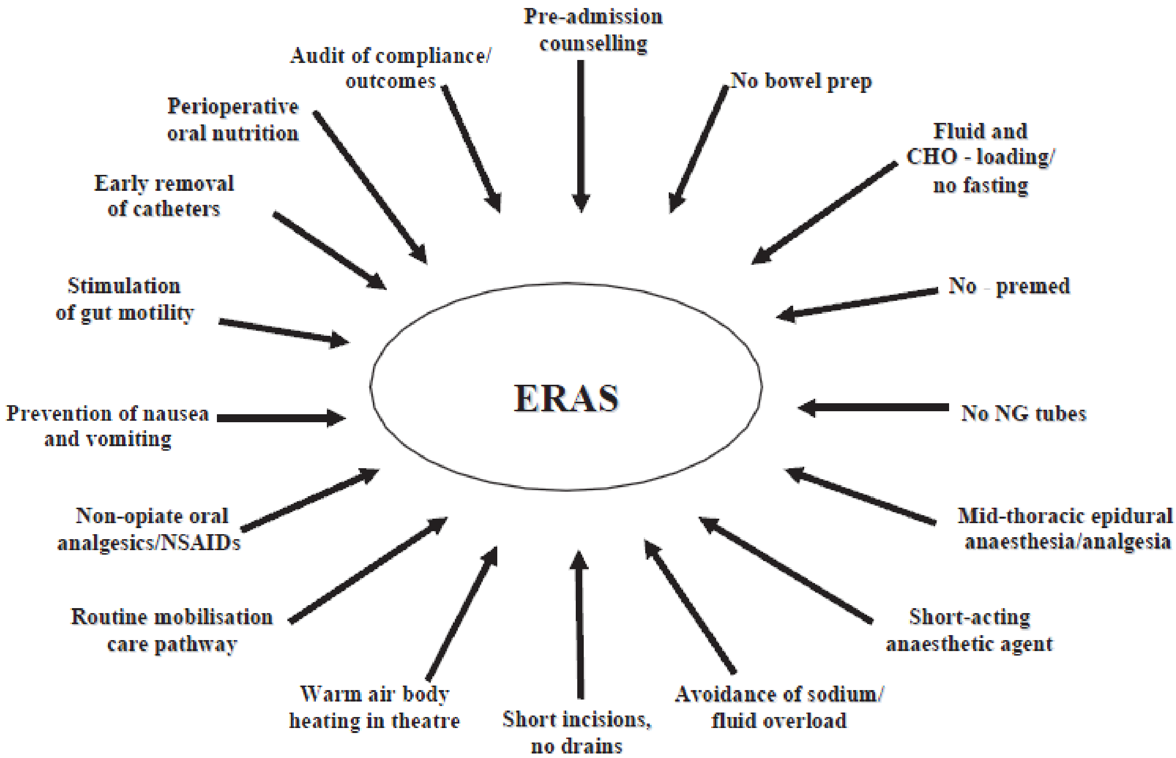


Figure 19: Main elements of the ERAS protocol (2005)

(from Clinical Nutrition 2005;24:466-477)

Laparoscopy is a part of ERAS protocols and there is no multicentre trial evidence has been reported regarding whether the benefits of laparoscopy still exist when open surgery is optimised within an enhanced recovery programme. To this effect a phase III, multicenter, randomised trial (EnROL Trial) of open versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme was undertaken in UK (Kennedy et al., 2014). This showed a significantly reduced length of stay in patients undergoing laparoscopic surgery, but otherwise similar outcomes in open and lap groups. The LAparoscopy and/or FAst track multimodal management versus standard care (LAFA trial) reported best outcomes in patients undergoing laparoscopic surgery in a fast-track programme, with lower morbidity in patients undergoing laparoscopic surgery (Vlug et al., 2011). In this study, patients undergoing open surgery and a standard (non-fast track) care had worst outcomes. Setting up and enhanced recovery programme is associated with significant costs and may not be feasible at every centre. Long term outcomes such as oncological clearance and survival have been shown to be comparable between the open and laparoscopic approaches to colorectal cancer resection (Huang et al., 2011, Bonjer et al., 2007). In such circumstances, laparoscopic colorectal resection seems to be the optimum treatment to be offered to suitable patients.

