Colorectal Cancer – The Prediction of Risk

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University of Leicester

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<table>
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<th>Description</th>
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<tbody>
<tr>
<td>2WW</td>
<td>Two Week Wait</td>
</tr>
<tr>
<td>APC</td>
<td>Adenomatous Polyposis Coli</td>
</tr>
<tr>
<td>ASA</td>
<td>American Society of Anaesthesiologists</td>
</tr>
<tr>
<td>AUC</td>
<td>Area Under Curve</td>
</tr>
<tr>
<td>CEA</td>
<td>Carcino Embryonic Antigen</td>
</tr>
<tr>
<td>CIBH</td>
<td>Change In Bowel Habit</td>
</tr>
<tr>
<td>CRC</td>
<td>Colorectal Cancer</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>DCBE</td>
<td>Double Contrast Barium Enema</td>
</tr>
<tr>
<td>EGF</td>
<td>Epidermal Growth Factor</td>
</tr>
<tr>
<td>EUA</td>
<td>Examination Under Anaesthesia</td>
</tr>
<tr>
<td>FAP</td>
<td>Familial Adenomatous Polyposis</td>
</tr>
<tr>
<td>FDA</td>
<td>Food &amp; Drug Authority</td>
</tr>
<tr>
<td>FOB</td>
<td>Faecal Occult Blood</td>
</tr>
<tr>
<td>FOS</td>
<td>Fibreoptic Sigmoidoscopy</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>Hb</td>
<td>Haemoglobin</td>
</tr>
<tr>
<td>HNPCC</td>
<td>Hereditary Nonpolyposis Colorectal Cancer</td>
</tr>
<tr>
<td>IBD</td>
<td>Inflammatory Bowel Disease</td>
</tr>
<tr>
<td>IDA</td>
<td>Iron Deficiency Anaemia</td>
</tr>
<tr>
<td>IMD</td>
<td>Index of Multiple Deprivation</td>
</tr>
<tr>
<td>MDT</td>
<td>Multi Disciplinary Team</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute of Clinical Excellence</td>
</tr>
<tr>
<td>ONS</td>
<td>Office of National Statistics</td>
</tr>
<tr>
<td>PCQ</td>
<td>Patient Consultation Questionnaire</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>PPV</td>
<td>Positive Predictive Value</td>
</tr>
<tr>
<td>PSQ</td>
<td>Patient Satisfaction Questionnaire</td>
</tr>
<tr>
<td>ROC</td>
<td>Receiver Operating Curve</td>
</tr>
<tr>
<td>TNM</td>
<td>Tumour Node Metastases</td>
</tr>
<tr>
<td>UHL</td>
<td>University Hospitals of Leicester</td>
</tr>
<tr>
<td>UICC</td>
<td>Union Internationale Contre Cancer</td>
</tr>
<tr>
<td>VEGFR</td>
<td>Vascular Endothelial Growth Factor receptor</td>
</tr>
<tr>
<td>WNS</td>
<td>Weighted Numerical Score</td>
</tr>
</tbody>
</table>
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I would like to thank Professor Will Steward and Mr John Jameson for supervising my research and this thesis. Their constant support and advice was invaluable to help me complete this work.

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Finally, I wish to thank my wife Deepa and my two sons Ankit and Arnav for their support and understanding.
PART I

Introduction

CHAPTER 1
I Aims and Hypotheses of the thesis project

Aims

(a) To assess the various current referral routes for patients with bowel symptoms and other signs suspicious of colorectal cancer.

(b) To assess the ‘Two week wait’ (2WW) fast-track referral system for colorectal cancer for compliance with current guidelines and colorectal cancer detection.

(c) To validate the Patient Consultation Questionnaire – Weighted Numerical Scoring (PCQ-WNS) system in the large and multicultural population of Leicester as an effective tool for prioritising colorectal referrals.

(d) To compare the PCQ-WNS system with the current 2WW referral system.

(e) To study colorectal cancer presenting as an emergency.

(f) To study colorectal cancer in Leicestershire’s Ethnic population.

(g) To investigate the diagnosis of proximal colon cancers.

(h) To assess patient satisfaction with the use of the PCQ and their overall treatment at the hospital.

Hypotheses

(a) The NHS guidelines are relatively sensitive to colorectal cancer detection if fully implemented but not specific resulting in a higher proportion of urgent fast track referrals.

(b) The PCQ-WNS system is effective in detecting risk of colorectal cancer with high sensitivity and specificity. The mean ‘score’ of referred patients having colorectal cancer is significantly higher than non-cancer patients. This provides risk stratification that allows effective prioritisation of patients for further assessment.
The PCQ-WNS system puts the patients in control of their own clinical pathway significantly improving patient satisfaction.

The incidence and presentation of colorectal cancer in Leicester’s immigrant ethnic population differs significantly from the native population.

The presentation and outcome of colorectal cancers presenting as an emergency differs significantly from those presenting electively.

II Colorectal cancer

Definition

Colorectal cancer by definition is cancer occurring in the colon or the rectum.¹

Incidence

Colorectal cancer is an important public health problem. Approximately one million new cases are diagnosed worldwide each year and there are approximately half a million deaths.² Recent reports have shown that in the United States, colorectal cancer was the most frequent form of cancer among persons 75 years or older. Overall it is the fourth most common cancer in the world affecting men and women almost equally. It represents 9.4% of all incident cancer in men and 10.1% in women.³

In the UK there are approximately 30,000 new cases of colorectal cancer registered each year and the disease represents the second most common cause of cancer death after lung cancer with over 17,000 per annum.⁴
Time trends

Although the mortality from colorectal cancer has declined as a result of advances in detection and treatment, the number of new cases of colorectal cancer worldwide has been increasing rapidly since 1975.\textsuperscript{3}

The incidence of colorectal cancer in England and Wales has been slowly rising during the last decades. The rise in incidence does not seem to be an effect of an ageing population as the rise is across the age bands.\textsuperscript{5} The biggest increase is seen in colon cancer in males. There seems to be no increase in the incidence of either colon or rectal cancer in females. Similar trends have been found in the rest of Europe and the United States.\textsuperscript{5}

Gender differences

The age-standardized incidence rates for colon cancer in England and Wales are 17.1 per 100,000 for males and 13.2 per 100,000 for females. The age-standardized incidence rates for rectal cancer in England and Wales for males and females are 13.6 per 100,000 and 7.8 per 100,000 respectively.\textsuperscript{5} In general, the incidence of colorectal cancer in England and Wales has been rising steadily, with the increase being more rapid in males than in females.\textsuperscript{6}

Geographical/Racial differences

Colorectal cancer is predominantly a disease of the western world. It is very common in North America, Western Europe, Australia and New Zealand, whereas the age-standardized incidence rate of colorectal cancer is very low in India and Africa.\textsuperscript{7} (see table 1.1)
### Table 1.1 Approximate incidence of colorectal cancer per 100 000 people

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>2</td>
</tr>
<tr>
<td>Asia</td>
<td>15</td>
</tr>
<tr>
<td>South America</td>
<td>15</td>
</tr>
<tr>
<td>West Europe</td>
<td>40</td>
</tr>
<tr>
<td>USA</td>
<td>35</td>
</tr>
</tbody>
</table>

The highest age-standardized incidence rates for colon cancer in males are found among the Japanese population in Hawaii (37.15 per 100,000) and for females in New Zealand (30.46 per 100,000). The lowest age-standardized incidence rates of colon cancers in both genders are found in Africa and India. The differences in incidence rates are more than tenfold. The highest age-standardized incidence rates for rectal cancer in males are found in Hungary (20.46 per 100,000) and for females in New Zealand (12.31 per 100,000). Furthermore, colon cancer is more common in developing countries than is rectal cancer.

**Age Differences**

Most colorectal cancers occur predominantly in older patients, with an average age at diagnosis of approximately 60 to 70 years. Nevertheless, colorectal cancers affect younger patients as well; although thankfully the incidence below the age of 40 years is low. The cancers that are seen in these younger patients reveal different tumour characteristics when compared with those seen in the older age group of patients. Studies have shown that in general, with increasing age, characteristics like tumour stage at diagnosis, tumour differentiation, and mucin production improved.
Socio-economic class differences

Sharp et al in Scotland revealed a clear trend in incidence of colorectal cancer across various categories of the Carstairs’ deprivation score, with the highest incidence in the least deprived areas.\textsuperscript{10} There seems to be an association between the incidence rates of colorectal cancer and higher social class, which may be diet-related. The association of diet with the incidence of colorectal cancer may, however, have a lag time of up to 35 years. These correlations reflect, therefore, the different diets of the social classes of 30 or more years ago. At present the lower socio-economic classes eat less fresh fruit and vegetables and more fried food when compared with the higher socio-economic classes. If the correlation of socio-economic class and the incidence of colorectal cancer is dependent upon diet, then we may expect to see a reversal of the trends in future decades.

Studies to investigate any correlation between socio-economic status and tumour stage at presentation have failed to show any consistent evidence that patients from deprived communities present with more advanced disease.\textsuperscript{11}

Incidence in migrants

Observations on migrants to the United States from Japan have shown that the mortality rates of colon cancer among Japanese males have risen in one decade almost to equal the higher risks prevailing for United States caucasians.\textsuperscript{12} A similar trend was seen among Polish and Chinese immigrants to the United States. The short time period in which colorectal cancer rates in migrant groups approach that of the host country is evidence that environmental factors are a strong influence in the carcinogenesis process.
On the other hand, studies conducted on the Asian population resident in England have shown a significantly lower incidence of colorectal cancer when compared to the indigenous population. A study in the city of Leicester which has a predominantly Gujarati Asian population confirmed this. If diet plays a part in the pathogenesis of colorectal cancer, then this observation may be explained by the fact that the Asian population tend to continue to use their native cuisine. Interestingly, it was also found that there was a trend towards an increased relative frequency of colorectal cancer in the younger Asian age group. The next few years will be an important time in determining whether or not this difference will persist or whether the incidence of colorectal cancer within the Leicester Asian population as a whole will increase.

**Site distribution**

The site distribution of colorectal cancer in the United Kingdom is typical of the western world, with two-thirds of the cancer in the rectum and sigmoid colon. In low-incidence countries, the sigmoid to ascending colon ratio is much lower. There have been several recent reports of a ‘proximal or rightward shift’ in the site distribution of colorectal cancer. The reason for this is not clear but there have been many suggestions. Improved diagnostic accuracy for proximal colon lesions, decreasing incidence of distal colorectal lesions, dietary influences or a combination of these factors have all been suggested. Irrespective of the underlying cause, if this apparent shift represents a true finding then this will have major implications for clinical services throughout the UK in terms of screening and preventive strategies. Flexible sigmoidoscopy, which has been shown to be an effective screening tool and which has been proposed to form the basis of a national screening program, will miss more proximal lesions. The continued rise in the proportion of such lesions not detected
by flexible sigmoidoscopy adds urgency to the need for a more complete and cost-effective screening method.

**Mortality**

The 5-year relative survival rate is currently in the region of 45%, and has improved slightly over the last 30 years from around 30% in 1971-75. The stage of the disease diagnosis determines the survival and so there is a wide variation in survival data. Analyses of survival data show that the global distribution of mortality rates mirrors the incidence rates. The age-specific mortality of colorectal cancer is high in Western Europe, North America, Australia, and New Zealand and low in India, Africa, and Latin America. Time trends show that the mortality has risen substantially in countries with low rates and has fallen gradually in countries with high rates.

Substantial differences in colorectal cancer survival also exist between Great Britain, Europe as a whole, and the United states. The age-standardized mortality rates for colorectal cancer in males and females in England, Wales, and Scotland are among the highest in the world.

Colorectal cancer survival in Britain is poor compared to comparable European countries. This is partly because patients tend to have a more advanced stage of the disease by the time they are diagnosed and treated. Possible explanations for this may include:

(i) patients are not certain when to go to their General Practitioner (GP) about their symptoms,

(ii) GPs, who see relatively few cases of cancer, may have difficulty identifying those at highest risk, or

(iii) the length of time taken in our hospitals to progress from first appointment through diagnostic tests to treatment.
Furthermore, the so called ‘Post-Code Lottery’ and variation in quality and provision of services across the country means that not all patients are getting the optimum treatment for their particular condition.¹⁹

Aetiology and Risk factors

Genetics

Clustering of cases of colorectal cancer within families is well known.²⁰ Possible causes include chance, common exposure to environmental risk factors, hereditary susceptibility or a combination of all of these. Two fundamental features have helped our understanding of the genetics of colorectal cancer. Firstly, the majority of colorectal cancers arise from pre-malignant adenomatous polyps and have a monoclonal composition.²¹ Secondly; there are several well-defined inherited syndromes that predispose to colorectal cancer. The two commonest are Adenomatous Polyposis Coli (APC) (see table 1.2) or the Hereditary Nonpolyposis Colorectal Cancer (HNPCC), both are highly penetrant. These contribute to less than 5% of the total large bowel cancer load. There are also more subtle mechanisms involving more weakly penetrant genes.²² Overall, the genotype is thought to play a part in the causation of colorectal cancer in about 30% of all cases.²³

Table 1.2 Polyposis syndromes

<table>
<thead>
<tr>
<th>Colonic manifestations</th>
<th>Extra colonic lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial adenomatous polyposis Syndromes</td>
<td>Retinal pigmentation</td>
</tr>
<tr>
<td>Familial adenomatous Polyposis</td>
<td>Osteomas, desmoids,</td>
</tr>
<tr>
<td>Gardner’s</td>
<td></td>
</tr>
</tbody>
</table>

23
Other gastrointestinal Cancers
Sebaceous cysts
Intracranial tumors

Oldfield’s
Turcot’s
Hamartomas
Peutz Jegher’s
Juvenile polyps
Perioral freckles

The sub site distribution of colorectal carcinoma in patients with FAP is similar to that in patients with sporadic colorectal cancer; in both, left-sided cancers are more frequent than right-sided cancers. Genetic studies have shown that APC is caused by mutations in the tumour suppressor gene \((apc\) gene) on chromosome 5. The HNPCC may account for as much as 6% of the patients with colorectal cancer. Two subtypes are described. Lynch syndrome I, or site-specific colorectal cancer is characterized by an early age of onset, on average 45 years, and a predilection for proximal colon cancers (70 percent). In Lynch syndrome II or cancer family syndrome, frequent carcinomas in other organs occur in addition to this. Four genes that may be responsible for HNPCC have been identified. Molecular genetics has confirmed the accumulation of genetic changes in the development of colorectal cancer. The most common changes are \(K-ras\) point mutations, mutations in growth suppressor gene \(p53\) on chromosome 17p and allelic loss in chromosome 5\((apc\) gene), and the growth suppressor gene DCC deleted in colorectal cancer on chromosome 18q. Mutations in these genes are common in sporadic colorectal cancer. Accumulation, rather than order, is most important; mutations in at least four to five genes are required for the formation of a malignant tumour, fewer changes suffice for benign tumorigenesis. This model provides a good explanation for individual
susceptibility to colonic neoplasms. Environmental mutagenic factors may determine which susceptible individuals grow polyps and carcinomas.

Colorectal cancer is generally a disease of advancing years; yet in FAP and HNPCC, development of cancer is usually under 50 years. Over 20 years ago, Lovett was the first to find that relatives of patients diagnosed at a young age were more at risk of developing colorectal cancer than relatives of those diagnosed in later years. Recent case control studies have confirmed a dramatic increase in risk to relatives of patients who were diagnosed younger than 45 to 50 years. This has profound implications for screening and disease prevention policies.

Over the years a confusing range of 'criteria' have emerged. The International Collaborative Group on HNPCC (ICG-HNPCC), established in 1989, proposed the Amsterdam criteria in 1990 (Box 1). These were not intended as a diagnostic definition but rather as a means to identify families very likely to be harbouring HNPCC. The aim of this was to allow genetic research to be targeted on a well-defined group that was likely to yield positive results. The Amsterdam criteria were modified by the ICG-HNPCC in 1999 (Box 2) to include HNPCC-associated cancers other than colorectal cancer (Amsterdam II criteria), so that a diagnosis of HNPCC might be made using either set of criteria. However, some HNPCC-affected families will still fail to meet them. Generally, an affected individual (i.e. with an HNPCC-related cancer) from a family fulfilling the Amsterdam I or II criteria would be offered testing.

Box 1  HNPCC: Amsterdam criteria I

- At least three relatives with colorectal cancer, one of whom should be a first degree relative of the other two.
- At least two successive generations should be affected.
- At least one colorectal cancer should be diagnosed before the age of 50 years.
- FAP should be excluded.
- Tumours should be verified by pathological examination.
Box 2  HNPCC: Amsterdam criteria II

- At least three relatives with an HNPCC-associated cancer (colorectal, endometrial, small bowel, ureter, renal pelvis), one of whom should be a first-degree relative of the other two.
- At least two successive generations should be affected.
- At least one colorectal cancer should be diagnosed before the age 50 years.
- FAP should be excluded.
- Tumours should be verified by pathological examination.

Diet

Ethnic and racial differences in colorectal cancer, as well as studies on migrants, suggest that environmental factors play a major part in the aetiology of the disease. The risk of developing cancer in the offspring of Japanese populations who have migrated to the United States has changed and the incidence of colorectal cancer now approaches or surpasses that in white people in the same population and is three or four times higher than among the Japanese in Japan.

For reasons such as these, colorectal cancer is widely believed to be an environmental disease with ‘environmental’ defined broadly to include a wide range of ill-defined cultural, social and lifestyle practices. It may be that up to 70-80% of colorectal cancers owe their appearance to such factors. Dietary factors appear to be among the most important of environmental determinants of colorectal cancer risk. Diet helps to explain the geographic variation in disease. Several foods and nutrients have been implicated in the development of colorectal cancers.

Evidence from epidemiological studies have consistently shown that intake of the typical ‘western diet’ of red and processed meats, sweets and desserts, French fries and refined grains, is positively related to risk of colorectal cancer. This evidence is obtained from ecological studies,
animal experiments and case-control and cohort studies. The correlation is stronger for colon cancer than it is for rectal cancer. Animal studies suggest that fat plays a larger role in colorectal cancer promotion than in its initiation. A plausible mechanism is through changes in faecal bile acid concentration.\textsuperscript{30}

It is difficult however to define the precise role of specific food factors, because diets high in saturated fats and animal protein tend to be low in fibre, fruit and vegetables. The overall pattern of certain diets therefore may be more important than specific components.

The inverse association of intake of dietary fibre with colorectal cancer is well documented, but there remain questions to be answered before a causal relationship between lack of fibre and colorectal cancer is established. It is not clear what type of fibre is most protective or how this protection is mediated. Faecal weight and colonic transit time do not seem to influences the risk of colon cancer.\textsuperscript{31} A dilutional effect on other faecal constituents with carcinogenic potential seems to be the most plausible mechanism.

The role of other dietary components is more uncertain. Some studies have shown the protective effects of antioxidants like vitamin E and carotenoids, others have refuted it.

\textit{Alcohol and Smoking}

There is little evidence that colon cancer is associated with consumption of alcoholic beverages. None of the published studies have shown any significant alcohol-related increase in the risk of colon cancer. Rectal cancer, however, has been positively associated with alcohol in a number of cohort studies.\textsuperscript{32}

Smoking has recently been positively linked to development of benign colorectal adenomas.\textsuperscript{33} More recently; a study has linked cigar
smoking to the development of rectal cancer and has also shown a correlation between cigarette smoking and cancer of the proximal colon.\textsuperscript{34}

**Colonic polyps**

The association between colonic polyps and colonic cancer has been established for a long time. The incidence of malignant change increases with both the size of the polyps and the degree of dysplasia. Tubular adenomas are less prone to malignancy than are villous adenomas. It is now believed that most, if not all, colonic cancers originate within an adenoma, and while most polyps do not become malignant it is clear that a polyp that has been growing for some years to achieve considerable size is more likely to do so. Equally clearly some pass through the adenoma phase quickly, underlying the dual process of tumour genesis and malignant transformation.

The prevalence of adenomas and the prevalence of colonic cancer run in parallel in epidemiological studies. Polyps are also frequently found in close proximity to cancers. The distribution of adenomas around the colon is the same as that of colonic cancers and some adenomas snared endoscopically disclose microscopic foci of cancer. The transformation of a benign adenoma into a cancer is thought to take, on average, about 5 years.

**Other Risk Factors**

Patients with Inflammatory bowel disease (IBD) have an increased risk of colorectal cancer. The association is better established for Ulcerative Colitis than it is for Crohn’s disease. Two independent risk factors for cancer among these patients have been well documented: younger age at diagnosis and extent of disease at diagnosis.\textsuperscript{35} Colorectal cancer in IBD patients is also characterized by a
more proximal localization when compared with colorectal cancer of non-IBD patients. Sclerosing cholangitis has also been found to have a strong association with development of colon cancer in patients with IBD.

Colorectal cancer promoters and inhibitors have been summarised in table 1.3

**Table 1.3 Colorectal cancer promoters and inhibitors**

<table>
<thead>
<tr>
<th>Promoters</th>
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<tbody>
<tr>
<td>Genetic</td>
<td>Familial adenomatous polyposis</td>
</tr>
<tr>
<td></td>
<td>Hereditary non-polyposis</td>
</tr>
<tr>
<td></td>
<td>Colonic cancer</td>
</tr>
<tr>
<td></td>
<td>Peutz-Jegher’s</td>
</tr>
<tr>
<td></td>
<td>Juvenile Polyposis</td>
</tr>
<tr>
<td>Diet</td>
<td>Fat</td>
</tr>
<tr>
<td></td>
<td>Bile acids</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Nuclear dehydrogenase-producing</td>
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<tr>
<td></td>
<td>Clostridia</td>
</tr>
<tr>
<td>Operations</td>
<td>Cholecystectomy</td>
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<td></td>
<td>Gastric surgery</td>
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<td></td>
<td>Ureterosigmoidostomy</td>
</tr>
<tr>
<td>Irradiation</td>
<td></td>
</tr>
<tr>
<td>Diseases</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td></td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>Inhibitors</td>
<td>Fibre</td>
</tr>
<tr>
<td></td>
<td>Selenium</td>
</tr>
<tr>
<td></td>
<td>Vitamins C and E</td>
</tr>
<tr>
<td></td>
<td>Carotene</td>
</tr>
</tbody>
</table>
Colonic cancers, in common with most epithelial tumours, are polyclonal with clones of cells exhibiting differing degrees of ‘malignancy’. The more undifferentiated or more ‘malignant’ clones are more likely to spread and metastasise. A tumour’s biological behaviour is the main determinant of the tumour’s propensity to spread locally and to metastasise and therefore, indicates the ultimate prognosis. This in turn is reflected to some extent by the histopathological features of a cancer. Tumour secondaries, which are often derived from selected clones of a polyclonal primary, are unlikely to behave in the same way as the primary tumour and will generally be more malignant.

Tumour biology is very much reflected by the stage of the disease, and therefore the amount of spread, at presentation. It is no surprise that there is a significant inverse relation between the length of history and the stage of the disease at diagnosis. Obviously tumours that are rapidly growing will become symptomatic in a shorter time and are more advanced at the time of presentation. Although the clinical and pathological stage is a ‘snapshot’ in the life of a tumour, it provides the most accurate prognostic index; this may be refined further by the histopathological features.

