THE ROLE OF MULTIDISCIPLINARY CARE IN THE OUTCOMES OF PATIENTS TREATED FOR COLORECTAL CANCER IN THE WEST OF SCOTLAND

by

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Summary

The aim of this thesis was to investigate the impact of the Managed Clinical Network (MCN) for colorectal cancer in the West of Scotland on outcomes for its patients. The alternative hypothesis was that greater changes to patient outcome had occurred over time than those that would have been expected in the absence of a Managed Clinical Network service structure.

The study was a retrospective cohort study merging locally derived clinical audit and nationally held Cancer Registry datasets. This facilitated a comprehensive examination of patient characteristics and survival outcomes in varied cohorts of patients suffering from colorectal cancer in the West of Scotland.

I employed longitudinal, cross sectional, univariate and multivariate methods of data analysis. Following a review of the current literature a baseline demographic summary of the population was produced. This allowed an examination of temporal changes in both survival and practice in the region in order to evaluate the key determinants underpinning differences before and after the inception of the new service structure. I went on to study specific aspects of patient management on outcome including effects of surgeon specialisation, effects of mechanical bowel preparation on short and long term outcomes and degree of equity of surgical provision for patients with rectal cancer. These aspects of care are thought to be measures of quality in patients with colorectal cancer and could be influenced by the inception of a Managed Clinical Network

Evaluation of the current literature regarding effects of Managed Clinical Network on outcomes for colorectal cancer patients demonstrated a paucity of studies investigating our alternative hypothesis.
Overall it appears that the introduction of the MCN has lead to improvements in survival for particular groups of patients only. We analysed the records of 37,890 colorectal cancer patients in the West of Scotland over a 25-year period and confirmed expected proportions of colonic to rectal lesions as well as equal sex distribution. We also report a higher ascertainment for data regarding Dukes' stage when compared to other published series.

Trends in relation to volume of work undertaken by surgeons on colorectal cancer patients in the West of Scotland demonstrate that there was increasing specialisation over the period under study. This is evidenced by the increase in proportion of resections performed by higher volume surgeons and is encountered in both colon and, to a lesser extent rectal cancer surgery. It seems that increasing specialisation has had resultant effects on overall survival for colon cancer patients but not for rectal cancer patients thus far.

With regard to specific aspects of patient care we were able to show that specialisation has increased with time in our region and that mechanical bowel preparation has no effect on either immediate or long-term outcome in patients undergoing surgery for colon cancer. We also showed that in the West of Scotland we provide a surgical service to rectal cancer patients that is unbiased with regard to sex and degree of socioeconomic deprivation. This contrasts to previous findings in England.

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Author's declaration

I declare that, except where explicit reference is made to the contribution of others, that this thesis is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Signature _____

Printed name _____

Abbreviations

ACPGBI – Association of Coloproctologists of Great Britain and Ireland

ANOVA – Analysis of Variance

APE – Abdomino-Perineal Excision

AR – Anterior resection

CEA - Carcinomatous Embryonic Antigen

CHI – Community Health Index

CRC – Colorectal cancer

CRM – Circumferential Resection Margin

CT – Computed Tomography

DEPCAT – Deprivation Category

DGH – District General Hospital

DVT – Deep Venous Thrombosis

EASR – European Age Standardised Rate

EUS – Endoanal Ultrasound

EVI – Extramural Vascular Invasion

GRO(S) – General Registry Office for Scotland

HealthSTAR - Health Services Technology, Administration, and Research

HMIC - Health Management Information Consortium

HPN – Home Parenteral Nutrition

IARC – International Agency for Research in Cancer

ICD – International Classification of Diseases

LCA – Local Council Area

MCN – Managed Clinical Network

MD – Doctor of Medicine

MDT – Multidisciplinary Team

MEL – Medical Executive Letter

NCIN – National Cancer Intelligence Network

NHS – National Health Service

NHSQIS – National Health Service Quality Improvement Scotland

PCR – Polymerase Chain Reaction

PE – Pulmonary embolus

POSSUM - The Physiological and Operative Severity Score for the enUmeration of Mortality

QIS – Quality Improvement Scotland

RCPath – Royal College of Pathologists

RFA – Radiofrequency Ablation

SASM – Scottish Audit of Surgical Mortality

SCAN – South East Scotland Cancer Network

SEC – Socio Economic Circumstances

SIGN – Scottish Intercollegiate Guidelines Network

SIGLE - System for Information on Grey Literature

SIMD - Scottish Index of Multiple Deprivation

SMR01 – Scottish Morbidity Record 1. In patient and day case hospital discharge records for non-psychiatric and non-obstetric specialities.

SMR06 – Scottish Morbidity Record 6. Cancer registration records

TME – Total Mesorectal Excision

UICC – International Union Against Cancer

WoSCSU – West of Scotland Cancer Surveillance Unit

5-FU - 5- Fluorouracil

Publications Presentations and Letters

Publications relating to this work

1. Mechanical Bowel Preparation does not influence outcomes following colonic cancer resection. G. A. Nicholson, I. G. Finlay, R. H. Diament, R. G. Molloy, P. G. Horgan and D. S. Morrison. British Journal of Surgery 2011. Vol 98, Issue 6, p866-871.

2. Quality of care in rectal cancer surgery. Exploring influencing factors in the West of Scotland. G. A. Nicholson, D. S. Morrison, I. G. Finlay, R. H. Diament, P. G. Horgan and R. G. Molloy. Colorectal Disease 2012. Vol 14, Issue 6, p731-739.

Presentations to learned societies relating to this work

1. BJS Prize Presentation. The Association of Coloproctology of Great Britain and Ireland 2009.
   Bowel Preparation: Complication rates and Survival Outcomes for Elective Colon Surgery in a Managed Clinical Network Setting.

2. Continued Improvement in Survival Following Surgery for Colorectal Cancer: The West of Scotland Experience R. Oliphant, G. Nicholson, P. Horgan, R. Molloy, D. S. Morrison.

Poster presentations to learned societies relating to this work

1. Digestive Diseases Week, Chicago, May 2009.
   Bowel Preparation in the West of Scotland. Complication rates and Survival Outcomes for Elective Rectal Surgery in a Managed Clinical Network Setting.

2. ASGBI International Surgical Congress, May 2010.
   Factors influencing type of rectal cancer resection in a population with a wide variation in socio-economic deprivation.

3. West of Scotland Surgical Association, October 2009.
   Factors Affecting Outcome in Emergency Colon Surgery in the West of Scotland.

4. West of Scotland Surgical Association, October 2009.
   Factors Affecting Outcome in Emergency Rectal Surgery in the West of Scotland

5. United Kingdom Association of Cancer Registries, August 2009.
   Will Screening for Colorectal Cancer in the West of Scotland cause a difference in the site of the lesion and introduce socio-economic bias?

6. United Kingdom Association of Cancer Registries, August 2009.
   Trends in Dukes' stage at diagnosis before introduction of screening in colorectal cancer patients in the West of Scotland.

7. Association of Surgeons in Training, April 2009.
   Survival Improves with time for colorectal cancer patients treated within a managed clinical network.

8. Royal College of Physicians and Surgeons of Glasgow Triennial Conference, November 2008.
   Survival outcomes of colorectal cancer patients referred to A&E compared to those referred to outpatient clinic

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   http://www.bjs.co.uk/details/yourviews/1057423/Mechanical-bowel-preparation-does-not-influence-outcomes-following-colonic-cance.html

1 Introduction and Literature Review

Specialist care is associated with better survival from cancer. This observation, along with evidence of geographical inequities in the quality of cancer care led to reorganisation of cancer services into Managed Clinical Networks throughout the United Kingdom, which began in the late 1990s. However, there is a lack of evidence that the reorganisation of services has resulted in either improvements in survival or a reduction in inequities of care, over and above those that would have occurred without reorganisation. Colorectal cancer is the second most common cause of cancer deaths in the United Kingdom and much of the evidence that led to service reorganisation came from analyses of colorectal outcomes. The aim of this thesis is to describe the impact of Managed Clinical Networks on colorectal cancer outcomes in the West of Scotland. However, before any evaluation of the effects of service reorganisation can be made - either temporally or geographically – other potential confounding factors that affect colorectal cancer survival need to be taken into account. These include patient characteristics, such as demographic and socio-economic factors, and disease factors, such as cancer site and stage. The West of Scotland has a high incidence of colorectal cancer, diverse socio-economic conditions, and high quality clinical information systems that make it useful for understanding determinants of cancer outcomes.

This chapter begins by describing colorectal cancer care in the context of the West of Scotland. A review of literature on the effects of patient and disease factors is then presented. Next, the effectiveness of the major treatment modalities is reviewed. Lastly, a review of literature on specialist care is made. This explores definitions of what constitutes specialist care and includes a systematic review of literature on the impacts of Managed Clinical Networks on patient outcomes.

1.1 Colorectal Cancer and its care in the West of Scotland

Background to development of managed cancer services in Scotland

Inevitably when development of cancer services in Britain is considered, the Calman-Hine report is cited. It is widely regarded as the piece of work that lead to the restructuring of cancer services in England from 1995 (7). The report followed 20 years of similar restructuring of cancer services in other countries. It was in 1974 though that Sweden took the lead when their Minister for Health introduced a care programme for cancer (SNAP 1996). In Denmark, a prototype version of the current SIGN guidelines for breast cancer has been in use since 1977. The Dutch and Americans have been using cancer care systems implemented as far back as 1995 (8). The fact that both Calman and Hine had backgrounds in cancer and with patient groups meant they were acutely aware of the needs of both service providers and potential service users. In England and Wales the Calman Hine report produced the initial impetus for reforms in cancer services (7). Although it was neither specific nor outlined any objective way of measuring improvement in cancer services, it led to a shift toward integrated cancer services. It was followed by a Scottish version less than a year later (Scottish Office Department of Health 1996) that outlined seven principles for integrated cancer care services throughout Scotland (see extract below). A review commenting on the evidence base for this reform followed the report (9). It outlined a broad scope for the reform and highlighted the differences in outcomes for patients suffering from different cancers. Emphasis was placed on the growing body of evidence for organised networks producing better outcomes although the authors recognised the disparity between different types of cancer. A further project in East Anglia agreed with the Selby review. It supported the Calman-Hine strategy but recognised that certain cancers were in need of priority change as opposed to an overhaul of all cancer services (10).

EXTRACT FROM A POLICY FRAMEWORK FOR COMMISSIONING CANCER SERVICES

GENERAL PRINCIPLES
The principles which should govern the provision of cancer care are:

All patients should have access to a uniformly high quality of care in the community or hospital wherever they may live to ensure the maximum possible cure rates and best quality of life. Care should be provided as close to the patient's home as is compatible with high quality, safe and effective treatment.

Public and professional education to help early recognition of symptoms of cancer and the availability of national screening programmes are vital parts of any comprehensive programme for cancer care.

Patient, families and carers should be given clear information and assistance in a form they can understand about treatment options and outcomes available to them at all stages of treatment from diagnosis onwards.

The development of cancer services should be patent centred and should take account of patients', families' and carers' views and preferences as well as those of professionals involved in cancer care. Individuals' perceptions of their needs may differ from those of the professional. Good communication between professionals and patients is especially important.

The primary care team is a central and continuing element in cancer care for both the patient and his or her family from primary prevention, pre-symptomatic screening, initial diagnosis, through to care and follow up or, in some cases, death and bereavement. Effective communication between sectors is imperative in achieving the best possible care.

In recognition of the impact that screening, diagnosis ad treatment of cancer have on patients, families and their carers, psychosocial aspects of cancer care should be considered at all stages.

Cancer registration and careful monitoring of treatment and outcomes are essential.

With these principles in mind, clear roles were set out for the first time in Scotland for interregional, regional, local *and* hospital-specific members of cancer centres.

The aforementioned framework reform was in response to the United Kingdom National Health Service Cancer Services Collaborative / Improvement Partnership.

The Cancer Services Collaborative programme commenced in 1999, before the publication of the National Health Service Cancer Plan. It built on the pioneering approach to service improvement developed by Don Berwick and colleagues at the Institute for Healthcare Improvement in the USA. In essence the Cancer Services Collaborative is applying lessons learned about process re-engineering in industry to the context of cancer care. It provides the model through which the principles from process re-engineering manifest in hospital medicine. It is then hoped that application of these principles will translate into improved quality of care and outcomes (11).

The principles were to initiate a paradigm shift in three ways. Firstly, the overall organisation of services would move from being general to specialised. Secondly, patients would be referred to specialists directly. It was envisioned that this would provide more uniform access for patients (12). Finally, to facilitate a more streamlined management plan the clinicians who previously were more autonomous would work within a multidisciplinary model of care (8). This, it was hoped, would make optimal use of resources resulting in optimal benefit to patients in terms of outcomes.

The following figure represents the points in the patient journey where the MDT is thought to exert an effect.

Figure 1 - Points of Influence of the MDT process

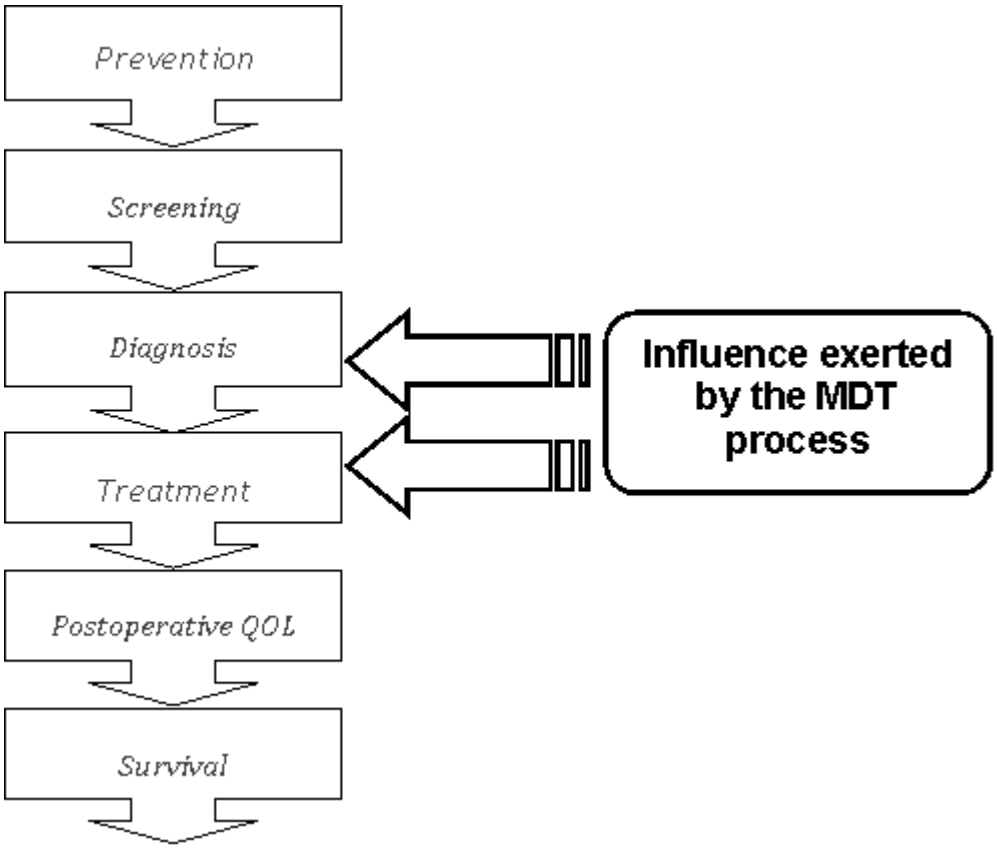


Figure adapted from Freeman and Chu (13).

Before drawing conclusions from the population as a whole it is important to have a degree of understanding of the pathological processes leading to development of colorectal cancer. A grasp of the current prognostic indicators is also important to allow us to draw sensible conclusions from results.

Within each region are a number of Health Boards. Within each Health Board are a number of MDTs. Using the West of Scotland as an example, there are a total of 11 MDTs operating in five Health Boards, covering 17 hospitals. This ranges from one MDT in the smallest three Health Boards to six MDTs in the largest (14). The population of the West of Scotland numbers 2,488,000. The Greater Glasgow and Clyde Health Board covers 1.2million people (15).

Managed Clinical Networks and Multi-Disciplinary Teams

There is a continuing body of evidence to support the treatment of colorectal cancer in high volume institutions where specialist colorectal surgeons are available (16). The impact of MCNs has been described for various conditions and locations outside the West of Scotland so a full assessment of the effects of treatment for colorectal cancer in all units in the West of Scotland is wanting (17,18).

Published data regarding the management of colorectal cancer throughout Europe (EUROCARE) resulted in Scotland fairing badly when compared to its European neighbours in terms of survival outcomes (19). This review of current literature provides an opportunity to explore more fully the impact that the Calman-Hine report has had in the West of Scotland with regard to colorectal cancer.

This review of current literature attempts to answer 4 questions:

- What is the current structure of MCNs with regard to colorectal cancer?
- Are they effective?
- What is known about the effects of either MDTs or MCNs on the outcomes of patients with colorectal cancer?
- What is known about the effects of specialisation and volume on outcome for colorectal cancer patients?

In order to manage effectiveness there generally has to be objective evidence to facilitate comparison between groups. Various papers report on whether or not recommendations are followed up or adhered to. These are usually in relation to guidelines or therapies (20). Measuring outcome following this (e.g. survival) remains less well reported.

Previous work evaluating impact of the MDT on patient survival in lung cancer patients demonstrated encouraging results (21). However, this was a single-centre experience and was not reporting on effects of a larger MCN setup. It is

hoped that larger networks should be able to replicate the outcomes of a single MDT.

Objective measures of outcome are generally sought to provide a means of comparison between populations. They are also widely employed and quoted for the purposes of audit thus upholding one of the tenets of Clinical Governance. In relation to colorectal cancer, 5 year survival is currently the gold standard objective measure (22). Any further attempts to tease out the weight added by each component of the MCN and MDT to patient survival outcomes increases the complexity of analysis. In the initial few years following Calmanisation articles relating to MCNs tended to be single centre reports or editorials with no objective, thus comparable, outcomes (17,23). MCN and MDT performance are thought to influence patient outcome positively so various attempts have been made to assess this in an objective way.
Most recently and most comprehensively, Hong and co-workers performed a wide-ranging literature review examining the potential relationship between multidisciplinary care and patient survival (24). Despite identifying 12 of 21 studies for review reporting statistically significant associations between MDT care and patient survival, only three of these were in colorectal cancer patients. The heterogeneity of study methodology and range of outcomes measured meant that a meta analysis was not possible. Only one study provided a before-after comparison in colorectal cancer patients. This study was limited to a single surgeon in a single hospital (25). Their final conclusion was that for all cancers, a causal relationship linking MDT care with improved patient survival could not be affirmed.

The factors that may affect outcome of cancer care can be divided into three categories. Firstly, patient characteristics. Secondly, characteristics of the care providers and thirdly, the structure of the care system. Table 1 summarises the areas where differences between hospitals or MDTs can arise. It is the aim of the NHS and cancer reform strategies to minimise these differences thus creating a service with equitable entry, treatment, and long-term outcome for all colorectal cancer patients. We are currently able to assess many of the patient characteristics. It would be additionally advantageous to measure co-morbid conditions.

Most consultants operating on colorectal cancer patients in the West of Scotland are declared specialists. The only exception to this is when an emergency resection is required. A further level of complexity is added when one considers that often there is more than one hospital contributing cases to a single MDT forum.

Table 1 - Factors that may affect access to and outcomes from colorectal cancer care services

Patient characteristics	Health care provider characteristics	Structure of the care system
Clinical – tumour stage and tumour morphology	Case volume	MDTs
Co-morbid conditions	Experience, training / certification	Case volume
Socio-economic status		Type – teaching vs. DGH
Age, sex, race	Age, sex, race	Location – urban vs. rural
Educational background		Facilities / design
Healthcare beliefs, attitudes, practices		Hospital characteristics
		Type and number of staff
		Quality assurance programme

Adapted from table 3 in (5)

Methods of measuring outcome

It should be noted that long-term outcomes can be assessed by regular follow-up. Strategies for this have been recently assessed but opinion remains divided in the field of colorectal surgery as to what represents an optimum follow-up strategy for colonic and rectal cancer patients. There remain several unresolved issues that lie outside the scope of this thesis (26).

An early attempt at measuring MDT performance in 2002 demonstrated that although MDT activity was widespread for colorectal cancer, a wide variation existed regarding its full implementation (27). Various problems were described therein. The authors' main conclusion was that a dedicated MDT clerk is essential to ensure smooth running of MDTs. The main drawback of this study is that it was a questionnaire. The vast majority of MDTs in the West of Scotland now have dedicated MDT clerical support staff, in line with QIS.

The most comprehensive report on outcomes in British colorectal cancer patients so far comes from Yorkshire (28). Morris *et al* also concluded that there is a variable extent to which Calman-Hine recommendations have been implemented. They employed the Kelly *et al* questionnaire approach to assessing growth of MDTs and their adherence to national criteria for the ideal team. This was done over a far wider population though. They then improved upon the Kelly approach by employing multilevel binary logistic regression models to their population based longitudinal study (n= 11548). They concluded that where institutions had followed Calman-Hine recommendations (i.e. had more surgical site specialisation), there was evidence of increased use of preoperative radiotherapy and increased proportion of anterior resections in rectal cancer patients

The paradigm shift in cancer care brought about by the Calman-Hine report should have affected public awareness. Whether or not this evolution would have happened without Calmanisation will never be known. For now though, we are concerned with ascertaining what definite changes in outcome have occurred since its inception.

An in depth analysis on a par with that performed by Morris and co-workers is wanting in Scotland. This would not only provide an almost direct comparison with their work but it would offer a unique glimpse into the current performance of the MCN for colorectal cancer and outcomes for its patients. This then provides a benchmark for future studies in Scotland, where a separately managed healthcare system exists compared to England.

Effective MDT working has various requirements. Leadership and team dynamics are considered imperative for the MDT to function optimally. Administrative support has also been highlighted in the past as an essential element in the smooth operation of an MDT. Protected time is a further issue that has been highlighted. Many MDTs operate over lunch hours, with no timetable slot devoted to the important decisions being made regarding patient management. Funding is the essential element that provides all of the aforementioned requirements. Under funded units will find it hard to adequately staff and resource an MDT that is to function optimally.

Certain aspects of the MDT are inherently harder to measure. Nonetheless they have been suggested as influencing the team dynamic and therefore potentially influencing patient outcome. These include more psychological and sociological areas such as communication between health professionals, job satisfaction, and psychological well-being of team members and patients alike. It is difficult to ascertain whether changes in these parameters translate into improved patient outcome.

On the other hand, there are more objective measures in the MDT environment that can act as benchmarks from which to compare performance. These encompass clinical outcomes, preoperative assessment, and recruitment into clinical trials. Frequency and results of audit remain important too. The following points summarise the aims and outcomes of the National Cancer Peer Review Programme

The National Cancer Peer Review Programme aims to improve care for people with cancer and their families by:

- Ensuring services are as safe as possible
- Improving the quality and effectiveness of care
- Improving the patient and carer experience
- Undertaking independent, fair reviews of services
- Providing development and learning for all involved
- Encouraging the dissemination of good practice

The outcomes of National Cancer Peer Review Programme are:

- Confirmation of the quality of cancer services
- Speedy identification of major shortcomings in the quality of cancer services where they occur so that rectification can take place
- Published reports that provide accessible public information about the quality of cancer services
- Timely information for local commissioning as well as for specialised commissioners in the designation of cancer services
- Validated information which is available to other stakeholders

Taken from www.cquins.nhs.uk (29).

As previously mentioned, the gold standard objective measure of outcome for colorectal cancer patients is survival at five years. There are currently no published data demonstrating an improved survival following treatment for colorectal cancer in an MDT. The most encouraging results to point towards this come from Paisley. MacDermid *et al* recently published outcomes on a series of patients who have an increased survival having been treated in an MDT versus those who have not been treated in an MDT. They looked only at the effect of chemotherapy and not at the entire MDT management process (25). Ideally, a before and after MDT comparison should be made. This is the case for a 2006 study by Stephens et al. They compared a group of 77 oesophageal cancer patients from 1991-1997 i.e. pre-MDT to a group of 67 MDT managed patients between 1998 and 2003 (30). They found the most important predictors of increased survival to be MDT management, lymph node metastases and ASA grade. The operating surgeon was not found to be significant. They did not adjust for the year of incidence.

McCarthy *et* al provide evidence of improvements in 1 year survival for breast and colorectal cancer in an MDT environment. Their wide-ranging study of compliance to current MDT standards revealed that compliance with certain tumour-specific clinical guidelines and cancer quality standards translated into survival gain at one but not five years. This was not the case for general standards relating to service coordination and service provision (31).

Recording of data

Quality outcome measures rely upon the completeness and quality of the original patient data. The data from the MCN represent a rich source of information on emerging and evolving practice patterns.

Ideally the precise objective measures used to produce the most meaningful results would guide the type of information collected. In the pragmatic world however, the situation is more likely to be that we tailor the outcomes measures to the available data. In essence we have to make do with what we have.

As will be outlined in the methods section, merging local West of Scotland MCN audit data with centrally held death records and Scottish cancer registry data created a novel dataset. Firstly, however, it is important to understand the origins of these data and how they are recorded, as the process of data collection and collation in itself is relatively new.

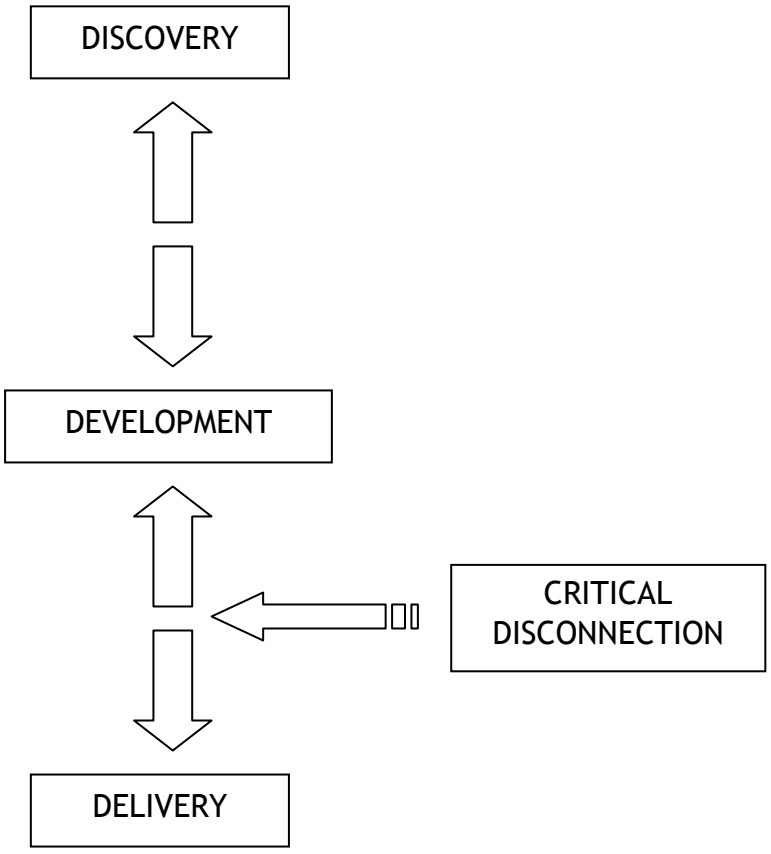
Managed Clinical Networks

Managed Clinical Networks (MCNs) have been variously described. A generally held definition is that they represent linked groups of health professionals and organisations from primary, secondary and tertiary care, working in a co-ordinated manner, unconstrained by existing professional and Health Board boundaries, to ensure equitable provision of high quality clinically effective services throughout Scotland (32). They aim to reduce the critical disconnect, cited as existing between the development of treatments and their translation to patients with colorectal cancer. Collaboration exists at different levels. Firstly, between government and the profession as a whole. Secondly between government and those who set the standards that MCNs are to achieve. Thirdly, between the standard setters and the managed networks themselves. The advantage of these various collaborations is that information is shared across a large population base affecting a maximum number of patients. Similarly, the network audit process enables far more detailed research to be conducted with far more numbers than would have been possible previously. A main

consideration is how much of this is translated into clinical practice in order to improve patient outcome.

The following figure highlights where the critical disconnection lies.

Figure 2 - Schematic representing the perceived point of critical disconnection between development of treatments and translation into patient benefit.



Adapted from Chu and Freeman in (33).

MCNs were first introduced as a result of a Scottish Executive medical executive letter (MEL) in 1999(32). At that point there were pre-existing networks in the Highlands and Islands as well as the diabetes network in Tayside. The label MCN was therefore introduced as an umbrella term for similar collaborations spanning the NHS whilst including the existing units. Existing services considering themselves as functional MCNs sought formal approval from their local Trust and Health Board.

This contrasted to the implementations in England and Wales where the centralised Cancer Centre model was adopted. Both models were introduced to

be more functional with regard to spread of population and location of services throughout their respective countries.
The overhaul of cancer services was underpinned by a set of principles. It was agreed that MCNs should have a set of principles to comply with too. These are contained within the MEL (32).

The need for a uniform set of standards was addressed by the Clinical Standards Board for Scotland (CSBS). They were also responsible for developing the key clinical and organisational performance indicators relevant to the service. The CSBS was responsible for developing minimum clinical standards for the management of the common cancers. The colorectal cancer standards were published in January 2001 but have now become part of Quality Improvement Scotland (QIS). The latest set of Clinical Standards were published in March 2008 (34).

A further HDL in 2002 re-stated the commitment of the executive to MCNs in terms of both funding and regular review. They were to draw on experiences to date and implement any necessary change. Focus was made on 11 key areas where clarification of roles was needed. These ranged from patient involvement to assistance available from the Health Department (35).

By their very nature and concept, MCNs are flexible and dynamic entities. They have been created for maximising patient care worldwide in areas ranging from home parenteral nutrition (HPN) and paediatric liver disease to cardiac services, breast cancer and paediatrics (18,36-38). MDTs for patients with learning disabilities have been around since at least 1983 (39). A formal preliminary evaluation of the development of cancer networks was published in 2002. This described swift organisational change within the NHS with regard to Cancer Services. It was confined to England and further limited by response rates as low as 33% to the survey questionnaire (40). A commentary on the survey remarked that it appears that implementation of the ground-breaking Calman-Hine report has been patchy, incoherent and incomplete (41). With this in mind it seemed more sensible to base further studies on objective measures at the MDT level before attempting to evaluate MCN function.

Current Structure

In Scotland there are currently three regional colorectal MCNs, namely the West of Scotland Cancer Network (WOSCAN), North of Scotland Cancer Network (NOSCAN), and South East Scotland Cancer Network (SCAN). The concept of coordinated care is promoted by each of these MCNs. Submission of all cases of colorectal cancer to MDT review is now considered mandatory but variation in attendance and process between MDTs still occurs despite their inception more than eight years ago. Most recent reports suggest continued heterogeneity across our region in terms of MDT coordinators, oncologists and clerical or audit staffing (42). It is the role of each MCN to audit this.

Variation in and reorganisation of rectal cancer services

A growing body of evidence exists to suggest significant variation in the type of rectal surgery performed across England and Wales (43-45). This variation has also previously been demonstrated to affect outcome (46). To date, this has not been investigated in any entire regional population.
A number of important studies provide relevant background to this piece of work as well as prompting numerous research questions and potentially influencing further reform of surgical service provision. There have been numerous important series pertaining to quality of rectal surgery and outcome published in the last six years. Two large retrospective population-based analyses highlight the large variation in ratio of APE to AR in the UK, following examination of a huge population of rectal cancer patients numbering 83,866 (43-45). They point to a decrease in APE with time and a statistically significant likelihood of receiving an APE for rectal cancer if the patient is male and / or socioeconomically deprived. Morris and co-workers also comment on the significant variation in type of major resection used between individual surgeons and hospital trust. This is independent of case-mix.

A prospective, randomised controlled trial looking at outcomes in rectal cancer patients in Holland quotes an improvement in survival for AR patients of 19.1% at seven years compared to APE ($p = 0.008$). They do not state if survival is overall, relative, or cause specific. They also state that 30.4% of APE patients had

positive circumferential margins compared to 10.7% in the AR group (p=0.002) (47). An advantage of their study is that they report results with tumours divided into different groups according to the tumour height from the anal verge. This very useful information is omitted from other major studies.
A large descriptive multicentre study of 1036 patients looks in particular at circumferential margin involvement (CMI) in restorative (i.e. AR) and non-restorative (i.e. APE) procedures (48). The conclusion is that APE is associated with a significantly higher CMI than AR.

Marr et al have also published data regarding a series of 561 rectal cancer patients demonstrating a statistically significant 11% reduction in cancer specific survival for patients undergoing AR compared to APE. Whilst affirming previous results from Tekkis et al regarding higher rates of CMI in APE patients, they also state that APE patients have a higher rate of local recurrence (LR). Their results stated a LR rate of 22.3% in APE patients versus 13.5% in AR patients, ($p = 0.002$; cancer specific survival 52.3% versus 65.8%, $p = 0.003$). There is however no mention of assessment of the case mix between the two groups under study. This could potentially explain some of the differences found (49).

The final important study in recent years is a prospective observational national cohort study involving 2136 rectal cancer patients and their oncological outcomes when comparing APE with AR for resections in the lower rectum. The main aim was to be able to select patients that would be suitable for radiotherapy (50). They examined various putative negative prognostic indicators concluding that if surgery is optimised; preventing intraoperative perforation and involvement of the circumferential resection margin, the prognosis for cancers of the lower rectum seems not to be inherently different from that for tumours at higher levels.

Rates of APE are slowly dropping with time in England, Canada and mainland Europe but there remains concern that some surgeons may still overuse this procedure thus resulting in some patients not only receiving an avoidable colostomy but also undergoing a more deforming operation (43)(51,52). Overall rates in the West of Scotland have not yet been ascertained to compare to

English figures (7). We aimed to perform this comparison, both with previous published data and nationally agreed standards.

Since 1995 the UK Government has undertaken wide scale reform of UK cancer services to ensure a ‘‘high quality of cancer care for all’’ and improve cancer survival in the UK (7). Quantifying and addressing variations in surgical practice is a key component in trying to achieve this. The Department of Health has published guidance stating that, wherever possible, surgeons should try to ensure anal sphincters are preserved (53).

Recently, there has been a growing appreciation of the importance of undertaking national comparative audit to monitor performance and outcomes across the NHS and realisation of the potential for routinely available health datasets to achieve this (54) (55). In consequence, this retrospective regional population based study sought, via linkage of cancer registry and routine, centrally collated clinical audit data, to examine variation in rectal cancer surgery throughout the West of Scotland between 2000 and 2005. We wanted principally to determine rates of use of APE and other rectal cancer operations across the region at a population level to determine if any significant variation could be explained by differences in patient characteristics such as Dukes’ stage of disease, age, gender, type of admission or socioeconomic deprivation level. In addition we sought to quantify the extent of variation in practice between MDTs, Health Boards and surgeons according to the volume of their practice. Although not a novel approach, this is the first time these aspects of rectal cancer surgery have been investigated at this level in our region (44).

In summary, the last six years have provided a number of large studies closely examining the variation in surgical practice for treating rectal cancer. The key findings are that the rate of APE resections is reducing with time. The two largest published studies to date have noted that men are more likely to undergo APE than women. Being both male and socioeconomically deprived are predictors of APE for a rectal tumour. There also exists significant variation, independent of case mix, in the rate of APE resections for rectal tumours between both individual surgeons and hospital trusts.

1.2 Colorectal cancer epidemiology

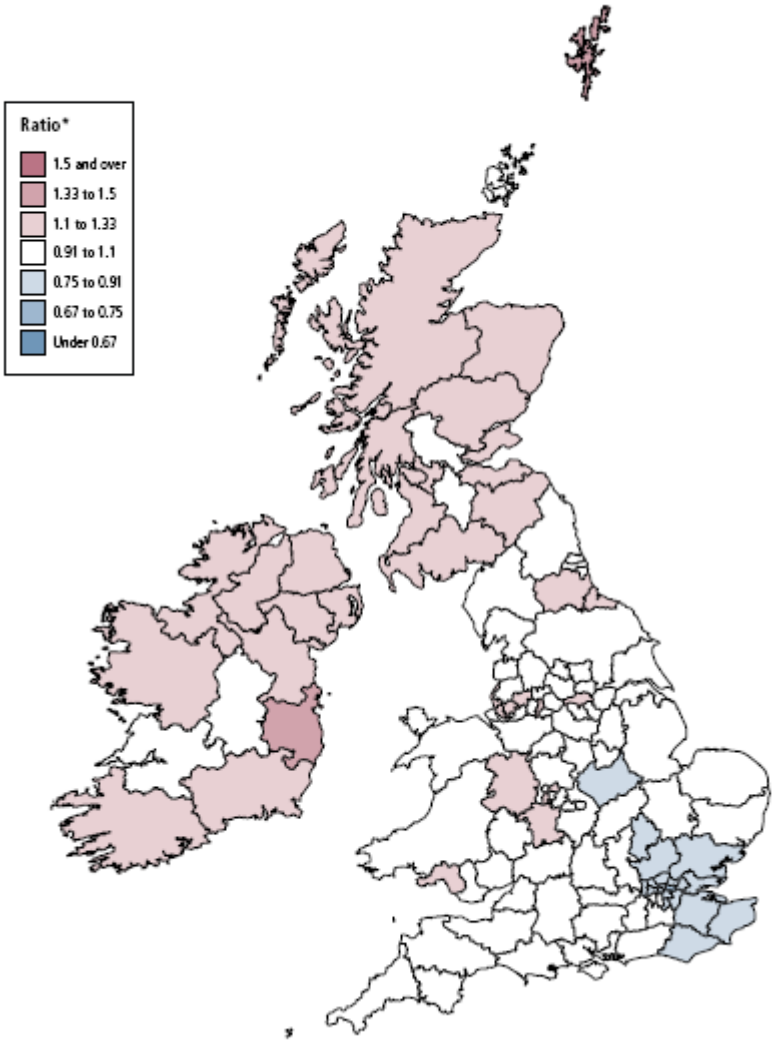
Colorectal cancer is currently the second most common cause of cancer death in the Western world (56). The age-standardised incidence rate for colorectal cancer in Scotland is around 64.3 per 100,000 in men and 41.5 per 100,000 in women. This is greater than the UK average of 52.9 per 100,000 for men and 34.9 per 100,000 in women (22). See figure three below. In contrast, the age-standardised European incidence rates for bowel cancer, EU-27, by sex are 60.5 per 100,000 for men and 37.2 per 100,000 for women. It therefore represents a significant health problem for the general population. The USA incidence per 100,000 and are age-adjusted to the 2000 USA standard population and were 54.43 in 2000 and 45.51 in 2007 (57).

In the West of Scotland the EASR incidence of 56.5 per 100,000 in 2008. The European Age Standardised Mortality Rate (EASR) was 20.6 per 100,000 in 2008 (58).

The 5 year relative survival for all colorectal cancer patient of both sexes in Scotland from 1998-2002 is 54.2% (58).

This compares to a 64.7% 5 year relative survival for all ages, all races and both sexes of patients with colorectal cancer in the USA from 1998 (57).

Figure 3 - Higher incidence of colorectal cancer in Scotland compared with England for males by health authority UK and Ireland 1991-2000 when comparing ratio of directly age-standardised rate in health authority to UK and Ireland average.



*Ratio of directly age-standardised rate in health authority to UK and Ireland average. Taken with permission from chapter 7 of (59).

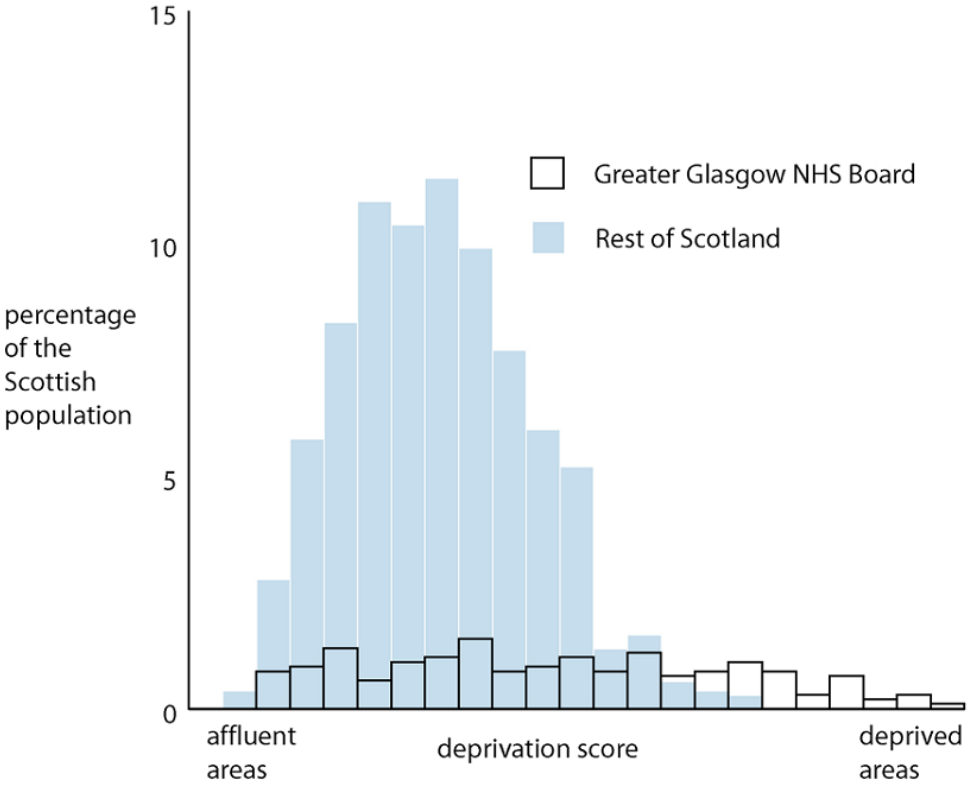
A similar picture exists for females.

There are likely to be a variety of ethnic, genetic and environmental causes for colorectal cancers. The fact that populations moving from one region to another adopt the new areas incidence for colorectal cancer points to an environmental aetiology. Indeed this is the case in around 80% of colorectal cancer patients. Increased intake of fruit, fibre and vegetables are all considered protective in

the risk of developing colorectal cancer. This contrasts with increased red meat intake and increased dietary fat both being implicated in increased risk of colorectal cancer.
Increased physical activity has been found to be protective whereas increased BMI (Body Mass Index) and centripetal obesity are now considered risk factors for developing the disease (60) (61).
Hormones are alternatively thought to have protective or causative roles in colorectal cancer patients.

An important consideration for many public health and large population studies documenting healthcare inequalities in the West of Scotland is socio-economic inequality and its translation into outcomes. Age, sex, geographic residence may be other markers or cofactors for underlying behavioural and genetic determinants of cancer incidence and survival (62-66). The West of Scotland has a larger proportion of deprived areas than the rest of Scotland. Figure four illustrates the distribution of Carstairs scores in Greater Glasgow NHS Board overlaid with the distribution of scores in the rest of Scotland. The distribution of socio-economic deprivation in Scotland is approximately normally distributed with a small right tail of more deprived populations. It is measured using the Scottish Index of Multiple Deprivation (SIMD).

Figure 4 – Distribution of deprivation scores within the Greater Glasgow NHS Board area and the rest of Scotland



Prognostic factors in colorectal cancer patients

As with many cancers, colorectal cancer in Scotland demonstrates an increased incidence with time from 50.2 per 100,000 in 1990 to 54.3 per 100,000 in 2008 EASR (European Age Standardised Rates) (58). At present men are more likely to be diagnosed with colorectal cancer than women (67). EASR 66.1 and 42.6 for men and women respectively in the West of Scotland in 2008 (58).

It is generally held that patients presenting as emergency admissions have poorer survival compared to elective cases. This outcome holds true following adjustment for age, stage, and socioeconomic circumstances (SEC) (68). Despite the introduction in 2000 of UK government rules for patients with suspected malignancy to be seen by a hospital specialist within two weeks of referral there have been challenges to the effectiveness of these guidelines (69) (70). To date there is also no published evidence that reducing the time to first treatment to 60 days reduces overall survival.

Urgency of admission has previously been correlated with increased proportions of postoperative complications. In the first nationwide population based survey

of colorectal cancer treatment McGrath *et al* reported the numbers of patients suffering from postoperative complications in emergency cases and elective cases respectively (71). 69.9% of 1311 patients had no post-operative complications. Surgery-related complications were recorded for 10.8% of patients. There was however, no attempt to assess whether the differences were statistically significant or not between the two groups.

Colorectal cancer incidence is higher and survival poorer in more deprived populations, and as a result overall mortality is higher (72). The poorer survival in patients from more deprived backgrounds was initially ascribed to a more advanced stage at presentation in more deprived patients (73). More recently two large studies have stated that the type of curative operation offered to patients suffering from colorectal cancer can differ according to their socioeconomic status (62)(44). This has not been examined across an entire region, inclusive of all hospital providers.

The incidence of colorectal cancer remains skewed towards a higher incidence in more deprived patients (72). Also across the deprivation categories there is a continuing trend for patients from more deprived backgrounds to exhibit decreased survival when compared with their more affluent counterparts (64,65,74). As a determinant of poor outcome in colorectal cancer patients, deprivation is thought to exert its effect in many ways. These are variously defined as lack of resources, inadequate information and knowledge, substandard living conditions, risk-promoting lifestyle, attitudes and behaviours, and poor nutrition. Many of these aspects of deprivation then contribute to increased incidence of co-morbid conditions such as COPD, diabetes and hypertension.

The pervading stoical West of Scotland culture may augment or diminish the expected negative effects of poor socioeconomic circumstances.

In the West of Scotland it can be argued that an overriding fatalistic or stoical culture exists to some degree. That is to say, there is an ingrained tendency for the majority of the population not to seek or accept cancer screening or care. It may be that given time, education and public health campaigning will result in a change in this attitude.

A number of studies point to differences in long-term outcome for patients with colorectal cancer according to their socioeconomic background. Most recently, Harris and co-workers performed a retrospective analysis of relationships between deprivation and survival in 486 rectal cancer patients (63). They demonstrated that despite a non-significant difference in stage at presentation, those from a deprived background had poorer overall survival compared to their affluent counterparts. Their study was confined to patients diagnosed with rectal cancer in a single hospital.

In the West of Scotland, Hole and colleagues have shown that cancer specific survival is better in more affluent patients even after adjustment for both stage of disease and mode of presentation(65). This was a retrospective study involving 2269 patients undergoing both palliative and curative resection for colorectal cancer. The excess mortality was confined to those patients undergoing apparently curative resection. No distinction was made between colonic and rectal cancers so that it is not possible to say whether the socioeconomic effects on survival were different between anatomical sites.
A study by Byers and co-workers in the USA concluded from their collaborative state registries study of 4422 colorectal cancer patients that patients from areas of low socioeconomic status have more advanced disease at time of presentation for breast and prostate cancers but not colorectal cancer (75). Colorectal cancer patients are liable to receive less aggressive therapy (adjuvant chemotherapy) if they have lower socioeconomic circumstances (SEC). This results in greater all cause mortality for colorectal cancer patients. They also found that low SEC was not a risk factor for mortality across all ages, only those patients aged <65 years. They suggest this may be as a result of medical insurance service provision changing around the age of retirement.
Other groups have studied the influence of deprivation on the postoperative phase of treatment for colorectal cancer. Smith and colleagues performed an analysis of a surgical association database of 7290 colorectal cancer patients, concluding that being more deprived was an independent risk factor for longer postoperative stay and is associated with higher postoperative mortality (64).
One of the principles of an MCN is to provide equitable care throughout the network. Assessing if this is happening in Scottish practice is an aim of this

thesis. The ethos linked to MDT care for colorectal cancer patients would be expected to reduce, if not eliminate, this inequality. This will be examined.

Novel prognostic indicators

As with many other cancers, researchers in the field of colorectal cancer strive to elucidate more accurate methods of stratifying prognosis according to reproducible, objective measures. One topical area of research is inflammation. It is now well recognised that patients with the same stage of disease mount differing local and systemic inflammatory responses to the presence of colorectal cancer (76). Of particular note is the modified Glasgow Prognostic Scale (mGPS). It is now a validated tool for gauging prognosis in curative resection colorectal cancer patients based on serum levels of inflammatory proteins (77). One further validated scoring tool combines four known prognostic indicators to derive a cumulative score for patients with node negative disease. The so called Petersen Index (PI) is not widely employed at present but represents a potential area in which to further tailor specific treatments to patients with the same TNM stage (77,78). The prognostic significance of peritoneal tumour cells has previously been tested in gastric cancer. This has now been demonstrated to be of strong prognostic significance in stage III colorectal cancer patients also (79).

Pathology - related prognostic factors

Pathology plays an important part in diagnosis and prognosis. The pathologist is a key member of the core multidisciplinary team and its approach to colorectal cancer patient care. A recent review by Quirke and Morris discusses the particular facets of the reporting process that are important to the MDT. They also make a clear point that recording data accurately in the national minimum core dataset could lead to improved outcomes for colorectal cancer patients (80).

It is worth taking some time to explore those aspects of the pathological process deemed important to the MDT as well as those features that have evolved to be important prognostic indicators. This will begin with an overview of the current

thinking regarding the pathogenesis of colorectal cancer and followed by a description of the pathological assessment made after resection of a tumour.

Adenoma – carcinoma sequence

The fact that 70% of colorectal cancers develop from adenomatous polyps and that the incidence of adenomas is 30-40% in Western populations is reason enough to justify government funding of a screening service given that a proportion of these adenomas will transform into carcinomas with time (67). Flat adenomas are more difficult to detect; they may have a higher rate of malignant change and can also develop into a more aggressive phenotype but only account for 10% of all polyps. The overall process of transformation from normal gut epithelium to malignant neoplasm is now well understood. A number of key molecular events have now been elucidated. These help to explain the adenoma-carcinoma sequence (81).

Diagnosis

The majority of patients with colon cancer will have the diagnosis confirmed histologically prior to consideration of surgical intervention. In contrast, all cases of rectal cancer require to be confirmed histologically before proceeding to surgical or neoadjuvant therapy (82). Biopsies are normally taken at time of sigmoidoscopy or colonoscopy. A small percentage of patients will have the diagnosis made from a metastatic deposit biopsy. This would be the case in a patient with an undiagnosed primary where biopsies are taken from liver lesions. Confirmation of the diagnosis is usually uncomplicated however confirmation may not be possible when samples are too superficial. In this case dysplasia or adenoma may be confirmed but not frank invasion.

Staging

Accurate staging is essential in formulating a management plan for all colorectal cancer patients. The relationship between pathologist, radiologist and surgeon is therefore necessarily close, as accurate staging is one of the main determinants of subsequent management.

The most common process occurs in three stages. Firstly a preoperative histological diagnosis is arrived at if possible; this comes from biopsy results. Secondly, the pathological staging is confirmed from the resected surgical specimen. Finally there is confirmation where an agreed stage of disease is recorded at a post-operative MDT meeting. This is the stage recorded in the regional MCN dataset.

Pre-Operative radiological staging is undertaken using CT scanning to assess both the anatomical location of the primary lesion and its relationship to adjacent structures. An assessment of distant spread to lungs or liver is also made. In addition MRI is employed for staging or rectal tumours.

Spread

There are generally four ways in which a cancer can spread:

- Directly into adjacent structures
- Via the lymphatic system
- Haematogenous spread
- Transcoelomic spread

There are various staging systems in use for assessing colorectal cancer. They all aim to be able to objectively assess degree of spread via the different routes outlined above thus arriving at an objective measure. This is then used to act as a guide to further management. Modified Dukes' staging for colorectal cancer was previously the accepted and most widely employed staging system in the UK. It is the system used to record stage for the majority of patients in this thesis (80).

Table 1 - Modified Dukes' Classification for staging of colorectal cancers

Stage	Description
A	Growth of primary tumour does not penetrate beyond muscularis propria; no nodal metastases
B	Growth of primary tumour extends beyond muscularis propria; no nodal metastases
C1	Lymph node metastases but apical lymph node free of tumour
C2	Metastases within apical lymph node(s)
D	Distant metastases

The alternative to Dukes' classification is the TNM staging system. It is the favoured method of colorectal staging in most countries outside of Britain and has been developed by the International Union Against Cancer (UICC) in Switzerland over the last 40 years. TNM allows for greater subdivision of patient groups. This is especially true of the T stage. More detailed comparisons can then be made with more equally matched patients in terms of treatment and outcome. There are three basic elements to the classification, namely tumour stage, nodal stage and presence of metastases. A summary can be found on the American Cancer Society website (83).

It is imperative that patients have their disease clinically staged at time of diagnosis as this then ensures correct treatment, thus optimising survival. It also acts as an objective research tool for assessing outcome. If a universally agreed staging system is employed it is far easier to make comparisons between populations in different countries.

The TNM classification has a number of recognised advantages over Dukes' classification. These include better global communication and objectivity and thus improved management of patients (80). In the United Kingdom there has been a gradual move towards the use of the TNM classification. Although it has been recorded on RCPath datasets since 1996, the vast majority of patient stage data in this thesis are recorded using Dukes' stage. This is as a result of the delayed and sporadic adoption of RCPath guidelines by pathologists across the UK (84).

Extramural vascular invasion

Extramural vascular invasion (EVI) is defined as tumour found within blood vessels located outside the muscular wall of the gut. These are almost always veins and are located within the fat surrounding the gut. EVI usually only occurs in T3 or T4 tumours. Courtney *et al* reported that EVI is an adverse prognostic indicator of survival in colorectal cancer patients whereas the presence of this finding was previously thought not to have independent prognostic value (85) (76). Talbot et al (1980) correlated EVI with development of hepatic metastases (86). Since EVI is now considered a variable in the joint national guidelines minimum data set for colorectal cancer histopathology reporting it will be interesting to note whether it holds prognostic significance in our dataset.

Lymph node metastases

There is a strong correlation between number of lymph node metastases and colorectal cancer patient survival (87). In addition, the presence of tumour within the apical node of the resection is consistent with an additional degree of adverse outcome (88). A more recent approach to assessing lymph node harvesting is to calculate the lymph node ratio of total nodes sampled to number of positive nodes. A higher ratio equates to a worse prognosis. This method also helps to overcome some of the inherent problems with simply assessing overall numbers of nodes harvested or nodes positive which can vary according to site of lesion and extent of exposure to preoperative chemotherapy and radiotherapy in colonic and rectal lesions respectively (89). A median of 12 harvested and analysed nodes is now considered important (82).