Minimal Access Surgery in Upper gastrointestinal resection

There is a high morbidity and mortality associated with oesophagectomy and different types of surgical techniques have been described and evaluated. Two stage Ivor Lewis (Lewis, 1946) oesophagectomy or three stage McKeown (McKeown, 1976) approach oesophagectomy involve thoracotomy and laparotomy with or without a cervical incision. In an attempt to reduce morbidity associated with thoracotomy, a transhiatal approach has been described involving laparotomy and a cervical incision (Orringer et al., 1999, Orringer et al., 2007). Cuschieri *et al* described a minimally invasive approach to oesophagectomy as early as 1992 (Cuschieri et al., 1992). Various approaches to minimally invasive oesophagectomy (MIO) have been reported including laparoscopy, thoracoscopy and the combination of these approaches with open surgery (Scheepers et al., 2008, Palanivelu et al., 2006, Bizekis et al., 2006). There is still however no consensus on the best approach to oesophagectomy.

In our analysis of HES data, the two groups (open and MIO) are matched in terms of age, gender and co-morbidity. The results showed that there was no significant difference between open and MIO in 30-day mortality (4.3% vs. 4.0%) or overall medical morbidity (38.0% vs. 39.2%). Incidence of respiratory complications in the MIO group (30.0%) was similar to the open group (31.4%) (p=0.365). Sub-group analysis of individual complications however showed that the patients in MIO group had a significantly lower rate of pleural effusion (16.2% versus 12.8% in the open and MIO groups respectively, p=0.004). The patients that underwent MIO, however, had a higher re-intervention rate compared with open group (21% vs. 17.6%; p=0.006). These included thoracotomy, minimally invasive interventions and endoscopy. With every progressive study year, the odds ratio for re-intervention increased. A re-intervention was associated with an increased post-operative morbidity with a three-fold increase in the risk of mortality. There was a six times higher risk of respiratory complications and renal failure in the presence of a re-intervention. We cannot determine from the data whether this is a causal association or a treatment for encountered complications. Recently published studies have demonstrated similar oncological outcomes following thoracoscopic (or combined with laparoscopy) oesophagectomy along with some benefits of reduced pulmonary complications (Chen et al., 2013, Hsu et al., 2014, Kubo et al., 2014, Ninomiya et al., 2014). There is a need for well designed randomised controlled trials to assess the superiority, if any, of minimally invasive oesophagectomy. The ROMIO (Randomised Open or Minimally Invasive Oesophagectomy) Study has been setup in the UK to establish the feasibility of a main trial which will examine the clinical and cost-effectiveness of minimally invasive and open surgical procedures for the treatment of oesophageal cancer (Avery et al., 2014).

As compared to oesophagectomy, minimally invasive gastrectomy has been slow to gain popularity in the UK. Our study spanning 10 years only identified 480 patients who underwent a laparoscopic (or laparoscopy assisted) gastrectomy. There was no significant difference identified in mortality or morbidity outcomes between open and laparoscopic groups. However, LG was associated with a lower length of stay (11 days versus 13 days, $p<0.001$). Previously published randomised controlled trials(Huscher et al., 2005), meta-analyses(Chen et al., 2009, Ohtani et al., 2010) and the interim analysis from the Korea Laparoscopic Gastrointestinal Surgery Study Group (KLASS) trial(Kim et al., 2010) also showed no significant differences in mortality and key morbidity outcomes between laparoscopic and open gastrectomy. LG has gained popularity in the East, and a high incidence of early gastric cancer in the East may explain the enthusiasm amongst surgeons there to undertake this procedure. Oncological outcomes following LG have also been recently shown to be comparable to the open technique, without any added risk of mortality or morbidity (Lee et al., 2014, Hu et al., 2014, Chen et al., 2014). A recent meta-analysis by Qiu and colleagues concluded that with comparable onocological outcomes, patients undergoing LG may benefit from a shorter hospital stay (Qiu et al., 2013).