Several staging methods are in use throughout the world, and each has strengths and weaknesses. The most commonly used ones are:

(i) The Dukes’ staging. (See table 1.4)

(ii) The Union Internationale Contre Cancer (UICC) Tumour Node Metastases (TNM) staging. (See figure 1)

The Dukes’ staging has the advantage of great simplicity but considerable disadvantages from lack of precision: it does not reflect accurately the depth of tumour penetration, the extent of spread outside the bowel, the number of lymph nodes affected by tumour, or the presence or
absence of metastases, all of which have an important bearing upon prognosis.

Table 1.4 Cancer staging – Dukes’ classification

<table>
<thead>
<tr>
<th>Letter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Tumour confined to bowel wall</td>
</tr>
<tr>
<td>B</td>
<td>Tumour involving or through serosa</td>
</tr>
<tr>
<td>C</td>
<td>Lymph nodes involved</td>
</tr>
<tr>
<td></td>
<td>C1 Apical node clear</td>
</tr>
<tr>
<td></td>
<td>C2 Apical node involved</td>
</tr>
<tr>
<td>D</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

(Dukes’ D has been added on as a modification of Dukes’ classification)

The anatomical site of the cancer has an influence on the stage of the disease and an independent effect upon prognosis. Right-sided colonic cancers tend to be more advanced in terms of pathological staging at the time of presentation, but the prognosis is comparable to left-sided tumours. Stages for stage, right-sided lesions have a better prognosis; this may reflect subtle differences in aetiology. Rectal tumours have a generally better prognosis, because of earlier presentation and easier accessibility.

Staging investigations give information about the primary tumour but also yield useful information regarding the presence or absence of occult hepatic metastases, a major factor in terms of survival. Patients with Dukes’ C tumours are more likely to have occult hepatic metastases than those with Dukes’ B tumours, while patients with Dukes’ A lesions are least likely to have hepatic metastases. Occult hepatic metastases account for the majority of deaths from colonic cancer. Only about 20 percent of patients die from local spread of the disease, which is also reflected in the clinical stage.

Age has little effect on the behaviour or prognosis of colonic tumours, except, in the small cohort of patients who develop the disease
under the age of 45 years. This group appear to have a particularly poor prognosis.

Figure 1 Cancer staging - UICC TNM classification

(American Cancer Society – Cancer reference information)

The UICC/TNM System describes the extent of the primary Tumour (T), the absence or presence of metastasis to nearby lymph Nodes (N), and the absence or presence of distant Metastasis (M).

T Categories for Colorectal Cancer

T categories of colorectal cancer describe the extent of spread through the layers that form the wall of the colon and rectum. These layers, from the inner to the outer, include the lining (mucosa), a thin layer of muscle (muscularis mucosa), the fibrous tissue beneath this muscle layer (submucosa), a thick layer of muscle that contracts to force the contents of the intestines along (muscularis propria), and the thin outermost layers of connective tissue (subserosa and serosa) that cover most of the colon but not the rectum.

Normal Intestine Tissue
(Cross section of digestive tract)

The layers of the colon wall

Tx: No description of the tumour's extent is possible because of incomplete information.

Tis: The cancer is in the earliest stage. It involves only the mucosa. It has not grown beyond the muscularis mucosa (inner muscle layer) of the colon or rectum. This stage is also known as carcinoma in situ or intramucosal carcinoma.

T1: The cancer has grown through the muscularis mucosa and extends into the submucosa.

T2: The cancer has grown through the submucosa, and extends into the muscularis propria.
T3: The cancer has grown completely through the muscularis propria into the subserosa but not to any neighbouring organs or tissues.

T4: The cancer has spread completely through the wall of the colon or rectum into nearby tissues or organs.

N Categories for Colorectal Cancer

N categories indicate whether or not the cancer has spread to nearby lymph nodes and, if so, how many lymph nodes are involved.

Nx: No description of lymph node involvement is possible because of incomplete information.

N0: No lymph node involvement is found.

N1: Cancer cells found in 1 to 3 nearby lymph nodes.

N2: Cancer cells found in 4 or more nearby lymph nodes.

M Categories for Colorectal Cancer

M categories indicate whether or not the cancer has spread to distant organs, such as the liver, lungs, or distant lymph nodes.

Mx: No description of distant spread is possible because of incomplete information.

M0: No distant spread is seen.

M1: Distant spread is present.

Stage Grouping

The following guide illustrates how TNM categories are grouped together into stages:

Stage 0: Tis, N0, M0: The cancer is in the earliest stage. It has not grown beyond the inner layer (mucosa) of the colon or rectum. This stage is also known as carcinoma in situ or intramucosal carcinoma.

Stage I: T1, N0, M0, or T2, N0, M0: The cancer has grown through the muscularis mucosa into the submucosa or it may also have grown into the muscularis propria, but it has not spread into nearby lymph nodes or distant sites.

Stage IIA: T3, N0, M0: The cancer has grown through the wall of the colon or rectum into the outermost layers. It has not yet spread to the nearby lymph nodes or distant sites.

Stage IIB: T4, N0, M0: The cancer has grown through the wall of the colon or rectum into other nearby tissues or organs. It has not yet spread to the nearby lymph nodes or distant sites.

Stage IIIA: T1-2, N1, M0: The cancer has grown through the mucosa into the submucosa or it may also have grown into the muscularis propria, and it has spread to 1-3 nearby lymph nodes but not distant sites.

Stage IIIB: T3-4, N1, M0: The cancer has grown through the wall of the colon or rectum or into other nearby tissues or organs and has spread to 1-3 nearby lymph nodes but not distant sites.
Stage IIIC: Any T, N2, M0: The cancer can be any T but has spread to 4 or more nearby lymph nodes but not distant sites.

Stage IV: Any T, Any N, M1: The cancer can be any T, any N, but has spread to distant sites such as the liver, lung, peritoneum or ovary.

Histopathological Grading

Grading depends upon the subjective interpretation of the degree of tumour differentiation at histological examination. To try and reduce variation between observers only two broad groups are used-
-Low or average grade tumours, which are well to moderately differentiated.
-High grade or undifferentiated,
Despite the apparent simplicity of this system, it provides useful prognostic information.
Patients with high-grade cancers fare worse than do those with well-differentiated lesions after taking account of tumour stage.

Typing, on the other hand, reflects the cellular characteristics. Mucinous, signet cell and small cell tumours are variants of the more common adenocarcinoma and the undifferentiated cancers. Signet cell and small cell tumours have a worse prognosis than adenocarcinoma, while mucinous lesions tend to recur locally. Occasionally rectal cancers turn out to be squamous cell types that are more responsive to chemotherapy and irradiation. Melanomas, which have a particularly poor prognosis, are found rarely in the rectum.

Histological features such as vascular, lymphatic or perineural invasion are prognostically unfavourable. By contrast, lymphocytic infiltration of the tumour and a histiocytic reaction in the regional lymph nodes are minor favourable prognostic features.
Identification of surface tumour antigens like the Carcino-embryonic antigen (CEA), oncogene expression and DNA ploidy are not yet in routine use.

**Prognosis**

Stage of the disease remains the most important indicator of prognosis (See table 1.5). The prognosis of patients with adequately treated stage 1 cancers is little different from that of an otherwise healthy population of the same age; 85 percent live 5 years or more after resection. Patients with cancer spread through the serosa only have 67 percent chance of living 5 years. Lymph node metastasis further adversely affects prognosis, with only about 37 percent of patients surviving 5 years. A few patients, some 5 to 10 percent, live 5 years even with hepatic metastases, although 85 percent of such patients die within 1 year of diagnosis.

**Table 1.5 Prognosis in colorectal cancer**

<table>
<thead>
<tr>
<th>TNM Stage</th>
<th>Rectal Cancer</th>
<th>Colon Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 N0 M0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>T2 N0 M0</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>T3 N0 M0</td>
<td>65</td>
<td>90</td>
</tr>
<tr>
<td>T4 N0 M0</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>Any T N1 M0</td>
<td>55</td>
<td>65</td>
</tr>
<tr>
<td>Any N M1</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>N2 M0</td>
<td>35</td>
<td>50</td>
</tr>
<tr>
<td>N3 M0</td>
<td>30</td>
<td>35</td>
</tr>
</tbody>
</table>
Clinical Presentation

Patients with colonic and rectal cancer have a broad range of clinical presentation, which can be classified, according to the anatomical site of the primary. (See table 1.6)

Caecal and right-sided tumours account for about 20 percent of large bowel cancers, while 70 percent occur distal to the splenic flexure and about 45 percent are at or below the recto sigmoid junction.

Table 1.6 Presenting symptoms in colorectal cancer

<table>
<thead>
<tr>
<th></th>
<th>Right Colon</th>
<th>Left Colon</th>
<th>Rectal Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anaemia</td>
<td>Left iliac fossa pain</td>
<td>Blood and mucus per rectum</td>
</tr>
<tr>
<td></td>
<td>Right iliac fossa pain</td>
<td>Lower abdominal colic</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Central abdominal colic</td>
<td>Constipation/ diarrhoea</td>
<td>Tenesmus</td>
</tr>
<tr>
<td></td>
<td>Diarrhoea</td>
<td>Blood +/- mucus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyrexia of unknown origin</td>
<td>Obstruction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Weight loss</td>
<td>Peritonitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Appendicitis</td>
<td>Weight loss</td>
<td></td>
</tr>
</tbody>
</table>
Management of Colorectal Cancer

Management of colorectal cancer is now multidisciplinary. All patients should be discussed and treated as appropriate by a team consisting of pathologists, radiologists, surgeons, oncologists and colorectal nurse specialists.

Diagnosis

The symptoms that suggest a diagnosis of colorectal cancer are well known but are also the topic of much debate. They form part of the written guidelines to GPs to help them identify patients at high risk of having colorectal cancer. The identification of high-risk patients forms the basis of this dissertation and is discussed in detail later. The most important and widely accepted high-risk symptoms are:  

(i) Change in bowel habit to loose and/or more frequent  
(ii) Rectal bleeding without anal symptoms  
(iii) Blood mixed with stool

These symptoms become more important if they present in a patient over 60 years of age, are present for a duration of more than 6 weeks, or are associated with important signs like palpable abdominal or rectal mass, abdominal distension, or presence of iron deficiency anaemia especially in a patient of more than 50 years.
Any of the above symptoms should prompt a digital rectal examination, as up to 80% of rectal cancers are palpable, followed by urgent investigation. The gold standard investigation for suspected colorectal cancer is colonoscopy.

This has been shown to be more sensitive and specific than Barium enema, but it must be acknowledged that small lesions can be missed on colonoscopy, and even in expert hands a 100% caecal intubation rate is not achievable. In addition, a colonoscopy service is highly dependent on sufficient expertise, and in the UK, double contrast barium enema (DCBE) is still widely used. However, this investigation can miss cancers, particularly in a patient with severe diverticular disease of the sigmoid colon, and on the right side of the colon spasm can be misinterpreted as a malignant stricture. Thus, unless the sigmoid colon is extremely well visualised, DCBE should be supplemented by flexible sigmoidoscopy and radiological evidence of lesions in the caecum should be treated with suspicion and confirmed by colonoscopy unless appearances are unequivocal.

Occasionally, both barium enema and colonoscopy will be unsatisfactory, either because of poor bowel preparation or through inability to retain contrast or air, especially in elderly patients. Some elderly patients would also be too frail for an invasive investigation like colonoscopy or even a barium enema. In such instances, careful spiral CT of the abdomen may be useful. CT is also attracting interest as, with appropriate software, it is now possible to carry out CT colography or ‘virtual colonoscopy’, which is effective in detecting polypoid lesions down to 6 mm in diameter. Although not yet widely available in the UK, this technology is fast becoming a standard investigation and will almost certainly replace barium enema as the radiological investigation of choice.
Screening

Screening for colorectal cancer seems attractive because of the great difference in prognosis between early and late stages of the disease.

Screening for colorectal cancer can be divided into two broad categories:

(i) Screening of high risk groups
(ii) Population screening

Screening of high risk groups

Family history: It is generally agreed that individuals at moderate risk of developing colorectal cancer on the basis of their family history should be advised to undergo a single colonoscopy at the age of 50 years. Such individuals are usually those with a first degree relative under 45 years of age diagnosed with colorectal cancer.

Two conditions, inherited as autosomal dominant traits, put the patient at very high risk of developing the disease. The first one is FAP, which accounts for 1% of all colorectal cancers. It is characterised by the appearance of multiple polyps throughout the colon and the inevitable development of colorectal cancer at a mean age of 40 years. Polyps first appear in late teens and early 20s. It is now possible to identify mutations of the *apc* gene responsible for the condition and the offspring of such an individual can be offered genetic counselling and screening. Carriers of the mutation should have early sigmoidoscopy and colonoscopy every 2-3 years. When polyps appear, the patient should undergo either a panproctocolectomy or a total colectomy, depending on the degree to which the rectum is affected.

The second inherited condition, HNPCC accounts for 5% of all colorectal cancers. The following criteria are used for diagnosis:

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39
1. The affected individual should have at least three relatives with a confirmed colorectal cancer (one of whom being a first degree relative of the other two).
2. At least two consecutive generations should be affected.
3. Colorectal cancers should be diagnosed at less than 50 years of age.

The germ line mutation in one of the DNA mismatch repair genes, responsible for this condition can be identified and affected individuals offered screening in the form of colonoscopy every 2 to 3 years starting at about 20 years of age.

**Sporadic Polyps:** Patients who have had colonoscopic removal of adenomatous polyps are at a higher risk than the general population of developing further polyps (approximately 40% risk at 3 years)\(^4\)
and presumably, therefore, of developing colorectal cancer. Enthusiasm for colonoscopic follow up of patients with colorectal adenomas must be balanced with a realistic approach to the use of endoscopy services. A randomised trial has shown that 3 yearly colonoscopy is as effective as one yearly colonoscopy in detecting significant lesions after polypectomy.\(^4\)

**Inflammatory bowel disease:** Patients with Ulcerative colitis or Crohn’s colitis are at a higher risk of developing colorectal cancer than the general population. In ulcerative colitis the cumulative risk is 2% at 10 years, 8% at 20 years, and 18% at 30 years. It therefore is reasonable to offer patients with left sided colitis or pancolitis of 10 years duration, colonoscopy every 3 years with mucosal biopsies plus biopsy of any suspicious lesion. This should be increased to yearly colonoscopy if disease has been present for 20 years. If at any time a high-grade dysplasia is found, colectomy should be advised, as there is a 40% chance of such a patient harbouring an invasive cancer.
Population Screening

As colorectal cancer is a common condition, particularly after the age of 50, and because there is a well-defined premalignant lesion, which is amenable to treatment, the disease would seem to be a prime candidate for population screening. The most widely used screening tests are Faecal occult blood testing, Flexible sigmoidoscopy, and Colonoscopy.

Only faecal occult blood (FOB) testing trials carried out in Minnesota, USA, Nottingham, UK, and Funen, Denmark have shown significant reductions in disease specific mortality. Such trials are essential in order to eliminate biases such as lead bias, which can give a false impression of an improved prognosis in screen-detected disease. The problem of false positives (and its subsequent impact on resources) continues to affect FOB testing and draws in to question its role as a screening tool that can be used on a national basis.

Prevention of colorectal cancer by offering screening endoscopy to the general population has been proposed recently. However, there has been widespread uncertainty about the viability of such a program. The major concerns are not about the efficacy of polypectomy in interrupting the polyp cancer sequence, but whether the benefits are worth the costs. Patient compliance and costs for the National Health Service (NHS) in the UK play a large role in this matter. A recent Scottish study assessed patient compliance by inviting patients for a screening flexible sigmoidoscopy. The uptake was found to be very poor in spite of the information given to the patients prior to the procedure. A screening program would result in a large increase in the workload of the average endoscopy unit and would require a substantial capital investment. A recent study at a large teaching hospital has shown that an additional 20% of colorectal sessions need to be
allocated to allow for adequate service provision for the incorporation of a screening program.\textsuperscript{47} The Imperial Cancer Research Fund (now Cancer Research UK) has investigated the role of once-only flexible sigmoidoscopy as a screening modality in a multicentre randomised study which has shown that this modality is feasible, safe and acceptable to patients,\textsuperscript{48} however the effect on mortality is not yet known. Further trials are needed to identify the most cost-effective approach for the general population.

\textit{Staging after Diagnosis}

Once the diagnosis of colorectal cancer has been made it is important to establish the extent of the disease both locally and in terms of distant spread. All patients should have preoperative chest and liver imaging, and there is good evidence that computed tomography (CT) is the most sensitive modality for both liver and lung metastases.\textsuperscript{49} Rectal cancer can be frequently inoperable due to its confinement with the pelvis. Many surgeons therefore commonly use CT or magnetic resonance imaging (MRI) of the rectum. However, there is no evidence that this approach is superior to digital rectal examination under anaesthetic (EUA) by an experienced surgeon in terms of determining operability.

There is no doubt that MRI is the most accurate modality for predicting histological spread of the tumour through the rectal wall and surrounding mesorectum and this is particularly helpful in planning preoperative radiotherapy.\textsuperscript{50} Gina Brown et al have shown recently that high spatial resolution MRI identified prognostic features of tumours in distal sigmoid, rectosigmoid and upper rectum, allowing accurate staging and planning for preoperative therapy.\textsuperscript{51} Endoluminal ultrasound is also widely used but this is more valuable in distinguishing between benign rectal adenomas and invasive carcinoma.\textsuperscript{52} It is now an established means
of assessing the depth of penetration of the bowel wall by the tumour. This information is useful when considering local treatment for a rectal cancer.

Synchronous tumours occur in about 5% of patients with colorectal cancer. Prior to any resection it is therefore important to ensure that the whole colon has been assessed if technically possible. Although this can be achieved by DCBE, colonoscopy is preferable because therapeutic procedures such as removal of adenomatous polyps can be undertaken if necessary. If preoperative colonoscopy is not feasible because of an obstructing tumour, visualisation of the remaining large bowel should be performed within six months of surgery.

**Surgery**

Surgery remains the definitive treatment for localised colorectal cancer and it is important that the patient undergoes appropriate preoperative preparation. Mechanical bowel preparation is widely used especially for left sided lesions although it is mainly for aesthetic reasons as there is no evidence that it has any significant benefit. Prophylaxis against deep vein thrombosis is important and the most commonly used method is low dose subcutaneous heparin. Prophylactic antibiotics to reduce the incidence of wound infection are well established and the current best practice is to give a single dose of intravenous antibiotics providing both aerobic and anaerobic cover within 30 minutes of induction of anaesthesia.

**Colonic cancer**

In the elective situation, right-sided cancers are treated by right hemicolecetomy and left sided cancers by left hemicolecetomy or sigmoid colectomy. For tumours in the region of the splenic flexure there is debate
as to whether segmental resection or extended right hemicolecctomy is appropriate.

In the emergency situation with an obstructing colonic cancer a right hemicolecctomy with primary anastomosis is appropriate for right-sided lesions. For left sided obstructing lesions, particularly in the sigmoid, it is still standard practice to perform a Hartmann’s procedure with an end colostomy and closure of the rectal stump. In favourable situations and when the surgeon is experienced, after an on-table colonic irrigation, a segmental resection or subtotal colectomy with primary anastomosis can be performed. However, one randomised trial has shown the latter procedure to be associated with poorer functional outcome.5 6

Clinical anastomotic dehiscence rates after colonic resection should be less than 5% but there is no consensus as to the best method of anastomosis. Randomised trials of stapling versus hand sutured anastomosis show no difference.57

Rectal cancer

The most important concept in recent years in rectal cancer surgery has been mesorectal excision.58 This involves careful dissection in the plane immediately outside the mesorectum so that the rectum and tumour can be removed as a package and damage to the pelvic nerves is minimised. It is generally agreed that for tumours of the upper third of the rectum it is safe to transect the mesorectum at 5cm below the tumour, whereas for tumours of the lower two thirds of the rectum total mesorectal excision is necessary. Abdominoperineal excision of the rectum should only be necessary for very low tumours and should account for no more than 40% of all rectal cancer operations.59 Providing a small rectal stump can be preserved an anastomosis is possible using stapling techniques. Unfortunately, however, this type of very low anastomosis is associated
with a high anastomotic leakage rate (up to 20%)\textsuperscript{60} and it is standard practice now in such cases to use a defunctioning loop ileostomy in order to minimise the effects of leakage.

If the principles of mesorectal excision are adhered to then overall local recurrence rates after rectal cancer surgery should be below 10%. Local recurrence is difficult to treat and ultimately fatal, so good surgery is of paramount importance for better long-term survival for patients with rectal cancer.

\textit{Laparoscopic colorectal surgery}

Since its inception in the early 1980s, laparoscopic surgery has revolutionised surgical procedures like cholecystectomy. It was only a matter of time before growing enthusiasm led to laparoscopic surgery being extended to colorectal resections in the early 1990s. However, the enthusiasm soon died down when reports were published citing poor oncological outcomes with laparoscopic surgery, dissemination of malignancy through the pneumoperitoneum and port-site metastases.\textsuperscript{61} Laparoscopic colorectal surgery was largely abandoned outside of clinical trials. Recently, with many multicentre randomised trials demonstrating oncological equivalence of laparoscopic resections, laparoscopic colorectal surgery has shown resurgence in a big way. The most important amongst these trials is the MRC-funded CLASICC (Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer) trial, which was set up in 1996. The initial data from this trial appears to confirm findings of randomised studies from other countries, namely that laparoscopic surgery can achieve similar results to open surgery in terms of lymph node harvest and resection margin clearance. Furthermore, many trials have shown statistically significant better short-term results with laparoscopic colorectal surgery in terms of reduced post operative pain, early bowel
movements, decreased hospital stay and overall a lower morbidity. This is primarily due to a significantly lower inflammatory and acute phase response in laparoscopic surgery as compared to open surgery. Leung et al\textsuperscript{62} studied 34 patients in a randomised controlled trial and demonstrated reduced levels of cytokines and C-reactive protein in laparoscopic anterior resection compared with open surgery. Braga et al\textsuperscript{63} in a randomised study of 79 patients showed that laparoscopic colorectal surgery induced a reduced acute-phase response and reduced postoperative pain. Many studies have examined quality of life after laparoscopic colorectal surgery as compared to that after open surgery. The so-called COST\textsuperscript{64} (Clinical Outcomes of Surgical Therapy) study from the USA showed advantages in quality of life in the short term.

Long-term benefits of laparoscopic colorectal surgery in terms of improved survival remain unproven so far. Some multicentre randomised trials have shown nonsignificantly better or equivalent survival rates with laparoscopic malignant surgery. In a well conducted randomised controlled trial in Barcelona\textsuperscript{65} of 219 patients with colon cancer, laparoscopic surgery not only gave significant benefits in terms of morbidity, recovery and postoperative stay but multifactorial analysis also demonstrated improved cancer-related survival in patients with stage III disease.

The future of laparoscopic surgery is bright and it is certainly here to stay. Having shown oncological equivalence and better postoperative outcomes for laparoscopic surgery as compared to open procedures, the emphasis of the various trials is now on training of surgeons and their learning curve. Increasing patient awareness and demand for laparoscopic colorectal surgery has further fuelled the need for more laparoscopically trained surgeons. Identification of appropriate surrogate measures of the learning curve and the currently ongoing preceptorship programs are steps in this direction. The indications for laparoscopic colorectal surgery are
changing as well, especially as more experienced surgeons become available and the range of equipment available increases.

**Adjuvant Therapy**

This can be subdivided into adjuvant chemotherapy and adjuvant radiotherapy.