A variety of novel techniques exist to detect lymph node metastases, including genetic and epigenetic DNA analysis (90). They are not yet used routinely either intraoperatively or in NHS laboratories but could improve detection rates in future if validated.

Local Recurrence

Local recurrence (LR) is defined either as regrowth of tumour in or around the tumour bed after previous removal of all macroscopically visible tumour, or if tumour returns after inadequate resection. This includes regrowth within the suture or staple line of an anastomosis, the adjacent mesocolon or adjacent lymph nodes (88).

The significance of local recurrence is that it dramatically reduces survival. If a patient is found to have local recurrence, they have a 90% chance of death as a result.
A 1996 MRC trial reported a 33% local recurrence rate at five years in patients with Dukes' B and C rectal lesions (91). This is in stark contrast to the 6% local recurrence rate quoted by Heald et al (1998) in their single centre results from 19 years' experience of the total mesorectal excision (TME) for rectal cancer (92).

Circumferential resection margin

The involvement of the circumferential resection margin (CRM) with tumour is a further risk factor for local recurrence. Quirke demonstrated in his classic 1986 work that the rate of local recurrence is directly related to the positivity of the CRM (93). It therefore aids in the decision as to whether or not a patient with rectal cancer is a candidate for postoperative radiotherapy. It is defined as the area of a rectal tumour not covered by a serosal surface, a non-peritonealised surgical resection margin (84). In contrast, involvement of a serosal surface by tumour is a risk factor for intraperitoneal spread of tumour. This influences staging and subsequent treatment. Current RCPath guidelines state a margin of <1 mm is regarded as an involved margin. It is not possible to say that a margin of >1mm ensures a disease free margin but it is currently recorded as a clear margin in the dataset (84).

Resection margins and local recurrence tend to be of more relevance to rectal resections as it is often harder to obtain sufficient clearance when operating in

the cramped anatomy of the pelvis compared to colonic resections in the abdominal cavity.

Clinical management and survival

It is now common to consider the stages in a patient's progression from diagnosis through treatment to recovery as part of a continuous pathway or journey. With this in mind, a sensible approach is to break down the pathway and examine each individual step in isolation. This can help to pinpoint distinct areas in the pathway that may be deficient.
As with any medical problem, the process begins with the patient seeking medical advice with a view to reaching a diagnosis.

Diagnosis, screening and primary care referral

The aim of screening is to enhance the pick-up rate of patients with colorectal cancer as a whole. It also aims to diagnose patients at an earlier stage of their disease. The Scottish bowel cancer screening programme will be fully implemented by the end of 2010. It is estimated that 160 lives per year will be saved as a result. Two published papers from different phases of a bowel screening pilot study have postulated that following introduction of screening, mortality rates from colorectal cancer could start to show a stronger socio-economic gradient than currently exists (94,95). This introduces the important point of lead time bias. Lead-time bias is the perceived improvement in survival for patients due to earlier diagnosis from screening, since screening adds a variable amount of apparent survival to all people who are diagnosed in the asymptomatic state, compared to symptomatic patients (96). A larger socio-economic gradient in diagnosis following screening goes against the ethos of both the NHS and Multidisciplinary team (MDT) care and will be discussed. Since screening is currently being rolled out across Scotland this thesis will offer a potential benchmark for future studies.
In relation to the West of Scotland there is also a need to scrutinise data *prior* to the inception of the National Colorectal screening programme. This will allow for future assessment of its effectiveness. From 2009 it is estimated that mortality

from bowel cancer will decrease by 16% thus saving approximately 150 lives per year (97).

Results have also been published from another European pilot study that justifies its expansion throughout the country. They demonstrated that 38693 (49·6%) of 78083 patients had an FOBT, with 2392 (6·2%) having a positive result. Positive predictive values were 4·0% for cancer, 28·1% for advanced adenoma and 36·6% for any adenoma (97).

Simultaneous work in developing countries has concluded that despite the clear benefits of screening for colorectal cancer, the cost of implementation has to be taken into account. In India and some African countries where there is already a less developed healthcare system, the creation of a screening service is far too expensive to implement. It is argued that the portion of the health care budget that would be devoted to screening could have quicker and further reaching effects upon a wider population if spent in other areas.

It has recently been concluded by Sankaranarayanan *et al* (2009) that screening is not cost effective and cannot be justified for most developing countries (98).

Primary care referral is an area of interest to patients and politicians alike. Again, waiting times issues are outwith the scope of this thesis. The process of referral from a GP to hospital remains a dynamic one. This is due both to the changing nature of the NHS and to the perceived speed at which patients can be assessed if referred along different pathways. Colorectal cancer patients can now be referred by genetic clinics, screening services; GP to clinic, GP to A&E, and an increasing proportion are being referred by NHS 24 to A&E. This last route has not yet, been assessed with specific regard to colorectal cancer patients.

Following diagnosis, it is imperative that patients undergo a thorough and uniform preoperative assessment. This includes staging of disease, general physical examination, measurement of routine biochemical and haematological parameters, and informed consent for intervention. Recently published work has confirmed that substantial variability exists in the preoperative evaluation of patients with colorectal cancer (99).

Patient selection

Recent surgical and anaesthetic techniques have improved the number of adequate oncological resections in the elderly. Patients must be deemed fit for surgery. Previously this may have been a single decision by the operating surgeon based on his previous experience. It would take into account their age, stage and comorbidity. Now, however, patients where there is a potential operative risk tend to be selected more on an aggregate of objective measures. These include cardiopulmonary tests (such as echocardiogram) and pulmonary function tests.

General preoperative considerations

Staging by CT and MRI is one of the most important preoperative considerations. It has already been discussed above in relation to all colorectal lesions but for rectal lesions ultrasound can be useful. Trans Rectal Ultrasound (TRUS) or Endoanal Ultrasound (EUS) is the most common technique for assessing the extent of invasion of the rectal wall. It is ideal for staging smaller superficial tumours (T stages T0, T1, T2) being considered for local resection and non-radical surgery. It is only good at estimating the lower so is helpful in selecting patients who may be suitable for local, endoanal or transanal excision. It is now considered accurate in staging gastro-intestinal tract tumours to allow an ultrasound staging system analogous to the pathological TNM system with a prefix ‘u’ denoting that this is an ultrasound rather than a pathological staging (100). The main determinant of LR is an involved CRM. EUS is poor at assessment of the CRM due to the inability to delineate the mesorectal fascia (101). MRI remains the investigation of choice for assessment of CRM. Tissue reaction in larger more locally invasive tumours makes EUS less reliable. It is also less reliable for assessing nodal metastases due to its reduced specificity at detecting the differences between benign nodes and those containing metastatic deposits.

Computed Tomography Staging

Computed Tomography (CT) scanning is inferior to both Magnetic Resonance Imaging (MRI) and TRUS in relation to accuracy in local staging of rectal carcinoma. This is due to its inability to adequately differentiate between the soft tissue planes in the rectal region. CT scanning remains of prime importance for global assessment of distant metastases in colorectal cancer patients. It remains the gold standard for assessment of hepatic and pulmonary metastatic deposits.

MRI staging

The current surgical strategy for all locally advanced rectal carcinomas is to attempt down staging prior to surgery. This treatment strategy is based on the relationship of the tumour to the mesorectal fascia, the optimal surgical circumferential resection margin that can be achieved by total mesorectal excision. MRI has been recognised as being useful in the ability to identify the CRM and accurately predict involved, threatened and clear margins and thus determine the MDT treatment decision. All patients who appear to have a threatened margin (<1mm) should be considered for preoperative neoadjuvant treatment in the form of short or long course chemoradiotherapy, whereas patients with clear margins can be treated by optimal surgery alone (101).

FDG PET Scanning

F-fluorodeoxyglucose (FDG) Positron emission tomography (PET) has been used for detection, staging and surveillance of disease in colorectal cancer patients and is considered a modality with emerging applications. FDG is a biological tracer that allows the evaluation of glucose metabolism. Elevated uptake of FDG has been shown in several types of malignant primary tumours thus highlighting tumour activity. FDG scanning also has the potential for demonstrating tumour metabolic activity before structural changes can be shown by CT imaging. In particular, FDG PET may be potentially useful for distinguishing local recurrences from postoperative scarring, for detecting hepatic and extra-hepatic metastases prior to any surgery or chemo-radiotherapy and for assessing

recurrent colorectal cancer when there are no indicators other than rising carcionoembryonic (CEA) levels. (102)
A systematic review by Patel et al (2011) concluded that combination PET/CT has a higher accuracy for detection of extra-hepatic and hepatic metastases than CT alone. These results were based on a small number of studies though (103).

The limitations of PET scanning include poor anatomic delineation, the fact that tumours <5mm cannot be detected, and high false negative results in patients who have had chemotherapy <1 month before the scan (104).
Normal physiologic and metabolic activity in the gastrointestinal tract can also be problematic and careful correlation with fused CT images is now recommended to improve specificity.
There is insufficient data at present to justify the routine use of FDG-PET in detecting recurrence in patients with colorectal cancer, mainly due to the lack of large randomised trials. In areas such as post-operative surveillance of colorectal carcinoma where the surgical treatment options and chemotherapy strategies are being constantly redefined, PET/CT may find additional future applications, particularly with the development of new, more specific radiotracers.

Antibiotic and DVT prophylaxis

Both antibiotic and Deep Venous Thrombosis (DVT) prophylaxis are considered standard measures in the pre-operative preparation of any colorectal cancer patient for surgery. Major abdominal surgery on a mitotic lesion is deemed an infection risk. SIGN 104 states that antibiotic prophylaxis is highly recommended for colorectal surgery, quoting an odds ratio of 0.24 and Number Needed to Treat (NNT) of 4 at a 1+ level of evidence (105).
Cancer is also a recognised risk factor for DVT. Both have been adopted as surrogate markers for quality of care by NHSQIS (34).

Bowel Preparation

Traditionally, preparation of the bowel for all elective and some emergency surgery was considered mandatory. Use of Mechanical Bowel Preparation (MBP) prior to large bowel surgery has been recommended since 1945. This dogma has been challenged in recent years. It is now considered normal practice in Europe to electively resect a colonic lesion without the requirement of bowel preparation (106-109). North American surgeons however, persist with preparation with MBP prior to surgery. Bowel preparation is still generally administered for resections of rectal tumours worldwide. It has been used with the aim of reducing postoperative complications. Early observational studies and subsequent decades of clinical experience indicated that preoperative bowel lumen cleansing was associated with decreased patient morbidity and mortality (110). It was hypothesised that bowel preparation acted by both reducing faecal bulk - and therefore mechanical stress on anastomoses – and by reducing colonic bacterial load (111) (112). However, several recent systematic reviews and meta-analyses of randomised controlled trials of mechanical bowel preparation have been carried out and all consistently found no convincing evidence for its short term benefits and some evidence for lower postoperative cardiac events among non-MBP patients (111,113-115) (116) (117).

A recent Cochrane review of 14 randomised controlled trials of mechanical bowel preparation concluded that there was no evidence it improved either morbidity or post-operative mortality (116). However, after the first update of the Cochrane review, the incidence of anastomotic leakage was observed to be significantly higher among patients treated with mechanical bowel preparation and a trend toward poorer short term outcomes remains in the latest update (111)(116). The primary outcome for the Cochrane review was anastomotic leakage and the majority of included studies followed patients for the post-operative period (30 days after surgery) only, with the longest follow-up being about two months (118).

There is evidence that some operative complications predict long-term outcomes, specifically survival, among colorectal cancer patients. Anastomotic leak is an independent prognostic indicator of poorer cancer-specific survival in

patients having had potentially curative resections and remains significant after exclusion of deaths within the postoperative period (119) (120)(121).

Stoma Nurse

It is hard to assess the individual influence of a stoma nurse's input into outcomes but there is no doubt that their role is important in the psychological preparation and well being of the patient in the perioperative period. A stoma nurse is recognised as integral to the MDT (34). They are involved in the education of the patient regarding stomas and potential complications. This was concluded in a randomised trial comparing 42 patients seen preoperatively in the community by a stoma nurse versus those seen postoperatively in hospital. Statistically significant results were obtained in favour of the intervention group for time to stoma proficiency, hospital stay and unplanned stoma-related community interventions per patient. No adverse effects of the intervention were noted. The average cost saving per patient was £1,119 for the study group compared with the control group (122).

In the postoperative period stoma nurses ensure that either the patient or their main carer is able to cope with changing the stoma bag. They also clarify situations where the patient or carer should seek further help.

Intent of operation

It is the aim of any MCN to ensure a common approach to these decisions and would therefore be interesting to study these in a regional, i.e. MCN, context. Prior to the inception of MCN (Managed Clinical Network) care for colorectal cancer patients the decision as to whether a resection was deemed curative or palliative was based on the surgeon's impression at the time of surgery.

Currently, more advanced preoperative assessment modalities in conjunction with the MDT process mean that the decision regarding therapeutic intent is more informed. Decisions regarding downgrading of tumours in order that they may become resectable now require consideration. This is particularly relevant for preoperative radiotherapy in rectal cancer.

Surgery in the management of colorectal cancer

Patients with colorectal cancer undergo either a laparotomy or a laparoscopic procedure to resect the tumour. In cases of advanced disease with involvement of adjacent organs an en bloc resection may take place. This employs the principles of total tumour clearance following known routes of lymphatic and haematogenous spread of tumours. The likelihood of lymph node involvement increases with depth of tumour invasion so the lymphovascular pedicle draining the tumour site is resected. If the tumour has spread directly into neighbouring organs they are either completely removed (e.g. spleen) or a wide margin of clearance is attempted. En bloc resection, coupled with the no-touch technique are methods first described by Turnbull *et al* in 1967. The no-touch technique minimises tumour shedding cells into the circulation as it is manipulated (123). It is now possible to detect these cells in draining vessels or intra-peritoneally using Polymerase Chain Reaction (PCR) technology. Both techniques remain strictly adhered to in the operating theatre. In fact, size of en bloc resection has been used as a surrogate marker of specialisation in colorectal surgery.

Resection of colonic tumours and high rectal or rectosigmoid tumours is normally completed with either a hand sewn or stapled anastomosis. With the advent of reliable, efficient and ergonomically designed stapling devices it is now possible to resect tumours and staple anastomoses deep in the pelvis. Surgery in the rectal area is regarded as requiring more skill as there is the potential for anal sphincter involvement and the related complication of rendering the patient incontinent. Operating deeper down in the pelvis is also technically more demanding as a result of lack of space. The Department of Health has published guidance suggesting that the sphincter should be retained in as many cases as possible. As a result the rates of abdomino-perineal excision (APE) have gradually been dropping over the years. Historically, 50% of patients with rectal cancer would normally require an APE (124). This drop has been mirrored by a similar rise in the number of rectal cancers being resected via the abdomen - an anterior resection (AR). Low or even ultra-low anterior resections are now performed routinely by colorectal surgeons for tumours close to the anal margin to allow sphincter preservation. This results in a higher objective quality of life for patients postoperatively (125).

Surgery is the mainstay of curative treatment for Dukes' A, B and C patients. This ranges from endoscopic polypectomy to mulitmodal treatment of advanced and disseminated disease. As a single treatment modality this is true for all Dukes' stage A and most stage B disease.

With regard to rectal tumours the popularisation and dissemination of the total mesorectal excision (TME) has standardised treatment for the vast majority this group of patients (92).

Heald recognised that the midline hindgut (rectum) and its mesorectum were embryologically derived together as a single unit. TME involves *en bloc* resection of the rectum and mesorectal tissue to the level of the levator ani muscles through sharp dissection through the avascular plane between the mesorectum and surrounding tissues (126).

Nerve preserving rectal resection

Preservation of the autonomic plexuses in close relation to the rectum (hypogastric, inferior hypogastric and pelvic splanchnic) became possible following initiation of novel resection techniques by the Japanese surgeons Hojo and Moriya (127). These techniques have been incorporated into the TME programme to allow lower rates of urogential nerve dysfunction.

The principles of embryological gut development have now been applied to resections of colonic tumours. A German group, describing their technique as the Complete Mesocolic Excision (CME) report increased five year survival. The technique has now been replicated in another centre and verified in a third (128).

Patients lower on the socio-economic scale have been found to be more likely to undergo APE than AR for cancer (43,44). This goes against the high quality of cancer care for all ethos proposed by MDTs and the government cited in the Cancer Plan 2000 (129). Similarly, another finding reported by Morris *et al* is that throughout England males were significantly more likely to receive an APE than

females. This finding was mirrored by the significant result that women were more likely to receive an anterior resection than men (44). This group found no significant differences between type of operation and age or stage at presentation. Stage at presentation was a statistically significant factor for patients admitted as emergencies only. These latter patients were also more likely than average to undergo a Hartman's procedure or an anterior resection.

There is evidence that rates of circumferential resection margin positivity vary between surgeons. So far, this has been shown to be able to predict outcome in rectal cancer patients (130).

Since the first recorded colonic resection in the early 1990s, laparoscopic colorectal surgery has become well established and validated as a suitable alternative to open colonic resection. It offers advantages in terms of reduced hospital stay, reduced postoperative pain, shorter time to return of bowel function, and improved abdominal aesthetics with regards to scar size. Its disadvantages include the steep learning curve to attain proficiency and the need to be willing and able to convert to an open procedure.

In its infancy, there was concern that laparoscopic resections lead to port site metastases and an increased frequency of intraperitoneal seeding of tumour. With the evolution of this technique various groups have now demonstrated no significant differences between open and laparoscopic methods (131). Other concerns regarding adequacy of resection margins, yield of lymph nodes and length of resected bowel with laparoscopic resections have all been demonstrated to be unfounded in randomised controlled trials (132,133).

Current guidelines suggest that any patient requiring removal of a colorectal neoplasm can be offered the option of an open or laparoscopic resection (82).

Current role of chemotherapy

Standardised regimes of neoadjuvant and adjuvant chemotherapy according to stage of disease continue to evolve. They have been adjuncts to surgery for over

25 years. Research efforts continue to be directed towards compounds with low side effect profiles that remain cytotoxic, antiproliferative and orally administered.

Capecitabine is one of the newer oral chemotherapeutic agents to have received a lot of trial attention in the last few years. Its effects have been studied in various phase I and II trials (134).
Current recommendations in Scotland date from 2003. They recommend that adjuvant chemotherapy should be considered for all Dukes' C patients unless contraindicated. The favoured regimen is bolus fluorouracil and low dose folinic acid (FUFA). This is given over five days, every month for six months (135). More recent evidence published in Col Dis indicated that following the introduction of MDT in one district general hospital, there was an improvement in the survival of patients due to optimal oncological input into their management plan (25).

Current role of radiotherapy

As rectal tumours tend to be more fixed in their location they are amenable to treatment with ionising radiation. The first successful radiotherapy for rectal cancer was administered in 1914 (126).

Radiotherapy regimes continue to evolve. It can be administered in a number of ways; preoperatively or postoperatively, over a short or long period, and in high or low doses.

The aim of preoperative radiotherapy is to downstage the tumour. This may then facilitate clear resection margins thus reducing the likelihood of local recurrence in future. These benefits were first demonstrated in the Swedish rectal cancer trial in 1997 however they did not translate into long-term survival advantages (136).

Adjuvant radiotherapy is now a standard part of the management bundle for selected rectal cancers. These groups include all stage II and stage III patients in North America. In some European countries a short 1-week course of radiation is employed in all cases of rectal cancer (137).

Two broad categories of radiotherapy treatment are currently favoured in the UK. Firstly, a dose of 45Gy in 25 fractions over five weeks is given to fixed rectal lesions. This is in an attempt to render lesions resectable. The second commonly administered course is 25Gy in five Gray fractions given the week before surgery. This is given to patients with resectable lesions with the intention of reducing local recurrence. The evidence base for these regimens comes from the Stockholm 2 trial and has been adapted by SIGN for the current Scottish Recommendations (136).

Evidence continues to accumulate towards further sub-selection of patients for radiotherapy, administered only to those patients with threatened or involved mesorectal margins. This theoretically decreases the chance of the surgeon breaching the tumour margin. It may also result in fewer complications from patients receiving radiotherapy unnecessarily (138).

Management of advanced disease

Around 33% of colorectal cancer patients will develop synchronous or metachronous hepatic metastases (139). One area of treatment for advanced stage colorectal cancer disease that has seen recent advances is resection for hepatic and lung metastases. Hepatic metastases occur before other distant metastases because the venous flow from the bowel passes to the liver via the portal system before entering the systemic circulation. Seeding therefore tends to occur here first. Operations that were previously deemed palliative are now potentially curative. As the resolution of computed tomography and ultrasound scanners improves so can both the selection of patients for resection of their metastases and their outcomes. Intraoperative ultrasound scanning of the liver is another technique employed to detect occult metastases at operation. This may result in the altering or abandoning of the resection if occult metastases are found to involve other lobes. There is now a tendency to assess patients for potential resectability of their metastases in terms of resection margins and having two contiguous segments of liver disease-free, rather than overall tumour size (140).

Radiofrequency ablation (RFA) is a further, adjunctive tool employed by surgeons. It uses high frequency alternating current to direct high temperature to localised areas. Coagulative necrosis and tissue dessication follows. RFA is reserved for regions of hepatic tissue which are not amenable to resection. This is usually due to proximity of the resection margin to vital blood vessels. RFA is used either as a single treatment or in conjunction with resection.

In patients with responsive tumours, chemotherapy is known to cause tumour shrinkage. Its use can therefore convert a patient with an unresectable liver lesion into a potentially resectable lesion (140).

Metastases to the lung are the second most common following the liver. As no satisfactory regimen of chemotherapy exists at present, surgery is the only chance for a potentially curative result. Again, high resolution CT imaging has aided in the earlier detection of previously occult pulmonary metastases. This has resulted in a reported five year survival rate of 24% to 63% for lung metastatectomy.

Lizasa and coworkers have shown that the two most important prognostic indicators in advanced disease are a high Carcinomatous Embryonic Antigen (CEA) and number of metastases (141).

The evaluation of long-term outcomes in this unfortunate group of colorectal cancer patients has now been published (142). Encouraging improvements in outcome following treatment in the MDT setting are also now coming to light in high impact journals. Lordan and colleagues have also shown in their 10-year study of outcome following hepatic resection for colorectal liver metastases that an MDT with a liver surgeon can positively and significantly influence the outcome of patients referred with hepatic metastases from colorectal cancer (56). As this is a specialist hepatobiliary unit the number of patients is comparatively small (n=331) but nonetheless offers an interesting insight into differences in survival benefit when a specialist liver surgeon is involved in the referral of patients from MDT for resection of tumour.

Post operative care and ERAS

Traditional barriers to rapid postoperative recovery following colorectal surgery are pain, paralytic ileus, and other organ dysfunction.

A modern multimodal approach involving a pain team, physiotherapists, occupational therapy and dieticians has generated the global term enhanced recovery. This results in a less protracted hospital stay for an increasing number of colorectal cancer patients. Enhanced Recovery After Surgery (ERAS) is the multidisciplinary and multimodal approach to enable rapid recovery and improved outcome for surgical patients by attenuating the stress response to surgery.

The most recent meta analysis of six randomised controlled trials with a total of 452 patients by Varadhan (2010) used outcome measures of length of hospital stay, complication rates, readmission rates and mortality in 452 patients. (143) Although the number of individual ERAS elements ranged from 4 to 12, with a mean of 9 they concluded that ERAS pathways appear to reduce the length of stay and complication rates after major elective open colorectal surgery compared to conventional perioperative care. There was no statistically significant difference in readmission and mortality rates between the two groups.

Palliation

A recent publication by SIGN outlines the current palliative management strategies for pain control in colorectal cancer patients deemed not suitable for resection of their tumour(s) (144).
At a recent meeting of the Scottish Managed Clinical Networks for Colorectal cancer it was indicated that there still remains a degree of heterogeneity in the representation of palliative care nurses or physicians at MDT meetings. This has implications for both blocking of beds in hospital and adhering to patients wishes when faced with a diagnosis of unresectable tumour and end of life care. A recently published abstract demonstrated that a community based palliative

care register can positively and significantly influence this. However, the presence of a palliative care representative at the MDT would be required for this to happen (145).

Follow-up and trials

Follow-up remains a controversial area. The reasons for following patients after treatment for colorectal cancer are early detection of recurrence for salvage surgery or palliative treatment, psychological support, the detection of metachronous tumour and research or quality assurance of treatment. What remains unanswered is duration and intensity of follow-up. Of these the most important is how long follow-up is needed. It appears to be the case that more intensive may be better than less intensive follow-up. Jeffrey et al (2007) concluded from eight studies in their Cochrane review that an overall survival benefit at five years exists for patients
undergoing more intensive follow up where the OR was 0.73 (95% CI 0.59 to 0.91). This benefit could be explained by the mortality benefit for performing more tests versus fewer tests (OR 0.64 (95% CI 0.49 to 0.85)), and liver imaging versus no liver imaging (OR 0.64 (95% CI 0.49 to 0.85)), or because there were significantly more curative surgical procedures attempted in the intensively followed arm (OR 2.41(95% CI 1.63 to 3.54)) There was significant heterogeneity between the studies though (146).

Renehan and coworkers (2004) have shown that follow-up is cost effective (147). What is not known is what exactly should be done, when and for how long. Results of three large ongoing randomized prospective trials are eagerly awaited. These are the Italian GILDA trial, the UK FACS trial, and the Scandinavian-based COLFOL trial (148). Furthermore, knowledge of long-term side-effects of adjuvant treatment is limited so longer follow-up should help to identify any that have not come to light thus far.

Patients entered into clinical trials have been shown to produce better outcomes than those not entered into trials (149). It is logical then that MDTs should endeavour to attain as high a trial inclusion rate as possible.

Schofield and Steele state that “it is reasonable to offer liver imaging to asymptomatic patients under the age of 70 in order to detect operable liver metastases once during the first two years after resection. (Recommendation Grade:A) Although there is no evidence that colonoscopic follow up improves survival, it does produce a yield of treatable tumours. It is recommended that a “clean” colon is examined by colonoscopy five years after surgery and thereafter at five yearly intervals up to the age of 70. (Recommendation Grade:B)” (150)

Future direction

Combined genetic and epigenetic analysis of sporadic colon cancer suggests that it can no longer be viewed as a single disease entity. There are at least three different subsets with distinct clinico-pathologic features, with important implications for prevention, screening, and therapy (151).

The MCN dataset

The analyses are based initially on a large clinical audit dataset as part of the MCN for colorectal cancer. These data are summarised then scrutinised in more detail in order to address the aims of the thesis and answer the research questions. This population includes patients from the 30 different hospitals in the West of Scotland region. 140 consultants were identified as being responsible for the patients in the MCN. Both hospital and consultant details were anonymised to ensure lack of bias when analysing results.

The general process of audit data capture is as follows:
Each local unit records data relating to their own direct input to the treatment and care of colorectal cancer patients.These data are recorded on separate, standardised MCN proformas, namely clinical, pathological and chemotherapeutic. This information is then added, at a local level, to an existing database of all colorectal cancer patients. See copies of these in the appendix.

Periodically, the MCN staff request a copy of these data in order that performance against the recognised QIS Standards of care can be measured (34).

The practicalities of audit data collection vary across the West of Scotland region. In some units the main clinical/surgical forms are filled in by the surgeon, the pathology form by the pathologist and the chemotherapy form filled in by the oncologist. Clinical audit staff support this process by ensuring that the various component audit forms are completed. They then attempt to fill-in the blanks from case notes or by referring back to the relevant clinician to attempt a higher rate of completeness. The data are then entered on to the local database. Previously the database was a Microsoft Access application developed by the MCN and installed locally within each unit. This was superseded by a web-based application whereby all data from the region (and potentially the entire nation) are recorded on a centralised MCN database directly by the staff in each unit. Audit staff at the MCN headquarters work to support the MDTs and increasingly are present at MDT review meetings - this is unlikely to be the point at which the audit process is initiated. It is more likely an opportunity for audit staff to 'fill in the blanks'. Nursing staff have their own component data set to complete but are not responsible for completion of other component parts e.g. clinical, surgical, etc

A number of patients may, for various reasons, evade enrolment into the MCN despite a diagnosis of colorectal cancer. These patients may have migrated out of the region, been diagnosed in a private hospital, or be death certificate only (DCO) patients.

The centrally held Scottish Cancer Registry dataset

The Scottish record linkage system was created in the late 1950s. Prior to this it was always recognised that the nation held a vast number of potentially useful computer records for each member of the population (152). These records had never been collated for research or administrative purposes. There were however multiple records for each person (153).

The increase in computational power allowed for a permanent, retrospective and prospective dataset to be created that could potentially link all records for each resident in Scotland. This would then help serve the requirements of larger epidemiological research studies.

There now exist numerous sets of Scottish Morbidity Record (SMR) data that span the entire spectrum of healthcare specialities. Those of relevance to this piece of work are SMR1 and SMR6. SMR1 records pertain to all hospital discharge records for non-psychiatric and non-gynaecological incidences whereas SMR6 records are incidences of cancer.

When linking any two records the crux lies in identifying that both relate to the same individual. To that end there are a set of five core items of identification used during the initial matching process; surname, first initial, year, month, and day of birth. Each of these core items carries a discrepancy rate of 3% for pairing records. The implication therein is that 15% of true links could be missed.

To allow for this probability matching is employed. A computer algorithm calculates a score that is proportional to the likelihood of two different records belonging to the same person. Records are then deemed to either match or not match based on the score. To further facilitate the matching process all surnames have a common phonetic algorithm (soundex) applied to avoid the most commonly confused sets of letters causing needless mismatches. Current computational power limitations and the sheer number of records involved means that comparing each individual record with each other individual record remains impossible. To that end records are checked in blocks. Linkage is then carried out in two passes. This results in less than 0.5% of true links being missed (154).

Quality of care

It is important to consider exactly what is meant by quality and how it can be measured in the context of MDT care. Maxwell, in his seminal 1984 BMJ paper suggested six dimensions to be borne in mind when assessing quality in healthcare. These are access to services, relevance to need, effectiveness for patients, equity in service provision, social acceptability, and efficiency and economy (155).

Lohr proposed the following definition in 1991: “Quality of care is the degree to which health services for individuals and populations increase the likelihood of

desired health outcomes and are consistent with current professional knowledge" (156)

Access to care

If access to care is compromised or biased towards particular groups of patients based on either their location or socioeconomic circumstances this can potentially affect patient outcome. The underlying structure of the healthcare system is therefore relevant. The Government and their influence is also relevant as they can dictate changes that ultimately affect quality of care. Finally, both physician and patient characteristics are known to affect access to care. A general practitioner facilitates appropriate access for patients from primary to secondary and tertiary care. Then in secondary care, the consultant screens referrals in order to prioritise their access to services.
Patients can affect their own access to care by leading chaotic lifestyles. This often leads to delays in attendance at hospital, delays in treatment, then compliance issues with treatment.

Processes of care

Screening and diagnosis are two processes of care known to affect quality. Full discussion of these topics falls outwith the remit of this thesis however potential effects of screening are discussed in chapter 8.

Treatments are a further important process of care. Whether it be single modality or a combination of chemotherapy, surgery, or radiotherapy, treatment is a large determinant of quality. Supportive care and follow-up are also processes of care where debate continues as to what represents best quality within a cost-effective environment. Finally, end of life care is a process that can be deemed as a contributory factor to overall quality in colorectal cancer patients.

Outcomes of care

Morbidity, mortality and cost of care are all objective measures and as such are used frequently as proxy measures of quality in colorectal cancer patients. Mortality can be measured in terms of both postoperative death and long-term mortality. Postoperative deaths are generally those occurring within thirty days of surgery and are usually considered as being deaths attributable to surgery rather than the underlying disease process.

Morbidity is harder to measure as there is no agreed or objective measure for a patient's degree of morbidity. If a patient's clinical status and/ or quality of life are improved by the process of care then they have had an improvement in their morbidity. Also, by performing an operation on a cancer the patient is benefitting by removing the potential for their cancer to lead to increased morbidity in future.

Cost is widely employed as an outcome measure, especially in the NHS. Patient length of stay and number of readmissions in a set time period are both used as measures of cost to the healthcare system and as outcomes of care and hence quality of care. Number of readmissions has also been employed as a proxy measure for comorbidity in some studies.

Measuring quality of care

There are both subjective and objective measures of quality. Objectively we can make an assessment of outcomes. These are primary or secondary and can be applied to all cancers. Primary outcome measures are recurrence and death. These are often thought of as being insensitive and somewhat impractical as there is a long time delay before meaningful information can be captured and a change in the system effected.

Quality can also be measured in the context of care processes. These directly affect patients so can be measured more quickly by assessing quantity of patients receiving given services such as adjuvant chemotherapy, rectal sparing surgery, or CT colonography. These are secondary measures.

There are also disease specific measures. These tend to address screening or therapy issues relating to a single disease. This contrasts to other aspects of care that transcend the disease barriers for example palliative care and pain management along with services offering care in the community.

Quality measures are by nature dynamic. They should reflect the current clinical climate based on best clinical evidence. They should therefore be revised over time. This thesis looks at data before the influence of screening will affect survival thus demonstrating the need to perform an analysis now and later following the impact of screening.

Measurements of quality can be assessed in relation to the extent to which guidelines are followed. Ideally guidelines should be evidence-based but the nature of some therapies for colorectal cancer is such that many chemotherapeutic agents are on trial. To that end, it is often expert committee opinion that leads to guideline formation in colorectal cancer care. Current attempts to measure quality of care in this country are limited to audit of adherence to clinical standards. This thesis will add to these findings as well as addressing other useful measures of quality pertaining directly to colorectal cancer care.

Stages in patient care can be identified where decisions to follow a certain line of treatment are made. If concordance with guidelines can be measured at each stage where a guideline is available then there is a basis for comparison between different Health Boards, hospitals or MDTs.

Evaluating quality in any study of healthcare generally requires four prerequisite elements:

- Identification of patients with the disease in question
- Reliable sources of data
- Data collection strategies
- Quality of care measures

The methods used to ensure all four of these prerequisites are attained will be outlined in the method chapter.

1.3 Surgeon Caseload, hospital volume and Sub specialisation

The past decade has generated a myriad of publications reporting on the relationships between surgeon caseload, hospital volume, subspecialisation, their interrelationships, and putative influence upon outcomes for patients requiring operations for cancer. It is now generally held that various factors relating to volume and specialisation can be positively associated with improved outcome for surgical patients. These include a higher surgeon caseload, a higher hospital volume, and surgeon subspecialisation (157). These influences have been reported on for a number of surgically resectable cancers including pancreatic cancer, breast cancer and colorectal cancer.
With reference to colorectal cancer a number of groups have confirmed a positive relationship between hospital volume and patient outcome (158) (159). Much less attention has been given to the effect of surgeon case volume, and to survival and long-term mortality outcomes although some studies confirm a positive relationship between surgeon caseload and improved outcome (16,52,160). The common adage underlying these findings is that practice makes perfect – more cases per surgeon in a hospital dealing with higher volume produces better outcomes (161,162).

Debate continues in three main areas though. Firstly, what threshold should be considered standard for distinguishing a low volume surgeon from a high volume surgeon? Arbitrary values for this range from seven to 25 cases per year (44,163). Some groups have also measured three levels of volume reporting outcomes in terms of low, medium, and high volume surgeons (164).
Secondly, when should a hospital be designated as a high volume hospital? (157).
Finally, how should subspecialisation be defined? This can vary from a surgeon declaring a specialist interest or being a member of a Society of Coloproctologists to a surgeon being declared specialist by a group of his peers (162).

The most recent systematic review and meta-analysis relating to gastrointestinal cancers was an objective review of the reported associations between hospital volume, surgeon caseload and mortality. It involved more than one million patients with a range of cancers of the GI tract. Of the 135 identified and analysed studies, only 42 pertained to colorectal cancer patients. The authors concluded that most studies addressed the issue of hospital volume as opposed to surgeon caseload. They found a significant volume effect was evident for the majority of gastrointestinal cancers; with each doubling of hospital case volume, the odds of perioperative death decreased by 0.1 to 0.23. They calculated that between 10 and 50 patients per year, needed to be moved from a "low-volume" hospital to a "high-volume" hospital to prevent an additional volume-associated perioperative death. This was dependent upon cancer type. They also called into question the validity of hospital surgical case volume as a reliable proxy marker for care quality as roughly 33% of all studies failed to demonstrate a significant hospital volume effect on mortality (165).

Also of note is the 2010 publication by Borowski and colleagues. They have added to the UK evidence base by publishing outcomes on hospital volume and surgeon caseload on short-term outcomes and five year survival from a large, population-based data set of patients with colorectal cancer. They concluded that medium and high volume surgeons were associated with significantly better operative mortality (odds ratio (OR) 0·74, P = 0·010 and OR 0·66, P = 0·002 respectively) and survival (hazard ratio (HR) 0·88, P = 0·003 and HR 0·93, P = 0·090 respectively) than low-volume surgeons. They found that rectal cancer survival was significantly better in high-volume versus low-volume hospitals (HR 0·85, P = 0·036), with no difference between medium- and low-volume hospitals (HR 0·96, P = 0·505). The benefit of this study was that it addressed both surgeon caseload and hospital volume however volume was split into three groups as opposed to two. They also highlighted that the volume-outcome relationship is not linear (164).

Changes in outcome relating to surgeon caseload and hospital volume are therefore likely to cause their effects via different mechanisms. Surgeon caseload (or experience) is more likely to affect preoperative and intraoperative decision making, patient selection, and choice of resection technique. The

influence of hospital volume involves systems and health service components of care including the way in which the MDTs function along with the pervading MCN or nationally agreed protocols for best quality of care, particularly in the postoperative period. A correlation between the two is also likely since the presence of a higher caseload surgeon (or surgeons) in a unit will usually lead to a hospital being classified as high volume. Studies should necessarily be designed to account for and adjust accordingly for these effects.

1.4 Aims of this thesis

i. To review current literature regarding the functioning and outcomes of Multidisciplinary Teams.
ii. To ascertain whether patients who receive MDT care in the West of Scotland for colorectal cancer have better survival than those who do not.
iii. To assess the influence of socioeconomic circumstances on casemix and survival.
iv. To describe temporal trends in the provision of specialist care for colorectal cancer patients in the West of Scotland.
v. To assess effects of specialist care on complications and overall survival following resection of colonic cancer.
vi. To describe patterns of surgical approaches to rectal cancer resection by surgeon and hospital.
vii. To describe socio-economic patterns in operative complications and overall survival in patients receiving surgical intervention for colorectal cancer both in a temporal manner (before and after MCN inception) and in a cross sectional way with MCN and non-MCN patients.

1.5 Objectives of this thesis

i. To perform an original, contemporary, wide-ranging, and methodologically rigorous literature review.
ii. To complete a linkage of an existing MDT clinical audit database with the patient-based linked Scottish cancer registry, General Register Office death records and acute hospital discharge data on colorectal cancer deaths thus creating a novel dataset.
iii. To compare two contemporaneous groups' survival outcomes, namely those who had entered an MDT care pathway and those who had not.
iv. To understand the variables conferring a survival advantage to colorectal cancer patients.
v. To investigate the effects of surgical specialisation in hospitals.

2 Methods

2.1 Literature Search

A systematic review of the literature was undertaken in October 2007. The timing of this was important, as enough time had elapsed from the inception of MCNs to allow results, opinions, and outcomes to come to light in the published literature.

The following search strings were used in Medline, Pubmed, Embase, All EBM reviews, the Cochrane database, ISI Web of Knowledge, CINAHL, HMIC (Health Management Information Consortium), HealthSTAR (Health Services Technology, Administration, and Research), and SIGLE (System for Information on Grey Literature): cancer, colorectal neoplasm, cancer policy, cancer policy implementation, Calman-Hine, specialisation, multidisciplinary team, Managed Clinical Network, program development, managed care program.

The overall yield using the above strategy was 381 abstracts. Two independent reviewers David Morrison and Gary Nicholson (DM and GN) then selected the abstracts they deemed to be relevant to the thesis topic. This resulted in a shortlist of 130 abstracts. The full text for each of these was obtained and entered into an online reference management database (Refworks, www.refworks.com). Copies of the search strategies for the main searches are available in the appendix.

The Department of Health, Scottish Executive and key government agency websites were also investigated for relevant titles.

Finally, searching of reference lists in obtained papers was performed to extract a further level of information. The references were imported into Refworks in order to remove duplicate records and record ordering of articles and reports.

2.2 Study Design

The study was a retrospective cohort study analysis of data merging locally derived (MCN clinical audit) and nationally held (Cancer Registry) datasets. This facilitated an examination of patient characteristics and survival in all patients suffering from colorectal cancer in the West of Scotland.
Two main precautions were taken against possible researcher bias. Firstly, all hospitals were given a unique hospital identifier. This information was held centrally in the MCN office and never disclosed to the author. When hospitals were grouped for analysis it was impossible for the author to know which hospitals were which. Similarly, each consultant surgeon was given a unique identifier. Again, the consultants' identity was kept from the author to avoid any possible bias in interpretation of results.

2.3 Study Population

Inclusion and exclusion criteria

The inclusion criteria were to have been diagnosed with colorectal cancer in the West of Scotland from 1st January 1980 to December 30th 2005. Diagnosis of colorectal cancer was based on the ICD (International Classification of Diseases) -9 (pre-1999) and ICD-10 classification system. Patients between the ages of 16 and 99 at diagnosis were included in the analysis; older patients were excluded as the quality and completeness of cancer registration data are poorer in this age group than for younger cases (166). It is also thought that patients at extremes of age display atypical pathophysiological responses to malignancy.

Individuals registered with more than one primary malignant tumour were included only once in the dataset, from the date of the diagnosis of their first tumour. A small number of registrations which could not be traced through the ISD or MCN datasets due to failed linking were also excluded. Cases registered only from death certificates and for whom no information was traced on the diagnosis of cancer during life ('death certificate only - DCO' registrations) were excluded. It has been recognised that the validity of the diagnosis is less in such cases (167). DCO registrations are more likely to arise in older age groups and,

since these cases tend to have a poorer prognosis, their inclusion in survival analyses may reduce survival estimates (168) (169).
The main issues regarding DCO cases are that i) there is no survival time for DCO registrations and ii) it is not reasonable to suggest anything about clinical care if a diagnosis was not made during life.

2.4 Originality

This work is original in that it is the first attempt to statistically analyse survival outcomes in a clinical audit dataset of this size in Scotland in relation to colorectal cancer. It covers a geographical area larger than most published UK studies of this type. Performance is known to differ between hospitals, between surgeons and between Health Boards. This thesis will take an original look at these areas in relation to colorectal cancer patients in the West of Scotland. The linkage of MCN audit data to the Cancer Registry is original but some of the work uses routinely-available CR data. The results hope to assess whether established quality indicators and clinical practice guidelines are effecting a change in colorectal cancer patient outcome.

Previous work in this area in the West of Scotland has been of an audit nature only. Whilst valuable in its own right, audit does not assess outcomes in terms of patient survival. This thesis adds this vital dimension, and lays the foundations upon which further work regarding the West of Scotland MCN outcomes can be based.

This work is not original in the sense that it is looking at outcomes of MDT patients with colorectal cancer. The MDT process has been validated in other cancers such as breast as a vector for improved survival of patients with cancer. Many of the variables examined have been studied individually in the past. It is already known that the baseline survival for colorectal cancer patients is increasing with time.

2.5 Ethics approval

Permission to use the linked SMR06 data was obtained from the Caldicott Guardians of each of the five West of Scotland Health Boards. The ISD Privacy Advisory Committee also gave permission to supply the WoSCSU (West of Scotland Cancer Surveillance Unit) with linked, patient-identifiable data. Full patient identifiers were required to allow linkage to other datasets. The linked cancer registry dataset was supplied by the Scottish Cancer Registry by permission of its Director, Dr. David Brewster. The Director of the WoSCSU (Dr. David Morrison), as the Data Controller, gave permission for extracts of the data to be used for this thesis. The Lead Clinicians of the West of Scotland colorectal cancer MCN gave permission on behalf of the MCN to supply the author with all necessary patient-identifiable records from the MCN dataset. Data release forms were completed and approved by the regional cancer MCN audit team who supplied the data. A copy of the agreement can be found in the appendix.

2.6 Study period

The data were analysed retrospectively. This took place during the period of dedicated MD research, namely August 2007 to August 2009.

2.7 Data - procurement, handling, validation, linking & missing data

Data were procured from two sources:

i. The West of Scotland MCN team at the MCN department of Glasgow Royal Infirmary.
ii. ISD Scotland provided all SMR06 (Scottish Morbidity Records) pertaining to cancer patients along with General Registry Office for Scotland (GRO (S)) data on registered deaths. This allowed comparison of data existing before the MCN database with that contemporaneous to it.

Data Handling and security

All versions of the dataset were password protected with TrueCrypt version 6.0a 256bit encryption (Copyright © 2008 TrueCrypt Foundation, www.truecrypt.org).

At no time did patient identifiable data leave the West of Scotland Cancer Surveillance Unit to be analysed. This was in agreement with locally held data security protocols. These were read and signed in accordance with the Data Protection Act 1998. Caldicott Principles were adhered to throughout.
A copy of the data security protocol is contained in the appendix.

Data Validation and linking

Linking initially validated the data. SMR06 contains details on all patients with a diagnosis of cancer. The search was confined to those patients attributed with an ICD (International Classification of Disease) C18, C19 or C20 diagnosis viz., colorectal cancer. The SMR06 dataset was matched with the MCN dataset on three main index variables - forename, surname and date of birth. This automatic match of patients was then added to with further patients found through a manual process for those patients where the automatic process had not worked.

Manual linking of patients was performed using further identifiers such as CHI (Community Health Index) number, postcode, or by simply checking for forename and surname transposition or unusual names which are not readily recognised by the soundex system, e.g. O'Boyle.

The following, table 2 shows current ICD-10 codes for colorectal cancer. All but C181 were used for inclusion into this study. It is generally felt that appendicular tumours are too histologically and pathologically distinct from other neoplasms of the colon to be included in analysis.

Table 2 - ICD-10 definitions

Code	Definition	included or not
C180	Malignant neoplasm of caecum	✓
C181	Malignant neoplasm of appendix	x
C182	Malignant neoplasm of ascending colon	✓
C183	Malignant neoplasm of hepatic flexure	✓
C184	Malignant neoplasm of transverse colon	✓
C185	Malignant neoplasm of splenic flexure	✓
C186	Malignant neoplasm of descending colon	✓
C187	Malignant neoplasm of sigmoid colon	✓
C188	Malignant neoplasm overlapping lesion of colon	✓
C189	Malignant neoplasm of colon unspecified	✓
C19X	Malignant neoplasm of rectosigmoid junction	✓
C20X	Malignant neoplasm of rectum	✓

Missing Data

A number of strategies exist to deal with missing data. These are summarised by Katz in Multivariable Analysis: A practical guide for clinicians (170).

- Delete cases with any missing data
- Create variables to represent missing data
- Make additional effort to obtain data
- Decrease the number of independent variables in the analysis
- Estimate the values of the missing cases

This final suggestion has been considered in more detail and was employed recently in a study by Nur *et al* regarding socioeconomic inequalities in colorectal cancer survival. The missing values were arrived at by using multiple imputation (171).

2.8 Definitions

Survival time was defined as the time from date of incidence to date of death or date of censor. Censoring is the method used to quantify survival time up to the point when a patient does not experience the outcome and stops being followed-up – either because the subject drops out or because the study ends. Drop out from study was not applicable in this thesis.
For example, in this thesis patients who are still alive on 30th September 2007 were censored on that date because death data are not complete on the cancer registration file after that date. In our population we were unable to assess how many people emigrated. Date of censor was 31st September 2007 for all survival analyses unless otherwise stated. In this study survival time is the entire time that the patient was followed-up. Throughout this thesis it is measured in years, as this is most appropriate and commonest unit used when describing survival in colorectal cancer patients.

30 day mortality

This represents the mortality within 30 days of surgical intervention and is synonymous with postoperative mortality. It is widely regarded as the time after which mortality is attributable to the disease process and not surgical intervention. It is of particular interest as it is seen as an opportunity for other parts of the MDT to influence postoperative care and recovery.

Survival

Convention for studies of clinical outcome in cancer patients has been to measure either overall, cause specific or relative survival at 3 months, 1 year, 3 years or 5 years. This can vary depending on type of cancer. 5 year survival is widely employed to compare outcomes in colorectal cancer from different populations. 5 years is deemed enough time to confidently assess the long-term effects of any treatment that the patient might be given.

Overall and cause-specific survival

The simplest estimate of survival is observed survival, which is an estimate of the probability that a group of patients with a given disease will be alive at a specified time-point after diagnosis, irrespective of the cause of death. As colorectal cancer generally affects older people, there are more likely to be more competing causes of death. This makes this method more inaccurate in older populations. In cause specific survival deaths attributable to the cancer of diagnosis are treated as deaths whereas deaths due to other causes are censored at the time of death.
Some confusion arises when certain loosely related causes of death are treated as being the specific cause. For example, ISD cite 15 different causes for colorectal cancer specific death, including "secondary malignant neoplasm", "benign neoplasm of colon" and "neoplasm of uncertain behaviour, site unspecified" among their primary causes of death regarded as 'cause-specific'. (Appendix 7, ISD Scotland: Scottish Cancer Intelligence Unit. Trends in Cancer Survival in Scotland 1971-1995, {{8854 ISD Scotland 2010}}

This contrasts with a Dundee group where colorectal cause-specific survival was calculated only for patients with a signed pathology report confirming they had an adenocarcinoma of either the colon or rectum (172).

Deprivation Category (DEPCAT) and Carstairs Scores

DEPCAT is a widely used proxy measure of socio-economic circumstances derived from the Carstairs score, postcode, and local council area. The Carstairs score is a z-score transformed (standard score) weighted sum of four separate variables that are thought to represent an objective measure of a postcode sector's socio-economic deprivation level. These are; degree of overcrowding; level of male unemployment; proportion of all householders from social classes four and five, and level of car ownership. The z-score systems used to generate Scottish Index of Multiple Deprivation (SIMD) by definition create a normal distribution. In contrast, residents of Greater Glasgow NHS Board area are found in a minority of the most affluent areas but represent the majority – and in many

cases the entirety – of the most deprived areas of Scotland. The West of Scotland thus has the scientific advantage of being able to generate large populations of both affluent and deprived patients with which to compare and contrast health outcomes.

The SIMD 2009 combines 38 indicators across seven domains namely: income, employment, health, education, skills and training, housing, geographic access and crime. The overall index is a weighted sum of the seven domain scores. The weighting for each domain is based on the relative importance of the domain in measuring multiple deprivation, the robustness of the data and the time lag between data collection and the production of the SIMD. The domain weightings were subject to sensitivity analysis to assess the effects of any changes in weights on the overall index ranks (173).

Each DEPCAT was calculated using an individual's postcode sector and their local council area (LCA) before cross-referencing this with the Carstairs 2001 table to arrive at a value between 1 (most affluent) and 7 (most deprived) for every patient. The standardised table is available for download as an SPSS or Excel file at (174). For example, the geographical area covered by G71 spans three different council areas. It is therefore possible for a person residing in G71 to have one of three different DEPCATs. Given that the population is not equally distributed throughout each deprivation category and that larger proportions occupy the middle 3 DEPCATs, it was agreed to further regroup the DEPCATs into 3, as follows: DEPCATs 1 and 2 were regrouped into an affluent category. DEPCATs 3, 4 and 5 were regrouped into an intermediate category and DEPCATs 6 and 7 were regrouped into a deprived category.

It has been considered that DEPCAT is not a true representation or objective measure of deprivation and that it gives way to the ecological fallacy. When interpreting results regarding socio-economic deprivation one must always consider that deprivation measurement and categorisation could be introducing a source of error. By categorising patients into distinct groups according to their socio-economic status we introduce a source of error. This is due to the fact that we are making aggregate measures of socio-economic status across geographical areas. We are not assessing each individual objectively. The error therefore is to

assume that any individual in any given area (or postcode in our case) has the average socio-economic deprivation score of that area when in fact he or she could have a worse or better than average socio-economic status. The inference of this is that some patients classed as one category on the socio-economic scale could in fact belong to another category. In the absence of any better method of making this difficult assessment we make do with depgroup (modified DEPCAT) in this thesis. Currently there is no better way of assessing degree of socioeconomic circumstances. This point should be borne in mind when interpreting results that rely heavily on DEPCAT as a prognostic indicator.

Definition of specialist

Debate continues as to the definition of what constitutes a specialist in the field of colorectal surgery. Currently, various definitions have been applied. Membership of the Association of Coloproctologists of Great Britain and Ireland (ACPGBI) has been used as a proxy measure for being a specialist. Regional peer opinion has also been employed to determine which consultant surgeons should be considered specialist (175). More objective measures have also been sought. If a surgeon is undertaking more than 20 colorectal operations per year then he can be said to have enough expertise be called specialist according to the ACPGBI (82). Similarly, for rectal cancer, a threshold of seven resections per year has previously been quoted for declaring a surgeon specialist (44). This is based on the fact that a third of colorectal cancer operations are rectal and seven is approximately a third of 20.

In this thesis we have used seven resections per year as the threshold for rectal cancer. We have then used both seven and a further division at ten resections per year for colon cancer surgery. This is firstly to be able to compare colon cancer outcome with rectal cancer at the same volume and secondly, to assess if the higher threshold of ten cases per year yields better outcome than seven, thus supporting the argument for specialisation in colonic surgery as well as rectal. Furthermore we decided that due to paucity of consultants performing greater than 20 resections per year, that this higher threshold would not include enough data to provide meaningful interpretations relating to our region. A lower threshold of 10 cases is therefore employed herein.

2.9 Analysis and Statistical Methods

Data were supplied from Glasgow Royal Infirmary's Managed Clinical Network office in Microsoft Excel format. This was imported into SPSS format for the purposes of data analysis. SPSS version 15.0 for Windows was used for all analyses (176).

Categorical and continuously distributed data

Comparison of categorical data was generally performed using the X^2 test. This either tested the assumption of independence between two variables or was used to compare the proportions across groups. Comparison of means from continuous, normally distributed data were t tested. The Chi-square test is one of association. It measures the difference in proportions between observed and expected results. In this study, examples of categorical data include Dukes' stage and age group. Age was also treated as a continuous variable where applicable. Continuous variables were tested using Cox proportional hazards models for significance before deciding whether they should be entered into multivariable survival models. The null hypothesis, H_0, of the chi square test is that the two categorical variables are independent of each other. A p value reflects the probability of an event having taken place by chance. This value can be set at any desired level but for the purposes of this thesis the significant level of p was taken to be 0.05 or less. At levels less than this, the null hypothesis is rejected, suggesting a real change or association has occurred. The author performed all statistical analysis with advice from Dr. David Morrison and medical statisticians Miss Nicola Greenlaw and Dr. Gwen Allardice (WoSCSU).