A large proportion of the current literature regarding minimally invasive upper gastrointestinal resection comes from the East. This is in keeping with the high prevalence of gastric malignancy in the countries in the Far East. Literature from Japan and Korea have consistently shown superior outcomes when compared with the West (Markar et al., 2013). Some of this variation can be explained by differences in demographics, chemo-radio therapeutic strategies, lymph node yield, etc. However surgical techniques also remain a key difference between the East and the West. Markar *et al* analysed data from trials from the East and West pertaining to gastrectomy for cancer and concluded that the persistence of better survival rates in the East after adjusting for age, sex, tumour depth and nodal status, type of gastrectomy and chemotherapy effect indicates that an unexamined factor, such as surgical technique, is a potential variable that may be responsible for the difference in outcomes (Markar et al., 2013). Also, minimally invasive upper gastrointestinal resection has a steep learning curve. In order to achieve an operative time for LG that is comparable to open surgery, it is estimated that one has to perform at least 40 cases and a discernible decrease in blood loss after LG is only seen after 20 cases (Kunisaki et al., 2008). Studies from the East have also shown that it takes a surgeon about 60-90 cases of LG before they can observe any improvement in morbidity outcomes (Jin et al., 2007, Zhang and Tanigawa, 2009). In our study, only 5 surgeons performed >15 LG procedures in the 10 year period. Thus it will a considerable time for English surgeons to achieve competency and demonstrate an advantage to the laparoscopic approach. Another challenge to UK surgeons in gaining proficiency in performing LG is the lower incidence of early gastric cancer. The National Oesophago-Gastric Cancer Audit (NOGCA) report of 2009 identified only 40% of gastric cancer cases as Stage 1 and these included those cases that were down-staged using neo-adjuvant chemotherapy. Given the current volumes, large, multi-centre, prospective, randomised trials, in the West would be essential in evaluating the role of MAS for oesophageal and gastric resection.

National Training Programme in Laparoscopic Colorectal Surgery (LAPCO)

In 2006, National Institute for Health and Care Excellence issued guidelines that laparoscopic (including laparoscopically assisted) resection is recommended as an alternative to open resection for individuals with colorectal cancer in whom both laparoscopic and open surgery are considered suitable. The National Training Programme (NTP) in Laparoscopic Colorectal Surgery (LCS) was commissioned in 2007, funded by the Cancer Action Team at the Department of Health to provide LCS training for colorectal consultants in England. This programme was an educational initiative which provided supervised training to colorectal surgeons in England. The steep learning curve associated with safely undertaking laparoscopic colorectal resection is associated with complications and high conversion rates (Miskovic et al., 2011). Training on simulators has its own limitations and performance in an operating theatre is considered 'gold standard' for consultants to be labeled competent. This was the rationale behind establishing such a programme. If shown to be superior than the open approach, a similar programme for upper gastrointestinal resection can go a long way in supporting the uptake of minimally invasive oesophagectomy and gastrectomy in England.

Surgeon caseload (volume)

The volume-outcome relationship for major cancer surgery such as oesophagectomy, gastrectomy, pancreatectomy and liver resection has been previously established and this has laid the foundation for centralisation of such cancer services in the UK (Begg et al., 1998, Glasgow and Mulvihill, 1996, van Lanschot et al., 2001, Kim and Kwon, 2014, Yoshioka et al., 2014). The rationale behind this is that high volume centres have the infrastructure and expertise to deal with complex surgery leading to improvement in outcomes such as mortality, morbidity and length of stay. However, this is still a topic of contention in many countries. Benefits of centralisation come at a price for the patients such as long travel and long waiting lists. A recent meta-analysis of sixteen studies on volume outcome relationship for oesophagectomy showed a survival benefit in favour of high volume centres and high volume surgeons (Brusselaers et al., 2013). The same study also demonstrated a lower risk of short term mortality in high volume centres. More importantly, surgeon volume was shown to be more strongly related to survival than hospital volume. Kim and Kwon undertook an analysis of outcome following laparoscopic gastrectomy at high and low volume centres (Kim and Kwon, 2014). Although this study reported cases undertaken by one surgeon, at different hospitals, the outcomes at the low volume centre were significantly worse. As early as 1996, it was shown from a California database that hospital volume influenced outcomes following pancreatic resection for cancer and laid a plea for centralisation (Glasgow and Mulvihill, 1996).

The volume thresholds used in most studies to define high and low volume centres are usually catered to the data in question and there has been no scientifically derived definition of high volume centres. Similarly, there is no robust evidence to show whether there exists a minimum or optimum number of cases a surgeon should undertake annually to have consistently good outcomes. We set out to derive this optimum/ideal number from HES data. In our study, surgeon volume ranged from 2-29 oesophagectomies, 1-14 gastrectomies and 2-31 pancreatectomies per surgeon per year. Using surgeon caseload as a continuous variable, from a risk adjusted model, we showed that caseload was a significant predictor of lower mortality, whereby each additional case of oesophagectomy, gastrectomy and pancreatectomy would reduce mortality odds by 3.4%, 7.2% and 4.1% respectively. Using CuSUM analysis, although a volume-mortality relationship could be demonstrated, we were unable to recommend a definitive minimum surgeon caseload for achieving low mortality. The mortality rates did not plateau, and it is possible that higher volumes than those in our study may yield better results. This study justifies the centralisation of upper gastrointestinal cancer services, and more recent data may be able to arrive at an optimum volume number.