**Adjuvant chemotherapy**

5-Fluorouracil (5FU) has been the cornerstone of adjuvant chemotherapy in colorectal cancer. Many randomised trials have proven benefit of 5FU based adjuvant chemotherapy for patients with stage III colon cancer if they are fit enough to receive it. Similar rules apply for patients with stage III rectal cancer. In 1989 and 1990 two important studies established the survival benefit of 12 months of 5FU plus levamisole over observation alone. Levamisole, an antihelminthic, was thought to enhance the efficacy of 5FU with its immunostimulatory properties. Soon after other studies showed survival advantage with a combination of 5FU and folinic acid (FA) which potentiates the action of 5FU on its target enzyme thymidylate synthase. The Quick and Simple and Reliable (QUASAR) study compared high- and low-dose FA with or without levamisole. Nearly 5000 patients were recruited and no significant difference was shown between groups, suggesting that levamisole is not necessary and that low-dose FA provides adequate modulation of 5FU.

Today, the standard treatment options for stage III (Dukes’ C) colorectal cancer patients are twofold. The first option is Oxaliplatin and 5FU/FA. This is based on the results of the MOSAIC study, which examined the impact of the addition of oxaliplatin to 5FU in the adjuvant context. Two thousand two hundred and forty-six patients who had undergone curative resection of Dukes’ B or C colon cancer were
randomised to bi-weekly 5FU/FA or FOLFOX (5FU/FA+oxaliplatin). A statistically significant improvement in 3-year disease-free survival was seen in the oxaliplatin treated patients, as was a 23% reduction in the risk of recurrence, compared to 5FU/FA alone. The second option is capecitabine, an oral fluoropyrimidine. The X-ACT study evaluated oral capecitabine versus 5FU/FA bolus in Dukes’ C patients and demonstrated better effectiveness and improved tolerability of the oral therapy. The choice of which option to use depends on patients’ co-morbidities and for less fit patients, the QUASAR regimen of weekly bolus 5FU is still used which appears to be less toxic as shown in this large British study.

Overall, adjuvant chemotherapy appears to confer a 5-10% improvement in absolute survival. The largest evidence base exists in patients with colon cancer and its applicability to patients with rectal cancer remains controversial. Nonetheless, in routine clinical practice, it is common to use the same criteria to select patients irrespective of the primary site of the tumour.

It is not so clear, however, whether or not patients with stage II cancer should receive chemotherapy and many randomised studies are trying to answer this question. Such patients already have a reasonable prognosis and very large studies are required to detect the likely size of any benefit from chemotherapy. Eight trials have been published addressing this issue; of which five were combined to form the International Multicentre Pooled Analysis of Colon Cancer Trials (IMPACT) B2 study. The benefit seen in these trials is only 1.5% and does not reach statistical significance. Many clinicians offer chemotherapy to some stage II tumours that have a worse prognosis like those with perforation, obstruction, vascular invasion, peritoneal involvement or poor differentiation. Currently, chemotherapy is not advised for patients with stage I cancer.
Adjuvant radiotherapy

In colorectal cancer, adjuvant radiotherapy tends to be confined to the pelvis because the large volumes of small bowel elsewhere in the abdomen and the difficulty of defining a suitable target volume generally preclude its use. Even in the pelvis every effort is given to minimising the treatment volume and avoiding structures such as the anal sphincter or pelvic bones where possible. Today there is unequivocal evidence that adjuvant radiation reduces the risk of local recurrence in resectable rectal cancer outlined in two recent overviews. There is less certainty about whether there is a benefit in overall survival. In the United States the emphasis has been on postoperative radiotherapy and there is evidence that this is more effective when combined with 5-fluorouracil based chemotherapy. However, in Europe emphasis has been on preoperative radiotherapy, and there is at least one randomised study indicating that preoperative treatment is associated with less morbidity and better disease control than postoperative radiotherapy.

There are three main indications for adjuvant radiation in rectal cancer. The greatest interest has focused on reducing the risk of local recurrence in patients with resectable rectal cancer. The second indication is to shrink locally advanced rectal cancer to facilitate successful resection. Finally, there is increasing interest in the use of radiation to shrink or ‘downsize’ resectable disease to achieve sphincter-preserving surgery.

In general, preoperative radiotherapy can be divided into three categories:

(i) Radiotherapy for the fixed rectal cancer in an attempt to render it operable. Most radiotherapists would recommend 45 Gy in 25 fractions over five weeks followed by an interval of about six weeks before surgery is attempted. However results of this approach are often disappointing.
(ii) Short course preoperative radiotherapy (SCPRT) on clearly operable disease in an attempt to reduce the risk of local recurrence. The Stockholm 2 trial demonstrated that 25 Gy in five fractions the week before surgery reduced local recurrence rates from 27% to 11% and was associated with improved survival. However, there was concern over the high local recurrence rate in the surgery only arm of this trial.

(iii) Long course preoperative radiation schedules using 1.8-2.0 Gy over 5-5.5 weeks. Despite evidence for improved local control, there is no trial evidence for improved survival using this strategy. Such schedules are combined with concurrent chemotherapy. A recent polish trial has completed recruitment comparing SCPRT with preoperative concurrent chemoradiotherapy (cCRT).

The main advantage of postoperative radiation is the ability to select patients considered at increased risk of local recurrence based on histopathological examination of resected specimen. Disadvantages are that a higher dose of radiation is needed and there are problems of compliance. The recent overview demonstrates clear evidence that adjuvant radiation significantly reduces the risk of local recurrence and is effective when used preoperatively or postoperatively. In Scandinavia, a policy of SCPRT is routine, whereas in North America selective postoperative chemoradiation for stage II and III patients is standard. In the UK, SCPRT is widely used but not yet routinely in every case.

With the widespread adoption of total mesorectal excision (TME) for rectal cancer, the outcome of surgery alone has improved significantly. Furthermore, the strong evidence supporting the hypothesis that local recurrence of rectal cancer is predicted by the presence of
microscopic cancer cells within 1 mm of the circumferential resection margin (CRM) has also been very influential. Therefore, in this new era several choices exist for adjuvant therapy, eg. routine SCPRT, selective SCPRT, neoadjuvant chemoradiotherapy or selective postoperative (chemo) radiotherapy.

Two major trials have investigated the role of SCPRT in this new era. The Dutch Colorectal Cancer Study Group trial and the MRC CR07 trial were both designed to compare SCPRT with a selective postoperative approach based on the CRM status, in operable rectal cancers. Results from the Dutch trial have shown a reduction in local recurrence with preoperative radiotherapy (2% vs. 8% at 2 years), which is associated with minimal complications. It is currently too early to detect any effect on survival. Results from the CR07 trial have also shown that preoperative radiotherapy results in a significant reduction in local recurrence and this was present across tumours of all stages, even early tumours. It was also commented that it was probably inappropriate to irradiate early tumours as the potential benefits were outweighed by the potential iatrogenic morbidity.

**Follow up**

Essentially there are four reasons for follow up:

1. Detection of metastatic disease at an early stage when treatment may be more effective. This is particularly true of liver metastases, which may be suitable for resection.

2. Detection of metachronous polyps or cancers, and it is generally agreed that patients should undergo colonoscopy every three years after a successful bowel resection.

3. Audit

4. Psychological support for the patients.
A recent meta-analysis of randomised trials has indicated that intensive follow up with CT and CEA estimation does result in improved survival. This is presumably by picking up those patients who are suitable for liver resection for metastatic disease. However it is not clear how often these investigations should be performed and further research is necessary. Towards this end, a multicentre, randomised, controlled trial is currently being undertaken in the UK, comparing intensive versus no scheduled follow-up in patients who have undergone resection for CRC with curative intent. This is the FACS trial (Follow-up After Colorectal Surgery). Its primary objective is to assess overall survival and the secondary aims are to assess quality of life of the survivors, cost of NHS service and the NHS cost per life years saved. The trial commenced in 2004 with 3 years for recruitment and 5 years for follow-up and seeks to recruit all patients who have undergone curative treatment for primary CRC.

Management of Advanced disease

Surgery for metastatic disease

There is now good evidence that survival may be prolonged by liver resection in patients with operable hepatic metastases. Geoghegan et al provided a state-of-the-art review of optimum treatment of liver metastases and examined developments in neoadjuvant therapy. They have shown that with careful patient selection, hepatectomy for colorectal metastases can be associated with a 5-year survival of around 30%. Although the most widely accepted criterion for resection is one to three resectable metastases in one lobe of the liver, many surgeons are now extending their indications. The timing of liver resection is also debatable. Some surgeons advocate immediate operation, others advocate a delay of 3-4 months with restaging at the end of this period. In this way patients with rapidly
progressive disease that is unlikely to benefit from resection will be spared fruitless major surgery. Some patients will have inoperable liver metastases to start with. Rene Adam from France\(^{83}\) has shown recently that improved neoadjuvant chemotherapy regimens for such patients (specifically the use of neoadjuvant oxaliplatin- and irinotecan-based regimens) have been able to achieve tumour downstaging so that 15 to 30\% of initially inoperable patients are able to have secondary, or rescue, surgery. If all disease can be removed while retaining sufficient functioning liver then liver resection should be attempted providing the patient is fit enough to withstand the surgery. If the disease is not surgically resectable, local destructive treatments have a role to play. Such local techniques would include microwave ablation, cryoablation and radio frequency ablation.

Pulmonary metastases may also be amenable to resection, but as only 10\% of patients develop such metastases and only 10\% of these have disease confined to the lung, very few are suitable for resection. Nonetheless, segmental resection of the lung may be associated with a 5-year survival rate of 20-40\%.\(^{84}\)

**Surgery for locally advanced disease**

When considering the treatment of locally advanced colonic or rectal cancer, either primary or recurrent, it must be remembered that surgical excision provides the only realistic hope of cure. Thus when the primary colonic tumour is invading adjacent structures such as the duodenum, stomach, kidney, ureter or bladder consideration should be given to en-bloc resection of the tumour with an adequate portion of the adjacent organ.

A major problem is the lack of an agreed definition of ‘locally advanced’ rectal disease. Transrectal ultrasound has now been accepted as
the reference investigation. However, the recognition of the importance of CRM has led to an increased interest in magnetic resonance imaging (MRI) for demonstrating the relationship of the tumour to the mesorectal fascia, the intended ‘CRM’ for a mesorectal excision. In recent years neoadjuvant cCRT has become the standard treatment for locally advanced rectal cancer, because of increased response rates seen in the very large number of phase II studies that have been performed. Many have used either infusional 5FU or bolus 5FU with FA but no direct comparison has been performed and there remains considerable uncertainty as to how to derive the optimum regimen.

Treatment of inoperable advanced disease

When colonic cancer is truly inoperable then surgical defunctioning or bypass may alleviate symptoms. Palliative radiotherapy is worth considering in patients with advanced rectal cancer as this may reduce symptoms. Recently there has been interest in stenting rectal and left sided inoperable cancers in order to alleviate obstructive symptoms but this will do little to reduce bleeding and mucus discharge. Stents are also used to relieve obstruction in cancers presenting as an emergency while the patient is being resuscitated and prepared for a definitive operation. However, use of stents in such an emergency setting is limited to only a few centres in the UK as it is dependent on the out of hours availability of both a surgeon and a radiologist trained in such procedures.

Palliative chemotherapy is the mainstay of the treatment of inoperable advanced colorectal cancer and the Mayo regimen of bolus 5-fluorouracil and folinic acid has been widely used. Modifications of this regimen (the De Gramont regimen of intermittent 5-fluorouracil and folinic acid infusion and the Lokich regimen of continuously infused 5-fluorouracil) appear to be more effective. A promising new approach is
the use of oral capecitabine, which appears to be more effective than the Mayo regimen. Also, two randomised trials have shown that patients who do not respond to or relapse on treatment with 5-fluorouracil and folinic acid may respond to the topoisomerase inhibitor irinotecan.\textsuperscript{88}

Marked improvements in median survival of advanced disease have occurred with the introduction of Oxaliplatin and segmental approaches using Oxaliplatin/ 5-fluorouracil or irinotecan/ 5-fluorouracil at relapses. Recent targeted therapies with the monoclonal antibody directed at the Epidermal Growth Factor (EGF) receptor (Cetuximab) and at Vascular Endothelial Growth Factor Receptor or VEGFR (Avastin), have demonstrated survival benefits when combined with chemotherapy and have recently gained Food and Drug Authority (FDA) approval. Hurwitz H et al have that addition of Bevacizumab, a monoclonal antibody against vascular endothelial growth factor, to fluorouracil-based chemotherapy regimen results in statistically significant and clinically meaningful improvement in survival among patients with metastatic colorectal cancer.\textsuperscript{89} Overall, the median survival now is 2 years depending on the exposure and the sensitivity of the drugs available.

It has to be stressed, however, that chemotherapy can only be viewed as a palliative measure in advanced disease. Few studies have compared chemotherapy with supportive treatment only, and the survival benefits, though significant are not great. In a randomised trial comparing irinotecan with best supportive care, such patients had a significantly improved survival and quality of life when given the active treatment.\textsuperscript{90} As our understanding of the genetic and biochemical basis of cancer improves it is hoped that new biological modifiers and gene therapy may have a part to play in the future.
III Prioritisation of colorectal referrals

A. Review of the ‘Two Week Wait’ referral system

Introduction

Colorectal cancer is the second most common malignancy in England and Wales. Altogether 30,000 new cases were diagnosed per annum towards the end of the twentieth century. Survival from bowel cancer in the UK has been worse than in the United States and Europe. This may have been due to late presentation, as the disease is probably incurable on diagnosis in almost a quarter of patients in the UK, although more recent figures suggest that this may be improving.

Concerns about delays in the diagnosis of colorectal cancer patients in the UK prompted the government to publish referral guidelines in the year 2000 for patients with suspected colorectal cancer. These aimed at identifying patients with new symptoms indicating a high probability of cancer who should then be seen by a hospital specialist within 2 weeks of referral by their GP. (See appendix)

The 2 Week Wait (2WW) referral guidelines for Colorectal cancer (CRC) have been the subject of audits and research studies in many teaching and district hospitals across the UK. While the implementation of the 2WW system has been very successful across the country in terms of complying with the 2 week ‘rule’ of a hospital appointment, the impact of the guidelines on their primary objective of early diagnosis of most colorectal cancers is being openly questioned and criticized. Some of the important problems brought to light since the introduction of this fast-track system are poor compliance with guidelines, a low overall cancer detection rate due to poor specificity and more colorectal cancers being diagnosed
outside the system (who may now be waiting longer than before to be seen by a specialist).95,96,97

The published literature on the 2WW referral system for colorectal cancer, since its inception, was reviewed. The aim was to review the experience of various hospitals across the UK with this system, highlight its primary shortcomings, explore the possible reasons for these failings and discuss possible alternatives. The appropriateness of the guidelines themselves is also discussed.

**Methods**

A Medline search was conducted for articles on the 2WW system published in mainstream peer-reviewed journals. The search terms were Colorectal Cancer, Two Week Wait rule, Referral guidelines and High-risk patients. Abstracts on the 2WW system presented at the Association of Coloproctology and the British Society of Gastroenterology meetings of the last 3 years are included as well as the author’s (Rai S) own audit of the system at the George Elliot District General Hospital, Nuneaton together with findings from our centre, the University Hospitals of Leicester. Implementation of the 2WW system, compliance with guidelines, cancer detection rate, impact of the system on the waiting times, and overall effectiveness in meeting its primary objective are evaluated.

**Data**

**Implementation**

There seems little doubt that, across the country, the proportion of ‘fast-tracked’ patients who receive an appointment with a hospital specialist within the stipulated 14 days has risen sharply since the commencement of
the system. The average figures in England were 81.2 and 81.8% during the first and second halves of 2001 respectively. In the second quarter of 2004, the average figure in England for implementation of the 2WW system rose to 93.2%. Many centres in the UK including our centre have reported percentages in excess of 90%. In our centre, over the years the figures have improved as follows: 85.3%(2001-02), 92%(2002-03) and 100%(2003-04).

Compliance with guidelines for 2WW referral

While the implementation of the 2WW targets at the secondary care level (hospitals) has been good, reports on the compliance with the published guidelines for appropriate ‘fast-track’ referral by the GPs at primary care level indicate that it has been variable but generally poor (See table 1.7).

<table>
<thead>
<tr>
<th>Centre</th>
<th>Total Fast-tracked</th>
<th>Number compliant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luton and Dunstable(^{103})</td>
<td>180</td>
<td>95(55%)</td>
</tr>
<tr>
<td>Univ of Aberdeen(^{104})</td>
<td>237</td>
<td>147(62%)</td>
</tr>
<tr>
<td>Cambridge, Addenbrooke’s(^{105})</td>
<td>462</td>
<td>303(65%)</td>
</tr>
<tr>
<td>Leighton Hosp Crewe(^{106})</td>
<td>508</td>
<td>274(54%)</td>
</tr>
<tr>
<td>Southport and Ormskirk(^{107})</td>
<td>100</td>
<td>41(41%)</td>
</tr>
<tr>
<td>Leeds(^{108})</td>
<td>149</td>
<td>144(96%)</td>
</tr>
<tr>
<td>Darlington(^{109})</td>
<td>178</td>
<td>92(52%)</td>
</tr>
</tbody>
</table>

Warwick et al from Southport and Ormskirk Hospital reported a significant increase in the ‘non-compliant’ fast-track referrals despite their modifying
the referral pro forma to allow easier identification of those qualifying for the 2-week rule.\textsuperscript{107}

Increased compliance with the 2WW referral guidelines has been reported in some centres including the University Hospitals of Leicester. Ambrose’s group from the University Hospital Leeds, reported 96% compliance with guidelines in the fast-tracked referrals.\textsuperscript{108} At the same time Chohan et al from Cambridge reported an apparent discrepancy between symptoms and signs recorded by GPs on the referral pro forma and those elicited in the Colorectal Clinic at the hospital.\textsuperscript{105} However improved compliance has not necessarily improved the yield of CRC in the fast-tracked population.\textsuperscript{108}

**Cancer detection rate**

Overall, the colorectal cancer detection rates of the 2WW system are low (See table 1.8). Thompson et al in Portsmouth have shown a 7% yield of CRC from the 2WW referrals as compared to 3.5% from ‘traditional’ referrals in a mixed general surgical outpatient clinic.\textsuperscript{110}

<table>
<thead>
<tr>
<th>Centre</th>
<th>No of 2WW referrals</th>
<th>No with CRC(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuneaton (Rai)</td>
<td>222</td>
<td>14(6%)</td>
</tr>
<tr>
<td>Leicester</td>
<td>1000</td>
<td>100(10%)</td>
</tr>
<tr>
<td>Crewe\textsuperscript{106}</td>
<td>508</td>
<td>57(11%)</td>
</tr>
</tbody>
</table>

The cancer rates are reported as being significantly higher in 2WW referrals that are appropriate and fit the guidelines, than in those that do not. (See table 1.9)
Table 1.9 Compliance with 2WW guidelines and cancer detection

<table>
<thead>
<tr>
<th>Centre</th>
<th>Compl refs</th>
<th>Cancers</th>
<th>Non-compl refs</th>
<th>Cancers</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>L&amp; D Hosp\textsuperscript{103}</td>
<td>95</td>
<td>24(25%)</td>
<td>85</td>
<td>2(2%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Aberdeen\textsuperscript{104}</td>
<td>147</td>
<td>18(8.9%)</td>
<td>90</td>
<td>3(3%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Adenbrooke's\textsuperscript{105}</td>
<td>303</td>
<td>59(19%)</td>
<td>159</td>
<td>5(3%)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The rate of detection of 'early' colorectal cancers (Dukes' stage A and B) through the 2WW system is even lower. The University of Aberdeen Hospital reported an early cancer detection rate of 4.6%.\textsuperscript{104} Other centres in the country have shown similarly low rates.\textsuperscript{111,112}

**Proportion of Colorectal cancers diagnosed through 2WW route**

More than half of the total colorectal cancers diagnosed in one year at any centre in the UK are not from the fast-tracked group of patients. Table 1.10 shows the contribution of the 2WW referral to the total number of colorectal cancers diagnosed at various centres.

Table 1.10 Contribution of 2WW system to total CRC detection

<table>
<thead>
<tr>
<th>Centre</th>
<th>% of total CRCs contributed by 2WW system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luton &amp; Dunstable\textsuperscript{103}</td>
<td>18%</td>
</tr>
<tr>
<td>Scarborough\textsuperscript{113}</td>
<td>33-50%</td>
</tr>
<tr>
<td>Sommerset\textsuperscript{114}</td>
<td>33-50%</td>
</tr>
<tr>
<td>Leeds\textsuperscript{115}</td>
<td>8%</td>
</tr>
<tr>
<td>Nuneaton (Rai)</td>
<td>16%</td>
</tr>
<tr>
<td>Burton\textsuperscript{116}</td>
<td>35%</td>
</tr>
<tr>
<td>Leicester</td>
<td>25%</td>
</tr>
</tbody>
</table>
In all these centres, the majority of colorectal cancers diagnosed were from outside the 2WW referral system. The sources were:

1. Colorectal cancers admitted as emergency (reported as between 15 to 25% according to definition of ‘emergency’)
2. GP referrals via ‘traditional’ outpatient appointments (triaged as ‘routine’, ‘soon’ or ‘urgent’ by the consultant).
3. Referrals from other departments in the hospital

Are the guidelines appropriate?

Apart from the working of the 2WW rule, a major emerging issue relates to the appropriateness of the guidelines themselves. The guidelines arose from a series of consensus discussions among the ‘great and the good’ during the late 1990s. Thus they were predictions about what the experts thought ‘ought to happen’ if these were introduced, and were not evidence-based in the strictest sense (i.e. not Level 1 evidence based on a Randomised Control Trial), but were largely a consensus view (Level 3 evidence). Proponents of the concept of using ‘high risk symptoms’ to select patients for the fast track have claimed a usefully higher diagnostic yield of CRC in patients who have these symptoms than in those who do not. Although Chohan et al from Addenbrooke’s have shown that the majority of their patients diagnosed with colorectal cancer presented with cardinal symptoms and signs outlined in the fast-track criteria, others have not shown such a correlation.

The specificity of the guidelines however is the main problem. It is all too easy to concentrate on the true positives, while overlooking the false positives. Debnath et al, Harikrishnan et al from Swansea and Thompson et al from Portsmouth amongst many others, have shown that rectal bleeding with change in bowel habit (CIBH) is the symptom
complex credited with the highest incidence of CRC (See figure 2). Up to 33% of the patients in their series with this symptom complex actually had CRC. In the context of trying to find any meaningful selection criteria this is quite high, but in the general sense of hospital referrals, it is low. A similar analysis can be made of their patients with the other symptoms. Thus one must conclude that even if one were successful in policing and implementing these selection guidelines in a rigorous fashion, the CRC detection count in the 2WW clinics will not be greatly increased.

The figure shows the correlation between various criteria and occurrence of CRC.