A logical approach to data analysis was adhered to throughout. In general, categorical variables were analysed using the Kaplan-Meier method with a log rank test. This was used in all univariate Kaplan-Meier models. Its major drawback is that it is unable to incorporate more than one variable in a model, hence the need for multivariate analyses. Visual inspection of log-minus-log plots was also undertaken. If lines are parallel, this indicates that the difference between categories is constant over time. If they become closer or further

apart with time, this infers the hazards are not proportional over time. Thus a single hazard ratio fails to describe the variable in question.

Univariate models

Univariate survival analysis was performed applying the Kaplan-Meier method. The Log-rank test was used to compare the survival times between groups of patients. The log rank test compares two or more groups of survival data by arranging both observed and censored survival times in rank order. It is a non-parametric hypothesis test based on the chi-square distribution. The null hypothesis (H_0) is that the risk of death is the same in both groups. The number of deaths expected at any time should be distributed equally between the two groups by the number at risk. Any difference between the observed and expected is evidence against the H_0.

Multivariate modelling

Multivariate survival analysis explored multiple factors employing Cox's proportional hazards model (170). This is a particular type of proportional hazards regression analysis introduced by Cox in 1972. It evaluates the contribution of individual prognostic factors to survival whilst adjusting for other potential indicators. It is the logarithm of the relative hazard that is being modelled. The main advantages of this method are that it accounts for variable lengths of follow-up and that it can adjust for confounding variables. 95% confidence intervals were chosen for all models unless otherwise stated.
Both stepwise multivariate models using SPSS and manual models were employed. Using manual models has the added advantage of forcing the program to include specific variables that may be clinically important in the model even if they are not statistically important. A stepwise multivariate model would automatically only include the statistically significant variables.

Co linearity and proportionality

Care was taken to avoid the potential problem of co-linearity. This becomes an issue when two or more overlapping variables are included in the same model. If variables were highlighted as inducing co linearity they were tested individually in the model to ensure no change in outcome of results. For example, MDT groups were not tested in the same model as hospitals or Health Boards since they all potentially overlap in their effects thus displaying co-linearity. Care was also taken to check the proportionality assumption for each variable. The proportionality assumption, as stated by Katz, is assuming that "the hazards for persons with different patterns of covariates are constant over time" (170). An example in relation to colorectal cancer is that we are assuming the relative risk of death from colorectal cancer in the first year following surgery in patients of different stages of disease is the same as the relative risk in the ensuing years, i.e. there is a linear relationship. Log minus log plots were taken for each variable in each proportional hazards model to check that the proportionality assumption held. These have the disadvantage that they are only applicable to individual variables.

Linear regression models

Linear regression modelling fits a straight line through a set of points in such a way that makes the sum of squared residuals of the model (that is, vertical distances between the points of the data set and the fitted line) is as small as possible. The goodness of fit summarises the discrepancy between observed values and the values expected under the model in question. Our alternative hypothesis in this thesis is that the introduction of an MCN caused improvements in overall survival for colorectal cancer patients greater than would have otherwise occurred. We would expect to see a positive increase in the slope of the line following the introduction of the MCN. This slope should be out of proportion to the change that would have otherwise occurred. A good model is one where we can accept the alternative hypothesis whereas a bad model is one where the alternative hypothesis is rejected either due to decreasing slope of line following MCN introduction.

In all plots α is the intercept of the line and ß is the slope.

Tables and Graphs

All tables and graphs are adapted from output generated in SPSS version 15.0 using Microsoft word or Excel.

3 Influence of demographic, socioeconomic and clinical factors on survival from colorectal cancer in the West of Scotland

3.1 Introduction

Survival from colorectal cancer is influenced by several factors: general health; the stage and site of cancer; and the treatment received. Before comparing survival among patients treated within a Managed Clinical Network with those who are not treated within one, the effects of casemix (patient and disease factors) need to be quantified. The alternative hypothesis in this thesis is that the introduction of an MCN caused improvements in overall survival for colorectal cancer patients greater than would have otherwise occurred. In this chapter the population of the West of Scotland from which the sample is drawn is described in ways that are relevant to understanding their survival from colorectal cancer. We then describe aspects of patients' clinical status and its relationship to survival in the West of Scotland population. This chapter therefore provides the basis by which the effects of changes in the organisation of care can be assessed in ensuing chapters.

Linkage of MCN and SMR06 datasets by names and dates of birth creates a uniquely comprehensive dataset allowing an accurate and region-wide assessment of broad, longitudinal outcomes and more specific clinical audit derived prognostic indicators for colorectal cancer patients. The linked dataset has two principal advantages. Firstly, it allows survival in MCN and non-MCN patients to be differentiated. Secondly, it allows more detailed clinical and pathological information on patients' treatment to be included in survival analyses. Furthermore the relationships between socioeconomic circumstances (SEC) and associated key variables in colorectal cancer patients in the West of Scotland can be interrogated before going on to describe their effects on operative complications and survival. We sought to firstly summarise the broad socioeconomic trends in colorectal cancer patients across the entire region. This covers both a larger, less selective population than previous work by Hole et al

(65). It also covers a wider time frame, incorporating the introduction of the MCN for colorectal cancer into patient management decisions.

3.2 Summary of literature

A number of studies have reported that differing socioeconomic circumstances are associated with different survival outcomes from colorectal cancer (44,63,65,73-75,177,178). The effects may be due to either disease factors (more advanced stage at presentation); patient factors (emergency rather than elective presentation and comorbidity) or differences in treatment – offering different types of operation to patients by surgeons with differing levels of expertise. The effects of delay in time to first treatment may also help to explain differences in survival. The impact of the Calman-Hine report has been assessed from a regional viewpoint in the North West of England (28). We aim to ascertain whether or not adopting the recommendations of the report in the West of Scotland has had any objectively measurable effect upon overall survival for this patient group.

3.3 Aims & Objectives

Aims

i. To describe the study population in terms of demographic and clinical characteristics relevant to understanding their survival from colorectal cancer.

ii. To quantify the effects of demographic and clinical factors on overall survival from colorectal cancer in the West of Scotland.

iii. To describe socio-economic patterns in operative complications and survival in patients receiving surgical intervention for colorectal cancer both in a temporal manner (before and after MCN inception) and in a cross sectional way with MCN and non-MCN patients.

Objectives

i. To summarise the demographics of the combined Cancer registry and MCN dataset and identify patients meeting the inclusion criteria from relevant data.
ii. To produce descriptive statistics.
iii. To produce survival models.

3.4 Method

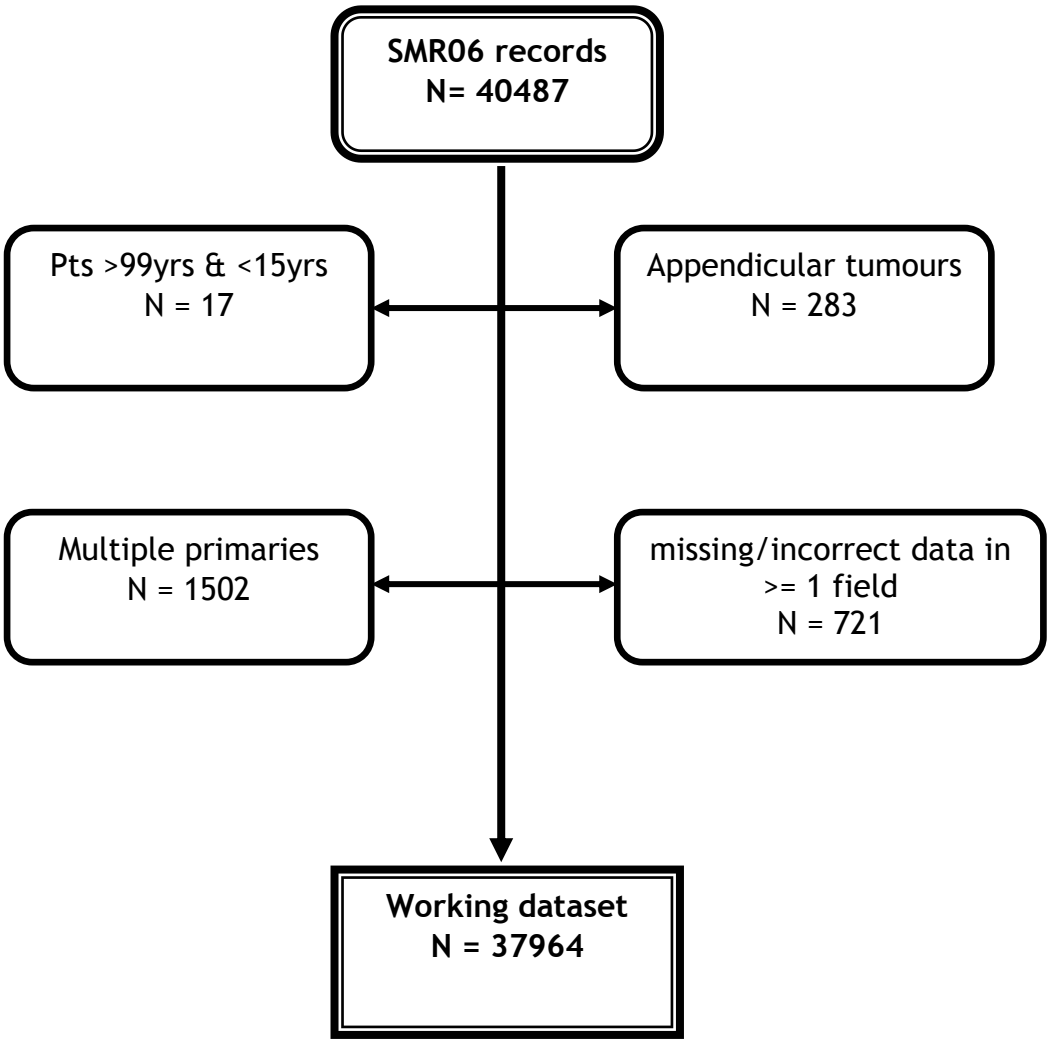
Inclusion criteria for this chapter:

The population under study included all patients diagnosed with a single colorectal cancer and treated in the West of Scotland from 01/01/1980 to 31/12/2005 with date of death data up to 30/09/2007. This allows for more complete follow up and thus more precise estimates of survival.

Linkage and derivation of dataset

The SMR06 records for all 40487 patients diagnosed with colorectal cancer from 1980 to 2005 were checked in order that only patients meeting the inclusion criteria for the study were selected. Figure 5 below demonstrates the exact numbers of patients excluded from the initial SMR06 records to arrive at the final working dataset.

Figure 5 - Flow diagram for case linkage and dropout



Multiple Primary cancers

Identification and exclusion of all separate records for new primary cancers in the same individuals was performed. A total of 1502 cases with more than one SMR06 entry were identified. This represents 2.7% of the total. These were due to patients having had synchronous tumours. They represent a group of patients that are thought to be different to most in terms of pathophysiology (179). The incidence of synchronous carcinoma is reported as being between 1.5% to 7.6% in other series of colorectal cancer patients (81).

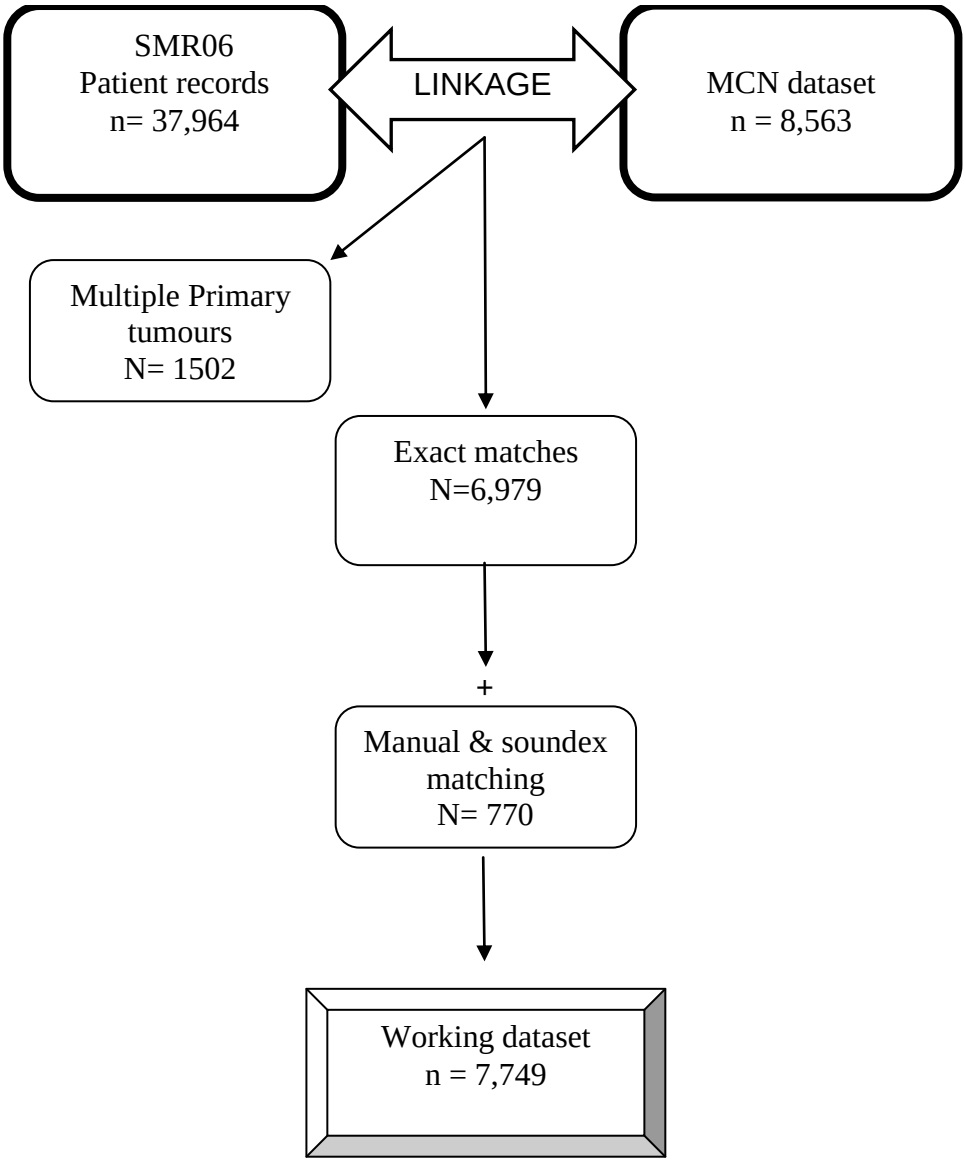
3.5 Results

In order that long term survival outcomes could be derived for the patients from the MCN clinical audit database, a linking process was undertaken to identify all patients with death records.

This section explores the trends from 1980 to 2005 regarding variables available for analysis as well as detailing relationships between socioeconomic circumstances, health board of origin, sex, Dukes' stage of disease and overall survival. This then highlights areas to be considered in more detail in further analyses. Furthermore, patients not enrolled in the MCN are compared with those enrolled in the MCN

Figure 6 shows the origins of the 7749 patients successfully linked to the cancer registry records from the MCN clinical audit database.

Figure 6 - Flow diagram summarising linking process of SMR dataset with MCN dataset to produce a working combined dataset following exact matches, Soundexing, and manual matching.



A total of 37964 patients were identified from the SMR06 data. These were all newly diagnosed colorectal cancer patients in the West of Scotland from 1st January 1980 to 31st December 2005. The age range was from 11 to 104 with a mean age of 70.76 and standard deviation of 11.679. 283 patients were excluded from analysis as they were diagnosed with cancer of the appendix. Despite this cancer being included in the ICD 10 classification of colorectal tumours it is an

atypical cancer which behaves differently compared to other colorectal tumours (180,181).

Completeness of data

The definition of completeness used in this thesis was the proportion of information entered into a field on the database. To that end, an entry of 'not applicable' was included as a bona fide entry as it indicates both that the field has not been left empty and that a member of the clinical audit staff has had to make a decision as to whether or not the field is appropriate to that patient. For example in the case of a colonic cancer patient, an MR scan would not be applicable as a part of the assessment of their tumour. In the MR scan field, the member of audit staff would enter 'not applicable' instead of leaving it blank. This then would count towards the completeness of the field.
With the passage of time, more variables have been added to both the cancer registry dataset and the MCN clinical audit database. This provides more information for analysis but has two main disadvantages. Firstly, comparison of older (pre-MCN) patient data with newer patient data is restricted to the fewer variables available at that time. Secondly, as the size and complexity of the newer dataset increases, it becomes more susceptible to inaccuracy.
The following table summarises the various variables available for analysis at different times.

Table 3 - Summary of available variables for all patients in the combined Cancer Registry/MCN audit dataset from 1980 to 2005 according to year group.

1980 onwards	1997 onwards	2000 onwards
Unique patient identifier	Earliest date of surgery	All clinical audit fields*
Sex	Age at surgery	
Date of incidence	Dukes' stage at diagnosis	
Site of cancer	Therapy objectives	
Health Board of residence		
Local council area		
Deprivation category		
Date of death		

*These fields are summarised in clinical audit proformas in the appendix.

A mean case ascertainment of 98% was achieved for the eight variables available from 1980 onwards. This is one of the main strengths of this study and is recognised in the field of cancer registry studies, (Dr. David Brewster, director, Scottish Cancer Registry, personal communication).

MCN audit data

The MCN clinical audit dataset contains clinical, pathological, oncological and nursing related variables. See appendix for a copy of the four proformas currently used for data collection. These include general demographics and details proforma, a pathology form, an oncology form, and a nursing form.
Of the 8,563 sets of patient details obtained from the MCN, 7749 (90.5%) matched with SMR06 records, using a combination of exact matches, Soundexing and manual matching techniques.

Cases with multiple tumours

1502 cases with multiple tumours were identified during the matching process (figure 5). Within this population there was a higher percentage of males, 58.5%, compared to the general population of colorectal cancer patients in the West of Scotland. The remaining variables had a similar distribution to those in the study population of patients with single tumours.

Table 4 summarises the overall demographics for colorectal cancer patients in the West of Scotland from 02/01/1980 to 29/12/2006. Ages are grouped to allow comparison with previously published series (65). Overall women were 3 years older than men (mean ages of women and men difference 3.0, 95% CI 2.8-3.2 years) There was also an increase in mean age with time overall, and for both sexes separately (ANOVA, P <0.001 for all 3 tests). Men increased in mean age at incidence from 67.43 in 1980 to 69.05 in 2005 with women increasing in mean age at incidence from 71.00 to 71.57 over the same time period.

No statistically significant difference was noted when comparing proportions of colon cancer patients from different deprivation groups with sex (p=0.836) whereas a statistically significant difference was found when comparing proportions of rectal cancer patients from different deprivation groups with sex. 32.7% of male rectal cancer patients were deprived compared to 29.7% of female rectal cancer patients. The affluent group contained 12.6% of the male patients whereas 14.9% of females' rectal cancer patients were in the affluent group. N = 10095, p<0.001. A higher proportion of male rectal cancer patients were from the deprived group compared to females, 32.7% and 29.7% respectively.

Table 4 - Descriptive demographics of the study population. All 37964 patients registered as having colorectal cancer in the West of Scotland from 1980 to 2005.

	Male	Female	Total
Sex (%)	19023(50.1)	18941(49.9)	37964(100)
Age Range	94(11-105)	93(14-106)	95(11-106)
Mean age (sd)	69.15 (11.1)	72.17 (12.0)	70.65 (11.7)
Median age	70.14	73.57	71.79
Age group <55	2027	1669	3696
55-64	4039	3112	7151
65-74	6765	5535	12300
>=75	6192	8625	14817
Colon cancer	13329 (47.9)	14521 (52.1)	27850 (100)
Rectal cancer	5694 (56.3)	4420 (43.7)	10114 (100)
Affluent*	2749 (49.1)	2845 (50.9)	5594 (100)
Intermediate*	10319 (49.9)	10364 (50.1)	20683 (100)
Deprived*	5907 (50.9)	5706 (49.1)	11613 (100)

*Data were missing for 76 patients regarding deprivation category

Health Board of residence

The aim of a Managed Clinical Network is to provide equitable standards of care across the area that it covers. We therefore compared demographic and clinical characteristics of patients from each of the five West of Scotland Health Board areas to determine if there were significant differences in casemix before calculating clinical outcomes. Firstly, absolute numbers of patients in each Health Board are considered in order to appreciate the variability throughout the West of Scotland.

Figure 7 demonstrates a wide range in absolute numbers of patients being diagnosed and treated in each Health Board.

Figure 7 - Health Board of residence for all colorectal cancer patients in the West of Scotland from 1980 to 2005. N=37964.

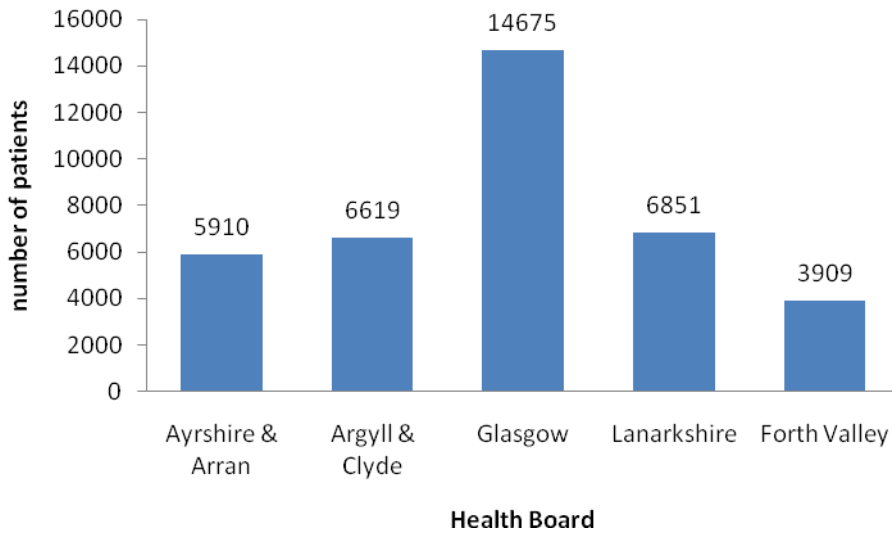
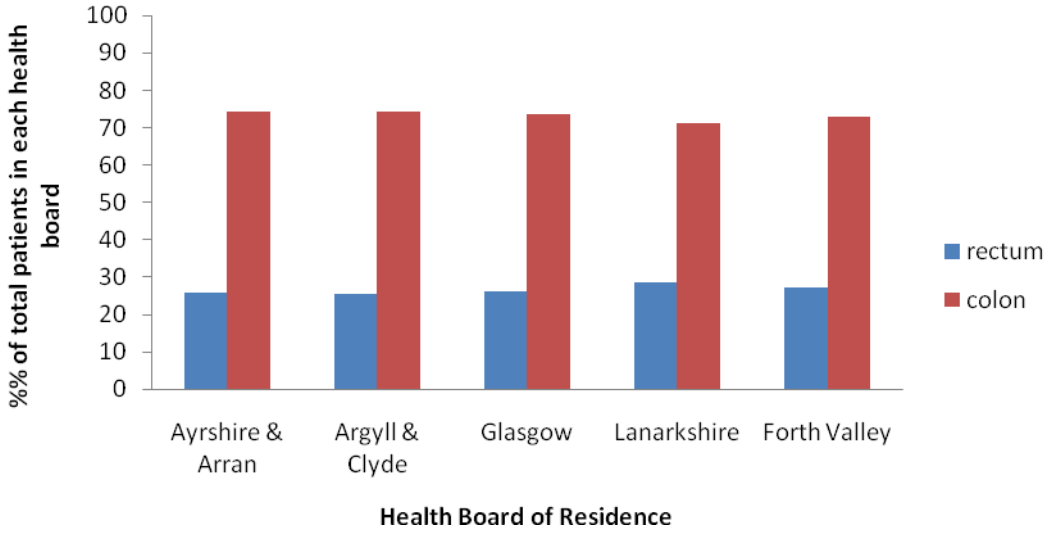


Figure 8 then highlights how these patients are distributed in relation to site of lesion. Overall 27850 patients (73.4%) and 10114 patients (26.6%) have colonic and rectal cancers, respectively. Furthermore, there is a statistically significant difference in these proportions across the region, $p< 0.001$. This appears to be explained by a higher proportion of rectal cancer patients in the Lanarkshire Health Board.

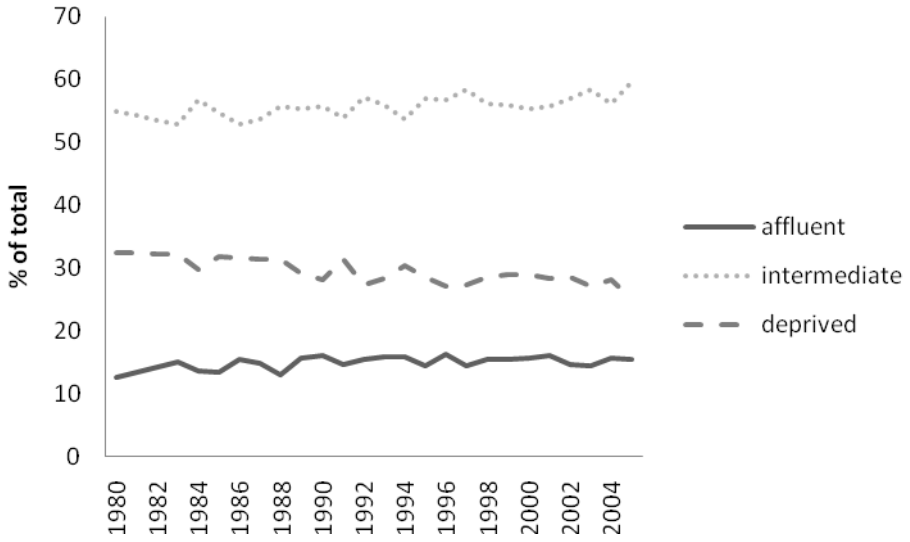
Figure 8 - Proportions of patients with colonic or rectal lesions in each Health Board. All patients with colorectal cancer in the West of Scotland from 1980 to 2005. N = 37890, p <0.001



Socioeconomic Circumstances

Figure 9 shows a drop in the proportion of deprived patients with time from 35% in 1980 to 30% in 2005. This is mirrored by an increase in the proportion of intermediate patients from 52% in 1980 to 60% in 2005, while the proportion of patients in the affluent deprivation group remains relatively constant with time according to this figure. A Chi square test for trend of deprivation group of patients divided into 5 yearly intervals for all colorectal cancer patients in the West of Scotland from 1980 to 2005 yielded a p value of <0.001.

Figure 9 - Deprivation group vs year of incidence for all colorectal cancer patients in the West of Scotland from 1980 to 2005. N = 37888.



Relationship between age and deprivation from 1980 to 2005

Affluent patients tend to be older than their more deprived counterparts. Although there is a trend noted with regard to deprivation and site of tumour, it is possible that this could be partly explained by age. The following analyses explore this.

Table 5 summarises the ANOVA results comparing age at diagnosis with deprivation group for all 37,964 colorectal cancer, all rectal, and then all colonic cancer patients in the west of Scotland from 1980-2005. Overall this suggests that there is a statistically significant relationship between SEC and patients with colonic cancer. This explains the significant trend seen in the population overall. Rectal cancer patients fail to demonstrate a significant difference in mean age between different degrees of SEC. Thus, age may be a confounding factor for the observed associations between colorectal cancers and socio-economic circumstances – and vice versa. Survival analyses should therefore be adjusted for both variables to reduce their confounding effects.

Table 5 - Summary statistic 1-way ANOVA of mean ages by deprivation group for all colorectal cancer, all rectal cancer, and all colon cancer patients in the West of Scotland from 1980 to 2005.

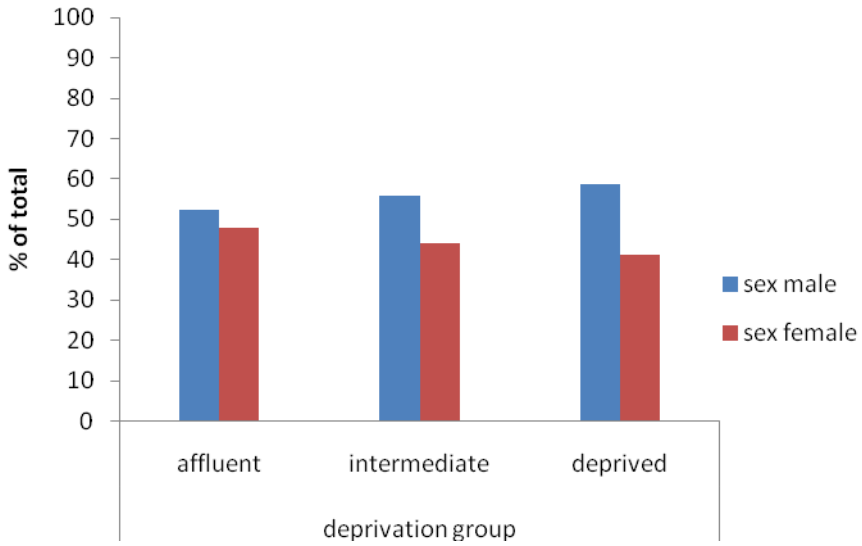
		Sum of Squares	df	Mean Square	p
colorectal cancer	Between Groups	2761.93	2	1380.97	<0.001
	Within Groups	5176137.58	37887	136.62	
Rectal	Between Groups	666.70	2	333.35	0.09
	Within Groups	1412041.28	10092	139.92	
Colon	Between Groups	1868.41	2	934.20	<0.001
	Within Groups	3750870.85	27792	134.96	

The relationship between sex and deprivation

There are significantly more men with rectal cancer across all deprivation categories. This is not the case with regard to colonic cancer patients. There was no statistically significant difference in the proportions of males and females in each deprivation group (df = 2, Chi square 5.129, p=0.08). Whilst there are no socio-economic differences in the proportions of men and women with colon cancer (df = 2, Chi square = 0.538, p=0.836), there were significantly greater proportions of affluent men with rectal cancers, as evidenced below.

Figure 10 highlights that for rectal cancer patients, there is a persistently higher proportion of male patients compared to females across the deprivation categories. In the affluent group 52.2% are male and 47.8% female. This difference is more pronounced in the deprived group where 58.7% of patients are male and 43.7% female. Overall the difference in proportions of male to female patients across the different deprivation categories is statistically significant, P<0.001.

Figure 10 - Comparison of sex with deprivation group for all patients with rectal cancer in the West of Scotland. n=10095 df = 2, Chi square = 16.90, p<0.001.

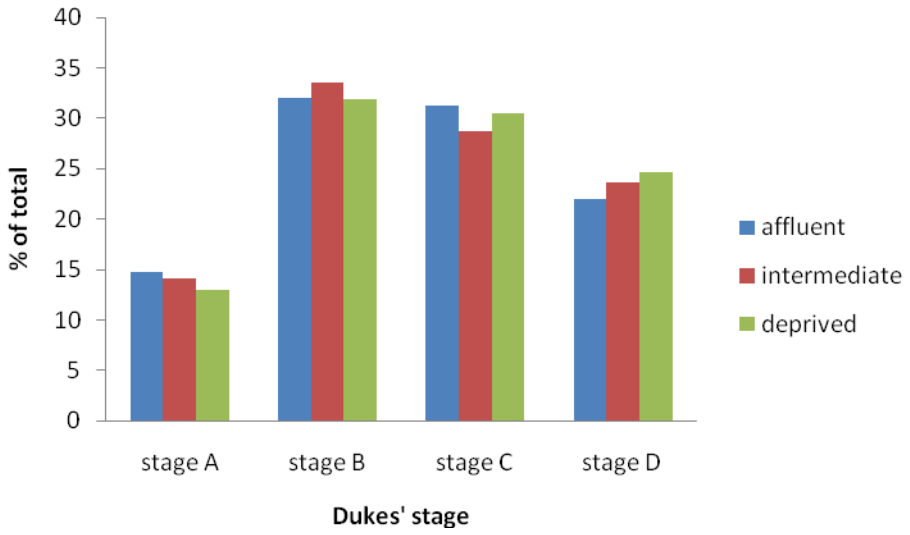


Exploring the relationship between Dukes' stage and deprivation

There are more affluent people with Dukes' A disease and more deprived people with Dukes' D disease. Figure 11 shows there is a larger proportion of affluent people with early stage disease and a larger proportion of deprived patients with advanced disease. 14.7% of affluent patients have stage A disease compared to 13.0% of deprived patients. 22.0% of affluent patients have stage D disease compared to 24.7% of deprived patients. n = 11126, p = 0.058. While there is no clear socio-economic trend overall, there does seem to be a consistent and clinically important relationship between increasing deprivation and later stage at presentation.

Additional testing of these variables using the Spearman rank test confirmed no correlation between SEC and Dukes' stage.

Figure 11 - Dukes' stage and deprivation group in all colorectal cancer patients from 1997-2005, excluding those with an unspecified Dukes' stage. n = 11166, p =0.058



No significant difference in stage at presentation compared to socioeconomic circumstances was found in any of the sub groups studied. These included colonic cancer patients only, rectal cancer patients only, male colon only, female colon only, male rectal cancer patients only, and female colon patients only. These findings are consistent with previous findings in Europe but not with trends reported in the USA.

Patients not enrolled into the West of Scotland MCN

An aim of the MCN is to review all patients diagnosed with colorectal cancer in the region. This should provide access to specialist care for all patients. We compared the characteristics of patients included and not included in the MCN. Figure 12 demonstrates the reduction in overall numbers of patients enrolled into MCN care between 2001 and 2005 as the colorectal cancer MCN was formed.

Figure 12 - Numbers of patients not enrolled into the West of Scotland MCN with time, from 2001 to 2005.

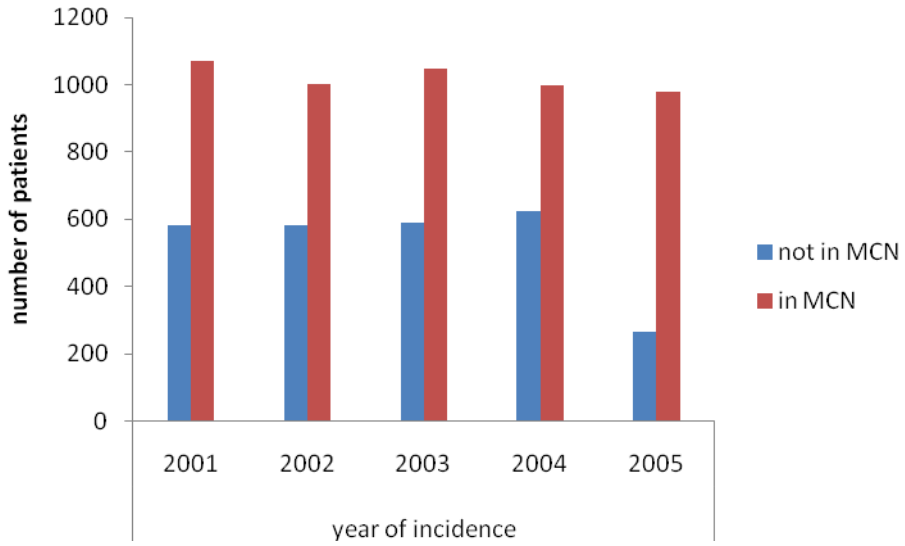


Figure 12 summarises temporal trend in patient enrolment into the MCN. Patients in the MCN were on average two years younger than those managed elsewhere, $p<0.001$ (95% CI -2.788 to -1.276).

Stage of disease is a recognised prognostic indicator for all cancers (182). It is therefore relevant to understand whether patients treated within an MCN differ from those not treated within an MCN with respect to their cancer stage. Table 7 shows the main differences in the populations of patients enrolled and not enrolled in the MCN. Of note is that there is a far lower proportion (16.9%) of patients with an unspecified Dukes' stage in the MCN compared to those not in the MCN (42.9%). Also, almost 30% of patients not enrolled in the MCN are in the Dukes' D category. In general, patients in the MCN have less advanced disease.

Table 6 - Descriptive demographics for all 7749 patients enrolled and not enrolled in the MCN from 2001 to 2005.

Numbers in brackets are % of total unless otherwise indicated.

		in MCN	not in MCN	p
Age at incidence	mean (range)	68.9 (21-97)	73.77 (24-105)	
	sd. (95% CI)	11.3 (68.60-69.22)	12.01 (73.31-74.22)	<0.01*
Deprivation status	affluent	767 (65.3)	408 (34.7)	
	intermediate	2956 (66.8)	1470 (33.2)	
	deprived	1336 (64.3)	760 (35.7)	0.12
Sex	male	2745 (65.6)	1441 (34.4)	
	female	2355 (66.1)	1208 (33.9)	0.63
	Total	2649 (34.2)	5100 (65.8)	

*tested using ANOVA

The descriptive statistics from table 6 show that there was a significant difference between the ages of patients enrolled and not enrolled in the MCN with those enrolled having a mean age of 3.8 years younger than their counterparts not in the MCN. There was no statistically significant difference between the two groups in relation to both deprivation status and sex.

Table 7 - Comparison of Dukes' stage with all colorectal cancer patients enrolled and not enrolled in the MCN from 2001 to 2005. N=7749, P< 0.001

		in MCN		Total
		Yes (%)	No (%)	
Dukes' stage	A	637 (12.5)	163 (6.2)	800 (10.32)
	B	1528 (30.0)	302 (11.4)	1830 (23.6)
	C	1483 (29.1)	273 (10.3)	1756 (22.7)
	D	589 (11.5)	774 (29.2)	1363 (17.6)
	Unspecified*	863 (16.9)	1137 (42.9)	2000 (25.8)
Total		5100 (100)	2649 (100)	7749 (100)

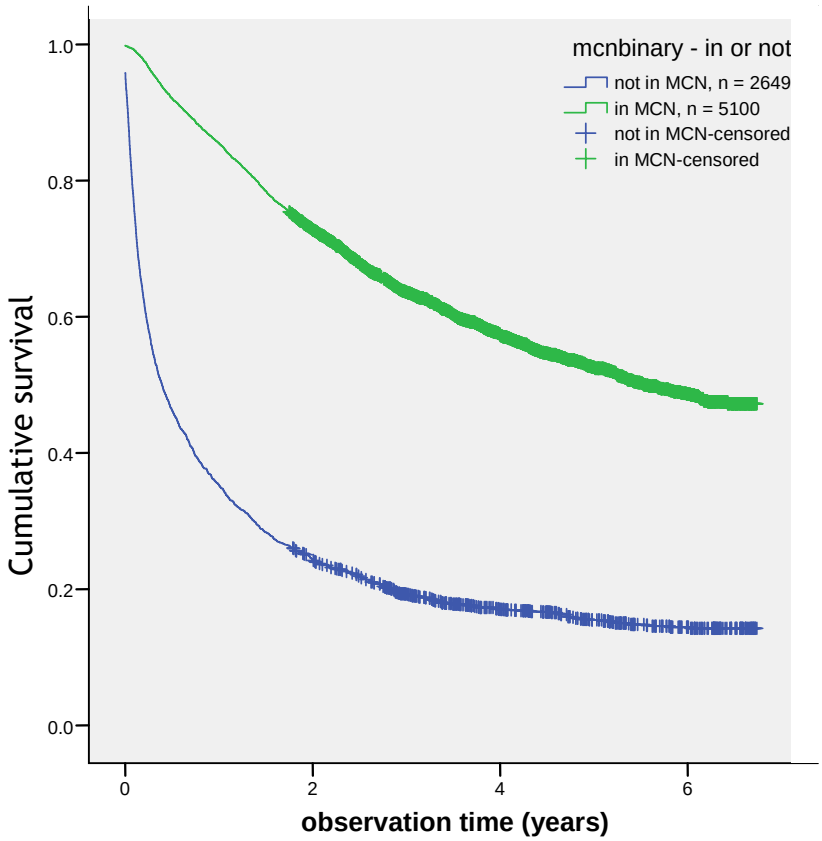
*The overall statistical significance did not change when the 2000 patients with Dukes' unspecified cancer were removed from analysis.

Given that there are demographic differences between the population of patients enrolled in the MCN and the population not, it is important to explore if there is a difference in overall survival.

Survival

The alternative hypothesis in this thesis is that the introduction of an MCN caused improvements in overall survival for colorectal cancer patients greater than would have otherwise occurred. We are interested in whether the reorganisation of services has accelerated or augmented the putative improvement. The following graphs represent the long-term changes with time for colorectal cancer patients, colon cancer patients, and rectal cancer patients. Three year survival was tested but did not add any important insights over and above those seen with five year survival. Graphs displaying these findings are in the appendix. In the following Kaplan Meier plot, Figure 13, a statistically significant difference in the overall survival of these two groups with patients in the MCN demonstrating a 5.15 year increase in median overall survival compared to those patients not in the MCN. These are contemporaneous groups, thus eliminating the effect of comparing groups of patients from before with after MCN inception.

Figure 13 - Kaplan Meier plot of overall survival comparison between those patients enrolled in the West of Scotland MCN and those not from 2001-2005. n =7749, Log Rank test, p<0.001.



Given the higher survival among patients treated within the MCN, table 8 explores factors that could explain this.

Age at incidence, degree of socioeconomic deprivation, degree of disease burden, having a colonic tumour and whether or not the patient has entered the MDT process all help to account for the difference in overall survival seen in the Kaplan Meier plot. These differences could be further explored if there were further clinical and pathological data available for the population of patients not entering into the MCN process.

Table 8 - Factors influencing overall survival for all 7749 patients diagnosed with colorectal cancer in the West of Scotland from 2000-2005. 2649 patients were not in MCN and 5100 were in the MCN

	p	Univariate HR (95% CI)	Multivariate HR (95% CI)
In MCN or not (in MCN baseline)	<0.01	2.01 (1.87-2.15)	1.71 (1.59-1.83)
Age at incidence	<0.01	1.03 (1.03-1.04)	1.03 (1.03-1.04)
affluent	<0.01	1	
Intermediate	0.05	1.09 (1.00-1.19)	1.16 (1.06-1.26)
Deprived	<0.01	1.23 (1.12-1.35)	1.28 (1.16-1.41)
Dukes' A	<0.01	1	
Dukes' unspecified	<0.01	6.82 (5.81-8.01)	6.17 (5.25-7.25)
Dukes' B	<0.01	1.81 (1.53-2.15)	1.82 (1.54-2.16)
Dukes' C	<0.01	3.05 (2.59-3.60)	3.22 (2.73-3.81)
Dukes' D	<0.01	11.92 (10.12-14.03)	12.72 (10.80-14.99)
Sex	1.00	1.00 (0.94-1.06)	
Site of lesion (rectum vs colon)	<0.01	1.24 (1.15-1.32)	1.14 (1.07-1.23)

Following the findings from table 8 we went on to explore the relationship between site of tumour and stage of disease as they were independent prognostic indicators. Table 9 shows a statistically significant difference in the incident proportions of rectal and colonic cancers according to stage with more rectal cancers presenting at Dukes' stage A compared to colonic cancers and more colonic tumours presenting at Dukes' D compared to rectal cancer.

Table 9 - Relationship between Dukes' stage at presentation and site of tumour for all 11166 patients from 1997-2005. Pearson Chi square <0.001

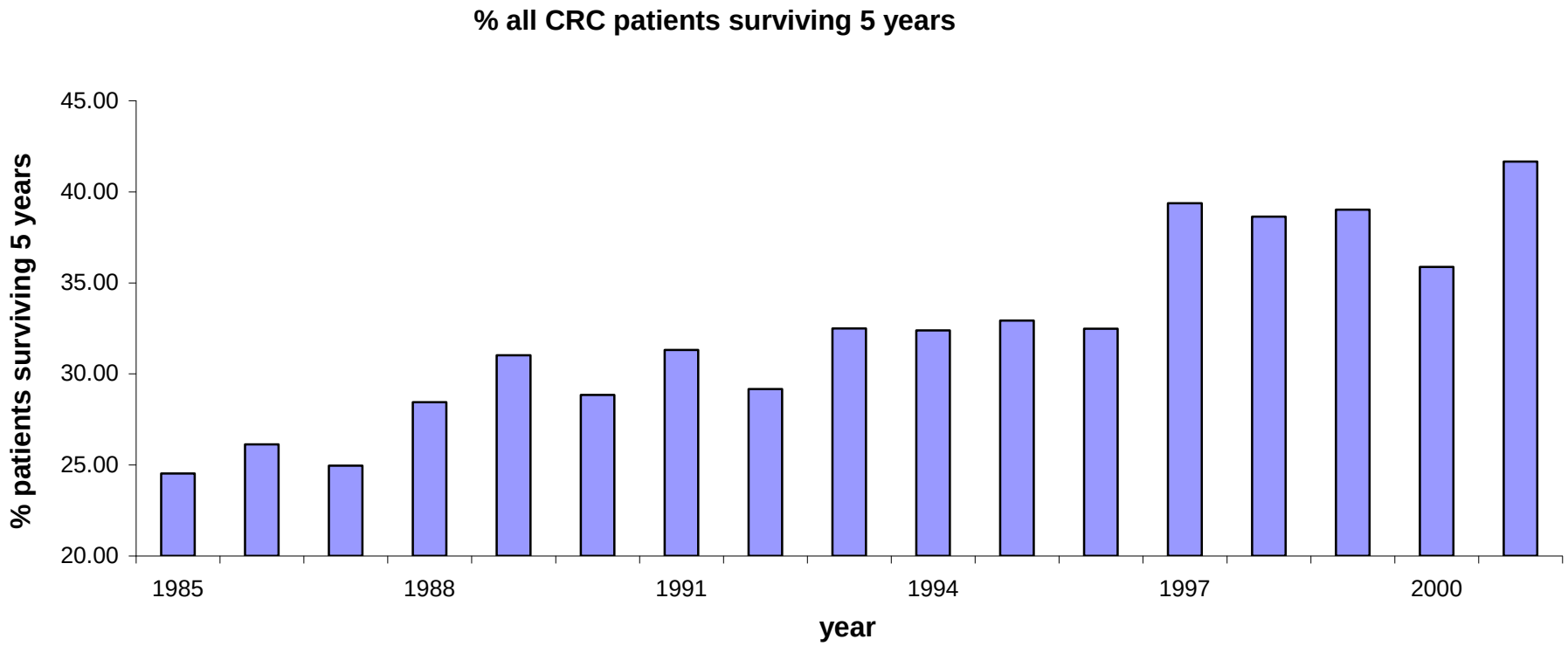
		rectum	colon	Total
Dukes' stage	stage A	609	940	1549
		21.8%	11.2%	13.9%
	stage B	776	2896	3672
		27.8%	34.6%	32.9%
	stage C	839	2465	3304
		30.0%	29.5%	29.6%
	stage D	572	2069	2641
		20.5%	24.7%	23.7%
Total		2796	8370	11166
		100.0%	100.0%	100.0%

Overall Five year survival

Figure 14 charts the increase in overall 5 year survival for the population of colorectal cancer patients in the West of Scotland region from 1980. There is an increase with time from fewer than 25% in 1985 to over 40% in 2001. There appears to be a stepwise increase between 1996 and 1997 from 32.48% to 39.37%.

Overall Five year survival

Figure 14 - Overall 5 year survival for all colorectal patients in the West of Scotland from 1980 to 2001.



The following figures (figures 16 and 17) display the trends noted for colonic and rectal cancer patients surviving five years. An overall increase in survival occurs with time from 22.5% in 1985 to 45.0% in 2001 for colon cancer patients. There are larger variations in survival with time for females with rectal cancer compared to males. This may well reflect the smaller numbers of patients with rectal compared with colonic cancers, with females having a lower incidence than men in the West of Scotland.

Figure 15 – Comparison of overall five year survival for all 27795 colorectal cancer with all 10095 rectal cancer patients in the West of Scotland from 1980 to 1996.

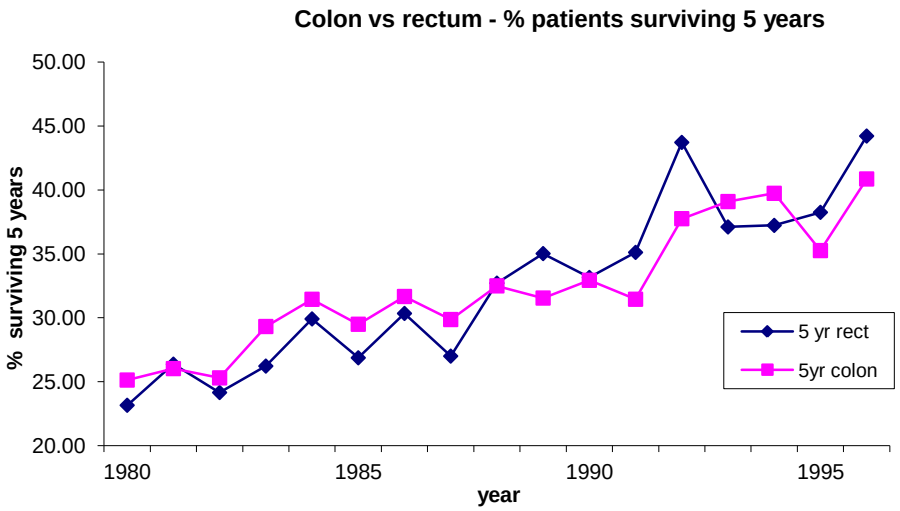


Figure 15 highlights that there appears to be very little difference in the overall 5 year survival trends for both sexes. Again, there is a general increase in survival with time from an average of 26% in 1985 to 42% in 1996. There is no obvious difference between sexes.

Figure 16 - Comparison of overall five year survival for all 17700 male and female colon cancer patients in the West of Scotland from 1980 to 2001.

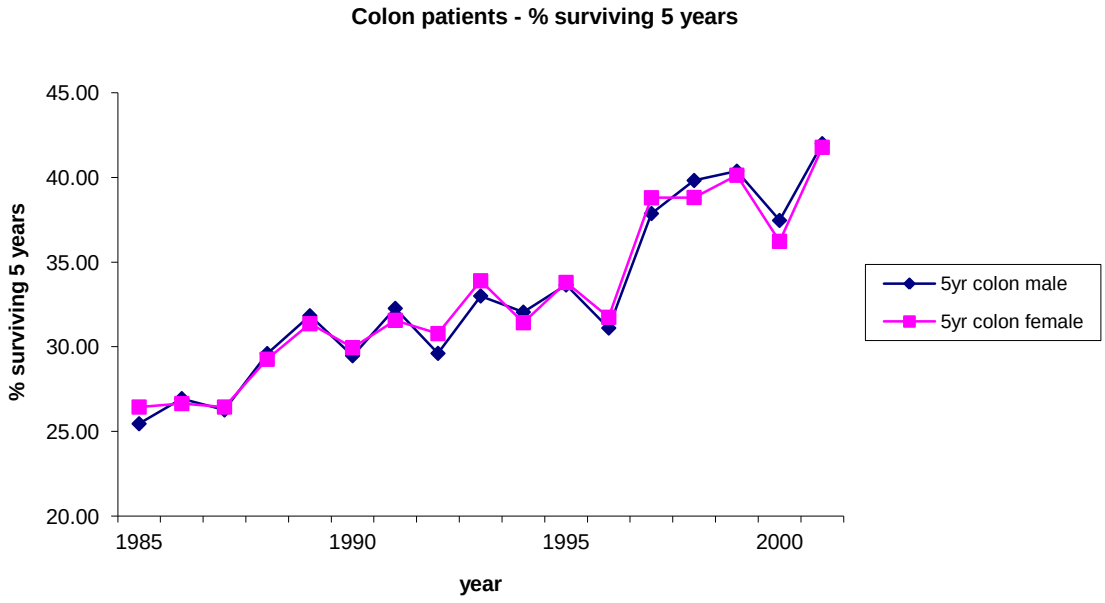


Figure 17 - Comparison of overall five year survival for male and female in all 10095 rectal cancer patients in the West of Scotland from 1980 to 1996.

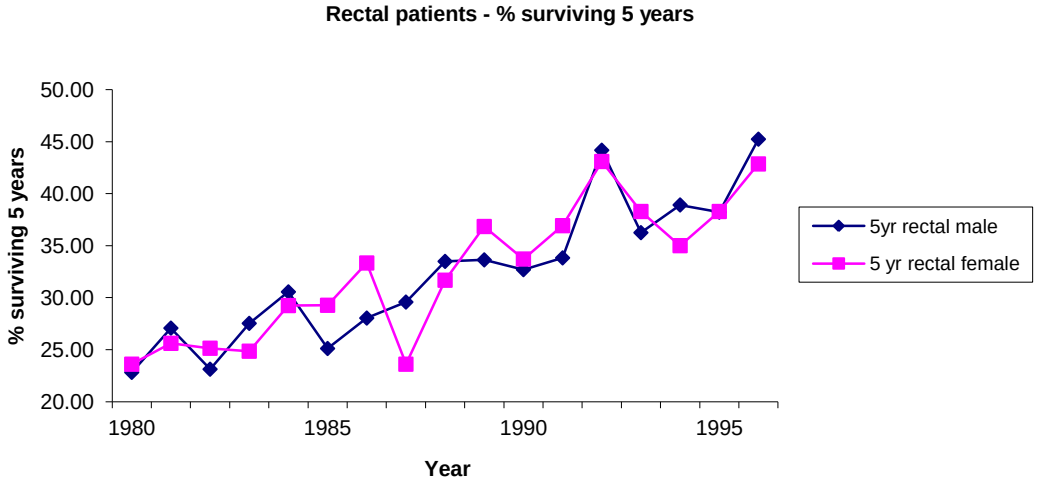


Figure 17 illustrates a greater increase in five year overall survival for rectal cancer patients compared to colonic patients between 1980 and 2001. The steeper rise in survival seems to occur in the mid 1990s when the TME technique was being learned, adopted and applied across the West of Scotland.

Linear Regression Models

Linear regression was used to quantify the increase in percentage of overall survival (the coefficient of the line) and to estimate any additional effect of the MCN after adjustment for time (per year).