8.6 Strengths and limitations

The main strength of this research is that the data source, and hence the results provide a national perspective. HES data are comprehensive to the English population and therefore comprise a record of the health outcome of all patients treated in the National Health Services (NHS). The NHS provides approximately 90% of healthcare in England. As such, this database offers a unique opportunity to investigate healthcare activity and outcome across an entire country. Submission of HES data is mandatory and thus is immune to the risk of reporting bias. Despite its administrative nature, important clinical parameters and outcome measures are available such as mortality, readmission and length of stay. A good understanding of the ICD and OPCS codes presents the opportunity to be able to derive further metrics such as medical morbidity, re-operation/re-intervention and failure-to-rescue.

Data accuracy

Critics of administrative databases frequently question the accuracy of these data. The data are input by clinical coders, who are thoroughly trained and provide an unbiased report of the patient episode. Comparison of HES to clinical registries in various specialties has been undertaken extensively and a systematic review of these studies demonstrated an overall accuracy of 83.2% with a 80.3% accuracy of diagnosis and 84.2% accuracy of procedures (Burns et al., 2012).

Clinical parameters

The primary purpose of HES is not for outcomes research. Despite the number of available variables, there are some data that would have a bearing on clinical outcomes, but do not find mention in HES. For example, BMI, smoking status, tumour stage, adjuvant and neo-adjuvant treatment, lymph node yield, operative times, intra-operative blood loss etc are not available from this dataset. Although various medical conditions can be coded for, the severity of the symptoms cannot be assessed. Difficulty of surgery cannot be ascertained. Although we studied the first resection as our index operation, patients who have had other procedures under different specialties such as urology/gynaecology, would pose a challenge to the surgeon. This could either make the surgery technically challenging or preclude the use of laparoscopy - which we cannot take into account.

Coding limitations

Certain codes have been introduced more recently which precludes these analyses from previous years. These include codes for interventional radiology, conversion from laparoscopic to open surgery, codes for ileo-anal pouch surgery to name a few. Some conditions currently do not have a code such as anastomotic leak and parastomal hernia. Different centres may have local policies regarding coding of secondary diagnosis codes. In cases where minimally invasive codes such as laparoscopy or thoracoscopy are used, one cannot determine whether the procedure was laparoscopic or laporoscopy-assisted.

Provider data

Each patient episode is coded to a particular Consultant team that was in-charge of treating the patient. In cases of surgery, the named consultant will be coded rather than who actually performed the operation. Mergers of hospitals and trusts have to be taken into account when studying volume or caseload. As we have studies elective resections for upper gastrointestinal cancer, being complex surgery, we would expect that even if the operation were performed by a trainee, they would be supervised by the named consultant. It is not possible to directly investigate the level of the operating surgeon or percentage of the operation performed by a trainee.

Cause of death

Tuffin *et al* reported on significant variation in causes of death certification of patients in an intensive care unit, between junior doctors involved in their care, their consultant intensivists and pathology consultants in an English hospital (Tuffin R, 2009). This study demonstrated amongst others, a pertinent issue of underlying causes of death being documented without accounting for significant co-morbidities which the patient may have had. The authors also noted that there may be differing opinions between consultants involved in the patients' care. These are two of several reports which highlight possible discrepancies in cause of death documentation on death certificates (German et al., 2011). To this end, the department of health in the UK has initiated improvement to the death certification process in 2008 (Health, 2012). A major change was to introduce an independent medical practitioner (who is part of the clinical governance team of the trust), who would have to review the patient's records and concur with the death certification by the primary medical team (and if need be refer to the Coroner), before burial or cremation is authorised.

Despite the aforementioned limitations, the current research forms a population based analysis. Similar studies from clinical registries may be possible, but currently there are no registries that enjoy 100% data ascertainment. More importantly, maintaining a health record on a clinical registry is estimated as £60 per record compared to £1 per record for an administrative database (Raftery et al., 2005). Such cost discrepancy between different population databases may be justifiable in the research context if superiority of data accuracy can be adequately established. Until formal comparison of available data sources is undertaken dismissal of administrative data for research purposes may be erroneous.

