SOME ASPECTS OF THE IMPACT OF CHRONIC ILL HEALTH ON PATIENTS WITH INFLAMMATORY BOWEL DISEASE:

GILLIAN ANNE MOODY
NOT WHAT THEY WANT BUT WHAT IS GOOD FOR THEM!

Oliver Cromwell, 1645.
STATEMENT:

The accompanying thesis submitted for the degree of Doctor of Medicine entitled Some aspects of the impact of chronic ill health on patients with inflammatory bowel disease is based on work conducted by the author at Leicester General Hospital, mainly during the period between 1st August 1991 and 1st August 1993.

All the work recorded in this thesis is original unless otherwise acknowledged in the text or by references.

None of the work has been submitted for another degree in this or any other University.

Most of the work has been published:

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HYPOTHESIS:

Patients with inflammatory bowel disease have an impaired quality of life.

It should be possible to develop a measurement of patients' quality of life, specific to inflammatory bowel disease.

AIMS

The aims of this thesis are:

1. To identify areas of patient need and to compare their views with physicians perceptions of care delivered.

2. To investigate specific areas of need and their frequency amongst a defined population. This will include assessments of:
   i) Sexual dysfunction amongst patients with inflammatory bowel disease.
   ii) Fertility amongst married patients with inflammatory bowel disease.
   iii) The attitudes of employers and insurance companies to patients with inflammatory bowel disease.
   iv) The incidence of colorectal cancer in patient with long standing ulcerative colitis

3. Integral to the study will be the development of a valid, reliable and concise assessment tool to measure the quality of life in patients with inflammatory bowel disease. This will be compared with validated tests such as the Sickness Impact Profile and will be assessed in patients with varying degrees of disease activity.
Justification for this thesis:

This thesis describes various aspects of the impact of chronic inflammatory bowel disease on quality of life. A concise validated, reliable and tested quality of life measure, designed for use in conjunction with the usual clinical parameters of disease remission is presented and tested for reliability and validity. Such a scale was developed by addressing key issues identified during joint discussions between patients and health workers and by exploring patients' perceived problems along with their strategies for coping.

Traditional interventions which have been demonstrated to be useful in other chronic illnesses were also investigated such as patient education, access to self-help groups and the role of alternative diets.
CHAPTER 1: INFLAMMATORY BOWEL DISEASE
1.1 INTRODUCTION:

In order to understand how a chronic and debilitating disease like ulcerative colitis or Crohn’s disease might affect a person’s quality of life it is important to be familiar with its clinical course and prognosis as well as some knowledge of its frequency and what its aetiology might be.

In the European Union between a quarter and a half a million people are affected by inflammatory bowel disease (IBD). This condition comprises a group of chronic disorders primarily affecting the gastrointestinal tract and includes ulcerative colitis (UC) and Crohn’s disease (CD), both of which are characterised by their chronic relapsing and remitting course with diarrhoea, abdominal pain and rectal bleeding. At present there is no cure for Crohn’s disease and although effective medical and surgical measures exist for patients with ulcerative colitis, patients need to come to terms with these diseases often during their most productive years. The clinical management of IBD can require repeated and frequent hospitalisation and so is responsible for a considerable cost to health care systems in Europe. In addition the chronic nature of these diseases and the need for medical and surgical intervention may have serious consequences for a patient’s quality of life. The purpose of this thesis is BOTH to investigate the reality of patients’ anxieties and to develop a measure to assess their impact.

This chapter reviews the clinical course of Crohn’s disease and ulcerative colitis as well as specific areas of difficulty including perineal disease in Crohn’s disease.

1.2 CROHN’S DISEASE:

The introduction of uniform criteria of case definition is an essential prerequisite for any international comparisons of IBD and such agreed criteria now exist for inflammatory bowel disease (Lennard-Jones 1989, Shivananda, Hordijk, Ten Kate et al 1991). Although many cases of ulcerative colitis and colonic Crohn’s disease can be accurately classified on the basis of composite findings, differentiation remains difficult in 10% of patients (O’Morain,
Tobin, Leen et al 1989). This is due to the limited morphologic response of the colon to disease, an incomplete expression of IBD, the occurrence of indeterminate colitis, and the clinical mimicry of IBD by other conditions, such as infection and ischaemia.

1.2.1 Historical aspects;
In 1932 Crohn, Ginzburg and Oppenheimer described 14 young adults with chronic inflammatory disease of the ileum associated with fibrotic stenosis of the gut and multiple fistulae (Crohn, Ginzburg & Oppenheimer 1932). Earlier reports included one by Dalziel in Glasgow in 1913 (Dalziel 1913), but it was only following Crohn’s publication that the disease became widely recognised. Recent reviews of the world literature suggests that Crohn’s disease is most common in North America and northern Europe, emerging in southern Europe and least common in other regions and this has been confirmed by a recent study throughout the European Union (Shivananda, Lennard-Jones, Logan et al 1996).

1.2.2 Clinical course;
Crohn’s disease can occur anywhere in the gastrointestinal tract from the mouth to the anus. In earlier studies ileocolonic disease accounts for more than half the cases but colonic disease alone is not uncommon and now represents a growing number of cases. Crohn’s disease comprises chronic inflammation involving all layers of the bowel wall and is often associated with granulomas and deep fissuring ulceration. There may also be a lymphocytic infiltration. Whilst non-caseating granulomas are diagnostic of Crohn’s disease, they are not always present and the diagnosis can be made in their absence. The inflammation is discontinuous with clearly demarcated inflamed areas separated by normal bowel (skip lesions). It differs in some important respects to ulcerative colitis in its propensity to present with a large number of distressing complications which can include perianal and perirectal abscesses and fistulae, intestinal obstruction or intra-abdominal fistulae or abscesses.

The disease predominantly occurs in people in their second, third and fourth decades but may appear at any age. It is suggested the mean age at diagnosis is 31 years for patients with ileocolic disease and 33 years when the disease is restricted to the colon. Patients with disease confined to the anorectum tend to be slightly older (39 years) with a shorter duration of symptoms (Kornbluth, Salomon & Sachar in Sleisenger & Fordtran 1993).
Any consideration of the clinical features of Crohn’s disease must emphasize the striking variability observed from patient to patient. The typical patient first described by Crohn was a young adult with persistent diarrhoea which was not frankly bloody. The diarrhoea is accompanied by fever and right lower quadrant pain. Anorexia, nausea and vomiting may also be present. Examination of the abdomen may reveal tenderness which can occasionally be rebound in nature, or a palpable firm irregular mass of matted loops of intestine. In some circumstances the similarity to acute appendicitis is so great that the diagnosis is made at an emergency laparotomy.

Symptoms may persist for days or weeks but early in the course of the disease they can subside spontaneously. However, in most cases they usually recur within several weeks or months (Kornbluth et al in Sleisenger & Fordtran 1993). This intermittent course of the disease can result in a delay in diagnosis which may be substantial (Shivananda et al 1991). When the disease is confined to the ileum, diarrhoea is usually of moderate severity with no more than 5 or 6 movements per day. These are loose and not usually bloody. Urgency and incontinence are only a feature if the colon is involved; for patients a frequency of defecation as great as this can be distressing (Godber 1989). Abdominal pain tends to be steady and localised to the right lower quadrant and superimposed upon this there may be intermittent periumbilical colic prior to defecation. There is also often a low grade fever.

Although Crohn’s disease most commonly presents with pain and diarrhoea its subsequent clinical course varies considerably. This is partly as a consequence of the variable distribution of the disease. When pathology is confined to the ileum small bowel obstruction is the most frequent clinical problem whereas patients with ileocolonic disease may develop perirectal complications.

In the majority of patients gradual deterioration occurs over a period of years with shorter and shorter asymptomatic intervals, difficulty in maintaining body weight and increasing fatigue and lassitude. However about 10% of patients remain completely asymptomatic for many years despite 2 attacks of regional enteritis (Kornbluth et al in Sleisenger & Fordtran 1993). A diffuse form of the disease is seen in 5% of cases where jejunum, ileum and colon are extensively involved and this form of the condition often progresses rapidly.
1.2.3 Outcome:

Longitudinal community based studies from Cardiff (Mayberry, Newcombe & Rhodes 1980 (c)) and Stockholm (Storgaard, Bischoff, Hendriksen et al 1979) have shown no reduction in mortality during the last thirty years although surgical and medical treatment has probably made life more tolerable. In most centres mortality is twice the expected figure for the general populations although this was not so in a comprehensive study from Copenhagen (Binder, Hendriksen & Kreiner 1985) or in Leicestershire where the overall mortality in 610 European patients with Crohn’s disease was not significantly greater than expected (SMR = 71.8%), (Probert, Jayanthi, Wicks et al 1992 (a)). Population based studies (Hellers 1979, Mayberry et al 1980 (c), & Binder, Hendriksen & Kreiner 1985) have identified patients at greatest risk as people under 20 years old at diagnosis, those with extensive disease, particularly affecting the small bowel, and newly diagnosed patients. In Birmingham (Prior, Gyde, Cooke et al 1981) when the effect of treatment on mortality was assessed, steroids where found to be associated with an increase in the SMR from 180 to 360. Of course, this may simply reflect the severity of disease in those needing steroids.

Patients with Crohn’s disease also have an increased risk of developing carcinoma of the gastrointestinal tract. The widespread nature of the disease predisposes the patient to diffusely infiltrating cancers as well as multiple cancers around localised areas of dysplasia or even at sites remote from macroscopic disease. Hoffman, Taft, Wheelis et al (1977) found a wide range for the relative risk of adenocarcinoma in the small intestine of between 6 and 220. In a review of 449 patients with Crohn’s disease, Weedon, Shorter, Ilstrup et al (1973) found 12 cases of cancer. They estimated that the probability of developing colorectal cancer over a 20 year period was 2.8%, which was 20 times greater than expected in an age and sex matched population. In Birmingham only nine deaths due to cancer were reported compared with the expected four which suggested the risk was much less than previously thought, although it probably increases with time (Prior et al 1981).

More recently the risks of developing colorectal cancer in extensive Crohn’s colitis have been re-examined. Gillen, Walmsley, Prior et al (1994) reviewed 281 adult patients living in the West Midlands of whom 44.5% had extensive colonic involvement and found an 18-fold increase in the risk of developing colorectal cancer, with an absolute cumulative frequency
of risk for developing cancer of 8% at 22 years from onset of symptoms.

Although patients often want to know their prognosis absolute statements in Crohn’s disease are rarely justified because of the clinical variability of the condition. Despite the usual clinical course and the many complications of the disease the vast majority of patients today have a normal life span although its quality may be significantly affected.

1.2.4 Perianal disease;
Perianal involvement is a significant factor in overall morbidity amongst patients with Crohn’s disease. Its reported incidence varies in hospital series from 8.5 to 93% (Atwell, Duthie & Goligher 1965, Lockhart-Mummary & Morson 1964, Schofield 1965). The higher figures probably reflect the inclusion of skin tags and haemorrhoids in the analysis. If only abscesses and fistulae are considered the frequency is closer to 20% of patients experiencing these complications (Williams, Hellinger, Larach et al 1995). Symptoms of perianal disease range from perianal pain and itching to a mucopurulent discharge with faecal soiling. A particularly unpleasant complication is the development of a rectovaginal fistula where either flatus or faeces are passed through the vagina. There may be a purulent discharge, chronic vaginitis or frank faecal leakage from the vagina with an associated faecal odour. Incontinence may indicate sphincteric involvement. Figures 1.1 and 1.2 demonstrate examples of significant perianal Crohn’s disease and cutaneous fistulae.

There has been considerable debate about the role of conservative treatment of perianal disease (Sweeney, Ritchie & Nicholls 1988) as compared with early and aggressive surgery (Williams et al 1995) but few investigators have concentrated on the impact of these distressing symptoms on patients quality of life (Allan, Linares, Spooner et al 1992, Irvine 1995). Allan and colleagues developed a clinical index to investigate the consequences of perianal disease. Parameters included in the score were symptoms related to tissue tension or inflammation (spontaneous perianal pain or itching), others related to sphincter dysfunction (painful defecation or anal leakage) and inhibition of normal activity because of perianal discomfort (locomotion, social and sexual intercourse). They concluded that anal pain, pain following defecation and inhibition of locomotion were the most discriminant symptoms of impaired quality of life. The effects of perianal disease on sexual intercourse have been given
FIGURE 1.1: CUTANEOUS FISTULAE IN CROHN'S DISEASE
Cutaneous fistulae on the anterior abdominal wall

Anal fistula in Crohn's disease

Reproduced with kind permission from Harcourt Brace and Company Medical Publishers
FIGURE 1.2: SEVERE PERIANAL DISEASE IN CROHN'S DISEASE
Inflammatory oedematous tags

Gross inflammation of the vulva extending from the anus

Inflammatory oedematous tags with severe ulceration
limited attention in the literature. Irvine (1995) developed an index for measuring disease activity for use specifically in perianal disease. It looked at similar parameters to Allen et al (1992) and concluded that few patients avoided sexual intercourse and that those who did generally tended to have more severe disease.

1.2.5 Aetiology:

The cause of Crohn’s disease remains elusive, some investigators believe it is secondary to some aspect of western civilisation, others believe infection may play a part, while considerable research has concentrated on immunological mechanisms. Likely theories include:

Genetic factors and family risk:

There has been interest in familial aspects of IBD since the 1960s (Almy & Sherlock 1966, Farmer, Michener & Mortimer 1980, Kirsner & Spencer 1963, Monsen, Brostrum, Berglund et al 1987 & Sherlock, Bell, Steinberg et al 1963). However, there are only a few studies which have measured the risk to first degree relatives of developing IBD (Mayberry, Rhodes & Newcombe 1980a, Weterman & Pena 1984 & Lashner, Evans & Kirsner et al 1986). Strong evidence of a genetic predisposition in Crohn's disease does exist but these levels of risk do not support a simple Mendelian pattern of inheritance, but suggest that several factors may be involved. Satsangi, Grootscholten, Holt et al (1996) have shown consistent clinical patterns in many families with IBD. Others have suggested that IBD arises in people with a genetic predisposition and who are exposed to an unidentified environmental factor (Probert, Jayanthi, Hughes et al 1993b).

Infective agents:

Ileocaecal disease occurs in animals and is caused by a variety of organisms. Attempts to transmit human Crohn's disease to animals have produced inconsistent results. Pathological similarities between Crohn's disease and tuberculosis have focused attention on the role of mycobacteria. Initially this centred on M. kansasii, but more recently the possible involvement of M. paratuberculosis has received attention (Vary, Andersen, Green et al 1990, Hermon-Taylor, Moss, Tizard et al 1990).
Another candidate for an infectious agent is the measles virus. Pounder and a group of researchers at The Royal Free Hospital have demonstrated measles virus nucleocapsids in diseased tissue in five out of six cases examined. The virus was particularly common in foci of granulomatous inflammation demonstrated using a gold labelling electronmicroscope technique (Lewin, Dhillon, Sim et al. 1995). They suggested that persistent measles infection in endothelial lymphocytes and macrophages causes a chronic granulomatous vasculitis. However, they concede that persistently infected immune cells aggregate in a focus of inflammation and may be unrelated to the primary cause of CD as they also isolated measles virus in one out of two cases of ileocecal tuberculosis (Wakefield, Ekbom, Dhillon et al. 1995).

**Immunology:**
There is evidence for the involvement of immune effector mechanisms in the pathogenesis of Crohn’s disease. Whilst humoral immune responses are normal in Crohn’s disease, cell mediated function may be defective (Harries, Danis & Heatley 1984). Patients have impaired skin sensitivity, a poor lymphocytic response to mitogens and decreased numbers of circulating T lymphocytes. This may be secondary to the disease itself or a consequence of malnutrition as the number of T cell lymphocytes return to normal with improved nutritional status.

The evidence to date does not distinguish between an appropriate response to antigenic stimuli to the mucosal immune system or a pathologically increased response to a minimally antigenic stimulus (Lowes & Jewell 1990). A number of immunosuppressants are used successfully in the treatment of Crohn’s disease but their mechanism of action remains unclear as the underlying triggers of the disease process elude investigators.

**Dietary factors:**
The relationship between diet and Crohn’s disease is one which has aroused interest since the earliest description of the condition. The possibility that a dietary antigen provokes a granulomatous reaction is attractive and an early candidate was silica (Chess, Chess, Orlander et al. 1950). The association between milk consumption and UC was reviewed by Wright and Truelove (1965) but Warthin (1969) later suggested that American troops with
the disease had a remission whilst taking combat rations which excluded milk products. This report was anecdotal and there was no attempt to validate its findings. Later James (1977) reawakened interest by reporting an association between the disease and eating cornflakes. Studies from Oxford (Rawcliffe & Truelove 1978), Bristol (Archer & Harvey 1978) and Cardiff (Mayberry, Rhodes & Newcombe 1980 (b)) failed to confirm a high intake of cornflakes but drew attention to several German studies (Martini & Brandes 1976, Miller, Ferves, Rohbeck et al 1976) which had reported a significantly increased consumption of sugar in Crohn’s disease. This association has been reported in a number of subsequent studies but its significance remains unclear.

**Smoking and Crohn’s disease:**

An important role for smoking in the development of Crohn’s disease has been established (Benoni & Nilsson 1984, Benoni & Nilsson 1987, Burns 1986, Francheschi, Panza, La Vecchia et al 1987 & Holdstock, Savage, Harman et al 1984). In an early study of 82 patients and matched community controls (Somerville, Logan, Edmond et al 1984) the relative risk of patients being smokers was 4; the relative risk was higher for smoking at the onset of disease (4.8) than for current smoking, (3.5). Confirmation of the role of smoking in the aetiology of Crohn’s disease comes from both the Royal College of General Practitioners Oral Contraceptive Study (Logan & Kay 1989) and the Oxford Family Planning Association Contraceptive Study (Vessey, Jewell, Smith et al 1986); in the latter the relative risk of developing Crohn’s disease was 3.4.