In order to gauge whether or not an increase in the percentage of patients surviving three years had occurred with time we employed linear regression to the values generated for overall three-year survival. We fitted three models using linear regression: a model with one explanatory variable, the year of incidence; a model with two explanatory variables, the year of incidence and a binary variable indicating whether the survival was pre-MCN or post-MCN; a model with three explanatory variables, the two previously mentioned and an interaction term between the year of incidence and pre/post MCN. The model including the interaction term tests for a significant difference in the slope parameters for the two groups (pre-MCN and post-MCN). If there is a significant interaction this implies that a difference in survival has taken place following the introduction of the MCNs. The following graphs demonstrate situations where a significant difference in the slope was obtained. No significant differences were found for five year overall survival so all plots refer to overall three year survival. In all plots α is the intercept of the line and β is the slope.

Figure 18 to 20 demonstrate only those linear regression models producing statistically significant results. In terms of three year overall survival, there were statistically significant results for all female colorectal cancer patients from 1997-2005, female rectal patients from 1980-2005, and all rectal patients from 1980-2005. In terms of five year overall survival, only female rectal cancer patients were found to have a significantly improved survival after the introduction of the MCN than would have been expected. In figure 18 there appears to have been a decrease in survival from 52% to 50% over time from 1996 to 2000, followed by an increase from 50% to 52% after the MCN was introduced. The paucity of data points is the most likely explanation for this.

Figure 18 - Linear regression. Overall three year colorectal cancer survival in all females in the West of Scotland from 1997-2005. Dashed vertical line represents the introduction of the MCN[1] Pre MCN α = 2454.51, β= -1.20, Post MCN α = -1384.46, β = 0.72. Year of incidence x MCN interaction, p = 0.022

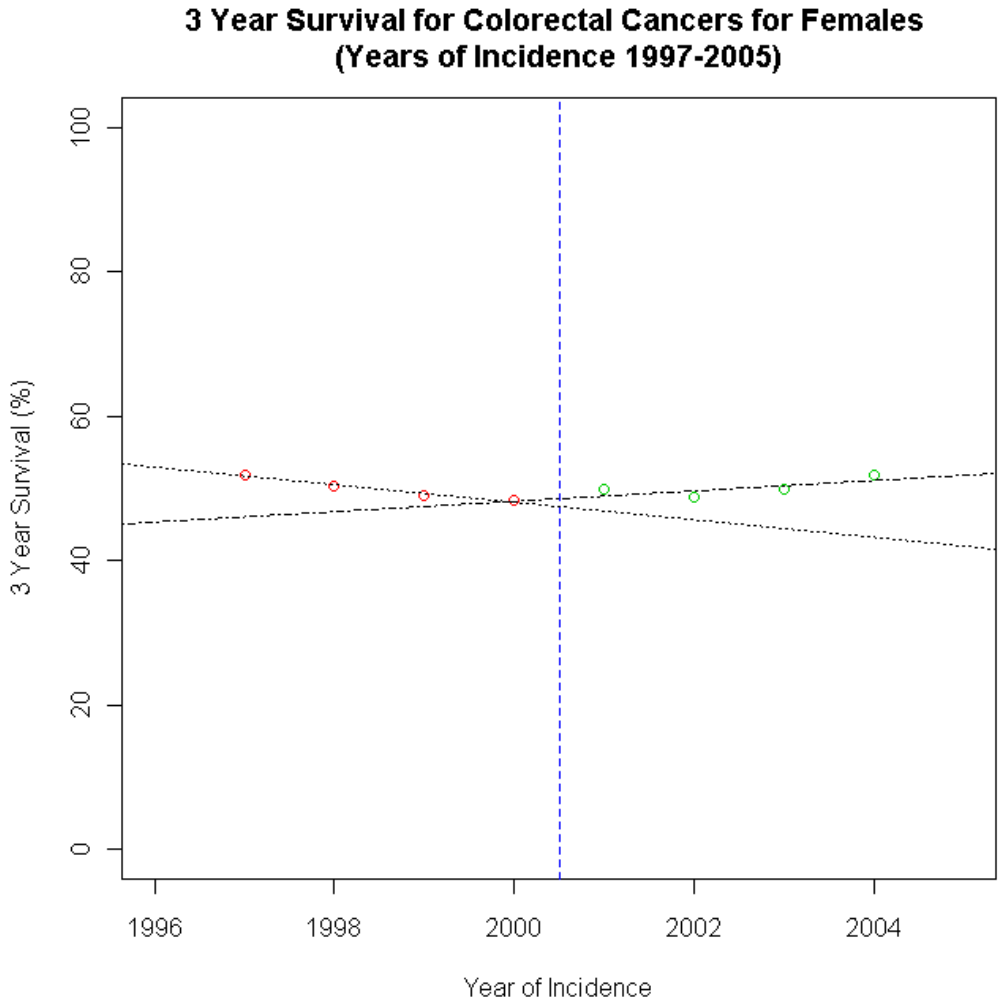


Figure 19 - Linear regression. Overall three year rectal cancer survival for females in the West of Scotland from 1980-2005. Dashed vertical line represents the introduction of the MCN. Pre MCN α = 2079.022 , β = 1.015
Post MCN α = -8194.1058 , β = 4.12
Year of incidence x MCN interaction, p = 0.031

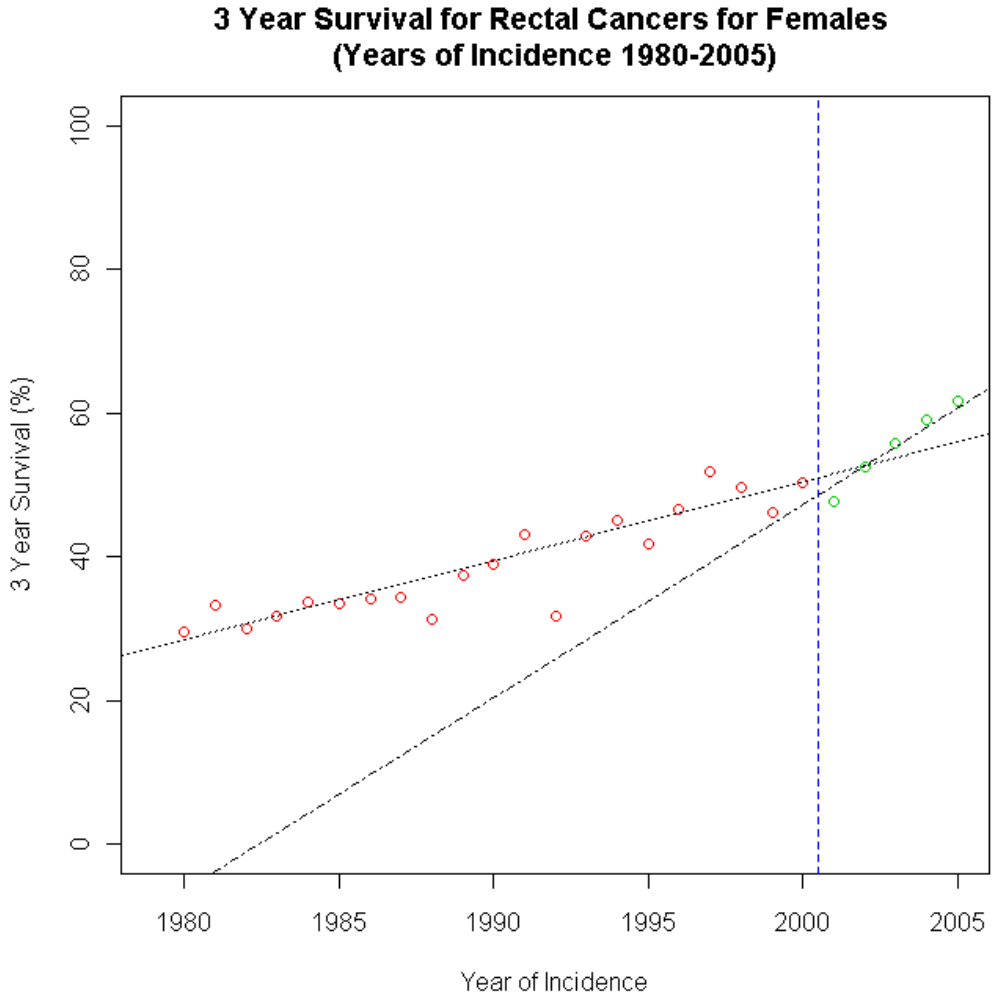


Figure 20 - Linear regression. Overall three year rectal cancer survival for all patients in the West of Scotland from 1980-2005. Dashed vertical line represents the introduction of the MCN. Pre MCN α = -2145 , β = 1.098
Post MCN α = -5326.7 , β = 2.69
Year of incidence x MCN interaction, p = 0.025

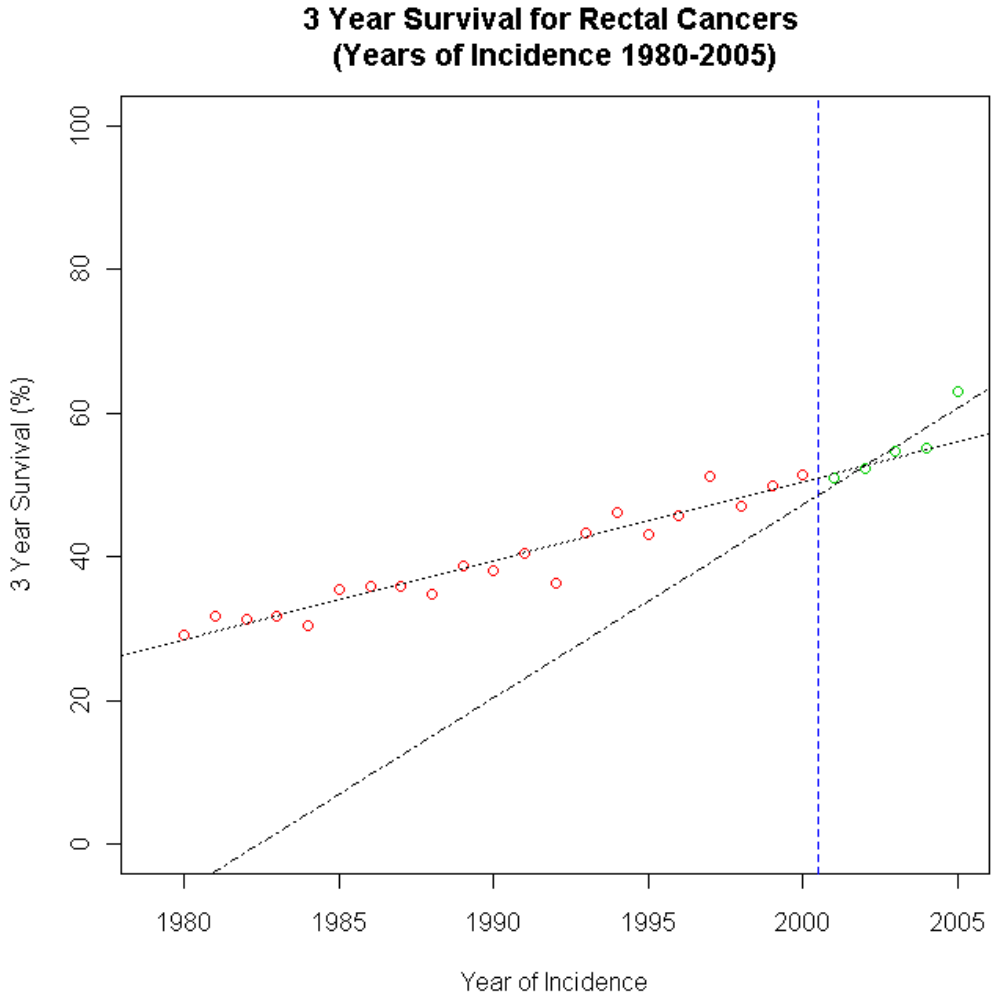
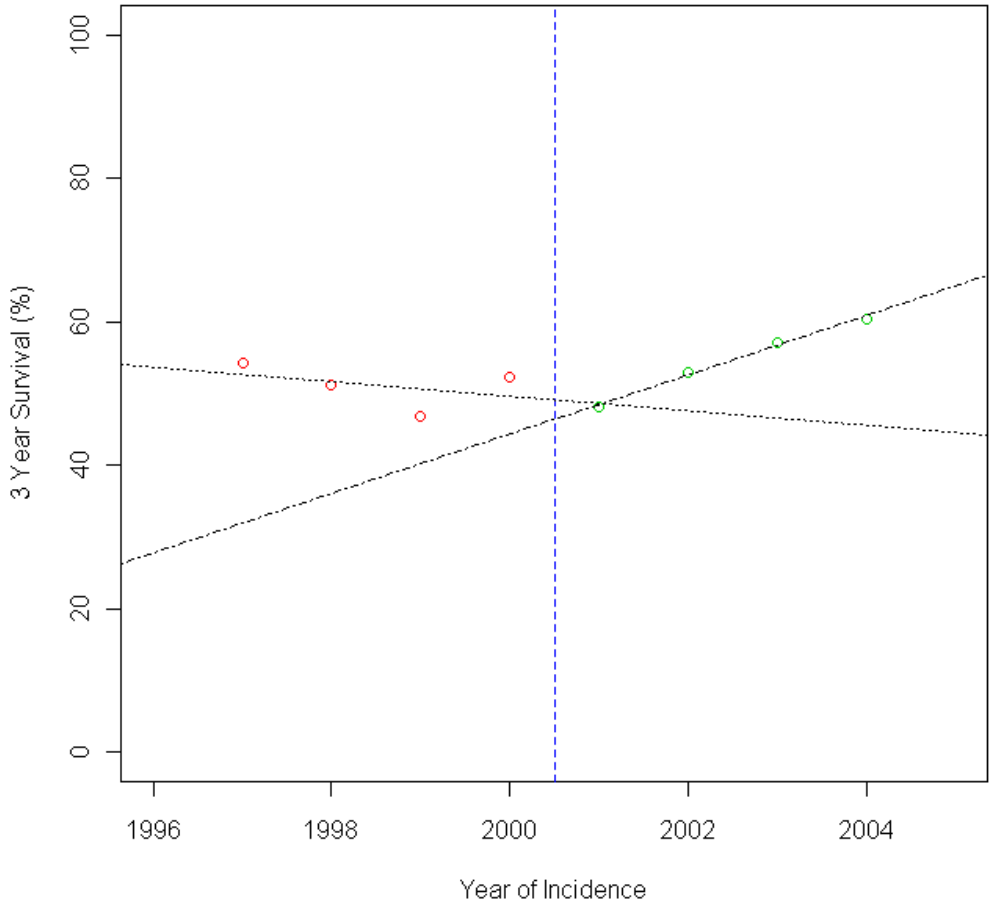


Figure 21 - Linear regression. Overall 5 year rectal cancer survival for females in the West of Scotland from 1997 to 2005. Dashed vertical line represents the introduction of the MCN. Pre MCN α = -2068.3914 , β = 1.059
Post MCN α = -6862.14 , β = 3.45
Year of incidence x MCN interaction, p = 0.022



Is the introduction of an MCN associated with increased overall survival?

A comparison amenable for inclusion in a Cox model is that of pre-MDT years with MDT years in order to provide a binary variable for pre and post inception of the MCN. The major drawback of this approach is that patient data before 2001 is limited to fewer variables.

All colorectal cancer patients undergoing curative intent surgery 1997-2005

The following table (Table 10) summarises the findings for both univariate and multivariate analysis for all colorectal cancer patients from 1997-2005 including a binary variable for pre and post MCN inception. All variables with the exception of the MCN variable remain individual prognostic indicators following adjustment in the multivariate model. Unadjusted survival was not significantly different when comparing patients from before inception of the MCN with those after the MCN

Table 10 - Univariate and multivariate findings for all 6851 colorectal cancer patients undergoing curative intent surgery from 1997-2005. (Pre MCN = 1997-2000. MCN = 2001-2005)

		Univariate		Multivariate
	p	HR (95% CI)	p	HR (95% CI)
MCN vs not	0.89	0.95 (0.87-1.03)	0.19	0.94 (0.87-1.03)
Age at incidence	0.00	1.04 (1.04-1.05)	0.00	1.04 (1.04-1.05)
affluent	0.00		0.00	
intermediate	0.01	1.76 (1.05-1.32)	0.00	1.23 (1.10-1.38)
deprived	0.00	1.28 (1.13-1.44)	0.00	1.27 (1.12-1.44)
Dukes' A	0.00		0.00	
Dukes' unspecified	0.00	1.71 (1.43-2.04)	0.00	1.70 (1.42-2.03)
Dukes' B	0.00	1.50 (1.34-1.68)	0.00	1.41 (1.26-1.58)
Dukes' C	0.00	2.04 (1.81-2.29)	0.00	2.15 (1.91-2.43)
Dukes' D	0.00	4.76 (3.81-5.96)	0.00	5.70 (4.56-7.13)
Male (baseline: female)	0.00	1.17 (1.03-1.20)	0.00	1.24 (1.15-1.34)

Survival in all colorectal cancer patients undergoing curative intent surgery from 2001-2005

Cancer registry data can provide only limited information into changing determinants of survival. Further information – particularly on clinical management – was available from MCN audit data. A further aim of this chapter is to ascertain factors influencing overall survival in patients undergoing curative intent surgery. It is in this subset of patients that the MCN process could affect the largest change in outcomes. Sufficient data for this population were only available for patients in the MCN. The following table displays the Cox proportional hazards model univariate and multivariate findings for all 3763 patients with colorectal cancer undergoing curative intent surgery from 2001 to 2005. It shows that age, deprivation category, Dukes' stage, extra mural vascular invasion, and sex were all significant prognostic indicators of long-term outcome. The MDT in which patients were treated was a significant independent variable on univariate analysis, but not when included in the multivariate model.

Multivariate modelling was then used in order to assess the relative contribution of various variables of interest to overall patient survival in the population undergoing curative intent surgery from 2001-2005.

Table 11 – Multivariate Cox proportional hazards model for all colorectal cancer patients undergoing curative intent surgery in the West of Scotland from 2001 to 2005. n = 3763. HR = Hazard Ratio. *continuous variable.

	p	Univariate HR (95% CI)	Multivariate HR (95% CI)
age at incidence*	.000	1.044 (1.04-1.05)	1.05 (1.04-1.05)
Deprivation – affluent	.041		
Deprivation – intermediate	.165	1.15 (0.98-1.35)	1.141 (0.95-1.37)
Deprivation – deprived	.014	1.35 (1.13-1.60)	1.28 (1.051-1.572)
Dukes' A	.000		
Dukes' B	.000	1.71 (1.40-2.10)	1.46 (1.056-2.015)
Dukes' C	.051	2.64 (2.20-3.22)	1.58 (1.216-2.053)
Dukes' D	.484	5.68 (4.27-7.54)	4.87 (3.215-7.375)
Differentiation – well	.084		
Differentiation – moderate	.975	1.03 (0.77-1.37)	0.99 (0.68-1.44)
Differentiation – poor	.332	1.50 (1.10-2.06)	1.22 (0.82-1.83)
Distal margin positive	.002	2.16 (1.48-3.12)	2.05 (1.29-3.24)
Extra mural vascular invasion	.000	2.03 (1.80-2.23)	1.61 (1.40-1.85)
Apical node positive	.000	2.37 (1.95-2.88)	1.68 (1.34-2.10)

The previous analysis was repeated substituting Dukes' stage with pathological tumour stage (pT) and pathological nodal stage (pN) as these are more specific measures than Dukes' stage. No difference was found although fewer patients had complete data on TNM stage. Dukes' was therefore retained as it gives the model more power.

All rectal patients undergoing surgery with curative intent

A separate analysis was undertaken for all rectal cancer patients in the West of Scotland from 2001 to 2005. This was for three main reasons. Firstly, rectal cancer patients are known to display better outcomes compared to colon cancer patients. This includes better one and five year relative survival for both men

and women (183). Secondly, there are a different set of objective pathological variables for this population, owing to the different anatomy of rectal tumours. Finally, the surgical management and preoperative treatments for rectal carcinoma can differ in important ways from that of colon cancer, as previously outlined.

Table 12 demonstrates that five of the seven variables tested retain their statistical significance as independent prognostic indicators in the 702 rectal cancer patients undergoing surgery with curative intent in the West of Scotland from 2001 to 2005. A positive circumferential margin had the largest influence on overall survival (HR 2.06, 95% CI 1.50-2.83) whereas age at incidence had the most modest significant effect on overall survival with a 4% increase in hazard per year. As before, this analysis was repeated substituting Dukes' stage with pathological tumour stage (pT) and pathological nodal stage (pN). No statistical difference was found although fewer patients had complete data on TNM stage so Dukes' was retained as it gives the model more power. Also, type of admission was omitted from this model as we were interested in planned care within the MCN setting rather than emergency surgery. Of note is that type of admission was a significant independent prognostic indicator, $p<0.001$.

Table 12 – Univariate and multivariate model for all rectal patients undergoing surgery with curative intent in the West of Scotland from 2001 to 2005. n = 702.

	P	Univariate HR (95% CI)	Multivariate HR (95% CI)
Circumferential margin +ve	<0.001	2.76 (2.08-3.66)	2.06 (1.50-2.83)
Distal margin positive	0.03	2.29 (1.28-4.08)	1.97 (1.05-3.68)
Extra mural vascular invasion	0.002	2.33 (1.83-2.96)	1.61 (1.19-2.18)
age at incidence	<0.001	1.04 (1.03-1.05)	1.04 (1.03-1.06)
Dukes' A	0.001	1.00	
Dukes' unspecified	<0.001	2.69 (1.87-3.90)	2.82 (1.73-4.58)
Dukes' B	0.02	1.77 (1.23-2.55)	1.75 (1.10-2.76)
Dukes' C	<0.001	2.86 (2.03-4.04)	2.43 (1.56-3.78)
Dukes' D	0.03	5.57 (3.04-10.20)	2.78 (1.10-7.03)
deprivation – affluent	0.61	1.00	
deprivation – intermediate	0.60	1.21 (0.86-1.69)	
deprivation – deprived	0.35	1.30 (0.91-1.87)	
sex - female as baseline	0.38	1.05 (0.85-1.29)	

Colon patients undergoing surgery with curative intent

Table 13 shows that eight of the ten variables entered into the multivariate model retained their individual prognostic significance. There was no independent effect observed according to which MDT a patient was treated in. A perforated tumour had the largest effect on survival in the multivariate model with an increased hazard of 74%. Emergency versus routine/urgent admission was also an independent negative prognostic indicator as were extra mural vascular invasion and worsening socioeconomic circumstances. Dukes' stage retained its negative prognostic significance as did age at incidence. Hospital MDT group and age were not statistically significant predictors of outcome in the adjusted multivariate model.

Table 13 - Multivariate results for all 2774 colon cancer patients undergoing surgery with curative intent in the West of Scotland from 2001 to 2005. n = 2774

		UNIVARIATE		MULTIVARIATE
	p	**HR (95% CI)**	**p**	**HR (95% CI)**
tumour perforation – no	0.00	1.00	0.00	1.00
tumour perforation – yes		2.12 (1.81-2.49)		1.74 (1.42-2.12)
Admission type - routine/urgent	0.00	1.00	0.00	
Admission type – emergency		1.97 (1.74-2.24)		1.50 (1.28-1.76)
peritoneal surface not involved	0.00	1.00	0.01	1.00
peritoneal surface involved		2.04 (1.77-2.35)		1.26 (1.05-1.50)
extra mural vasc invasion – no	0.00	1.00	0.00	1.00
extra mural vasc invasion – yes		1.94 (1.69-2.24)		1.52 (1.29-1.79)
Affluent	0.00	1.00	0.03	1.00
Intermediate	0.10	1.17 (0.97-1.41)	0.21	1.15 (0.93-1.42)
Deprived	0.00	1.40 (1.14-1.71)	0.01	1.34 (1.07-1.69)
bowel prep – no	0.00	1.00	0.00	1.00
bowel prep – yes		1.85 (1.62-2.12)		0.72 0.61-0.85)
Dukes' A	0.00	1.00	0.00	1.00
Dukes' unspecififed	0.00	2.34 (1.75-3.12)	0.01	1.56 (1.11-2.18)
Dukes' B	0.00	1.68 (1.30-2.17)	0.60	1.08 (0.81-1.44)
Dukes' C	0.00	2.54 (1.98-3.28)	0.00	1.52 (1.14-2.04)
Dukes' D	0.00	5.41 (3.85-7.59)	0.00	4.26 (2.89-6.29)
age at incidence	0.00	1.04 (1.04-1.05)	0.00	1.05 (1.04-1.06)
MDT	0.43			
Sex	0.21	1.09 (0.96-1.23)		

Determinants of survival in all rectal cancer patients undergoing curative intent surgery 1997-2005

Unadjusted survival from rectal cancer was 18% lower (HR 0.82, 95% CI 0.70 to 0.96) following introduction of the MCN. However, after adjustment for patients' age, Dukes' stage and sex, survival was found to have increased by 23% (HR 1.23, 95% CI 1.05 to 1.44) after introduction of the MCN

Table 14 - Univariate and multivariate findings for all 1921 rectal cancer patients undergoing curative intent surgery from 1997-2005. (Pre MCN = 1997-2000. MCN = 2001-2005).

		Univariate HR		Multivariate HR
	p	(95% CI)	p	(95% CI)
Pre and post MCN	0.01	0.82 (0.70-0.96)	0.11	1.23 (1.05-1.44)
Age at incidence*	0.00	1.04 (1.03-1.05)	0.00	1.04 (1.04-1.05)
affluent	0.14			
intermediate	0.05	1.25 (1.00-1.56)		
deprived	0.07	1.25 (0.98-1.60)		
Dukes' A	0.00			
Dukes' unspecified	0.00	1.65 (1.24-2.20)	0.00	1.91 (1.43-2.57)
Dukes' B	0.00	1.56 (1.28-1.89)	0.00	1.50 (1.23-1.82)
Dukes' C	0.00	2.13 (1.74-2.60)	0.00	2.29 (1.87-2.81)
Dukes' D	0.00	3.27 (1.93-5.56)	0.00	3.76 (2.21-6.38)
Sex§	0.02	1.19 (1.03-1.39)	0.00	1.25 (1.07-1.45)

*continuous variable, §female baseline

All colon cancer patients undergoing curative intent surgery 1997-2005

Table 15 demonstrates that for all 6851 colon cancer patients in the West of Scotland undergoing curative intent surgery between 1997 and 2005 we found that age at incidence, deprivation group, Dukes' stage and sex were all statistically significant independent prognostic indicators in both univariate and multivariate analyses. The binary variable for pre and post MDT was not statistically significant on univariate analysis.

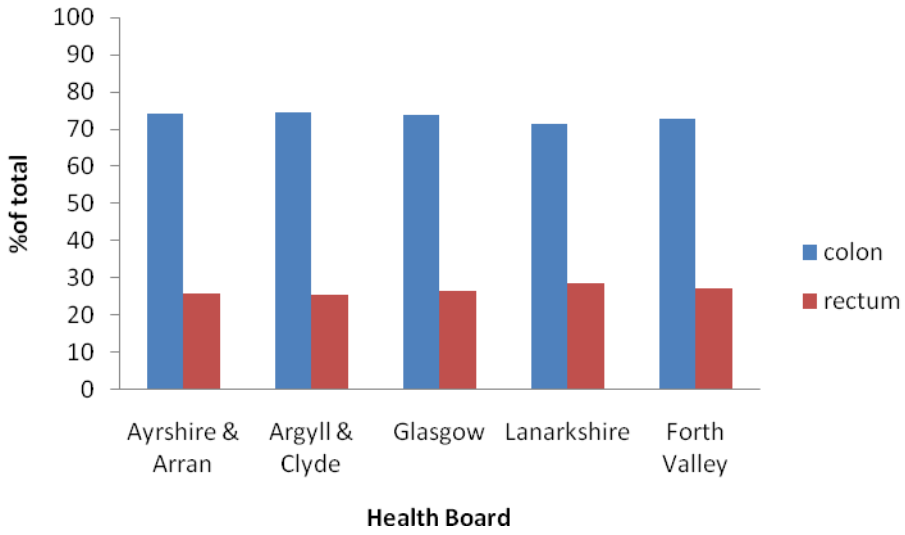
Table 15 - Univariate and multivariate findings for all 6851 colonic cancer patients undergoing curative intent surgery from 1997-2005. (Pre MCN = 1997-2000. MCN = 2001-2005). *continuous variable

	p	Univariate HR (95% CI)	p	Multivariate HR (95% CI)
Pre and post MCN	0.99	1.00 (0.91-1.10)		
Age at incidence*	0.00	1.04 (1.04-1.05)	0.00	1.05 (1.04-1.06)
affluent	0.00		0.00	
intermediate	0.03	1.16 (1.02-1.32)	0.07	1.19 (0.99-1.44)
deprived	0.00	1.29 (1.12-1.49)	0.00	1.46 (1.19-1.78)
Dukes' A	0.00		0.00	
Dukes' unspecified	0.00	1.76 (1.40-2.19)	0.00	2.21 (1.65-2.95)
Dukes' B	0.00	1.48 (1.29-1.70)	0.00	1.67 (1.29-2.15)
Dukes' C	0.00	1.99 (1.72-2.31)	0.00	2.63 (2.04-3.39)
Dukes' D	0.00	5.14 (3.99-6.61)	0.00	6.52 (4.63-9.15)
Sex (♀ baseline)	0.04	1.10 (1.00-1.20)	0.01	1.19 (1.05-1.35)

Figure 22 confirms the heterogeneity in distribution of deprivation across the region in relation to 27,795 patients with colonic cancer. Glasgow Health Board has the largest proportion of deprived colon cancer patients (51.8%) whereas Forth Valley has the highest percentage of affluent patients (26.3%) with colon cancer. These differences are examined with reference to rectal cancer patients below.

The following figure summarises the relationships between Health Board and proportions of patients with rectal and colonic cancers therein. Lanarkshire has the largest proportion of rectal cancer patients (28.7%) as well as the second lowest proportion of deprived patients (see figure 3 above). This contrasts with Argyll and Clyde where the largest proportion of colonic cancers occur (74.40%) and the proportion of affluent patients is higher. There is no clear cut linear or reciprocal relationship between these two factors.

Figure 22 - Proportions of colon and rectal cancers across Health Boards in the West of Scotland from 1980-2005. n = 37890, chi squared = 21.54, df = 4, p<0.001.



Exploring site of lesion in relation to Socioeconomic Circumstances

Affluent patients tend to have more colonic and fewer rectal cancers. From 1980 to 2005 data regarding site of lesion are available. The relationships between socioeconomic circumstances and distribution of colonic and rectal lesions are illustrated below.Table 16 represents the statistically significant larger proportion of deprived patients presenting with rectal cancer (27.4%) compared to affluent patients (24.1%). In contrast, there is a larger proportion of affluent patients with colonic cancer (75.9%) compared to deprived patients (72.6%), X^2 = 7.73, df = 2 p<0.001.

Table 16 – Comparing proportions of colonic and rectal cancer patients in the West of Scotland population from 1980-2005 according to deprivation group. n = 37890, χ2 = 15.86, df = 2, p<0.001

SEC	Rectum (%)	Colon (%)	Total
Affluent	1372 (24.5)	4222 (75.5)	5594 (100)
Intermediate	5552 (26.8)	15131 (73.2)	20683 (100)
Deprived	3171 (27.3)	8442 (72.7)	11613 (100)

This result was further explored by comparing the proportions of patients with rectal and colonic in different deprivation groups from two separate time

periods, namely, 1980-1985 and 2000-2005. These results are summarised in Table 17 below.

In both periods, the same relationship between site of lesion and SEC was found, namely that more deprived patients have a higher proportion of rectal lesions compared to colonic lesions. Affluent patients demonstrate the reciprocal of this with a higher proportion of colonic lesions.

Table 17- Comparison of proportions of patients with rectal and colonic cancer in different periods of time, 1980-1985 and 2000-2005. n =17126.

Time period	n	rectal (%)	colonic (%)	Chi square	df	p
1980-1985	7805	2156 (27.6)	5649 (72.4)	15.63	2	<0.001
2000-2005	9321	2529 (27.1)	6792 (72.9)	7.73	2	0.021

This finding could be confounded by age.

Socio-economic circumstances, type of admission and type of surgery

The following table, table 17 highlights the higher proportion of affluent patients admitted electively compared to deprived patients – 60.73% compared to 50.76% respectively. There is an inverse trend in emergency admissions with affluent patients having the lowest proportion (39.27%) compared to deprived patients, with the highest proportion (49.33%). These trends are statistically significant, p<0.001.

Table 18 - Socioeconomic circumstances compared to type of admission for all patients diagnosed with colorectal cancer in the West of Scotland from 2000-2005. Chi 26.50, df 2, P <0.001. n = 6252.

SEC	Elective (%)	Emergency (%)	Total (%)
Affluent	563 (60.73)	364 (39.27)	927 (100)
Intermediate	2015 (55.91)	1589 (44.09)	3604 (100)

Deprived	872 (50.76)	849 (49.33)	1721 (100)
Total	3450 (55.18)	2802 (44.82)	6252 (100)

We also compared all 4315 patients presenting electively for *colon* cancer surgery with 1113 presenting as an emergency between 2000 and 2005 and found no statistically significant difference in the proportions of patients from each deprivation group. Chi 4.203, df 2, p = 0.122.

Is there any difference in time taken to first treatment with regard to deprivation status?

Following the results from table 17 above, we would expect that as there is a statistically significant difference in the proportions of elective and emergency admissions compared to socioeconomic status there could be a difference in time to first treatment according to socioeconomic circumstances.

Of the 7749 patients with colorectal cancer in the West of Scotland from 2000-2005, 5668 (73.1%) had data regarding time taken from date of diagnosis to date of first treatment. Of these, 5656 patients waited up to a year for treatment. There was no difference seen between groups from different social circumstances. This information is displayed in figure 23.

Figure 23 - Boxplot of time taken to first definitive treatment for all 5656 patients with colorectal cancer and valid data from 2000-2005 according to deprivation group. n =5668.

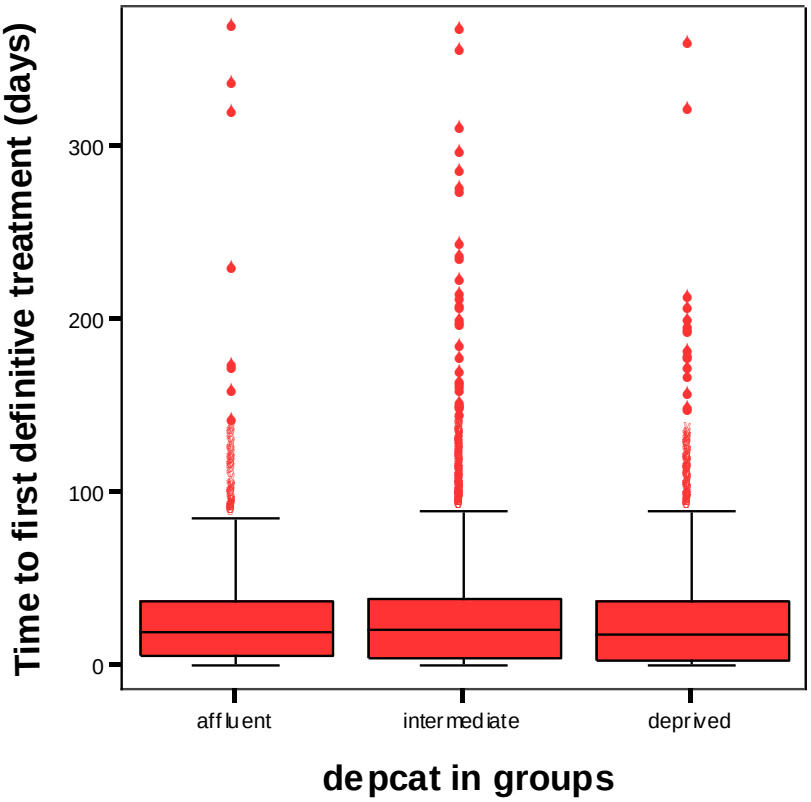


Table 19 displays the 1-way ANOVA analysis undertaken to test for a significant difference in mean time taken to first definitive treatment. The mean times to first definitive treatment for affluent, intermediate and deprived patients were 30.57, 32.29 and 30.66 days respectively. There was no statistically significant difference found, p = 0.34.

Table 19 - 1-way ANOVA of socio-economic group by time to first definitive treatment from date of diagnosis for 2786 colorectal cancer patients from 2000-2005.

	N	Mean	Std. Deviation	Std. Error	95% CI Lower Bound	95% CI Upper Bound
affluent	450	30.57	27.80	1.31	28.00	33.15
intermediate	1627	32.29	30.30	0.75	30.82	33.76
deprived	709	30.66	28.06	1.05	28.59	32.73
Total	2786	31.60	29.35	0.56	30.51	32.69

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1875.29	2	937.65	1.09	0.34
Within Groups	2396843.43	2783	861.24		
Total	2398718.72	2785			

Relationship between socioeconomic circumstances and decision to undergo surgery.

Table 20 shows proportions of all patients within each DEPCAT group receiving surgery or not. This result indicates that there is no statistically significant evidence that surgical treatment is associated with patients' socio-economic circumstances. There is a 1.7% difference between affluent and deprived, and a socio-economic trend from affluent to deprived. It indicates that the chances of receiving surgery are not affected by SEC. When subdivided into rectal and colonic cancer patients there was no statistically significant difference found with n=1993 (p=0.164) and n=5029 (p=0.905) respectively.

Table 20 - Comparison of deprivation group with decision to undergo surgery in all colorectal patients in the West of Scotland from 2000 to 2005. n = 7022, p = 0.474

Deprivation category	receiving surgery n (%)	not receiving surgery n (%)
Affluent	919 (85.3)	158 (14.7)
Intermediate	3411 (84.3)	633 (15.7)
Deprived	1590 (83.6)	311 (16.4)

The above findings were further explored using univariate and multivariate Cox proportional hazards modelling in order to determine which factors exert an independent influence upon outcome. Of all the factors tested on univariate analysis, all retained their significance in the multivariate model apart from site of tumour. By not having surgery, the HR was 2.04. If a patient presents as anything but an elective case, the HR was 2.78. There was an increasing HR noted with worsening SEC with affluent as a baseline. Worsening disease stage was also an independent prognostic indicator with a HR of 34.74 for Dukes' D disease compared to Dukes' A as baseline. Increasing age retained its significance as an independent prognostic indicator in the multivariate model. A 5% increased risk of death (HR 1.05) was seen with every years increase in age.

Table 21 – Combined univariate and multivariate analysis of factors determining patient outcome in all colorectal cancer patients in the West of Scotland from 2000 to 2005. n = 7022. *continuous variable.

		Univariate		Multivariate
Variable	**p**	**HR(95% CI)**	**p**	**HR(95% CI)**
surgery yes or no (yes baseline)	<0.001	10.19 (8.29-12.52)	<0.001	2.04 (1.48-2.82)
presentation for surgery (elective baseline)	<0.001	3.26(2.83-3.75)	<0.001	2.78 (2.37-3.26)
affluent	0.00	1.00	<0.001	1.00
intermediate	0.03	1.14(1.01-1.28)	0.01	1.25 (1.05-1.50)
deprived	0.00	1.35(1.18-1.53)	<0.001	1.57 (1.29-1.91)
Dukes' stage A	<0.001	1.00	<0.001	1.00
Dukes' stage unspecified	<0.001	3.55(3.00-4.21)	<0.001	3.33 (2.60-4.25)
Dukes' stage B	<0.001	1.92(1.62-2.27)	<0.001	1.74 (1.39-2.19)
Dukes' stage C	<0.001	9.17(7.71-10.92)	<0.001	3.54 (2.82-4.43)
Dukes' stage D	<0.001	41.46(32.72-52.53)	<0.001	34.74 (25.04-48.19)
colon or rectum (colon baseline)	<0.001	1.27(1.16-1.40)	0.21	0.91 (0.79-1.05)
age (by year)*	<0.001	1.04(1.04-1.05)	<0.001	1.05 (1.04-1.05)
sex (female baseline)	0.21	1.05	0.97	

Patients were divided into 2 groups. Firstly, those from 1997 to 1999. Then 2000 to 2005, i.e. pre-MCN inception and MCN respectively. Our hypothesis is that any differences noted with regard to type of surgery performed could be due to the effect of open discussion of cases in the MDT forum. We found that patients from 1997-1999 from more affluent circumstances were significantly (p=0.018) more likely to receive a curative surgical procedure. As noted above, socio-economic deprivation is not associated with more advanced stage at presentation. This pertains to all colorectal cancer patients before the inception of the MCN, that is, before 2000. Given that there is no difference in stage at presentation, as presented above, there may be other reasons to explain this difference. There was no difference found when comparing proportions in the same group from 2000 onwards. MCN implementation, Intent of surgery vs Deprivation group in all colorectal cancer patients undergoing surgery in the West of Scotland from 2000-2005. n=6776, p=0.172

Further subgroup analyses confirmed this trend for patients with colonic tumours. Those with rectal cancer did not display the same trend however. This may be due to the lower number of overall cases of rectal cancer.
Table 22 provides evidence for the factors determining the decision as to whether the intent of operation was deemed curative or palliative.
Only Dukes' stage and presentation for surgery were statistically significant determinants in relation to operative intent. These retained their significance in the multivariate model.

Table 22 – Univariate and multivariate findings for all 4873 colorectal cancer patients undergoing surgery from 2000-2005 in the West of Scotland. Factors linked with operative intent.

Variable	Univariate		Multivariate	
	p	OR (95% CI)	p	OR (95% CI)
Age	0.64	1.00 (1.00-1.01)	0.00	1.01 (1.00-1.02)
Sex	0.38	0.94 (0.81-1.08)	0.51	1.06 (0.89-1.27)
Deprivation group				
Affluent	0.08	1	0.09	1
Intermediate	0.08	1.22 (0.98-1.51)	0.38	1.13 (0.86-1.47)
Deprived	0.03	1.31 (1.03-1.66)	0.04	1.34 (1.01 – 1.79)
Dukes' A	0.00	1	0.00	1
Dukes' B	0.00	0.07 (0.04-0.14)	0.00	3.98 (2.07-7.68)
Dukes' C	0.00	0.34 (0.26-0.45)	0.00	12.09 (6.28-23.26)
Unspecified	0.03	0.77 (0.61-0.97)	0.00	8.59 (4.51-16.37)
Dukes' D	0.00	15.37 (11.67-20.26)	0.00	189.86 (98.04-367.69)
Presentation for surgery (elective baseline)				
Emergency	0.00	3.38 (2.89-3.96)	0.00	3.00 (2.48-3.64)

Surgical complications and socio-economic deprivation

We sought to determine the extent to which postoperative complications are related to colorectal cancer patients in the West of Scotland. Thirteen commonly measured surgical and general medical complications were tested for their relationships with all 6321 colorectal cancer patients together, then separately with 4467 colonic cancer patients, and 1854 rectal cancer patients. No statistically significant association was found between greater socio-economic deprivation and any of the complications.

Survival analyses

Kaplan-Meier survival curves provide a helpful visual indication of survival differences between risk groups with logrank p-values indicating whether there are overall differences between them. However, Kaplan-Meier plots are univariate and therefore do not adjust for confounding effects such as the age differences between patients from different socio-economic groups. Cox Proportional Hazards Models (CPHM) allow for multiple adjustment of risk factors between groups. Additional information on casemix was available in the Cancer Registry from 1997 onwards and from 2000 onwards, further information was available from the MCN audit which was linked to Registry data. These are 1980-2005, 1997-2005 and 2000-2005.

Figure 24 indicates that increasing socio-economic deprivation was associated with significantly poorer all-cause survival (logrank test, $p = 0.037$) among all 11030 colorectal cancer patients treated by surgery in the West of Scotland between 1997 and 2000.

Figure 24 – All-cause Kaplan-Meier plot for all 3870 patients undergoing surgery for colorectal cancer in the West of Scotland from 1997 to 2000. n =11030. Log rank = 0.037

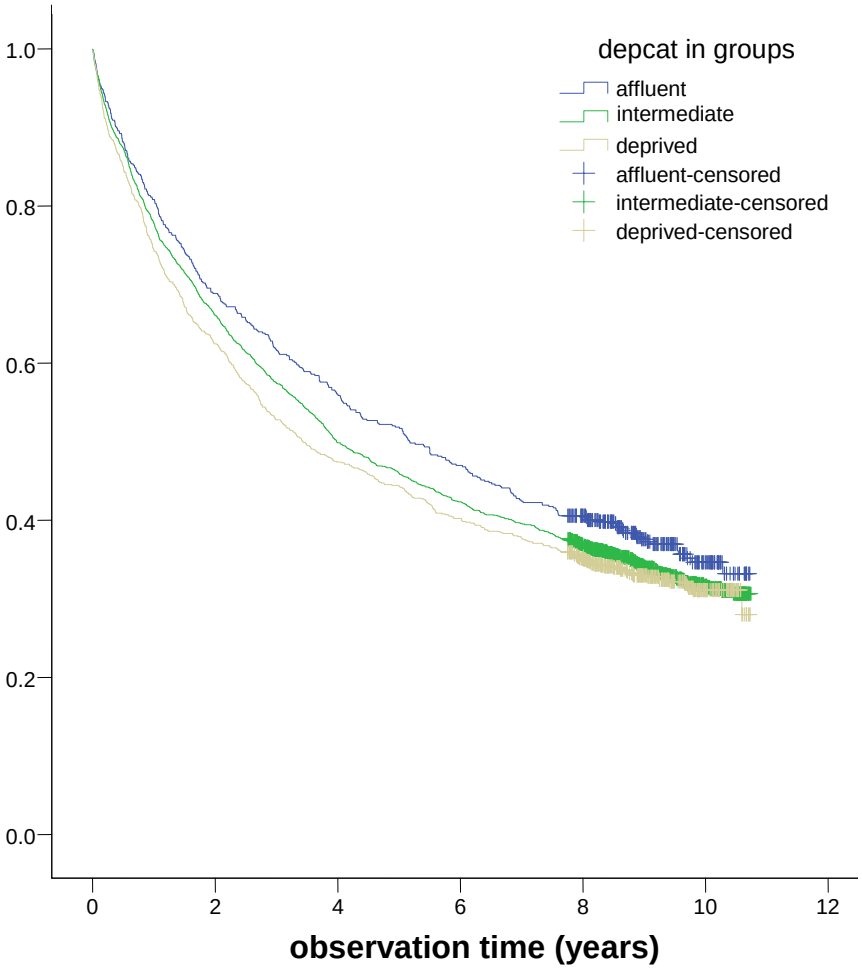
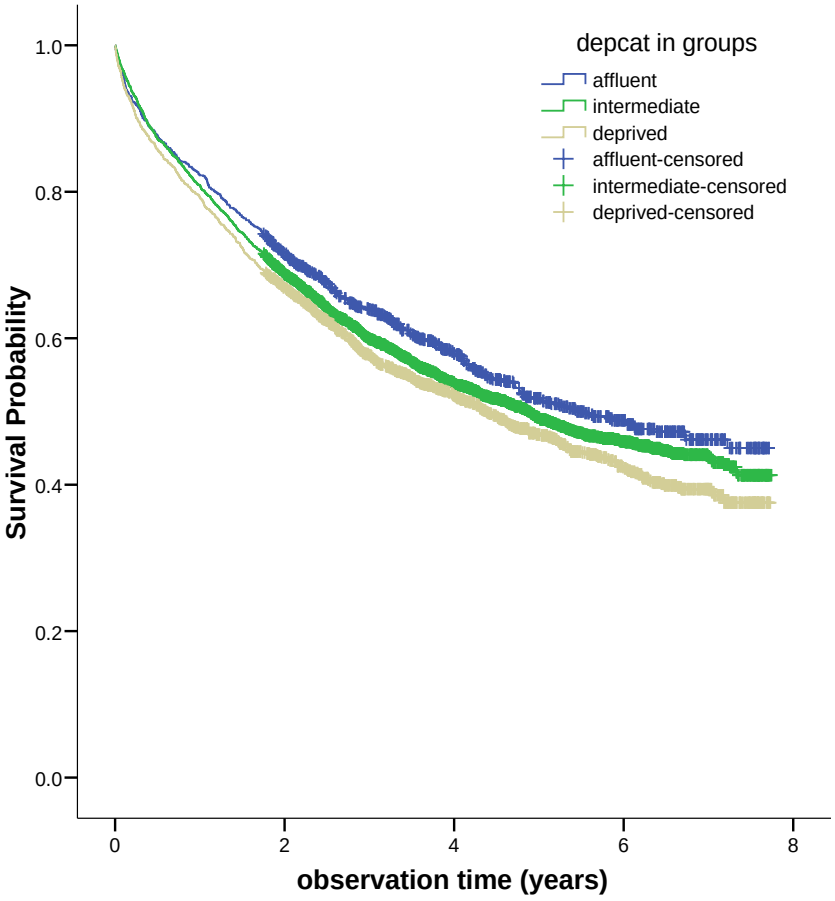


Figure 25 demonstrates a statistically significant and consistent relationship between worsening socioeconomic circumstances and poorer overall survival for all 7160 colorectal cancer patients undergoing surgery from 2000 onwards.

Figure 25 - All-cause Kaplan-Meier plot for all patients undergoing surgery from 2000 to 2005 according to socioeconomic circumstances. n = 7160, p = 0.003



All colorectal cancer patients

From 1980 to 2005, univariate analysis of all 37,964 patients with colorectal cancer yielded statistically significant differences for age group, deprivation group, Health Board of residence, year of incidence, and site of tumour. Inclusion of these five significant variables in the multivariable model returned results indicated that only site lost its individual prognostic significance for overall survival. In particular, being deprived confers an excess hazard of 15% compared to affluent patients, following adjustment for age group, Health Board of residence, and year of incidence.

Table 23 presents unadjusted (univariate) and adjusted (multivariate) hazard ratios for all-cause mortality among colorectal cancer patients in the West of Scotland between 1980 and 2005. Increasing age, worsening socioeconomic

circumstances, Health Board of residence and year of incidence were all significant predictors of all cause survival in both univariate and adjusted analyses. Compared with patients in the most affluent areas, patients in intermediate and deprived areas had increased mortality of 6% and 15% respectively. Compared with patients <55 years of age, those aged over 74 were at over 2.5 times greater hazard of death. Only Health Board five had a significantly different survival from the baseline area, Health Board one, with 12% greater hazard (HR 1.12, 95% CI 1.07 to 1.17). Hazards fell by 2% each successive year.

Table 23 - Univariate and multivariate results for all 37890 colorectal cancer patients with colorectal cancer in the West of Scotland from 1980 to 2005. SEC, age group, Health Board of residence, and year of incidence all contribute to explaining differences in overall survival.

	Univariate		Multivariate	
	p	HR (95%CI)	p	HR (95%CI)
Sex (female baseline)	0.30	1.01 (0.99-1.03)		
affluent	0.00	1	0.00	1
intermediate	0.00	1.08 (1.04-1.12)	0.00	1.06 (1.03-1.110)
deprived	0.00	1.17 (1.13-1.21)	0.00	1.15 (1.11-1.19)
Age <55	0.00	1	0.00	1
Age 55-64	0.00	1.24 (1.18-1.30)	0.00	1.26 (1.20-1.32)
Age 65-74	0.00	1.55 (1.48-1.62)	0.00	1.58 (1.51-1.65)
Age >=75	0.00	2.44 (2.34-2.55)	0.00	2.54 (2.43-2.66)
Health Board 1	0.00	1	0.00	1
Health Board 2	0.33	1.02 (0.98-1.07)	0.78	1.01 (0.96-1.05)
Health Board 3	0.13	1.04 (0.99-1.08)	0.47	1.02 (0.97-1.06)
Health Board 4	0.00	1.07 (1.03-1.11)	0.53	0.99 (0.95-1.03)
Health Board 5	0.00	1.09 (1.04-1.14)	0.00	1.12 (1.07-1.17)
Year of incidence	0.00	0.98 (0.97-0.98)	0.00	0.97 (0.97-0.98)
Site (colon baseline)	0.00	1.06 (1.04-1.09)	0.17	1.02 (0.99-1.04)

Table 24 focuses on patients from 1997 onwards. The addition of Dukes' stage and operative intent add a further two statistically significant, independent prognostic indicators of overall survival. Initially, the variables from the previous

table were used. Year of incidence lost its independent effect in this model. All other variables remain statistically significant. Deprivation remains an independent predictor of mortality even after adjustment for age, stage and site of lesion, exerting a 24% increase in hazard for deprived patients when compared to the affluent group. There were significant variations in hazard ratio between Health Board areas ($p<0.01$) such that residents of Boards three and four were at 13% and 14% lower hazard, respectively, compared with Board one.

Table 24 - Cox proportional hazards modelling results for all colorectal cancer patients undergoing surgery from 1997-2005.

		Univariate		Multivariate
	p	**HR (95% CI)**	**p**	**HR (95% CI)**
affluent	0.00		0.00	
intermediate	0.00	1.10 (1.04-1.17)	0.01	1.09 (1.02-1.17)
deprived	0.00	1.23 (1.15-1.31)	0.00	1.24 (1.15-1.34)
Age <55	0.00		0.00	
Age 55-64	0.01	1.15 (1.04-1.26)	0.00	1.23 (1.11-1.36)
Age 65-74	0.00	1.44 (1.32-1.57)	0.00	1.57 (1.43-1.73)
Age >=75	0.00	2.44 (2.24-2.66)	0.00	2.38 (2.17-2.62)
Health Board 1	0.01		0.00	
Health Board 2	0.26	0.95 (0.88-1.04)	0.27	0.95 (0.87-1.04)
Health Board 3	0.32	0.96 (0.98-1.04)	0.00	0.87 (0.80-0.95)
Health Board 4	0.38	1.03 (0.96-1.11)	0.00	0.86 (0.79-0.93)
Health Board 5	0.17	1.06 (0.98-1.14)	0.96	1.00 (0.92-1.09)
Year of incidence	NS			
Intent of operation (curative baseline)	0.00	6.75 (6.44-7.08)	0.00	4.10 (3.86-4.35)
Site (rectum baseline)	0.00	1.15 (1.10-1.20)	0.00	1.15 (1.09-1.22)
Dukes' Stage A	0.00		0.00	
Dukes' unspecified	0.00	6.16 (5.57-6.80)	0.00	2.92 (2.62-3.27)
Dukes' stage B	0.00	1.65 (1.49-1.82)	0.00	1.40 (1.26-1.55)
Dukes' stage C	0.00	2.70 (2.44-2.98)	0.00	1.75 (1.58-1.95)
Dukes' stage D	0.00	9.88 (8.94-10.92)	0.00	3.41 (3.04-3.83)

3.6 Summary – Demographics and Determinants of Survival

Overall survival is poorer among patients from more deprived areas. Compared to their affluent counterparts, deprived patients with colorectal cancer have a 24% increased hazard following adjustment for age, stage of disease, Health Board of residence and operative intent.