Figure 2 CRC correlated with symptom complexes (Thompson et al100)

In addition, audits across the UK have shown an overall poor specificity of the guidelines themselves, and it is now becoming increasingly clear that patients can meet the national guidelines and still be regarded by the recipient consultant as an 'inappropriate fast-track referral’, while patients who do not meet the guidelines can present with symptoms that lead to the same consultant having a high suspicion of CRC.
appropriate for urgent evaluation. Barwick et al\textsuperscript{108} at Leeds have shown a low specificity for all criteria for fast-track referral. A retrospective study by Soo et al in 2001 showed that 30\% of patients with CRC admitted under a single surgeon would not have met the referral criteria.\textsuperscript{120} Jones et al from Guy’s and St Thomas Hospital in a critical BMJ editorial have shown a relatively poor positive predictive value of the existing fast-track referral criteria\textsuperscript{121} of about 30\%. Warwick et al from Southport and Omskirk hospital\textsuperscript{122} have shown that use of guidelines for urgent referral of patients suspected to have CRC did not result in a higher pick-up rate than the traditional referral routes. Clark et al from University Hospital of Lewisham have shown that even if the criteria are applied accurately to all fast-tracked colorectal referrals, a significant proportion of CRCs will still be missed.\textsuperscript{119}

Vieten et al from Bristol have shown that only 37\% of their CRCs were referred through the 2WW system. The system was found to be neither specific nor sensitive for picking up CRC.\textsuperscript{123}

At the University Hospitals of Leicester (UHL), we have found a declining CRC pick-up rate within the fast-tracked population in spite of high compliance rates. Regular monthly audits by the 2WW office at Leicester have found that over 90\% of all such referrals every month are compliant with the guidelines for fast-track referral. In the year 2003 less than 10\% of all fast-tracked 2WW referrals were found to have CRC.

**Impact on waiting times from referral to diagnosis**

The time taken to see a surgeon is only one part of the wait for definitive treatment of CRC. Successful implementation of the 2WW rule due to the government’s target-driven approach has definitely shortened this period for this subgroup. Foster et al from Leeds\textsuperscript{115} have shown that the 2WW
patients had a significantly shorter wait in almost all aspects of the patient pathway when compared with standard surgical clinic patients. Aryal et al from Burton-upon-Trent have also shown a significantly shorter time interval from referral to treatment for the fast-tracked patients. However, while the time to see a specialist has been shortened by the 2WW rule, other waiting times in the patient pathway and more importantly other non-urgent referral routes have not been addressed and these times are in danger of being adversely affected. This is particularly relevant, as we now know that the majority of CRCs are diagnosed outside the 2WW system. There is no doubt now that in some centres CRC patients diagnosed outside the 2WW system are waiting longer for treatment. Pullyblank et al from Gloucester in a study over a one-year period had 149 patients diagnosed with CRC. Of these 45 were from the 2WW system and 33 were from ‘traditional’ GP referrals, the rest being emergencies or internal referrals. These 33 patients had to wait twice as long for initiation of treatment. Furthermore, two thirds of the non fast-tracked patients actually did fulfill the criteria for fast-track referral on review of their GP referral letters. The importance of recognizing high-risk symptoms in patients referred via other routes was stressed.

In the year 2003, we at the UHL, highlighted continuing hold-up in the process of delivery of care to patients with suspected CRC (Kelly et al). As part of the Cancer Services Collaborative ‘roll out’, cancer networks across the country were asked to carry out a mapping exercise to delineate the patient’s journey. The main reported ‘bottle-necks’ or delays were radiology, endoscopy, oncology followed by the waits for start of treatment. Earlier, we had also shown at the University Hospitals of Leicester that by implementing changes in a number of areas within the patient’s journey from referral to treatment, a 32% reduction in waiting times can be achieved. Waiting times for assessment, diagnosis and
treatment of outpatients with CRC continue to fall well outside the government’s guideline aspiration of two months.\textsuperscript{127}

\textbf{Discussion}

Delays in recognising colorectal cancer in patients resulting in a relatively poor outcome are a problem that seems to be, if not unique, at least deeply problematical for the NHS in the UK. Colorectal cancer survival figures in the United States, Australia and other countries in Europe like France have been significantly better.\textsuperscript{92} Not only is the overall capacity in hospital outpatient clinics and diagnostic facilities (endoscopy, barium enema, ultrasound, CT and MRI scanning) significantly lower in the UK, the pivotal role of the GP as gatekeeper means that patients cannot easily consult one specialist after another until they reach a diagnosis (or give up), as they do abroad. Since we cannot double our facilities overnight, the government has been concentrating on encouraging us to use what we already have to its best advantage, hence the referral guidelines.

Unfortunately the national implementation of referral guidelines in the form of the 2WW rule has failed to achieve the goal it set itself - to improve the speed of diagnosis and treatment of CRC. The combination of the fast-track system’s inability to identify an overtly high proportion of the total number of CRCs seen at any centre in the UK and the negative effect on some individuals in the large number of CRCs diagnosed outside the system, are thought to be main reasons for its poor showing. Audits across the country have highlighted many criticisms of the 2WW system.

The simple ‘shorthand’ of symptoms and physical signs, on which the guidelines are based, has been reported as an unreliable indicator of CRC.\textsuperscript{95} On the other hand, some, but by no means all, authors have shown that about 60\% of the CRCs identified when analysed retrospectively
appeared to fit the guidelines, suggesting that the guidelines, if properly implemented, might be useful. Poor compliance with guidelines leading to a poor CRC pick up has been documented at many centres. There is a significantly improved CRC detection in fast-tracked referrals that do comply with guidelines compared to those that don’t.

At the same time improved compliance with the guidelines in many centres, including Leicester, has not necessarily improved the yield of CRC identified through the system. This leads us to the belief that the guidelines, even if accurately applied, are simply insufficiently specific to identify most of the CRCs. High-risk symptoms such as persistent rectal bleeding and change in bowel habit, two criteria used in the guidelines, have been shown to have a poor positive predictive value, being only 30%. Consequently, with the present system a large number of fast-tracked referrals need to be processed in order to pick-up a small number of CRCs.

It is important to realise that there are two sets of figures to be considered: the overall pick-up rate of CRC in the fast-tracked population, and the proportion of patients proven to have CRC who went through the 2WW system. The two figures are not the same. In most centres the CRC pick-up rate in the 2WW clinics is about 10% or less, whereas only some 25% of all CRCs go through the 2WW clinic. Clearly, if all (elective) referred patients went through the 2WW clinic (as it happens in many centres abroad), up to 75% of all CRCs would be diagnosed in these clinics but the cancer pick-up rate would still be 10%.

Poor compliance and lack of specificity of the guidelines has resulted in the present 2WW system identifying only a third (or even less) of all the CRCs diagnosed at any centre in the UK. Thus the majority of the CRCs are diagnosed outside the 2WW system. More worryingly, many patients who are referred non-urgently are now waiting longer to be seen
by a specialist, as the large number of 2WW referrals is overwhelming the system. There has been a 60% increase in the total number of 2WW referrals across England from 13,410 referrals in 2001-02 to 21,234 referrals in the second quarter of 2004. A ‘target based’ implementation of the 2 week rule for appointments has further helped ensure this.

Several abstracts at the British Society of Gastroenterology meeting in 2001 suggested that the 2WW standard is being met at the expense of a substantial increase in waiting time for routine referrals, notwithstanding the new government target of a maximum of 17 weeks for all referrals to be seen by a specialist. One of these studies identified a doubling of the routine waiting time. A significant number of patients referred routinely with ‘lower risk’ symptoms, who nevertheless prove to have cancer, are now experiencing longer waiting times than before. These patients have a less well-defined clinical picture but paradoxically they may harbour slow growing malignancy at an earlier stage, with better prospects of cure.

Although, patients referred via the 2WW fast-track system themselves encounter reduced waiting times for almost all components of appointment, assessment and treatment, studies on patients with confirmed CRC have shown that many continue to experience delays far greater than the 62 day target set out in the 2005 rule for cancer. Many factors have contributed to this scenario. A substantial increase in urgent fast-tracked referrals without a matching improvement in Out-Patient and Diagnostic services, and an overemphasis on only one component of the patient pathway (which has failed to provide a significant yield of CRC) are probably the most important.

Similar outcomes have been reported using the 2WW system for breast tumours and urological cancers. There has been a decline in the breast cancer detection rate and an increase in the waiting time for patients not referred urgently by the GPs. Patients with urological cancers
continue to experience an overall significant delay in treatment in spite of the 2WW rule.\textsuperscript{130}

Eccersley et al\textsuperscript{103} have pointed out that urgency of referral is not related to disease stage. In their experience Dukes’ stage of CRC was similar whether the patients were seen urgently or routinely. Furthermore, the delay in patients seeking medical advice was twice as long as the delay caused by waiting for specialist opinion in the hospital. There is also epidemiological evidence that availability of diagnostic services including screening does favourably influence stage of the disease.\textsuperscript{131} This explains the current renewed interest in screening for CRC.

Changes

Given our limited capacity in the UK, we believe that better recognition of high-risk patients and improved resources are the key to improving outcome of CRC. While resources and funding are government-dependent, much can be done to improve recognition of patients at high risk of harbouring CRC. Review of the current guidelines for referral and discussions on their effective use and implementation have gone on for several years without any significant impact on improving the management of CRC. The time must be ripe for a new approach to the problem. Here we summarize some of these recommended in literature and from our own experience in Leicester.

1. The Cancer Services Collaborative (CSC) project was established in 1999 in nine centres across England. Its remit was to streamline the time taken for patient journey from referral to treatment in common solid tumours. We in Leicester have shown that by implementing changes in a number of areas within the patient’s
journey, a significant reduction in waiting times can be achieved. Individual trusts need to do regular ‘mapping exercises’ to identify hold-ups in the patient journey locally and make changes where needed.

2. **The Leicester ‘Straight-to-test’ Diagnostic Protocol.** Patients referred under the 2WW system are usually seen by a specialist first who then requests a diagnostic test. A new ‘diagnostic protocol’ was piloted in Leicester over 2 years. Its central tenet is ‘test first, clinic appointment second’. The 2WW office that receives the details of patients fast-tracked by the GPs requests a diagnostic test for these patients based on a previously agreed protocol, prior to appointment with a specialist. An audit has shown a significant reduction in waiting time for diagnosis. (See appendix)

3. **Cade and Selavachandran et al** from Crewe have introduced a completely new approach. Patients are asked to complete a detailed 60-domain questionnaire based on their bowel and other symptoms, medical and family history. They claim, with considerable evidence, that the risk of CRC can be predicted from the response by using their software program. This is done by calculating a weighted numerical score based on symptom complexes rather than individual symptoms alone. This has been shown to have a significantly high sensitivity and specificity and a high positive predictive value. It is said to be an effective tool at the primary care level for GPs to prioritise colorectal referrals, without significantly affecting their workload. Validation of this system and its comparison with the 2WW system is the topic of this MD thesis project (Rai S). This system is currently also being validated at other centres in the UK.

4. **Thompson et al in Portsmouth** advocate ‘Fibre optic sigmoidoscopy plus full blood count for all’ as the solution.
Although this combination might fail to identify a significant number of right-sided colon cancers, it would diagnose up to 90% and probably more of patients presenting electively with CRC. However, at present the UK just does not have enough nurse or medical endoscopists, or the facilities to implement such a program in full. Currently at our centre, up to a quarter to a third of all new ‘traditional’ colorectal referrals via GP letters are triaged for a ‘direct access’ flexible sigmoidoscopy by the consultants. If all referrals were to have an endoscopy, this would increase the demand for all endoscopy facilities including the number of nurse endoscopists and the number of endoscopy sessions needed by up to 3 or 4 times. Current hopes of implementing flexible sigmoidoscopy screening for polyps or CRC will compound these difficulties even further.

5. Novell et al in Luton have recently suggested a common urgent pathway for all colorectal referrals as the way forward. They have shown this to be of particular benefit for the majority of patients not referred via the 2WW system, who also contribute the most to the total number of colorectal cancers diagnosed. However the implications of this system on the available limited resources is obvious.

Conclusion

Introduction of guidelines had the good intention of improving management and outcome of CRC in the UK. They have raised many controversies and have failed to make any obvious impact on surrogate indices for mortality from CRC. Efforts to improve compliance with the
current system and the modifications suggested have only secured marginal improvements for subgroups, but not improved the overall picture.

We believe that what is needed is a fresh approach to the problem. Thompson’s suggestion of a combination of flexible sigmoidoscopy and haemoglobin estimation for all referrals is both expensive and difficult to implement in full. The Luton solution of taking a flexible mix of 2WW referrals and rapid assessment of all other referrals may work when organised by enthusiasts, but runs the risk of stretching resources and recruiting even more (‘negative’) referrals. A combination of the Questionnaire-based early recognition system as suggested by Cade et al (the topic of this thesis) and the Leicester ‘Straight-to-test’ protocol could combine all approaches and be a step forward in finding cost-effective viable answers.

B. An urgent need to prioritise colorectal referrals effectively

More than one in three people in England will develop cancer at some stage of their lives. One in four will die of cancer. This means that every year, over 200,000 people are diagnosed with cancer, and around 120,000 people die from cancer. Better prevention, earlier detection of cancer and improved treatment and care, are thus of great importance to society.19

Colorectal cancer (CRC) is the third most common cancer in both men and women representing 30,000 cases per annum in England and Wales. Cancer survival in Britain is poorer than in comparable European countries (overall 5-year survival of less than 40%) mainly because patients tend to have a more advanced stage of the disease by the time they are treated. This may be due to delays at various levels. There could be
'patient delay' in reporting of their symptoms to the GP, delay by the GPs in failing to identify high-risk patients or 'hospital delay' because of the time taken in hospitals to progress from first appointment through diagnostic tests to treatment.¹⁹

Furthermore the 'postcode lottery' and variation in quality and provision of services across the country means it is likely that not all patients are getting the optimum treatment for their particular condition.¹⁹ However, if found at an early stage it is universally accepted that there is potential for a complete cure in CRC (Dukes' A disease has 90% 5 year survival). CRC is often preceded by a benign adenomatous polyp that in itself gives rise to symptoms leading to the potential of early detection.

Colonoscopy is the investigation of choice for detection of CRC but is expensive and carries small but definite risks (1/1000 suffer perforation, 3/1000 major haemorrhage and 1-3/10,000 die as a result of the procedure. Data from the Trent/Wales audit also suggested that complete colonoscopy is achieved in less than 50% of cases with higher results being operator dependent. Faecal occult blood tests have been assessed as a tool for CRC detection, but compliance, high false positive rates and low specificity were problematic. The Joint Advisory Group (JAG) on gastrointestinal endoscopy published guidelines in 2004 (downloadable from the JAG website: www.thejag.org.uk) recommending that a caecal intubation rate of at least 90% should be achieved during colonoscopy in the absence of structuring or significant faecal contamination.

With the current number of hospital referrals, financial constraints and limited resources the established system has struggled to provide a quality service.¹³⁸ Referrals nationally in general surgery have expanded by 90,446(6.6%) between 1997 and 1999.¹³⁸ Government drive established the 2-week wait rule and CRC guidelines in the hope of providing primary and secondary care with a method to prioritise and streamline referrals. Several
high-risk symptoms and signs were used as criteria for urgent referrals. Booklets and posters for the guidelines were given to general practitioners to assist in implementing these guidelines. Not surprisingly, hospital referral workload has increased with the GPs referring more patients with referrals often based more on anxiety and litigation than evidence-based practice. At the Association of Coloproctology and the British Society of Gastroenterology annual meetings, many paper presentations and posters have regularly addressed the efficacy of this 2-week wait system based on the NHS guidelines. Some reports suggested the symptoms are not specific resulting in overwhelming referral rates. Others demonstrated effective cancer detection but failed to show the proportion of cancers missed that came through the conventional routes. Some reported a low compliance rate by the GPs and inappropriate referrals using the guidelines. One study reported that CRCs detected through the conventional referral route are now waiting longer to be seen at the hospitals.

A method of improving the current referral system is therefore urgently needed. For the system to be effective a systematic approach is needed that must control the following two cardinal factors:

1. High risk symptoms
Distal colorectal cancer presents with primary colorectal symptoms and accounts for 65-70% of all CRCs with 90% occurring over the age of 50 years. The work of Thompson and Fijten has clearly demonstrated that in the majority of distal CRCs, high-risk symptoms have a high sensitivity to cancer detection. But since limited resources are a major problem, a high specificity is needed. In spite of the NHS high-risk criteria being relatively specific for colorectal cancer, they are still not effective in balancing the demand with the available resources. Work from Leighton
Hospital, Crewe, Cheshire has demonstrated that introducing additional symptoms and symptom complexity clusters to the high-risk criteria achieve improved sensitivity and specificity.\textsuperscript{133}

However, adding a list of extra symptoms and symptom complexes will burden the already overwhelmed GP leading to ineffective implementation.

2. Effective implementation and compliance with guidelines at the Primary Care level

The GP is inundated with guidelines rendering him incapable of implementing all of them. In addition, the time allocated to each patient (7 minutes on average) allows only a limited history to be taken. Doctors’ anxiety about increasing litigation has resulted in inappropriate referrals. Streamlining and compliance can be achieved by providing a colorectal consultant experience in a computerised format that increases patients’ involvement in controlling their own clinical pathway is easy to use by the patient and analyse by the GP and does not add to the ever-increasing workload of the GPs.

By controlling factors 1 and 2 it would be possible to influence the size of the referred population. However different units across the country have different management policies for investigating their referrals. More important than the time from referral to being seen is the time from referral to diagnosis and this is largely influenced by the time waiting for investigation. To be able to effectively audit the efficacy of the 2-week rule a unified investigation protocol is required. This will enable balanced comparison between units and a better recognition of factors that need to be investigated which contribute to the delay in the diagnosis of colorectal cancer. The ongoing efforts to develop a uniform investigation policy
across the 3 University Hospitals of Leicester (the Leicester Diagnostic Protocol)\textsuperscript{132} should be a step towards improving early detection of colorectal cancer.

C. The Leighton Hospital System for Colorectal Referrals\textsuperscript{133}

A system that is effective in identifying and fast-tracking those who are at high risk of colorectal cancer has been achieved. The Leighton Hospital system for colorectal referrals has 3 components:

1. The Patient Consultation Questionnaire (PCQ):
The PCQ (see appendix) is a comprehensive questionnaire that assesses colorectal symptoms, their duration and progression. It also asks about the patient’s medical history and relevant family history. In majority of cases this would be equivalent to an out patient consultation. The patient completes the PCQ. It is easy to understand and complete and can effectively help prioritise patients and rationalise investigations. It is given to the patient ideally at his visit to the GP surgery. Currently in Leighton it is sent to the patient on receipt of the referral letter and it is returned before clinic attendance. Using the PCQ information, appropriate investigation can be chosen and appropriate information sent to the patients before attendance at the clinic. Hard copies for the notes and subsequent discharge letters are automatically generated.

2. Weighted Numerical Score (WNS) or the Selva score
A scoring system that assigns a numerical value behind each symptom and symptom clusters is obtained via the PCQ. It is automatically calculated by
the computer package when the PCQ data is entered into the replicated electronic form (see appendix). The Weighted Numerical Score (WNS) reflects the severity of symptoms and risk of colorectal cancer. This also provides a dual benefit because it categorises patients with relatively important conditions such as colitis and polyps > 1cm as urgent. This maximises the benefit for the urgently referred population. Using a cut-off of 70 for the WNS, it was found that patients with scores of more than 70 had up to 25% risk of having colorectal cancer whereas those scoring less than 70 had less than 2% chance of having colorectal cancer (see table 1.11). Higher the score more is the risk of having colorectal cancer. Combining the PCQ and WNS allows developing a system that provides a high specificity and sensitivity, stratifies risk of the referred population, is automated and maximises compliance.

<table>
<thead>
<tr>
<th>WNS</th>
<th>No. of Patients</th>
<th>No. with colorectal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>967</td>
<td>1</td>
</tr>
<tr>
<td>40-49</td>
<td>398</td>
<td>8</td>
</tr>
<tr>
<td>50-69</td>
<td>571</td>
<td>20</td>
</tr>
<tr>
<td>&gt;70</td>
<td>332</td>
<td>66(25%)</td>
</tr>
<tr>
<td>Total</td>
<td>2268</td>
<td>95</td>
</tr>
</tbody>
</table>

3. One-stop Colorectal clinic
A comprehensive history obtained from the PCQ complements the GP referral letter. Appropriate investigations can be decided before attendance at the clinic. Endoscopies and treatment are undertaken at a single visit maximising the use of resources and minimising the time to diagnosis. At the one stop clinic, immediate diagnosis was achieved in over 80% of
cancers. The remaining patients had their diagnosis established after polyp histology revealed carcinoma or after barium enema result.

The **PCQ-WNS** system provides colorectal consultant experience in a computerised format that not only increases patients’ involvement in controlling their own clinical pathway, but also helps to streamline referrals and improve compliance. Many, perhaps most, patients presenting with colorectal cancer have multiple vague symptoms rather than a handful of clear-cut ‘obvious’ ones.

A full 4-page 60-point detailed history does help an expert, but even then there are ‘wood for the trees’ problems. By transferring this detailed history from the questionnaire onto a computer program (which can easily be done by a data clerk without taking up the GP’s time), a quick analysis of the patient’s history is possible, to look for the relevant combination of symptoms which can predict a high risk of colorectal cancer. This is what computers do best.

**D. The University Hospitals of Leicester (UHL): referral pattern**

The colorectal referral pattern in the UHL is similar to most centres in the UK. The primary sources of colorectal referrals are:

1. **The General Practitioners**
   The GPs refer patients in two ways:

   (a) Fast tracked Two Week Wait (2WW) referrals to a central 2WW office by faxing patient details on a Colorectal Cancer Referral form. The 2WW office arranges for these patients to have a preliminary ‘diagnostic test’
(endoscopy or radiology) as per the ‘Leicester straight to test diagnostic Protocol’, prior to their first consultation with a Colorectal surgeon or a Gastroenterologist.

(b)‘Traditional’ referrals through letters (by post). These letters are either unmarked or marked as ‘urgent’, ‘soon’, or ‘routine’ by the GP. Based on the information provided in the letter, the Colorectal surgeon or the Gastroenterologist asks to arrange for either a diagnostic test or an outpatient clinic appointment and grades the urgency at his/her discretion.

2 ‘In-house’ or internal referrals from ‘non-colorectal’ surgeons and Physicians

3 Patients with colorectal symptoms admitted as emergencies

The recently introduced ‘Leicester straight to test diagnostic protocol’ at the UHL, whereby fast-tracked colorectal referrals have a diagnostic test prior to their first appointment with a consultant, was an attempt aimed to shorten the referral to diagnosis time. The initial pilot of this system has shown promising results\textsuperscript{132} and the system has now been fully adopted.

Across the UHL the total number of colorectal cancers (CRCs) diagnosed annually is about 400. At the present time only 10% of patients referred under the fast track 2WW system are diagnosed with colorectal cancer. This 10% contributes to only about a third of the total CRCs diagnosed annually. The remaining cancers are referred through traditional routes (including GP letters by post, internal referrals and emergencies). Paradoxically, more than 90% of those referred under the 2WW system were seen at the hospital within the stipulated 2-week period. In other words we have been extremely successful in seeing the ‘wrong’ patients.
quickly through the 2-week wait fast-track system. Similar outcomes have been demonstrated in other centres in the UK.
PART II

Validation of the PCQ-WNS system at Leicester and its comparison with the ‘two week wait’ referral system

CHAPTER 2
This is a prospective multi-centre cohort study that involves colorectal units across the 3 University Hospitals of Leicester and the peripheral Community Hospitals in the county of Leicestershire. These hospitals together serve a catchment population of approximately 1 million. Leicester has the highest proportion of ethnic minorities of any county in the UK with 39.4% of the population being of an ethnic background (predominantly Indian who constitute 25.73% of the population). The mean age of the population in Leicester was 35.45. These are figures from the 2001 census conducted by the Office of National Statistics (ONS). The total population mix is therefore truly multicultural.