**1.3 ULCERATIVE COLITIS;**

**1.3.1 Historical aspects;**

Ulcerative colitis was first described by Wilks and Moxon in 1875 following an autopsy on a patient who had died of bloody diarrhoea (Wilks & Moxon 1875). The identification of ulcerative colitis as a distinct disease entity was hampered by a tendency to believe all diarrhoeal illnesses were a form of infectious dysentery and Wilks and Moxon were the first to question this belief. For many decades the condition was considered a disease exclusively of Europe and North America but is now reported with increasing frequency from Africa, Asia and South America.
The severity of the condition varies and many patients with proctitis have a mild illness and probably never attend hospital. As a consequence the diagnosis may not be confirmed and such cases are often not represented in published studies. A study from Nottingham has suggested the prevalence of asymptomatic ulcerative colitis may be as high as 34 per 100,000 (Mayberry, Ballantyne, Hardcastle et al 1989).

1.3.2 Clinical course;
Ulcerative colitis most commonly affects individuals in their second, third or fourth decades. It is more often seen in women and was originally thought to be a disease predominantly of Europeans and Jews although recent studies have shown a comparable incidence in South Asians (Probert, Jayanthi, Pinder et al 1992 (b)). Symptoms are often first associated with an upper respiratory tract infection, a "stomach" upset, severe emotional upset or stress and a variety of different lifestyle factors.

It is a disease of variable severity, clinical course and ultimately prognosis. The onset of symptoms maybe insidious or abrupt. Symptoms can range from small amounts of rectal bleeding to fulminant diarrhoea with colonic haemorrhage and prostration. 60-70% of patients will have intermittent symptoms with complete remission between attacks. Up to 5%-10% of patients experience only one attack alone with up to 15 years free of further symptoms whilst a similar number will have continuous symptoms and experience no remission (Jewell in Sleisenger & Fordtran 1993).

The severity of the disease both in the presenting episode or in subsequent relapses has important therapeutic and prognostic implications. Most immediate deaths occur in those patients with severe disease. Death rates from severe refractory disease have also remained constant over the last 30 years. However significantly fewer patients with moderate disease now die of their ulcerative colitis. The best indicators of disease severity are generally agreed to be clinical signs and symptoms. Large volume diarrhoea indicates that the colonic mucosa has been involved to such an extent that sodium and water reabsorption are significantly impaired. Frequent bowel movements may be a reflection of colonic or rectal irritability and as such number of stools is not a reliable indicator of severity (Jewell in Sleisenger & Fordtran 1993, Ayres, Gillen, Walmsley et al 1996). As with Crohn’s disease it may,
however cause significant problems with a patient’s quality of life (Kelly 1992) A large amount of blood in the stool, a fall in haemoglobin concentration and hypoalbuminaemia are all signs of severe and widespread mucosal destruction. Similarly sustained high fever, tachycardia and marked elevation of inflammatory markers are indicators of severe inflammation whilst rapid weight loss resulting from anorexia and increased catabolism have a similar implication. Sustained abdominal pain and tenderness imply transmural involvement.

The clinical classification of ulcerative colitis into mild and severe disease is arbitrary but is useful for prognosis. Mild disease is often classed as disease associated with fewer than four bowel actions per day. It is not associated with weight loss, fever, tachycardia, anaemia or hypoalbuminaemia. Severe disease is defined as that associated with more than six stools a day, considerable colonic bleeding, fever, tachycardia, weight loss, anaemia and hypoalbuminaemia.

**Mild disease:**
This is the most common form of the disease affecting about 60% of patients (Jewell in Sleisenger & Fordtran 1993). Most commonly the distribution is segmental and just involves the distal colon. The course of mild colitis may be the same as for more severe forms, indeed 10-15% of patients will extend their disease to affect a much larger part, if not the entire colon. Anorectal complications as well as extra colonic manifestations of ulcerative colitis are noted in mild disease as in more severe forms (Jewell in Sleisenger & Fordtran 1993).

Neither colonic bleeding nor diarrhoea are severe in mild colitis and systemic signs and symptoms are absent. Occasionally patients may complain of short episodes of anorexia and fatigue or mild lower abdominal tenderness and rarely they may present with extra colonic manifestation in isolation. Long term prognosis is perceived to be generally good, immediate mortality is almost zero and risk of colorectal cancer is minimal (Ayres et al 1996).

**Moderate disease:**
This affects up to 25% of all patients with ulcerative colitis and symptoms are often more intense. During the initial attack diarrhoea is a major symptom, stools are frequent, loose and
contain blood, crampy abdominal pain is prominent and may wake the patient at night. There may be a low grade fever, the patient can be tired and unable to take part in his or her usual daily activities. There may also be anorexia and weight loss and extra colonic manifestations such as back ache and arthritis may be present (Jewell in Sleisenger & Fordtran 1993). The disease can progress to fulminant colitis characterised by high fever and profuse diarrhoea, rapid deterioration manifesting itself as massive bleeding or rapid and progressive dilatation of the colon. Since the advent of corticosteroids the immediate mortality of this condition has significantly fallen although longterm prognosis is still disputed (Ayres et al 1996).

**Severe or fulminant disease:**
This affects 15% of patients. They often have a sudden onset of symptoms which rapidly progress to a critical illness, although occasionally onset may be insidious. There is profuse diarrhoea, rectal bleeding and an intermittent or sustained fever. Anorexia and weight loss are early and prominent features. Physical examination reveals an acutely ill patient with fever, tachycardia, dehydration and profound weakness. A microcytic anaemia and hypoalbuminaemia are universally found. Progression to severe bleeding or a toxic megacolon necessitates emergency surgery.

**1.3.3 Outcome:**
The outlook for recovery from the first attack of ulcerative colitis is very good and mortality in the first year is usually associated with the severest forms of the condition (Jewell in Sleisenger & Fordtran 1993). Figures of 4-6% of patients dying during their first attack are quoted by some centres (Ayres et al 1996). Disease severity is thought to be the best indicator of prognosis rather than extent of disease. Also in general those with a short illness prior to hospitalization seem to have an increased mortality compared to those with an insidious onset. Another factor in determining prognosis is age of onset where age confers an increased risk of death.

Death is relatively uncommon, but may be due to the disease itself, complications of medical therapy, or following surgical intervention. The average rate is about five deaths per million
per year. However, there is good evidence that mortality rates vary from country to country and are lowest in southern Europe (Probert, Jayanthi, Wicks et al 1993a, Hendriksen, Kreiner & Binder 1985). Such simple mortality rates can be misleading for a variety of reasons. If a disease is uncommon or infrequently diagnosed few people appear to die from it. A second explanation can be successful treatment as perhaps in a study from Copenhagen (Hendriksen et al 1985) where patients had survival rates similar to the rest of the community. Mortality studies from Leicester also showed no excess mortality amongst 1014 patients with UC (SMR = 93%), (Probert et al 1993a). In contrast, a detailed study of the fate of patients with IBD in Stockholm county (Brostrom 1986) reported no improvement in survival over the previous 25 years. Patients who maybe at increased risk of death include middle-aged and older people (Bonnevie, Binder, Anthonisen et al 1974, Softley, Myren, Clamp et al 1988), men (Kristensen, Koudahl & Jarnum 1977), recently diagnosed patients (Bonnevie et al 1974), patients during the year following radical surgery (Mosbech 1960, Gyde, Prior, Dew et al 1982), and patients with extensive colonic involvement (Gilat, Fireman, Grossman et al 1988). Men with UC appear to be at a lowered risk of death from either cardiovascular disease or lung cancer, and this may be due to their non-smoking habits (Gyde, Prior, Dew et al 1982).

Patients with early onset, extensive disease or disease for longer than 10 years are known to be at increased risk of cancer. In studies from Sweden (Storgaard, Bischoff, Hendriksen et al 1979) and Czechoslovakia (Maratka, Nedbal, Kocianova et al 1985) the risk of developing colonic cancer in total colitis was estimated at 4 to 5 fold that in the normal population. In Copenhagen (Hendriksen & Binder 1980) patients were regularly monitored in the hope that such follow-up might lead to early detection. Over an 18 year period cancer affected only 1.4% of their patients. Even when a policy of biennial review for all patients with total colitis of more than ten years duration is followed cancer seems to develop in those who default from the screening program (Jones, Grogono & Hoare 1985). Such an approach gives a work load of 30 colonoscopies/10^5 population/ year and in view of the ineffectiveness of screening may not be economically justifiable. A more detailed review of risk of colorectal cancer in ulcerative colitis as it impinges on quality of life appears in chapter eight.
1.3.4 Aetiology:

Ulcerative colitis is an inflammatory condition of unknown and possibly multiple causes. Infective, genetic, immunologic and psychosomatic theories again have all been advanced as possible mechanisms but as yet none have met all the criteria necessary to identify them as the cause.

Infective agents:
With its similarities to dysentery and other infectious diarrhoeas an infective organism remains a possible cause of ulcerative colitis. Ever since Felsen (1936) reported an unexpectedly large number of patients who developed ulcerative colitis following an epidemic of bacillary dysentery the search for an infective agent has continued with varying degrees of enthusiasm.

High titres to cytomegalovirus have been demonstrated in patients with ulcerative colitis when compared with well matched controls, and in another study patients with ulcerative colitis who developed cytomegalovirus infection were more likely to need surgery for toxic megacolon (Berk, Gordon, Choi et al 1985, Swarbrick, Kingham, Price et al 1979). However as ulcerative colitis is exceedingly rare in unrelated members of the same household (husband and wife) environmental or infective factors are unlikely to be the sole cause.

Genetic and Familial prevalence:
The data so far are inconclusive. With a prevalence rate of about 100 per 100,000 for ulcerative colitis it has been suggested that the familial incidence should be in the order of 1% but the incidence of inflammatory bowel disease in families is more like 15% (Farmer et al 1980, Monsen et al 1987). Explanations could include: simple dominant inheritance with low penetrance; polygenic inheritance or a genetic predisposition to causal environmental factors. Binder, Weeke, Olsen et al (1996) compared 152 patients with matched controls of the same social class. In eight families a relative was affected compared with only one in the control group. The comparative risk of developing ulcerative colitis in a first degree relative of a patient with the condition was 15 times the normal risk in a study from Leicester.
(Probert et al 1993b). In the recent Oxford review of case notes of patients with UC 12% of parents and 7% of first degree relatives had UC (Satsangi, Jewell, Rosenberg et al 1994).

**Dietary factors:**
A possible link between ulcerative colitis and milk consumption was first suggested in the days of Bonnie Prince Charlie who cured himself of the "bloody flux" by withdrawing milk from his diet. In this century Andresen et al (1925 & 1942) again drew attention to the role of milk in exacerbations of the disease and the value of milk free diets has been advocated by Truelove (Truelove 1961).

**Smoking and ulcerative colitis:**
Several studies (Boyko, Koepsell, Perera et al 1987, Jick & Walker 1983, Penny, Penny, Mayberry et al 1985 & Rudra, Motley & Rhodes 1989) have confirmed the observation by Harries, Baird & Rhodes (1982) that patients with UC were often non-smokers. It is of some interest that ulcerative colitis is common amongst non-smoking communities such as Mormons (Penny et al 1985). These observations have led directly to the investigation of nicotine as a therapeutic option although trials to date have shown mixed results (Thomas, Rhodes, Mani et al 1995, Thomas, Rhodes, Rangunath et al 1996).

1.4 Conclusion:

Thus IBD is a chronic relapsing and remitting and as yet medically incurable disease. It has wide clinical variability and its symptoms might be distressing and disturbing to the suffer. Initial symptoms could be unpleasant, disruptive, socially embarrassing and difficult to explain. The examinations and investigations that lead to diagnosis may also lead to further distress. Because of this I felt the need to investigate the impact of these disease on patients and also the need to develop a measure to assess these difficulties objectively. Few investigators have examined these issues in detail. This thesis investigates these issues further and incorporates them into a quality of life measure. The next chapter reviews the historical perspective of quality of life as well as detailing the necessary ingredients for a good measure to assess quality of life.
CHAPTER TWO: QUALITY OF LIFE
2.1 INTRODUCTION:

Inflammatory bowel disease is a chronic disease of a relapsing and remitting nature. Epidemiological studies have shown a world wide distribution of this condition but have done little to provide a cure or identify a definitive cause. Few patients die of their inflammatory bowel disease today but they make frequent visits to both primary health care doctors and hospital specialists.

Until recently the literature was largely devoid of any reference to long-term prognosis although some investigators suggested an optimistic future for such patients with a normal "quality of life" but with no data on which to base their comments (Gazzard, Price, Libby et al 1978, Hendriksen et al 1980 & Binder et al 1985). Whilst the impact of inflammatory bowel disease has largely been based on clinical disease parameters investigators now recognise the failure of such clinical measures in assessing functional disability, psychosocial functioning and drug toxicity.

General measures of health are necessary tools for surveys on health and for making comparisons between disease states. Recent studies have concentrated on validation of general measures of health such as the short Form 36 (SF36) for routine use within the NHS (Jenkinson, Ziebland, Fitzpatrick et al 1991). Seventeen patients aged 16 to 86 with either low back pain, menorrhagia, suspected peptic ulcer or varicose veins were compared with 900 patients from general practitioners lists. The authors concluded that such a questionnaire should not be used in isolation and that a disease specific measure of clinical outcome was mandatory (Jenkinson, Coulter & Wright 1993). A disease specific questionnaire focuses on domains relevant to a disease or condition and on the characteristics of the patients with that condition. This is particularly important for clinical trials where a specific intervention is being evaluated. Disease specific questionnaires can also be used to encourage patients to participate in the management of their disease, promote understanding of its natural history and guide their future expectations (Farmer, Easley & Farmer 1992). Disease specific questionnaires can also reduce the time patients need to complete the measure. Such questionnaires increase the acceptability of the measure to patients by including only relevant
dimensions and thus may increase patient responsiveness (Jenkinson et al 1993).

Since the work of this thesis was conducted a Canadian measure, the IBDQ, (Irvine, Feagan, Rochon et al 1994) has been introduced in clinical trials and is likely to raise the profile of this hitherto neglected area both in everyday practice and in the context of drug trials and surgical interventions. The IBDQ was specifically developed for use in large scale clinical trials and does not specifically address the day to day needs of individual patients. Thus a measure to explain an individual's illness experience and health outcomes is still necessary (Garrett, Drossman & Patrick 1990).

This chapter discusses the ingredients that make up a tool suitable for measurement of quality of life and the implications for its use. It also reviews the development of quality of life measures both in general health and specifically in inflammatory bowel disease. Chapter 9 describes the development and validation of such a measure - the Quality Index in Crohn's and Colitis.

2.2 HISTORICAL ASPECTS:

The increasingly technical world of scientific medicine is now becoming aware of the need to assess social outcomes of treatment. Although much has been written about quality of life and its subjective evaluation by doctors, psychologists and other health professionals, it is clear that there is no single measurement tool which satisfactorily addresses this issue. In 1946 the World Health Organisation defined health as "complete physical, mental and social well-being and not merely the absence of disease and infirmity." Since then there have been a number of imprecise attempts at remodelling this definition with quality of life firmly in mind. However as the 19th century philosopher Lord Kelvin said "When you can measure what you are speaking of and express it in terms of numbers, you know something about it. When you cannot express it in terms of numbers, your knowledge of it is of a meagre kind". With this approach the need for valid reproducible survey tools has become critical.

In the USA, the financial burden of health care has also stimulated the search for objective outcome measures to ensure purchasers receive value for money. Checks on the efficiency
or effectiveness of medical interventions have been major stimuli to work on quality of life. A less acceptable aspect is the use of such tools critically to compare clinical performance and delivery of care (Goldfield & Nash 1989). In contrast greater resource allocation may result from work on quality of life which demonstrates need (Kaplan & Ware 1989).

Against this background patients often believe doctors underestimate their difficulties. This may reflect traditional training practices, but is still true for graduates of "progressive" institutions. There is a clear need for functional assessment tools to prioritize patients' problems and through appropriate interventions improve their quality of life. Use of such tools may favourably influence doctors' performance, but their value must be assessed in terms of benefit to patients rather than to carers.

A truly comprehensive quality of life evaluation must address the four domains of psychological, social, occupational and physical well-being (Fallowfield 1990). It will include assessments of depression, anxiety, inter-personal relationships, employment, sleep and eating patterns, mobility and pain. The medical profession has traditionally examined these issues through disability, morbidity and mortality indices. Such tools are crude and seldom reflect the specific effects of chronic conditions. Wenger (1984) observed that "the major therapeutic goal for most patients with chronic illness is not a cure for the disease, but rather an improvement in function and life quality resulting from alleviation of symptoms of illness and a limitation of the progression of the disease."

2.3 THE TOOLS:

In the late 1980's and early 1990's there was a shift towards the view that what is important to patients can only be discovered by interviewing them (Deyo 1991). Until recently some investigators have been quick to criticise the value of quality of life research based on the belief that the data are "soft" and inferior to laboratory measurements. However, such work is rapidly gaining recognition and one of the driving forces is the emergence of market forces, quality assurance and the prospect that "money will follow the patient" (Goldfield & Nash 1989).
DEFINITIONS:
The "tools" used in such work must meet the same criteria as other measurements. Crucial aspects of any scientific measurement of quality of life will include: (Bowling 1990)

1. **Repeatability** - the measure must be consistent when applied to the same subjects at different times unless real changes have occurred in the meanwhile. There are several ways of testing repeatability or reliability:

   (i) **multiple** - Two instruments developed simultaneously are used to assess the same attribute and their correlation calculated.