A mean case ascertainment of 98% was achieved for the eight variables available from 1980 onwards. We found that median age at incidence was three years higher in women compared to men. There was an increase in mean age at incidence with time for both sexes separately and overall (ANOVA, P <0.001 for all 3 tests). Men increased in mean age at incidence from 67.43 in 1980 to 69.05 in 2005 whereas women increased in mean age at incidence from 71.00 to 71.57 over the same time period.

No statistically significant difference was noted when comparing proportions of colon cancer patients from different deprivation groups with sex (p=0.836) whereas a statistically significant difference was found when comparing proportions of rectal cancer patients from different deprivation groups with sex. 32.7% of male rectal cancer patients were from the deprived group compared to 29.7% of female rectal cancer patients. The affluent group contained 12.6% of the male rectal cancer patients whereas 14.9% of female rectal cancer patients were in the affluent group. N = 10114, p<0.001. We noted a higher proportion of rectal cancer patients in the Lanarkshire Health Board compared with other health boards.

A reduction in the proportion of deprived patients with time from 35% in 1980 to 30% in 2005 was noted. This was mirrored by an increase in the proportion of intermediate patients from 52% in 1980 to 60% in 2005, while the proportion of patients in the affluent deprivation group remained constant with time. We found that affluent patients tended to be older at time of incidence compared to their more deprived counterparts. Furthermore, there were significantly more men with rectal cancer across all deprivation categories. This was not the case with colonic cancer patients. There was no statistically significant difference in the proportions of males and females with colorectal cancer in each deprivation group but we found that affluent patients tend to have more colonic cancers and

fewer rectal cancers. Also, there were more affluent people with Dukes' A disease and more deprived people with Dukes' D disease in this population.

Regarding patients enrolled in the MCN, there was a 5.15 year increase in median overall survival compared to those patients not in the MCN. Of the measurable variables age at incidence, degree of socioeconomic deprivation, degree of disease burden, having a colonic tumour (as opposed to rectal) and whether or not the patient had entered the MDT process all help to account for the difference in overall survival seen between those enrolled in the MCN and those not. In terms of five year overall survival, only female rectal cancer patients were found to have a significantly improved survival following introduction of the regional MCN compared to the baseline improvement that would have been expected without an MCN.

For all 3763 patients with colorectal cancer undergoing curative intent surgery from 2001 to 2005 age, socioeconomic circumstances, Dukes' stage, extra mural vascular invasion, and sex were all significant prognostic indicators of overall long-term outcome. The MDT in which patients were treated was a significant independent variable on univariate analysis, but not when included in the multivariate model. In all rectal cancer patients undergoing curative intent surgery from 1997-2005 survival was found to have increased by 23% (HR 1.23, 95% CI 1.05 to 1.44) after introduction of the regional MCN in 2001.

We found that the chances of receiving surgical intervention for colorectal cancer are not determined or influenced by socioeconomic circumstances. This demonstrates an equitable and unbiased provision of service. This is a key tenet of the MCN model and aim of the cancer services reorganisation.

No statistically significant association was found between greater socio-economic deprivation and any of the immediate postoperative complications recorded.

Increasing age, socio-economic deprivation, Health Board of residence and year of incidence were all significant predictors of all cause survival in both univariate and adjusted analyses for all 37890 colorectal cancer patients in the West of Scotland from 1980 to 2005. Compared with patients in the most

affluent areas, patients in intermediate and deprived areas had increased mortality of 6% and 15%, respectively. Compared with patients <55 years of age, those aged over 74 were at over 2.5 times greater hazard of death.

3.7 Discussion

Regarding demographics of our population, we found results consistent with previous series (67). There was a significant increase in mean age at incidence with time in the West of Scotland from 1980 to 2005. Of the entire colorectal cancer population in the region from 1980 to 2005, 19023 (50.1%) were male. The mean age of males was 69.15 compared to 72.17 for women. Three year overall survival has increased from around 30% in 1980 to approximately 45% in 2004 with rectal cancer survival increasing more markedly from 30% in 1980 to approximately 55% in 2004. The increase was more pronounced for female patients with rectal cancer. We have demonstrated a statistically significant larger proportion of Dukes' A tumours at the rectum along with a higher proportion of Dukes' C & D stage tumours in the colon. Stage A disease at incidence is more common in the rectum than colon. Women tend to present with more proximal lesions compared to men, who tend to present with more distal lesions. A higher proportion of non-MCN patients had Dukes' stage D disease (44.4% versus 23.7% respectively). Non-MCN patients were also significantly older. Site of lesion remains a significant independent prognostic indicator. There was significant variation in overall survival between Health Boards despite adjustment for age, sex, stage and SEC.

Trends with age

The mean age at diagnosis has recently been reported as 73 in a large review of the US literature on colorectal cancer (184). This compares well to the mean age of 71 in the West of Scotland. This difference may be a significant difference as it involves large populations. It could be explained by the fact that the population in the West of Scotland is more deprived, the methods of data collection are more accurate, and the case ascertainment percentage is higher. Methods of cancer detection may also be more widely employed in our population as we have a different healthcare system compared to the US. The

population of the West of Scotland may also be less prone to migration, a common cause of underreporting of incident cases of cancer.

In the United States, men are more likely to develop colorectal cancer and to die from it than their female counterparts. Women tend to develop colorectal cancer later in their lives than men (184). Data presented in the results section confirm these two findings in our population with men outnumbering women by 19023 to 18941 at a mean age of 69.15 compared to 72.17 ($p<0.001$). It is thought that this is due to a biological protective effect of oestrogens as women are found to develop colorectal cancer more frequently after the menopause. To date though, this has only been supported by a large study showing a protective role of exogenous hormones in the risk of colorectal cancer among women (185). Unfortunately there was no way to account for degree of comorbidity in our patients. Only 1618 patients of a total 11070 undergoing surgery (i.e. 14.62%) had ASA grade assigned. This was felt to be too small a number to provide meaningful results. One method of attempting to account for this would be to match patient details with SMR01 records. The number of hospital admissions during the six months prior to diagnosis could then be calculated and be used as a proxy marker for comorbidity.

We have shown that there was a significant increase in mean age at incidence with time in the West of Scotland from 1980 to 2005. This was statistically significant for both sexes together and individually ($P <0.001$ ANOVA).
We wanted to know whether there was an age bias when selecting intent of operation in the West of Scotland. Our results indicate that of the 5196 patients with these data, there was no significant difference in operative intent between age groups ($p= 0.827$). Unfortunately these data have only been recorded since the inception of the MCN so there is no way to tell whether or not the MCN has had an effect in the decision making process with regard to intent. We were also unable to assess the degree to which elderly patients are given chemotherapy for metastatic disease. This is an area where there has traditionally been a lot of bias towards younger patients due to the perception that older colorectal cancer sufferers will fare worse than their younger counterparts when given chemotherapy. This issue is summarised succinctly in a recent editorial (186).

Of the 11063 patients from 1997-2005 with data regarding age at surgery there was no statistically significant difference between the year of incidence and the age group at surgery (p=0.051). This was also confirmed by testing ANOVA using age as a continuous variable.

Numerous questions abound with regard to age and colorectal cancer patients. These become more important as the population demographics change towards a more elderly population. One could also argue that as patients who will be undergoing resection become older, they require a wider range of specialities to provide input into their management as they are more likely to have more co morbidities. This provides a reason for MDT discussion and has repercussions for changes in service provision.

In an MDT the prevailing attitude should be equality of treatment at any age, dependent upon suitability for treatment. Previous reports suggest that there is a bias towards younger patients when selecting for suitability for chemotherapy (187). Prior to this, a Dutch group had already reported in a series of 294 patients who were stage and site matched, that there were no statistically significant differences in postoperative complications and cause specific survival when comparing a group of young patients (mean age 63) and a group of older patients (mean age 80) (188).

A further issue regarding age is that of age at surgery. With an increasingly older population (proven above) one would expect to find a significantly larger proportion of patients in the >75 age group with time. It would appear from our data that this is not the case. This may point towards a bias in patient selection for surgery but it may also mean that the decision to palliate patients is being made appropriately.

Trends with gender

Of the entire colorectal cancer population in the region from 1980 to 2005, 19023 (50.1%) were male. The mean age at incidence for males was 69.15 compared to 72.17 in women, mean difference of 3.02 years with a corresponding 95% confidence interval (2.78,3.25) assuming equal variances.

This result indicates that women are in general older by three years at time of incidence compared to men, confirming findings from a large U.S. review paper by Payne (184). These appeared to be spread equally between Health Boards but chi square testing revealed a statistically significant difference between Health Boards in relation to sex. This is likely to be due to the large number involved. It is accounted for in any conclusions drawn from the data.

Women have a greater risk of proximal colorectal cancer, which tends to be more advanced when diagnosed. Despite this, women experience a better survival outcome compared to men for this type of tumour. The better overall survival prospects are thought to relate in part to biological and genetic factors and in particular to sex differences in the immune function, where female sex steroids offer women protection both from the disease and also in terms of survival (184). We measured overall survival for all 14097 patients with colorectal cancer from 1997-2005. There was no statistically significant difference between the groups at a mean follow-up of 4.6 years (Log Rank = 0.55). This is due the fact that adjustments had not been made for age, stage and site.

There are variations between women and men in the type and location of colorectal cancer experienced (outlined below), which relate in part to biological factors including hormones and gene expression. For example, right-sided colon cancer is highest among women, men more often have cancer of the left colon, and men are more frequently diagnosed with rectal cancer. These findings suggest sex or biological differences between men and women. Research on hormonal factors also suggests a biological basis for the gap (185). Women tend to develop colorectal cancer at a later age, which may reflect the protective effect of female hormones prior to the menopause, and possibly also Hormone Replacement Therapy (HRT). Studies of the association between HRT and colorectal cancer suggest it reduces the risk of colon cancer but not rectal cancer (189). Further evidence to support this theory comes from the US where a reduction in women's colorectal cancer rates was witnessed in the 1950s when hormonal treatment came into use. It was not witnessed in men until the 1980s or 1990s. There is also an association between cancers of the female

reproductive system and colorectal cancer (184). Despite this, women, on average are older at presentation for colorectal cancer in our region.

The largest colorectal care survey ever undertaken in Australia found that men were more likely to suffer from colorectal cancer than women and that rectal cancer was more common in men than women (71). We have confirmed both of these findings herein with a total of 10114 rectal cancer patients from 1980 to 2005, 5694 (56.3%) of whom were men.

Overall survival

To our knowledge, this is the first time that this type of linear regression modelling has been applied to explore the effects of introducing an MCN in relation to overall survival of colorectal cancer patients.

Three year survival

It has been demonstrated that from 1980 to 2004 there was a steady increase in three year overall survival for both sexes in colon cancer and rectal cancer. Three year overall survival has increased from around 30% to approximately 45% in 2004 with rectal cancer survival increasing more markedly from 30% in 1980 to approximately 55% in 2004. The increase was more pronounced for female patients with rectal cancer. In all cases of rectal cancer, the most pronounced increase in survival was seen to happen around the mid-1990s. This can best be explained by the introduction and adoption by rectal surgeons of the TME technique for resecting the rectum and mesorectum en bloc (92). Only now are surgeons beginning to treat colonic resection with the same embryological approach to enable more accurate resection of the tumour, the so-called CME – complete mesocolic resection. This technique aims at the separation of the mesocolic from the parietal plane and true central ligation of the supplying arteries and draining veins right at their roots. It is almost never performed in the UK (190).

Our novel approach to assessing long-term survival differences using linear regression models generated some significant new findings for colorectal cancer

patients in the West of Scotland. We tested all permutations of three year overall survival from before and after inception of MDT care. Firstly we tested long-term differences from 1980 onwards. We then looked at 1997 onwards. The significant findings were than from 1980 onwards three year overall survival for rectal cancer has significantly improved. It has also significantly improved for females alone but not males alone. This suggests that the survival improvement for females is so great that it explains the increase noted for both sexes. A possible explanation is that women have a better stage at presentation or there are more female cases so their increase in number exerts a bigger effect on survival. In fact though, there are more male cases of rectal cancer and they have a lower Dukes' stage at presentation. These findings could also have been confounded by casemix, or the paucity of data points resulting from too short a follow-up period.

Data for overall three year survival from ISD shows a steady increase in survival with time from 1980 onwards (58). This was not demonstrated in our linear regression model for overall three year survival in colorectal cancer patients. It may simply be a reflection of the shorter time frame of our data recording coupled with a smaller number of patients than those in the ISD database.

Five year survival

It has been shown that similar patterns of survival exist at five years, as do three years for colorectal cancer patients in the West of Scotland. The larger differences in survival between male and female rectal cancer patients appear to be attenuated slightly in terms of five year survival. However, these figures reflect overall survival so perhaps cancer specific or relative survival models would attenuate the difference further.

Nonetheless, a switch from colonic tumour patients surviving longer to rectal patients surviving longer is noted in the five year data. Again this seems to have happened around 1993 and could be partly attributed to the introduction of TME.

Our novel approach of linear regression modelling was not applied to five year overall survival as it was felt that the data were not mature enough to provide

any meaningful results. The West of Scotland data would be worth analysing in this way once deaths from 2010 are complete.

Trends with Site of Tumour

Survival following resection of colorectal cancer relates in part to location of the cancer, with better prognosis for distal cancers (see Table **24**). Distal cancers tend to present at an earlier stage too, particularly in men, whilst in women the majority of colorectal cancers are right sided.

Site of lesion has been shown to bear strong correlation to stage of disease in a large U.S. study examining 40% of the American population. They concluded that stage of presentation was more advanced with more proximal disease (191). We have been able to confirm these findings in the West of Scotland. We have provided evidence of a statistically significant larger proportion of Dukes' stage A tumours at the rectum along with a higher proportion of Dukes' C & D stage tumours in the colon.

Univariate analysis of our dataset confirmed a significant difference in survival between rectal lesions and other colonic sites. This agrees with published data from ISD, with stated observed 5 year survival rates of 43.75% for rectum and 41.25% for colon and respectively (192). Although it is encouraging that we have been able to corroborate previous findings regarding trends with site, the problem remains with accurate anatomical description. There are currently no internationally agreed definitions for exactly where the proximal and distal boundaries of the rectosigmoid area are. As a result there is a tendency to either group it along with rectum or with colon, thus creating a potential source of error when attempting to interpret outcomes from different studies. This is further compounded by variation in reporting by pathologists. It is hoped that published guidelines will be adhered to thus helping to reduce the uncertainty in this area (193).

Trends with Stage

Staging of disease is an extremely important part of patient work up as described in the introduction. Ideally, it is optimal to diagnose patients at as early a stage as possible. To that end, recording of stage data is equally important, in order to facilitate this. We have shown that with time the number of patients not having a Dukes' stage recorded has risen from 12.3% in 1997 to 23.1% in 2005 with a peak of 31.1% in 2003. Whilst this has important implications for adjuvant treatment selection there are a few reasons why this may have occurred.
Some patients with a polyp cancer are diagnosed and treated at colonoscopy. A diagnosis of cancer is made histologically. No Dukes' stage is ever attributed as they have already had complete resection of a tumour. Staging will not affect treatment.
More pathologists are turning towards the TNM classification for staging colorectal cancer patients.

Those patients in whom a polyp is resected and found to be cancerous should all go on to be discussed at an MDT and receive the appropriate treatment. The royal college of pathologists' minimum dataset was introduced in 1996 so the reduction in Dukes' stage recording should not be due to reduction in reporting by pathologists (84). It is possibly due to recording errors by the audit team when collating data to be sent to the MCN database (Margaret Balsitis, personal communication).

We have also compared our data with those most recently published by the National Cancer Intelligence Network (NCIN) (194). It is encouraging that we have a higher rate of stage data in the West of Scotland however the trend towards an increased number of patients without Dukes' Stage recorded requires addressing.

Our comparison with the NCIN data demonstrates a further difference in stage proportions. In the West of Scotland stage D disease accounts for 18.73% of cases with stage data. This compares to only 9.2% from the eight cancer registries reporting in England. These data cover the period before, during and after

inception of MCNs so perhaps if they were broken down and compared over more recent years the discrepancy would be less. If these data are accurate, it bodes well for the potential success of screening in the West of Scotland, as patients in this region may benefit more from down staging of disease. By removing all patients with unknown stage it has been shown that a higher proportion of stage D patients persists in the West of Scotland. Down-staging of disease at diagnosis will confer a survival benefit. This is the hope with increasing public awareness and the current screening programme in Scotland (195).

The incidence of stage I disease in the United States is now 30%. This compares to 13.9% and 13.1% of known stage A patients in the West of Scotland and NCIN series respectively (194). It is thought that this increase is due in the main to better screening. Increased public awareness of symptoms and lower threshold to attending a physician also remain important (139).
For people who have none of the risks described earlier, digital rectal examination and testing of the stool for hidden blood are recommended annually beginning at age 40. Flexible sigmoidoscopy is recommended every 5 years at age 50 or older. A double contrast barium enema every 5 to 10 years, and colonoscopy every 10 years are acceptable alternatives (196).

Our findings with regard to age suggest a significant difference in stage at presentation with differing age group. Fewer stage D patients were found in the older age groups, with a higher proportion of patients in stages B and C occurring in the middle two age groupings. It was necessary to explore this further in terms of sex differences. Stage A and stage D disease was more common in males whereas there was a preponderance of females with stage B disease. Stage C disease was found to have almost equal incidence between sexes. With regard to the West of Scotland there is a significant change in stage distribution at presentation with time for males only. Pearson Chi squared test = <0.001. This was not significant for females (Pearson Chi squared test = 0.190). This is for all patients in the MCN so does not exclude palliative procedures nor those patients who did not go ahead with, or were unfit for, surgery.

The next finding concerns site and its relationship to stage. We confirmed the known trend that as one travels distally along the gastrointestinal tract, the

likelihood of patients presenting with an earlier stage tumour increases ($p<0.001$). A more proximal tumour will present later as it takes more time to become symptomatic. This is thought to be due to the wider lumen of the proximal colon and the liquid nature of its content. There is more space for the tumour to grow into before either obstructing the bowel or causing pressure symptoms by pressing on to adjacent structures. This echoes previously cited findings by Cheng at al that "The disease stage was highly correlated with the anatomical site of location. Localised disease increased from 31.9% among cancers of the proximal colon to 37% in the descending colon and 41.5% in the distal colorectum. The percentage of regional disease stage decreased from proximal to distal" (197). This is in comparison to rectal cancers - they will produce more easily recognisable symptoms (e.g. bright blood compared to altered blood, tenesmus, and change in bowel habit) and hence are diagnosed at an earlier stage.
A further statistically significant result was found by comparing just stage A and B disease in the rectum versus colon. Stage A disease is more common in the rectum than colon.

Again, we have confirmed previous findings from the USA for our population, namely that that there is a statistically significant difference between sex and site for lesion. Women tend to present with more proximal lesions compared to men, who tend to present with more distal lesions (184).

It is thought that these differences are due to underlying genetic heterogeneity between the sexes. Difference sex hormone profiles are also putative causes for the observed difference. McGrath et al also found that patients with rectal cancer were both more likely to be male and also more likely to have a stage A tumour when compared to colonic tumour patients (71). This was a statistically significant finding and is confirmed in our series.

The Influence of the MCN

One of the aims of this thesis is to compare outcome of the group of patients in the MCN with those not in the MCN. As has been shown, the number of patients not entered into the MCN dramatically decreased from 2001 onwards, as the

evolving network captured more patients and their clinical data. The average figure for each year thereafter is around a set point 400 patients. One would expect this number to remain constant with time, as there will always be a number of patients not registered with the MCN because they are DCO diagnoses; private hospital patients, those diagnosed and remaining in care homes to be palliated, or those that are treated in another region then migrate into the West of Scotland before dying here. These rates can vary significantly between countries due to different laws surrounding autopsy without consent. In countries where no consent is required for a post mortem examination there will be a higher rate of cancer diagnosis after death (198).
Since those patients not in the MCN have no clinical audit data associated with them we were only able to compare variables relating to age at incidence, site of lesion and Dukes' stage, i.e. the cancer registry variables. In summary, the groups were very heterogeneous. Two-sample t testing revealed a statistically significant difference in age at incidence, with patients not in the MCN being 2 years older on average. A higher proportion of the non-MCN patients had Dukes' stage D disease (44.4% versus 23.7% respectively). This reflects the fact that many of the patients not entering MDT care may be too unwell and are therefore palliated at home or the diagnosis is made at post mortem.

In relation to site of lesion, the numbers were similar. The only discrepancy was in terms of unspecified lesions. Of those in the MCN only 9% had a lesion of unspecified site whereas 15.3% of patients not in the MCN had an unspecified site. This may reflect the fact that site of lesion is more important for patients in the MCN as it influences their surgical and chemotherapeutic management. Many patients not in the MCN may not need to have their site recorded as it will have no influence on outcome.

A significantly higher proportion of rectal cancer patients were found in the Lanarkshire Health Board. Also a higher proportion of male rectal cancer patients were from the deprived group compared to females, 32.7% and 29.7% respectively.

We demonstrated that site of lesion remains a significant independent prognostic indicator and that there was significant variation in overall survival

between Health Boards despite adjustment for age, sex, stage and SEC. This may be due to other hitherto unidentified variables accounting for differences or it may indicate a true difference in outcome due to differences in service provision in some Health Boards.

An aim of the MCN is to capture as many cases of colorectal cancer as possible. Following comparison of groups enrolled and not enrolled in the MDT process it seems that the MCN selected younger individuals with better prognoses and more accurate staging data. Various explanations could account for this as outlined previously. It is also likely that with the passage of time the process of patient identification and data capture becomes more efficient at identifying patients with colorectal cancer. This will reduce the selection bias of the MCN process.

Analysis to determine whether there has been an increase in patient survival showed that being treated before the MDT era or within an MDT does not act as an individual indicator of prognosis. This is possibly due to the relatively short period of time over which differences have been studied.

In relation to socioeconomic circumstances, the distribution of socioeconomic deprivation in the West of Scotland has altered such that there has been a shift from fewer deprived patients in our region to more in the intermediate group ($p<0.001$). The proportion of affluent patients with colorectal cancer seems to have remained constant with time. If this trend continues then it should translate into a measurable survival improvement. The effects of screening would need to be accounted for also.

The findings regarding postoperative complications demonstrated no direct correlation with a patient's preoperative SEC in any of the subgroups studied. This means that long-term differences in survival are not explained by events occurring in the peri-operative period in this population, and is an argument for excluding the first 30 days post-op from future survival analyses.

Long-term survival demonstrated a significant difference between deprivation groups with poorer survival in more deprived populations. We showed this consistently among patients from 1997 onwards and then in the cohort from 2000 onwards, i.e. under the influence of an MDT decision making process.

Novel linear regression modelling showed that for select subgroups of patients there has been an increase in three year overall survival as a result of having been treated by the MDT process. These subgroups include all female colorectal cancer patients from 1997-2005, female rectal cancer patients from 1980-2005 and all rectal cancer patients from 1980-2005. Only female rectal cancer patients demonstrated a survival benefit from MDT treatment over five years.

These findings suggest that the MDT process has somehow benefitted women with rectal cancer over men from MCN inception. This is perhaps due their differing anatomy and relative ease for rectal cancer resection. It could also reflect a difference in underlying demographics and co morbidities between the sexes. Unfortunately there are not enough data from before 2000 to further explore this.

Socioeconomic Circumstances

We sought to examine the potential bias inherent in the MCN system towards those from deprived socio-economic backgrounds. In order to do this we looked at different stages in the process from diagnoses to end of follow-up. This was done firstly in relation to stage at presentation. Then we looked at deprivation and its effect on time from referral to treatment. We ascertained if there were any differences in type of operation received in relation to deprivation before assessing immediate 30-day outcome after surgery. Finally we looked at long-term outcomes in terms of the effect of deprivation on survival. Accepting that unbiased patient selection, management, and outcome in relation to deprivation is a marker of an equitable service this allows assessment of the service quality to be made.
The proportions of patients in each deprivation group are consistent with previously published data on Carstairs scores for Scottish postcode sectors from the 2001 Census by Philip McLoone (199).

A central component of the MDT ethos is to provide an equal standard of care to patients from all backgrounds. Using depgroup (modified DEPCAT) as our objective measure for socio-economic deprivation we have ascertained that in our population there is no difference in deprivation status compared to stage at

presentation. This result holds when examining rectal cancers alone, colon cancers alone, and further by examining each sex within these subgroups.
In the present study we found no statistically significant difference in stage at presentation according to deprivation group. The overall p value for all colorectal cancer patients was 0.058. No other subgroups under study achieved statistical significance. The current literature regarding this topic comes mainly from the UK although 2 US studies are commonly cited. Opinion is divided as to whether or not deprivation influences stage at presentation. Some groups have found no relationship between deprivation and stage at presentation whereas others *have* found an association (65,200,201)(64,73,202).

In relation to entering the MDT process, it has also been shown that deprived patients may experience delay to referral and may also be less able to access services such as specialist surgery or adjuvant therapy (203,204).
Although this may act more as a political point we have demonstrated that waiting longer than 62 days from time of referral to first definitive treatment has no detrimental effect on outcome. This is presumably because consultants employ their own clinical judgement to expedite cases they deem to need treatment more quickly than others.

Once a patient has entered into the MDT process, it has been reported that they are more likely to receive certain types of operations if they are more socio-economically deprived. Patients lower on the socio-economic scale have been found to be more likely to undergo APE than AR for cancer where there is a choice of operation (43,44). It is thought that overall an APE negatively impacts quality of life in addition to having lower long-term cost-effectiveness for the NHS when compared to anterior resection. In our series of 1390 patients having either an APE or AR we found no statistically significant difference when comparing proportions of patients from each deprivation group with type of operation.

In a series of 653 cases of colorectal cancer patients a group from the North East of Scotland reported few differences in proportions of patients receiving surgery with relation to deprivation however they did report that more deprived patients were statistically less likely to be offered radiotherapy as an adjunct to

treatment. This is grade C evidence (177). We are not currently in a position to explore this aspect further in our cohort. Instead we examined the intent of operation according to deprivation group. We found no statistically significant difference between operative intent and deprivation in 3524 colonic cancer patients or 1399 rectal cancer patients undergoing surgery. This, however does not ignore the fact that the decision as to whether a resection is curative or palliative is based solely on the surgeon's impression at time of surgery. Therefore one surgeon may label a case as curative where there is a borderline resection adequacy whereas another surgeon would label it palliative. This problem has previously lead to the suggestion that the 'true' hazard ratio for cancer survival rates in curative resection cases in some hospitals is probably higher than that calculated (68).

It has been previously demonstrated that socially deprived patients have poorer cancer-specific survival than their less deprived contemporaries. We already know that more deprived patients are not as healthy as their affluent counterparts. This holds true with regard to longevity also, with affluent individuals living longer (74). McArdle and Hole reported in 2002 that among other factors (namely sex, stage and age) deprivation significantly influenced survival following potentially curative resection for colorectal cancer. This was a larger study covering 11 different hospitals in the central belt of Scotland, a region with a large socio-economic spread and large population (65). More recently Smith (2006) and colleagues have proffered results demonstrating that social deprivation was an independent risk factor for increased length of stay and associated with increased postoperative mortality (64). We were not able to confirm this finding in our population. We found that of the 163 colorectal cancer patients who died within 30 days of surgery there was no statistically significant difference in deprivation group at the 5% probability level ($p = 0.088$).

Then when looking at overall survival (not cancer-specific survival as with Hole and McArdle) in a univariate model for deprivation, we found a significant difference in survival for all colorectal cancer patients at 6 years. This difference was however explained by age, sex, Dukes' stage, bowel preparation, tumour differentiation and extra mural vascular invasion in a Cox multivariate model.

As a set of results these are encouraging. They provide evidence for the case supporting the equal provision and outcomes of the Regional Colorectal cancer service to all patients despite the large degree of heterogeneity in social deprivation within our region. The Dukes' stage finding is in relation to only those patients who had stage of disease recorded so results have to be taken in light of this. It is always important to bear in mind that deprivation is also a variable that is inherently difficult to measure objectively. It is also possible that these measures are demonstrating the ecological fallacy, namely that individual patients' socioeconomic circumstances are not measured, only an aggregate estimate of the circumstances of a group of patients from one postcode area.

A further finding cited in 2003 is that the more deprived in society are less likely to take up the offer of screening for colorectal cancer thus potentially increasing the gulf between themselves and the less deprived in relation to survival outcome (94). However, Rachet et al have demonstrated, within the framework of a randomised controlled trial, that it is possible for the most socially deprived patients to attain the survival rates of the most affluent patients (205). There is a lag of around five years in this happening. We have demonstrated that our current service is selecting patients equally, treating them equally, and producing equal outcomes in regard to deprivation, irrespective of uptake of screening.

The current literature regarding this topic comes mainly from the UK although two US studies are commonly cited. Opinion is divided as to whether or not deprivation influences stage at presentation. Some groups have found no relationship between deprivation and stage at presentation (65,200,201) whereas others *have* found an association (64,73,202).
In relation to entering the MDT process, it has also been shown that deprived patients may experience delay to referral and may also be less able to access services such as specialist surgery or adjuvant therapy (203,204).

3.8 Conclusions

It appears that the introduction of the MCN has lead to improvements in survival for particular groups of patients only.

The number of multiple primary cancer cases in this region is consistent with other similar series elsewhere. The percentage of male multiple primary cases was higher than the number of females in the West of Scotland colorectal cancer population.

A higher proportion of male rectal cancer patients have deprived socioeconomic circumstances compared to their female counterparts, 32.7% and 29.7% respectively ($p<0.001$). Patients not enrolled in the MCN were found to be 2.03 years older than those experiencing MCN care. There was a lower proportion (17.6%) of patients with an unspecified Dukes'

stage in the MCN compared to those not in the MCN (41.1%). Also, more than 25% of patients not enrolled in the MCN are in the Dukes' D category. In general, patients in the MCN have less advanced disease. There was no difference in the proportions of patients from different socioeconomic backgrounds when comparing those in the MCN with those not in the MCN. Patients in the MCN demonstrated a 1.45 year increase in mean survival compared to those patients not in the MCN.

Age at incidence, degree of socioeconomic deprivation, degree of disease burden, having a colonic tumour and whether or not the patient has entered the MDT process were all independent variables found to account for the difference in overall survival seen in the Kaplan Meier plot of patients enrolled and not enrolled in the MCN. This difference could be further explored if there were further clinical and pathological data available for the population of patients not entering into the MCN process.

An increase in overall five year survival with time for all colorectal cancer patients from fewer than 25% in 1985 to over 40% in 2001 was seen. There was a disproportionate rise in 5 year survival for rectal cancer patients compared to

colon cancer patients with time. This appeared to begin in the mid 1990s and is thought to be attributable to advances in rectal cancer resection surgery. There was no independent effect observed according to which particular MDT a patient was treated. This demonstrates that the type of treatments received throughout the region are similar enough to provide homogeneous outcomes. Further analysis using multivariate modelling showed that age at incidence, socioeconomic circumstances, Dukes' stage and sex all help to explain overall survival to differing degrees in colorectal cancer, colonic cancer and rectal cancer patients. Overall survival is poorer among patients from more deprived areas.
Compared to their affluent counterparts, deprived patients with colorectal cancer have a 24% increased hazard following adjustment for age, stage of disease, Health Board of residence and operative intent.

We have herein identified important influences on survival that need to be included in any comparison of survival between treatment sites. Also, given that the MCN ethos is to provide equitable access to care and equity of management regardless of patients' socioeconomic circumstances, many of these factors might be expected to have been reduced after the formation of the MCN, leading to survival improvements.

We have analysed the records of 37,890 colorectal cancer patients in the West of Scotland over a 25-year period and confirmed expected proportions of colonic to rectal lesions as well as equal sex distribution. We also report a higher ascertainment for data regarding Dukes' stage when compared to other published series. There was a large, statistically significant variation in socio-economic conditions found between the five Health Boards. Overall, affluent patients tend to present more with colonic lesions than rectal cancer. Affluent patients also tend live longer than deprived patients, thus adding a further possible factor to explain differential survival outcomes between patients of different socioeconomic circumstances.

The proportion of men with rectal cancer was significantly higher in the deprived group when compared to the proportions on the other two deprivation groups. In terms of Dukes' stage, the overall relationship is that a consistent and clinically important relationship between deprivation and later stage at presentation exists with more affluent people presenting with Dukes' A and

more deprived patients presenting with a greater, stage D, disease burden. We were able to attest that there was no statistically significant difference in time to wait to first treatment according to socioeconomic circumstances. This was despite the fact that we have also shown that more deprived patients attend more frequently as non-elective cases.

A larger proportion of deprived patients underwent palliative procedures ($p=0.018$). This finding was not replicated in the years following MDT creation ($p=0.360$). SEC, age, stage and whether or not the patient had been discussed in an MDT all bore influence independently upon whether or not the patient underwent palliative or curative resection.

4 Degree of specialisation and Outcomes in management of MDT patients.

4.1 Introduction

There is a continuing body of evidence to support the treatment of colorectal cancer in high volume institutions where specialist colorectal surgeons are available (206). Both volume and specialisation can therefore be used as independent proxy measures for good quality care. The impact of MCNs has been described for various conditions and locations outside the West of Scotland (17,18). A full regional assessment of the effects of treatment for colorectal cancer by designated specialists has not been made in the West of Scotland. In this chapter we aim to assess whether the proportions of consultants performing procedures at differing thresholds have changed with time, i.e. following introduction of the MCN in the West of Scotland.

Particular reference is made to rectal cancer surgery. It is recognised that the management of rectal cancer is more complex than colon cancer. More complex preoperative staging, imaging, and more technically demanding surgical procedures are all required in the MDT approach to managing patients with rectal cancer. For these reasons it has been suggested that perhaps rectal cancer patients' outcomes may be affected to a greater degree by the MDT process compared to colonic cancer patients (164). Although immediate postoperative complications demonstrate no difference between general and specialist surgeons, stoma rates do differ significantly (207).

Debate continues as to the definition of what constitutes a specialist in the field of colorectal surgery. Currently, various definitions have been applied. Membership of the Association of Coloproctologists of Great Britain and Ireland has been used as a proxy measure for being a specialist. Regional peer opinion has also been employed to determine which consultants are specialists (175). More objective measures have also been sought. If a surgeon is undertaking more than 20 colorectal operations per year then he can be said to have enough expertise be called specialist.

In this chapter we use seven resections per year as the threshold for both colonic and rectal cancer resections. We have then used seven and a further division at ten resections per year for colon cancer surgery. This is firstly to be able to compare colon cancer outcome with rectal cancer at the same volume and secondly, to assess if the higher threshold of ten cases per year yields better outcome than seven, thus supporting the argument for specialisation in colonic surgery as well as rectal. Furthermore we decided that due to the small proportion of consultants performing greater than 20 resections per year, that this higher threshold would not include enough data to provide meaningful interpretations relating to our region. A lower threshold of 10 cases is therefore employed herein.

4.2 Aims & Objectives

Aims

i. To assess if there has been an increase in the proportion of operations carried out by surgeons performing higher volumes of colorectal cancer operations in the West of Scotland since the MCN was formed.
ii. To determine if overall survival is better for patients operated on by higher volume surgeons.

Objectives

i. To analyse variables from the MCN dataset pertaining to consultant in charge.

ii. To derive levels of caseload per year per consultant.

iii. To further analyse site of tumour and type of presentation with regard to their effects in relation to volume.

iv. To construct overall survival plots for differing surgeon volumes.

v. To construct further univariate and multivariate models.

4.3 Method

In addition to general methodology mentioned previously, a set of variables were created from the dataset in order that named consultant volume was able to be measured at differing thresholds. It was not possible to construct these variables prior to inception of the MCN as named consultant data were only recorded from 2000 onwards.

4.4 Results

In total, 5937 patients underwent any type of surgery for colorectal cancer in the West of Scotland MCN from 2001 to 2005. Overall, 4773 (80.39%) patients had a named consultant. These patients form the population under study in this chapter, and are summarised in Table 25. In 2004 and 2005 the proportion of patients with no named consultant was higher than in other years.

Of these 4773 patients, 3464 (72.57%) had a colonic cancer and 1309 (27.43%) a rectal cancer.

Table 25 - Proportions of the 5937 patients undergoing surgery with, or without, a named consultant per year.

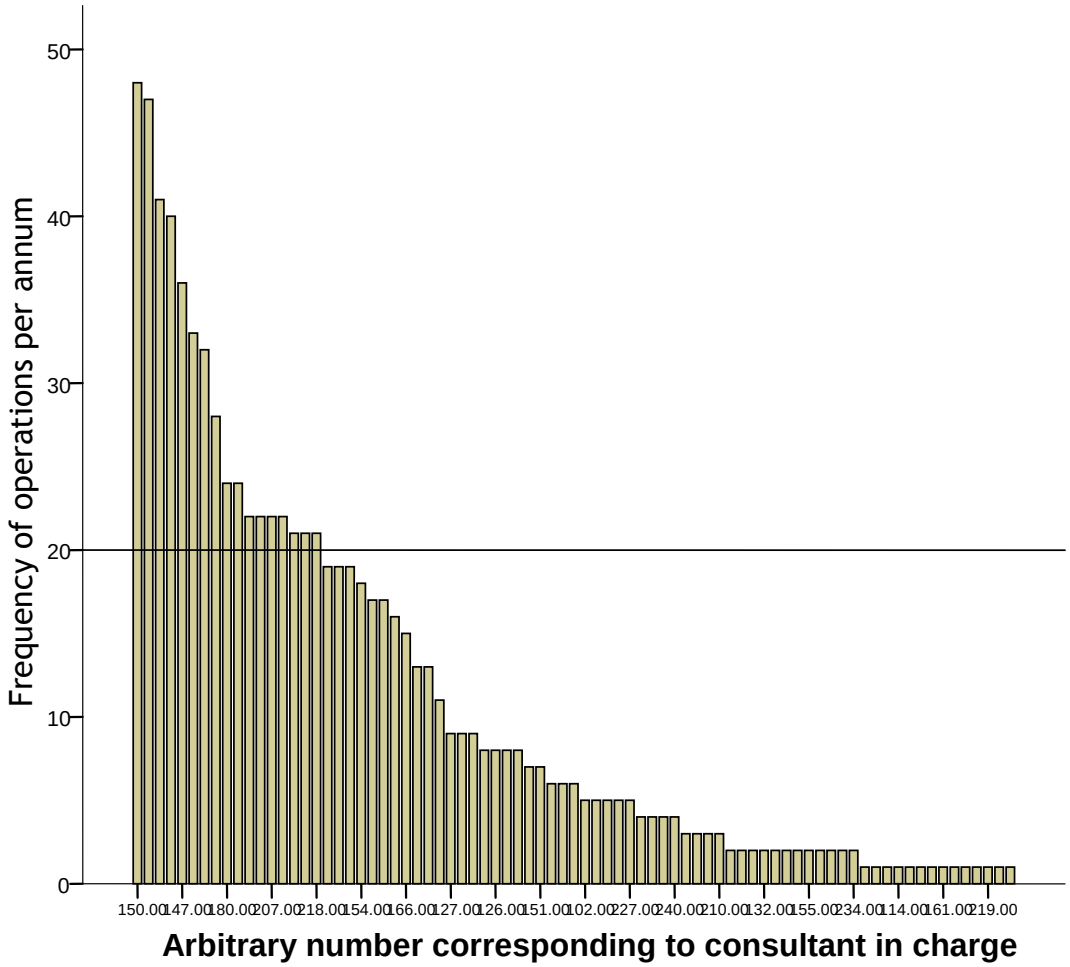
		Named consultant n (%)		Total
		no	yes	
year of Incidence	2001	260 (19.30)	1087 (80.70)	1347 (100)
	2002	185 (15.29)	1025 (84.71)	1210 (100)
	2003	215 (17.77)	995 (82.23)	1210 (100)
	2004	286 (23.95)	908 (76.05)	1194 (100)
	2005	218 (22.34)	758 (77.66)	976 (100)
	Overall	1164 (19.61)	4773 (80.39)	5937 (100)

ALL COLORECTAL CANCER PATIENTS

The following results are grouped into all colorectal cancer patients undergoing surgery, all colon cancer patients undergoing surgery, and all rectal cancer patients undergoing surgery. This is due to the fact that rectal cancer surgery is viewed as the realm of the specialist whereas emergency colonic resections are additionally undertaken by generalists. In extreme cases though, a general surgeon will still undertake the emergency, life-saving, temporising operation. Further divisions into elective and emergency surgery have also been performed for each group to fully explore patterns in care by consultants of differing volumes.

In figure 26 there is a wide spread in number of cases attributed to the 79 named consultants for this year, 2001. 17 of these (21.5%) were the named consultant for > =20 cases, namely specialist consultants.

Figure 26 - Number of cases performed per numbered consultant for all 863 colorectal cancer patients undergoing elective colorectal surgery in 2001. Line set at 20 cases per year.



In figure 27 there is a wide spread in number of cases attributed to the 60 named consultants for this year, 2005. 12 of these (20%) were the named consultant for >=20 cases, namely specialist consultants.

Figure 27 - Number of cases performed per named consultant for all 605 colorectal cancer patients undergoing elective surgery in 2005. Line set at 20 cases per year.

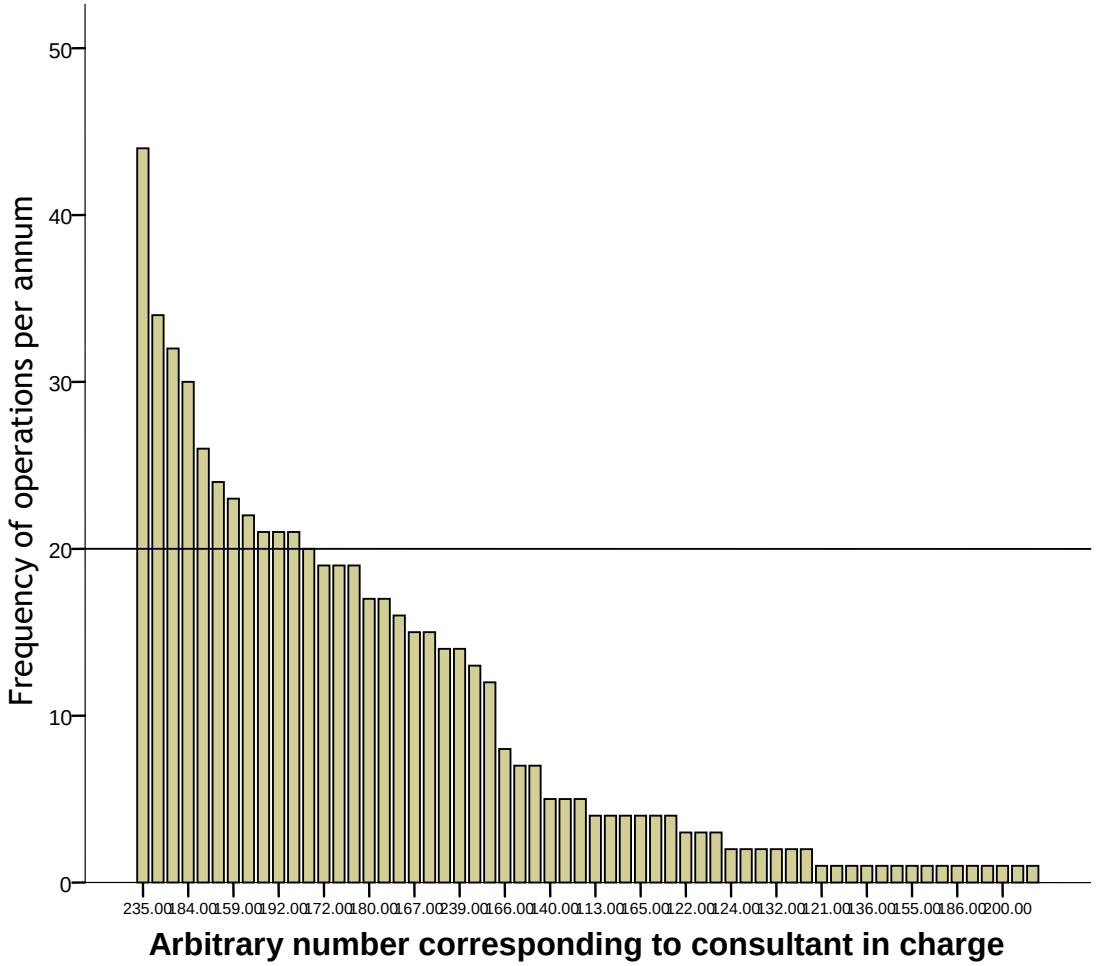


Figure 28 shows that there was a significant increase in the proportion of patients treated by higher-volume surgeons in the first 5 years of the MCN. In 2001 52% of patients were operated on by a low volume surgeon. 21% of patients were operated on by a high volume surgeon. In 2005 these figures had reduced and increase to 42% and 26% respectively.

Of note is that overall, 46% of patients were still treated by “non-specialist” low-volume surgeons.

Figure 28 - All 4773 colorectal cancer patients undergoing surgery in the West of Scotland with a named consultant from 2001 to 2005. Linear-by-linear chi-square p <0.001.

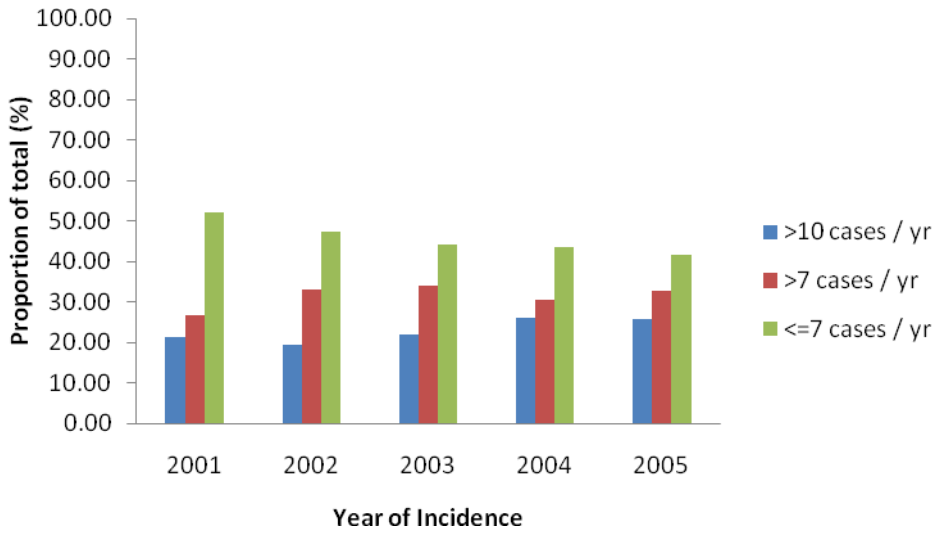


Figure 29 shows a similar significant increase in the proportion of patients being treated by high-volume surgeons over time when looking at elective cases only. In 2001 only 24.8% of cases were undertaken by a high volume surgeon (>10 cases / year) with almost half (46.9%) of elective cases being performed by the lowest volume surgeons. By 2005, high volume surgeons were performing 30.3% of all operations with the lowest volume surgeons performing 35.5%.

Figure 29 - All 3789 colorectal cancer patients undergoing ELECTIVE surgery with a named consultant in the West of Scotland. Pearson Chi square P <0.001

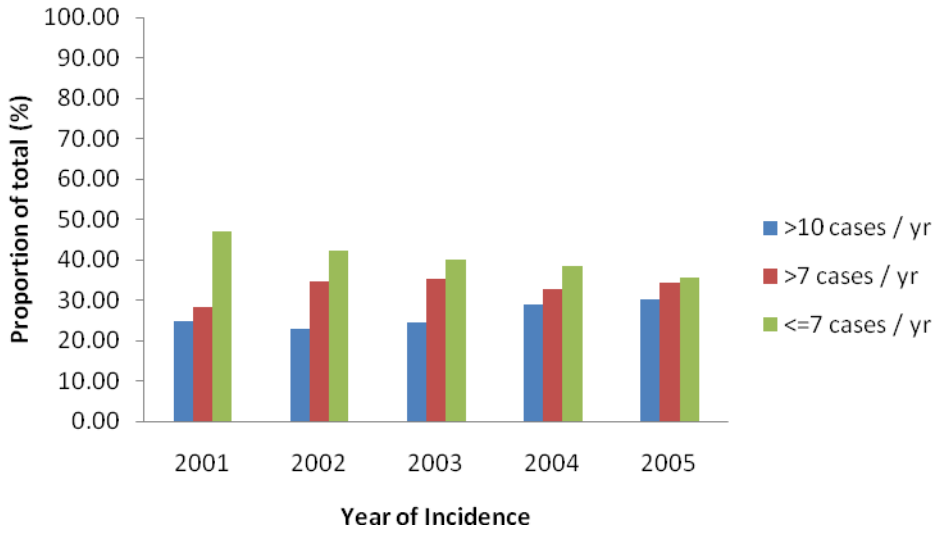
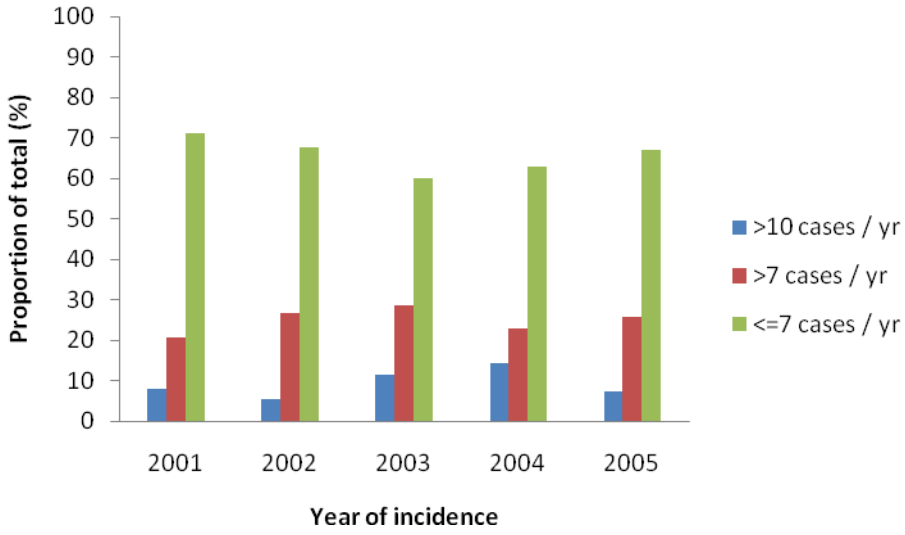


Figure 30 shows there is no convincing evidence of an increase in high-volume surgeons for emergency patients over time. The other important feature of this graph is that a much larger majority of emergency patients are treated by non-specialists/low-volume surgeons.

Figure 30 - All 964 colorectal cancer patients undergoing EMERGENCY surgery with a named consultant in the West of Scotland. P = 0.048



4.5 Colon Cancer Patients

In relation to colon cancer resection by different volumes of operating surgeon, there is a statistically significant change in proportions with time. As shown in Figure 31, only 18.4% of cases were performed by a high volume surgeon. This had grown to 22.1% by 2005. Lowest volume consultants reduced their overall contribution from 56.3% to 47.8% over the same period.

Figure 31 - All 3464 colon cancer patients undergoing surgery in the West of Scotland with a named consultant. p = 0.03

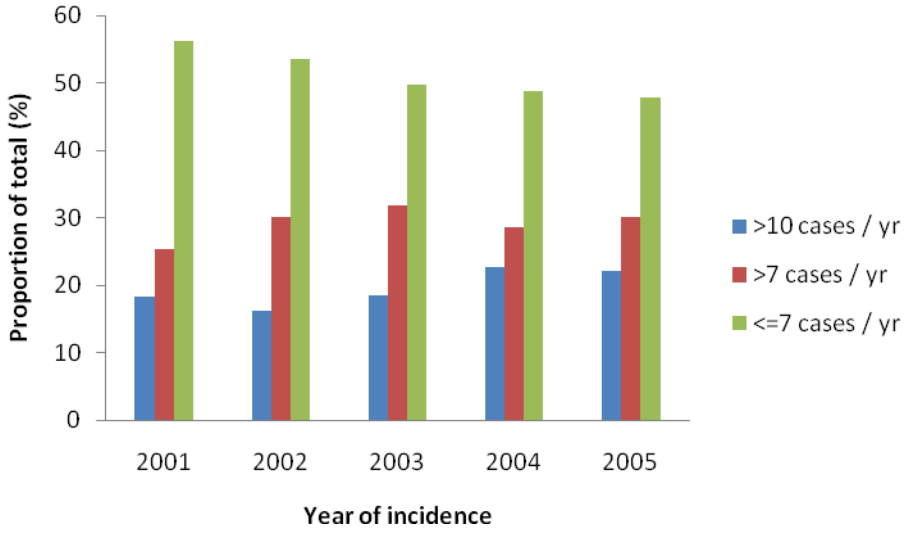
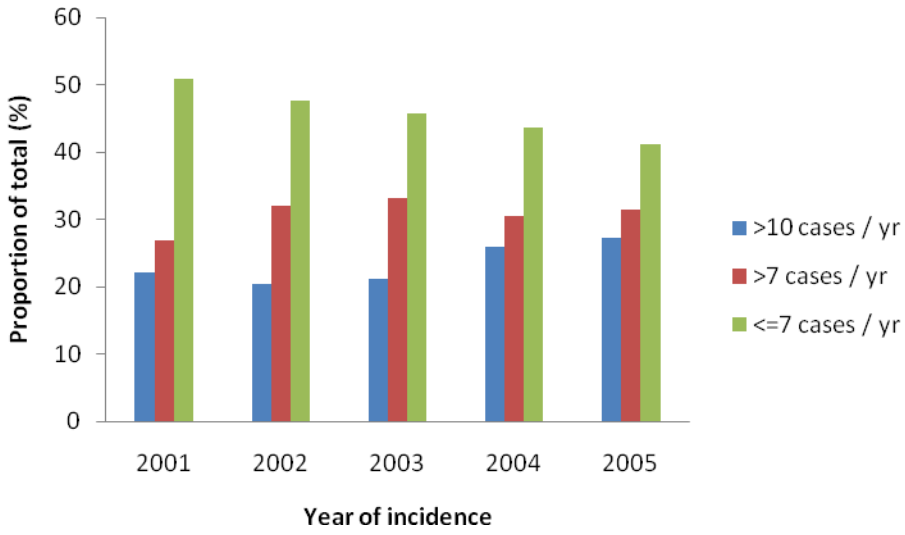


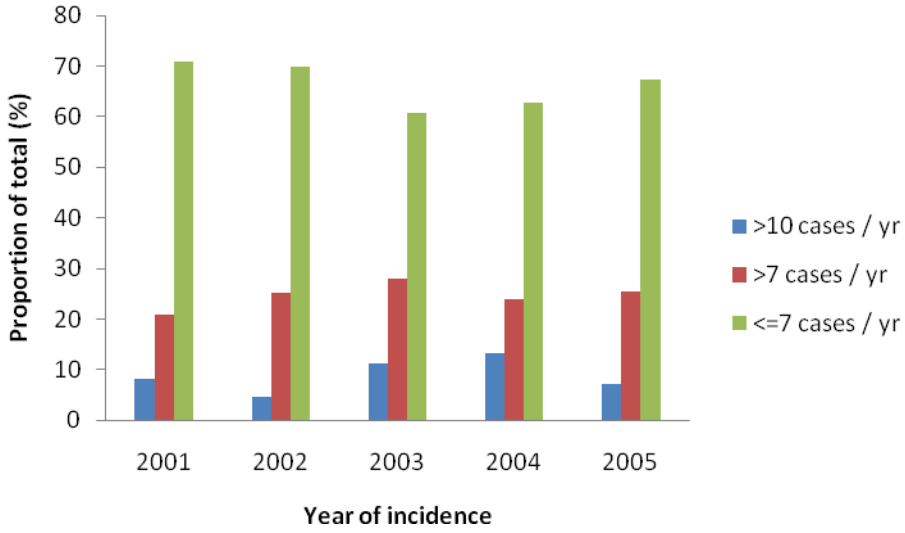
Figure 31 shows that for all 2353 colon cancer patients undergoing elective surgery in the West of Scotland there is a statistically significant increase in the proportion of patients being treated by high-volume/specialist surgeons (p = 0.025). The proportion of high volume surgeons is initially higher for elective surgery compared to all types seen in Figure 31 (22.1% vs 18.4%). The magnitude of change seen for elective surgery is larger though, with a change of +5.1% with time for elective surgery compared to a 1.7% change for all types of colon surgery.