Patients and Methods

A. Inclusion criteria

A prospective cohort study was undertaken between September 2003 and August 2004 at the 3 University Hospitals and the peripheral Community Hospitals in Leicestershire. We included all referrals from GPs to Hospital Colorectal surgeons and Medical Gastroenterologists for patients with

Lower bowel related symptoms
Unexplained anaemia
Positive faecal occult bloods
Palpable rectal mass
Palpable abdominal mass

Patients from a total of 18 hospital consultants (Surgeons and Gastroenterologists) were recruited in the study.
Apart from these, colorectal cancer patients diagnosed as emergencies during this period were included in the study and their case notes were reviewed.

B. Methods

Procedures
All 2WW faxed colorectal referrals were sent a ‘PCQ pack’ in the post along with the appointment for a diagnostic test (as per the new UHL Diagnostic Protocol) by the staff at the 2WW office. The PCQ pack contained a covering letter from the consultant the patient was assigned to, a Patient Information Sheet describing details of the study, a PCQ and a stamped addressed envelope (addressed to the principal investigator) for returning the completed questionnaire. Copies of the faxed referral forms and patient’s Colorectal Imaging Forms (with details of the test requested as per protocol) were kept for records.

The ‘Traditional’ colorectal referral letters from GPs were assessed by consultants who marked them as suitable for a PCQ or not (with a prominent sticker), as well as suitable for assessment either in the Out Patient Clinic (‘urgently’, ‘soon’ or ‘routinely’) or assessment through a test (direct access endoscopy or radiology) urgently, soon or routinely. The respective clinic co-ordinator or consultant secretary sent out a PCQ pack in the post for all the suitable referrals. For each patient sent a PCQ pack, a copy of their GP referral letter was kept for records.

A similar procedure was adopted for colorectal referrals to the peripheral Community Hospitals in Leicestershire.
All completed PCQs were returned to the principal investigator (Rai S). Data from the PCQs returned by the patients was entered onto the Computer Software provided by the Leighton Hospital, and a Weighted Numerical Score (WNS) or Selva score was calculated for each patient.

All referrals were followed up through their course of investigations in the hospital as per the current practice until a firm diagnosis, benign or malignant, was made. This was done by reviewing:

Clinic letters to GPs dictated by consultants
Pathology reports
Radiology reports
Endoscopy reports

The reports were accessed through the hospital network and department databases. Details of the dates of investigations, their results and diagnoses were entered on the software.
At all times the consultants and their clinical teams were kept ‘blinded’ from the patients’ Weighted Numerical Scores.

Patients with a confirmed diagnosis of colorectal cancer (whether referred by GP or admitted as emergency) had their case notes reviewed in detail. These were identified with the help of the Multi Disciplinary Team (MDT) co-ordinators at the 3 main hospital sites. Information was collected on Microsoft Excel based databases. Separate databases were made for CRCs admitted as emergency, and those in the Ethnic minorities. Patients from ethnic minorities were identified from their names. The author, being of an ethnic background, was able to identify such patients.
Patients from Ethnic background had the option of asking for a PCQ in their own Language. The PCQ was translated into 4 ethnic languages: Urdu, Punjabi, Gujarati and Bengali. The initially sent PCQ in English had a note attached in 5 languages explaining how to request for another language PCQ. Those phoning in with such a request were sent the required PCQ promptly by post.

A Patient Satisfaction Questionnaire (PSQ) was sent to a sample of the referred patients who responded to the PCQ to assess their satisfaction on a variety of issues like waiting times, assessment, diagnostic tests and treatment as well as ease of answering the PCQ.

**Out comes measured**

1. Referral routes and compliance with guidelines
   - Patient demographics (age, sex ratio, ethnic background).
   - Various referral routes from GPs (2WW and traditional letter referrals).
   - Compliance with guidelines for fast-track referral.

2. Prioritisation of colorectal referrals
   - 2WW referrals processed through the 2WW office as per ‘Diagnostic protocol’.
   - Consultants review of the ‘traditional’ referral letters marked as
     - Suitable for a diagnostic test (direct access).
     - Assessment in the clinic first.
   - Assessment of referred patients
     - Tests ordered by 2WW office as per protocol.
     - Tests requested by consultants on review of ‘traditional’ referral letters.
• Sensitivity/ Specificity of cancer detection of
  - The PCQ/WNS system, using various cut-offs for the score
  - The 2WW system
  - Each of high-risk symptoms or simply age more than 60 years

3. Colorectal cancer in the ethnic population
• Incidence
• Demographics
• Stage of CRC
• Language issues
  - Preferred language to complete the Questionnaire
  - Help from friends and relatives

4. Patient Satisfaction
• Ease of using the PCQ
• Patient satisfaction with primary care (GPs) and the secondary care (the Hospital)

5. Colorectal cancer presenting as an emergency
• Demographics
• Presentation (obstruction, perforation, bleeding)
• Outcome

Statistical Methods

Statistical help and advice was sought from the statisticians at the Trent Institute at Leicester and also from Mohammed Ballal who is experienced in statistics and was involved in the validation of the PCQ-WNS system at Crewe, Cheshire.
Sample size calculations were done using the current incidence of colorectal cancer in Leicestershire and with the aim of detecting a significant difference between the 2WW referral system and the PCQ-WNS system in terms of sensitivity, specificity and the positive predictive value. For a study with a power of 80% and an alpha error of 0.05, it was estimated that a total of 1422 referrals (or responses to the PCQ) would be needed with at least a total of 62 colorectal cancers.

Analyses were done using the SPSS version 12. Patients with CRC and those without CRC were compared using the Student’s t tests. A Receiver Operating Curve (ROC) analysis was done to assess the discriminatory power of WNS system.

All the symptoms on the PCQ were dichotomised (present = 1, absent = 0). The association of the symptoms with colorectal cancer was analysed. The sensitivity, specificity, positive predictive value and the referral rate were calculated for each symptom, the 2WW system and for the PCQ-WNS system. The significance of the differences in proportions was calculated using the Chi-square tests.

**Ethics approval**

A full ethical approval was obtained from the Leicestershire Local Research Ethics Committee (Project Number 8628, Ethics reference 7006).
CHAPTER 3

RESULTS
A total of 3555 colorectal referrals were made by the GPs during the period of the study, of which 1274 were 2WW referrals (36%). The rest were traditional GP letter referrals. These figures were obtained from the 2WW office and the Information Technology (IT) department of the hospital who analysed the clinic activity of the various hospital consultants. This 2WW referral rate of 36% at Leicester is comparable to figures from other centres in the UK.

During the study period, in spite of best of intentions, logistical constraints meant that only 3128 PCQs were sent out to patients (out of the 3555 referrals made). These PCQs were sent out simultaneously and consecutively to the patients as the referrals were made at each of the hospital sites. Of these only 188 (6%) were to patients of the ethnic Indian origin. The overall response rate was 51% with 1590 PCQs completed and returned by the end of the study period. The first consecutive 1422 PCQs were incorporated in the study (as per the sample size calculations). Eighty-three colorectal cancers were detected in this study group of 1422 patients. In spite of the fact that only half the patients returned a completed PCQ, there was no reason to believe that these patients formed a select group or that there was any bias. We endeavoured to send a PCQ to almost all referred patients who were then recruited in the study consecutively as the PCQs were returned.

All patients diagnosed as having colorectal cancer are captured prospectively on our UHL colorectal cancer database. Using this database we determined that during the period of the study a total of 322 colorectal cancers were diagnosed in Leicester. Excluding the emergency colorectal cancers, 239 of these cancers (74.5%) were admitted following referral by the GP. Amongst these, 124 (52%) were referred under 2WW rule and 115 (48%) were referred through the traditional GP letter route.
The age, sex and cancer distribution of the 1422 patients who completed and returned their questionnaires (52% female, 48% male) is shown in tables 3.1 to 3.3. Fifty six percent of these were more than 60 years old.

Table 3.1 Age & sex distribution of patients who completed a PCQ

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up To 40.0</td>
<td>70</td>
<td>81</td>
<td>151</td>
</tr>
<tr>
<td>40.0 To 50.0</td>
<td>94</td>
<td>82</td>
<td>176</td>
</tr>
<tr>
<td>50.0 To 60.0</td>
<td>134</td>
<td>160</td>
<td>294</td>
</tr>
<tr>
<td>60.0 To 70.0</td>
<td>164</td>
<td>161</td>
<td>325</td>
</tr>
<tr>
<td>70.0 To 80.0</td>
<td>148</td>
<td>167</td>
<td>315</td>
</tr>
<tr>
<td>Over 80.0</td>
<td>82</td>
<td>79</td>
<td>161</td>
</tr>
<tr>
<td>Total</td>
<td>692</td>
<td>730</td>
<td>1422</td>
</tr>
</tbody>
</table>

Table 3.2 Cancer distribution in patients who completed a PCQ

<table>
<thead>
<tr>
<th>Sex</th>
<th>Non-cancer</th>
<th>Cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>637</td>
<td>55</td>
<td>692</td>
</tr>
<tr>
<td>Female</td>
<td>702</td>
<td>28</td>
<td>730</td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
</tr>
</tbody>
</table>

Table 3.3 Age & cancer distribution in patients who completed a PCQ

<table>
<thead>
<tr>
<th>Age</th>
<th>Non-cancer</th>
<th>Cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up To 40.0</td>
<td>151</td>
<td>0</td>
<td>151</td>
</tr>
<tr>
<td>40.0 To 50.0</td>
<td>172</td>
<td>4</td>
<td>176</td>
</tr>
<tr>
<td>50.0 To 60.0</td>
<td>279</td>
<td>15</td>
<td>294</td>
</tr>
<tr>
<td>60.0 To 70.0</td>
<td>302</td>
<td>23</td>
<td>325</td>
</tr>
<tr>
<td>70.0 To 80.0</td>
<td>283</td>
<td>32</td>
<td>315</td>
</tr>
<tr>
<td>Over 80.0</td>
<td>152</td>
<td>9</td>
<td>161</td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
</tr>
</tbody>
</table>
The ethnic background of the 1422 patients and their sex and cancer distribution is shown in tables 3.4 & 3.5.

Table 3.4 Ethnic background and sex distribution

<table>
<thead>
<tr>
<th>Ethnic Origin</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black - African</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Black - Caribbean</td>
<td>5</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Black - Other</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chinese</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Indian</td>
<td>82</td>
<td>37</td>
<td>119</td>
</tr>
<tr>
<td>Pakistani</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>White</td>
<td>599</td>
<td>681</td>
<td>1280</td>
</tr>
<tr>
<td>Total</td>
<td>692</td>
<td>730</td>
<td>1422</td>
</tr>
</tbody>
</table>

Table 3.5 Ethnic background and cancer distribution

<table>
<thead>
<tr>
<th>Ethnic Origin</th>
<th>Non-cancer</th>
<th>Cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black - African</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Black - Caribbean</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Black - Other</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chinese</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Indian</td>
<td>114</td>
<td>5</td>
<td>119</td>
</tr>
<tr>
<td>Pakistani</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>White</td>
<td>1202</td>
<td>78</td>
<td>1280</td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
</tr>
</tbody>
</table>

The majority (90%) of the responders included in the study were white and the second largest group was patients of Indian origin (8.4%). As Indian patients constituted only 6% of those to whom a PCQ was sent, it follows that they responded better (63%) as compared to the whites (44%).

The various referral routes and the cancer distribution for the 1422 patients who responded to the questionnaire is summarized in table 3.6. The 2WW
referrals constituted 35% of all GP referrals and contributed to 55 of the 83 colorectal cancers (66%) diagnosed in the study group. Data from the audit done by the 2WW office for referrals made each month has shown that the compliance rate of the 2WW referrals (with the 2WW referral guidelines) was above 90%.

Table 3.6 Referral routes and cancer distribution

<table>
<thead>
<tr>
<th>Referral Mode</th>
<th>Non cancer</th>
<th>cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two Week Wait Fax</td>
<td>450</td>
<td>55</td>
<td>505</td>
</tr>
<tr>
<td>Letter (including internal referrals)</td>
<td>889</td>
<td>28</td>
<td>917</td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
</tr>
</tbody>
</table>

Analysis of the priority assigned by GPs to their traditional referral letters reveals that most (78%) were unmarked. Only 4% of the traditional GP letter referrals marked as ‘urgent please’ were diagnosed with cancer (see table 3.7).

Table 3.7 Priorities assigned by GPs to their letter referrals

<table>
<thead>
<tr>
<th>Priority Request by GP</th>
<th>Non cancer</th>
<th>cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Stated</td>
<td>681</td>
<td>23</td>
<td>704</td>
</tr>
<tr>
<td>Routine</td>
<td>91</td>
<td>1</td>
<td>92</td>
</tr>
<tr>
<td>Soon</td>
<td>36</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>Two Week Rule</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Urgent</td>
<td>61</td>
<td>3</td>
<td>64</td>
</tr>
<tr>
<td>Total</td>
<td>873</td>
<td>27</td>
<td>900</td>
</tr>
</tbody>
</table>

Table 3.8 shows the priority and/or the diagnostic test assigned by the consultants to the GP letter referrals. The most common investigation
requested by the consultants was a fibreoptic sigmoidoscopy (FOS) in more than 60% of cases.

Table 3.8 Priority assigned and tests requested by consultants for traditional GP referrals

<table>
<thead>
<tr>
<th>Test/ Priority assigned by consultants</th>
<th>Non cancer</th>
<th>cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barium Enema</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Diagnostic Protocol</td>
<td>24</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>Direct Access FOS (Routine)</td>
<td>333</td>
<td>5</td>
<td>338</td>
</tr>
<tr>
<td>Direct Access FOS (Soon)</td>
<td>159</td>
<td>2</td>
<td>161</td>
</tr>
<tr>
<td>Direct Access FOS (Urgent)</td>
<td>22</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>Direct Access FOS + Barium Enema</td>
<td>12</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Direct Access OGD + Barium Enema</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Direct Colonoscopy (soon)</td>
<td>38</td>
<td>1</td>
<td>39</td>
</tr>
<tr>
<td>Direct Colonoscopy + OGD</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Direct access FOS + OGD</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Routine Barium Enema</td>
<td>28</td>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>Routine Out Patients Appointment</td>
<td>138</td>
<td>2</td>
<td>140</td>
</tr>
<tr>
<td>Soon Barium Enema</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Soon Out Patients Appointment</td>
<td>65</td>
<td>4</td>
<td>69</td>
</tr>
<tr>
<td>U/S Abdomen</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Urgent Barium Enema</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Urgent Out Patients Appointment - Not Over book</td>
<td>29</td>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>Urgent Out Patients Appointment - Over book</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>873</td>
<td>27</td>
<td>900</td>
</tr>
</tbody>
</table>

Table 3.9 lists the symptoms in the questionnaire and their sensitivity, specificity and positive predictive value (PPV) for colorectal cancer. The symptoms assessed were bleeding per rectum (Blood PR), change in bowel habit (CIBH) and anal symptoms. These values were also calculated by strictly applying the NHS high-risk criteria (1 to 3, symptoms only) to the data. This was to assess as to what the outcome would have been if the NHS high-risk criteria were strictly followed.
### Table 3.9 Sensitivity, specificity and PPV for detecting CRC

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood PR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>466</td>
<td>25</td>
<td>491</td>
<td>70%</td>
<td>35%</td>
<td>65%</td>
<td>6%</td>
</tr>
<tr>
<td>Yes</td>
<td>873</td>
<td>58</td>
<td>931</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CIBH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>715</td>
<td>18</td>
<td>733</td>
<td>78%</td>
<td>53%</td>
<td>48%</td>
<td>9%</td>
</tr>
<tr>
<td>Yes</td>
<td>624</td>
<td>65</td>
<td>689</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NHS Criteria 1 = PR bleed with CIBH to more frequent stools or looser stools (or both) for > 6 wks

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NHS criteria 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1032</td>
<td>47</td>
<td>1079</td>
<td>43%</td>
<td>77%</td>
<td>24%</td>
<td>10%</td>
</tr>
<tr>
<td>Yes</td>
<td>307</td>
<td>36</td>
<td>343</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NHS Criteria 2 = age > 60 years and persistent PR bleed without anal symptoms

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NHS criteria 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1036</td>
<td>39</td>
<td>1075</td>
<td>53%</td>
<td>77%</td>
<td>24%</td>
<td>13%</td>
</tr>
<tr>
<td>Yes</td>
<td>303</td>
<td>44</td>
<td>347</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NHS Criteria 3 = age > 60 years and CBH to more frequent or loose stools (or both) for > 6 wks

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NHS criteria 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1200</td>
<td>63</td>
<td>1263</td>
<td>24%</td>
<td>90%</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>Yes</td>
<td>139</td>
<td>20</td>
<td>159</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NHS criteria (combined)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>749</td>
<td>24</td>
<td>773</td>
<td>71%</td>
<td>56%</td>
<td>46%</td>
<td>9%</td>
</tr>
<tr>
<td>Yes</td>
<td>590</td>
<td>59</td>
<td>649</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The most common presenting symptoms were bleeding PR (65%) and change in bowel habit (48%).

Table 3.10 lists the sensitivity, specificity and positive predictive value for detecting colorectal cancer using different cut-offs for the weighted numerical score (Selva score).

Table 3.10 Sensitivity, specificity and PPV for detecting CRC using the WNS system

<table>
<thead>
<tr>
<th>Selva score</th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>486</td>
<td>4</td>
<td>490</td>
<td>95%</td>
<td>36%</td>
<td>66%</td>
<td>8%</td>
</tr>
<tr>
<td>&gt;=40</td>
<td>853</td>
<td>79</td>
<td>932</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Selva score</th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>705</td>
<td>7</td>
<td>712</td>
<td>92%</td>
<td>53%</td>
<td>50%</td>
<td>11%</td>
</tr>
<tr>
<td>&gt;=50</td>
<td>634</td>
<td>76</td>
<td>710</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Selva score</th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>917</td>
<td>19</td>
<td>936</td>
<td>77%</td>
<td>68%</td>
<td>34%</td>
<td>13%</td>
</tr>
<tr>
<td>&gt;=60</td>
<td>422</td>
<td>64</td>
<td>486</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Selva score</th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;70</td>
<td>1108</td>
<td>30</td>
<td>1138</td>
<td>64%</td>
<td>83%</td>
<td>20%</td>
<td>19%</td>
</tr>
<tr>
<td>&gt;=70</td>
<td>231</td>
<td>53</td>
<td>284</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3.11 shows the sensitivity, specificity and positive predictive value for detecting colorectal cancer, using the 2WW referral system which incorporates the NHS high risk criteria (symptoms), signs like palpable
rectal or abdominal mass elicited by the GP as well as investigative findings like unexplained iron deficiency anaemia.

Table 3.11 Sensitivity, specificity and PPV for detecting CRC using the 2WW system

<table>
<thead>
<tr>
<th></th>
<th>non cancers</th>
<th>Cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>non 2WW</td>
<td>885</td>
<td>28</td>
<td>913</td>
</tr>
<tr>
<td>2WW</td>
<td>454</td>
<td>55</td>
<td>509</td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Referral Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>non 2WW</td>
<td>66%</td>
<td>66%</td>
<td>36%</td>
</tr>
<tr>
<td>2WW</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>2WW</td>
<td>11%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
</tbody>
</table>

The stratification of the weighted numerical score (WNS) into bands (≥40, ≥50, ≥60, ≥70) showed increasing sensitivity with lower thresholds of the score, with a cut-off of 40 being 95% sensitive in detecting CRC. With higher thresholds of the WNS, the sensitivity decreased but the specificity improved. For similar cancer detection rates (or sensitivity), the specificity of the weighted numerical score cut-off of 70 was significantly better than the 2WW system (P value < 0.001). Therefore, for similar numbers of cancers detected, a significantly lower number of urgent referrals needed to be seen with the WNS system (284 patients) than with the 2WW system (509 patients), (Tables 3.10 & 3.11), (P value < 0.001). The WNS also had a better positive predictive value for detecting CRC than the 2WW system (Tables 3.10 & 3.11), (P value < 0.001).

The cancer detection rate (or sensitivity) of age > 60 years as the sole criterion, was significantly better than that of the 2WW system (P value < 0.025), although its specificity was significantly poorer (P value < 0.001), (Table 3.12).
Table 3.12 Sensitivity, specificity and PPV for detecting CRC using age > 60 years

<table>
<thead>
<tr>
<th>Age</th>
<th>non cancers</th>
<th>Cancers</th>
<th>Total</th>
<th>Sensitivity (cancers detected)</th>
<th>Specificity</th>
<th>Referral Rate</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>572</td>
<td>15</td>
<td>587</td>
<td>82%</td>
<td>43%</td>
<td>59%</td>
<td>8%</td>
</tr>
<tr>
<td>&gt;=60</td>
<td>767</td>
<td>68</td>
<td>835</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1339</td>
<td>83</td>
<td>1422</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The weighted numerical score showed a clear correlation with cancer risk (Table 3.13). With increasing weighted numerical score, the patient’s risk of cancer proportionally rises. A score of above 70 shows a cancer risk of one in five, whereas a score of less than 40 gives a cancer risk of one in 123.

Table 3.13 Cancer risk and the WNS

<table>
<thead>
<tr>
<th>Selva score</th>
<th>No. of referrals (%)</th>
<th>% of total detected</th>
<th>cancers (%)</th>
<th>No. of cancers ratio (1 in)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>490 (34%)</td>
<td>5%</td>
<td>4 (1%)</td>
<td>123</td>
</tr>
<tr>
<td>40-49</td>
<td>222 (16%)</td>
<td>4%</td>
<td>3 (1%)</td>
<td>74</td>
</tr>
<tr>
<td>50-59</td>
<td>224 (16%)</td>
<td>14%</td>
<td>12 (5%)</td>
<td>19</td>
</tr>
<tr>
<td>60-69</td>
<td>202 (14%)</td>
<td>13%</td>
<td>11 (5%)</td>
<td>18</td>
</tr>
<tr>
<td>&gt;=70</td>
<td>284 (20%)</td>
<td>64%</td>
<td>53 (19%)</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>1422 (100%)</td>
<td>100%</td>
<td>83 (6%)</td>
<td>17</td>
</tr>
</tbody>
</table>

The mean Weighted Numerical Scores for various disorders diagnosed are shown in figure 3. Important benign conditions such as colitis or large polyps, scored high as well. Overall, a WNS (Selva score) of > 50 was an indicator of the patient having an important benign or malignant pathology. Only half the patients in the study group (710 patients) scored more than 50 (See table 3.10) and therefore needed urgent attention.
The validity of the PCQ-WNS system (or the Selva scoring system) was demonstrated by a significantly higher mean Selva score in colorectal cancer patients as compared to those without cancer (mean of 76.3 [95% CI 71.3-81.3] as compared to a mean of 48.9 [95% CI 47.6-50.2]; \( P < 0.001 \)) (see figure 4). The significance of the difference in Selva score between the two groups of patients was assessed using the Student’s \( t \) test.

A Receiver Operating Curve (ROC) analysis has shown that the PCQ-WNS scoring system has a high discriminatory power for prediction of colorectal cancer. The ROC curve determines the ability of a test to discriminate between a positive and a negative result. The area under the
curve (AUC) is measured in a range of 0-1, and values close to 1 indicate a high discriminatory power. The AUC for the WNS was 0.805 (standard error of 0.03) (see figure 5).