   (ii) **split-half** - Internal consistency is assessed with the index or scale being split into two halves. The association between scores from each half is calculated.

   (iii) **test-retest** - The test is administered to the same population on two occasions and results compared.

2. **Validity** - This assesses the degree of confidence which can be placed on inferences drawn from scale scores. It concentrates on the meaning of the information contained in the score, a valid score contains information about the specific aspect under investigation and not some other variable. With no uniformly agreed general or specific scales, the search for an ideal assessment tool continues. Validity can be classified as either empirical or non-empirical and there are different types of each; (Ware jr, Brook, Davies et al 1981)

   **A. Non empirical scales**; often rejected as unsuitable, such assessments are easy to perform and prevent the misuse of "validated" tools for inappropriate topics. Examples include

   (i) **content** - Are all aspects of the topic to be assessed present in the scale or index? (Bowling 1990).

   (ii) **face** - Does the scale or index measure the variables it sets out to assess? (Bowling 1990).

   **B. Empirical scales**; these are more difficult to measure as available empirical information falls short of what is required

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(i) **criterion** - Does the scale measure these variables accurately? This may be assessed through comparison with a gold standard, but when there are no clearly defined or direct measures of quality of life available this may be impossible (Fallowfield 1990).

(ii) **construct** - assemblance of empirical evidence to support the inferences that a particular measure has meaning. This must be an on-going process similar to gathering support for a complex scientific theory where no single set of observations can provide crucial or critical evidence. This involves testing methods and theory simultaneously. Such an approach must be used when there is no single gold standard by which comparison can be made (Fallowfield 1990).

3. **Responsiveness**;

This is a measure of association between change in quality of life before and after some event (eg treatment). A quality of life scale should be constructed to be sufficiently responsive so that effective clinical treatments produce significant changes in the scale (Testa & Simonson 1996).

4. **Sensitivity**;

Although a measure maybe responsive to big changes in quality of life the scale of the measure may not be adequate enough to reflect much smaller changes. Meaningful changes for a single patient are typically much smaller than the differences between patients and thus interventional studies may require a greater sensitivity in the tool being used (Testa & Simonson 1996).

These measures can be used to compare approaches to assessing health status and allow investigators to demonstrate their work is reproducible and correlates well with established procedures. Such features are usually associated with laboratory based investigations and when present in social surveys should ensure the results are believed.

Recently the the British Medical Research Council have produced an informal but standardised method for assessing any questionnaire measure (Fayers, Hopwood, Harvey et
al 1997). It is divided into several sections; context of use, development, validity, reliability and sensitivity. Each of these sections has a series of questions which an investigator should address when assessing such measures.

**UTILITY THEORY:**

The concept of health state utilities originated in the 1970’s with the Standard Gamble technique. Utilities are paired comparisons, the first alternative being a treatment with two possible outcomes; an individual has to choose between a good (probability \( p \)) and bad outcome (probability \( 1-p \)). The second alternative has an outcome which is intermediate between the good and bad outcomes of the first alternative. The probability of the second outcome is varied until the respondent is indifferent between the two alternatives at which point the health utility of the health state in the second alternative can be calculated. This approach has been developed further with attempts made to make it more "user friendly" including the Time Trade Off method (Lane 1987).

Utility may be the best way to measure quality of life. It can help to guide decision making in the face of uncertainty. It is a general concept for measuring the value individuals attach to the consequence of various courses of action. Its scope is global and is patient and decision specific; it can describe present health states, predict the desirability of future health states and discriminate between different prognostic and diagnostic categories. Although developing such utilities is not straightforward once assigned they are easy to interpret (Torrance 1987).

To develop utilities it is simplest to trade-off between two reference consequences - the best (complete recovery) and worst (death) are assigned utilities of 1 and 0 respectively. The utility of the consequence under investigation can be calculated by assessing different expected outcomes and assigning them a number between 1 and 0 depending on the probability of success or risk of death. By averaging the utilities associated with each possible outcome the expected utility is computed.

Drawbacks include the notion that prognosis should be firmly omitted from such measurements as it is not part of a health state description (Lane 1987), but likely to change with time. Although for scientific purposes this may be appropriate, prognosis is intimately
involved with patient centred decisions on treatment and should be addressed in such assessments. Utilities are complicated to develop and require time and effort to complete - this may itself introduce bias from care free appraisal or distortion through too much thought. This partly explains why few investigators in IBD have adopted this approach.

2.4 REVIEW OF QUALITY OF LIFE STUDIES:

General measures:
Scales have been invented for all manner of illnesses particularly cancer and chronic disorders. Some have been tested and retested for reliability and validity but no-one can quite agree as to what should be measured in the first place i.e. there is no gold standard (Bowling 1990). The Sickness Impact Profile (SIP) is an example of a general health measure of a behavioral nature based on measures of sickness related dysfunction (Bergner, Bobbitt, Kressels et al 1976). It covers patients' perceptions of daily living including physical, psychosocial and independence scores (sleep, rest, eating, working, eg: I sleep most of the day, I rest most of the day etc.). The Nottingham Health Profile (Hunt, Mc Kenna, Mc Ewan, et al 1980 & Hunt, Mc Ewan, Mc Kenna et al 1981) is another general measure of health. It was developed from lay perceptions and reflects how people feel at various levels of illness. However, because it concentrates on negative feelings people are unlikely to complete it when fit and consequently it is less sensitive at lower levels of dysfunction (Kind & Carr-Hill 1987, Brazier, Herper, Jones et al 1992).

Most scales are concerned with ill-health and usually give little attention to well-being. Exceptions include a scale developed by Kaplan in the early 1980's for use in chronic obstructive airways disease. This quality of well-being scale correlated well with the SIP and although originally designed as a general measure it adapted well as a disease specific model (Kaplan, Atkins & Timms 1984). In contrast Spitzer's Quality of Life Index for use in patients with cancer overlooked any positive feelings patients may have (Spitzer, Dobson, Hall et al 1981).

There is a bias in health professionals' perception of quality of life with a lack of consideration for what patients feel. Evidence for this comes from a review by a patient with
IBD (Godber 1989). Some scales designed by physicians, for use by physicians show wide discrepancies from assessments made by patients of their own quality of life. Others suggest that doctors reports are likely to be inadequate; they are after all as biased observers as the patients themselves (Slevin, Plant, Lynch et al 1988). These arguments centre around objective versus subjective measures, whereas objective measures have been favoured traditionally. When a variable can be measured by direct observation it is argued that this is of greater reliability than one where interpretation of the observation is required. For example the total number of people with condition "X" equals 100 - a more specific and reliable measurement than one inferring 60 people with condition "Y" have difficulty getting to the toilet on time - a less easy to measure situation requiring a considerable degree of interpretation. Some observers doubt that such interpretations render subjective research invalid (Ware, Brooke, Davies et al 1981, Hunt 1988). Other studies have used comparative physician rated scales despite the lack of correlation with either patients views or those of other health professionals. This is against a background of disagreement within the medical profession and the different core of knowledge held by patients and physicians (Ware et al 1981).

The emergence of a group of professional but non-clinical health assessors is not the solution to these difficulties. There seems some fundamental confusion in the minds of such investigators who often divorce prognosis from health status of individuals. There is a belief that patients are able to make decisions about their own health care quite independently of the ultimate outcome of their illness (Lane 1987), but in practice long term prognosis is intimately entwined with quality of life.

**Specific measures of quality of life in IBD:**

Interest in quality of life issues for people with inflammatory bowel disease has been sporadic and studies have used a variety of assessment tools which have limited any effective comparison. Individual studies vary from those suggesting a good quality of life to others reporting significant impairment. In the 1970's the social toll of Crohn's disease was thought negligible (Gazzard, Price, Libby et al 1978). Most people were believed to live optimistic,
useful lives and continue in full time employment. Gazzard used a combination of the Morbid Anxiety Index (Salkind 1972) and the Eysenck Personality Questionnaire (Eysenck & Eysenck 1977) together with a combination of clinical and biochemical features to assess quality of life amongst 85 patients with inflammatory bowel disease. Further support for this view came from a study of married ileostomists who had adapted well to a stoma and whose sexual problems were minimal (Burnham, Lennard-Jones & Brooke 1977). In Denmark patients with ulcerative colitis seemed to adapt well to their condition and suffer few social or professional disabilities (Hendriksen et al 1980). In this study an unstructured non-validated questionnaire was used to interview 122 randomly selected patients attending an out-patients department regarding their professional, emotional and family conditions. Another study from Denmark also reported an optimistic prognosis in Crohn’s disease (Binder et al 1985) and a survey of permanent ileostomists (Kennedy, Lee, Claridge et al 1982) revealed that nearly all had normal occupations and enjoyed recreational activities.

In contrast in the 1980’s inflammatory bowel disease was shown to significantly impair quality of life (Drossman, Patrick, Mitchell et al 1989 & Garrett & Drossman 1990). Drossman et al (1989) developed a rating of IBD patient concerns proportionately weighted according to the views of 150 patients with IBD. It included issues such as "having an ostomy bag, low energy levels, loss of bowel control and fear of developing cancer" in its top ten. Drossman, Leserman, Li et al (1991) used this rating of IBD patient concerns in combination with The Sickness Impact Profile (Bergner et al 1976) and a comparative physicians rating scale. They concluded that their measure correlated reasonably with the general health scales but that physician rating of disease activity did not correlate with overall health related quality of life. These assessments were cumbersome and took between 60 and 90 minutes for patients to complete. As participants were paid, their objectivity could be questioned.

Issues such as educational achievement have also been examined, with one study suggesting that although patients lost more time from school they gained equivalent academic successes to their healthy peers (Mayberry, Probert, Srivastava et al 1992). There have been conflicting reports on employment prospects. In some studies despite periods of long term unemployment, job prospects were regarded as good, whilst others have shown a significant

Thus a more acceptable, validated measure of quality of life in IBD is clearly needed. The Inflammatory Bowel Disease Questionnaire was developed in Canada for use in clinical trials (Guyatt, Mitchell, Irvine et al 1989). 97 patients were asked to describe problems experienced because of IBD. The 32 most frequent and important "complaints" were included in the IBD questionnaire. This included fear of being incontinent and fear of developing colorectal cancer. This questionnaire acts as an indicator of health status of the respondent at a single point in time and as disease activity varies over time it needs to be repeated at frequent intervals. This index was specifically designed for use in clinical trials and not as a device for use by patients and medical staff to assess impact of disease and the planning of longterm objectives and management strategies on an individual basis. More recently Irvine has used the IBDQ in clinical trials and shown its reproducibility, but these trials have only taken place in Canada and their adaptability to UK patients has yet to be validated (Irvine, Feagan, Rochon et al 1994). In America Farmer & Easley (1992) have also developed a quality of life questionnaire for use in inflammatory bowel disease. This is a 47 item questionnaire for use in ambulatory patients; the main objectives were that it could be completed by patients and be applicable in day to day life. It includes items about difficulties in: having intimate relationships; having children; obtaining a job and obtaining insurance. However the index excludes symptomatology or measures of disease activity, was not compared with a disease activity score and has not been validated in the UK.

Similar limitations are frequently seen in reviews of quality of life following surgery for IBD. Most publications are concerned with the efficacy of one or more treatments and neglect their overall and long term impact on life style (O'Young & Mc Peek 1987). Issues that have been examined include: (Meyers 1983)

(i) Abdomino-perineal resections compared with sphincter saving procedures.
In general patients with Crohn’s disease regard intestinal resections as providing long term improvement in quality of life. Only a small number would decline further surgery (Meyers 1980). This is in sharp contrast to a report from Rotterdam (Shivananda, Van Blankenstein, Hordijk et al 1989) where high opinions of surgery fell with the need for repeated intervention, as conversely the view of medical treatment improved. A recent Canadian study (Mc Leod, Churchill & Locks 1991) of the quality of life of patients with ulcerative colitis preoperatively and postoperatively used time trade-off techniques and a direct questioning of objectives. The direct questioning of objectives (a type of utility score developed in conjunction with the patient) was specifically designed for use in patients on home parenteral nutrition (Detsky, Mc Laughlin, Abrams et al 1986). Mc Leod et al (1991) in a study of 93 patients suggested quality of life is improved (according to an improved utility score) irrespective of the surgical procedure whether it be a conventional ileostomy, a Koch pouch or an ileal reservoir. Another American study interviewed 51 patients with Crohn’s disease retrospectively some 5-10 years after the operation for failed medical management of their disease (Meyers 1980). The authors concluded that the majority of patients (92%) had an improvement in their quality of life post-operatively. However this study is flawed because of a number of problems including re-call bias, no pre-operative assessment and the use of non-validated assessment tools. The conclusions of these studies contrast with a recent British study in which conventional ileostomies were preferred to continent procedures (Probert, Jayanthi & Mayberry 1996). However this study can also be criticised for the same reasons; re-call bias, non-randomisation and use of non-validated tools.

2.5 CONCLUSION;

Thus I believe quality of life assessments need to include aspects of education, employment and family life and pinpoint areas of need. The increasingly used IBDQ (Irvine et al 1994) was designed to complement traditional measures of outcome in clinical trials and does not aim to identify individual patients problems. A scale for use in clinical practice should pin
point individual patient needs and guide health professionals to target resources at appropriate
patients. A disease specific measure for use by patients and health professionals is needed
to meet these criteria and serve as a framework on which to build individual patient
management plans. Interventions may then be directed at the areas identified and are likely
to include counselling, access to self-help groups and information booklets as well as
conventional medical treatment. Identifying particular needs will enable us to educate
employers, teachers and insurance companies who are so often ignorant of patients strengths
and weaknesses.

Thus an ideal quality of life instrument for use in IBD should:

1. reflect patient concerns about disease, prognosis and treatment
2. be consistent when re applied to the same subject (repeatable)
3. measure the specific aspect under investigation accurately (validity)
4. be able to measure change after an intervention (responsiveness)
5. be able to detect small changes in individual patients (sensitivity)

There is still a need for a disease specific (inflammatory bowel disease) quality of life
questionnaire for use by patients and health care professionals in Britain. It should address
all of these issues but be concise enough for practical everyday use.
CHAPTER THREE: FEARS AND CONCERNS OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE
3.1 INTRODUCTION

The traditional view has been one in which doctors and nurses know what is best for their patients and early randomised controlled trials used outcome measures that were developed by professionals. The value of such an approach does not stand up to careful scrutiny and it is now clear that health professionals are inaccurate at measuring quality of life in patients with chronic diseases (Slevin, Plant, Lynch et al 1988, Ware 1976). McNeil, Weichselbaum & Paulker (1978) demonstrated that doctors, nurses, medical students, volunteers and patients could not agree over the most appropriate treatment choice for bronchogenic carcinoma. Slevin et al (1988) also showed that there were wide discrepancies between professionals' and patients' assessment of quality of life in cancer patients and he concluded that doctors were least accurate at assessing quality of life. Others too have shown that there are wide discrepancies between patients' and doctors' ratings of outcome following specific therapies including out-patient care (Ortho-Gomer, Britten & Rehnquist 1979), treatment of low back pain (Thomas, Hislop & Waters 1980) and the effect of anti-hypertensive drugs on quality of life (Jachnuck, Brierley, Kachnuch et al 1982).

Reasons for these discrepancies may reflect the way in which health professionals and patients each view ill-health. Health professionals are interested in disease models, a medical conception of pathological abnormalities indicated by a set of signs and symptoms. Patients are experiencing ill-health, a person's conception of feelings of pain and discomfort leading to a change in usual functioning or feeling (Bowling 1990). Because of this complex relationship between disease and ill-health a patient's health status cannot be explained by symptoms and disease related measures alone.

In a national study of over 900 patients with inflammatory bowel disease in the USA Drossman et al (1991) assessed a questionnaire containing 25 inflammatory bowel disease specific concerns including loss of bowel control, fear of developing cancer and ability to have children. They concluded that patient's anxieties about personal illness are a disease-specific component of health status that may affect satisfaction with care, adjustment to illness and even the planning of treatment.
Thus to develop a sensitive quality of life measure it is essential to ask patients what concerns them. The aim of the investigation described in this chapter was to identify a core of issues and concerns experienced by patients with inflammatory bowel disease and their methods of dealing with ill-health. Patients were able to express their concerns freely in a non-clinical environment and these were used to develop a non-disease/ non-clinical model of quality of life issues in IBD.

A questionnaire developed from this discussion group investigating the importance to patients of such issues and coping strategies was administered to a randomly selected group from the database (described below) (n=164) and compared with the attitudes of consultant members of the British Society of Gastroenterology (n=78).

3.2 The Leicester database

Patients and methods;

All the patients with IBD investigated in this thesis have been randomly selected from a rigorously assembled epidemiological database of more than 2,500 patients which formed the basis of Dr CSJ Probert's MD thesis approved in 1993 (Leicester University) and entitled Inflammatory bowel disease: an epidemiological study of South Asians and Europeans in Britain. The results of the incidence studies were published as referenced (Probert, Jayanthi, Pinder et al 1992, Jayanthi, Probert, Pinder et al 1992).

Data were collected retrospectively for these studies from 1st January, 1972 to 31st December, 1989 inclusive. Potential cases were identified from both hospital and general practice sources. Disease registers of general practitioners throughout the county and of adjoining counties whose catchment area crossed into Leicestershire were reviewed as well as records held in pathology and endoscopy departments, hospital activities analysis (HAA) and Korner data from the Leicestershire Health Authority. In addition personal registers were examined and consultants in private practice asked to identify patients with inflammatory bowel disease. People from Leicestershire treated in adjoining districts were identified from the records held by Oxfordshire, Trent and East Anglia regional health authorities (HAA and Korner data). Finally, supra-regional referrals to Birmingham, Oxford and London were
identified from source cases. Case notes and microfiche records were obtained for all potential cases. The two private hospitals in the district do not have facilities to identify patients treated with IBD, but such cases were identified directly either from general practitioners or specialists in private practice.