Figure 32 - All 2353 colon cancer patients undergoing elective surgery in the West of Scotland with a named consultant (p = 0.025).



In contrast to all types of surgery and elective surgery there appears to be no change in the proportions of emergency cases being operated on by a specialist. This is evidenced in figure 33 below for all 918 colon cancer patients undergoing emergency surgery in the West of Scotland (p = 0.084). Also of note is the fact that throughout the period of study, low volume surgeons are the named consultant in greater than 60% of the total number of emergency operations.

Figure 33 - All 918 colon cancer patients undergoing EMERGENCY surgery in the West of Scotland with a named consultant (p = 0.084).

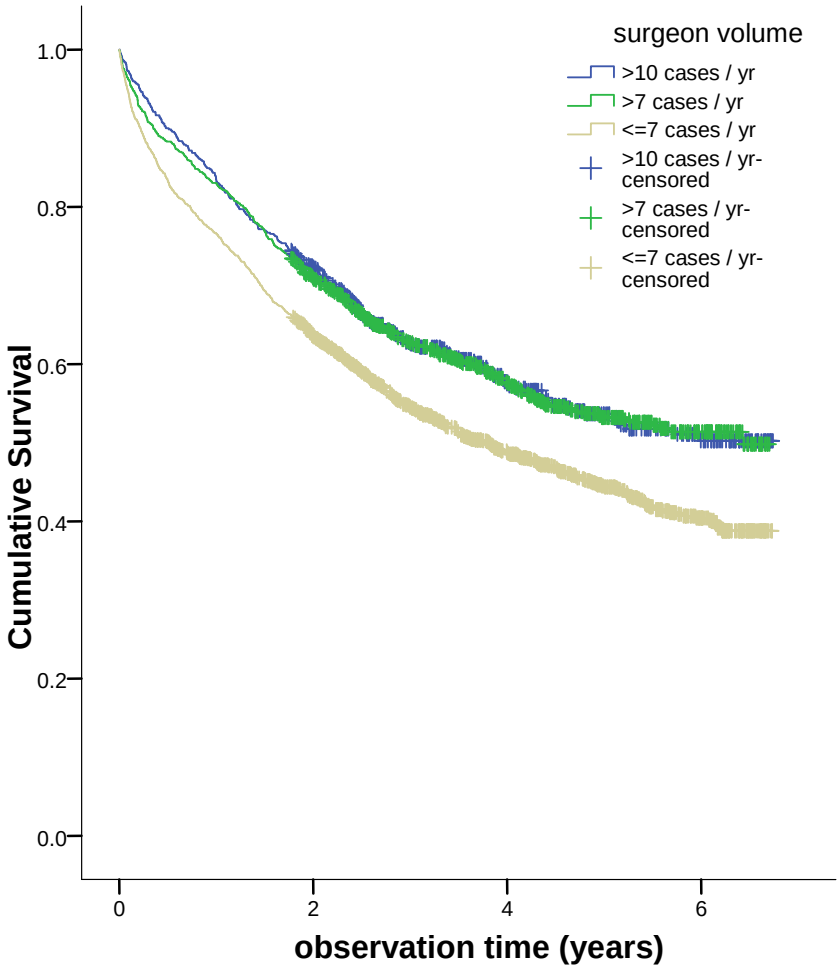


Overall survival in all colon cancer patients undergoing surgery

Having described temporal trends in relation to specialisation it is important to ascertain whether specialisation in itself carries an advantage to patients in terms of overall survival.

In figure 34 there is a statistically significant difference (Log rank <0.001) in overall survival between colon cancer patients being treated by low and medium or high volume consultants. There appears to be no significant difference between the medium and high volume cases.

Figure 34 - Kaplan Meier plot for all colon cancer patients undergoing surgery in the West of Scotland from 2001 to 2005 according to volume of operating surgeon. n = 3464, Log Rank <0.001.



We have also shown in figure 34 that low-volume/non-specialist care is associated with emergency presentation. In the following unadjusted survival plot, we show that there is a significant difference in overall survival for all colon cancer patients undergoing surgery with a named consultant according to presentation. This is therefore an important variable to include in a multivariate

model to further explore and account for differences in outcome perceived to be due to specialisation.

In figure 35 there is a statistically significant difference (Log rank <0.001) in overall survival between colon cancer patients according to their presentation for surgery. Again, this is a further important variable to include in a multivariate model to further explore and account for differences in outcome perceived to be due to specialisation.

Figure 35 - Kaplan Meier plot for all colon cancer patients undergoing surgery in the West of Scotland from 2001 to 2005 according to presentation for surgery. n = 3450, Log Rank <0.001.

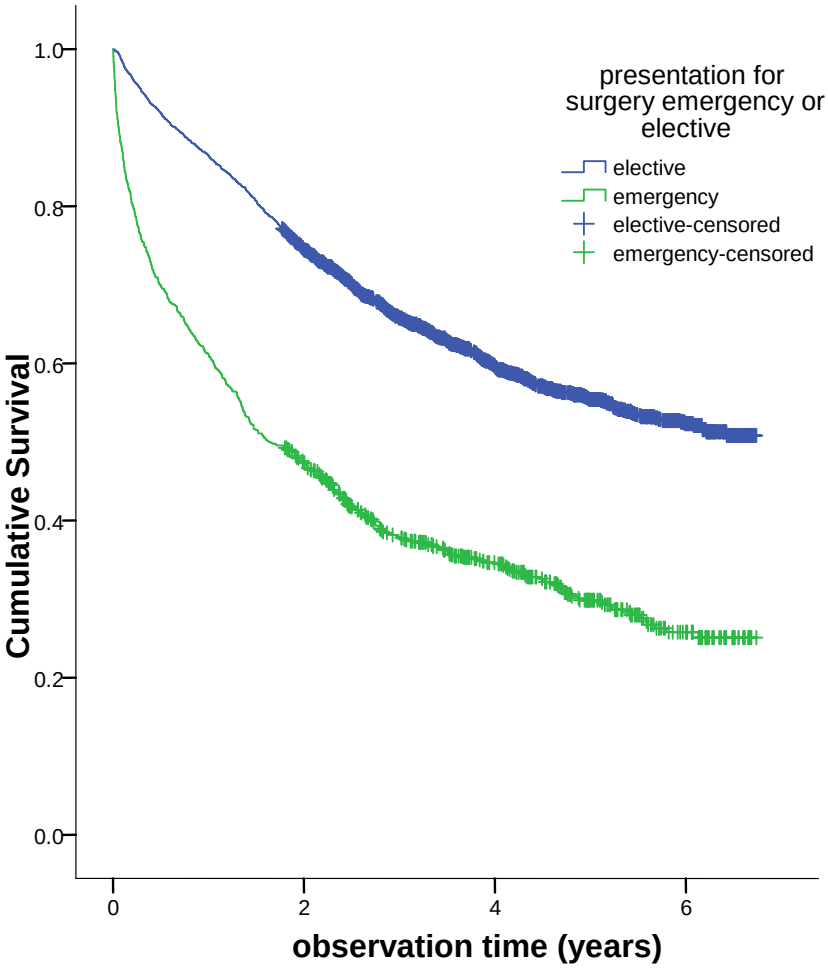


Table 26 highlights the results from univariate and multivariate analysis of all 3464 patients undergoing surgery with a named consultant. It shows that age, presentation for surgery, volume, socioeconomic status and site of cancer were all found to be independent prognostic indicators of overall survival. Following adjustment in the multivariate model, only age at incidence, presentation for surgery, volume of procedures per year, and socioeconomic circumstances remained independent prognostic indicators for overall survival in this large group.

Table 26 - Univariate and multivariate Cox regression results for all 3464 patients undergoing surgery for colorectal cancer with a named consultant

Variables in the model	UNIVARIATE		MULTIVARIATE	
	p	HR (95% CIs)	p	HR (95% CIs)
volume >10	0.00	1	0.02	
volume >=7	0.87	1.01 (0.87-1.18)		0.14 (0.91-0.81)
volume <=7	0.00	1.34 (1.18-1.53)		0.35 (1.06-0.94)
elective presentation	0.00	1	0.00	
emergency presentation		2.36 (2.14-2.61)		2.41 (2.18-2.65)
Age at incidence	0.00	1.03 (1.02-1.03)	0.00	1.03 (1.02-1.03)
sex - female	0.14	1		
sex - male		1.08 (0.98-1.19)		
affluent	0.00	1		
intermediate	0.01	1.17 (1.03-1.34)	0.00	1.21 (1.06-1.38)
deprived	0.00	1.32 (1.15-1.52)	0.00	1.35 (1.17-1.55)
rectum	0.00	1.00	0.53	1.00
colon		1.37 (1.24-1.52)		1.03 (0.93-1.15)

4.6 Rectal Cancer Patients

Overall 1309 patients with a named consultant had surgery for their rectal cancer. Of these, six had data missing regarding volume of cases performed by their named consultant.

Table 27 summarises the proportions of surgeons performing surgery on patients presenting as an emergency or as an elective case. More than double the number of elective cases were operated on by surgeons carrying out more than seven resections per year. In contrast, only marginally more emergency operations were carried out by lower volume surgeons.

Table 27 - Summary of comparison of all 1303 rectal cancer patients undergoing surgery, comparing presentation for surgery with surgeon volume, using a cut-off of seven cases per year.

		surgeon volume		Total
		>7 cases / yr	<= 7 cases / yr	
type of surgery	elective	871 (69.29)	386 (30.71)	1257 (100)
	emergency	22 (47.83)	24 (52.17)	46 (100)
	Total	893 (68.53)	410 (31.47)	1303 (100)

Figure 36 - All 1309 MCN rectal cancer patients with named consultants undergoing surgery at different volume thresholds. P = 0.004

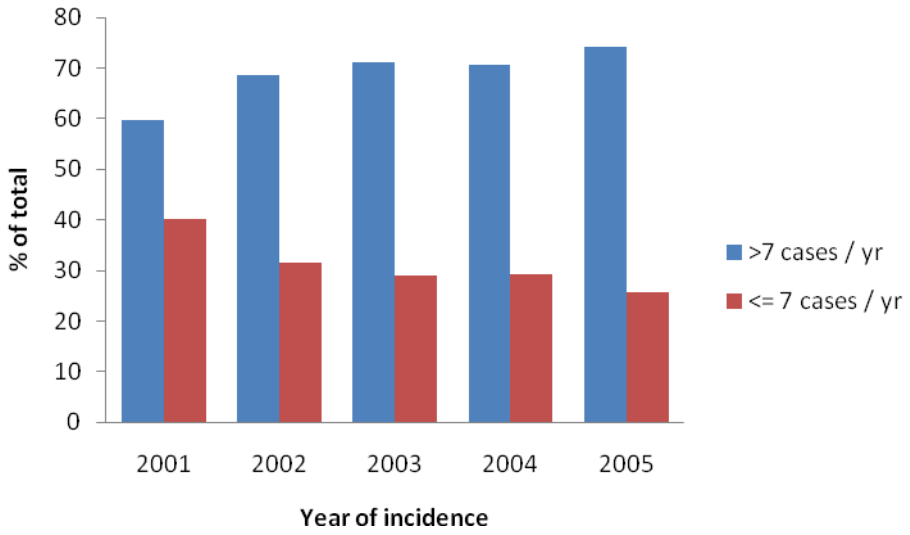
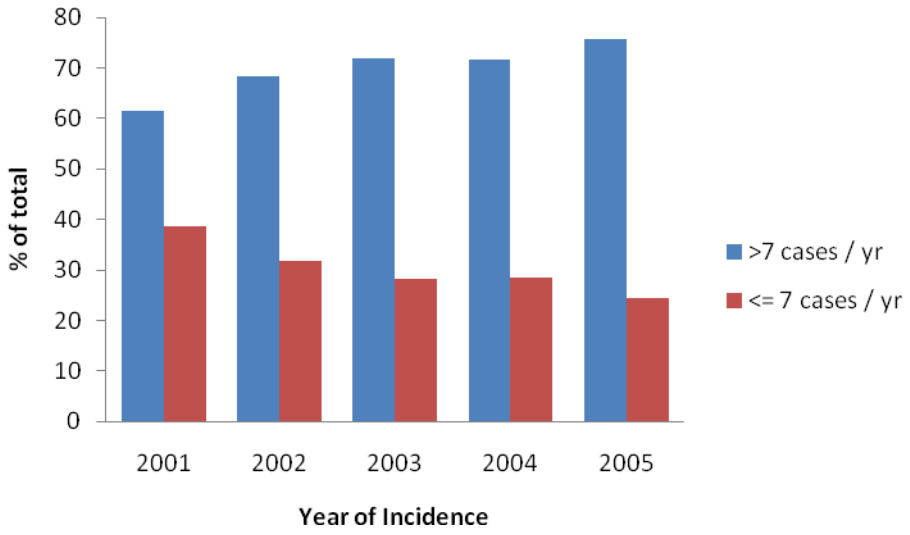


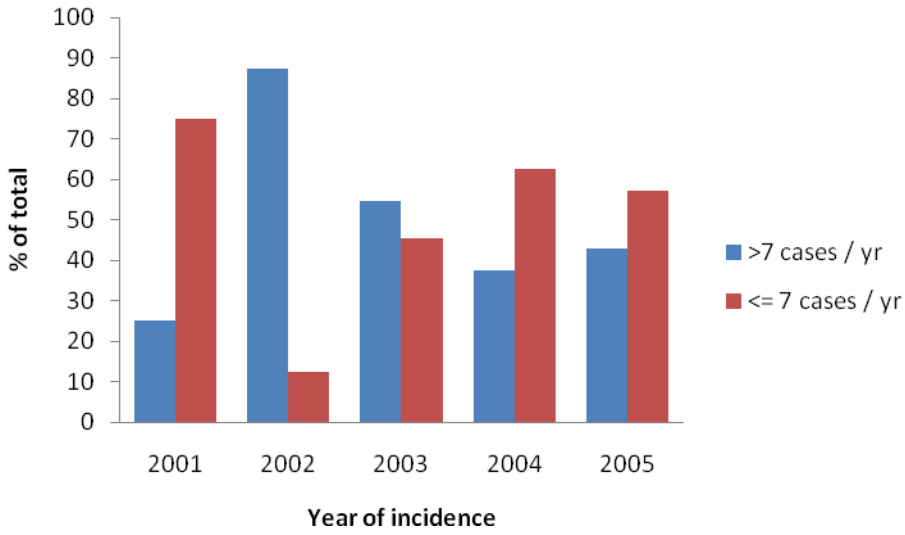
Figure 37 - All 1257 rectal MCN cancer patients undergoing ELECTIVE surgery with a named consultant at different volume thresholds. P = 0.090



Figures 36 and 37 chart the changes in proportions of rectal cancer patients undergoing surgery overall and elective surgery, with time. There is a significant change with time for all patients undergoing surgery towards more specialist care but not for elective rectal resections.

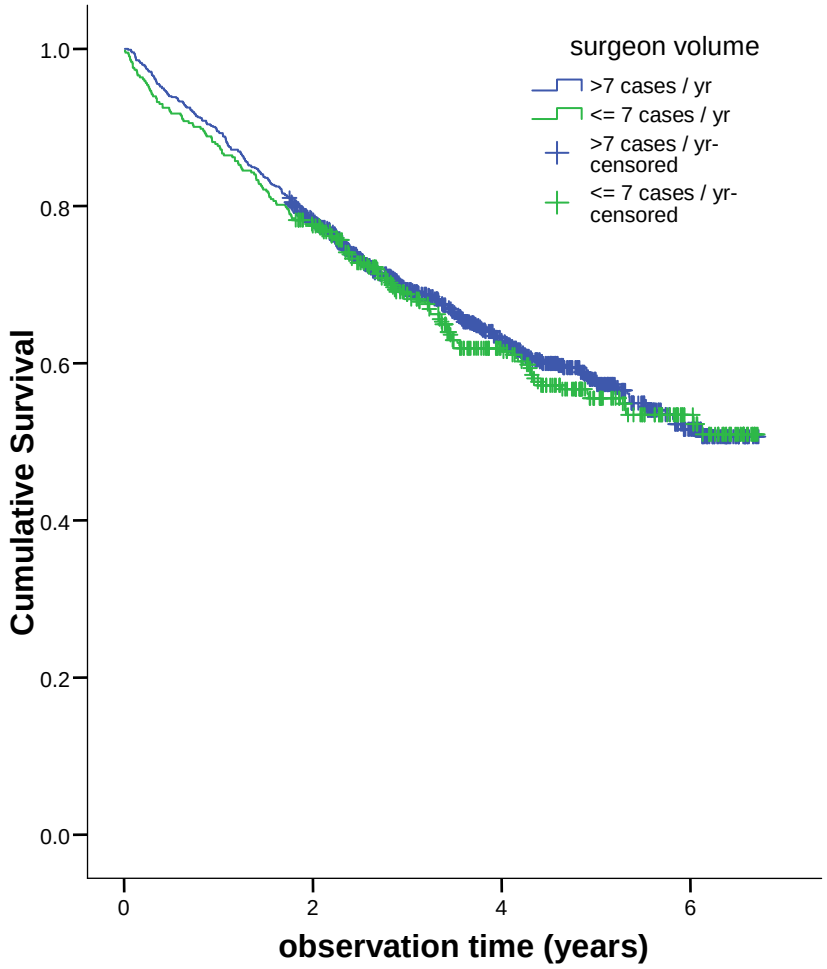
Figure 38 shows that there was no trend with time for emergency surgery on rectal cancer patients according to surgeon volume. Given that the total number of patients is 46, a larger number of cases over a longer timeframe may result in a different pattern.

Figure 38 - All 46 rectal MCN cancer patients undergoing EMERGENCY surgery with a named consultant. Pearson Chi-square, p = 0.086.



In contrast to Figure 34 for colon surgery, Figure 39 shows that there appears to be no statistically significant difference in overall survival for rectal cancer patients according to the volume of named consultant. We have used seven cases per year as a cut-off so it may be that there is a significant difference in survival at another volume threshold. There were no significant differences noted according to volume when elective patients and emergency patients were tested individually.

Figure 39 - Kaplan Meier plot for all 1309 rectal cancer patients with a named consultant undergoing surgery in the West of Scotland from 2001-2005. Log Rank 0.628



In figure 40 there is a clear difference in overall survival for rectal cancer patients according to presentation for surgery. There is a relatively small number of emergency presentations (n=46) compared to elective (n=1257).

Figure 40 - Kaplan Meier plot assessing overall survival differences comparing presentation for surgery for all 1303 rectal cancer patients with a named consultant in the West of Scotland from 2001-2005. Log Rank <0.001

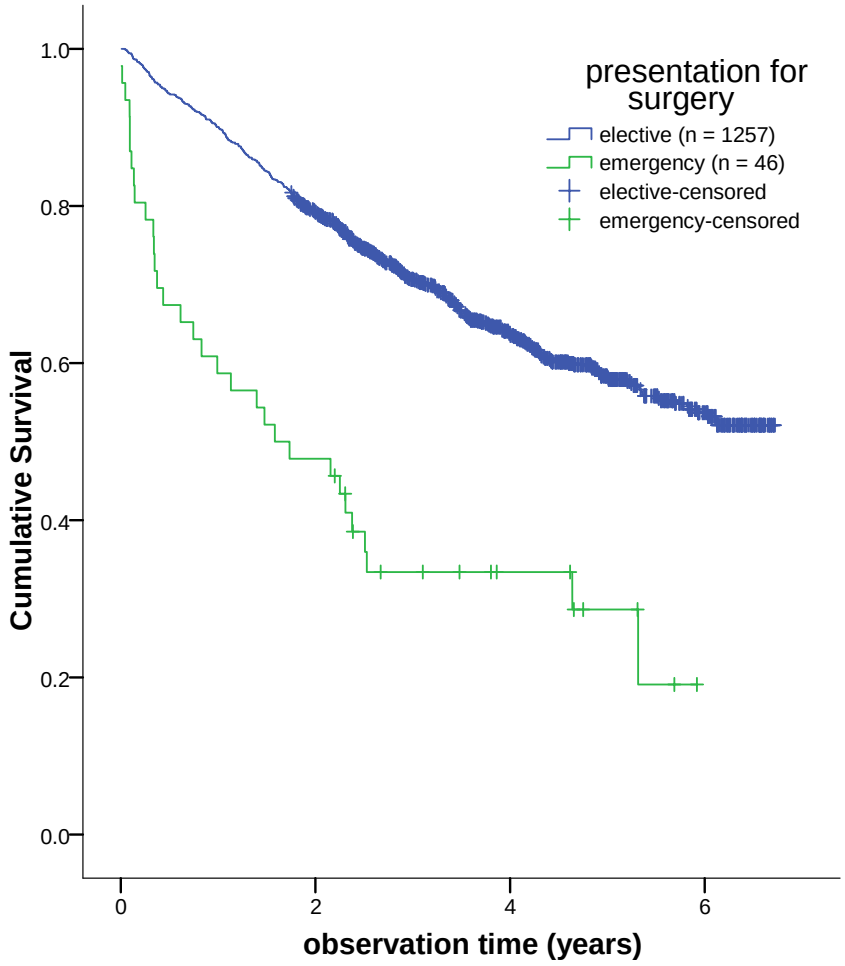


Table 28 - Summary of all log rank results for Kaplan Meier plots regarding surgical volume in all colorectal cancer patient groups with named consultants in the West of Scotland from 2001-2005.

	n	log rank
Colon - all	3464	<0.001
Colon - elective	2532	0.004
Colon - emergency	918	0.532
rectal - all	1309	0.628
rectal - elective	1257	0.823
rectal - emergency	46	0.395

In contrast to Table 26 for all colorectal cancer patients, table 29 shows the univariate and multivariate findings for rectal patients only. Only age at incidence and presentation for surgery remain independent as prognostic indicators following adjustment for sex, volume and socioeconomic circumstances. The increased hazard ratio of 2.70 for emergency presentation compared to elective presentation is noteworthy as it compares well with that seen for colorectal cancer patients in Table 26 (2.40).

Table 29 - Univariate and multivariate Cox regression results for all 1309 patients undergoing surgery for rectal cancer with a named consultant

Variables in the model	p	UNIVARIATE HR (95% CI)	p	MULTIVARIATE HR (95% CI)
volume >7	0.63	1.00		
volume <=7		1.05 (0.87-1.26)		
age at incidence	0.00	1.03 (1.02-1.04)	0.00	1.03 (1.02-1.03)
sex - female	0.19	1.00		
sex - male		1.13 (0.94-1.35)		
elective presentation	0.00	1.00	0.00	1.00
emergency presentation		3.10 (2.17-4.44)		2.70 (1.88-3.87)
affluent	0.28	1.00		
intermediate	0.23	1.19 (0.89-1.58)		
deprived	0.11	1.28 (0.95-1.75)		

4.7 Discussion

Although there was a reduction in the total number of surgeons performing colorectal surgery from 79 to 60 over the period of study the proportion of named consultants for >=20 operations was -1.5% over the same time frame. The number of patients with a named consultant also reduced over the period of study with 2004 and 2005 having the poorest proportion of named consultants. This should be considered when interpreting these results as it raises the issue of accurate data collection.

We have shown that there was an increase in surgery by high-volume surgeons between 2001 and 2005 from 21% to 26% of the total (
Figure 28). This indicates increasing specialisation with time. The specialisation was confined to elective colorectal cancer operations only.
The majority (46%) of surgery for colon cancer is still performed by low-volume surgeons (Figure 31). Additionally, a much larger majority (66%) of emergency surgery is performed by low-volume surgeons (Figure 33). This makes sense, given that, unlike the SCAN area, WOSCAN does not have a specialist colorectal emergency service at present. A further important point is that the majority of emergency patients are treated by non-specialists/low-volume surgeons.

Based on the findings of the multivariate analysis in Table 26, it appears that surgeon volume remains an independent prognostic indicator in this large group of patients. This follows adjustment for age, type of presentation for surgery, and socioeconomic circumstances.

The majority (68.5%) of all rectal cancer surgery, in contrast, is carried out by high-volume surgeons (Table 27). However, this effect appears to be confined to elective surgery only. A relatively small number (n=46) of emergency rectal surgery cases were carried out from 2001 to 2005 so perhaps this trend would change in a larger cohort over a longer period of study. Ideally a comparison of before inception of the MCN with after the MCN was created would provide clear evidence of an MCN effect. This is not possible due to lack of specific named consultant data prior to 2000.

The majority of emergency rectal surgery is carried out by low-volume surgeons (Figure 38). The proportion of emergency cases being performed by low volume consultants is far lower for rectal cancer than colon cancer. This reflects the fact that general surgeons will still perform definitive surgical procedures for colon cancer patients whereas rectal cancer patients may only be stented, or have a temporary defunctioning colostomy fashioned by a general surgeon thus providing time for staging, imaging and a definitive rectal cancer resection. There is a convincing increase in higher-volume surgeons carrying out elective rectal cancer surgery over time.

Overall survival in colon cancer patients is related to both type of presentation for surgery and surgeon volume, as evidenced in both Figure 34 and Figure 35. Univariate and multivariate modelling (Table 26) further explores survival for the larger group of all colorectal cancer patients concluding that age at incidence, presentation for surgery, volume of procedures per year, and socioeconomic circumstances remain independent prognostic indicators for overall survival. Site of cancer was significant on univariate analysis. The effect was attenuated in the multivariate model though. We can therefore say that surgical volume is an important consideration in outcome for this population and may have implications for service provision in terms of providing specialist colorectal services for all patients previously operated on by lower volume surgeons. With reference to rectal cancer patients, we were not able to demonstrate a significant difference in overall survival using a volume threshold of seven cases per year. There was a statistically significant difference in survival for this group in relation to presentation for surgery (Figure 40).

Following adjustment in the multivariate model, only age at incidence and presentation for surgery remained independent prognostic indicators of overall survival (Table 29). This suggests that despite an ongoing trend towards specialisation for rectal cancer surgery in our region, that the process may well have been taking place prior to inception of the MCN. The very low number of emergencies for rectal cancer also suggests that there is a greater tendency to temporise.

We are unable to tell whether the named consultant was simply the consultant in charge of the patient or whether the named consultant performed the procedure. We are also unable to tell if the patient had their definitive cancer resection at the time of operation or whether they went on to have further procedures following temporising surgery by a non-specialist.

Overall, 4773 (80.4%) of patients had a named consultant with 1164 (19.6%) having no named consultant in the MCN. In the former group we are not able to say if the consultants were all surgeons since gastroenterologists and other palliative care physicians could be nominated as consultant in charge in some cases. In order to lessen this source of error we selected only those patients undergoing surgery.

Only one method of objectively measuring volume has been used herein.
It is entirely possible that some consultants were newly appointed, nearing retirement, or retired during the period of study. This may mean that a more exact and objective measure of number of cases should be sought to assess caseload. It may be that some senior consultants perform the majority of their resections in the private sector. These are not included in the current dataset. Some consultants in smaller hospitals may not achieve the threshold of seven resections per year for rectal cancer yet may consider themselves specialist.
It appears that there is a statistically significant difference in overall survival for all colon cancer patients according to the yearly volume of operations performed by consultant. This is not the case for rectal cancer patients. This finding was confirmed for rectal cancer patients both in elective cases and emergency cases. Although these models are overall survival models they are not adjusted for common prognostic indicators such as age, stage and socioeconomic circumstances.
A further variable worthy of exploring is seniority of operating surgeon. Although each patient has a named consultant it is possible that in some cases the named consultant was not the main operating surgeon.

4.8 Conclusions

Trends in relation to volume of work undertaken by surgeons on colorectal cancer patients in the West of Scotland demonstrate that there was increasing specialisation over the period under study. This is evidenced by the increase in proportion of resections performed by higher volume surgeons and is encountered in both colon and, to a lesser extent rectal cancer surgery.

It seems that increasing specialisation has had resultant effects on overall survival for colon cancer patients but not for rectal cancer patients thus far. To that end consideration should be given for service provision for colonic cancer by dedicated specialists only. This is important as the reason for having a colorectal subspecialty was that *rectal* cancers needed a specialist but colonic cancer procedures were deemed to be general operations. Further work should firstly address the issue of ensuring a named consultant surgeon for each patient undergoing resection and whether they consider themselves to be a specialist or not. It is clear that with the passage of time there may be more obvious survival benefits demonstrated from specialisation. The same methodology employed here should therefore be repeated in a population with more mature follow-up data. Unfortunately there were no data available regarding named consultants prior to inception of the colorectal MCN. This would have enabled a before and after study to be undertaken.

5 Effects of mechanical bowel preparation on post-operative complications and long-term survival after elective resection of colon cancer

The decision as to whether to administer mechanical bowel preparation (MBP) or not to patients undergoing elective resection of colon cancer remains under debate. We suggest that the selective omission or administration of MBP in the correct populations of patients is an aspect of care that may have been improved through MCN working. We wished to explore the hypothesis that mechanical bowel preparation is associated with poorer long-term survival as a result of increased anastomotic leakage. The MCN and its audit data provide the context for investigating this as well as an idea of how well current recommendations regarding MBP are adhered to. We carried out a retrospective study of a large cohort of surgically-treated colon cancer patients to determine the relationship between mechanical bowel preparation and overall survival after five years.
We are not aware of any study regarding mechanical bowel preparation where long term follow-up has been reported.

5.1 Introduction

Recent meta-analyses have indicated that pre-operative mechanical bowel preparation confers no clear benefit and may be harmful for colorectal cancer patients in up to three months post-operative follow-up (113-115,208). However, the effects of bowel preparation on longer-term outcomes have not been reported. The use of mechanical bowel preparation remains a constant topic of discussion for colorectal surgeons regarding their management of cancer patients. Worldwide, there are ongoing debates regarding its benefit. This chapter uses the merged dataset to arrive at conclusions relating to how MBP affects the population in our region in order that surgeons can be better informed of the effects of MBP on their patients.

The overall short-term results of meta-analyses of randomised controlled trials of MBP have shown no clear benefit and, in some cases, worse postoperative complication rates (although no difference in postoperative mortality) (113-115,208). The results of individual RCTs have also consistently shown no benefit, an exception being a lower risk of peritonitis among MBP patients reported by Contant and others (117,209,210) (211). Mechanical bowel preparation is generally unpleasant for patients and time consuming for nurses to oversee in the elderly or infirm. It was previously associated with a variety of complications such as dehydration, nausea, vomiting, mucosal lesions, hypokalaemia and other electrolyte disturbances (111,212). Although these side-effects still occur, they are less frequently observed through use of safer, more cost effective and better tolerated solutions and better maintenance of perioperative hydration (109). There are a number of ways in which MBP has been thought to act. It may decrease intraoperative contamination with faecal material thereby reducing the incidence of post-operative wound infection and residual intra-abdominal infection. It may prevent mechanical disruption of the anastomosis by the passage of hard faeces and improves the handling of the bowel intra-operatively. It may reduce the bacterial count within the colon. Conversely, it may also be associated with bacterial translocation through the bowel wall hence possibly contributing to post-operative infectious complications (213,214).There is little evidence to support these claims and yet bowel preparation remains standard practice in many hospitals in the USA (215).

5.2 Aim & Objectives

Aim

i. To assess the impact of MBP on short term (30 day), longer term outcomes and complications following resection of colon cancer in a defined population in the West of Scotland region, and to assess and quantify if there is any survival advantage from preoperative bowel preparation prior to surgery for colon cancer.

Objectives

i. To analyse the combined dataset with reference to postoperative complications.

ii. To assess longer term overall survival as affected by mechanical bowel preparation.

iii. To ascertain factors influencing overall survival in patients who had received and not received mechanical bowel preparation prior to surgery for colon cancer.

5.3 Method

We carried out a retrospective cohort study on all patients undergoing potentially curative surgery for colon cancer (International Classification of Diseases, 10th edition, C18) after routine hospital admission in the West of Scotland between January 2000 and December 2005. Exclusion criteria were: emergency admissions; patients with rectal lesions; those with multiple tumours; and those not undergoing surgery (for example, palliative patients or those undergoing colonoscopic treatment). Emergencies were excluded on the basis that acute obstructive symptoms may be a contra-indication to mechanical bowel preparation and overall prognosis is likely to be poorer than in the elective or urgent setting (216).
We linked clinical audit data gathered by the West of Scotland Colorectal cancer Managed Clinical Network to Scottish Cancer Registry and General Register Office (Scotland) death records (SMR06/GRO(S)) to create a novel dataset. Linkage was carried out by exact matches of forenames, surnames and dates of birth and by phonetic algorithms (Daitch-Mokotov Soundex and New York State Identification and Intelligence System) where exact matches could not be obtained. All patients' clinical audit records were successfully matched to the Cancer Registry. Death records up to 30th September 2007 were obtained. Postoperative complications had been prospectively recorded on a standard clinical audit proforma used for all cases of colorectal cancer throughout the region. Anastomotic leak, DVT (deep venous thrombosis), wound infection, fistula formation, intra-abdominal abscess, myocardial infarct, pulmonary embolism, and chest infection were all recorded as complications.

The West of Scotland (population 2.4 million) is an area of Western Europe with a high incidence of colon cancer and wide variations in socio-economic deprivation (192). To categorise socio-economic deprivation, we used the validated DEPCAT (deprivation category) classification (199). This uses four Census variables that have been shown to best correlate with health outcomes – overcrowding, car ownership, proportion of population in occupational Social Classes IV and V and male unemployment – to classify patients' residential postcode sectors (population around 4000) on a categorical scale from 1 (most affluent) to 7 (most deprived) . We further grouped DEPCATs into three

conventional categories: affluent (DEPCATs 1 and 2), intermediate (3-5) or deprived (6-7).

5.4 Results

A total of 1730 patients underwent potentially curative routine or urgent resection for colonic cancer (886 male and 844 female, mean age 69.7 years, SD 10.6) between January 2000 and December 2005. The median follow-up period was 3.52 years (mean 3.57, SD 1.73), range 0.1 to 6.7. A summary of their demographics, Dukes' stage and socio-economic characteristics is shown in Table 1. Men were significantly more likely to receive MBP compared with women ($p=0.022$); patients with Dukes' A tumours were more likely to receive MBP than those with Dukes' D (92.7% vs. 83.6%, $p<0.001$) although there was no clear trend associating Dukes' stage with likelihood of MBP; routine admissions were more likely than urgent admissions to receive MBP (86.7 vs 71.6%, $p<0.001$); and elective admissions were more likely to receive MBP than emergency admissions (87.0 vs 32.5%, $p<0.001$).

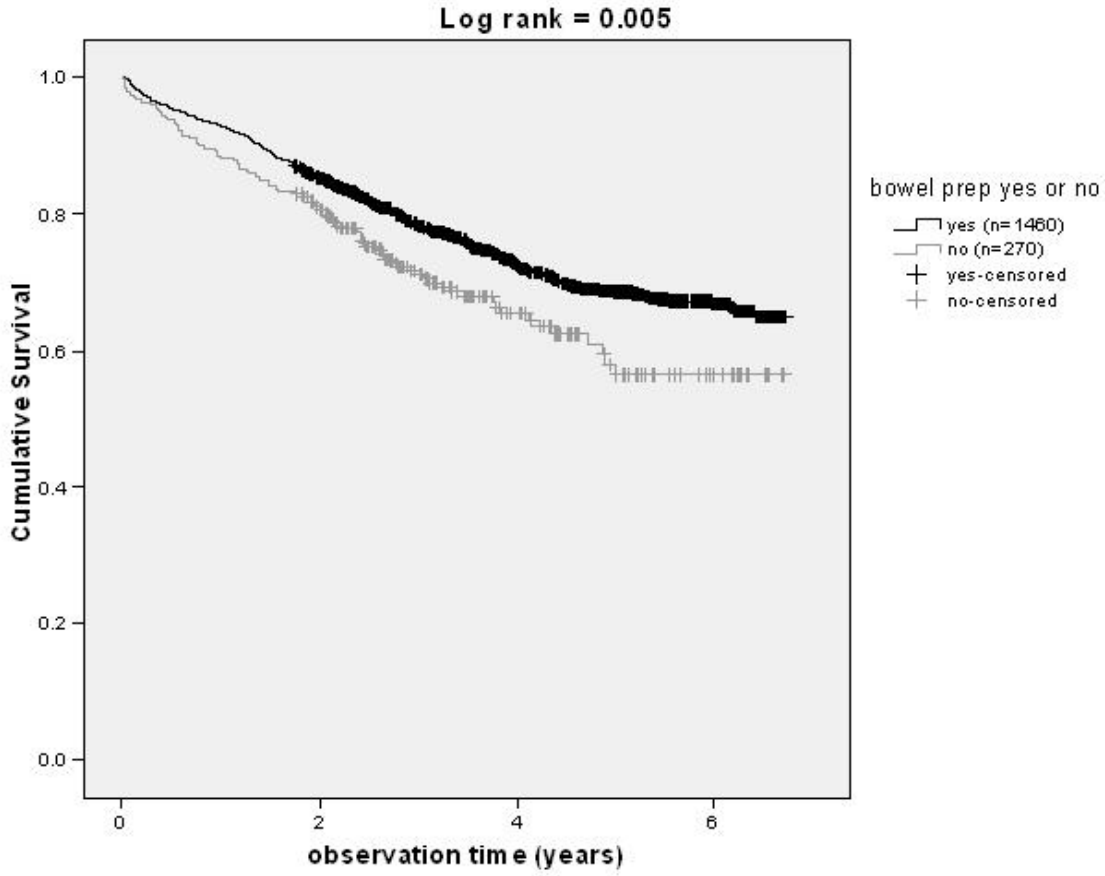
Table 30 - Baseline characteristics of 1730 patients undergoing surgery for resection of colon cancer, 2001-05. P-values for Pearson chi-squares except *, t-test of independent samples.

All figures in brackets are %		Total (%)	Bowel prep given (% of total)	Bowel prep not given (% of total)	p value
n		1730 (100)	1460 (84.4)	270 (16.6)	
sex	male	886 (51.2)	765 (86.3)	121 (13.7)	
	female	844 (48.8)	695 (82.3)	149 (17.7)	0.022
Age	Mean	69.71			
	(SD)	(10.64)			
	Range	70 (24-94)			0.037*
Dukes' stage	A	288 (16.6)	267 (92.7)	21 (7.3)	
	B	649 (37.5)	545 (84.0)	104 (16.0)	
	C	504 (29.1)	431 (85.5)	73 (14.5)	
	D	55 (3.2)	46 (83.6)	9 (16.4)	
	Unspecified*	234 (13.5)	171 (73.1)	63 (26.9)	0.005
Deprivation category	Affluent	294 (17.0)	251 (85.4)	43 (14.6)	
	Intermediate	988 (57.1)	840 (85.0)	148 (15.0)	
	Deprived	442 (25.5)	364 (82.4)	78 (17.6)	0.385
Type of Admission	Urgent	264 (15.3)	189 (71.6)	75 (28.4)	
	Routine	1466 (84.7)	1271 (86.7)	195 (13.3)	<0.001
Presentation for surgery	Elective	1649 (95.3)	1434 (87.0)	215 (13.0)	
	Emergency	80 (4.6)	26 (32.5)	54 (67.5)	<0.001

* Unpecified Dukes' stage not included in Chi square analysis

All cause survival was significantly higher (Log Rank p = 0.005) among patients treated with MBP in up to 7 years' follow-up after surgery – see Figure 40.

Figure 41 - Kaplan-Meier survival estimation of all-cause survival for patients receiving and not receiving mechanical bowel preparation before elective or urgent colonic cancer resection.



This was further explored with univariate and multivariate Cox regression analysis to allow adjustment for confounding by age, stage, socio-economic circumstances, type of admission, presentation for surgery and surgical complications. Results are shown in Table 31. Patients who received mechanical bowel preparation had 28% lower mortality on univariate analysis, HR 0.72 (95% CIs, 0.57 to 0.91). Following adjustment for age, sex, disease stage and type of admission the survival advantage remained but after the addition of urgency of surgery to the model, the adjusted all-cause mortality for MBP was 0.85 and no longer statistically significant (p=0.22).

Increasing age, male sex, advancing Dukes' stage and emergency presentation for surgery were independently associated with greater mortality. Urgent admission to hospital was not associated with significantly increased hazards in the adjusted model.

Table 31 - Univariate and multivariate hazards of all cause mortality after elective colon surgery adjusted for age, sex, Dukes' stage, mechanical bowel preparation, socio-economic circumstances (DEPCAT), type of admission, any surgical complication, and presentation for surgery.

		UNIVARIATE		MULTIVARIATE
	p	HR (95% CI)	p	HR (95% CI)
bowel prep – no		1		1
bowel prep - yes	0.00	0.72 (0.57-0.91)	0.22	0.85 (0.67-1.10)
age (continuous)	0.00	1.05 (1.04-1.06)	0.00	1.05 (1.04-1.06)
sex female		1		1
sex male	0.04	1.20 (1.01-1.44)	0.00	1.31 (1.10-1.57)
affluent	0.11	1		
intermediate	0.27	1.16 (0.89-1.50)		
deprived	0.04	1.34 (1.01-1.78)		
Dukes' stage A	0.00	1	0.00	1
Dukes' stage unspecified	0.00	2.09 (1.46-3.00)	0.00	1.82 (1.27-2.63)
Dukes' stage B	0.01	1.48 (1.08-2.04)	0.04	1.40 (1.01-1.92)
Dukes' stage C	0.00	2.20 (1.61-3.02)	0.00	2.14 (1.56-2.94)
Dukes' stage D	0.00	6.56(4.31-9.99)	0.00	7.37 (4.83-11.25)
admission type – routine		1		1
admission type – urgent	0.04	1.31 (1.01-1.69)	0.15	1.21 (0.93-1.58)
any surgical complication	0.48	0.86 (0.58-1.29)		
elective surgery		1		1
emergency surgery	0.00	1.94 (1.38-2.74)	0.00	1.92 (1.32-2.79)

We found no difference in the proportions of surgical complications for anastomotic leak, intra-abdominal abscess, and fistula formation between both sets of patients – see Table 32. In addition, we measured rates of three further complications that have been previously noted as occurring more often in patients receiving bowel preparation, namely myocardial infarction, deep venous thrombosis, and pulmonary embolism (210). We found no statistically significant difference in frequency of these complications between patients who did and those who did not receive MBP.

Table 32 - Main postoperative (within 30 days of surgery) surgical complications in patients who received Mechanical Bowel Preparation (MBP). Pearson chi-square p-values of differences between MBP and non-MBP groups.

Complication	n	Received MBP	p value
Anastomotic leak	38	34 (89.5%)	0.38
Intra abdominal abscess	7	6 (85.7%)	0.82
Fistula	3	3 (100%)	0.46
Wound infection	71	59 (83.1%)	0.76
Myocardial infarct	31	25 (80.6%)	0.56
Deep venous thrombosis	6	5 (83.3%)	0.94
Pulmonary Embolism	5	5 (100%)	0.34
Chest Infection	64	58 (90.6%)	0.162
Not recorded	34	30 (88.2%)	0.533
Any complication	215	187 (84.4%)	0.265

5.5 Discussion

Patients who received mechanical bowel preparation before colon surgery had no better survival than those who did not in up to seven years' follow-up. A survival advantage of 28% remained after adjustment for age, sex, socio-economic circumstances, Dukes' stage and type of admission but was no longer significant after the addition of urgency of surgery to the multivariate model (HR 0.85, 95% CI 0.67 to 1.10). This suggests that the observed survival benefit was because of other factors related to emergency surgery. There are several possible explanations for our findings. The first is that selection biases accounted for the improved survival among patients who received mechanical bowel preparation which confound any real association. We included a validated measure of socio-economic circumstances, the DEPCAT, so that the confounding effects of underlying morbidities, such as smoking-related illnesses, would be attenuated. The second explanation might be that differential misclassification of patients occurred, such that those with better prognostic factors were systematically recorded as having poorer characteristics among patients receiving mechanical bowel preparation. Thus, after adjustment in a multivariable model, outcomes would be better than expected among the MBP group. This seems unlikely because the unadjusted Kaplan-Meier survival plot indicates improved survival among the cohort who received mechanical bowel preparation. The overall results of meta-analyses of randomised controlled trials of MBP have shown no clear benefit and, in some cases, worse postoperative complication rates (although no difference in postoperative mortality).(113-115,208) The results of individual RCTs have also consistently shown no benefit, an exception being a lower risk of peritonitis among MBP patients reported by Contant and others.(117,209,210) (211) It is possible that while no measurable reduction in postoperative complications occurs with MBP, there are other, subtler biological effects that confer improved long-term survival. Further work is needed both to replicate our findings and to explore biological mediators of survival such as C-reactive protein and albumin that might explain the long-term risks associated with emergency surgery (77,217) Potentially modifiable aspects of patient care and management are also putative explanations.

5.6 Conclusions

Long-term survival among colon cancer patients is not improved through mechanical bowel preparation prior to surgery nor does it reduce postoperative complications. Given that randomised controlled trials have consistently shown no short-term benefit of MBP, we suggest that there remains little argument in favour of its continued use.

There is no convincing evidence that mechanical bowel preparation affects short term outcomes for elective surgery for resection of colonic cancer. Meta-analyses suggest that postoperative complications may be greater among patients who receive bowel preparation. Despite this, it continues to be used routinely in many countries.

The long-term survival of patients treated with mechanical bowel preparation has not been previously reported. We followed-up 1730 patients for up to 7 years and found that a 28% greater survival among non-emergency hospital admissions for colon cancer surgery could be explained by lower emergency surgery rates. There was no significant survival advantage for patients given mechanical bowel preparation after adjustment for other risk factors. There is little evidence to support the continued use of mechanical bowel preparation prior to colon cancer surgery.

6 Type of rectal surgery as a proxy marker for quality of care

6.1 Introduction

This chapter addresses a further aim of this thesis, namely assessing extent of variation in treatment for rectal cancer within the West of Scotland and to what extent this has an impact on patient survival. In order to do this it has focussed on a current, nationally agreed objective measure of quality of surgery for rectal cancer patients - the APE (abdomino perineal excision) to AR (anterior resection) ratio. Rectal cancer patients have been chosen specifically as decisions relating to the timing and choice of surgical procedure are highly dependent upon the modern MDT process. Attaining the nationally agreed measure could therefore be regarded as a reflection or result of the MCN effect. As will be outlined, the APE: AR ratio can be viewed as a proxy measure for subspecialisation in rectal surgery. Subspecialisation in itself is thought to provide better surgical outcomes for patients as previously discussed (162).
There are growing numbers of putative indicators of quality of care in rectal surgery. These cover the entire perioperative period and have been explored and incorporated into various guidelines for treating this complex cohort of patients (82,218). Among them are clear circumferential resection margins (CRMs), number of patients receiving pre operative chemoradiotherapy and reduced numbers of patients with postoperative local recurrence of tumour. Underlying these measurements is the assumption that patients are accurately staged and therefore selected appropriately for surgery. As has been previously discussed, patients in our region have staging data that compares well with other, larger published series (82).

Rectal cancer is a common disease in the UK with 13 000 cases and 5000 deaths per year. In 2007, 379 men and 285 women died due to the disease in Scotland (22). Traditionally, there were two main perceived barriers to improved outcomes for patients with rectal cancer compared to colon cancer. These were a higher colostomy rate and higher local recurrence rate respectively.

In order to circumvent these problems, two major advances occurred. Firstly, technological advances in stapling devices: Smaller, more reliable and more ergonomically designed staplers allowed secure anastomoses to be made lower in the pelvis than before. This helped to reduce the APE to AR ratio as more patients became suitable for AR surgery. Secondly, the advent of total mesorectal excision (TME) lead to a reduction in local recurrence at the circumferential resection margin thus further improving outcomes and ultimately survival for rectal cancer patients compared to those with colonic lesions (52). It is now widely accepted that if the surgical principles of TME are adhered to the overall local recurrence rate should be <10% across all stages of rectal disease (219).

The NHS was founded on a set of principles dictating delivery of speciality and sub speciality services to all patients in the UK independent of socioeconomic background, race or sex. It is widely accepted that this vector of service delivery results in improved outcomes and more specifically, improved resection margins in rectal cancer patients. Providing a service to patients with rectal cancer in this manner is therefore extremely important.

Technological advances in CT resolution coupled with the greater availability of MRI scanning have resulted in improved preoperative staging. More precise and informed decisions can now be made regarding preoperative treatment plans. Postoperative reduction in CRM positivity has also been noted (220). Decisions regarding palliative and curative intent of surgery are now more accurate as a result.

Key differences between rectal and colonic cancer

There are various aspects of rectal cancer surgery that distinguish it from colon cancer surgery. The first and most obvious is anatomical location. The currently agreed definition of a rectal tumour has previously been stated by the Expert Advisory Committee of the ACPGBI. They maintain any tumour whose distal margin is seen at 15cm or less from the anal verge using a rigid sigmoidoscope should be classified as a rectal cancer (82). This is a grade C recommendation.

Secondly, and as a result of the anatomical location, rectal tumours are technically more difficult to resect. Locally advanced lesions present significant challenges for resection. Local invasion of the mesorectum and adjacent pelvic structures such as ureters, bladder and sacral nerves may occur. This, coupled with the narrow confines of the pelvis (especially in men), makes any attempt at resection particularly demanding for the surgeon (52). As mentioned in the introduction and background to this thesis, the management of rectal cancer is evolving. Preoperative ultrasound and / or MRI staging, preoperative radiotherapy, and depending on quality of resection, preoperative chemo radiotherapy are all modern adjuncts to surgical management of rectal carcinoma.

Given that rectal cancer is inherently more difficult to resect and involves a more complex approach to management it has come under much more quality control scrutiny.

Current surgical management of rectal cancer

Surgery is the mainstay of curative treatment for localised rectal cancer and is a major element of the multimodal management approach to more advanced curative and palliative staged disease. Abdominoperineal excision (APE), anterior resection (AR) and Hartmann's resection are three common options for the surgeon when excising a cancerous rectal lesion although many others exist (see appendix). Traditionally the curative procedure for lower rectal tumours was the APE which requires the removal of the anal sphincter complex. This necessitates a permanent colostomy. Whilst APE remains the only option in selected patients with very low rectal tumours where optimal oncological clearance is needed, for the majority the more modern technique of AR can be performed (221). This allows the retention of the sphincter complex and was generally considered preferable for the patient as it was assumed that a better quality of life resulted (222). More recently the Cochrane collaboration has published a review article stating that this assumption is not met. Patients with a permanent stoma do not seem to have a poorer quality of life than those without. They also concede that

firm conclusions cannot be drawn as it is a difficult area to produce objective outcomes (125).

In the NHS then, recommendations for reduced stoma rates in rectal cancer patients are more likely to be based on the long-term cost benefits in AR patients. This is because the ongoing care and expense associated with stoma care in APE patients is removed. It must be borne in mind that a degree of morbidity is seen in those patients undergoing AR too. Common symptoms include diarrhoea, incontinence, and chronic pelvic pain (125). APE therefore currently remains a valid operation for tumours of the low rectum in proximity to the sphincter complex and in patients where it is felt that the functional results obtained with a low restorative resection would significantly affect quality of life or compromise continence.

The introduction of the relatively modern total mesorectal excision (TME) technique and the use of low or ultra-low AR have led to significantly improved local disease control and overall survival for more patients with tumours in the lower rectum (52) (50). This is at the expense of poorer function in terms of bowel control and is coupled with the higher risk of nerve damage and subsequent bladder and erectile dysfunction. Positive circumferential resection margins are known to be a strong prognostic indicator of local recurrence in rectal cancer resection patients but there are currently no guidelines that state what proportion of positive resections margins in rectal patients is acceptable as an indicator of good quality surgery (84,223).

Current literature does not span the entire rectal cancer population of a defined region where there is a different organisation of health care resources. It would be of benefit to compare these to test whether we have a system that is more or less discriminatory in terms of patient sex and socioeconomic circumstances. To that end we wanted to explore both variation in type of operation offered to rectal cancer patients then provide a closer analysis of factors that could contribute to or explain the variation.

6.2 Aims & Objective

Aims

i. To assess if there was any variability in the ratio of types of major resection for rectal cancer throughout the region.

ii. To further explore this in order to ascertain factors that could explain the variability.

Objective

i. To logically and thoroughly analyse the combined dataset with regard to surgical procedures performed on patients with rectal cancer.

6.3 Method

Methodology was in keeping with that mentioned on page 73. In addition, there was an additional coding methodology adhered to in order that operations were correctly categorised (44). This can be seen in more detail in appendix 3.