**Figure 4** Box plot of WNS (Selva score) for cancer and non cancer patients

![Box Plot](image)

**Figure 5** Discriminatory power of the WNS
(AUC = area under curve)

![Receiver-operating curve for WNS](image)
CHAPTER 4

DISCUSSION
All referrals to hospitals have increased nationally over the last few years. There has been a 60% increase in the total number of 2WW referrals across England from 13,410 referrals in 2001-02 to 21,234 referrals in the second quarter of 2004. Various factors have contributed to this rise, of which fear of litigation and anxiety on the part of GPs has been important. This has resulted in further strain on the already overstretched NHS resources and has had a detrimental effect on efforts to improve management of colorectal cancer in the UK.

In the year 2000, the UK government implemented the 2 Week Wait rule and colorectal cancer guidelines to provide primary care (the GPs) and secondary care (the hospitals) with a method to help streamline and prioritize colorectal referrals. It aimed to detect patients at a high risk of having colorectal cancer, who can then be fast-tracked through the system for an early diagnosis and treatment.

In spite of the best of intentions, the 2WW system has failed to perform to its expectations. The yield of CRC from the 2WW referral route has been consistently poor in most centres in the UK. Various audits of the 2WW system across the country have tried to pinpoint the reason(s) behind its failure. Initial studies showed poor compliance with the guidelines as a major contributing factor, despite attempts at some centres to modify the proforma to improve compliance. Some authors suggested that strict adherence to guidelines can improve the colorectal cancer pick up rate.

However, what has become increasingly apparent in recent years is the inherent unreliability of the ‘high-risk’ symptoms and signs as indicators of colorectal cancer. The NHS guidelines even if properly implemented have been shown to be simply insufficiently specific to pick up most colorectal cancers. Thus, in the present system a large number of fast-tracked referrals are being processed to pick up a relatively small number of colorectal cancers.
Selvachandran et al from Crewe, UK have developed a computer program based Patient Consultation Questionnaire (PCQ) which is easy to complete by the patient, provides a comprehensive history and provides a significantly improved, reliable and specific cancer risk assessment than the NHS guidelines. This study has validated this questionnaire based cancer risk assessment tool in the large and ethnically diverse population of Leicester. The ethnic population of Leicester, which contributes up to 30% of the total, is predominantly of Indian origin. This study has shown that the response to the PCQ can be even better in this group of patients, suggesting that language need not be a barrier. However, we found that the overall referral rate to the hospital is significantly less in the ethnic population (6%) despite their significant contribution to the total population (30%). This could be due to a true lower incidence of colorectal cancer in the ethnic groups or due to their poor reporting of colorectal symptoms to the GPs.

This study has shown that the 2WW system in its current format has poor specificity, resulting in a high urgent referral rate and consequently a poor colorectal cancer detection rate. The NHS guidelines (symptoms only), on which the 2WW rule is largely based, even if strictly implemented are not specific enough, resulting in a large proportion of colorectal referrals being falsely classified as ‘fast-track’. In fact age more than 60 years alone as a criterion for fast track referral is more sensitive than the guidelines in detecting CRC (although much less specific).

This study has shown that the PCQ based weighted numerical score improves specificity resulting in improved colorectal cancer detection rate in a significantly smaller urgently referred population. The higher the score, the better is the specificity and positive predictive value for colorectal cancer.
Using a WNS score of >70, 225 fewer patients needed to be seen at
the hospital than if the 2WW system was used, to detect the same number
of colorectal cancers. Only half the patients in the study group scored more
than 50 on the WNS system and all of these were subsequently diagnosed
with important benign or malignant conditions that needed prompt
attention. The PCQ-WNS system can therefore reduce the number of fast-
track referrals, thus making better use of limited resources without
compromising patient care and has the additional benefit of ensuring
prompt treatment for important benign conditions as well.

Alternate ways have been suggested to help improve early diagnosis
of colorectal cancer. The Leicester ‘straight-to-test’ diagnostic protocol
where pre-agreed diagnostic tests are organised as the first assessment for
patients referred under the 2WW rule, has helped improve early
diagnosis.\textsuperscript{132} Thompson et al from Portsmouth\textsuperscript{134} have suggested a
combination of flexible sigmoidoscopy plus haemoglobin estimation for all
referrals, whereas Novell et al from Luton\textsuperscript{136} have proposed and tested a
common urgent pathway for all colorectal referrals. The implication of
these approaches on the limited available resources is obvious.

The patient consultation questionnaire based weighted numerical
score is an efficient and cost effective way of prioritising colorectal
referrals from GPs. We propose that a pilot project should be undertaken in
selected centres in the UK to test the use of this system in place of the
current 2WW rule.
PART III

CHAPTER 5

COLORECTAL CANCER PRESENTING AS AN EMERGENCY AND COMPARISON WITH ELECTIVE REFERRALS
Introduction

Despite efforts to identify high-risk patients early and prioritise their referral for an early diagnosis of colorectal carcinoma (CRC), a significant proportion of these tumours, particularly those of the colon, continue to present as emergencies. Advances in medical care and application of diagnostic techniques like Barium enema, colonoscopy and new imaging methods, have improved early recognition. However, between 8 and 29% of colorectal cancer patients present with obstruction, and between 3% to 8% present with perforation at the site of the tumour. A proportion of patients present with a combination of both when perforation occurs in distended colon proximal to the obstructing cancer, and a significant number present with bleeding and or symptomatic anaemia.

For patients presenting with CRC as an emergency, the overall prognosis is poorer as compared to patients presenting as an elective admission. Despite advances in emergency peri-operative care, the post-operative mortality rate is higher among the emergency population with a mortality rate of up to 20% after an emergency operation.

The reasons for this high mortality include-

a) Advanced age and co-morbidity

b) Obstruction or perforation itself (Hypovolemia/sepsis) with poor general condition of the patient, and

c) Advanced tumour stages with a higher incidence of lymph node metastases and therefore a decreased curative resection rate in patients with obstructing colorectal cancer.

In emergency surgery the resection rate is inferior than under elective conditions (85% elective versus 77% emergency) and the curative resection rate is also lower (70% versus 60% elective versus emergency, respectively). Many reports have therefore described significantly lower
survival rates for patients with obstructing CRCs when compared with non-obstructing colorectal cancer. In such circumstances the primary goal of surgery is to provide palliation of symptoms.

The continuing presentation of a significant proportion of CRC patients as acute surgical emergencies, in most cases as the first contact with primary or secondary care, stresses the urgent need for an effective screening program for CRC. Such a screening program needs to ensure compliance and should be directed at the section of population that generates proportionately the greatest number of emergency CRC admissions. The Nottingham screening trial of faecal occult blood testing did not reduce the overall incidence of emergency CRC surgery. This was probably because of non-compliance as the highest incidence of emergency CRC was seen in the non-responders. In Leicester, while significant improvements have been made in early diagnosis and management of patients referred by GPs with colorectal symptoms, up to a quarter of all the CRC patients are diagnosed while presenting as an acute surgical or medical emergency.

The aim of this study was to assess the clinical presentation, treatment and outcome of patients with CRC who present as an acute surgical or medical emergency. In addition, several clinical factors that may influence development of morbidity or mortality were evaluated. A comparative analysis has also been done between CRCs presenting as an emergency and those presenting as an elective admission. The objective was to identify specific features if any, which make this cohort of patients different thereby allowing us to propose methods to reduce their number. This would be a significant step in improving the overall prognosis and survival in patients with CRC.
Patients and Methods

Between 1\textsuperscript{st} September 2003 and 31\textsuperscript{st} August 2004 (the duration of the PCQ validation project), 322 patients underwent treatment for CRC in the 3 University Hospitals of Leicester. From this population, 83 patients (25\%) were admitted as emergencies. The remaining 249 were a mix of 2-week wait (2WW) referrals and traditional GP letter referrals. The hospital CRC database was interrogated to obtain information about all of these patients. In addition, 77 of the emergency referrals and 131 of the elective referrals had their medical notes available for a detailed review. Information from the medical notes was isolated onto Microsoft Excel based databases.

The information reviewed/collected included a) name, age, sex, address with post code and any significant past medical history b) clinical presentation and its duration c) reasons for emergency admission d) investigations and diagnosis e) tumour site f) presence or absence of distant metastases at first diagnosis g) American Society of Anaesthesiologists (ASA) grade h) type of first treatment i) outcome/complications j) death within 30 days of surgery k) Dukes’ stage of the tumour

Results

A. Colorectal cancers admitted as emergencies (83 in total)

I Sex distribution: We found a slight male preponderance in the sex distribution with 49 (59\%) of the patients being male.
II. Age distribution: The age distribution is as shown in the figure 6 below. Almost half (50%) of the patients belonged to the 76-95 year age group.

Figure 6. Age distribution of emergency CRC patients

III. Site of the tumour: The majority of the tumours were found in the sigmoid colon (24%), followed by the caecum (21%) and the rectum (15%). (See figure 7)

Figure 7. Site of tumour in emergency CRC patients
IV Presence of distant metastases at the time of diagnosis

A total of 15 out of the 83 (18%) emergency admissions had distant metastases at the time of first diagnosis (Therefore 18% of emergency admissions were Dukes’ D at the time of first diagnosis)

V Type of surgery:

A total of 60 patients underwent surgery. A curative resection was performed in only 20 (33%) of the patients. See figure 8.

Figure 8. Type of surgery in emergency CRC patients

VI ASA Grade:

47 (78%) of the patients operated belonged to ASA grade II or III. Of these 24 (40%) belonged to Grade II and 23 (38%) belonged to Grade III. See figure 9.

Figure 9. ASA grade in emergency CRC patients
VII Died within 30 days of surgery:
8 out of the total of 60 operated (14%), died within 30 days of surgery.

VIII Dukes’ stage of the tumour:
A total of 49 patients had the tumour resected and staged. Twenty-six (53%) patients were staged as Dukes’ Cl. Only 12 of the patients (25%) belonged to stage A or B. See figure 10.

Figure 10. Dukes’ stage of tumour in emergency CRC patients (of those who had the tumour resected and staged)

IX Duration of symptoms:
The medical notes of 77 patients presenting as an emergency were available for review in detail. These patients had a median duration of symptoms of 4 weeks.

B. Colorectal cancers admitted electively (249 in total)
I Sex distribution:
There was a similar male predominance with 141 (57%) of the patients being male.
II Age distribution:
In this group of patients almost half the patients (48%) belonged to a younger age group of 56-75 years. See figure 11.

Figure 11. Age distribution in elective CRC patients

III Site of Tumour:
The predominant site of tumour in the patients with CRC presenting electively was the rectum in 98 patients (40%). This was followed by the sigmoid colon in 58 patients (24%). Only 24 of these patients (9%) had a caecal tumour. See figure 12.

Figure 12. Site of tumour in elective CRC patients
IV Presence of metastases at the time of diagnosis:
35 out of the total 249 patients (14%) admitted electively were found to have metastases at the time of first diagnosis (therefore 14% of the elective admissions were Dukes’ D at the time of first diagnosis)

V Type of surgery:
A total of 169 patients underwent surgery. This group had a higher curative resection rate with 78 patients (46%) undergoing a curative operation. See figure 13.

Figure 13. Type of surgery in elective CRC patients

VI ASA grades of those operated (a total of 169):
The vast majority of patients in this group belonged to a lower ASA grade II (64%). See figure 14.
VII Died within 30 days of surgery:
6 out of the 169 operated (4%) died within 30 days of surgery.

VIII Dukes’ stage of the tumour:
A total of 153 patients had their tumour resected and staged.
Eighty six of these (56%) belonged to Dukes’ stages A & B
See figure 15.

Figure 15. Dukes’ stage of tumour in elective CRC patients (of those who underwent resection of the tumour and staging)
Duration of symptoms prior to presentation:

The medical notes of 131 patients with CRC presenting electively were available for review in detail. These patients had a median duration of symptoms of 12 weeks prior to presentation.

The difference in the median duration of symptoms prior to presentation in the emergency as compared to elective colorectal cancer patients was statistically significant (P value < 0.000002, using the Mann Whitney U test). See figure 16.

(W = weeks of symptoms prior to presentation)

Figure 16. Difference in duration of symptoms (Elective Vs Emergency)
**Post code of residence Vs Clinical presentation:**

In 2004, the ‘Indices of Deprivation were provided by the Office of National Statistics (ONS) as a means of comparing different measures of deprivation in different parts of England. The various deprivation indices are for:

Income
Employment
Education
Skills and Training
Health
Barriers to housing and services
The Living environment
Crime

The data is ranked in such a way that a lower rank indicates a greater deprivation. A rank of 1 therefore represents the most deprived. These indices are calculated for Local Authorities and for smaller blocks of land called the Output Areas (previously this was calculated for electoral wards). In addition there is a combined Index of Multiple Deprivation or IMD, which combines all the above indices. England has been subdivided into 32,482 Output Areas for the calculation of the IMD. Thus on the IMD, a rank of 1 is the most deprived (Benchill ward in England) and a rank of 32,482 is the least deprived (Aldenham east). Using the following website of the Office of National Statistics

http://neighbourhoodstatistics.gov.uk/default.asp?nsid=false&CE=True&SE=True the IMD rank of a particular output area can be calculated by inputting the postcode of residence.

We determined the individual IMD ranks of the areas of residence of patients with colorectal cancer from our databases. The median IMD rank
of the patients with CRC presenting electively was **20,584** (ranging from 210 - 32,253).

The median IMD rank for emergency CRC patients was **20,564** (ranging from 1193 – 32,136).

This comparison has shown that the patients with CRC presenting as an emergency:

1. had a shorter duration of symptoms prior to presentation,
2. were more likely to be in the older age group of more than 75 years,
3. have a higher chance of having a distant metastasis at the time of diagnosis,
4. have a lower chance of undergoing a curative resection,
5. are more likely to be unfit with a significant systemic disease and therefore a higher ASA grade,
6. are more likely to die within 30 days of surgery,
7. have a poorer Dukes stage of the carcinoma,

as compared to those patients who present electively.

There was a difference in the site of cancer distribution as well. The emergency CRCs were primarily located in the caecum or the sigmoid colon, whereas the cancers presenting electively were mainly rectal.

On the other hand the degree of deprivation of the area of residence of a patient makes no difference to the type of clinical presentation of the patient’s CRC (elective or emergency).

**Clinical Presentation and reasons for emergency admission:** These details were studied during the review of the medical notes of 77 patients with colorectal cancer who presented as an emergency.

a) The emergency admission was either under the Physicians or the surgeons. The distribution was as follows:
Medical admission: 31
Surgical admission: 46

b) Reasons for emergency admission: (hospital team's diagnosis after initial assessment). See figure 17.

Figure 17. Reasons for emergency admission of CRC patients

The main reasons for emergency admission were therefore:
Bowel Obstruction 25 patients (32%)
Symptomatic anaemia 18 patients (23%)
Bleeding per rectum 9 patients (11%)
Other significant reasons were perforation causing peritonitis (6 patients or 7%) and symptomatic liver metastases (4 patients or 5%).

Bowel obstruction and perforation together constituted 44% (34 out of 77 patients) of all emergency admissions. The distribution of the site of the tumour in these patients was as follows:
Sigmoid colon 13 (38%)
Descending colon 8 (23%)
Transverse colon (with perforated caecum) 1
Caecum (causing small bowel obstruction) 4
Ascending colon (perforated tumours) 2
Disseminated abdominal malignancy causing bowel obstruction 2
Splenic flexure (obstruction) 2
Rectum (one perforated tumour) 2

c) Mode of referral / Previous GP consultation:
9 of the 77 patients (11%) admitted with colorectal cancer were admitted via the department of Accident and Emergency (A&E), 1 was an internal referral and the remaining 67 (87%) were admitted to the hospital as an emergency by their GP.

None of the 9 emergency admissions via A&E had been seen by their GP in the recent past for any bowel or related symptoms. Similarly, of the remaining patients admitted by their GPs, 39 had not been seen previously by the GP for any bowel complaints or related symptoms. See figure 18.

![Figure 18. Prior GP consultation in emergency CRC patients](image)

Therefore, a significant number of patients (48 out of 77 or 62%) admitted as an emergency and subsequently diagnosed as having colorectal cancer were not seen by their GPs in the recent past for bowel or other symptoms related to their emergency admission.
Patients presenting with symptomatic anaemia:
A significant proportion of our patients with colorectal cancer presenting as an emergency (19 out of the total of 77 or 24% whose medical notes were reviewed in detail) presented with symptomatic anaemia (dizziness, general malaise, shortness of breath on exertion, blackouts or falls) or anaemia as the main presenting complaint. These patients had their mode of referral, past history and subsequent management reviewed as follows:

a) 17 of the 19 patients presenting with anaemia were admitted as emergency medical admissions with the physicians. The other 2 were emergency surgical admissions.

b) The site of tumour in 14 of these patients was in the right colon (caecum, ascending colon or hepatic flexure)

c) There was a significant delay in the diagnosis of cancer in 16 of these patients (84%). A significant delay in diagnosis was arbitrarily defined as more than 62 days, which is twice the government target of 31 days from referral to diagnosis. The delay could be attributed to the GP in 6 of these and to the admitting physicians in the remaining 10.

The delay by the GP was primarily due to the anaemia being treated empirically with Iron for some length of time before any bowel investigations or referral to the hospital. The delay at the physician level was due to failure to promptly investigate for a colonic lesion as the possible cause of the anaemia. An upper gastrointestinal endoscopy was requested urgently, whereas either no colonic investigation was ordered or a Barium Enema or colonoscopy was requested as an outpatient routinely. These colonic investigations happened after a considerable delay, were sometimes falsely reported
(two of the Barium enemas) or were incomplete (colonoscopies), resulting in further delays. The delay in the diagnosis of right-sided colon cancers presenting with significant anaemia has been investigated in more detail in the chapter 7.

Discussion
Colorectal cancer presenting as an emergency continues to present as a significant problem to all surgeons involved in the management of these patients. An emergency operative intervention is usually required in patients presenting with obstruction or perforation. These patients make up 7% to 40% of all patients undergoing surgery for colorectal cancer. More recently it has been shown that in the UK, about 20% of patients with colonic cancer will present as an emergency while 16% will present with obstruction. Our study has shown that up to 44% of emergency colorectal cancers presented with obstruction or perforation. These were acute surgical admissions. In our series too, as reported previously, obstruction and perforation occurred most frequently in cancer of the left colon (sigmoid and the descending colon). In addition we have also shown that a significant number of emergency colorectal cancer patients present with symptomatic anaemia to the physicians as a medical admission. Most of these patients have cancer of the right colon. Overall rectal tumours in our study presented less often as an emergency and this confirms with what has been reported previously. Patients presenting as emergencies due to colorectal cancers, tend to belong to an older age group and our study has shown similar results. There was no significant difference in the sex ratio between emergency and electively presenting colorectal cancers. However there was an overall predominance of colorectal cancer in men.
Colorectal cancers presenting as an emergency tend to be more advanced and therefore distant metastases are more commonly found at the time of presentation.\textsuperscript{167,168,169} Our series has shown that up to 18% of all emergency colorectal cancers had distant metastases (Dukes’ D) at the time of presentation as compared to 14% in those colorectal cancers that presented electively. Similarly tumour stages have been reported to be higher in these patients as compared to those presenting electively.\textsuperscript{158} In our study, more than half the patients with emergency colorectal cancers who underwent a resection were found to have Dukes’ stage C\textsubscript{1} tumour, as compared to elective colorectal cancer patients undergoing resection whose tumour stages were predominantly Dukes’ A&B. None of the elective patients were found to be Dukes’ D at surgery, presumably as they were all adequately staged pre-operatively (Dukes’ D staging being a contraindication for surgery)

Patients presenting as an emergency with colorectal cancer tend to be older and therefore have an increased incidence of associated medical conditions resulting in a higher ASA. Our study has confirmed this. These patients also tend to have an overall lower curative resection rate.\textsuperscript{154,158} Our study has shown a curative resection rate of 33% for complicated colorectal cancers as compared to 46% for uncomplicated cancers.

The combination of older age, associated medical conditions, advanced tumour stage and a poor chance of a curative resection results in a significantly higher 30-day mortality in patients with colorectal cancer presenting as an emergency. Our study has shown a 30-day mortality of 14% in patients with emergency colorectal cancers as compared to 4% in those with elective colorectal cancers.

Emergency patients have been shown to have a shorter history of presenting symptoms as compared to elective patients.\textsuperscript{166} In our series, the median duration of symptoms prior to an emergency admission was 4
weeks as compared to a median of 12 weeks duration for elective colorectal cancer patients.

Studies from Scotland have shown that patients with colorectal cancer from deprived communities may present with more advanced disease.\textsuperscript{170} This finding however has not been replicated in other studies, which have found no such correlation.\textsuperscript{11} In our study we attempted to assess the area of residence of patients in terms of its Index of Multiple Deprivation (IMD) as per the most recent rankings assigned by the Office of National Statistics (ONS). We found no significant difference between the deprivation status of patients with complicated colorectal cancers and those with uncomplicated cancers.

Colorectal cancers presenting as an emergency continue to be a significant proportion of the colorectal cancer workload at any centre in the UK. Improving general awareness about colorectal symptoms in the community and encouragement to report such symptoms to the GPs, especially within the older population, should help reduce the numbers of colorectal cancers presenting as an emergency. This should in turn affect the outcome of colorectal cancer management in a positive way.

This study has highlighted two important aspects of colorectal cancers presenting as an emergency that have not been described in the literature before:

A. \textit{Consultation with the GP prior to emergency presentation.}

We have shown in our study that up to 62\% of the patients in our series with complicated colorectal cancer did not have any consultation with their GP prior to their emergency presentation. They either presented as an emergency via A&E or the on-call GP who referred them to the hospital medical or surgical admission unit. This could be attributed to
- a short history of clinical symptoms
- lack of any significant symptoms
- general apathy on the part of the patients in reporting symptoms (due to older age ?)

B. *Delay in the diagnosis of right sided colon cancers*

A significant proportion (27%) of patients in our series who presented as an emergency, presented with symptomatic anaemia in the form of shortness of breath on exertion, fainting episodes or collapse as the main presenting feature. Eighty one percent amongst these were diagnosed with colorectal cancer (right sided in most cases) after an unacceptable length of time (more than 62 days, which is twice the government target). Various factors contributed to this delay:

i) Lack of any specific symptoms or signs

ii) Empirical iron therapy for anaemia commenced by the GPs,

iii) Lack of or delayed / incomplete colonic investigations instituted by the attending physicians

This aspect has been studied in more detail in chapter 7.

**Conclusions**

Colorectal cancer remains a major cause of cancer morbidity and mortality. Efforts to improve early detection and diagnosis by identifying and fast tracking high risk patients presenting with colorectal symptoms to the GP and improved resources for investigations and diagnosis at the hospitals have helped reduce the diagnosis and treatment times of colorectal cancer.
However, a significant number of colorectal cancers continue to present as an emergency medical or surgical admission. These patients may not have been seen previously by their GP, are older with significant co-morbid conditions, tend to have more advanced tumours at the time of diagnosis which may get delayed in tumours of the right colon, and are more likely to die from an emergency operation which is usually palliative.