For all candidate cases demographic details and the results of laparotomy, histopathological, microbiological, radiological and endoscopic investigations were noted. All potential cases were reviewed using a structured proforma based on criteria of case definition defined by Lennard-Jones in 1989. Patients in whom the diagnosis was entirely clinical were excluded. Microbiological tests were reviewed when available and those patients with a positive stool culture and non specific histological changes were excluded; stool culture is particularly important in Leicestershire because of the possibility of South Asian patients becoming infected during travel overseas. Patients with secondary colitis due to ischaemia or radiation were also excluded as were those cases with apparent acute self-limiting colitis. Only patients diagnosed whilst residing in the county during the study period were included in the incidence studies.

Case Definition:
Crohn’s disease
The diagnostic criteria of Crohn’s disease (CD) were based on the clinical history and investigations. A history of abdominal pain with, or without, diarrhoea which may be bloody was necessary. Features sought on investigation were discontinuous disease of the large or small bowel on endoscopy and/or radiology, with characteristic discrete ulcers and strictures. Histological features were transmural inflammation with lymphoid aggregates and goblet cell preservation; non-caseating granulomas were characteristic but not essential for a potential case to be classified as CD.

A strict scoring system was not applied, but characteristic features were sought from investigations recorded in the case-notes and these were used to classify the candidate patients as cases or non-cases. Once again, patients in whom the diagnosis of CD was entirely clinical were excluded. Cases of indeterminate colitis, defined as continuous inflammatory disease limited to the colon with equivocal histological or endoscopic
appearance, were distinguished from CD.

All the patients identified during these studies are held on a hand-written alphabetical filing system which constitutes the Leicester data base. It was kept up to date for the following 2 years as part of the European North-South incidence studies (Shivananda et al. 1996). It is comprehensive and representative including medical as well as surgical cases.

**Ulcerative Colitis and Proctitis**

Ulcerative colitis (UC) was defined as idiopathic, continuous colitis and proctitis as idiopathic disease confined to the rectum. Those in whom the upper limit of the disease was not delineated were defined as UC.

The same criteria were used throughout the study and for all ethnic groups, a proforma was used to ensure uniformity. An acceptable clinical history of passage of blood and mucus per rectum with or without diarrhoea, with characteristic endoscopic, histological or radiological finding was essential to the diagnosis. All histology reports for each patient were reviewed. A 10% sample of histology slides were reviewed by an independent pathologist and the diagnosis confirmed.

An important and integral part of the definition of UC and proctitis is their recurrent nature. Patients with single attacks consistent with acute self-limiting colitis were specifically excluded. Persistent or recurrent symptoms after a follow up of at least one year were an essential requirement for the diagnosis of ulcerative colitis or proctitis to be accepted. Consequently the last date of diagnosis for inclusion in the study was 31st December 1989, with all cases reviewed until the end of 1990.

**Randomisation techniques:**

The data base comprises all cases of known IBD in Leicestershire diagnosed between 1972 and 1989 and is thus likely to represent all spectrums of disease extent and severity. As the data base is not computerised we could not generate random patients easily. Thus more crude randomising techniques such as choosing every tenth name on the data base were employed.
I do not believe this created an unreasonable bias in the selection of patients. A more satisfactory randomisation technique would have been to computerise the data base and generate random patients for each of the studies reported in this thesis. This would have eliminated any suspected bias associated with using co-operative patients.

3.3 METHOD:

Sources for recruitment of patients:
Patients were selected by choosing every tenth name on the Leicester inflammatory bowel disease data base (previously described).

The discussion groups:
Twenty patients with IBD were invited to attend a series of discussion groups with an experienced clinician (John Mayberry) and a psychologist (Chris Gillespie) to ascertain a core of problems specific to IBD together with possible solutions or methods of coping. A series of brainstorming sessions were held. In these meetings patients were split into two groups either led by a clinician or by a psychologist. Sessions were taped so that contents could subsequently be reviewed and valuable ideas not lost. Each group was asked to concentrate on describing problems specific to IBD. In the following meeting the team leaders changed groups and encouraged the patients to outline solutions or ways of coping with the problems they had described earlier.

The questionnaires:
After all the sessions the groups came together and agreed upon ten major issues and seven ways of coping which were then incorporated into two draft questionnaires. These lists were tabulated and a letter inviting the reader to score each statement with a number from 1 to 5 devised. One corresponded to "not important" and 5 with "extremely important". The final questionnaire was further tested on members of the committee of a local self help organisation for people with IBD (Appendix 3.1). The questionnaire on coping was also piloted on this group (appendix 3.2).

The Patients:
Questionnaires were sent to 100 patients with Crohn's disease and 100 with ulcerative colitis,
using every tenth name selected from the data base of patients with IBD in Leicestershire. Data were analyzed after three successive mailings. 10% of patients who responded were approached again at four months to test the reliability of the questionnaire.

**Consultant members of the BSG:**
The same questionnaire was also sent to the first 100 consultant surgeons and first 100 consultant physicians listed as members of the British Society of Gastroenterologists (BSG). Data were analyzed after two successive mailings.

**3.4 RESULTS:**

*Summary of discussion groups:*
The themes of the two discussion groups were very similar and ranged from concerns about cancer, risk to family members to the attitude of employers and insurance companies. Other concerns regarded the uncertainty and unpredictability of symptoms and the urgent need for a toilet (Table 3.1)

To help develop coping strategies these concerns were grouped according to:

**a. physical symptoms;** including pain, diarrhoea, bleeding, weight gain (steroid side effect), weight loss and rashes.

To deal with these symptoms patients suggested:
"grin and bear it", distracting activities (reading, knitting, listen to music), exclusion diets.

Fear of surgery was also a motive for getting fit.

**b. psychological symptoms;** including anger, being fed-up, anxious, depressed, fearful, resentful and concerned about body image.

To deal with these feelings patients suggested:
relaxation therapy, breathing exercises, imagery, homeopathy, health shops and reading.

Above all patients wanted to know the truth about their illness and its treatment.

**c. social difficulties;** sexual relationships, getting to work, keeping a job, going out, location of toilets.
To deal with these problems the following strategies were suggested: Public awareness; education of employers, insurance companies, shops/public sector and schools. More localised informal support groups involving GP’s, the hospital and trained counsellors.

The final questionnaires were agreed from these in depth discussions (see appendix 3.1 & 3.2)

**Response rate to questionnaire:**

(i) **Patients:**
There was an 82% response rate from patients with IBD, \( n = 164 \). 37 replies were from men with CD, 42 from women with CD, 38 from men with UC and 47 from women with UC.

(ii) **Consultants:**
In contrast the response rate from consultants was much lower, 50% from consultant physicians \( n = 50 \) and only 29% from consultant surgeons \( n = 29 \).

The scoring system coded 5 for extremely important, 4 for very important, 3 for quite important, 2 for not so important and 1 for not important. The *risk of cancer, risk to family members and dependence on drugs* were scored as extremely important by significantly more patients than consultants, see figure 3.1 \( (X^2=21, \ p < 0.0001, \ X^2 = 11.7, \ p < 0.001, \ X^2 = 24.15, \ p < 0.0001 \) respectively). However significantly more doctors than patients scored the effects of IBD on social life as extremely important, \( (X^2=14.4, \ p < 0.001) \). All groups considered *fear of incontinence, drug side effects and the attitudes of employers and insurance companies* as extremely or very important (score 4 or 5). There were no statistical differences between responses amongst male and female patients nor between those with CD and UC. Similarly significantly more patients than doctors thought the following coping strategies were extremely important: *keeping relaxed* \( (X^2=6.19, \ p < 0.05) \), *keeping occupied* \( (X^2=5.05, \ p < 0.05) \) and "*grinning and bearing it*" \( (X^2=25.2, \ p < 0.0001) \) (see figure 3.2). Significantly more doctors than patients thought joining a self-help group was very or
extremely important (score 4 or 5) ($X^2=8.09$, $p<0.005$).

Less than 20% of patients scored any issue as less than quite important (i.e. score 2 or less) (see figure 3.3). There were few significant aggregations of issues as many of patients uniformly scored every issue the same and the effect of small numbers confounded interpretation in those cases where this was not so. Those issues that particularly stood out with greater than 50% scoring 4 or higher were risk of cancer, fear of incontinence and drug side-effects. Greater than 70% of patients who scored one of these issues as 4 or higher were likely to have also scored the other two issues as very important. This was also true for those that thought the attitude of employers very important, they scored the attitude of insurance companies and public ignorance similarly. A poor response rate made the interpretation of doctors’ views difficult. Surgeons who thought that the effect of IBD on social life was very important were also likely to have scored fear of incontinence and drug side-effects in a comparable way.

The responses to the coping strategies questionnaire (see figure 3.4) were similar with the exception of joining a self-help group; just under 60% of patients felt all strategies were important ways of coping (i.e. a score of 3 or more). There was no clustering of patients’ responses with most scoring everything either 3 or 4. Except for “finding out the truth”, which nearly all doctors scored as extremely important, the rest of the scores by patients were randomly scattered with small numbers preventing meaningful analysis. In addition 16% of patients ($n=26$) voluntarily added that diet was an extremely important factor for coping with their inflammatory bowel disease.

In contrast surgeons were more likely than physicians to consider the risk to family members ($X^2=6.4$, $p<0.01$), tiredness ($X^2=6.6$, $p<0.01$) and keeping fit ($X^2=5.1$, $p<0.05$) to be extremely important to patients (see figures 3.1 & 3.2). All doctors believed the effects on social life of inflammatory bowel disease to be important to patients (see figure 3.1), ($X^2=8.4$, $p<0.01$).
3.5 DISCUSSION:

By utilising the freely voiced concerns of patients with IBD and their suggested strategies for coping with a chronic illness a non-health professional biased assessment tool can be developed. This technique has been employed by others in the field including Guyatt et al (1989), Drossman et al (1991) and Farmer et al (1992). However I am not aware of any other gastroenterology group in the UK who have adopted this technique. Drossman et al (1991) reported a 25 point rating of IBD patient concerns in numerical order. In keeping with our patients loss of bowel control (rated number 7), fear of cancer (number 8) and effects of medication (number 2) scored highly in their study. However fears regarding employment and insurance were not rated specifically although "ability to achieve full potential" (number 9) was. In our study patients were also concerned about issues of ill-health such as drug side-effects, dependence on treatment and tiredness and in common with other chronic illness patients adopt a resigned or "grin and bear it" attitude.

Patients were in fear of faecal incontinence. A preliminary report on lay counselling has suggested many patients were afraid of leaving the house as a consequence of worries about the location of a toilet and the threat of faecal incontinence (Godber 1989). No national surveys of the general population have enquired about such concerns and whilst mobility (severe rheumatoid arthritis, severe chronic bronchitis and asthma etc) will affect a persons' ability to walk to a toilet, few investigators comment on whether loss of bowel control is a particular worry. A recent MORI poll (Jacobs & Worcester 1991) however did report that nearly two thirds of people interviewed felt health was the single most important determinant of happiness.

Patients are particularly concerned about their risk of developing colorectal cancer although doctors did not believe this to be the case. This agrees with a recently published study where most patients with ulcerative colitis were aware of the increased risk of cancer but less than half knew it was possible to screen for the condition by means of a colonoscopy or that once detected surgery was necessary to remove the cancer (Robinson, Hart & Mayberry 1996).
Patients were also concerned about the attitude of employers. Surgeons were more likely than physicians to consider the attitude of employers an important concern for patients with IBD. This contrasts with earlier reports where patients with IBD were believed to have good employment prospects with most claiming a full work capacity (Binder et al 1985, Gazzard et al 1978 & Hendriksen et al 1980). A recent case-controlled study suggested young patients with IBD gained equivalent qualifications to their peers, but they failed to gain equivalent employment (Mayberry, Probert, Srivastava et al 1992). Both doctors and patients agreed effects on social life were important. Despite this many doctors seem to believe that patients "lead optimistic and useful lives" (Gazzard et al 1978, Hendriksen et al 1980).

Sixteen percent of patients volunteered diet as extremely important. Support for this belief comes from a study of 137 patients with Crohn's disease in Canada. They were randomised to two groups, one of which received counselling on diet while the other group did not. Patients who received dietary counselling had a significant reduction in disease activity, disease severity, number of admissions to hospital and dependence on corticosteroids (Imes, Pinchbeck & Thomson 1988).

Patients want to know the truth about their illness and are concerned about risk of cancer, risk to family members and side effects of treatment. In the early 1980's a study of patients with Crohn's disease from Newport in Gwent showed more than half felt they were not given enough information about their disease (Rees, Mayberry & Calcraft 1983). Doctors mistakenly believe self-help groups are an important avenue for dealing with illness, whilst in our study patients did not see them in this light. This contrasts with earlier reports which suggested self-help groups might be beneficial (Probert & Mayberry 1991, Mayberry 1987). However both these studies had flaws as one was based on responses from members of an established self-help group (Mayberry 1987), and the other on small numbers of patients attending an out-patient clinic (Probert & Mayberry 1991). Another study reported patient dissatisfaction with information given to them regarding their disease and the authors concluded that educational programmes for patients and carers alike should incorporate information regarding new treatments, aetiology, diet, symptoms, longterm evolution and risk of cancer (Martin, Castagluolo, Leone et al 1992). This corresponds to the discussion group's conclusions regarding the need for public awareness to be increased with education.
of employers, insurance brokers, the public sector and schools being highlighted. One solution to this problem suggested by our patients was the creation of small local support groups including counsellors and a local GP as opposed to national organizations such as NACC (National Association of Crohn’s and Colitis).

A concern from this study was the limited response rate of doctors to this questionnaire survey. They underestimated the concerns of patients with IBD and were unable to predict what worries them most. However, the response rate from physicians and surgeons was disappointingly low which makes interpretation difficult. If taken at face value it may suggest a lack of interest amongst doctors regarding patients’ fears and consequently their quality of life. Other more likely reasons may be a perception that such issues and concerns cannot be "cured" by a drug or surgery and therefore are not the domain of doctors. Also others may just be too busy to return such questionnaires. Of course, market surveys rarely generate more than a thirty percent response rate in the community.

3.6: CONCLUSION

The needs and concerns of individual patients will be different, but there is an increasing body of evidence to suggest fear of incontinence, risk of cancer, education and employment issues and drug side-effects are common anxieties for many patients with IBD. These areas of concern should be addressed as they may lead to improved compliance with treatment and so hopefully to a better quality of life. Together with the need to assess outcomes of treatment such fears should be incorporated into quality of life measures. Educational packages should be developed and made available to patients, employers, insurance brokers and teachers alike. Thought needs to be given to small local support groups which could include professional counsellors and local GP’s.

These needs and concerns have been studied in more detail in subsequent chapters and finally were incorporated into a tool to measure quality of life.
TABLE 3.1: THE FEARS AND CONCERNS OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE:

<table>
<thead>
<tr>
<th>Issues from Group 1</th>
<th>Issues from Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>*  fear of the unknown,</td>
<td>*  uncertainty</td>
</tr>
<tr>
<td>fear of cancer</td>
<td></td>
</tr>
<tr>
<td>*  restriction on life</td>
<td>*  strain on family, children</td>
</tr>
<tr>
<td>(annoyance, spoiling, school, social life, illness centred)</td>
<td>and finance</td>
</tr>
<tr>
<td>*  resentment</td>
<td></td>
</tr>
<tr>
<td>*  greater public awareness</td>
<td>*  public ignorance</td>
</tr>
<tr>
<td>(not disabled/invalid)</td>
<td></td>
</tr>
<tr>
<td>*  &quot;being caught short&quot;</td>
<td>*  not enough toilets,</td>
</tr>
<tr>
<td>having to live close to a toilet</td>
<td>always needing to</td>
</tr>
<tr>
<td>*  negative effect on mood</td>
<td>anticipate need of toilet</td>
</tr>
<tr>
<td>and behaviour</td>
<td>*  mood changes, temper</td>
</tr>
<tr>
<td>*  always tired</td>
<td>depression</td>
</tr>
<tr>
<td>*  more research/audit of treatment</td>
<td>*  no energy</td>
</tr>
<tr>
<td>audit of drugs</td>
<td>*  more information on</td>
</tr>
<tr>
<td></td>
<td>tablets, doctors/chemists</td>
</tr>
<tr>
<td>*  reliance on drug treatment/</td>
<td>ignorance</td>
</tr>
<tr>
<td>side-effects of treatment.</td>
<td>*  employers and insurance</td>
</tr>
<tr>
<td></td>
<td>companies attitudes</td>
</tr>
<tr>
<td></td>
<td>*  risk to family members</td>
</tr>
<tr>
<td></td>
<td>*  dependence on drug</td>
</tr>
<tr>
<td></td>
<td>treatment</td>
</tr>
</tbody>
</table>

Overall both groups had similar concerns and fears which included fear of incontinence, dependence on drugs, lack of energy and public ignorance.
THE 10 ISSUES INVESTIGATED AMONGST PATIENTS WITH IBD AND CONSULTANT MEMBERS OF THE BSG:

1. Public ignorance
2. Attitude of employers
3. Risk of cancer
4. Fear of incontinence
5. Effects on social life
6. Risk to family members
7. Attitude of insurance companies
8. Drug side-effects
9. Tiredness
10. Dependence on tablets
Fig 3.1 Numbers in Percent Who Thought Various Issues Were Very Important. (Score = 5):

KEY ON ADJACENT SHEET

- □ Patients
- ● Physicians
- □ Surgeons
THE 7 COPING STRATEGIES INVESTIGATED AMONGST PATIENTS WITH IBD AND CONSULTANT MEMBERS OF THE BSG:

1. Keep fit

2. Keep relaxed/ keep serene

3. Keep occupied

4. Join a self-help group

5. Find out the truth

6. Counselling

7. Grin and bear it
Fig 3.2 Numbers in Percent Who Thought Each Coping Strategy Was Extremely Important (Score = 5):

KEY ON ADJACENT SHEET

- □ Patients
- □ Physicians
- □ Surgeons
Fig 3.3 Proportions of Doctors and Patients Scoring Issues As Not Important (Score = 1 or 2):
Fig 3.4 Proportion of Doctors and Patients Scoring Coping Strategies As Not Important
(Score = 1 or 2):
CHAPTER 4: THE ATTITUDE OF EMPLOYERS AND INSURANCE COMPANIES TO PATIENTS WITH INFLAMMATORY BOWEL DISEASE
4.1 INTRODUCTION:

In chapter 3 the patients who participated in the discussion groups considered the attitude of employers and that of insurance companies as areas of concern which should be addressed. These issues were also a common concern amongst patients and doctors who answered the anonymous questionnaire. Chapter four investigates whether there is any evidence these views are justified and that employers and insurance companies do discriminate against patients who admit to having inflammatory bowel disease. The results of these two sub-sections help define the role that these concerns should play when designing a health related quality of life assessment.