Inclusion and exclusion criteria

Patients diagnosed with rectal cancer requiring surgical intervention in the West of Scotland from 2001 to 2005 were included in the study. Patients deemed to have advanced disease not amenable to surgical intervention, or those undergoing endoscopic treatment were excluded to minimise confounding effects on results.

A number of patients with tumours at other sites within the bowel (n=15) were also coded as receiving APEs in our larger dataset of colonic and rectal cancer patients. They were excluded.

6.4 Results

The characteristics of the population of rectal cancer patients in the West of Scotland from 2001 to 2005 can be seen in table 1. In total, 1574 patients met the inclusion criteria. The majority of patients were male (61%). The median age of all patients was 68. This represents a population skewed towards the right of a normal age distribution. This is in keeping with the incidence of rectal cancer. Of note is that 14.61% of patients had data missing regarding type of operation. This is highlighted in order to comment upon the degree of completeness of the dataset.

Table 33 - Demographics and characteristics of the 1574 patients in the West of Scotland undergoing a surgical procedure for rectal cancer from 2001 to 2005.

Variable		Frequency	%
Sex	Male	960	60.99
	female	614	39.01
Age	mean (SD)	67.03 (11.54)	
	range	75 (22-97)	
	median	68	
Operation type	APE	325	20.65
	AR	710	45.11
	Hartmann's	37	2.35
	Other	272	17.28
	Total	1344	85.39
	Missing	230	14.61
Intent	curative	1163	73.89
	palliative	179	11.37
	not recorded	232	14.74
Admission type	emergency	185	11.75
	routine or urgent	1212	77.00
	unknown	177	11.25
Dukes' stage	unspecified	316	20.08
	stage A	322	20.46
	stage B	381	24.21
	stage C	434	27.57

	stage D	121	7.69
deprivation group	affluent	216	13.72
	intermediate	935	59.40
	deprived	418	26.56
	Unknown	5	0.32
age group	<=60	422	26.81
	61-70	488	31.01
	71-80	480	30.50
	>80	184	11.69
Surgeon volume	>7 cases / yr	896	56.93
	<=7 cases / yr	413	26.24
	missing	265	16.84
year of incidence	2001	350	22.24
	2002	316	20.08
	2003	313	19.89
	2004	331	21.03
	2005	264	16.77
Health Board	Ayrshire & Arran	75.3*	17.60
	Argyll & Clyde	69.0*	18.23
	Glasgow	57.0*	31.45
	Lanarkshire	62.0*	21.92
	Forth Valley	60.3*	10.80
Tumour perforation	Yes	101	6.4
	No	1098	69.8
	Other†	375	23.8
	Total	1574	100.00

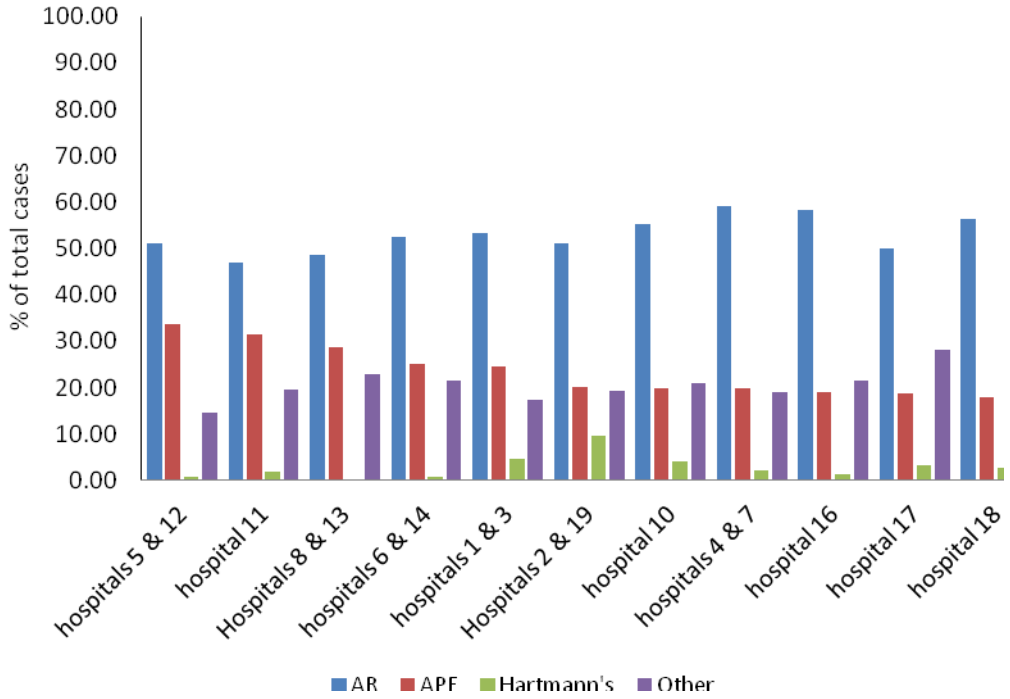
*Values are expressed as a rate per 100,000 of Health Board population. Health Board population numbers are derived from GRO Scotland. † not recorded, Inapplicable, or missing.

Variation between MDT groups

In figure 42 below the greatest proportion of ARs were performed in hospitals 4 &7 (59.12%) whereas the lowest was in hospital 11 (47.06%). The largest proportion of APE resections were performed in hospitals 5 &12 (33.79%) with only 17.95% in hospital 18. The proportion of "other operations" varied from 14.48% in hospitals 5 &12 to 28.13% in hospital 17. Similarly, a large variation in numbers of recorded Hartmann's operations occurred. None were recorded in hospitals 8 & 13 whereas hospitals 2 & 9 recorded 9.62% of operations for rectal cancer as being Hartmann's procedure. Overall, a statistically significant difference was observed in the proportions of operations performed between MDTs ($p = 0.004$).

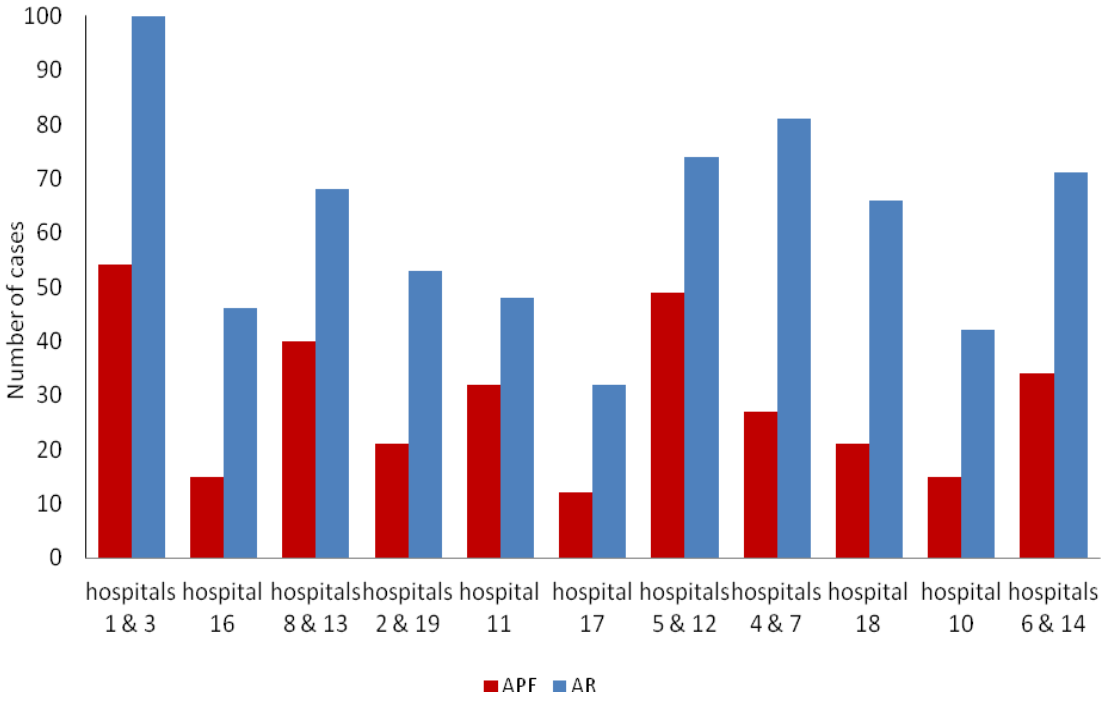
Figure 42 also highlights the variation in rectal operations performed for cancer patients within the MCN (Managed Clinical Network). Nine of the 11 MDTs were attaining the now recommended rate of <30% APE for all rectal tumour resections (82). There was a constant proportion AR operations being performed across the region, ranging from 47% of total to 59% of total operations performed). A larger variation existed with regard to Hartmann's procedures. It appeared that in hospitals 8, 13, 6, 14, 5 and 12 there were very few Hartmann's procedures taking place whereas almost 10% of all rectal cancer resections were Hartmann's in the MDT at hospitals 2 & 9.

Figure 42 - Summary of variation in use of main rectal cancer surgical operations by MDT in the West of Scotland. APE, abdominoperineal excision; AR, anterior resection. n = 1318, P=0.004



By concentrating on only the two major operations for rectal cancer a non-significant variation across all MDTs is demonstrated (p=0.122). This is shown in figure 43 below.

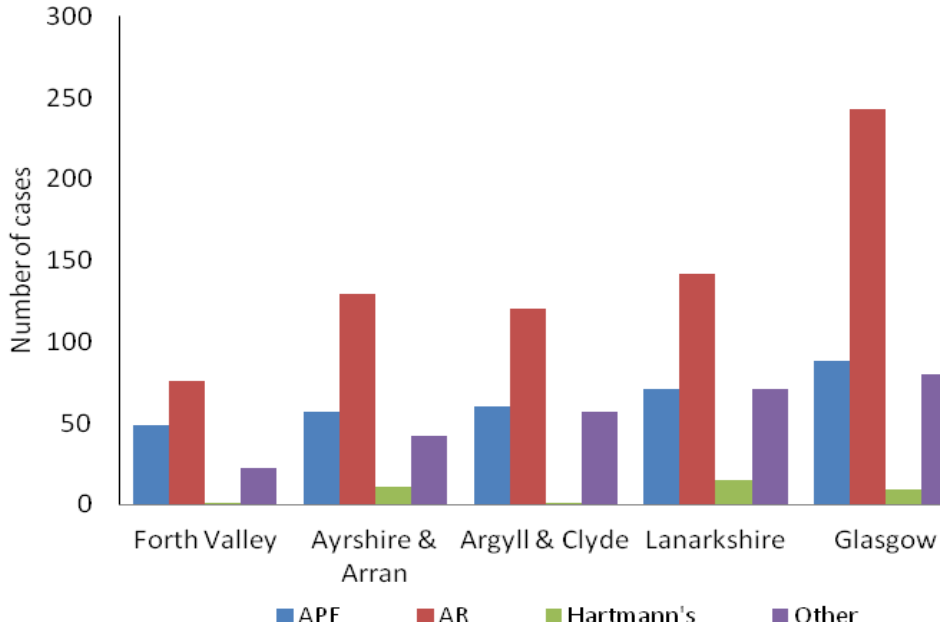
Figure 43 - Variation in use of only APE and AR rectal cancer surgical operations by MDT in the West of Scotland. n = 1018, p = 0.122.



Variation between different Health Boards

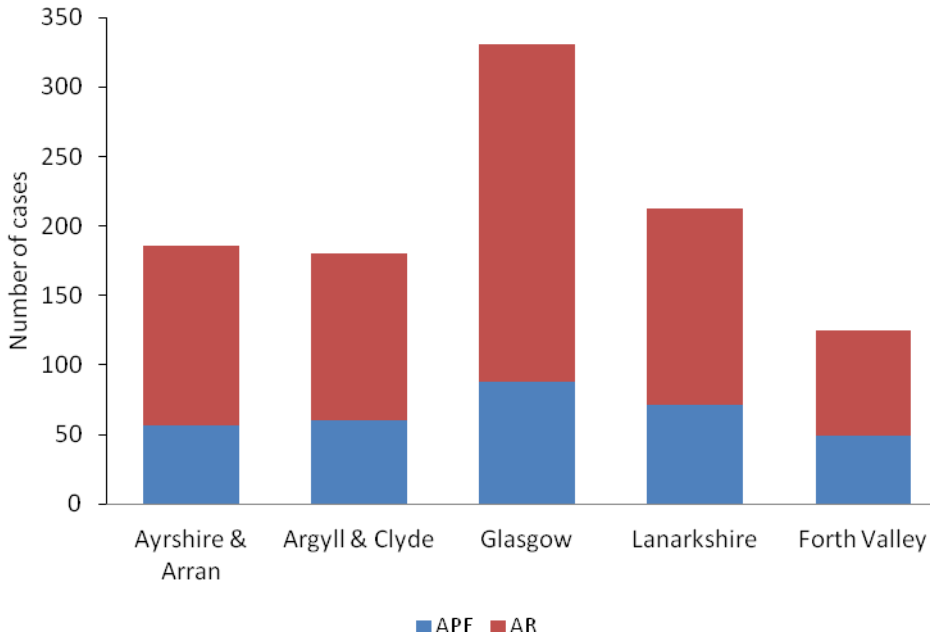
A statistically significant difference is observed in the proportions of operations performed between Health Boards (p = 0.001) This is possibly due to the large variation in number of operations recorded as other. In order to test this, a further comparison has been made, excluding all Hartmann's operations other than AR and APE.

Figure 44 - Variation in use of main rectal cancer surgical operations by Health Board in the West of Scotland. APE, abdominoperineal excision; AR, anterior resection. n = 1344, p =0.001



Again, by selecting only APE and AR operations the statistically significant variation seen across the region disappears. Despite there being a wide variation in total numbers of procedures carried out with over 300 in Glasgow and less than 150 in Forth Valley, the difference in proportions of APE to AR is not statistically siginificant (p=0.098).

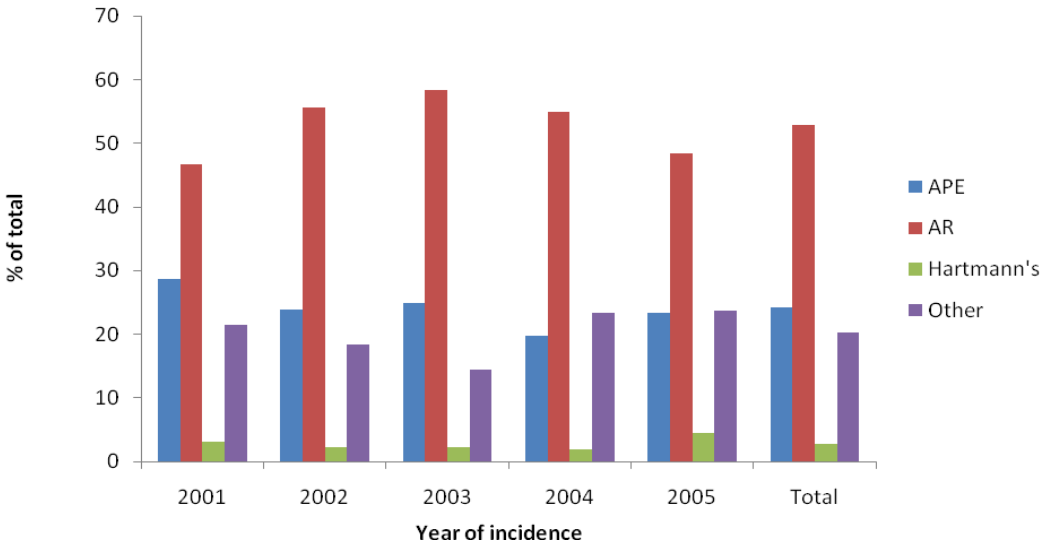
Figure 45 - Variation in use of only APE and AR rectal cancer surgical operations by Health Board in the West of Scotland. n = 1035, p = 0.098



Variation with time

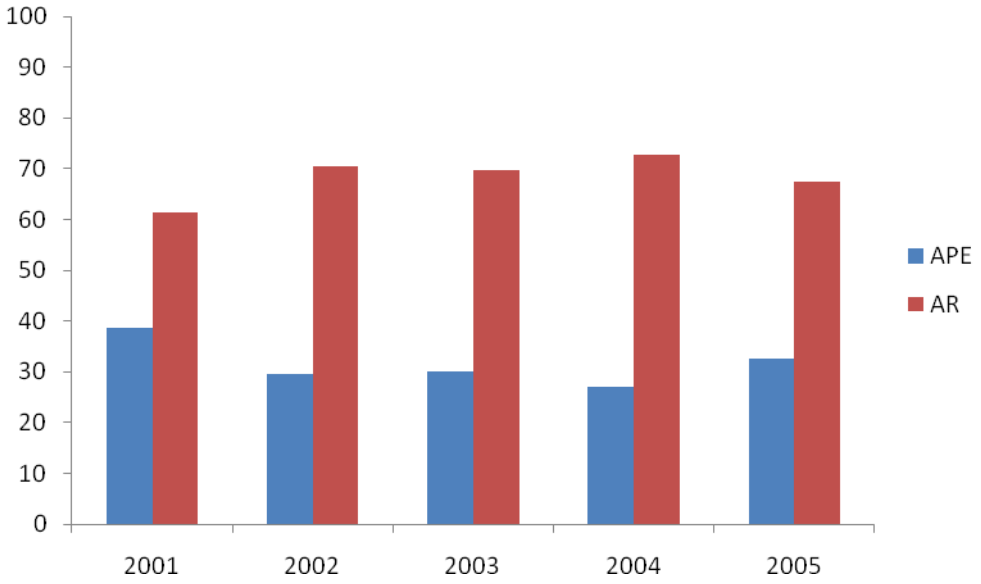
In figure 46 the ratio of APE to other operations was highest in 2001. This reduced with time. The proportion of APE rectal operations was largest in 2001. The proportion of ARs was highest in 2003. Overall, a statistically significant difference was seen (p = 0.034) in proportions of operations performed for rectal cancer however this seems to be due to variation in type of operation and not due to a consistent trend towards less APEs and more ARs. In order to assess this a closer look at APE to AR ratio is required.

Figure 46 - Change in proportions of rectal cancer operations performed with time in the West of Scotland from 2001-2005. n =1344, p = 0.034



As seen above with both MDT and Health Board, the variation noted when looking at all rectal cancer operations disappears when selecting only APE and AR. In figure 47 although a reduction in the overall number of APEs perfomed can be seen with time it was not statistically significant (p=0.121). If the length of time over which data were analysed was to be increased, a significant trend might emerge.

Figure 47 - Change in proportions with time of the 2 main rectal cancer operations, APE and AR. n = 1017, p =0.121



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Comparing the population of rectal cancer patients receiving APE with those receiving AR

Table 34 shows that the groups of patients undergoing APE are well matched in terms of sex, stage and deprivation category with those undergoing AR. A far higher proportion of patients undergoing APE were emergency admissions (14.2% compared to 8.9%). This contrasts to the 18% reduction in odds of undergoing APE as an emegency admission stated by Morris et al (44). Chi square testing of deprivation groups produced a p value of 0.576. This is particularly noteworthy and will be discussed below. Surgeon volume is an ongoing area of debate in relation to surgical outcomes (164). This table demonstrates a statistically significant difference in proportions of patients undergoing resection by surgeons operating on differrent volumes of patients. Again, this confirms previously published findings (44). Intent of operation was also found to be statistically significant (p=0.034) indicating that a higher proportion of patients undergoing curative resection have a sphincter saving operation. Of particular note is that we found no statistically significant difference between proportions of APE and AR in relation to sex nor deprivation group. In total, 26.2% of the APE patients had a positive circumferential margin whereas only 10.1% of AR patients had a

positive circumferential margin. These figures agree with those previously published in both Holland and Leeds (47) (49).

Table 34 - Chi square test results used to assess differences in proportions of APE and AR in relation to ten variables of interest when comparing proportions of APE and AR only.

		APE	AR	p
		n = 325	n = 710	
		(31.4)	(68.6)	
Age mean (SD)	66.31(11.01)			
Gender	Male	193 (59.4)	428 (60.3)	0.785
	Female	132 (40.6)	282 (39.7)	
Type of admission	Emergency	46 (14.2)	63 (8.9)	0.028
	Other	275 (84.6)	633 (89.2)	
	Unknown	4 (1.2)	14 (2.0)	
Depgroup	Affluent	49 (15.1	90 (12.7)	0.576
	Intermediate	188 (57.8)	425 (60.1)	
	Deprived	88 (27.1)	192 (27.2)	
Dukes' stage	A	58 (17.8)	88 (12.4)	0.121
	B	95 (29.2)	207 (29.2)	
	C	97 (29.8)	239 (33.7)	
	D	15 (4.6)	34 (4.8)	
	unspecified	60 (18.5)	88 (12.4)	
Year of incidence	2001	82 (38.14)	133 (61.86)	0.117
	2002	65 (29.95)	152 (70.04)	
	2003	67 (21.91)	157 (70.1)	
	2004	54 (26.5)	150 (73.5)	
	2005	57 (32.57)	118 (67.43)	

Surgeon volume	> 7 cases / yr	202 (29.66)	479 (70.33)	0.030
	<= 7 cases/yr	108 (36.73)	186 (63.27)	
Intent of operation	Curative	280 (86.2)	648 (91.3)	0.034
	Palliative	31 (9.50)	39 (5.50)	
	not recorded	14 (4.30)	23 (3.20)	
Health Board	Ayrshire & Arran	57 (30.64)	129 (69.35)	
	Argyll & Clyde	60 (33.33)	120 (66.66)	
	Glasgow	88 (26.59)	243(73.41)	
	Lanarkshire	71 (33.33)	142(66.67)	
	Forth Valley	49 (39.20)	76 (60.80)	0.089
MDT Group	hospitals 1 & 3	54 (31.58)	117 (68.42)	
	hospital 16	15 (24.59)	46 (75.41)	
	hospitals 8 & 13	40 (37.04)	68 (62.96)	
	hospitals 2 & 19	21 (28.38)	53 (71.62)	
	hospital 11	32 (40.00)	48 (60.00)	
	hospital 17	12 (25.00)	32 (72.73)	
	hospitals 5 & 12	49 (24.14)	74 (60.16)	
	hospitals 4 & 7	27 (25.00)	81 (75.00)	
	hospital 18	21 (24.10)	66 (75.86)	
	hospital 10	15 (26.32)	42 (73.68)	
	hospitals 6 & 14	34 (32.38)	71 (67.62)	0.122
CRM positivity	Yes	70 (26.20)	58 (10.10)	
	No	197 (73.80)	517 (89.90)	<0.005
Tumour perforation	Yes	27 (9.31)	43 (6.41)	
	No	263 (90.69)	628 (93.59)	0.112

Univariate and multivariate findings

Of the 13 variables assessed on univariate analysis, only age (as a continuous variable), Dukes' stage and circumferential margin positivity were found to be statistically significant.

Table 35 - Results from univariate binary logistic regression analysis with APE as the dependant variable.

Explanatory variable	p	OR	95% CI
Age continuous	0.01	0.99	0.976-0.996
Age categorical	0.23		
<=60		1.00	1.00
61-70		1.04	0.76-1.43
71-80		0.91	0.659-1.25
>80		0.65	0.40-1.04
Sex	0.51		
Male		1.00	1.00
Female		1.09	0.85-1.40
Deprivation group	0.69		
Affluent		1.00	1.00
Intermediate		0.86	0.60-1.23
Deprived		0.91	0.61-1.35
Dukes' stage	0.02		
A		1.00	1.00
B		1.51	1.05-2.18
C		1.31	0.91-1.88
D		0.64	0.35-1.19
Unspecified		1.07	0.72-1.59
Type of admission	0.51		
Urgent/routine		1.00	1.00
Emergency		1.13	0.79-1.62
Year of incidence	0.23		
2001		1.00	1.00

2002		0.85	0.59-1.22
2003		0.89	0.62-1.28
2004		0.06	0.44-0.93
2005		0.90	0.61-1.32
Intent of operation	0.05		
Curative		1.00	1.00
Palliative		0.66	0.44-1.00
Circumferential margin	<0.001		
Negative		1.00	1.00
Positive		2.60	1.83-3.69
Volume of surgeon	0.15		
< 7 cases per year		1.00	1.00
>= 7 cases per year		0.82	0.63-1.08
Health Board	0.05		
Health Board		1.00	1.00
Health Board (1)		0.64	0.41-0.99
Health Board (2)		0.65	0.42-1.01
Health Board (3)		0.53	0.36-0.80
Health Board (4)		0.64	0.42-0.98
MDT groups	0.16		
MDT group		1.00	1.00
MDT group(1)		0.98	0.60-1.60
MDT group(2)		0.64	0.33-1.26
MDT group(3)		1.20	0.71-2.03
MDT group(4)		0.78	0.42-1.45
MDT group(5)		1.37	0.78-2.42
MDT group(6)		0.63	0.30-1.31
MDT group(7)		1.56	0.93-2.60
MDT group(8)		0.74	0.42-1.31
MDT group(9)		0.65	0.36-1.20
MDT group(10)		0.69	0.35-1.35

Table 36 - Results from multivariate binary logistic regression analysis with APE as the dependant variable.

	p	OR	95.0% C.I.for EXP(B)	
			Lower	Upper
Age*	0.03	0.98	0.97	1.00
Depgroup	0.13			
Affluent		1.00	1.00	
Intermediate	0.07	0.65	0.41	1.03
Deprived	0.06	0.61	0.36	1.01
Stage of disease	0.31			
Dukes' A		1.00	1.00	
Dukes' unspecified	0.74	1.10	0.64	1.90
Dukes' B	0.99	1.00	0.64	1.57
Dukes' C	0.14	0.71	0.45	1.12
Dukes' D	0.36	0.67	0.28	1.58
Sex	0.58			
Male		1.00	1.00	
Female		1.09	0.80	1.50
Volume	0.61			
< 7 cases per year		1.00	1.00	
>= 7 cases per year		0.91	0.65	1.29
Type of admission	0.67			
Urgent/routine		1.00	1.00	
Emergency		1.12	0.68	1.84
Year	0.35			
2001		1.00	1.00	
2002	0.06	0.64	0.40	1.02
2003	0.11	0.68	0.43	1.09
2004	0.18	0.72	0.44	1.16
2005	0.26	0.75	0.46	1.23
Operative intent	0.53			
Curative		1.00	1.00	
Palliative		0.82	0.44	1.52

Circumferential margin	<0.001			
Negative		1.00	1.00	
Positive		3.49	2.32	5.27

* age measured in continuous whole years. It became non-significant (p = 0.73) when grouped as an ordinal categorical variable.

The following table demonstrates that of the three variables found to be statistically significant on univariate analysis (age as a continuous variable, Dukes' stage and circumferential margin positivity) only the last retains its significance when entered into a multivariate model with the other two. Following adjustment for the other covariates, a positive circumferential margin confers a mortality risk of 3.68 times more than would be seen in a patient with a negative margin.

Table 37 - Combined univariate and multivariate results.

Factor	**Univariate OR (95% CI)**	**Multivariate OR (95% CI)**
age (continuous)*	0.98 (0.97-0.99)	
Depgroup		
Affluent	1.00	
Intermediate	0.86 (0.60-1.23)	
Deprived	0.91 (0.61-1.35)	
Stage of disease		
Dukes' A	1.00	
Dukes' unspecified	1.07 (0.72-1.59)	
Dukes' B	1.51 (1.05-2.18)	
Dukes' C	1.31 (0.91-1.88)	
Dukes' D	0.64 (0.35-1.19)	
Sex		
Male	1.00	
Female	1.09 (0.85-1.40)	

Volume		
< 7 cases per year	1.00	
>= 7 cases per year	0.82 (0.63-1.08)	
Type of admission		
Urgent/routine	1.00	
Emergency	1.13 (0.79-1.62)	
Year		
2001	1.00	
2002	0.85 (0.59-1.22)	
2003	0.89 (0.62-1.28)	
2004	0.06 (0.44-0.93)	
2005	0.9 (0.61-1.32)	
Operative intent		
Curative	1.00	
Palliative	0.66 (0.44-1.00)	
Circumferential margin		
Negative	1.00	1.00
Positive	2.60 (1.83-3.69)	3.58 (2.38-5.36)

6.5 Discussion

Comparison with previous studies

In terms of population demographics our sex distribution of 60.99% male to 39.01% female compares well to that reported in previous series. The most recent UK paper quoted proportions of 63.2% males to 36.8% females. Tilney et al cite a sex distribution of 62.15% and 37.85% for males and females respectively (43,44). In contrast to these large scale studies, we found no evidence that males were more likely to undergo APE rather than AR.
The mean age of our population (67.03) is also within 1 year of that reported by Tilney et al in their January 2008 study (43).

In our population the percentage of emergency admissions (11.75%) is almost double that quoted in other similar series (5.8%) (44). It is possible that inter-regional differences exist in interpreting the term emergency. Otherwise this may point to the fact that patients with rectal cancer present later in their disease process in our region. This observation is supported by the proportion of patients in our cohort with Dukes' stage D disease (7.69%) compared to 3.7% in the large Morris et al cohort. Dukes' D disease is more likely to present as an emergency as patients are more likely to obstruct or decompensate physiologically if they have a large, obstructing tumour or metastases respectively.

It appears that on average, patients diagnosed with rectal cancer in the West of Scotland present younger than those in other published series. A smaller proportion of patients are not only in the oldest age group (>80 years) but in the next oldest age group also (71-80 years). This amounts to 11.69 and 30.5 percent of the total compared to 12.2 and 33.1 percent in the large English series (44). There also remains a proportion of patients with Dukes' stage of disease unspecified. In our series this was 20.08% of the population. That in the larger Morris population is 25.5%. Our data are therefore more complete in relation to staging of disease.

Previous groups have noted a socioeconomic bias in the form of increased use of APE in more deprived patients. We were not able to demonstrate this in our

population suggesting that there is possibly less deprivation bias in patient selection processes for type of operation in the West of Scotland. This is particularly relevant given that ISD Scotland report a statistically significant trend with P<0.005 for both incidence and mortality in patients with rectal cancer in more deprived populations (192). If the incidence is rising in more deprived populations then we can expect to be treating more of these patients and should be offering them the same treatment as more affluent patients.

Oncological outcomes

It has been previously noted that inferior oncological outcomes occur following APE. In particular, the circumferential resection margin (CRM) positivity has been cited as being positive more often in APE operations when compared to AR (224) (48) (49). This was one of only two variables in this study retaining their significance in predicting likelihood of APE following regression analysis (table 3). We therefore confirm that APE results in poorer resection quality in terms of margin involvement in our population despite adjustment for case mix.

Regional Variation

During the study period there were 17 hospitals grouped into 11 different functioning MDTs. These 11 MDTs together constitute the MCN for colorectal cancer in the West of Scotland. When considering all rectal cancer procedures, statistically significant variation was seen across MDTs in the region (figure 1). When concentrating on only APE and AR this disappeared (figure 2).

This could partly be explained by a difference in case mix between MDTs with some hospitals encountering a higher proportion of patients with lower rectal tumours. It could also be explained by an internal difference in coding between hospitals. A further possibility is surgeon preference for performing certain operations for particular rectal lesions. This difficulty with variation in coding of operations has been noted previously (44,54). Fortunately though, a recent comparison of administrative data with the Association of Coloproctology of Great Britain and Ireland database concluded that there was a good correlation of accuracy between the two. This was particularly the case for rectal cancer operation data (55).

Furthermore, we looked at the variation between Health Boards. A similar picture to that at MDT level is seen when looking at numbers of rectal cancer resections across different Health Boards. The encouraging finding is that all have an APE rate below the 30% rate recommended by the ACPGBI, except Forth Valley (82). These guidelines were produced in 2007 however, which is later than the period under study. A statistically significant difference is observed in the proportions of operations performed between Health Boards ($p < 0.05$). This is more likely to be due to the larger variation in numbers of "other" and Hartmann's operations being performed than a large difference in the APE to AR ratio. Indeed this was borne out in table 2 where Health Board was found to be not significant ($p=0.089$) when comparing proportions of APE to AR operations without Hartmann's and other included.
Again, when only APE and AR are analysed in relation to distribution of these operations across different Health Boards there was no statistically significant difference found ($p = 0.098$).

Variation according to sex

Unlike previous studies we found no significant difference in proportions of patients receiving an APE according to sex ($p = 0.58$). See table 36.
We also found no significant difference in the proportion of patients receiving APE compared to AR in relation to deprivation group, unlike Morris et al. Both of these findings would suggest that the service offered to patients in this population could be viewed as less discriminatory on the basis of sex and deprivation.

Variation with time

The agreed aim of mid and high rectal cancer surgery is to preserve the sphincter complex as far as possible thus ensuring relatively normal bowel function. It has also been said that reducing permanent stoma rates reduces the future financial burden on the NHS. With time then, we would hope to reduce the rate of APEs performed. Figure 47 demonstrates that although there is a significant difference in the proportions of all procedures performed with time, it is not a constant reduction. Moreover, by concentrating only on the

relationship between APE and AR with time we are able to show no significant difference in proportions of operation performed with time. (p= 0.121) Whilst other centres have been able to show a definite reduction in APE rate with time it may be that we are not considering a trend over a long enough time frame in this series. It may also be that the region has potentially attained its lowest possible APE rate at an earlier stage. We may therefore be unlikely to see a significant drop with time.

Most importantly, the overall APE rate over the study period never exceeds the recommended rate of 30% (82). This is an arbitrary number that has been arrived at through consensus recognising that it is difficult to determine what the ideal ratio of anterior resection to APE should be. A further recommendation is that if any doubt exists as to type of operation then experienced second opinion should be sought. It would be useful to know how often a second opinion is sought by surgeons, and in what circumstances.

Rates of use of APE over time have been shown to be consistently dropping across other published series (43,45,225).

The next stage in analysis was to explore the various significant results from binary logistic regression. Table 36 shows that when using APE as the dependent variable, only age and positive circumferential margin remain statistically significant indicators of whether or not a patient is likely to have had an APE resection instead of an anterior resection.

Strengths and weaknesses of this study

Incorrect or absent recording of operation type is a potential source of error in this study. Rate of APE may be falsely low as 12.09% of operations were not categorised. The fact that this study depends upon accurate OPCS codes has not been overlooked. We are aware that both accuracy and quality of coding rely on accurate input from audit staff. Not until their performance is regularly audited or until consultant surgeons are coding their operations themselves and having their practice audited by peers will we see a reduction in coding error and missing codes. Reassurance is taken from the conclusions of a recent study

stating that administrative data regarding rectal cancer patients has a good correlation of accuracy with prospectively collected data from the ACPGBI (55).

Should intent of operation be used as a reliable discriminator? The decision as to whether an operation is deemed curative or palliative is now generally made by a team at a colorectal MDT whereas historically it was made by the consultant in charge. To that end it is now less subjective. More accurate staging data also adds to the objectivity of this decision. It is recommended that the term curative resection should be based on surgical and histological confirmation of complete excision. Surgeons should expect to achieve an overall curative resection rate of 60%, but it is appreciated that this will depend at least in part on the stage at which patients present (82). We feel this was perhaps an unreliable variable but is becoming more objective with time. As such, stronger conclusions will be able to be drawn as objective pathological evidence is added.

There will always be a subset of patients for whom there is no option but to perform an APE. The main factor in determining this is distance (or height) of the tumour from the anal verge. It has been suggested that in these patients a more radical version of the traditional APE may need to be performed in order to ensure adequate oncological resection margins (226). A major drawback of this study is not being able to adjust for height of tumour. This would allow for more insight into how operations are applied according to height of tumour and how influential height is in making a decision regarding type of operation.

Data regarding the proportion of procedures carried out laparoscopically is lacking. It is imperative that these data are also analysed as laparoscopic surgery has a steeper learning curve thus having a greater potential to produce more variation in practice across a region as trainees learn from the outset of training and consultants adopt the newer laparoscopic techniques.

Implications for clinical practice

Quantifying and addressing the variations in surgical practice is a key component in trying to achieve a high quality of cancer care for all.

Herein we have demonstrated that we are able to combine sources of routinely collated colorectal cancer data to view rectal cancer surgical practice at a regional level, covering a population of 2.2million. This is the first time this has been done for an entire, defined population of rectal cancer patients.

Our population in the West of Scotland is age and sex matched with other populations. We have a higher proportion of patients presenting as emergencies and with more advanced disease at a younger age. This has implications for more investment in educating the population with regard to early signs and symptoms of rectal cancer as well as encouraging further uptake of the successful bowel screening project.

In contrast to a large published series, and following multivariate binary logistic regression modelling, we show only statistically significant differences in the number of patients receiving an APE in relation to circumferential margin positivity. Univariate modelling revealed that patients undergoing APE were more likely to be older and have positive circumferential margins than those undergoing AR. These differences were then attenuated following adjustment in the multivariate model, with the exception of circumferential margin positivity.

These findings differ from previously published series in that a patient is no more or less likely to receive an APE in our region according to their sex or deprivation. The service in our region appears to be less discriminatory with regard to these parameters.

Implications for further research

Further work should assess the adherence to both NICE and ACPGBI guidelines relating to laparoscopic resections for rectal tumours. A further aspect for investigation would be that of node harvest, adherence to the NICE guidance of removing and examining a minimum of 12 lymph nodes from their resected surgical specimens.

We are not able to accurately assess the height of each rectal tumour from the anal verge or proportion of perforated tumours. This would facilitate a far more accurate analysis of this population of patients as well as offering further insight into the reasons for the observed differences in practice. In addition, comparison could be made with other published series.

6.6 Conclusions

Variation exists in surgical treatment for rectal cancer in the West of Scotland. Unlike previously reported findings from elsewhere in the UK, we have been able to demonstrate that patients are no more or less likely to undergo an APE resection according to their sex, intent of operation or underlying socioeconomic circumstances. We therefore conclude that the service being offered to patients in our region is currently an equitable one.

We have also confirmed (thus further validating) previous findings that CRM positivity retains statistical significance in a multivariate model and is associated with an APE resection rather than AR for rectal cancer.

7 Final Discussion

Summary

This thesis completes a more detailed analysis of survival outcomes for colorectal cancer patients in the West of Scotland than has been previously possible. This has enabled assessment of the degree to which services for colorectal cancer patients have affected the likelihood of desired health outcomes. I have created a merged dataset combining accurate cancer registry data with detailed clinical audit data to provide a unique insight into factors contributing to changes in overall survival for colorectal cancer patients since the inception of regional multidisciplinary team management strategies in 2001. I have also been able to nest current overall survival outcomes in the context of long-term survival by comparing contemporary outcomes with historical data from the cancer registry.

To understand the impact of a reorganization of services, in this case the MCN, it was necessary to understand how survival with colorectal cancer has changed over time. This was measured both before and after inception of the novel service structure. The unadjusted overall survival figures from chapter three initially suggested an increase in overall five year survival with time with a disproportionate rise in survival for rectal cancer patients. Further analysis demonstrated this increase to be linked to female patients with rectal cancer only.

In the MCN era, differences in overall survival across the region's Health Boards and MDTs were seen. We were then able to adjust for known common confounders such as age, stage and deprivation to ascertain whether these persisted.

After taking these factors into account we found that the observed effects of the common confounding variables observed on univariate testing were generally attenuated and explained in proportional hazards models. For all curative intent surgery on colorectal cancer patients in the West of Scotland we have now confirmed that age at incidence, stage of disease, distal margin positivity,

extramural vascular invasion, apical node positively and sex (in favour of women) were all found to exert significant individual prognostic influence upon survival.

Having shown that survival has improved since 2001, to what extent can it be explained by known determinants of survival? Following on from the aforementioned results there were new findings. We have now shown that bowel preparation exerts no significant survival advantage to patients either immediately postoperatively or in longer-term follow-up. We then investigated what other aspects of the reorganization might be responsible. Firstly, greater specialist care and particular aspects of this care, namely type of resection for rectal cancer in the form of APE or AR. With regard to type of resection for rectal cancer, the main finding was that there was no statistically significant difference in type of operation received in relation to patient's socioeconomic circumstances. This suggests that the disparity noted in other parts of the UK is not occurring in the West of Scotland (43,44).

We were able to demonstrate that the influence of socioeconomic circumstances did not remain a significant prognostic indicator for long-term overall survival in all colorectal cancer patients undergoing elective surgery for their cancer. This can be seen as a marker for service quality in that its selection of patients is not biased in terms of their deprivation.

Unfortunately our data and analyses are not yet mature enough to be able to accurately assess the net impact of the MCN on 5-year overall survival. We are able to say that in relation to 3 year overall survival there is a significant improvement for rectal cancer patients when comparing figures from 1980 to 2000 with those after inception of the MCN structure. There also appears to be an improvement in 3 year overall survival when comparing all female colorectal cancer patients from 1997 to 2000 with those post 2000 (i.e. in the MCN). This evidence is encouraging for exponents of MCN care.

Quality of data

It has previously been noted that "Scottish health networks have developed impressive guidelines for collecting reliable data on the impact of cancer services on outcomes" (227). The practicalities of audit data collection vary across the West of Scotland. In some units the main clinical/surgical forms are filled in by the surgeon, the pathology form by the pathologist and the chemotherapy form filled in by the oncologist. Clinical audit staff support this process. They ensure that the various component audit forms are completed. They then attempt to complete missing entries from case note information or by referring back to the relevant clinician to attempt a higher rate of completeness. This may be a process that could potentially be improved by application of lean thinking to allow greater case ascertainment/ accuracy.

Scotland's cancer registration system compares well with those in other countries. Case ascertainment is believed to be approximately 95%. Computerised probability linking is quoted as being 99% accurate and procedure coding is thought to be correct in the vast majority of cases too (96%) (154). The initial, larger, SMR06 dataset is therefore accurate enough to be considered as reliable. The second dataset used is derived from the West of Scotland MCN database. As highlighted in the results section, there are areas of this dataset that vary in terms of their completeness. In some cases there is a disappointing trend towards reduction in completeness with time. This has been taken into consideration when interpreting results.

The use of linked routine data sources can paint a unique picture unavailable to alternative methods of data collection. It transcends the barriers of sample bias that can be introduced when dealing with datasets from individual hospitals or sets collected by small teams. An advantage of using routinely collected data is the insight they provide into the recent past in the West of Scotland. It should be borne in mind that the patients have not been recruited into this study thus eliminating a further potential source of bias. Whereas results from specialised centres may be misleading due to referral bias and the possible effect of

specialisation in its own right, cancer registries allow the analysis of true epidemiological trends.

A series of 1911 patients in Australia had a 96% ascertainment for Dukes' staging (71). Using Dukes' stage as an exemplar, our data are 78.8% complete for this variable from 1997 onwards but only 74.2% complete from 2001 onwards. This may reflect a change in practice from recording Dukes' stage to TNM in some centres. It may also reflect an increase in number of patients deemed to be palliative from the outset. This therefore forgoes the need to record their Dukes' stage.

Artefact

Artefact can arise through random error, confounding, and bias. Both random error and confounding factors are taken into account in statistical testing. Bias is discussed forthwith.

Bias

Bias can be either selection bias or measurement/observer bias. Is what we are recording truly an observation of what we are trying to measure or is it odd in some way? In order to test this I endeavoured to compare the novel findings with those previously published elsewhere.

The linkage of data can introduce bias to the results. Firstly, there are a number of cases that inevitably fail to match. This means we are not accounting for the entire population of colorectal cancer patient in our analyses.

Selection biases are a further well-known source of bias. There are varying numbers of DCO patients with colorectal cancer patients in different countries. A proportion of DCO patients will have died of colorectal cancer but may not have this fact recorded on their death certificates. This is bound to influence incidence and survival estimates. To what extent is not known.
A certain proportion of patients will escape capture by the MDT and cancer registry process.

There are a variety of potential reasons why patients may never enter into the MDT care pathway for treatment of their colorectal cancer.

- They are deemed too unwell at time of diagnosis to warrant any further intervention and are channelled straight into a palliative care pathway.
- Other co morbidities and their treatment preclude the patient from being assessed by the colorectal MDT, e.g. end-stage organ failure. With time, almost all patients are now included in MDT discussion in order to ensure their capture i.e. for completeness of audit.
- Post mortem diagnosis of colorectal neoplasm.
- Migration to another area of the country.
- Diagnosis in a private hospital.

We know this is not such a large problem in Scotland as reported elsewhere in the UK (198).

Exclusion and restriction of patients from analysis also introduces bias. This is a common criticism of the methodology for trials testing effects of chemotherapeutic agents. They tend to exclude patients at the extremes of age. In terms of exclusion, we omitted patients younger than 15 years and older than 99 years from analysis. Although this does introduce bias we are primarily interested in the effects on survival of patients in this age group as they represent the vast majority of those undergoing treatment for colorectal cancer.

Bias and confounders are artifices of the scientific process. They should therefore be minimised through rigorous methodology wherever possible. We have endeavoured to do this.

Missing information

Following matching of cases in the MCN dataset with those in the registry we were then able to assess how much information was missing. The proportion of matched cases with unknown values in various variable fields has previously been cited as an indicator of data quality. In his Review article Bray states that this can be due to problems with “the data collection system, or access to

necessary source documents; item and code values that are defined; or misapplication of coding rules." (198)

I have demonstrated in our dataset that there was certainly a degree of missing information. Having highlighted above how this information is collected we can assume that there are multiple points in the process where missing information could arise. Various measures can be instituted to overcome these problems. These range from reabstracting and recoding of a proportion of cases by a third party. This ensures reproducibility of results amongst data collectors. A computer-based, national system where data are entered directly at the time of MDT discussion would reduce the number of steps that data take to get from MDT to the MCN database. A nationally agreed minimum dataset such as that used by the Royal College of Pathologists would provide a baseline with which to compare patients across the nation (153).
Perhaps, in the current climate of data transparency and individual consultant performance, the most important of the fields with a large proportion of data missing was the "consultant in charge" variable. Had this field been more accurate, a far more detailed analysis could have been undertaken relating to consultant specific outcomes and specialisation.

In future perhaps a more appropriate methodology would be to apply a multiple imputation strategy. This is a validated and standardised way of accounting for missing data in epidemiological and clinical research situations and applies to most studies as they inevitably have some missing data. A recent review by Sterne et al highlights the various types of missing data and their consequences. They then go on to describe the application of multiple imputations and highlight some pitfalls (228). Results of a survey in the USA comment on predictors of completeness for their population (229). They note a marked variation for completeness of data when comparing information on patients in different hospital types and different age groups. These trends differ with respect to type of therapy received.

Factors affecting quality

Descriptions of the quality of care can be targeted towards factors regarding either access to care, processes of care in hospital and then outcomes of care. In this thesis I was concerned with the processes of care and their outcomes.
I recognise that there are a multitude of factors known to contribute to the worldwide variation in the outcomes of cancer care. I was necessarily restricted to analysing those regarding colorectal cancer patients in the West of Scotland region. Furthermore I was concerned with ascertaining the particular aspects of quality care that are potentially modifiable to improve outcomes for colorectal cancer patients. I initially summarised long-term outcomes for all colorectal cancer patients. I was then trying to dissect the various measurable aspects of their care to assess the aspects of care that impact on survival.

Age

Traditionally surgeons tend to evaluate patients on the basis of chronological age and not biological age. Novel work in Glasgow regarding biological age of tumours could help to provide a more accurate assessment thus improving patient selection(230).

The percentage of elderly patients taking part in trials is reported to vary from 2.5% to 35%. This does not represent the same proportion of these patients in the colorectal cancer population though (231). In future, it would be more appropriate to both recruit more patients and to recruit those representative of the colorectal cancer population. Current guidelines dictate that all colorectal cancer MCNs should have an active recruitment drive to clinical trials, especially in chemotherapy (135). Recently published data from the NCIN show worse relative survival in older populations. Unfortunately we were unable to estimate relative survival for our population but we are able to quantify numbers entering clinical trials – one of the putative reasons for poorer outcome in this group. In the West of Scotland MCN in 2007 only 1.3% of patients were offered a trial and accepted. For 4.7% of colorectal cancer patients there was no trial available. Overall, 9.2% of the patients were ineligible for trials; 0.6% were offered a trial and refused; and 2.9% were not offered a trial for clinical /other reasons.

(Vidhya Gunaseelan, data manager for the West of Scotland MCN), personal communication).
These data are unpublished and have not been validated by each of the Health Boards but they do point to an area where improvement could be made to improve the lot of colorectal cancer patients, particularly the elderly.

Pathology

Employing Kaplan-Meier then multivariate analyses to determine prognostic indicators is not a new method in colorectal cancer pathology. Newland et al concluded that 6 different variables retained their prognostic significance in a multivariate model in 1994. “In order of diminishing potency, these were: apical lymph node involvement; spread involving a free serosal surface; invasion beyond the muscularis propria; location in the rectum; venous invasion and high tumour grade.” (232). The prognostic power of apical node positivity was again corroborated by Audisio in 2001 (88). A further paper reports a strong correlation between number of lymph node metastases and colorectal cancer patient survival (87). Most recently clarification of the prognostic significance of peritoneal tumour cells has been sought. Katoh and colleagues concluded that for patients with stage III colorectal cancer, peritoneal tumour cells is the most significant predictor in relation to risk of recurrence (79).
Of the aforementioned variables, we have been able to measure most in our dataset. We found that apical node positivity correlated very strongly with a diagnosis of either Dukes’ C disease. This was therefore acting as a quality control measure for the staging data of our patients. Both extramural vascular invasion and degree of histological differentiation were also significant on univariate analysis. With regard to total number of lymph nodes examined, there was no statistically significant difference on univariate analysis when all groups were analysed together (n=3285, Log Rank = 0.076). This then became significant when the two extreme groups were analysed (log rank = 0.016). Current standards dictate that the minimum number of nodes harvested should be 12. What is understood is that increasing degree of node harvest increases the possibility of finding tumour in a node. This then increases the patient’s chances of converting their stage of disease from Dukes’ B to Dukes’ C with implications for need for adjuvant chemotherapy. Our findings would suggest that even

increasing the number as high as 19 would confer additional survival advantage, but this advantage would perhaps be lost in a multivariate model.

This was not the case for rectal cancer patients though, as there was a slight convergence in survival between the two extreme groups at around 6 years post incidence. Further confounding factors are the differences in practice among pathologists. There are many factors influencing the number of nodes identified. Adipose tissue and whether it is mesorectal, mesocolic or subserosal, length of specimen, time of fixation, and diligence of pathologist all have bearing on the final result. Nodes tend to shrink after chemoradiotherapy and are more difficult to find. Inflammation may cause reactive enlargement of nodes so in the setting of an adherent, fistulating or perforated tumour it may be easy to find multiple nodes. Once the apical node is identified and assessed for positivity, this aids in more accurate staging.

Positive lymph node ratio has recently been described as a calculation which optimises patient staging and alters patient treatment stratification in relation to current practice. This was in a series of 495 colorectal patients spread across two hospitals (89). This could be tested in our larger population.

Extramural Vascular Invasion

As demonstrated previously, EVI is a significant prognostic indicator. This confirms recent work by Courtney *et al* whilst refuting the previous hypothesis of Jass (76,85).

Circumferential Resection Margin

Circumferential resection margin applies to rectal cancer patients only. We have examined the potential role of circumferential resection margin (CRM) positivity in relation to predicting survival. CRM status is thought to be a strong positive predictor of outcome. It is generally held that a positive CRM has a strong correlation with local recurrence, systemic failure and thus poorer survival (130,220). The univariate findings from the results section support this in our population of 1126 rectal and rectosigmoid patients with a Log Rank of <0.001.

This variable was also found to be one of seven variables remaining statistically significant in a Cox regression model of 17 separate elements previously found to have had a statistically significant impact on survival in Kaplan-Meier models.

Ethnicity

Data on ethnicity are not routinely collected in the West of Scotland despite the fact that our region is constantly becoming more ethnically and culturally diverse. What is known is that people of Scottish and Irish origin living in England have mortality above average compared to English nationals (184). This trend was noted to hold true for women from North and West Africa also. Work by Mandelblatt and colleagues has demonstrated a significant difference in the mean age at diagnosis of colorectal cancer between differing ethnic groups (73). They suggest that this is linked to poverty too. It would be both relevant and interesting for this type of data to be collected prospectively in our region to ensure there is equality across races and that it translates into equal survival outcomes. One such study performed in Middlesex has shown that colorectal cancer presents at a significantly younger age in all ethnic minority groups when compared to the native Caucasian population with the Asian population presenting at the youngest age of all (233). This group also showed a significant increase in the number of right-sided lesions in the Afro-Caribbean population compared to others. Analysis was limited to 256 patients. This small number is the main drawback of the study.

The most recent paper to report on trends in colorectal cancer in relation to race paints a dim picture. DeLancey *et al* conclude that despite a generalised decrease in colorectal cancer mortality since 1975, the disparity between blacks' and whites' is increasing (234).

Disability

Currently there are no published papers dealing with the issue of disability and colorectal cancer surgery or MDT care. One 2006 paper discusses this in relation to breast cancer, concluding that inequality in treatment exists. Various reasons for this are suggested including social stigmatism, misperceptions about patient abilities to cope, quality of life and preferences for care.

Type of Admission and Mode of Referral

The most obvious trend in types of admission is the shift in numbers from routine to urgent. This occurred between 2003 and 2004. We think this is linked to the introduction of Government guidelines for patients with suspected malignancy (69). One published audit from a district general hospital of 180 urgent referrals challenged the effectiveness of these guidelines. Eccersley and colleagues mention that although the chances of having cancer as an urgent referral are higher than in other groups, the majority of patients that have cancer are not found in this group. They are found outside the new system (70).

It is unsurprising to find that type of admission has a statistical significant impact on outcome with emergency admissions having worse outcome compared to elective. This holds true after matching for age, stage and deprivation group in colon cancer patients only. The type of admission does not retain significance in a Cox proportional hazards model for rectal cancer patients.
Various questions abound regarding type of admission and emergency procedures. Firstly, should general surgeons be undertaking emergency operations on colorectal cancer patients or should there be a 24 hour on-call service for these patients?

A comparison between our data and other published series can also be made in terms of admission type. Burton et al demonstrated in 2006 that of their emergency cases, the highest proportion were left sided cancers (20%) (235). They included sigmoid lesions in this group. Our data also show left sided lesions as being the largest proportion of emergency admissions in the West of Scotland. Our numbers are much larger and cover an entire region compared to the district general hospital population reported by Burton.

Type of admission has previously been correlated with postoperative complications. In the first nationwide population based survey of colorectal cancer treatment McGrath *et al* simply noted numbers of patients suffering from postoperative complications in emergency cases and elective cases (71). There was no attempt to assess whether the differences were statistically significant or not. I took this a stage further in this study by examining whether or not there

was a significant difference between the main complications and types of admission. Only anastomotic leak and wound infection show significant differences between types of admission. PE, MI, intra abdominal abscess, fistula and DVT appear to occur at similar rates across admission type.