Any effort that hopes to improve the overall management and survival in colorectal cancer cannot afford to ignore this significant cohort of patients that appear at present to form a separate entity. Colorectal cancer screening programs would hopefully help reduce the number of emergency colorectal cancers by detecting cancers in relatively asymptomatic patients and generally improving awareness in the community. It cannot be overemphasized that any proven iron deficiency anaemia in a patient needs to be comprehensively investigated with both an upper and a lower gastrointestinal imaging. Empirical iron therapy or transfusions to treat symptomatic iron deficiency anaemia without complete colonic investigations can lead to unacceptable delay in diagnosis and a worsened prognosis.
CHAPTER 6

COLORECTAL CANCER IN THE ASIAN POPULATION OF LEICESTER: INCIDENCE AND PRESENTATION
Introduction

Worldwide, colorectal cancer (CRC) varies with race and ethnicity. The highest incidence of CRC is found in whites of European descent\(^1\), but a more advanced stage at diagnosis and consequently a higher mortality has been reported in the ethnic races.\(^2\) The reason for such disparities is multifactorial. These have been divided into biological or genetic factors or non-biologic factors like diet, environment, poor understanding of the disease and socio-economic differences that affect access to health care.\(^1,2,3,4,5\) These disparities highlight the need for a better understanding of CRC biology and epidemiology that will allow development of CRC screening and treatment programs that incorporate strategies to target high risk groups.

While many studies have shown racial/ethnic differences in CRC in populations in the United States,\(^1,2,3,4,5\) only modest research has been done in the United Kingdom to highlight any such differences.\(^6\) Leicester has one of the largest concentrations of ethnic minorities in the UK. Our aim was to study the incidence and stage of presentation of CRC in the ethnic population of Leicester and compare this with that of the rest of the population in Leicester.

Patients and Methods

As part of our Patient Consultation Questionnaire (PCQ)\(^7\) validation project at Leicester, we sent the PCQ to all patients referred to the hospital consultants (colorectal surgeons and gastroenterologists) by the general practitioners with colorectal symptoms, over a one-year period between September 2003 to August 2004. Patients who responded were scored (the Selva score) using their responses and were also followed up to
a final diagnosis. A total of 1422 patient responses were included in the project. We also analysed data from our University hospitals of Leicester (UHL) colorectal cancer database for the same one-year period to study the differences in the stage of CRC at diagnosis, amongst the various patient groups.

Results

Amongst the total of 1422 patients who responded to the PCQ, 1280 were from the indigenous white background and 78 of these were found to have CRC, an incidence of about 6%.

The second largest group of 128 patients were from an Asian background (Indian, Bangladeshi, Pakistani or Chinese), and of these, 5 were diagnosed with CRC, an incidence of about 3%.

On interrogating our CRC database for this one-year period, we found a total of 16 patients of Asian origin diagnosed with CRC. Fourteen of these had their tumour resected and staged. Their stage distribution is shown in table 6.1

Table 6.1 Stage distribution of Asian CRC patients (of those resected)
N=14

<table>
<thead>
<tr>
<th>Dukes’ Stage</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dukes’ A</td>
<td>2</td>
</tr>
<tr>
<td>Dukes’ B</td>
<td>2</td>
</tr>
<tr>
<td>Dukes’ C</td>
<td>9</td>
</tr>
<tr>
<td>Dukes’ D</td>
<td>1</td>
</tr>
</tbody>
</table>
From amongst the remaining 306 patients on the database diagnosed with CRC over this 12-month period, 188 patients had their tumour resected and staged. Their stage distribution is shown in table 6.2.

**Table 6.2 Stage distribution of non-Asian CRC patients (of those resected)**

<table>
<thead>
<tr>
<th>Dukes’ Stage</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dukes’ A</td>
<td>26</td>
</tr>
<tr>
<td>Dukes’ B</td>
<td>65</td>
</tr>
<tr>
<td>Dukes’ C</td>
<td>96</td>
</tr>
<tr>
<td>Dukes’ D</td>
<td>1</td>
</tr>
</tbody>
</table>

The two tables show the differences in the stage at resection of CRC between the Asian background patients and the indigenous whites with CRC. Seventy one percent of the Asian patients had stage C or D disease, whereas only about 53% of the white patients had CRC in this stage.

**Discussion**

The incidence and natural history of CRC varies significantly in different racial and ethnic groups. While genetic factors could account for such disparities, it is now well established that environmental factors have a significant impact as well. Carethers et al from California USA have focused on the genetic differences in terms of chromosomal aneuploidy and micro-satellite instability. Various other authors have studied environmental factors. Palmer et al from Boston studied the
influence of social inequalities on CRC. Seow et al from Singapore have studied dietary influences.\textsuperscript{174}

The importance of environmental influences is well established by studies that show a difference in the CRC incidence between the migrant population and their descendants born in the host country. Flood et al from Seattle USA have shown that the incidence of CRC is two-fold higher in Japanese men born in the United States than those born in Japan.\textsuperscript{178} Mayberry et al from Leicester United Kingdom have shown a relatively increased incidence of CRC in the younger Asian population born in the UK as compared to their older counterparts.\textsuperscript{13} Steward et al, also from Leicester, have shown that although the incidence of CRC is lower in the South Asians as compared to the rest of the population in Leicester, it is rising in the younger South Asian population\textsuperscript{180}

Chien et al from the United States have shown that the black population with CRC presented with more advanced stage disease and had higher mortality rates as compared to the non-Hispanic white population.\textsuperscript{172} Our study has shown that the Asian population (Indian, Pakistani, Bangladeshi and Chinese) in Leicester have a significantly higher risk of being diagnosed with an advanced stage of CRC as compared to the white population (Table 6.1 & 6.2). Mayberry and Steward et al from Leicester,\textsuperscript{13,180} have shown a significantly lower incidence of CRC in the Asians as compared to the white population. Six years on, our study has confirmed this. The reasons for an overall low incidence of CRC in the ethnic population but its presentation in a more advanced stage can only be speculated upon. Poor and delayed reporting of colorectal symptoms amongst the ethnic population due perhaps to cultural reasons may be to blame. On the other hand it may very well be a true low incidence of CRC in the ethnic population.
Conclusion

Colorectal cancer varies widely in the various racial and ethnic groups. Genetic differences obviously contribute to these disparities, but environmental influences have a significant impact too. The most compelling evidence for this comes from differences seen in CRC characteristics between the migrants and their own descendents born in the host country.

The Asian population in the UK have a lower incidence of CRC as compared to the white population and therefore do not contribute significantly in numbers towards any research studies. They do however have a greater risk of having advanced stage disease and therefore contribute significantly towards mortality from CRC. We recommend that more research is needed in the UK targeting this important group of patients if we are to better understand the carcinogenesis, epidemiology and the nature of the environmental influences affecting CRC. This would help in improving the overall management of CRC by better designing of preventive, screening and treatment programs for CRC.
CHAPTER 7

DELAY IN THE DIAGNOSIS OF PROXIMAL COLON CANCERS
Introduction

Early diagnosis and prompt commencement of treatment has been the main objective of all initiatives in the past few years to help improve the management and overall survival from colorectal cancer (CRC). The two-week wait (2WW) referral system to help prioritise colorectal referrals and the recently concluded pilots for colorectal cancer screening are a step towards this objective. Symptoms and signs such as rectal bleeding, change in bowel habit, symptomatic iron deficiency anaemia (IDA), palpable abdominal or rectal mass, have been used as part of the two week wait system to help early detection of colorectal cancer.

We have already highlighted the poor specificity of these so called high-risk symptoms in predicting the risk of colorectal cancer in a patient. In our study of colorectal cancers presenting as an emergency we found a significant number being admitted as an emergency under the physicians for symptomatic IDA. (See chapter 5) We also found that the majority of these patients (73%) had proximal colon cancers and most of them had the cancer diagnosed after a considerable delay, which could be considered unacceptable.

Iron deficiency anaemia is a well recognised complication of colorectal cancer.\textsuperscript{181,182} Symptomatic anaemia is often the only significant presenting feature in elderly patients with right-sided or proximal colon cancers, who have few or no other colorectal symptoms.\textsuperscript{183} Failure to thoroughly investigate the cause of the anaemia in these patients can lead to a considerable delay in the diagnosis.\textsuperscript{183}
Aim

The aim of our study was to explore the various reasons for the delayed diagnosis of proximal colon cancer in patients who presented to a hospital consultant with significant IDA.

Patients and Methods

Using our hospital colorectal cancer database we identified all patients who were diagnosed with cancer of the proximal colon (proximal to the splenic flexure) over a one-year period at our hospital from September 2003 to August 2004. The time taken to make the diagnosis from first presentation (to the hospital consultant) was measured for each patient. An unacceptable delay in the diagnosis was arbitrarily defined as being more than 62 days from first presentation to date of working diagnosis, which is twice the government target of 31 days from GP referral to diagnosis. The criteria for anaemia were defined as per current national two week wait referral guidelines of haemoglobin (Hb) <11g/dl for men of all ages and <10g/dl for women (post menopausal).

Results

Of a total of 322 patients diagnosed with CRC during the one-year period from September 2003 to August 2004, 60 patients were diagnosed with proximal colon cancers. The diagnosis was delayed in 20 of these patients by more than 62 days from the time of first presentation. Nineteen of the 20 patients (95%) had been referred to a consultant physician (Figure 19) and 13 of these were women. The median age of the patients with delayed diagnosis was 78 years (age range 63-93 years). All of the 20 patients were anaemic (as per 2WW guidelines) with 13 of these receiving
blood transfusions. Fourteen (70%) of the patients with delayed diagnosis were admitted as an emergency (Figure 21), 11 of these received blood transfusion for symptomatic anaemia (these patients had a median Hb value of 7.0). In our study, all non-elective admissions were defined as emergency presentations. The median duration of the delay in diagnosis was 5 months.

In the non-delayed group of patients, 15 (35%) were referred to physicians and 25 (65%) to the surgeons (Figure 19).

The various reasons for the delay in diagnosis are shown in figure 20. The most common reason was failure to investigate the colon adequately. This occurred in 13 patients who did not have prompt colonic imaging at first presentation. In 3 of these 13 patients, the anaemia was wrongly attributed to gastric erosions found on gastroscopy, presence of co-existing hairy cell leukaemia and co-existing multiple myeloma respectively. Other causes for delay were:

i) Incomplete colonoscopies in 3 patients that were not followed up with further investigations.

ii) False negative imaging (double contrast barium enema) in 3 patients, and

iii) Clerical error in one (a positive finding on imaging not reported promptly)
Figure 19

i) Referral Distribution (delayed diagnosis)

ii) Referral Distribution (non-delayed diagnosis)
Reasons for delay in the diagnosis of proximal colon cancers

Figure 20

Mode of admission of patients with delayed diagnosis

Discussion

Proximal colon cancers can form up to a third of the total number of colorectal cancers diagnosed in any centre. They tend to present with few bowel symptoms and mostly non-specific complaints, especially so in
elderly patients.\textsuperscript{181,183} This often results in delays in the diagnosis.\textsuperscript{183} In our study, the median age of the patients with delayed diagnosis of their proximal colon cancer was 78 years. Furthermore, elderly patients tend to have a higher incidence of right-sided colon cancers than the left.\textsuperscript{181} Iron deficiency anaemia is a recognised complication and a common presenting feature of colorectal cancer.\textsuperscript{181,182} It is now well established that the incidence of anaemia is higher in patients with cancer of the right colon than those with cancer of the left.\textsuperscript{183,185,186} Therefore, it is not uncommon for elderly patients with proximal colon cancers to present with non-specific complaints and iron deficiency anaemia.\textsuperscript{181,183} Iron deficiency anaemia of $<11\,\text{g/dl}$ in men and $<10\,\text{g/dl}$ in women constitutes the national referral guideline for anaemia within the fast-track 2WW referral system. However, it must be borne in mind that using anaemia alone as an investigative tool in diagnosing proximal colonic cancers, without adequate colonic imaging in patients presenting with colorectal symptoms, would be a mistake. The author (Rai S) has shown in a different study that anaemia per se is a poor predictor of right-sided colon cancers.\textsuperscript{187} It was shown in the study that even after raising the cut-off level for a ‘low’ haemoglobin as per national guidelines, a significant number of patients with proven proximal colonic cancers were not found to be anaemic. The importance of adequate colonic imaging in symptomatic patients was stressed. Therefore, where on one hand presence of anaemia should prompt complete colonic imaging, absence of anaemia on the other does not rule out a proximal colon cancer.

Delay in the diagnosis of colorectal cancer has been attributed to delay in the patients presenting to the General Practitioner (GP) with their complaints (patient delay). Lack of any specific bowel complaints in elderly patients with right-sided colon cancers, who may consider any symptoms to be part of ‘growing old’,\textsuperscript{181} certainly contributes to ‘patient
delay'. Another cause for delay can be commencement of iron therapy for anaemia empirically by the GPs (without any bowel investigations) as we have shown in chapter 5.

In this study, we concentrated on the delay from the time of first presentation to the hospital (electively after a GP referral or as an emergency admission) to the time a definitive diagnosis was made (hospital delay).

Harris et al have reported unacceptable delays of 6 months or more from the time of initial presentation to definitive diagnosis of colorectal cancer. Incomplete imaging of colon was the most common reason found. Other causes were inappropriate iron therapy, false negative imaging results and clerical error. Our study has shown that inadequate colonic imaging in patients presenting with symptomatic iron deficiency anaemia to a hospital consultant either electively or as an emergency was the most common cause of the delayed diagnosis (it was not requesting colonic imaging urgently enough or requesting inadequate imaging like FOS alone, or not requesting colonic imaging at all as in 8 patients). Interestingly, in our study, in all cases with delayed diagnosis except one, the hospital consultant was a physician. This is in contradiction to the finding by Stebbing et al who found no difference in the delay between referrals to physicians and surgeons.

The majority of the patients in our study with delayed diagnosis initially underwent an upper gastrointestinal endoscopy to investigate their anaemia. Where a benign lesion was found like oesophagitis or gastritis, this was wrongly thought to be the cause for the anaemia and as a consequence complete colonic imaging was not requested (or followed up). The patient presenting with some upper gastrointestinal symptom may also have influenced this decision. However, McIntyre et al from Nottingham have shown that clinical symptoms and signs are poor
indicators in determining the investigations that will detect a cause for the anaemia. There is also evidence that colonic neoplasia may be missed in patients presenting with iron deficiency anaemia unless colonic investigations are performed on all patients even when an alternative cause has been found.\textsuperscript{188} Cook et al have shown that as many as 16\% of patients with IDA found to have a benign cause for anaemia on upper GI endoscopy also have a colonic neoplasm.\textsuperscript{189} Three of our patients had their anaemia attributed to coexisting gastric erosions, Hairy-cell leukaemia and multiple myeloma respectively.

Various studies have highlighted the need for both upper and lower GI tract investigation for IDA. Guthrie et al have shown the value of a Double Contrast Barium Enema (DCBE) in investigating patients with unexplained iron deficiency anaemia even in the absence of bowel symptoms,\textsuperscript{190} while Hardwick et al have shown bidirectional endoscopy (upper GI endoscopy and colonoscopy) under the same sedative to be an effective method of investigating patients with IDA.\textsuperscript{191}

The proportion of colorectal cancer patients with an emergency presentation has been variously reported between 14\% to 50\%,\textsuperscript{165} with elderly patients having higher rates when compared to the young. In our study, 70\% of the patients (14 out of 20) with delayed diagnosis of their cancer, presented as an emergency of which 12 (85\%) were above the age of 70 years. There is a lot of confusion in the literature about the definition of an ‘emergency’ presentation. In our study the definition of an emergency presentation is used to cover all non-elective admissions.

**Conclusion**

Unexplained IDA in a patient can be a significant predictor of the presence of CRC. Significant delays can occur in the diagnosis of CRC due
to (i) ‘patient delay’, with patients failing to promptly report their bowel symptoms to the GP, (ii) commencement of iron therapy for anaemia empirically by the GPs without bowel investigations, or (iii) ‘hospital delay’ with failure to promptly and adequately investigate the large bowel in patients presenting with significant iron deficiency anaemia requiring a blood transfusion, especially elderly patients presenting as an emergency. The large bowel should be imaged in all such patients even if a probable alternate cause for the anaemia has been found.

Physicians in particular need to be aware of proximal colon cancers as an important if not common cause of IDA and should endeavour to image the colon promptly and adequately in all such patients.
CHAPTER 8

PATIENT SATISFACTION SURVEY
Introduction

The patient consultation questionnaire (PCQ) \(^{133}\) contains 60 domains that ask a detailed history from the patient about their colorectal symptoms, other related symptoms, medical conditions and any significant family history. The questions about the colorectal symptoms focus on their details, their duration, presence of any symptom complexes (two or more symptoms together) and their progression with time (worsening or resolution). The scores attributed to these questions enable the software program linked to the questionnaire to produce a weighted numerical score (the WNS or the Selva score). This score reflects the risk of that patient having colorectal cancer. The patients themselves complete the PCQ and it provides the clinician with a detailed history from the patient and a score. The WNS allows the clinician (the General Practitioner) to fast track the relevant patients for assessment by a hospital consultant.

The PCQ was developed by Selvachandran et al from Leighton Hospital, Crewe and their prospective study on its use has shown it to be significantly more effective and efficient in detecting high-risk patients, who need urgent assessment, than the current NHS guidelines. \(^{133}\) Our study has validated this questionnaire in the large and varied population of Leicestershire as an effective tool for prioritising colorectal referrals.

Aim

As part of our validation project in Leicester, we assessed how easy or difficult it was for patients to complete the 4-page PCQ. This was particularly relevant in Leicester, which has a significant ethnic minority population who do not speak English as their first language. The aim of our patient satisfaction survey was to assess user-friendliness of the PCQ
and gauge the overall satisfaction of the patients with their experience at the hospital.

Methods

To overcome the language obstacle, we translated the questionnaire into 4 different ethnic languages spoken in Leicester. As explained in chapter 2, patients received PCQs from the 2WW office or from the consultants after they had vetted the GP referral letters. A translated questionnaire was available to those who requested it. An extra question was added to the PCQ asking the patients if they needed any help (from friends or family) in completing the questionnaire.

We designed a patient satisfaction questionnaire (PSQ) to ask patients about the ease of completing the questionnaire, how it compared with giving their history to the clinician, the waiting times for appointment, their experience at the hospital with the diagnostic test or the treatment offered and overall satisfaction with their care.

The PSQ (see appendix) was sent to a cross section of the patients who had responded to the initial PCQ. These were patients who had been recruited in the study over a random 3-month period (from the total 1 year duration of the project).

Results

A total of 3128 PCQs were sent out to patients. The overall response rate was 51% with patients from an ethnic background (predominantly of Indian origin) responding better than the indigenous white population (see chapter 3). The first consecutive 1422 patients who returned a completed PCQ were recruited in the study. Of these only 8 patients (<1%) requested
for a translated questionnaire (3 Arabic and 5 Gujarati). The overwhelming majority therefore were able to complete the English questionnaire.

63 of the 142 ethnic minority patients (45%) who responded to the questionnaire needed help from family members or friends to complete the questionnaire whereas, only 118 of the 1280 responders (9%) from the indigenous white background needed such help (p value < 0.001). Interestingly, more than 80% of those who needed help (from both the ethnic minority and the white population) belonged to the >40 years age group (See tables 8.1 & 8.2). This however was not significant (p value < 0.2).

Table 8.1 PCQ completion help

<table>
<thead>
<tr>
<th>Ethnic origin</th>
<th>No</th>
<th>Yes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black - African</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Black - Caribbean</td>
<td>7</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Black - Other</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chinese</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Indian</td>
<td>60</td>
<td>59</td>
<td>119</td>
</tr>
<tr>
<td>Pakistani</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>White</td>
<td>1162</td>
<td>118</td>
<td>1280</td>
</tr>
<tr>
<td>Total</td>
<td>1241</td>
<td>181</td>
<td>1422</td>
</tr>
</tbody>
</table>
### Table 8.2 Those who needed help to complete the PCQ

<table>
<thead>
<tr>
<th>Ethnic origin</th>
<th>Age</th>
<th>40.0 -70.0</th>
<th>&gt;=70.0</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black - African</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Black - Caribbean</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Black - Other</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chinese</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
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<td>2</td>
</tr>
<tr>
<td>White</td>
<td>8</td>
<td>32</td>
<td>78</td>
<td>118</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>16</td>
<td>71</td>
<td>93</td>
<td>181</td>
</tr>
</tbody>
</table>

A total of 101 patient satisfaction questionnaires were returned out of a total of 158 (63%). The age and sex distributions of these patients are shown in the figures 22 and 23.
Figure 22. Age distribution of those who responded to a PSQ

![Age Distribution Chart]

Figure 23. Sex distribution of those who responded to a PSQ

![Sex Distribution Chart]
Eighty-one patients (80%) found completing the patient consultation questionnaire easy or relatively easy (Figure 24).

Sixty-seven patients (66%) of the patients found it less embarrassing filling out the PCQ than discussing their colorectal symptoms with their GP (Figure 25).

**Figure 24. Ease of completing the PCQ**

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

1 - Difficult  5 - Easy

**Figure 25. Completing the PCQ Vs relating history to the GP**

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>20</td>
<td>25</td>
<td>10</td>
</tr>
</tbody>
</table>

1 - More  5 - Less
At Leicester, the patients referred via the 2WW referral system have a diagnostic test organised within the stipulated 2 weeks before being seen by a consultant. Even those referred by the GPs through the traditional letter have an endoscopy or a radiological test first (as decided by the referred consultant reviewing the letter). Therefore a significant majority of patients undergo a diagnostic test before being seen by the consultant. There was a mixed response to our query as to how comfortable the test was and whether it was what the patients expected from the information given to them (Figure 26 and 27).

**Figure 26. How comfortable was the diagnostic test**

Question 7a If you had a test at the hospital (X-ray, Camera test or scan): How did you find the test?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Not Comfortable</td>
<td>5 - Comfortable</td>
<td>11</td>
<td>12</td>
<td>26</td>
</tr>
</tbody>
</table>

11 - Worse than Expected
40 - Better than Expected
Figure 27. Information about the diagnostic test

Question 7b If you had a test at the hospital (X-ray, Camera test or scan): Was the test as you expected?

The majority of the patients (71%) however found having a diagnostic test before seeing a hospital consultant as acceptable (Figure 28).

Figure 28. Diagnostic test prior to clinic appointment

Question 8 If you had the test at your FIRST visit to the hospital, would you rather have seen a consultant in a clinic beforehand?
Figures 29 to 33 show the responses to some of the other queries posed to the patients. These included queries about the time taken to receive the appointment, information given to the patients and their experiences at the hospital.

**Figure 29. Referral to Hospital appointment time**

Question 1 Do you feel the time interval between referral from your GP and being seen in the Hospital was acceptable?

![Bar chart showing the responses to the question about referral time](image)

**Figure 30. Information given to the patients**

Question 2 Did you receive adequate information before coming to the Hospital?

![Bar chart showing the responses to the question about information given](image)
Figure 31. All queries satisfactorily answered?

Question 5 When you attended the hospital the first time, were all your questions satisfactorily answered?

![Bar chart showing satisfaction levels from 1 (Unsatisfactory) to 5 (Very Satisfactory).]

Figure 32. Able to ask questions at the hospital?

Question 6 Were you given enough opportunity to ask questions at the Hospital on your first visit?

![Bar chart showing opportunity levels from 1 (Not Enough) to 5 (Enough).]
Figure 33. Satisfied with the hospital treatment?