4.2 THE ATTITUDE OF EMPLOYERS TO PEOPLE WITH INFLAMMATORY BOWEL DISEASE:

4.2.1 Introduction:

Many patients with inflammatory bowel disease (IBD) express anxiety about their employment prospects (Wyke et al 1988, Duclos et al 1990 & Mayberry et al 1992). Little practical advice is available and this can be inaccurate. In order to assess whether prejudice exists against patients with IBD a survey of employers was undertaken in which their attitude to people with IBD was investigated. This was done so that provision for more objective information could be made available to patient counsellors.

4.2.2 Method:

Questionnaires (see appendix 4.1) were sent to personnel officers at 195 companies. These included 61 of the largest firms throughout Britain and a second group of those employing more than 250 people identified by Chambers of Commerce in Cardiff and Leicester. The questionnaire recorded total number of employees, those known to have Crohn's disease or
ulcerative colitis, whether information was kept on file about IBD and to whom this was available. Questions dealt with the influence of IBD on employment, the effects of newly diagnosed IBD on continued employment and the effect of various diseases on promotion prospects. Attitudes to health and screening facilities were also noted.

4.2.3 Results:

Fifty three questionnaires were completed, 39 from local companies and 14 from national companies (27% response rate). A further 17 were returned by companies unprepared to complete them; reasons stated included:

i) no employees with IBD
ii) never heard of IBD
iii) no records available.

The companies employed 1,096,662 people, (range 250-250,000). 84% of respondents had heard of IBD; however this figure may have been biased by the fact that some returns were completed by medical officers or company nurses. Amongst 35 of the companies, employing 304,537 people, 33 people with Crohn’s disease and 26 with ulcerative colitis were known. The remaining companies did not answer this question. The combined minimum prevalence of IBD (Shivananda et al 1996) is at least $150/10^5$, which would suggest a minimum of 457 people with either Crohn’s disease or ulcerative colitis should be employed by these companies. The 59 people known to employers were significantly fewer than expected, ($X^2=240$, $p<0.001$).

36% of companies kept medical files containing information on IBD, which were available to managers in 21% of cases of those that kept such files. Personnel officers from only two companies said they would reject a job application from an IBD patient. Four were prepared to employ a patient regardless of his or her disease. However, most (93%) would rely on routine pre-employment medical examinations before reaching a final decision.

If patients suffered a relapse, 60% of companies would offer lighter work although 75%
expected an eventual return to full employment. 16% of companies would pay for private
care and 70% gave paid leave to enable employees to attend out-patient clinics. There was
a similar sympathetic attitude to patients undergoing surgery, especially for those needing a
stoma.

Facilities for preventive medicine are rather limited in most companies who replied. Only
53% cater for special diets and few hold well person clinics (23%) or are members of
private medical insurance schemes (38%). Screening is available in some companies for
hypertension (45%), hypercholesterolaemia (36%), breast cancer (23%), cervical cancer
(23%) and bowel cancer using faecal occult blood testing (9%).

Most personnel managers felt that ill-health did not influence promotion prospects but that
each employee would be assessed individually. However many diseases were acknowledged
to jeopardise promotion in the companies who replied: epilepsy (21%), multiple sclerosis
(17%), liver disease (17%), ischaemic heart disease (15%), chronic obstructive airways
disease (15%), hypertension (11%), asthma (9%), arthritis (9%), coeliac disease (8%),
ulcerative colitis (8%), Crohn’s disease (8%) and diabetes mellitus (6%).

4.2.4 DISCUSSION:

25% of companies who responded to the survey would not continue to employ somebody if
they developed IBD and up to a third would not provide time off work to attend hospital.
Less than 10% of respondents felt that having IBD jeopardised promotion prospects.
However 60% of employers would consider a move to lighter duties if asked for by
somebody affected by IBD.

The response rate from employers in this study was disappointingly low and so makes
interpretation difficult. Reasons for low response rates and methods for improving them have
been taxing market researchers since the earliest days of mail surveys. Herzog & Bachman
(1981) believe that motivation is one of the key determinants and other factors such as, types
of question, questionnaire length and topic under investigation are less important.
In market research, investigators have used two methods to increase response rates:

(i) follow up techniques such as telephone reminders
(ii) monetary incentives (Kanuk & Berenson 1975, Duncan 1979 & Janssens & Pessemier 1980).

Some investigators believe personalisation increases response rates (Duncan 1979, Scott 1961) whereas Downs & Kerr (1986) concluded that there was little difference between anonymous mail surveys and personalised ones. However, this approach was probably not relevant in a survey of companies. Whilst in our other surveys we employed follow-up techniques we elected not to re-mail non-responding companies. I felt there would be little benefit to the non responding companies to return the questionnaires and that replies following a reminder may have been inaccurate because of low motivational interest.

Occupational issues have been examined in many chronic illnesses (Robinson, Yateman, Protopapaet et al 1990, Songer, La Porte, Dorman et al 1989 & Mc Clellan & Garrett 1990). It is accepted that whilst insulin dependent diabetics have no greater levels of absenteeism than their non-diabetic counterparts they still receive a greater number of job refusals, particularly if they admit to the condition (Robinson et al 1990). Another study suggested that people with diabetes mellitus were more likely to experience problems obtaining employment and staying employed than healthy people (Songer et al 1989). In New Zealand people with asthma experienced difficulties in obtaining time off work to attend clinic. The authors concluded asthma had a detrimental effect on employment prospects as a consequence of the need for long term medical care (Mc Clellan & Garrett 1990). However, employers attitudes can be informed for instance in myocardial infarction, explaining longterm prognosis to employers improves return to work by such patients (Cay & Walker 1988).

People with inflammatory bowel disease are concerned about employment prospects and advice given to them is often inadequate (Mayberry et al 1992). Some patients fail to attend job interviews because of the possibility of symptom recurrence (Godber 1989). In a study of the "social toll" of Crohn’s disease there was no association between disease activity or number of operations and the patients work record. However, anxieties about promotion prospects or a better job were uniform throughout the group interviewed (Gazzard, Price,
Recently it has also been shown that young patients with Crohn's disease acquire equivalent qualifications at school, but fail to gain employment equivalent to their unaffected peers (Mayberry et al 1992). Some evidence to the contrary comes from Copenhagen where most patients did not feel that ulcerative colitis restricted their ability to work. Few patients were unemployed or sick, with most claiming full work capacity (Hendriksen et al 1980). An Italian study also claimed patients had a generally good quality of life and that their work capacity was not significantly reduced. However all patients who had changed jobs or retired had undergone surgery (Tragone & Lanfranchi 1989). Many diseases influence promotion prospects and, although some patients with IBD in the UK have had promotions withdrawn (Godber 1989), most employers claim not to discriminate against them.

Within the limits of a poor response rate, these results suggest that many people in Britain either fail to tell employers of their IBD when applying for jobs or that in practice there is discrimination against them. Companies seem to employ significantly fewer people with IBD than expected. Despite this employers claimed not to discriminate against patients with these conditions. If IBD develops during employment, personnel officers claim few people would lose their job. Although there are no statutory regulations on rights to attend medical clinics during working hours, paid leave during illness appeared to be widely available.

There may not be wide enough recognition of the nature of IBD amongst personnel officers and employers. Companies need adequate literature to enable managers to make informed decisions about employees' illnesses. Indeed one American study suggested that a comprehensive workplace health promotion programme could reduce days taken off because of ill-health or to attend hospital for ongoing treatment or surgery amongst all employees (Bertera 1990).
4.3 DISCRIMINATION BY INSURANCE COMPANIES AGAINST PATIENTS WITH INFLAMMATORY BOWEL DISEASE:

4.3.1 INTRODUCTION:

The traditional view has been that both Crohn's disease and ulcerative colitis are associated with a significantly increased mortality. This follows a number of studies in the 1970's and 1980's (Storgaard et al 1979, Mayberry et al 1980 (c), Prior et al 1981). However, more recent studies have questioned these views with reports of a normal life expectancy in both ulcerative colitis and Crohn's disease (Probert et al 1992 (a), Langholz, Munkholm, Davidsen et al 1992). These are in sharp contrast to the older data and current publications for insurance companies on morbidity and mortality in IBD (Brackenbridge & Elder 1992). These discrepancies are of particular consequence as a preliminary report on lay counselling amongst patients with IBD, insurance and mortgages were identified as areas of concern (Probert et al 1991).

The aims of this study were to investigate the attitude of major insurance companies to patients with IBD and contrast this with their replies to a consultant gastroenterologist (JFM) who had requested guidelines for patients with these conditions. Patients' experience of insurance companies was investigated in a parallel study of 69 people with IBD from Leicestershire.

4.3.2 Method:

Attitude of major insurance companies:

A standard letter (see Appendix 4.2) requesting information on the likelihood of additional loading on life assurance linked to a mortgage for a male patient with Crohn's disease of six years duration was sent to 50 major insurance companies. The companies chosen did not have a special interest in inflammatory bowel disease. Other details supplied included age (31 years), activity of disease (inactive for five years) and history of surgical procedures (one small bowel resection five years ago). Information only was requested and a formal
application for an insurance policy was not made to avoid any suggestion of fraudulent activity (Esmail & Everington 1993). Companies replied to the patient’s (GM) home address and were only mailed once.

Attitude of insurance companies to a consultant requesting guidelines for patients:
A similar letter was constructed from a consultant gastroenterologist (JFM) to the same 50 insurance companies. It requested simple guidelines which could help patients with IBD when applying for insurance, in particular life assurance. Companies were asked to reply to the hospital and were only mailed once.

The experience of patients in Leicestershire.
A simple questionnaire (appendix 4.2 (c)) investigating the experience of patients with IBD when applying for insurance was devised. It sort details of the age and sex of the patient and asked if they had ever applied for any of the following policies:

(i) low cost endowment
(ii) flexible whole life
(iii) term assurance
(iv) mortgage protection.

Patients were also asked if a medical report had been requested from their family doctor or specialist. They were asked if an additional loading was placed on any policy because of IBD and its extent. Any advice given by their insurance company about the best policy with regards to their illness was also sought. The questionnaire was sent to 100 patients with IBD by selecting every tenth name from the Leicestershire data base (previously described). The questionnaire was mailed on two occasions and 10% of patients were contacted four months later to test its reliability.

4.3.3 Results:

(i) Information to patient:
39 insurance companies responded to the request for information, (response rate=78%). Three companies no longer offered such policies and 12 were unprepared to comment without completion of an application form and/or medical examination. Of the remaining 24, 7 thought the patient would be accepted at normal rates and 17 expected the patient would be charged an increased premium. Only one company referred the patient to an alternative group specialising in insurance of patients with IBD (not one of the companies originally approached).

Guidelines to Consultant:
Only 27 companies replied to the letter requesting general guidelines including the three who no longer offered such policies (response rate= 54%). An overview of the complex rating system is documented in Table 4.1. There were 17 replies from the patient’s and consultant’s request for information which overlapped.

Of the seventeen overlapping replies, five companies (30%) informed the patient to expect increased premiums whilst advising the consultant that a similar patient could expect normal rates. Six companies conferred (35%), telling both patient and consultant to expect normal rates whilst either one or both of the six remaining companies (35 %) felt unable to advise without specific personal details obtained directly from an application form, a medical examination or a consultant’s report.

Patients experience:
69% of patients responded to the questionnaire. The results are tabulated in Table 4.2. Over half (54%) had applied for an insurance policy. Low cost endowment was the commonest option (49%), with applications for other policies being evenly distributed. More than a third of patients had needed a medical examination (36%) or report from their GP (41%) before being accepted. 39% of patients received a loading on policies because of IBD and two patients were turned down altogether.

4.3.4 DISCUSSION:
The history of insurance companies is long and interesting (Brackenbridge & Elder 1992).
The first known life policy was issued in 1583 following strictly on the lines of a marine policy. It was not until the late seventeenth century that the demand for life insurance was met. Assurance was administered by various societies under a tontine system. This consisted of groups of people who banded together with the object of insuring their lives to make provision for their widows and children. Only the very young and elderly were excluded. This system was open to abuse, the most serious being the practice of insuring a person's life without their knowledge. This enabled more unscrupulous members of the society to gamble on the lives of others which were at best none too sound and hence many schemes failed financially.

This failure was secondary to a lack of any scientific selection. The first serious attempt to establish population mortality rates was made by John Gaunt (Brackenbridge & Elder 1992), the son of a draper, who in his spare time analyzed the records of weekly christenings and burials in the city of London which were kept following the 1603 Plague. In 1662 Gaunt published *Natural and Political Observations* made upon the bills of mortality from which he compiled a "table of survivors", a fore-runner of life tables. Around the same time, in 1693, Edmund Halley, the Astronomer Royal, studied records of births and deaths regularly kept in Breslaw in Silesia since 1584. He compiled an estimate of the degrees of mortality of mankind drawn from curious tables of births and funerals at the city of Breslaw.

It was not until the next century that James Dodson showed that life assurance was viable with premiums properly graduated according to age in the 1750's. This advance was further assisted by the Life Assurance Act of 1774 and by the compulsory registration of births, marriages and deaths in 1837. William Farr, compiler of abstracts in the General Register Office, developed a national system of vital statistics from which the first English life tables appeared in the Registrar General's Fifth Annual Report of 1843.

As the life assurance business expanded the Institute of Actuaries was established in 1848. The first medical test to be used in association with life assurance was routine testing of urine at the end of the nineteenth century. This was soon followed by body build (height and weight) and then blood pressure measurements. Rating by tables is based on the principle that a standard life is 100%. An extra mortality risk associated with a particular impairment will
then be added to this basic or standard life along with any other independent mortality risk. In America it is thought that approximately 94% of applicants are accepted at standard rates (Medical Imperial Study 1983).

IBD is considered to have a 170% mortality rate in men and 200% in women in the USA. The data for this are taken from analysis of 10,200 insurance policies in the USA between 1952 and 1976 (Brackenbridge & Elder 1992). In the UK patients with IBD are considered to have a 190% mortality (Brackenbridge & Elder 1992). These data are taken from two studies from two tertiary referral centres, one with 671 patients in Leiden (Weterman, Biemond & Pena 1990) and the other of 769 patients in Birmingham (Andrews, Lewis & Allan 1989). These studies contradict the most recent mortality data on IBD from Denmark and the UK which suggest that after the first year of diagnosis there is no additional mortality from the conditions (Probert et al 1992a, Langholz et al 1992, Probert et al 1993a). The "life tables" used by many insurance companies (Medical Imperial Study, 1983) are clearly out of date, especially when referring to an increased mortality in IBD.

Tables 4.3 - 4.8 describe how Medical Selection of Life Risks "rates" patients with IBD and patients with diabetes for insurance purposes. Despite the very different mortality associated with IBD and diabetes little distinction appears to be made in the risk tables. Patients need to be aware of the various approaches adopted by leading insurance companies and should consider several different proposals before accepting an unnecessarily high premium.

Insurance companies appear to have limited interest in assisting the medical profession in providing patients with information about the consequences of illness on insurance premiums. The difficulty in obtaining valid data for this study lies in the escape clause used by so many insurance companies. Each application is considered individually and no comment can be made on hypothetical cases. Insurance companies also quote one rate to a professional enquirer, whilst the figure given to a prospective client may be quite different.

This was the first attempt to obtain objective information on insurance assessment in IBD and no other accurate published data are available. By creating a "patient" we believe the information acquired was reliable. The only other data available have been published on
ankylosing spondylitis. In a short report from the National Ankylosing Spondylitis Society (NASS) on over 3000 people with ankylosing spondylitis, 73% of patients who had taken out a policy after diagnosis with-held the fact they had ankylosing spondylitis from the insurance company. More than 30% who admitted they had ankylosing spondylitis received loaded policies while a further 3% were rejected (Jones 1994).

The experience of patients in Leicestershire resembles the information supplied to our "patient". People with IBD are discriminated against by leading insurance companies. A significant number will not offer insurance to patients at the standard rates which are suggested to a professional enquiry, and indeed some withhold insurance altogether. Few insurance companies seem aware of the existence of companies which specialise in suitable policies for people IBD.

4.4 CONCLUSION

In chapter 3 patients were clearly concerned regarding employment prospects and obtaining insurance. We have shown these concerns to be real; insurance companies put unnecessary loading on premiums and employers do not always allow employees time off to visit outpatients. Patients may even hide the fact they have IBD from their employers. Patients are right to be concerned regarding their future employment prospects as there is a lack of understanding about IBD amongst employers.