8.7 Future research

Minimally invasive surgery

This thesis has given an overview of gastrointestinal resectional surgery in England. In particular, role of minimally invasive surgery for both upper and lower gastrointestinal resections has been discussed. Further research, in the form of randomised controlled trails, with clinical data such as stage of tumor, BMI, smoking status etc are needed to fully ratify the potential benefits of using this approach. Especially in colorectal resection, the benefits of laparoscopic surgery independent of the benefits of enhanced recovery programmes are key to establish this technique as the preferred option. Use of MAS in oesophagectomy and gastrectomy has a long way to go from an English perspective. Following centralisation, there has been higher numbers of minimally invasive oeosphageal and gastric resections. Randomised controlled trials, with a focus on oncological benefit and long term survival are needed. Biochemical studies such as Troponin levels following surgery in patients in the open versus MAS arms could shed more light on the differences in physiological response to tissue trauma. The role of laparoscopic surgery in other high risk patients such as those with renal failure, high BMI, etc. could be undertaken by linking HES with primary care data. In addition, robotic surgery is gaining wide interest, however it is currently limited to a few centres worldwide. Before accepting this approach, it has to be thoroughly evaluated by trials designed to study outcomes comparing robotic surgery to conventional laparoscopic surgery.

Ideal mortality metric

The deaths occurring following major surgery, between thirty days and one year need to be investigated further. Although the cause of death analysis has been undertaken in this report, to attribute these delayed deaths to the stress of surgery and anaesthesia would need further research. Risk stratification studies evaluating 90-day mortality or 180-day mortality and their role as quality metrics may be able to demonstrate the excess mortality that is not captured with traditional mortality measures and risk prediction tools such as ASA/POSSUM scores. Especially in the elderly, research involving assessment and quantification of frailty and impact of targeted strategies such as involving geriatric physicians early in patients undergoing emergency surgery would be prudent in the light of an expanding elderly population.

International comparisons

Collaborations with other countries, even across continents, and pooling of administrative data may provide the base for meaningful international comparisons and bench marking. Various coding systems could be translated to generate risk-adjusted models for various outcome measures. A similar initiative is called The Global Comparators (GC) Project and coding systems from England, Europe and USA were mapped to compare outcomes following colorectal surgery (Munasinghe et al., 2014).

CONCLUSIONS

The studies undertaken as a part of this research have provided an insight into gastrointestinal resection in English NHS hospitals. I have demonstrated that using HES data, national outcomes and trends can be reported. Given the limitations of the administrative nature of HES data, meaningful metrics such as morbidity can be derived. Routinely collected, mandatory national databases such as HES have the potential to be used in measuring quality and performance of health services. Accuracy of coding will remain an issue of contention, but strategies to ensure an accuracy as close to hundred percent as possible can be implemented, thus enhancing the scope of outcomes research from HES.

The absolute mortality figures following gastrointestinal resection (upper and lower) in England are worse than some studies from the USA, Europe and the Far East. However, one has to exercise caution while comparing case series with administrative data. The morbidity rates however corroborate with published literature. The superiority of laparoscopic colorectal resection over the open approach, in terms of reducing risk of mortality, morbidity and length of stay has since been demonstrated in various randomised trials. My work has shown minimally invasive oesophagectomy and gastrectomy to be safe with comparable outcomes to open surgery. Further studies, and carefully designed trials are required to establish benefits of this approach, if any. Centralisation of the upper gastrointestinal cancer services in England has been justified by our study showing an inverse volume-mortality association.

I posed the question of how representative a thirty day mortality metric is in patient undergoing major surgery, especially in high risk patients such as elderly and those undergoing emergency surgery? I have demonstrated significant morbidity and death beyond the initial hospital stay and attempted to explain this using cause of death analyses. Further work using receiver operating curve (ROC) analyses is proposed to identify a more accurate mortality measure and to test predictive power of currently established scores such as ASA, POSSUM, Charlson's index, etc. in quantifying this risk pre-operatively. I have shown that quoting 30-day mortality risk in elderly patients undergoing emergency surgery such as colorectal resection may not be appropriate, especially when contemplating surgery versus conservative treatment. The perioperative journey extends to the community with a significant proportion of adverse outcomes occurring up to one year. This also paves way for studies on frailty as a measure of risk rather than age alone and a multi-disciplinary approach to post-operative care of the elderly in hospital, at intermediate care and in the community.

The conceptual framework of this research has been designed along the Donabedian model, which proposes structural inputs, process relationships, and outcomes as interrelated domains that lead to quality improvement. The studies in this thesis, answer some of the clinical questions pertaining to gastrointestinal resection and also raise some others. I have laid the foundation for further clinical research to be undertaken in order to measure the quality of services in the National Health Services.

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