Question 10 Was the treatment you received explained to you satisfactorily?

1 - Not Satisfactorily 5 - Satisfactorily

Figure 34. Overall care at the hospital

Question 12 How satisfied are you with your overall care at the hospital

1 - Not Satisfied 5 - Very Satisfied
Discussion

In the current atmosphere of increasing numbers of colorectal referrals nationally combined with limited availability of resources within the NHS and the pressure to improve the management of cancer in the UK, an increasing need is being felt to develop an efficient and cost effective method of prioritising colorectal referrals. The two week wait referral system introduced by the government to help the GPs identify and fast-track ‘high-risk’ patients suspected to have colorectal cancer, has failed to make a significant impact. As a consequence significant efforts have been made nationally to try and find a viable alternative. Suggestions to treat all referrals as urgent or to endoscope all referrals have obvious disadvantages in terms of resources and manpower needed for their implementation.

The patient consultation questionnaire developed by Selvachandran combines an exhaustive patient history through a questionnaire with a computerized scoring system. The system has been shown to be significantly more specific than the NHS guideline based 2WW system making colorectal cancer detection more efficient. Moreover, the system does not have any significant associated resources or manpower implications.

Our survey of patients, who completed the PCQ and were subsequently investigated and or treated at the hospital, has shown that generally these patients found completing the questionnaire easy and also less embarrassing than discussing their colorectal symptoms with the doctor. Even patients from the ethnic minority who do not speak English as their first language were able to complete the questionnaire, albeit with some help from friends and family, and most did not feel the need for a translated questionnaire although this was readily available to them. We
have therefore shown that language need not be a barrier to using the questionnaire. Most of those who needed help in completing the questionnaire (amongst both the ethnic and the white population) belonged to the >40 years age group (see table 8.2). This may be due to a smaller number of English speaking patients in the older ethnic population as compared to the third generation younger group. The older population in general may have needed help to complete the questionnaire due to associated medical conditions.

A significant number of patients referred (both through the 2 week wait rule and traditional letter route) have a diagnostic test prior to appointment with a consultant at the hospital. Most of the patients when questioned found this entirely acceptable (Figure 28). However the diagnostic tests performed were sometimes not what the patients expected (Figure 26). Improved communication and more detailed written information about the tests should help overcome this concern.

There was general satisfaction with the overall care of the patients at the hospital (figure 34).

Conclusion

The patient consultation questionnaire is a user-friendly document which is easy to complete and can be an effective tool in prioritising colorectal referrals. We propose a pilot study to test its use in the population as a viable alternative to the current 2WW referral system.
Future work, Presentations and Publications

The Future:

The successful validation of the PCQ-WNS system at Leicester and the demonstration of its advantage over the current 2WW referral system to prioritise colorectal referrals in Leicester, some further projects have been planned as a follow on from this thesis project. These are as follows:

1. Discussions with the Department of Health (DoH), Cancer Policy team are ongoing. The validation of the PCQ-WNS system in Leicester and a similar assessment of the system done in Wales has been discussed with the DoH and the author (Rai S) has made a formal presentation of the main findings of this thesis. The DoH is now looking at the feasibility of a pilot project in the UK to use the PCQ-WNS system as an alternative or adjunct to the current 2WW referral system.

2. Pilot project at Leicester. Discussions are underway for planning a pilot project at Leicester where a group of GPs or GP practices would be invited to consider using the PCQ-WNS system at their surgeries to study the user-friendliness of the PCQ-WNS system. Once agreed upon, the software and the other help would be provided to the GPs. The author (Rai S) hope to be actively involved in such a project along with other Colorectal surgical and Gastroenterology consultants at Leicester.
Presentations:

1. Rai S, Thomas WM, Jameson JS. Prioritisation of Colorectal referrals. Leicester Digestive Diseases Week, Leicester May 03.


Publications:


3. **Rai S**, Kelly MJ. Prioritization of colorectal referrals - a review of the ‘Two week wait’ referral system and recent advances. To be published as a chapter in the book titled *Recent advances in colorectal cancer* 2006; *in press*.

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APPENDICES

1. 2WW Referral guidelines
2. The UHL straight to test pathway and protocol
3. Patient Consultation Questionnaire (PCQ)
4. Transfer of data from paper to electronic form (PCQ/WNS)
5. Patient satisfaction Questionnaire (PSQ)
Appendix 1
Guidelines for ‘Two week wait’ referrals
It is recommended that these symptoms and sign combinations WHEN OCCURING FOR THE FIRST TIME should be used to identify patients for urgent referral under the two week wait standard.

- Rectal bleeding and change in bowel habit to increased frequency of defaecation and/or looser stools and persistent for at least 6 weeks
- Rectal bleeding without anal symptoms over 60 years
- Palpable intraluminal rectal mass felt pr on digital rectal examination in all ages
- Palpable abdominal mass in all ages
- Change in bowel habit, increased frequency of defaecation and/or looser stools and persistent for at least 6 weeks in patients over 60 years
- Unexplained iron deficiency anaemia microcytic, hypochromic hb below 10g/dl in post menopausal women and 11g/dl in men of all ages, thought likely to be due to Colorectal cancer

NB: Patients with the following symptoms and no abdominal or rectal mass, are at very low risk of cancer*:

- Rectal bleeding with anal symptoms
- Change in bowel habit to decreased frequency of defaecation and harder stools without bleeding
- Abdominal pain without clear evidence of intestinal obstruction
- Anal symptoms include soreness, discomfort, itching, lumps and prolapse as well as pain

* If there is significant cause for concern for this group of patients please make a standard referral to the Consultant's clinic in the usual way.

URGENT REFERRALS OF SUSPECTED COLORECTAL CANCER (TWO WEEK WAIT) SHOULD ONLY BE MADE VIA THE FOLLOWING ROUTES:

Glenfield Hospital: Fax: (0116) 250 2777 (Referrals) Tel: (0116) 250 2613 (Queries)

Leicester General Hospital: Fax: (0116) 258 4733 (Referrals) Tel: (0116) 258 4735 (Queries)

Leicester Royal Infirmary: Fax: (0116) 258 5840 (Referrals) Tel: (0116) 258 6257 (Queries)

For direct referrals to community hospitals, see contact numbers on reverse of pro-forma

Leicestershire and Rutland Cancer Services

Version 3 – April 2003
2 WEEK WAIT REFERRAL

Please state if you have any preference of consultant for this referral

PATIENT:

Surname ...........................................(Mr/Mrs/Miss/Ms) 
First name .................................................................
Address ..................................................................
……………………………………………………………..Post Code ................................
Date of Birth .............................................. Age ...........
Telephone No. (Home) ..........................................................
Telephone No. (Daytime) ....................................................
Religion ................................................ Language Spoken
NHS No. ........................................ Hospital No. ........................................

GP Name and Details:

RELEVANT HISTORY * (please tick box)

Rectal bleeding and change in bowel habit to increased frequency of defaecation and/or looser stools and persistent for at least 6 weeks

Rectal bleeding without anal symptoms over 60 years

Palpable intraluminal rectal mass felt on digital rectal examination in all ages

Palpable abdominal mass in all ages RIF □ LIF □ EPIGASTRIC REGION □

Colorectal Cancer diagnosed in another centre

Change in bowel habit to increased frequency of defaecation and/or looser stools and persistent for at least 6 weeks in patients over 60 years

Unexplained iron deficiency anaemia microcytic, hypochromic hb below 10g/dl in post menopausal women and 11g/dl in men of all ages, thought likely to be due to Colorectal cancer

DURATION OF SYMPTOMS

< 6 weeks □ > 6 weeks □

IMPORTANT PATIENT FACTORS

Does the patient have diabetes? YES □ NO □

Is the patient unable to climb a flight of stairs unaided? YES □ NO □

Does the patient have renal failure? YES □ NO □

Does the patient have MRSA? YES □ NO □

Signed ........................................ Date ........................................

ACTION

Please fax completed form to the appropriate hospital (dedicated 2-week wait fax line)

Leicester General Hospital (0116) 258 4733
Leicester Royal Infirmary (0116) 258 5840
Glenfield Hospital (0116) 250 2777

* Fax numbers for the community hospitals are listed on the back of this form

2 WEEK WAIT PATIENTS WILL BE ‘FAST TRACKED’ THROUGH THE SYSTEM. WE WOULD WELCOME A REFERRAL LETTER TO BE FAXED WITH THIS FORM GIVING ANY OTHER RELEVANT INFORMATION, BUT IT IS NOT ESSENTIAL.

*If your patient’s symptoms do not correspond with these criteria, you may still make an “urgent referral” direct to the consultant’s clinic in the usual way
Appendix 2
The Leicester ‘Straight-to Test’
Diagnostic Protocol
Referral and Booking Process for University Hospitals of Leicester Colorectal Diagnostic Investigations Protocol

2 Week Wait Referrals

2WW referral faxed by GP to hospital site-specific 2WW office

Referral information reviewed i.e. symptom, age, and important patient factors

Does the patient meet the required criteria for the proposed investigation?

YES

Using diagnostic investigations protocol, identify proposed investigation 'under protocol'

2ww staff to complete generic colon imaging request form and date

2ww staff makes initial contact with relevant dept (phone/fax/visit)

Where possible, leave the relevant dept with date and time of appt for the proposed investigation. Where applicable, make fu appt in op.

2WW staff sends notification fax of 2ww referral to GP, along with date and time of diagnostic investigation within 24 hours of receipt of referral

NO

If not enough information on referral proforma/letter, 2ww staff to ring GP

If patient having FOS/ BAE copy request form and referral letter, to enable each dept to have their own copy

As locally agreed contact named GI clinicians in order to identify the diagnostic investigation

Ensure Consultant receives referral information and colon imaging form and to make decision upon choice of test within 24 hours of receipt of referral into hospital.

Radiologist CR Surgeon /admin & clerical staff to inform 2ww staff to collect referral
Referral and Booking Process for University Hospitals of Leicester Colorectal Diagnostic Investigations Protocol

Named Consultant/Dear Doctor letter

- Referral letters reviewed by Consultant on a daily basis suspected cancer referrals identified
- Diagnostic investigation identified using protocol by consultant
- Consultant to attach completed generic colon imaging form to referral letter and place in protocol tray (in secs’ office)
- Referral letters reviewed by Consultant on a daily basis suspected cancer referrals identified
- Where possible, leave the relevant dept with date and time of appt for the proposed investigation & make follow up appointment where applicable.
- Medical secretaries to telephone 2ww team to inform that referrals are ready for collection
- 2ww staff makes initial contact with relevant dept (phone/fax/visit) see booking protocol for contact details
- If patient having FOS/ BAE copy request form and referral letter, to enable each dept to have their own copy
<table>
<thead>
<tr>
<th>PRESENTING SYMPTOMS</th>
<th>AGE CRITERIA</th>
<th>DIAGNOSTIC INVESTIGATIONS*</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Bleeding, Change of Bowel Habit to increased frequency of defaecation and/or looser stools and persistent for at least six weeks</td>
<td>All ages</td>
<td>Flexible Sigmoidoscopy and Barium Enema Coloscopy Colonoscopy CT Colonography</td>
<td>Patients presenting with these symptoms will have a whole colon examination on the same day using full bowel preparation. The patient will then be reviewed in Outpatients for the results. Patients under 45 should not have an X-ray colon test (unless F/sig -ve and referred by GI Consultant), IRMER Regulations.</td>
</tr>
<tr>
<td>Rectal Bleeding without anal symptoms</td>
<td>Recommended over 60 years &amp; Discretionary over 45 Years.</td>
<td>Flexible Sigmoidoscopy Guidance Note: Aim to reach the splenic Flexure</td>
<td>Patients presenting with this symptom will attend a direct access, named Consultant Rectal Bleed clinic and will be reviewed by a Colorectal Surgeon.</td>
</tr>
<tr>
<td>Change of Bowel Habit, increased frequency of defaecation and/or looser stools persistent for at least six weeks</td>
<td>Over 60 years</td>
<td>Barium Enema CT Colonography Colonoscopy</td>
<td>Patients presenting with these symptoms will have a whole colon examination. The patient will be reviewed in Outpatients with the results.</td>
</tr>
<tr>
<td>Patients with palpable abdominal mass</td>
<td>All ages</td>
<td>Ultrasound Scan CT</td>
<td>Patients presenting with this symptom will have an ultrasound scan carried out by a Consultant GI Radiologist (GI MDT). The patient will then be reviewed in Outpatients with the results.</td>
</tr>
<tr>
<td>Patients with palpable Intraluminal Rectal Mass</td>
<td>All ages</td>
<td>Sigmoidoscopy and biopsy(FOS or Rigid)</td>
<td>Patients presenting with this symptom will attend a direct access, named Consultant appointment in Endoscopy or Outpatients.</td>
</tr>
<tr>
<td>Patients with unexplained iron deficiency anaemia microcytic, hypochromic Hb below 11g/dl in men Hb below 10g/dl in women</td>
<td>All ages Post Menopausal</td>
<td>Barium Enema CT Colonography Colonoscopy</td>
<td>Patients presenting with this symptom will have a whole colon examination. Patients under 45 should not have an X-ray colon test unless referred by a GI Consultant, IRMER Regulations. The patient will then be reviewed in Outpatients with the results.</td>
</tr>
</tbody>
</table>

Patients presenting with these specific symptoms should be referred via the 2 week wait referral standard upon where the appropriate diagnostic test will be organised. Please do not order any diagnostic investigation prior to referral for these patients.

* The selection of diagnostic investigations will be in accordance with individual patient factors and local resources. Please indicate on the referral proforma if the following important factors apply to your patient: Diabetes Difficulty in taking bowel preparation Limited mobility
Colon Imaging Request Form

Patient Unit Number

Patient Name

DOB

Barium Enema and Flexible Sigmoidoscopy (same day)

Flexible Sigmoidoscopy only

Barium Enema only

Ultrasound

CT Scan

CT Cologram

Colonoscopy

Date

Cancer Administration Team
Glenfield Hospital
Ext: 2613
Appendix 3
The Patient Consultation Questionnaire
Leicester Royal Infirmary
University Hospitals of Leicester NHS Trust
Leicester LE1 5WW

Bowel Symptoms Assessment Questionnaire

It is VITAL that you DOUBLE CHECK to see that you have answered all the questions.

Hospital No: CROSC Ref No:

Your Full Name: [Patient label]
Your Date of Birth: 
Your Age: 
Marital Status: 
Your Telephone Number: 
Your Occupation: 
Your Country of Birth: 

Please place a tick ☑ in the appropriate boxes

1. Have you seen blood from the back passage? (If “Yes” continue below. If “No” go to question 2 on next page.)
   Yes ☐ No ☐
   a. State whether blood is
      Fresh or Bright red ☐
      Old or Dark ☐
      Both Fresh & Old ☐
      Uncertain ☐
   b. is the blood
      Seen on toilet paper only ☐
      Separate from stool ☐
      Mixed with stool ☐
      Separate and mixed in stool ☐
      Uncertain separate or mixed ☐
   c. When you see blood in stool is it
      Small amount ☐
      Large amount ☐
   d. How often have you seen blood when opening your bowels?
      Every day ☐
      Every few days ☐
      Every week ☐
      Every few weeks ☐
      Every month ☐
      Every few months ☐
      Only once or twice in the past year ☐
   e. For how long have you seen blood when opening your bowels?
      Less than four weeks ☐
      4 – 6 months ☐
      1 – 2 years ☐
      1 – 3 months ☐
      6 – 12 months ☐
      Over 2 years ☐
   f. During the past four weeks has the bleeding
      Got worse ☐
      Improved ☐
      Remained the same ☐
      Completely Settled ☐

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2. Do you have any changes in your bowel habit?
   If "Yes" continue below. If "No" go to question 3 below.
   a. What changes have there been in your bowel habits?
      - Loose Motion (or Diarrhoea)
      - Constipation (that is less frequent and harder stools)
      - Alternating loose motion and constipation
      - Normal Motion or Stools
   b. Do you open your bowels more frequently than normal to you?
      - Yes, 2 – 4 times more per day
      - Yes, 5 – 6 times more per day
      - Yes, 7 – 10 times more per day
      - No
   c. Is the increase in opening your bowels worse at any particular time of day?
      - Yes, in the morning
      - Yes, at night
      - No
   d. Do you have to "rush" to have your bowels open? Yes
   e. For how long have you had these symptoms?
      - Less than four weeks
      - 4 – 6 months
      - 1 – 2 years
      - Over 2 years
   f. During the past four weeks has the change in bowel
      - Got worse
      - Improved
      - Remained the same
      - Completely Settled
   g. What has been your normal bowel habit?
      - Normal Motion or Stools
      - Constipation (that is less frequent and harder stools)
      - Loose Motion
      - Alternating loose motion and constipation

3. Do you see
   - Slime (jelly-like fluid) in your motion Yes
   - Slime and blood mixed in your motion No

4. Do you feel that you have not emptied your bowels satisfactorily when your bowels are opened? Yes

5. Do you have symptoms around your back passage? Yes
   (If "Yes" continue below. If "No" go to question 6 on next page.) No
   - Pain on opening your bowels
   - Irritation and itching
   - Lump or swelling at back passage
   - Leakage or soiling at back passage
   - How long have you had these symptoms?
      - Less than four weeks
      - 4 – 6 months
      - 1 – 2 years
      - Over 2 years

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6. **Do you have pain in your tummy (abdomen)?**
   (If “Yes” continue below. If “No” go to question 7 below.)
   - **Yes**
   - **No**
   a. Lower tummy pain
      - Left sided tummy pain or discomfort
      - Spasms of tummy pain
      - Right sided tummy pain or discomfort
      - Pain all over tummy
   b. Do you get bloating of your tummy (swollen & uncomfortable) recently?
      - **Yes**
      - **No**
   c. For how long have you had these abdominal symptoms?
      - Less than four weeks
      - 1 – 3 months
      - 4 – 6 months
      - 1 – 2 years
      - Over 2 years
   d. During the past four weeks has the abdominal symptoms got worse
      - Got worse
      - Improved
      - Remained the same
      - Completely settled

7. **Have you lost weight recently?**
   (If “Yes” continue below. If “No” go to question 8 below.)
   - **Yes**
   - **No**
   - Over half a stone in three months
   - Weight loss does not concern you
   - Due to dieting

8. **Do you have loss of appetite?**
   - **Yes**
   - **No**

9. **Have you felt excessively tired?**
   - **Yes**
   - **No**

10. **Do you take regular medication?**
    - Iron tablets
    - Steroids / Prednisolone tablets
    - Medication for diabetes
    - Tablets for thinning blood / Warfarin
    - Any other medication (please state which)

11. **Have you had any of these illnesses in the past?**
    - Bowel polyps
      - **Yes**
      - **No**
    - Colitis (Inflammation of the bowel)
      - **Yes**
      - **No**
    - Cancer *
      - **Yes**
      - **No**

*If you have had cancer – in which part of the body? ___________________________
12. Have any of your close relatives suffered cancer?  
   (If “Yes” continue below. If “No” go to question 13 below.)

   (*When stating grand parents, aunts and uncles please tick father’s or mother’s side.)

<table>
<thead>
<tr>
<th>Relation</th>
<th>Father’s side</th>
<th>Mother’s side</th>
<th>Age when Cancer found</th>
<th>Part of body</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

13. Please give us any other information that you think may be relevant

_________________________________________________________________________
_________________________________________________________________________
_________________________________________________________________________

14. Did you obtain help to answer this questionnaire?  

   Yes  [ ]  No  [ ]

Signature: ___________________________  Date: _______________

Thank you.

Please remember to return your questionnaire in the envelope provided

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Appendix 4
Transfer of data from paper to electronic form
To enable us to arrange tests and treatment without delay please fill in this form and send it back to us as soon as possible.

Name: [Name] Donald
DOB: 4th May 1944
Hosp no.: 7654321A

If you have seen blood from the back passage, please tick "Yes" in the appropriate box.

1. Have you seen blood from the back passage?
   - Yes □ No □

2. Did you see the blood in fresh or bright form?
   - Fresh or Bright □

3. When you see blood in fresh form, do you see it on tissue only or also in the stool?
   - Tissue only □

4. How often have you seen blood when opening your bowels?
   - Every few days □

5. For how long have you seen blood when opening your bowels?
   - 6 - 12 months □

6. Abdominal Symptoms
   - Lower Abdo Pain □
   - Upper Abdo Pain □
   - Spasms Abdo Pain □
   - Nausea □
   - Vomiting □
   - Abdominal Mela □

Weighted Numerical Score: 59
Appendix 5
The Patient Satisfaction Questionnaire
PATIENT SATISFACTION QUESTIONNAIRE
University Hospitals of Leicester

You had recently taken part in a survey in which you had most kindly completed a bowel symptoms questionnaire around the time of your visit to the hospital for your bowel related problems. To help us improve our services further please answer the following questions which will only take a couple of minutes of your time. Once again, your responses will be completely confidential and anonymous and in no way affect any future treatment that you may have at the hospital.

Please answer the questions using the scale of 1 to 5 by circling the number that best represents how you feel

Please return the completed questionnaire to us in the envelope provided

1. Do you feel the time interval between referral from your GP and being seen in the Hospital was acceptable?

Unacceptable 1 2 3 4 5 very acceptable

2. Did you receive adequate information before coming to the Hospital?

Unacceptable 1 2 3 4 5 very acceptable

3. How did you find completing the Bowel Symptoms Questionnaire around the time of your visit to the hospital?

Difficult 1 2 3 4 5 Easy

4. Was it less embarrassing filling out the Bowel Symptoms Questionnaire than telling the doctor your symptoms at the surgery/Hospital?

More 1 2 3 4 5 Less

5. When you attended the hospital the first time, were all your questions satisfactorily answered?

Unsatisfactory 1 2 3 4 5 Very satisfactory

6. Were you given enough opportunity to ask questions at the Hospital on your first visit?

Not enough 1 2 3 4 5 Enough
7. If you had a test at the hospital (X-ray, Camera test or scan):
   (a) How did you find the test?

   Not comfortable 1  2  3  4  5 Comfortable

   (b) Was the test as you expected?

   Worse than 1  2  3  4  5 Better than expected

8. If you had the test at your FIRST visit to the hospital, would you rather have seen a consultant in a clinic beforehand?

   Yes did not matter Not applicable

9(a) Did you have further treatment for your bowel related symptoms?

   Yes No

   (b) If you did have further treatment, please state the treatment you had:

                      Where ____________________________ When ____________________________

10. Was the treatment you received explained to you satisfactorily?

    Not satisfactorily 1  2  3  4  5 Satisfactorily

11. How much pain did you have after treatment?

    Severe 1  2  3  4  5 None

12. How satisfied are you with your overall care at the hospital?

    Not satisfied 1  2  3  4  5 very satisfied

13. Did your symptoms improve after treatment?

    Not improved 1  2  3  4  5 much improved
14. We would welcome any comments you may have on how to improve the services we provide at the hospital.

Please answer these last 3 questions before finishing.
Please circle the answer that applies to you:

A) Your age
   15-25  26-35  36-45  
   46-55  56-65  66-75  
   76-85  86-95  96-105  

B) Your Sex
   Male   Female

C) Hospital
   Seen at
   Leicester Royal
   Leicester General
   Glenfield

Many thanks for taking time to complete this questionnaire.

If you have any queries regarding this questionnaire please do not hesitate to contact Mr Sajal Rai, Research Fellow, Glenfield Hospital, on 0789 9954923.