These areas of need should be highlighted in any quality of life assessment and may stimulate the education of prospective employers of patients with IBD and insurance underwriters. Also identifying particular patients with these problems may allow appropriate intervention and help to be given.
### TABLE 4.1: An overview of the response to a letter from a Consultant Gastroenterologist requesting guidelines for insurance in relation to patients with IBD.

<table>
<thead>
<tr>
<th>Crohn’s disease</th>
<th>Ulcerative colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 2 years of diagnosis</td>
<td>Additional premium for 2 year</td>
</tr>
<tr>
<td>Within 1 year of a major attack</td>
<td>Heavy loading</td>
</tr>
<tr>
<td>Medical therapy alone, disease free for 5 years</td>
<td>No loading</td>
</tr>
<tr>
<td>Age under 40 years</td>
<td>Greater loading</td>
</tr>
<tr>
<td>Disease free following ileostomy or restorative surgery more than 2 years ago</td>
<td>No loading</td>
</tr>
<tr>
<td>Severe cases</td>
<td>Rated heavier even if disease free for more than 5 years</td>
</tr>
<tr>
<td>Within 1 year of surgery</td>
<td>Postpone application for 12 months</td>
</tr>
</tbody>
</table>

Patients with inflammatory bowel disease generally receive an additional loading on their insurance premiums even when currently well.
### TABLE 4.2: The experience of patients in Leicestershire when applying for insurance policies (n=69).

<table>
<thead>
<tr>
<th></th>
<th>Male CD (n=18)</th>
<th>Male UC (n=18)</th>
<th>Female CD (n=17)</th>
<th>Female UC (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied for insurance</td>
<td>12</td>
<td>9</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>(i) Low cost endowment</td>
<td>8</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>(ii) Flexible whole life</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>(iii) Term assurance</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>(iv) Mortgage</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Required medical examination</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Required GP report</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Accepted at increased premium</td>
<td>5</td>
<td>5*</td>
<td>3</td>
<td>2*</td>
</tr>
<tr>
<td>Supplied with helpful information</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Two patients refused an insurance policy

Thirty nine percent of all patients with IBD applying for an insurance policy received an additional weighting to their policy.
### Table 4.3: Ulcerative colitis treated medically

<table>
<thead>
<tr>
<th>Time since diagnosis</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 year</td>
<td>+100 to +250*</td>
</tr>
<tr>
<td>2nd year</td>
<td>+75 to +200*</td>
</tr>
<tr>
<td>Thereafter</td>
<td>+50 to +150*</td>
</tr>
</tbody>
</table>

* Depending on extent and severity of disease, frequency of relapse and quality of cancer surveillance. Additional rates if prolonged or repetitive courses of corticosteroids.

Source: Brackenbridge et al 1992

### 4.4: Ulcerative colitis treated surgically.

<table>
<thead>
<tr>
<th>Time since surgery</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 6 months</td>
<td>Postpone insurance premium</td>
</tr>
<tr>
<td>Thereafter</td>
<td></td>
</tr>
<tr>
<td>i Panproctocolectomy and conventional ileostomy</td>
<td>+25 to 75</td>
</tr>
<tr>
<td>ii Panproctocolectomy with ileoanal anastomosis and pouch</td>
<td>+25 to +75</td>
</tr>
<tr>
<td>iii Simple colectomy with ileorectal anastomosis</td>
<td>+25 to +75</td>
</tr>
</tbody>
</table>

4.5: Crohn’s disease treated medically

<table>
<thead>
<tr>
<th>Time since diagnosis</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 year</td>
<td>+100 to +250*</td>
</tr>
<tr>
<td>2nd year</td>
<td>+75 to +200*</td>
</tr>
<tr>
<td>Thereafter</td>
<td>+50 to +150*</td>
</tr>
</tbody>
</table>

* As for table 4.3

Source: Brackenbridge et al 1992

4.6: Crohn’s disease treated surgically

There is no additional rating. If the disease is severe, referral to a medical examiner is necessary.

Source: Brackenbridge et al 1992
4.7: Type I or Insulin dependent diabetes mellitus (IDDM)

<table>
<thead>
<tr>
<th>Age at application</th>
<th>Basic rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 15</td>
<td>Postpone</td>
</tr>
<tr>
<td>16 - 30</td>
<td>+250</td>
</tr>
<tr>
<td>31 - 50</td>
<td>+100 to +150</td>
</tr>
<tr>
<td>51 and over</td>
<td>Standard to +50</td>
</tr>
</tbody>
</table>

Source: Brackenbridge et al 1992

4.8: Type 2 or Non-insulin dependent diabetes mellitus

<table>
<thead>
<tr>
<th>Age at application</th>
<th>Basic rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 30</td>
<td>Rate as IDDM</td>
</tr>
<tr>
<td>31-40</td>
<td>+100</td>
</tr>
<tr>
<td>41 and over</td>
<td>Standard to +50</td>
</tr>
</tbody>
</table>

Individual applicants diabetic control and compliance are also considered. Additional rates payable for any complications including retinopathy and coronary heart disease.

CHAPTER 5: SEXUAL DYSFUNCTION IN INFLAMMATORY BOWEL DISEASE
5.1 INTRODUCTION:

Although in chapter three I did not specifically enquire about patients' views on intimate relationships other investigators have noted this to be a concern (Drossman et al 1989, Farmer et al 1992). I therefore elected to investigate whether having IBD interfered with personal and sexual relationships. I did not examine the more specific issues relating to sexual performance but only whether patients were able to have sexual intercourse and how often. I also wanted to collect data on the reasons patients' might fail to have a sexual relationship.

Sexual function is integral to any quality of life assessment. It may be affected by a number of mechanisms including:

(i) trauma or disease affecting the spinal cord
(ii) trauma or disease affecting the sexual organs including the after effects of surgery
(iii) mental or physical chronic ill-health.

The problems individuals suffer are consequent upon which of these mechanisms is responsible for their disability. Trauma and neurological disease obviously present a very different set of issues compared to patients with IBD. An inability to move or feel either legs or arms calls for very different ways of investigating patients' needs and offering help.

Whilst much is written about sexual dysfunction in chronic ill-health there are few valid or reliable techniques for its measurement. Sexual function studies have mainly concentrated on men and have usually taken the form of either physical or psychological assessment but rarely both (Reily 1985, Pearman 1972). Reily (1985) reported that men with diabetes mellitus had an increased incidence of sexual dysfunction secondary to neuropathic and angiographic abnormalities and that as many as 60% of men had erectile failure within five years of diagnosis.

The picture is less clear for women with diabetes mellitus. Indeed this is true in general of
sexual dysfunction in women. The data reported largely concentrate on the physically handicapped. A number of investigators have used discussion groups to investigate this area (Helsinga, Schellen & Verkuyl 1974, Hale, Norman, Boyle et al 1978 & Campling 1979). Helsinga et al (1974) reported on a group of people who had sustained a spinal cord injury and the questions most frequently asked were "Am I going to live?" followed by "What are my sexual responses like now?". There is now literature available for women with physical disabilities (Hale et al 1978, Campling 1979) and some investigators believe counselling and information in hospital immediately after spinal cord injury could reduce later sexual difficulties by preventing conjecture and uncertainty through fact (Cole, Chilgren & Rosenberg 1973, Cole 1975).

Sexual functioning has been assessed following pelvic surgery using unstructured qualitative interviews. Early studies in men following abdomino-perineal resection for rectal carcinoma, reported that up to 95% of patients experienced some sexual difficulties including impotence (Jones 1942, Williams, Watson & Goligher 1951 & Weinstein & Roberts 1977). Similar figures were initially found by Dennis (1945) after total proctocolectomy for ulcerative colitis, but more recent studies suggest an incidence of sexual difficulties of around 2%. Bauer, Gelernt, Salky et al (1983) reported on 291 patients undergoing a proctocolectomy, mainly for ulcerative colitis using a personal interview. They did not assess sexual function pre-operatively nor did they employ valid, reliable techniques administered by pre-trained interviewers to investigate the frequency and nature of sexual problems post-operatively. Despite these limitations they suggested that with careful surgical dissection only 1.5% of men had problems after surgery. Work on sexual difficulties following an ileostomy has suggested that most patients adapt well to their stoma and that when difficulties arise they are secondary to surgical complications (Burnham et al 1977). Burnham et al (1977) in association with the Ileostomy Association of Great Britain analyzed over 300 returned questionnaires investigating sexual problems. Less than 10% of men and women found the presence of a stoma made sexual intercourse difficult. However 30% did admit to embarrassment regarding their stoma and more than half felt it made them look less attractive.

following an ileo-anal anastomosis. In a retrospective uncontrolled study of 49 patients (23 women) at a median of almost 4 years after surgery they tried to assess sexual function pre-operatively, with a stoma and following reconstructive surgery. Each patient was interviewed personally using an unstructured and non-validated questionnaire. The interview covered frequency of sexual intercourse, ability to achieve orgasm and its quality, frequency of masturbation, ejaculation, impotence, soiling and pouch discomfort. It is not clear how the answers to these questions were interpreted and most surprisingly there did not seem to be any change in sexual function following a pouch operation.

Irvine (1995) has developed an index to measure the impact of perianal Crohn’s disease (The Perianal Crohn’s Disease Activity Index - PCDAI). One dimension assesses restriction of sexual function with 5 grades ranging from no restriction of sexual activity to being unable to engage in sexual intercourse. They concluded that most patients did not avoid sexual intercourse despite their perianal disease. Those that did tended to have the severest disease. Fatigue and intestinal symptoms were also volunteered as reasons for reduced frequency of sexual intercourse.

There have been few detailed studies of sexual function in patients with inflammatory bowel disease. Some investigators have suggested normal sexual functioning using global, non-validated measures of quality of life, (Gazzard et al 1978, Hendriksen et al 1980 & Binder et al 1985). Reasons for the apparent absence of problems may reflect a lack of readiness to discuss sexual difficulties with doctors but could be due to a lack of validated, reliable measures for investigating this topic.

The case-control studies reported in this thesis were conducted in 1990 and investigate the frequency and nature of sexual problems in men and women with inflammatory bowel disease. The problems identified may form the basis on which better counselling programmes can be developed. Section 5.2 reports on the initial study of 55 women from Cardiff and Leicester with Crohn’s disease and a similar number of community "buddy" controls. Section 5.3 reports on 150 men and women with IBD in Leicestershire using the same questionnaire.
5.2 SEXUAL DYSFUNCTION AMONGST WOMEN WITH CROHN'S DISEASE

5.2.1 Patients and Methods:

Fifty five women with Crohn’s disease were identified from the epidemiological data bases in Cardiff and Leicestershire (previously described). Women over aged greater than 16 and less than 50 were selected consecutively from the respective data bases. A female researcher (G. Moody) invited each patient by telephone to participate in a structured interview. This technique has been widely used during aetiological investigations in cervical carcinoma (Cullimore 1990). The structured questionnaire was developed during studies of risk factors in cervical adenocarcinoma (Cullimore 1990). It was modified after a pilot study amongst a different group of patients with Crohn’s disease allowing for their additional comments. The interview was conducted in a quiet room at a later date away from general clinical activity. During the interview background information on age, diagnosis, marital status as well as such clinical details as site of disease and surgery were collected. After good rapport was established obstetric and gynaecological history, sexual behaviour and any associated problems were investigated (Appendix 5.1). A conscious decision was made to avoid both controversial and "difficult to assess" areas such as sexual abuse, homosexuality, orgasm and anal intercourse. I felt that to explore such areas with patients would destroy the trust and confidence built up with their consultants over a period of years and might have stopped some patients participating in the studies. Some investigators do not believe these issues to be of any magnitude amongst patients with IBD and indeed in a study of sexual victimisation in patients with bowel disorders by Walker, Katon, Roy-Byrne et al (1993) it was shown that patients with IBD had a lower rate of sexual abuse compared to irritable bowel controls. There was also a definite reluctance on the part of the clinicians caring for patients with IBD in Leicester, including their general practitioners, to expose them to such a line of questioning.

Each patient was asked to identify a friend or "buddy" of similar age who would be willing to participate in such an interview. Replies were compared using $X^2$, Fisher's exact test and t-tests where appropriate.
5.2.2. Results:

Of the 55 women with Crohn's disease approached 50 agreed to participate, and in addition they identified 50 buddy controls. Patients and controls were well matched for age (mean 34.7 SD ± 6.1 and 33.6 SD ±6.0 years respectively, t = 0.92 n.s.). Women with Crohn's disease had been married for a mean of 13.1 years (S.D. ±7.7) which was significantly longer than the 9.6 years (S.D. ±6.4) (t=2.1 p<0.05) of controls. The divorce rate was 16% in patients and 6% in controls (Fisher exact test p=0.09, ns). 73% (n=24) of married patients and 98% (n=39) of the married controls were sexually active (X²=9.4, p<0.005), 75% (n=9) of the patients and 86% (n=6) of controls with a stable, but unmarried relationship were sexually active (X²=0.3 ns). Duration of marriage was not related to frequency of sexual intercourse in either patient (correlation coefficient r = -0.13) or control group (r = -0.02).

Women with Crohn's disease described sexual problems more often than controls. Of those women with a stable relationship (married or unmarried) 27% of patients had no sexual intercourse compared with 4% of controls (X²=8.9, p<0.005). Amongst those who were sexually active patients had intercourse on average 1.9 times per week compared with 2.2 times per week amongst controls (t=0.74, ns). In this study dyspareunia was defined as sufficient pain to interfere with or prevent sexual intercourse and it was significantly commoner in patients (n= 24, 60%) than controls (n=14, 34%) (X²=6.5 p<0.01). Dyspareunia was independent of the site of disease (large vs. small bowel X²=0.85 ns), (Table 5.1). There was no association between abdominal surgery for Crohn's disease and dyspareunia, (X²=0.01 ns). Women with dyspareunia had 1.6 surgical procedures (SD±1.9) compared with 1.4 (SD±1.8) amongst those without dyspareunia (t=0.34 ns). There was no association between sexual problems and perianal disease (X²=2.8 ns) or fistulae (X²=0.8,ns). However, women with both perianal disease and fistulae were more likely to have dyspareunia than those with neither (X²=4.2, p<0.05). Life-time reported experience of vaginal candidiasis was also significantly greater in patients (56%) than controls (32%), (X²=5.8, p<0.05), and may have contributed to any dyspareunia. Other reasons for this reduced frequency of sexual activity included abdominal pain (24% of patients), diarrhoea (20%) and fear of faecal incontinence (14%).

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In this study there was no significant difference between total number of pregnancies; patients had 94 pregnancies and controls 86 ($X^2=8.4$ ns). Although the overall number of pregnancies was similar, women with Crohn's disease had experienced greater difficulties in achieving conception, in 22% there was a 2 year delay compared to 7% of controls ($X^2=7.2$, $p<0.01$). In addition there were more problems at delivery amongst patients ($X^2=16.1$, $p<0.05$), with an increase in both elective and emergency caesarian sections ($X^2=9.2$, $p<0.05$). Forceps deliveries were less common amongst the patient group ($X^2=5.6$, $p<0.01$).
Table 5.1: Dyspareunia Amongst Female Patients with Crohn’s Disease and Controls:

<table>
<thead>
<tr>
<th>Site of disease</th>
<th>Comparison</th>
<th>$X^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small bowel</td>
<td>Controls</td>
<td>6.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Large bowel</td>
<td>Controls</td>
<td>9.4</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Large bowel</td>
<td>Small bowel</td>
<td>0.85</td>
<td>ns</td>
</tr>
</tbody>
</table>

Patients were divided into those with predominantly small bowel involvement and those with disease confined to the colon according to their case notes.

Dyspareunia is independent of site of disease
5.3 PERCEIVED SEXUAL DYSFUNCTION AMONGST PATIENTS WITH IBD

5.3.1 Patients and methods:

300 patients with inflammatory bowel disease (IBD) were selected at random from the community data base for IBD in Leicestershire (previously described). Every tenth name on this register was selected until 100 women with ulcerative colitis (UC), 100 men with UC and 100 men with Crohn’s disease (CD) had been identified. Women with Crohn’s disease were not approached in this arm of the study. Each patient was posted an invitation to take part in a questionnaire study of possible personal and sexual problems arising from their IBD. 188 of the 300 patients (63%) agreed to participate and they were subsequently sent a modified version of the original questionnaire on sexual problems (see appendix 5.1).

Details sought included demographic data, patients' perception of the severity of their illness, data relating to treatment, family history and fertility. The last section dealt with frequency of sexual intercourse and any difficulties experienced, as well as adverse effects on relationships with partners. Women were specifically asked about dyspareunia which was defined as pain severe enough to interfere with sexual intercourse. For purposes of analysis infertility was defined as failure to conceive within one year. Again this questionnaire did not investigate controversial areas such as sexual abuse, homosexuality, anal intercourse or orgasm for the reasons already stated.

All patients were asked to identify a suitable person to act as a "buddy control" and in addition controls were recruited from the community through local general practitioners. Responses from the two control groups were reviewed at the end of the study to ensure comparability. A randomly selected group of questionnaires (n=20) were further validated by direct interview with patients four months after the main study.
5.3.2 RESULTS:

150 questionnaires were returned by patients who agreed to participate in the study (response rate = 80%). 50 were from women with UC, 46 from men with CD and 54 from men with UC. The response rate within each group was comparable ($X^2=0.53$, degrees of freedom=2, ns). Forty seven female controls and 75 male controls also completed the questionnaire, 76 of whom were buddy controls and 46 drawn from general practice.

The range of disease severity (recorded on the data base as previously described) was similar in all groups of patients, ($X^2= 4.31$ df=4, ns). There were no differences in demography between patient and control groups; in age range ($t=0.67$ ns), marital status or numbers with regular partners; ($X^2 = 14$, df=12 $p=0.3$, ns.) or in mean duration of marriage (range of means 16-19 years) (Table 5.2). The "buddy control" group and the community controls were comparable with no statistical differences (Table 5.3).