It has been previously noted in the West of Scotland that Deprivation was associated with type of admission (65). We have demonstrated within our dataset that this trend remains. We examined all 7727 patients, finding a p value of 0.001 for the relationship between type of admission and deprivation category.

Mode of referral

There has also been a shift in mode of referral with time in our dataset. More patients are now being referred to A&E as opposed to colorectal outpatient clinics. Whether this represents a breakdown in relationship between primary care and secondary care. We have demonstrated that this trend has an adverse effect on patient outcomes {{8886 Nicholson,G.A. 2008}}. Whether this trend and its effect on survival is replicated in other regions is unknown.

Intent of operation

The decision as to whether or not an operation is deemed palliative or curative rests either with the consultant in charge at the time of operation or is decided upon postoperatively based on pathological measures. Whilst their opinion should be valued as an expert opinion, consultants designating operative intent introduces a potential source of bias in the results as they could be inadvertently or subconsciously designating a potentially curative operation as palliative. This would then exclude that patient from many of the analyses in this thesis.

We compared our findings with other published figures. The overall percentage of curative intent procedures in our MCN dataset was 76.4%. This compares well with the 78.6% quoted by another Glasgow group from their retrospective study of 481 patients with potentially curative colorectal cancer in 2000 (236).

These figures are close but the fact that the more recent figure is lower may reflect the fact that the selection criteria are in evolution. Patients previously deemed suitable for potentially curative resection may now be more likely to have a trial of neoadjuvant chemotherapy first or are deemed palliative from the outset. The increased precision of MRI for staging rectal cancers also means that this subset of patients can be more accurately staged and categorised as either curative or palliative.

Type of Operation

Is there significant bias with relation to what type of patient receives what type of operation? A more recent, national perspective on resection for rectal cancers showed that socially deprived patients are more likely to undergo APE resection than anterior resection. It is though that this negatively impacts quality of life in addition to having lower long-term cost-effectiveness for the NHS when compared to anterior resection (237). Patients lower on the socio-economic scale have been found to be more likely to undergo APE than AR for cancer (43,44). This goes against the "high quality of cancer care for all" ethos of MDTs and the government (The NHS cancer Plan 200). Similarly, another finding reported by Morris *et al* is that throughout England males were significantly more likely to receive an APE than females. This finding was mirrored by the significant result that women were more likely to receive an anterior resection than men (44). The results herein do not confirm the aforementioned findings. In our population there was no evidence of a statistical difference in either deprivation category or sex when comparing with type of operation performed, this was despite employing the same methodology to categorise operations.

Morris and co-workers found no significant differences between type of operation received and age or stage at presentation. Stage at presentation was a statistically significant factor for patients admitted as emergencies only. These patients were also more likely to receive a Hartman's procedure or an anterior resection than average. Again, our results disagree with these reported trends. We show no significant difference in type of admission. We show a significant difference ($p = 0.018$) in age group and type of operation, and a significant

difference upon comparing Stage at presentation with type of operation (p = 0.007).

Postoperative mortality

Postoperative mortality is seen as a potential area that can be influenced by the MDT process. There is reliance upon the skill and experience of pathologist, radiologist and surgeon to accurately stage disease. If the correct management decisions are made at the time of MDT meeting then patients deemed unfit for surgery will not be put at risk of unnecessary operation. This then has a positive effect on postoperative mortality rates. Similarly, enhanced recovery programmes and improved intra-operative monitoring can maximise improvement in postoperative mortality. A recently published series of outcomes from 7290 colorectal cancer patients in England quoted an overall operative mortality of 6.7% (64). This compares extremely well to our region, where we have a rate of 6.8%. I have shown that there is no statistically significant difference in thirty-day mortality for all colorectal cancer patients undergoing surgery from 1997-2005. These are crude, unadjusted figures.

One area of current interest is whether deprivation has an independent effect on peri operative outcome. We have previously demonstrated that no difference in stage at diagnosis occurs in relation to deprivation in the West of Scotland so we sought to discern whether there was a significant difference in postoperative mortality according to deprivation group. Results published by Smith *et al* found deprivation to be an independent risk factor for postoperative death. Another recently published paper by Harris *et al* demonstrated no significant difference in postoperative mortality in a series of rectal patients from one hospital MDT when comparing deprivation (63). We have been able to confirm these latter findings in our population of rectal cancer patients. The advantage we have over Harris is that our series covers an entire region. Whilst giving us the benefit of larger numbers, we are also introducing the added confounding factors associated with measuring aggregate outcomes from many different MDTs in the MCN. They will inherently consist of different team members and have a different case mix of patients with different surgeons operating on them.

We found a similar result when examining the link between deprivation and postoperative outcome in 2768 colon cancer patients undergoing surgery with curative intent ($p = 0.530$). There are no currently published series examining this in colon patients only however Smith *et al* found a statistically significant result when looking at all colon and rectal cancer patients together. They concluded that there must be a cause and effect relationship between deprivation and mortality.

We conclude that deprivation does not in itself result in a poor postoperative result in our population. In terms of long-term outcome though, deprivation is a known individual prognostic indicator in our population. We could reason that the process of patient selection for operation, the subsequent management delivered, and the peri operative care received are not biased in relation to deprivation but that once the patient returns home, there are some environmental, social, psychological or underlying biochemical factors that somehow contribute to a poorer outcome than their affluent counterparts.

We then went on to explore the intra-regional variations in postoperative mortality. We report that there is no statistically significant difference in postoperative mortality between the Health Boards or looking at a level below, in MDTs. This finding holds true when selecting curative resection patients only. It also holds true for emergency admission patients.

Patients not receiving surgery

The main population of interest in this work is those patients having surgery, as we are primarily interested in their outcomes. However, a proportion of the population did not receive surgery. It was interesting to note how the demographics, stage at presentation, type of presentation and DEPCAT of this group varied with time.

Sex - Overall 505 (56.6%) male and 387 (43.4%) female. There is very little difference here between the patients receiving surgery, 54% male and 46% female. We found no significant change in proportion of men to women not having surgery despite the fact that women live longer.

Age - The majority of patients not receiving surgery were in the >=75 years group (54.4% of the total) compared to those receiving surgery (36% of the total).

Stage - As one would hypothesise, the vast majority of patients not undergoing surgery are those with Dukes' stage D disease (41.7% of total). This compares to only 17.6% in the group of patients that had a surgical procedure. One would also expect that a large proportion of the 54.1% of patients without a specified stage would also be Dukes' D.

DEPCAT - The distribution of socioeconomic circumstances in those not receiving surgery is very similar to those receiving surgery.

This finding confirms the lack of bias in selection of patients for surgery. This holds with time. With a Chi Square value of 0.649 when comparing SEC with year of incidence.
Type of admission – The percentage of patients not receiving surgery and presenting as an emergency is higher than that for patients having surgery – 39.3% compared to 26.1% respectively.

Site of cancer - In the group of patients not receiving surgery there was a far higher percentage of patients with rectal lesions compared to those receiving surgery (41.0% vs 27.4%) In all other sites, the percentage of patients undergoing surgery was higher than those not having surgery.

Patients not undergoing surgery

Patients not undergoing surgery are older and present at a later stage than those who have surgery. There appears to be no difference between the groups in relation to sex and degree of socioeconomic circumstances.
Patients who do not undergo surgery are more likely to have a rectal lesion than any other site in the large bowel.

Time taken to definitive treatment

The Clinical Standards regarding management of bowel cancer services from March 2008 state that the time from urgent referral to time of first treatment should be no more than 62 days (34). These guidelines are based on two other sets of guidelines thus making it unclear as to whether or not there is any evidence base to this cut- off point (238,239). Of note is that the mean time to wait for all patients was 34.22 days.
Further univariate analysis of the urgent referrals only revealed that there was a significant survival advantage for the patients waiting more than 62 days to first definitive treatment. (Log Rank 0.042) This perhaps reflects the clinical discretion of the operating surgeon, knowing that some urgent referrals could easily wait longer than 62 days without detriment to their outcome. It would appear then, that establishing a 62 day rule for time from urgent referral to first definitive treatment has no significant survival benefit to patients as it still relies upon the surgeon's experience and judgement.

Stoma type

It is an essential criterion of the Clinical Standards for the management of bowel cancer services that permanent stoma rate is not more than 40% in patients with rectal tumours. In this way, a permanent stoma (or lack of) is used as a measure of surgical performance and a proxy guide for the quality of cancer surgery. (34)

Following selection of all rectal cancer patients undergoing curative intent surgery for their tumour, I have shown that the overall rate of permanent stomas is 40.7% in the West of Scotland from 2001 to 2005. This includes patients admitted as an emergency. If emergency admissions are removed, the overall figure rises by 0.2% but this is influenced by a very high rate in 2001. The general trend is for a reduced overall rate with time in rectal cancer patients undergoing elective and urgent curative intent surgery.

I have been able to demonstrate in a univariate model that all patients receiving a permanent stoma have statistically significantly worse survival when compared with those patients with a temporary stoma. Permanent stomas are most likely

to be fashioned for patients with low rectal cancer having an APE. When this particular group of patients was selected the survival advantage conferred from having a temporary stoma was not statistically significant. I have shown that with regard to both year of incidence and type of admission there is no statistically significant difference in the type of stoma fashioned. Overall 54.2% of patients received temporary stomas with 45.8% receiving permanent stomas. Further subtype analysis of these groups would determine whether the rate of permanent stomas could be reduced.

Limitations exist when analysing stoma types with these data. Firstly, we do not know what proportion of temporary stomas were reversed. This is a potential source of bias due to misclassification in the results. We are also not able to assess accurately how much more ill patients receiving permanent stomas were. This would allow adjustments to be made.

Clinical Nurse Specialist

One of the key members, designated part of essential criterion 2b.2 of current clinical standards is a cancer clinical nurse specialist (CNS). There is no doubt that the role of the CNS is important. Their knowledge and experience help in many aspects of the management of patients from clinic, through administration to follow-up. There is no doubt that they aid in improving the patient's overall experience and resultant quality of life but can the effect of their intervention into a patient's experience of surviving cancer be objectively measured in some way? The simple answer is no, not directly. Despite the role of the CNS in the MDT being deemed essential, their input alone provides no currently measurable benefit to patient outcome.

Multivariate findings

The purpose of multivariate analysis is to control for *known* confounding variables. This then results in a more accurate assessment of the contribution that each of the known univariate variables has on overall survival. In the process of analysis further variables may be discovered to have a previously

unrecognised influence on survival. The main example from this thesis is that of mechanical bowel preparation.

All Colorectal cancer Patients

Of the 2740 colorectal cancer patients undergoing surgical resection with curative intent, age at incidence, Dukes' stage, degree of tumour differentiation, distal margin positivity, extra mural vascular invasion, apical node positivity, and male gender were all found to contribute independently towards a poorer outcome. These variables have previously been identified as prognostic indicators, as mentioned above.

Preoperative and perioperative considerations

Good quality care should begin with a good quality team making good quality decisions about carefully selected and staged patients. Before this happens though, there is a wait from time of referral to treatment. The Scottish Government have now met their 62 day target for colorectal cancer patients from date of urgent referral to treatment. I have confirmed in my analysis that the length of time from date of incidence to date of first definitive treatment was not found play a significant role in the long term survival of curative intent colorectal cancer patients.

Even before the decision has been made to operate it is important to appreciate that MDT care for patients is associated with a large reduction in variation of decision making. Pfeiffer and Naglieri previously demonstrated that decisions made by an MDT are superior to those made by team members acting independently (39). Their work was regarding patients with learning difficulties. More recently, this has been replicated in the upper GI then colorectal cancer settings (240,241).

The decision-making process can now be further honed. Various risk stratification tools for selected Dukes' stage B and stage C patients have now been validated (77). It is possible that these will be widely adopted into clinical

practice as standard ways for ensuring decisions regarding treatment are made in a uniform manner.

Preoperative management includes physiological optimisation of patients with other comorbidities. The anaesthetist usually oversees this facet of patient management. TED stocking and thromboprophylaxis with a low molecular weight heparin for all patients is mandatory. These are recommendations laid down by SIGN and are regularly audited in MCN reports (105). Antibiotic prophylaxis per-operatively is also recommended. I have provided evidence herein that there is a very high concordance with SIGN guidelines with regard to administration of antibiotics. This applies to both elective and emergency surgery. This increased number of patients having this variable "not recorded" in 2004 and 2005 is disappointing though.

The use of mechanical bowel preparation remains controversial for rectal cancer operations. Its use for colonic resections is now considered unnecessary in most elective colonic resections (111). This is mainly due to the similar postoperative complication profiles seen in both groups. I have provided evidence that the trend in the West of Scotland is towards reduced use of bowel preparation for all colorectal cancer patients. I have also shown that in our population of elective resections, there is no statistically significant difference in postoperative complications between the two groups. This remains of limited power though due to the small number of patients suffering complications.
One of the main findings from the multivariate analyses was that the use of mechanical bowel preparation remained a positive prognostic indicator, even following adjustment for other well recognised predictors. The reason for this currently remains unknown but a recent experimental pilot study has indicated that different types of mechanical bowel preparation can have an objective effect on the mucosal cell turnover rate (214). Whether or not these hitherto undiscovered mechanisms can influence long-term survival of curative resection patients remains to be seen.

Specialist colorectal surgeons resect a larger portion of colon and perform wider en bloc dissection when required. This was demonstrated as far back as 1994 (242). In 2000 a group from the Western Infirmary in Glasgow reported that

lower local and overall recurrence rates were achieved by colorectal surgeons when compared to vascular or general surgeons. Follow-up in these patients was limited with a median period of 45 months. Another limitation was that only two specialist colorectal surgeons' patient outcomes were studied along with six vascular / transplant surgeons and four general surgeons (236). Numbers of surgeons were therefore small and could not be said to be representative of a region.

An additional consideration is that none of the patients studied underwent any form of adjuvant chemotherapy or radiotherapy. This means they cannot be directly compared to our population in terms of outcomes.

TME revolutionising rectal cancer resections and becoming the gold standard operation APR is still necessary in 25% of patients with a lesion within 12cm of the anal verge (92) (243).

Postoperative considerations

Postoperative management is again a combination of inputs from different members of the MDT. The anaesthetist is usually involved immediately postoperatively. Then the roles of the pain team, physiotherapists and surgeon come in to play. The stoma team may also have input at this stage. Various aspects of postoperative care can again be audited objectively. These are laid out in the SIGN 77 publication regarding postoperative management in adults (244).
Care of the patient begins as soon as they attend their primary care physician with symptoms or are diagnosed via screening. The quality of their care can therefore start being measured from there. The following factors can all influence the overall quality of care that a patient receives:

- Timely diagnosis
- Correct diagnosis
- Correct histopathogical and radiological staging
- Delivery of diagnosis & explanation of treatment
- Informed consent to treatment

- Appropriate neoadjuvant or adjuvant chemo or radiotherapy
- Education regarding a stoma if appropriate
- The most suitable operation performed by a suitably trained surgeon
- Appropriate follow-up

Specialist colorectal surgeons resect a larger portion of colon and perform wider en bloc dissection when required (242).

Grilli *et al* concluded in 1998 that "While most studies suggest that cancer patients treated at specialized institutions have better outcomes, analysis of the process of care does not help to determine why this occurs, as the indicators used often have a questionable linkage to outcome" and "Overall, the literature in this area suffers from major methodological flaws and is of limited value in disentangling the components of specialisation more likely to lead to a better process and outcome of care"
(245)

The most recent Cochrane review for patients treated for non-metastatic colorectal cancer has concluded that there is an increased survival benefit from intensive follow-up. Although this conclusion may seem common sense it remains unclear which elements are the crucial determinants in follow-up and, more importantly for the NHS, how cost-effective they are (26).

Conclusions

MCN care represents the main management model for colorectal cancer patients in the UK. This study acts as the best available analysis of current trends in survival for colorectal cancer patients in the West of Scotland as a result of having been treated in the first generation MCN. We have demonstrated that whilst the overall survival of patients is improving, it is only improving more than pre-MDTs for female rectal cancer patients.

We have demonstrated that there is equal entry to the system of care, equality in type of operation offered, and equal postoperative outcome for patients across the socio-economic spectrum.

There continues to be a disparity in use of bowel preparation in patients undergoing elective resections for cancer but this reflects the continued worldwide uncertainty as to its use in colorectal cancer surgery.

We have shown that no significant difference in operative intent between age groups ($p= 0.827$) existed. This again points to a system that is treating patients equally. This also bodes well for the aging colorectal cancer population.

It is anticipated that through further evolution, MDT care will force the transformation of colorectal cancer from a cause of eventual demise into a chronic disease, treatable in the vast majority of cases.

It is clear from the results I have proffered that there remains a great degree of heterogeneity in data recording and quality. This is generally accepted as being better quality than anywhere else in the UK but still requires to be as accurate as possible in order to obtain the most correct and objective results. A recent poster presentation pointed to the fact that data quality is improved by clinician rather than administrator data recording (246).
The current situation is for the majority of surgeons to delegate data recording to audit staff. The question is whether it would be a better use of their time to record data themselves (thus improving quality) or spend more time adequately training administrative staff to the degree where there recording of data is on a

par with consultants. It is hoped that a real-time online system will replace that currently used to reduce the amount of error inherent in the system.

Differences in survival

It is unlikely that each individual MDT will comprise exactly the same elements. This is multi-factorial and includes the constraints of local service provision, size of each MDT, and experience of its members therein.

Further patients specific factors contributing to the region's heterogeneity in outcomes include:

- Differing tumour stage at presentation
- Difference in ratio of palliative to potentially curative procedures performed in each MDT
- Difference in proportions in type of admission
- Different frequencies of operative complications (related both to type of admission and patient co morbidity)
- Preoperative patient comorbidity

8 Future Work

The analysis of surgical outcomes should play as big a part in clinical governance as caring for patients themselves. It is through this continued scrutiny of process and results that excellence in patient care will flourish.

This works on micro, meta and macro levels thus involving the MDT, MCN and national levels of policy. It is therefore the responsibility of colorectal nurse specialists, clinicians, trusts and politicians to detect, investigate and implement change on the basis of outcomes.

Laparoscopic resection of colorectal tumours is now a well-validated and frequently used technique worldwide. Shorter postoperative hospital stay, reduced need for analgesia, improved cosmetic result and quicker return to normal bowel function are all benefits of a laparoscopic operation. Unfortunately, this modality of treatment is under-utilised and under recorded in the West of Scotland compared to most other UK regions.

In future, if data are collected prospectively it would be useful to include BMI, amount of exercise taken, whether they'd had a splenectomy, neoadjuvant chemotherapy, neoadjuvant chemoradiotherapy, ASA status, and grade of anaesthetist as potential predictors in univariate models for inclusion in multivariate models. ASA is of particular importance as it would allow simple comparison and further validation of an accepted model of mortality risk prediction for patients with colorectal cancer (247).

If amount and duration of chemoradiotherapy prescribed are recorded along with the proportion of patients that manage to complete the course this offers insights into both service quality and service structure. This would be invaluable if linked to survival outcome.

Hopefully, the future of colorectal cancer services will see integration of the MCN datasets and uniform analysis of outcomes nation-wide. A major issue is that there are currently no regionally or nationally integrated data collection systems. A bespoke IT system for cancer services, or colorectal cancer in

particular, is wanting. This would have a number of obligatory fields for data entry thus ensuring an accurate minimum core dataset for all patients for the purposes of audit and research. Currently there is no regionally or nationally agreed strategy for the process of data analysis. This has the potential to cause overlap of analyses or duplication of work within regions. There is also the further possibility that data are analysed differently making inter-regional comparisons difficult if not impossible, if outcomes are measured in different ways.

Ideally, further analyses should encompass all other aspects of MDT care with the potential to influence outcome. This includes chemotherapy, radiotherapy, imaging, and correlation with biochemical measurements including CRP and CEA.

We have made no attempt to assess the role of enhanced recovery in outcomes for colorectal cancer patients. As this is a facet of the care pathway it would be worthwhile investigating in the future.

Cause specific and relative survival measures for this population are necessary. This allows international comparisons to be made with our regional, and national colorectal cancer populations.

Specific points from the MCN dataset:

Operative intent is poorly completed. It has become worse with time. 13.4% in 2001 to 23.9% in 2005 had no operative intent completed. It acts as an inclusion variable for patients. Many were therefore needlessly excluded due to poor data collection. It is a further potential source of bias.

Recording of Dukes' stage has also become worse with time. This is across all stages and not simply a reflection of many Dukes' D palliative patients not being recorded. It is not clear whether this is due to the increased use of TNM as a preferred method of staging in some hospitals.

Perhaps the worst recorded variable with the potential for greatest impact is the consultant in charge variable. Overall, there was a named consultant for 64.8%

of patients from 2001 to 2005, however this ranged from 67.8% in 2001 to 59.8% in 2004. Without this information it is impossible to calculate accurate volume figures for each consultant. 30 day mortality and survival cannot be attributed to each consultant nor adjusted for individual case mix.

Relative survival

Relative survival is currently the most accurate way of determining survival in cohorts of this type. It tries to overcome the inherent drawback of observed survival, namely, that observed survival is always likely to reduce with time in older patients as their risk from dying from other causes increases with time. Future work should aim to repeat analyses contained herein employing relative survival analysis.

Lymph node ratio

Lymph node status remains one of the most important pathological parameters measured as presence of tumour in lymph nodes determines the need for adjuvant chemotherapy. Although some node negative patients do receive chemotherapy this is usually only in the setting of a clinical trial (139). Apical node positivity is an independent adverse prognostic indicator. As such it adds an extra grade of severity to a patient's TNM staging. It has been used successfully as an adverse prognostic indicator but does this variable have any significance in the role of MDT care?

Other considerations using the combined dataset

One useful variable missing from this dataset is an objective measure of comorbidity. Would POSSUM therefore be a valid tool for assessment of comorbidity in this population? If so, it would then be possible to ascertain what extent comorbidity and deprivation act independently or synergistically to lower survival?

It would be interesting to assess whether consultants should or do fill-in their own audit forms and to what extent does it introduce bias if they do?

To help clarify the ongoing issues surrounding follow-up it would be useful to use this dataset to determine at what stage in their follow-up do “follow-up detected” recurrences occur. This could direct future policy.

Again, in relation to follow-up, do high volume surgeons follow-up more frequently than their lower volume colleagues or vice versa?

A further level of detail in some of these patients would be assessing whether it is possible to link these data with regional laboratory results to examine prognostic significance of CEA and LFTs in this large population. Using the data in this thesis it would be possible to analyse how survival differs in the subset of patients with synchronous/ metachronous tumours. This is a patient group for whom there exists a paucity of long-term follow-up and survival data in the literature.

The last consideration would be to include patient data regarding treatment with chemotherapy and radiotherapy. It is possible to include these variables in order to further ascertain the precise nature of the determinants of improved survival and how these manifest through the MDT environment.

9 Appendix

MCN Data Collection Proformas

9.1 General demographics and details proforma

9.2 Pathology form

9.3 Oncology form

9.4 Nursing form

Patient Demographic Details - use patient label if available

Forename .....
Surname .....
Address .....
.....
Postcode .....

CHI No .....
Date of birth .....
Sex Male ☐ Female ☐
Hospital of Diagnosis .....
Unit Number .....

Referral and 1st Presentation for Colorectal Symptoms

Date of cancer referral ...../...../.....
Date referral received ...../...../.....
Type of presentation Emergency ☐ Elective ☐ Not recorded ☐
Urgency of referral Urgent ☐ Soon ☐ Routine ☐ Not recorded ☐

Source of cancer referral
Primary Care Clinician ☐ ColoR screening ☐
Incidental ☐ Review clinic ☐
Cancer Genetic Clinic ☐ Self referral to A&E ☐
GP ref directly to A&E ☐ Not recorded ☐
Referral from private healthcare ☐

Clinical Contacts (Clinician/Consultant in Charge along patient pathway for colorectal cancer)

Clinician 1	**Specialty**	**Date first seen** ...../...../.....
Clinician 2	**Specialty**	**Date first seen** ...../...../.....
Clinician 3	**Specialty**	**Date first seen** ...../...../.....
Clinician 4	**Specialty**	**Date first seen** ...../...../.....

Diagnostic Investigations (pre and peri-operative)

Primary tumour	**Performed**		**Completed**			**Cancer**	**No cancer**	**Equivocal**	**Not recorded**
Rigid siggy	Y ☐	N ☐	Y ☐	N ☐	→	☐	☐	☐	☐
Flexible siggy	Y ☐	N ☐	Y ☐	N ☐	→	☐	☐	☐	☐
Colonoscopy	Y ☐	N ☐	Y ☐	N ☐	→	☐	☐	☐	☐
Ba Enema	Y ☐	N ☐	Y ☐	N ☐	→	☐	☐	☐	☐
CT colonography	Y ☐	N ☐	Y ☐	N ☐	→	☐	☐	☐	☐
Water soluble contrast enema	Y ☐	N ☐	Y ☐	N ☐	→	☐	☐	☐	☐
Metastatic Disease			**Performed**			**Cancer**	**No cancer**	**Equivocal**	**Not recorded**
Chest x-ray or CT			Y ☐	N ☐	→	☐	☐	☐	☐
Liver: CT ☐			Y ☐	N ☐	→	☐	☐	☐	☐
MRI ☐			Y ☐	N ☐	→	☐	☐	☐	☐
US ☐			Y ☐	N ☐	→	☐	☐	☐	☐

Site of Primary Tumour

Caecum ☐ Appendix ☐ Ascending colon ☐
Hepatic flexure ☐ Transverse colon ☐ Splenic Flexure ☐
Descending colon ☐ Sigmoid colon ☐ Colon unspecified ☐
Rectum ☐ Not recorded ☐

For synchronous tumours rather than ticking the box please mark poorest stage as 1, and then next as 2 and so on.

Date of Diagnosis ...../...../..... (pre-operative)
Mode of diagnosis Histology ☐ Cytology ☐ Imaging ☐ Clinical ☐

Management

Mode of first treatment Surgery ☐ Endoscopic treatment ☐ RT ☐ Chemo ☐ ChemoRT ☐
Other therapy ☐ No active treatment ☐ Pt refused all therapies ☐ Pt died before trt ☐ Not recorded ☐

Managed Clinical Network for Colorectal Cancer
Pathology Data

Patient Demographic Details - use patient label if available

Patient name .....
Date of birth .....
Hospital .....
Date of operation ...../ ..... / .....
Surgeon .....
Date of receipt ...../ ..... / .....

Sex Male ☐ Female ☐
CHI No.....
Unit No.....
Path Report No .....
Pathologist .....
Date of reporting...../ ...../.....

Gross Description

Site of tumour .....
Maximum tumour diameter: .....mm
Distance of tumour to nearer longitudinal margin .....mm
Presence of tumour perforation (pT4) Yes ☐ No ☐

Metastatic Spread

Number of lymph nodes examined.....
Number of positive lymph nodes.....
(pN1 1-3 nodes, pN2 4+ nodes involved)
Apical node positive (Dukes C2) Yes ☐ No ☐
Not identifiable ?
Extramural vascular invasion Yes ☐ No ☐

Rectal tumours

Tumour is: Above ☐ At ☐ Below ☐ the peritoneal reflection
Distance from the dentate line (AP only): ..... mm

Histology

Type: Adenocarcinoma Yes ☐ No ☐
(to include mucinous and signet ring adenocarcinoma)
If no, other .....

Differentiation by predominant area:
Well ☐ Moderate ☐ Poor ☐ Undifferentiated ☐

Background abnormalities

Adenoma(s) Yes ☐ No ☐
Synchronous carcinoma(s) Yes ☐ No ☐
(Please complete a separate form for each tumour)
Ulcerative colitis Yes ☐ No ☐
Crohn's disease Yes ☐ No ☐
Familial adenomatous polyposis Yes ☐ No ☐

Other comments.....

Local invasion

Submucosa (pT1) ☐
Muscularis propria (pT2) ☐
Beyond muscularis propria (pT3) ☐
Tumour cells have breached the peritoneal surface ☐
or invaded adjacent organs (pT4)

Tumour involvement

Tumour involvement	**N/A**	**Yes**	**No**
Doughnut	☐	☐	☐
Margin (cut end)	☐	☐	☐
Peritoneal surface	☐	☐	☐
Non peritonealised margin	☐	☐	☐
Residual tumour biopsy	☐	☐	☐
Rectal tumours only			
Circumferential margin	☐	☐	☐

Histological measurement from tumour to circumferential margin: .....mm

Pathological staging

Complete resection at all margins Yes ☐ No ☐

TNM pT ☐ p**N** ☐ pM☐

Dukes

Dukes A (growth limited to wall, nodes negative) ☐
Dukes B (growth beyond muscularis propria, nodes negative) ☐
Dukes C1 (nodes positive and apical node negative) ☐
Dukes C2 (Apical node positive) ☐
Histologically confirmed liver mets Yes ☐ No ☐

Managed Clinical Network for Colorectal Cancer
Pathology Data

Additional Comments and Notes
These data are collected on behalf of the Managed Clinical Network for Colorectal Cancer **On completion, please forward this form to your local Audit Support Office**

Managed Clinical Network for Colorectal Cancer
Oncology Data

Patient Demographic Details - use patient label if available

Patient name .....
Date of birth .....
CHI No .....
Hospital .....
Name of Consultant Oncologist .....

Sex Male ☐ Female ☐
Postcode.....
Unit No .....
Date first seen ...../ ..... / .....

If no treatment: Patient refused ☐ Patient too frail ☐ Died prior to treatment☐ Inappropriate ☐

Radiotherapy Primary radical ? Pre-operative? Post operative ?

Date first seen ..... / ..... /..... **Site of Radiotherapy** .....

Type of radiotherapy: Adjuvant preoperative ☐ Adjuvant postoperative ☐ Chemoradiotherapy ☐
Primary radical ☐ Palliative (totally inoperable) ☐ None-no documented contraindication ☐
None-documented contraindication ☐ Patient refused treatment ☐ Not recorded ☐
Date radiotherapy started ...../...../..... **Date radiotherapy completed** .. ../...../.....
Total dose administered..... **cGy** Not recorded ☐
Total fractions given..... Not recorded ☐
Treatment completed Yes ☐ No ☐ Not recorded ☐
Specify reason if treatment incomplete .....

Chemotherapy

Type of chemotherapy: Adjuvant ☐ Neoadjuvant ☐ Primary ☐ Palliative ☐ None-no documented contraindication ☐ None-documented contraindication ☐ Patient refused treatment ☐ Not recorded ☐
Date chemotherapy started ...../...../.....
Chemotherapy agent: Bolus FUFA over 5 days every 4 weeks ☐ Bolus FUFA weekly ☐
Intermittently infused FUFA (Bosset) (+ RT) ☐? Continuous flourouracil (Lokich) (+RT) ☐ Bolus FUFA (+RT) ☐
FUFA infusion (de Gramont) ☐ Capecitabine ☐ Raltitrexed ☐ Not recorded ☐ Inapplicable ☐
Route of delivery: Intravenous ☐ Portal vein infusion ☐ Oral ☐ Intra-arteria l☐? Not recorded ☐ Inapplicable ☐
Treatment completed Yes ☐ No ☐ **Date chemotherapy completed** ...../...../.....
Specify reason if treatment incomplete .....

Clinical Trials

Patient entered in clinical trial: Yes ☐ No ☐ Ineligible ☐ Patient refused ☐ Not offered ☐
No trial available ☐ Not recorded ☐ **Trial entry date** ...../...../.....
Trial entered: QUASAR ☐ CLASSIC ☐ CRO7 ☐ EORTC/CITCCG 40983 ☐ FOCUS ☐ VICTOR ☐ CLOCC ☐ Not recorded ☐
Other ☐ Please specify ..... Outwith trial ☐
If patient is entered in more than one trial please indicate by ticking all relevant boxes.

Death Details **PATIENT HAS DIED Yes ☐ No ☐**

Date of death ...../...../.....
Primary cause of death: Colorectal cancer ☐ Other cancer ☐ None cancer death ☐? Surgical treatment related ☐
Radiotherapy treatment related ☐ Chemotherapy treatment related ☐ Not recorded ☐
Other, specify .....

Additional Comments and Notes may be written on the reverse of this form

These data are collected on behalf of the Managed Clinical Network for Colorectal Cancer
On completion, please forward this form to your local Audit Support Office

West of Scotland Managed Clinical Network for Colorectal cancer

Nursing Data

Patient Demographic Details - use patient label if available	
Forename	**CHI No** .....
Surname	**Unit No** .....
Address	**Date of birth** ...../...../.....
.....	**Sex** Male☐ Female ☐
.....	
Postcode	**Hospital of Diagnosis** .....

Referral	
Previous referral to Cancer Genetic Clinic	Yes ☐ No ☐ Pt refused ☐ Not recorded ☐
Referred to **Stoma** Care Nurse?	Yes ☐ No ☐ If yes: Pre-op ☐ Post-op ☐
Date of referral to **Stoma** Care Nurse	...../...../.....
Primary assessment by **Stoma** Care Nurse?	Yes ☐ No ☐ If yes: Pre-op ☐Post-op ☐
Date of assessment by **Stoma** Care Nurse	...../...../.....
Stoma site marked pre-operatively by the **Stoma** Care Nurse Specialist or appropriately trained person?	Yes ☐ No ☐ N/A ☐
Referred to **Colorectal** Nurse Specialist?	Yes ☐ No ☐ If yes: Pre-op ☐ Post-op ☐
Date of referral to **Colorectal** Nurse Specialist	/ /
Primary assessment by **Colorectal** Nurse Specialist?	Yes ☐ No ☐ If yes: Pre-op ☐ Post-op☐
Date of assessment by **Colorectal** Nurse Specialist	...../...../.....

MDT	
Nurse Specialist present at pre-treatment multidisciplinary team review?	Yes ☐ No ☐ N/A ☐ Date ...../...../.....
Nurse Specialist present at post-operative multidisciplinary team review?	Yes ☐ No ☐ If yes: Date ...../...../.....

Information and communication					
CNS present when patient is given diagnosis?	Yes ☐ No ☐ If yes: Date ...../...../.....				
Patient given information by the named Nurse Specialist regarding their disease and treatment ?	**Verbal**	Yes ☐	No ☐	Declined ☐	
	Written	Yes ☐	No ☐	Declined ☐	
Information given relating to stoma and stoma care?	**Verbal**	Yes ☐	No ☐	Declined ☐	N/A ☐
	Written	Yes ☐	No ☐	Declined ☐	N/A ☐
Was the patient issued with relevant contact telephone numbers to access information, advice and support?		Yes ☐	No ☐		

Family History Yes ☐ No ☐ Not recorded ☐

Referral to Cancer Genetic Clinic Yes ☐ No ☐ Pt refused ☐

Comments

9.5 Data agreement

West of Scotland Cancer Network

Data Sharing Agreement

This document is a formal agreement between the West of Scotland Cancer Network and the recipient(s) of the data described herein. This agreement requires that the data provided are used only for the purposes stated in this agreement and that access to these data is restricted only to those persons stated. Use of these data is conditional on adherence to the following:

1. Data provided will, at all times, be used and stored in accordance with local NHS policies and guidance and in accordance with the following legislation and guidance:

    a. Data Protection Act 1998
    b. Human Rights Act 1998
    c. Common Law Duty of Confidentiality
    d. Freedom of Information (Scotland) Act 2002
    e. Caldicott Guidance

2. Data remain, at all times, the property of the source hospital which reserves the right to withdraw their data at any time.

3. Access to data shall be limited to those individuals who require it.

4. Appropriate administrative, technical and physical safeguards will be established to protect the confidentiality of data and to prevent unauthorised use or access to it.

5. Publication of results from analyses of these data will require explicit approval of the relevant disease-specific MCN Advisory Board or it's designated group or individual to which these results will be provided in full.

6. The results from the analyses of data will be provided only to stated recipients.

7. Linkage with other data sets described in this agreement should not involve the transfer of MCN data to any other party or system unless stated in this agreement.

8. Following completion of the specified work, unless otherwise stated in this agreement, all data supplied must be deleted and the MCN Office must be notified in writing that this has been done.

Data requested by: (please print name, designation and organisation)	David S Morrison Director West of Scotland Cancer Surveillance Unit	Date requested: 14 March 2008	
Main data user and contact (name, designation, organisation and location):	Mr Gary Nicholson Surgical Research Fellow West of Scotland Cancer Surveillance Unit 1 Lilybank Gardens, Glasgow, G12 8RZ	Contact details:	Email: garynicholson@nhs.net Tel: 0141 330 3281

The eight variables available for analysis from 1980 onwards.

Variable	**N**	**% completeness**
Unique patient identifier	37,966	100
Sex	37,966	100
Date of incidence	37,966	100
Site of cancer	37,966	100
Health Board of residence	37,966	100
Local council area	37,964	99.9
Deprivation category	37,964	99.9
Date of death	32152	Not applicable*

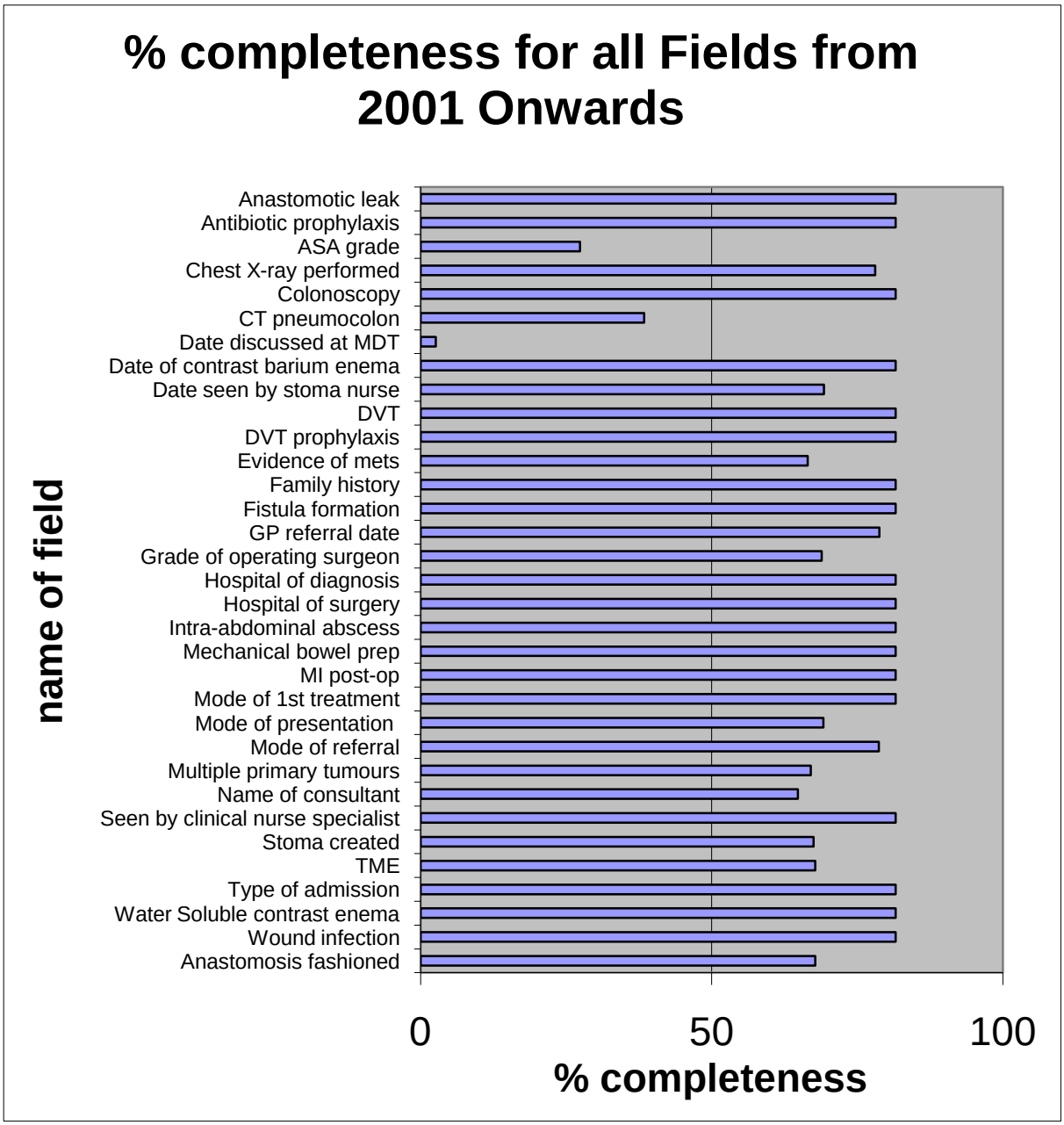
* many patients would still be alive

The four additional variables available from 1997 onwards.

Variable	**Number of entries**	**% completeness**
Earliest date of surgery	14098	78.9
Age at surgery	11063	78.5
Dukes' stage at diagnosis	14098	100*
Therapy objectives	14098	83.6

*** This includes "stage not specified" as an entry into the field, hence 100% completeness.**

From 2001 onwards, the following remaining variables were recorded for all patients with COLORECTAL CANCER in the West of Scotland



Pathology variables and their respective completeness from 2001 to 2005.

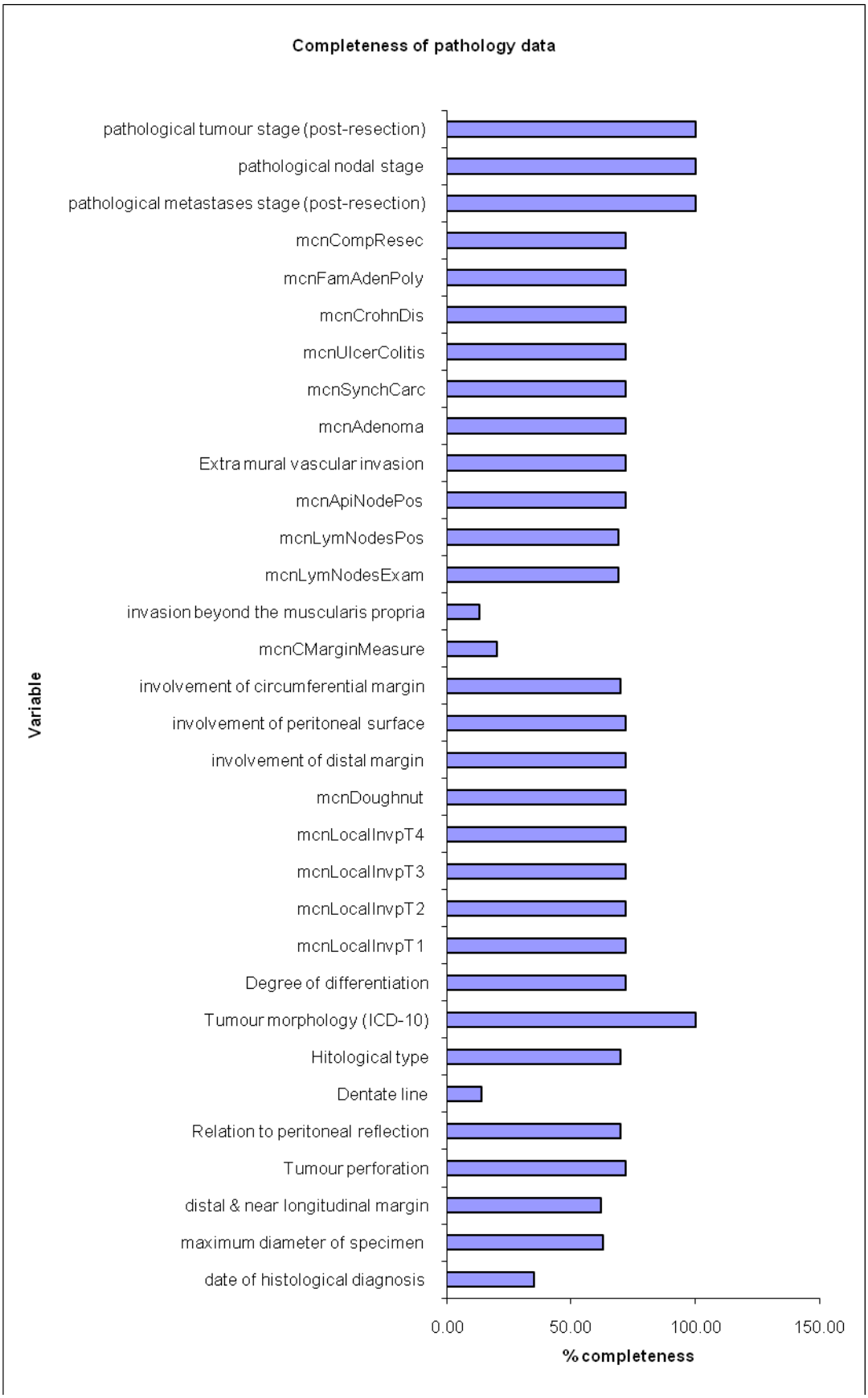

Completeness of pathology data
pathological tumour stage (post-resection)
pathological nodal stage
pathological metastases stage (post-resection)
mcnCompResec
mcnFamAdenPoly
mcnCrohnDis
mcnUlcerColitis
mcnSynchCarc
mcnAdenoma
Extra mural vascular invasion
mcnApiNodePos
mcnLymNodesPos
mcnLymNodesExam
invasion beyond the muscularis propria
mcnCMarginMeasure
involvement of circumferential margin
involvement of peritoneal surface
involvement of distal margin
mcnDoughnut
mcnLocalInvpT4
mcnLocalInvpT3
mcnLocalInvpT2
mcnLocalInvpT1
Degree of differentiation
Tumour morphology (ICD-10)
Hitological type
Dentate line
Relation to peritoneal reflection
Tumour perforation
distal & near longitudinal margin
maximum diameter of specimen
date of histological diagnosis
Variable
0.00
50.00
100.00
150.00
% completeness

Table of sites of cancer for all duplicate cases identified

site of cancer	ileocaecal valve	187	12.5
	ascending colon	108	7.2
	hepatic flexure	40	2.7
	transverse colon	129	8.6
	splenic flexure	31	2.1
	descending colon	81	5.4
	Sigmoid colon (excluding	272	18.1
	rectosigmoid junction)		
	Overlapping lesion of colon	8	0.5
	Colon, unspecified	249	16.6
	rectosigmoid junction	86	5.7
	Rectal ampulla	311	20.7

9.6 OPCS Coding for APE and AR procedures

OPCS code	group	Category	OPCS definition
H331	1	APE	ABDOMINOPERINEAL EXCISION OF RECTUM AND END COLOSTOMY
H332	2	AR	PROCTECTOMY AND ANASTOMOSIS OF COLON TO ANUS
H333	2	AR	ANT.RESECT.RECTUM AND ANASTOMOSIS OF COLON TO RECTUM USING STAPLES
H334	2	AR	ANTERIOR RESECTION OF RECTUM AND ANASTOMOSIS- NOT ELSEWHERE CLASSIFIED
H335	3	Hartmann's	RECTOSIGMOIDECTOMY & CLOSURE OF RECTAL STUMP & EXTERIORISATION OF BOWEL
H336	2	AR	ANTERIOR RESECTION OF RECTUM AND EXTERIORISATION OF BOWEL
H338	4	Excision of rect unspecified	OTHER SPECIFIED EXCISION OF RECTUM
H339	4	Excision of rect unspecified	UNSPECIFIED EXCISION OF RECTUM
H041	4	Panproctocolectomy	PANPROCTOCOLECTOMY AND ILEOSTOMY
H042	4	Panproctocolectomy	PANPROCTOCOLECTOMY- ANAST. ILEUM TO ANUS AND CREATION OF POUCH- H.F.Q.
H043	4	Panproctocolectomy	PANPROCTOCOLECTOMY AND ANASTOMOSIS OF ILEUM TO ANUS- N.E.C.
H048	4	Panproctocolectomy	OTHER SPECIFIED TOTAL EXCISION OF COLON AND RECTUM
H049	4	Panproctocolectomy	UNSPECIFIED TOTAL EXCISION OF COLON AND RECTUM

H051	4	Total colectomy	TOTAL COLECTOMY AND ANASTOMOSIS OF ILEUM TO RECTUM
H052	4	Total colectomy	TOTAL COLECTOMY AND ILEOSTOMY AND CREATION OF RECTAL FISTULA- H.F.Q.
H053	4	Total colectomy	TOTAL COLECTOMY AND ILEOSTOMY- NOT ELSEWHERE CLASSIFIED
H058	4	Total colectomy	OTHER SPECIFIED TOTAL EXCISION OF COLON
H059	4	Total colectomy	UNSPECIFIED TOTAL EXCISION OF COLON
H101	4	Excision of sigmoid colon	SIGMOID COLECTOMY AND END TO END ANASTOMOSIS OF ILEUM TO RECTUM
H102	4	Excision of sigmoid colon	SIGMOID COLECTOMY AND ANASTOMOSIS OF COLON TO RECTUM
H103	4	Excision of sigmoid colon	SIGMOID COLECTOMY AND ANASTOMOSIS- NOT ELSEWHERE CLASSIFIED
H104	4	Excision of sigmoid colon	SIGMOID COLECTOMY AND ILEOSTOMY- HOWEVER FURTHER QUALIFIED
H105	4	Excision of sigmoid colon	SIGMOID COLECTOMY AND EXTERIORISATION OF BOWEL- N.E.C.
H108	4	Excision of sigmoid colon	OTHER SPECIFIED EXCISION OF SIGMOID COLON
H109	4	Excision of sigmoid colon	UNSPECIFIED EXCISION OF SIGMOID COLON
H091	4	Excision of left hemicolon	LEFT HEMICOLECTOMY AND END TO END ANASTOMOSIS OF COLON TO RECTUM
H092	4	Excision of left hemicolon	LEFT HEMICOLECTOMY AND END TO END ANASTOMOSIS OF COLON TO COLON
H093	4	Excision of left hemicolon	LEFT HEMICOLECTOMY AND ANASTOMOSIS- NOT ELSEWHERE CLASSIFIED
H094	4	Excision of left hemicolon	LEFT HEMICOLECTOMY AND ILEOSTOMY- HOWEVER FURTHER QUALIFIED
H095	4	Excision of left hemicolon	LEFT HEMICOLECTOMY AND EXTERIORISATION OF BOWEL- N.E.C.
H098	4	Excision of left	OTHER SPECIFIED EXCISION OF LEFT

		hemicolon	HEMICOLON
H099	4	Excision of left hemicolon	UNSPECIFIED EXCISION OF LEFT HEMICOLON

9.7 Search strategy for literature review

CINAHL combined search

1. cancer.mp.
2. Calman-Hine.mp.
3. Specialisation.mp.
4. Multidisciplinary team.mp.
5. Managed Clinical Network.mp.
6. 1 and 2 and 3 and 4 and 5
7. 1 and 2
8. 3 and 7
9. 3 and 4
10. from 7 keep 1,3,5,8-9,14,17

Outcome of Calman Hine Cinahl

Library search strategy

1. exp Neoplasms/
2. exp Colon/
3. exp Rectum/
4. 1 and (2 or 3)
5. ((colo$ or rect$) adj5 (cancer$ or neoplas$)).mp.
6. exp Colorectal Neoplasms/
7. or/4-6
8. (managed adj3 network$).mp.
9. exp "Quality of Health Care"/
10. exp Health Care Delivery/
11. exp Health Policy/
12. exp Practice Guidelines/
13. exp Managed Care Programs/
14. or/8-13
15. exp Treatment Outcomes/
16. exp Survival/
17. exp Cancer Survivors/
18. exp Survival Analysis/
19. exp Study Design/

20. or/15-19
21. 7 and 14 and 20
22. calman hine.af.
23. 21 or 22
24. exp Cancer Screening/
25. exp Colorectal Neoplasms/pc [Prevention and Control]
26. or/24-25
27. 23 not 26

HMIC database search

1. Adenocarcinoma/ or Colorectal Neoplasms/ or management of colorectal cancer.mp.
2. limit 1 to (full text and humans and "review articles")
3. "Delivery of Health Care"/ or Program Development/ or Scotland/ or managed clinical network.mp. or Program Evaluation/ or Managed Care Programs/
4. 1 and 3
5. from 4 keep 18,43,48,57,73,76-77,91,93,100-101,105-106,122-125,134,156
6. Managed clinical network.mp.
7. from 6 keep 1,3,5,8,10,12,15-18
8. from 7 keep 1-10
9. from 6 keep 1,4,6-8
10. from 6 keep 1-8
11. colorectal cancer.mp. or exp colorectal cancer /
12. exp CANCER SERVICES/ or exp NHS/ or exp INTERPROFESSIONAL COLLABORATION/ or exp managed clinical networks/ or exp SERVICE PROVISION/ or managed clinical network.mp. or exp SCOTLAND/
13. 11 and 12
14. from 13 keep 8,21,23-25,27,32-34

Initial EMBASE

1. Adenocarcinoma/ or Colorectal Neoplasms/ or management of colorectal cancer.mp.
2. limit 1 to (full text and humans and "review articles")

3. "Delivery of Health Care"/ or Program Development/ or Scotland/ or managed clinical network.mp. or Program Evaluation/ or Managed Care Programs/
4. 1 and 3
5. from 4 keep 18,43,48,57,73,76-77,91,93,100-101,105-106,122-125,134,156
6. Managed clinical network.mp.
7. from 6 keep 1,3,5,8,10,12,15-18
8. from 7 keep 1-10
9. from 6 keep 1,4,6-8
10. from 6 keep 1-8

Outcome of Calman Hine Medline
Library search strategy
1. exp Neoplasms/
2. exp Colon/
3. exp Rectum/
4. 1 and (2 or 3)
5. ((colo$ or rect$) adj5 (cancer$ or neoplas$)).mp.
6. exp Colorectal Neoplasms/
7. or/4-6
8. exp Cancer Care Facilities/
9. exp Guideline Adherence/
10. exp Practice Guidelines/
11. exp Medical Oncology/st
12. exp Managed Care Programs/
13. (managed adj3 network$).mp.
14. or/8-13
15. exp Treatment Outcome/
16. exp "Outcome Assessment (Health Care)"/
17. exp Survival Analysis/
18. exp Survival Rate/
19. exp Epidemiologic Methods/
20. or/15-19
21. 7 and 14 and 20
22. calman hine.af.
23. or/21-22

24. exp *Diagnostic Imaging/
25. exp Mass Screening/
26. exp *Mass Screening/mt [Methods]
27. exp *Colonoscopy/
28. exp Colorectal Neoplasms/pc [Prevention & Control]
29. or/24-28
30. 23 not 29

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