Women with UC had a later menarche at 13.1 years ± 1.7 although this was not significantly different to controls (12.8 years ± 1.6, $t=0.92$, ns). Although dyspareunia was commoner amongst the 40 female patients who were sexually active (15/40 = 38%) than the 38 controls (7/38 = 18%) the difference did not reach statistical significance, ($z$ test = 2.6, ns). Ten patients and nine controls were abstinent at the time of the survey and so did not report dyspareunia.

The total number of pregnancies was similar in all groups with a mean of 2.7 per patient studied, (female colitics vs controls, $z = 1.7$, ns, male colitics vs controls $z = 0.44$, ns, male CD vs controls $z = 0.38$, ns and male CD vs male UC; $z = 0.03$, ns). The partners of men with ulcerative colitis and to a lesser extent those with Crohn's disease took significantly longer to conceive, (defined as successful conception taking longer than 1 year to achieve), (male UC vs controls; $X^2=19.4$, $p<0.0001$ and male CD vs controls; $X^2=5.9$, $p=0.02$, Yates correction).

There was no difference in the frequency of sexual activity using contingency tables for $X^2$
analysis (Table 5.4) between patient groups and controls, \((X^2 = 12.78, 12\text{df}, \text{ns})\). When comparing those with infrequent or no sexual activity again using contingency tables for \(X^2\) analysis there was no difference, \((X^2=6.98, 4\text{df}, \text{ns})\). Similarly there were no statistical differences in frequency of sexual activity between the two control groups. However patients reported numerous reasons why their sexual activity might be impaired (Table 5.5) including fear of faecal incontinence \((n=17)\), tiredness \((n=16)\), abdominal pain \((n=13)\) and proximity of toilet facilities \((n=11)\).

In the assessment of reliability there were no differences in responses from the sub-group of 19 (>10%) who were re-interviewed in person 4 months later.

### 5.4 Discussion:

It is important in subjective studies which attempt to measure quality of life that data are obtained by reliable and valid measures. To achieve this a questionnaire was developed from one used in a study of risk factors in cervical adenocarcinoma (Cullimore 1990), which was used to collect similar personal details. My questionnaire was piloted on a small group of women with Crohn’s disease from the city of Leicester and the wording modified in line with patients comments. All the women with Crohn’s disease were interviewed face to face and compared with "buddy controls". The use of "buddy" and community controls is now a well established technique in studies of inflammatory bowel disease (Mayberry et al 1992). Buddy controls are likely to be of a similar age and educational background and to share the same interests. Draw backs to this method, however, would include the idea that "like attracts like" and that perhaps people with similar problems will also tend to be drawn together. To get round this difficulty we also used patients registered with the study groups’ general practitioners. In this study the results between controls were comparable and so they were treated as an homogeneous group. The data on frequency of sexual intercourse correlated with a review of sexual activity in the normal British population by MORI (Jacobs & Worcester 1991) which reported the average number of times couples had sexual intercourse as 1.9 times per week.

In the second study I believe I have selected a representative cross section of a large
community based population register of patients with inflammatory bowel disease was selected. Such a random sample is likely to be representative of the disease as a whole, including patients with mild as well as severe disease. The questionnaire’s reliability was assessed in a randomly selected group of men who were re-interviewed in person after a four month interval. These responses were comparable to their initial answers.

Only 63% of patients approached expressed an interest in the study and only 80% of these participated. This reflects the difficulties associated with investigation of sexual function. The less personal and anonymous nature of a mailed questionnaire may be responsible for underestimating the frequency of these problems. It is possible that face to face interviews, with a sensitive interviewer may have discovered a reduced frequency of sexual intercourse for which questionnaires were less appropriate. Reasons for this belief include the similarity of problems and fears quoted by both groups.

Inflammatory bowel disease does not significantly affect personal relationships in all the groups of patients studied. There were no significant differences in duration of marriage or divorce rates. Although the divorce rate in women with Crohn’s disease was 16%, this was not significantly greater than the 6% amongst controls. Gazzard et al (1978) investigated 85 patients with Crohn’s disease using a battery of tests to measure personality and mood together with their own untested quality of life questionnaire. He suggested that despite decreased sexual activity there was little effect on personal relationships. Duration of marriage also, was not related to frequency of sexual activity in this investigation.

Patients with ulcerative colitis and men with Crohn’s disease report similar concerns to women with Crohn’s disease but in practice these did not appear to prevent sexual relationships. All groups were fearful of faecal incontinence and anxious about abdominal pain and diarrhoea during sexual intercourse. Women with Crohn’s disease have significantly more sexual problems than controls. A significant minority are sexually inactive because of dyspareunia, abdominal pain, diarrhoea and fear of faecal incontinence during intercourse. For others dyspareunia leads to a reduced frequency of sexual intercourse (Hamilton, Brown, Davies et al 1977, Brooke 1979 & Lichtarowicz & Mayberry 1987) but this problem is not widely known and little advice is available to sufferers.
Despite the general impression that patients with chronic IBD may have difficulties in this area it has received limited attention from the medical profession or in scientific publications. Most work on quality of life in patients with IBD has failed to include a detailed account of sexual function and those that do mention it usually allude to "a normal and fulfilled life" (Hendriksen et al 1980, Binder et al 1985). Investigators have usually felt patients with IBD do not have sexual difficulties and there is widespread reluctance to assess aspects of sexual function such as orgasm or same sex relationships. Hendriksen et al (1980) suggested that 122 randomly selected patients with UC in Denmark had a similar frequency of sexual intercourse to 83 age matched community controls. In another study from Denmark, Sorensen, Olsen & Binder (1987) reported that 106 patients with CD had similar sexual problems and a similar frequency of sexual intercourse to 75 previously healthy patients admitted to hospital for an acute illness of less than 28 days duration.

Several studies have concentrated on problems following ano-rectal surgery or a stoma (Burnham et al 1977, Kennedy et al 1982). They all concluded that although there are initial problems, patients lead a "normal life" in the longterm. More recently Damgaard et al (1995) retrospectively investigated sexual function following firstly a stoma and then reconstructive surgery. They used a personal interview but without a validated questionnaire and covered particularly sensitive areas. Although there was no deterioration of sexual function following surgery neither was there any improvement. This is surprising given the fact these patients will all have had severe colitis pre-operatively and are likely to have had significant diarrhoea associated with generally poor health. The reasons for these results may reflect the fact that the study took place many years after the surgery and thus patients re-call is likely to be biased. It is also likely that with surgeons involvement in the study this may have introduced an element of interviewer bias in favour of surgery. The interviewers also did not employ validated or sensitive questionnaire.

Differences between women with CD and other patients with IBD are not entirely surprising as women with Crohn’s disease often have specific complications including perianal and vaginal disease. Certainly the medical and surgical treatment of perianal disease taxes many clinicians and some would favour early aggressive surgery (Williams et al 1995) whilst others adopt a more conservative approach (Mc Kee & Keenan 1996). Perianal disease alone did
not seem to contribute to the reduced sexual intercourse in women with CD which is in agreement with the work of Irvine (1995). The PCDAI which has been validated in Canada suggests only patients with severe perianal disease abstain from sexual intercourse and that it is often intestinal symptoms and fatigue that lead to abstention or reduced frequency of sexual intercourse in agreement with the findings of the present study.

Both men and women with inflammatory bowel disease reported concerns about diarrhoea, abdominal pain and fear of faecal incontinence. These concerns can affect quality of life, and command importance as explanations for loss of sex drive. Burnham et al (1977) together with the Ileostomy Association investigated problems amongst married ostomists and concluded most adapt well with no evidence of subsequent sexual dysfunction. In contrast Kennedy et al (1982) found psychological problems associated with sexual activity were not unusual following ileostomy surgery. Long term follow-up stoma nurses could detect and perhaps alleviate their difficulties, although recent work would cast doubt on this assumption e.g. Bhakta, Probert, Jayanthi (1992) found that both European and Asian patients were dissatisfied with counselling from stoma therapists.

This study shows a significant numbers of women with Crohn's disease experience serious sexual problems. Whilst men with IBD and women with UC do not appear to have a reduced frequency of sexual intercourse, they also report similar fears and concerns. Questionnaire based studies tend to highlight problems at a specific point in time and may fail to reflect the relapsing nature of the disease. The use of a sympathetic interviewer may overcome some of these limitations. However, sexual problems are so personal that it would be surprising if all difficulties were identified in a single interview with a stranger. Nevertheless there is a definite need for wider recognition of sexual problems amongst people with inflammatory bowel disease.

5.5 Conclusion:

In conclusion patients with IBD are concerned about sexual function because of fear of faecal incontinence, abdominal pain, fatigue and dyspareunia. These difficulties actually prevent women with Crohn's disease from leading a normal sex life. This may be a reflection of
severe perianal disease in women with Crohn's disease.

These two studies highlight the need for sympathetic investigation and clinical management of this area. Although only women with Crohn's disease have a significant level of involuntary sexual abstinence, fear of incontinence, diarrhoea and pain are common to all patients with IBD. Where appropriate, referral to agencies such as Relate (the marriage guidance organisation), SPOD (Sexual and Personal problems of the Disabled) and clinical psychologists with an interest in sexual problems may be necessary. Greater awareness by doctors and nurses may alleviate some of the stress, anxiety and embarrassment faced by patients in busy clinics.

Thus although sexual problems were not an issue broached in the public forum of the discussion groups in chapter three it is clearly a concern to many patients with IBD. In particular fear of faecal incontinence which may lead to a reduced frequency of sexual intercourse was certainly a major concern in the open group discussions and as such both of these areas need to be incorporated into an overall quality of life measure.
### TABLE 5.2: AGE AND DURATION OF MARRIAGE AMONGST PATIENTS AND CONTROLS:

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=150)</th>
<th>controls (n=122)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men with CD</td>
<td>Men with UC</td>
</tr>
<tr>
<td>Mean age ± SD</td>
<td>40.2 ± 8.6</td>
<td>40.2 ± 7.9</td>
</tr>
<tr>
<td>Mean duration of marriage ± SD</td>
<td>16.8 ± 7.29</td>
<td>18.65 ± 6.23</td>
</tr>
</tbody>
</table>

Age and age at marriage of 150 patients and 122 controls were recorded in a study of personal and sexual problems of a community based group of patients with IBD in Leicestershire.
### TABLE 5.3: COMPARABILITY OF COMMUNITY AND "BUDDY CONTROLS"

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP Controls n = 41</td>
<td>38.5 ± 8.8</td>
<td>38.5 ± 10.0</td>
<td>t = 0, ns</td>
<td>38.8 ± 11.1</td>
<td>39.3 ± 11.5</td>
<td>t = 0.15, ns</td>
</tr>
<tr>
<td>&quot;Buddy&quot; Controls n = 32</td>
<td>38.5 ± 10.0</td>
<td>38.5 ± 10.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 22</td>
<td>39.3 ± 11.5</td>
<td>39.3 ± 11.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t = 0.15, ns</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean duration marriage</td>
<td>12.6 ± 8.9</td>
<td>16.1 ± 9.5</td>
<td>t = 1.6 ns</td>
<td>16.7 ± 9.9</td>
<td>13.8 ± 10.3</td>
<td>t = 0.84, ns</td>
</tr>
<tr>
<td></td>
<td>16.7 ± 9.9</td>
<td>16.7 ± 9.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of sexual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>intercourse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 / week</td>
<td>5</td>
<td>9</td>
<td></td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>2 / week</td>
<td>17</td>
<td>8</td>
<td></td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>3 / week</td>
<td>6</td>
<td>6</td>
<td></td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>4 / week</td>
<td>3</td>
<td>3</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>* Infrequent or never</td>
<td>12</td>
<td>6</td>
<td></td>
<td>6</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

* Patients who had sexual intercourse on a monthly basis, less often or not at all were all grouped together as "infrequent".

Community and "buddy" controls were identified by patients with IBD and General practitioners in Leicestershire.
### TABLE 5.4: FREQUENCY OF SEXUAL INTERCOURSE OF PATIENTS WITH IBD IN LEICESTERSHIRE

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Women (n=97)</th>
<th>Men (n=175)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UC</td>
<td>controls</td>
</tr>
<tr>
<td>1/week</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>2/week</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>3/week</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>4/week</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Infrequent or never *</td>
<td>19 (13)</td>
<td>9 (7)</td>
</tr>
</tbody>
</table>

* Patients who had sexual intercourse on a monthly basis, less often or not at all were grouped together as "infrequent." The number of patients who were married or who had a stable relationship are in brackets.

Patients and controls were asked to complete a questionnaire on sexual activity.
TABLE 5.5: REASONS FOR REDUCED FREQUENCY OR TOTAL ABSTENTION FROM SEXUAL INTERCOURSE IN PATIENTS WITH IBD IN LEICESTERSHIRE.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Women with ulcerative colitis (n=24)</th>
<th>Men with Crohn’s disease (n=34)</th>
<th>Men with ulcerative colitis (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern over stoma</td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Tiredness</td>
<td>2</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhoea/urgency</td>
<td>1</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Proximity of toilet facilities</td>
<td>3</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Fear of incontinence</td>
<td>10</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Depression/moodiness</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Patients and controls were asked to identify reasons for any reduction in sexual activity.
CHAPTER 6: FERTILITY AND OUTCOME OF PREGNANCY IN MEN AND WOMEN WITH INFLAMMATORY BOWEL DISEASE
6.1 INTRODUCTION:

Crohn’s disease (CD) and ulcerative colitis (UC) commonly affect young adults during their reproductive years. In chapter three patients were clearly concerned about the risks of having IBD on their family. Whilst several studies (De Dombal, Burton & Goligher 1972, Mc Ewan 1972, Willoughby & Truelove 1980, Khosla, Willoughby & Jewell 1984 & Mayberry & Weterman 1986) have investigated fertility in women with CD and UC and to a lesser extent in men (Levi, Fisher, Hughes et al 1979, Korelitz 1985 & Burnell, Mayberry & Calcraft et al 1986), few have examined large numbers of patients from the same community exposed to similar medical and surgical practice.

Women with CD are thought sub-fertile and at risk of an early menopause (De Dombal et al; 1972, Khosla et al 1984 & Mayberry & Weterman 1986). This may be due to a combination of disease activity, advice against pregnancy and reluctance by women to conceive because of fear both of relapse of their disease and also the risk of the disease affecting their offspring as expressed by patients in the free discussions described in chapter three. Reduced sexual activity as a result of pain, fear of incontinence, abdominal discomfort and diarrhoea are also likely to play some role. In contrast, women with ulcerative colitis are thought not to be infertile (Mc Ewan 1972, Willoughby & Truelove 1980).

Whilst reduced fertility in men with IBD is recognised, it is usually secondary to sulphasalazine therapy (Toth 1979, Toovey Hudson, Hendry et al 1981, Conn & Holdsworth 1984, O’Morain, Smethurst, Dore et al 1984 & Shatter, Kershaw & Berrisford 1984). Within weeks of initiating treatment there can be a reduction in motility and numbers of spermatozoa, together with the appearance of abnormal forms, including megalos varieties (O’Morain et al 1984). Such seminal abnormalities caused by sulphasalazine could theoretically put the foetus at risk of congenital abnormalities but this has never been investigated.

This study reports the experience of nearly 1200 male and female patients with IBD in Leicester over a twenty year period. Its aims were to ascertain whether patients had
(i) A similar fertility rate to the background population  
(ii) Experienced delays in conception  
(iii) Abnormal pregnancies and  
(iv) A high rate of congenital malformations compared to the background population.

6.2 METHODS:

Patients:
Nearly 2,500 patients with IBD were identified during the assembly of the epidemiological database in 1989 (previously described). Some 400 of these were cases in the Indian migrant community who were excluded from this study because of their poor response rate in earlier work (unpublished data). Of the European patients 1743 were thought to be alive and contactable at the commencement of the study, subsequently 304 were found to have either moved away (n=126), died (n=138) or were untraceable (n=40). Over 1400 patients were therefore eligible for the study.

Methods:
A questionnaire (appendix 6.1) investigating the fertility of European patients was developed from a previously validated proforma for collecting information on sexual dysfunction in IBD (adapted from appendix 5.1). The questionnaire was piloted on committee members of a local self-help organisation and after minor modification sent to 1439 patients with IBD.

The questionnaire:
The questionnaire (see appendix 6.1) sought details of marital status, duration of marriage and age at diagnosis. Patients were asked to record the total number of pregnancies and note if any conception took longer than 12 months. Details about miscarriages, stillbirths and terminations were also collected. Patients were asked about caesarian sections and forceps procedures they had experienced. Enquiry was also made about significant illnesses or abnormalities in their offspring. Patients were asked whether they had taken sulphasalazine during the time of conception and pregnancy. Disease site and activity were not investigated in this study. Analysis took place after three successive mailings of the questionnaire using Lotus version Release 2.01 spreadsheets, student's t tests and $X^2$. 100 patients were
approached again six months later to check on the reliability of their answers to the questionnaire.

6.3 RESULTS:

Response Rate:
1159 questionnaires were returned, 1108 were completed and 51 came from patients who refused to participate, usually because of older age. The overall response rate was 81% after three successive mailings. The response rate was similar for both sexes and between disease groups. The total sample comprised 472 men and 636 women; 439 patients had Crohn’s disease and 669 had ulcerative colitis.

Representativeness of replies:
280 patients failed to return the questionnaire after three successive mailings. There were no apparent differences between the responding and non-responding groups in age (mean age of non-responders = 54.4±15.8, mean age of responders 52.2±16.2, t=2,ns), proportions of men and women or disease groups. Patients with a range of disease distribution, severity and activity responded to the questionnaire and the sample was representative of people with IBD in Leicestershire.

Repeatability:
10% (100 patients) of the responder group were selected at random and asked to complete the same questionnaire again six months later. There were no significant changes from the first mailings but included three couples, pregnant during the first survey, who had successfully completed their pregnancies.

Fertility:
The number of male and female patients with CD and UC who responded are recorded in Table 6.1 together with the total number of live births before and after diagnosis. The mean age of respondents was 52.2±16.2 years and their mean age at diagnosis was 36.3±15.8. There were 853 patients who were either married or had a long-term regular heterosexual partner at the time of the survey (77%). The mean duration of the relationship was 26.5 ±
14.7 years. There were 156 single patients (14%), 51 who had been widowed (4.6%) and a further 48 (4.4%) who were divorced.

There were 1933 completed pregnancies (90.7%). The crude infertility rate for the group was 21%, for men with CD it was 27% and men with UC 24%. 60% of the men who had fathered children admitted to taking sulphasalazine. Women with CD had an infertility rate of 19% and for women with UC it was 15%. The mean number of children for the whole group was 1.7±1.3 and for those aged 45 and under at the time of diagnosis it was 1.6±1.3. For Leicestershire the fertility rate is 1.85 (Birth statistics 1990). If applied to our group 2050 live births would be expected compared with the observed 1933. As expected all patient groups had significantly more children before diagnosis than after, (male CD, z=24.4, p<0.0001, female CD, z=8.4, p<0.0001, male UC, z=17.9, p<0.0001 and female UC, z=12.7, p<0.0001), (see table 6.1). 167 (7.8%) pregnancies ended in miscarriage (n=161) or stillbirth (n=6) and 33 (1.5%) pregnancies were terminated, (see table 6.2).

208 (23.8%) couples experienced a delay of greater than twelve months in achieving conception for one or more of their children, including 58 families where this delay was repeated for more than one pregnancy; 69% of these pregnancies were achieved after diagnosis. Forty nine men with CD experienced a delay, 85% after diagnosis. Over half of these men with CD reported taking sulphasalazine. Twenty six men with UC also experienced a delay, 65% after diagnosis. Fifty five percent of these men with UC reported taking sulphasalazine. Fifty three women with CD experienced a delay in achieving conception, 75% after diagnosis. Fifty three percent of these women with CD reported taking sulphasalazine. Eighty women with UC also experienced a delay, 63% after diagnosis, and 53% of them reported taking sulphasalazine.

Outcome of pregnancy:
Table 6.2 reports the numbers of miscarriages, termination, caesarian sections and forceps procedures experienced by women with IBD compared with the wives of men with IBD. In doing this I used the wives of men with IBD as controls, allowing the assumption that these women are representative of a cross-section of seemingly healthy or "normal" women in the community. Women with CD had more miscarriages than women with UC, X²=3.9,
p<0.05, they also had more forceps procedures than women with UC, $X^2=7.1$, p<0.01. There were no differences between these groups in numbers of terminations or caesarian sections ($X^2=2.7$, ns and $X^2=0$, ns, respectively).

When the wives of men with IBD were used as controls and compared to women with IBD, women with CD had significantly more miscarriages than the wives of men with CD, ($X^2=26.1$, p<0.0001). Whereas there was no difference between women with UC and the wives of men with UC, ($X^2=1.5$, ns). Women with CD had significantly more caesarian sections and forceps procedures than the wives of men with CD, ($X^2=38$, p<0.0001 and $X^2=9.3$, p<0.005 respectively). In contrast women with UC had similar numbers of both procedures to the wives of men with UC, ($X^2=3$, ns and $X^2=1.6$, ns, respectively). There were slightly more terminations amongst women with UC when compared with wives of men with UC, ($X^2=5.5$, p<0.05), while there were no such differences in the two CD groups, ($X^2=3.7$, ns).

133 parents reported significant illness or abnormality in their children. IBD and atopic illness formed the majority of documented illnesses although these figures cannot be considered representative as some parents may not have recorded these conditions believing them not to be relevant (n = 21 and n = 54 respectively). Major congenital malformations incompatible with life included anencephaly (n=5) and other congenital malformations, eg tracheo-oesophageal fistula (n=5), childhood leukaemia (n=5), cleft palate (n=4), and congenital heart disease (n=5) were also reported. The percentage of births overall with a serious congenital malformation was 2% which is comparable with 1.8% reported for Leicestershire (Congenital malformation statistics 1990). In men with CD it was 1.5%, but over 2% in all other groups, (Table 6.3). 39 of the congenital abnormalities occurred after diagnosis and in 29 cases the parents reported a history of taking sulphasalazine (Table 6.3). Patients with an offspring who had a congenital malformation were significantly more likely to have taken sulphasalazine, $z=4.3$, p<0.0001. This however may reflect how most patients in the study cohort would have been prescribed sulphasalazine as first line therapy before the newer aminosalicylic compounds were available.
6.4 DISCUSSION:

The response rate of the study was reasonably high at over 80% and combined with large number of patients who participated the results can be considered representative of people with IBD in Leicestershire. Results were not analyzed by site of disease and indeed has been shown unimportant in a number of earlier reports (De Dombal et al 1972, Mc Ewan 1972, Willoughby et al 1980 & Burnell et al 1986).

Until recently young men with IBD were likely to receive sulphasalazine as first line therapy until they complained of infertility. Almost 25% of men had no children which is 15% higher than the national average (Burnell et al 1986). This may be related to sulphasalazine treatment (Toth 1979, Toovey et al 1981, Conn et al 1984, O’Morain et al 1984 & Shaffer et al 1984) which was taken by 60% of participants in the study.

Crohn’s disease:

This study confirms the reduced number of children born to men with Crohn’s disease reported by Burnell et al (1986). In that study the fertility of 70 men with CD was compared with a group of age matched controls. Men with CD had a mean of 1.6 children compared with a mean of 1.9 in the controls. No correlation was found with sulphasalazine or steroid therapy in the present study. Men with CD had a significant fall in birth rate after diagnosis having 333 children before diagnosis compared to 86 after. This is comparable with Burnell et al’s finding (1986) that there was a threefold reduction in births after diagnosis. Men with CD (16%) also reported a delay in achieving conception which although well recorded in women with CD has not been recognised previously in men (Khosla et al 1984, Mayberry et al 1986).

Women with Crohn’s disease had less children than the background population in Leicester (1.2), with a higher level of infertility (19.4%). These findings are comparable with other reports including a European study which investigated fertility and pregnancy in 275 women with CD in 5 different countries (Mayberry et al 1986). In this study there was a significant reduction in births after diagnosis with a large number of women failing to conceive at all
despite not using contraception. In contrast an earlier study from Oxford concluded there was
only a 12% involuntary infertility rate amongst 54 married women (Khosla et al 1984). However, patients who had been advised against pregnancy and patients who did not wish
to have a family were excluded. Both factors are likely to be affected by re-call bias.

Women with CD had more miscarriages and caesarian sections than women with UC. They
also had more miscarriages, forceps procedures and caesarian sections than the wives of men
with CD. Several studies have also found an increased number of miscarriages and stillbirths
Dombal et al 1972, Martinbeau, Welch & Weiland 1975, Levi et al 1980, Nielsen,
reported 22 spontaneous abortions amongst 82 pregnancies in 44 married women with CD
but these were strongly biased by one woman having 9 successive spontaneous abortions.
Others associate a higher spontaneous abortion and still birth rate with either site of disease
(Fielding & Cooke 1970, Martinbeau et al 1975), its severity during pregnancy or first
presentation during pregnancy (Nielsen et al 1984, Miller 1986). Steroids have been
implicated in the increased risk of stillbirths among women with asthma and rheumatoid
arthritis (Reinisch, Simon, Karow et al 1978,) and increased abortion and stillbirth rates,
reduced litter sizes and reduced DNA synthesis in mice (Azad Khan & Truelove 1980,
Jamerot, Into-Malmberg & Esbjomer 1981). However no such associations have yet been
demonstrated amongst women with IBD (De Dombal et al 1972, Mc Ewan 1972). It is
perhaps not surprising that a structurally destructive disease which can cause severe perianal
problems should lead to an increased miscarriage rate and need for assisted delivery.

Whilst many studies have reported on the frequency of abnormal babies born to patients with
IBD these have concentrated on women (De Dombal et al 1972, Levi et al 1979, Korelitz
1985). There appears to be no increased risk of congenital abnormalities in women with CD
although some investigators suggest severe, untreated disease can have adverse effects on
foetal development (Schofield et al 1970, Nielsen et al 1984). Sulphasalazine has not been
shown to affect foetal development (Toth 1979, Toovey et al 1981, Nielsen et al 1984).
However this report casts some doubt on this view. In the present study men with a
congenitally abnormal child were significantly more likely to have taken sulphasalazine, as
were women with UC. This is the first study to suggest that the effects of sulphasalazine on sperm may lead to significant abnormalities. These findings are tentative but give some cause for concern and need confirmation.

_Ulcerative colitis:_

Patients with UC had comparable numbers of children to the background population in Leicestershire (Birth statistics 1980-1990). However, 15% of patients experienced a significant delay in achieving conception (9% of men with UC and 23% of women). These variables have not been studied in depth by other authors as most believe the fertility of patients with UC to be normal (Mc Ewan 1972, Willoughby & Truelove 1980). Whilst the fertility rate is normal in the study reported here colitis appears to influence some aspects of conception in UC, particularly in delaying conception.

The outcome of pregnancy in 352 women with UC in this study compares favourably with other centres (Mc Ewan 1972, Willoughby & Truelove 1980). Willoughby and Truelove (1980) investigated 147 women and concluded the outcome of pregnancy was essentially normal and that disease activity had to be severe and uncontrolled for problems to develop.

Once again men with UC who had a congenitally abnormal child were more likely to have taken sulphasalazine. This was also the case in women with UC. It is biologically possible that sulphasalazine interferes with foetal development. It is known to cross the placenta (Jarnerot et al 1981) and again further study is needed to confirm these findings.

6.5: _CONCLUSION:_

Patients with UC may have normal fertility but can experience delays in conception and a reduced potential for pregnancy after diagnosis. A factor which confounds these problems is the continued widespread use of sulphasalazine. Men and women with CD have significant changes in fertility which cannot be explained by drug treatment alone.

Sulphasalazine causes morphological abnormalities in spermatozoa and may increase the chances of men with IBD having congenitally abnormal offspring. In our study there was no
significant difference in the observed numbers of congenitally abnormal offspring compared to the expected figures for Leicestershire. However it was interesting to note that those men with IBD and women with ulcerative colitis with congenitally abnormal children were likely to have taken sulphasalazine. Further studies are needed to prove that sulphasalazine (and other 5-aminosalicylic acids which have yet to be studied in detail) are safe for both men to take whilst their partners are trying to conceive and for women to take both when trying to conceive and during early pregnancy. To lessen these fears and concerns patients in the reproductive years should probably no longer be prescribed sulphasalazine. This study gives some support to the concerns of patients about the safety of their medications and the potential risk to their offspring and provides some justification for the inclusion of such factors in any measure of quality of life.
TABLE 6.1: Pregnancy experience of patients with IBD in Leicestershire before and after diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Grand total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>CD</td>
<td>UC</td>
</tr>
<tr>
<td>Patients</td>
<td>472</td>
<td>317</td>
<td>155</td>
</tr>
<tr>
<td>Births before diagnosis</td>
<td>724</td>
<td>391</td>
<td>333</td>
</tr>
<tr>
<td>Births after diagnosis</td>
<td>194</td>
<td>108</td>
<td>86</td>
</tr>
<tr>
<td>Total</td>
<td>918</td>
<td>499</td>
<td>419</td>
</tr>
<tr>
<td>TPFR*</td>
<td>1.9</td>
<td>1.5</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Total period fertility rate

Women and men with IBD had significantly more children before diagnosis than after, pre-diagnosis fertility rate is little different to the expected rate for the population of Leicestershire.
TABLE 6.2: The outcome of pregnancy in women with IBD in Leicestershire compared with the wives of men with IBD.

<table>
<thead>
<tr>
<th></th>
<th>Female CD n = 284</th>
<th>Female UC n = 352</th>
<th>Wives of men with CD n = 317</th>
<th>Wives of men with UC n = 155</th>
<th>Total n = 1108</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage</td>
<td>49</td>
<td>66</td>
<td>20</td>
<td>32</td>
<td>167</td>
</tr>
<tr>
<td>Termination</td>
<td>13</td>
<td>12</td>
<td>5</td>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>Forceps</td>
<td>56</td>
<td>67</td>
<td>18</td>
<td>29</td>
<td>170</td>
</tr>
<tr>
<td>Caesarian section</td>
<td>22</td>
<td>43</td>
<td>10</td>
<td>19</td>
<td>94</td>
</tr>
<tr>
<td>Total number pregnancies</td>
<td>379</td>
<td>719</td>
<td>541</td>
<td>461</td>
<td>2100</td>
</tr>
</tbody>
</table>

Women with CD had more miscarriages, forceps procedures and caesarian sections than the wives of men with CD, $X^2=26.1$, $p<0.0001$. 
TABLE 6.3: The distribution of congenital malformations amongst the children of men and women with IBD in Leicestershire.

<table>
<thead>
<tr>
<th></th>
<th>Male CD</th>
<th>Male UC</th>
<th>Female CD</th>
<th>Female UC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>congenital malformation*</td>
<td>7</td>
<td>10</td>
<td>8</td>
<td>14</td>
<td>39</td>
</tr>
<tr>
<td>Took sulphasalazine regularly</td>
<td>6</td>
<td>8</td>
<td>5</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>% of total births</td>
<td>1.5</td>
<td>2.4</td>
<td>2.4</td>
<td>2.1</td>
<td>2</td>
</tr>
<tr>
<td>z value*</td>
<td>2.7</td>
<td>2.7</td>
<td>1</td>
<td>2.7</td>
<td>4.3</td>
</tr>
<tr>
<td>p value* &lt;</td>
<td>0.05</td>
<td>0.05</td>
<td>ns</td>
<td>0.01</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

* Comparing proportion of parents who had a child with a serious congenital malformation and took sulphasalazine with those who had a child with a congenital malformation but did not take sulphasalazine.

Men and women with IBD who took sulphasalazine were more likely to have a congenitally abnormal offspring than those who did not.
CHAPTER 7: THE PERCEIVED VALUE OF A LOCAL SELF HELP GROUP FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE:
7.1 INTRODUCTION:

Patient support groups in the UK have grown in number over the last decade and are often a point of reference for those who are newly diagnosed. Traditionally such groups have not had a strong medical input, and although run by patients for patients, there can be a marked lack of accurate information regarding the people who join such groups and why. Chapter three reported how doctors rather than patients believe such groups fulfil a useful role. This chapter investigated the need for such a group in Leicestershire and the role its members believe it could fulfil.

Leicestershire has a population of approximately 750,000 with over 2,000 known cases of inflammatory bowel disease (Probert et al 1992, Jayanthi et al 1992). It has a large migrant population from East Africa and the Indian sub-continent who are well represented amongst patients with IBD, but it is thought that their membership of such self-help groups may be under-represented. In the East Midlands, there are several active self-help organisations including Crohn's in Childhood (CICRA) in Derby, The Ileostomy Association (IA) and an East Midlands branch of the National Association for Colitis and Crohn's disease (NACC) which was based in Nottingham. With most of these groups based some distance from Leicester the need for a truly local organisation became important in the minds' of a number of gastroenterologists and people with inflammatory bowel disease (IBD). As a result it was decided to establish a new branch of NACC in Leicestershire and to approach all known cases living in the area to investigate their attitude towards such a proposal.

We investigated some of the characteristics of those patients who attended an inaugural meeting of this new local self-help group together with those patients expressing an interest in joining the group. Details of what they hoped to get from the organisation were also sought. This type of information would give additional insight into areas where patients felt quality of life could be improved. Twelve months later a random sample of patients (n=90, every tenth name on the database) who had joined and a similar number who had not (every tenth name from records held by Leicester NACC), were re-mailed to investigate whether this self-help group had fulfilled a useful function.
7.2 METHOD:

All 2084 people with inflammatory bowel disease (IBD) in Leicestershire were mailed an invitation to an inaugural meeting of a local self-help group. This was posted several weeks prior to the meeting. The mailing list was based on the Leicestershire data base already described in this thesis in chapter three. Neither the parent organisation nor the local organisers of the self-help group were involved in the mailing and were unaware of the names of patients. A questionnaire (appendix 7.1) was included in the invitation to elicit what responders felt the role of such a group should be. The questionnaire was initially piloted on members of the committee and cultural advice on wording was obtained. The questionnaire was coded so responders could be identified and characterised. Patients were asked whether they would join the proposed local group and which of the traditional services offered by such organisations they favoured. Such services included:

(i) an information resource
(ii) social events
(iii) opportunities to discuss problems with fellow sufferers
(iv) promoting the needs of IBD sufferers in the local community

Responders were asked to list further suggestions on services which could be provided. As the basis for the study was an invitation to an inaugural meeting of a local self-help group patients were mailed once only and results analyzed one month later. The meeting was also advertised in the local news media (radio and newspapers), and at clinics for IBD in Leicestershire. It had the support of all gastroenterologists in the district.

Twelve months later a similar questionnaire was sent to 90 of the patients who joined the group and 90 who had not (Appendix 7.2). Every other patient who had answered the initial questionnaire was selected until the desired number was achieved. The questionnaire investigated whether the self-help group had fulfilled any of the above functions. Non-joiners were asked to complete a questionnaire detailing reasons for their disinterest. Results were analyzed after three successive mailings.
7.3 RESULTS:

Of the 2084 patients contacted, 253 replied that they were interested in the group and of perhaps becoming members. One hundred and thirty eight people actually attended the inaugural meeting of the group. There was a disinterest rate of 87% in the inaugural meeting and its associated questionnaire with only a 7% attendance at the meeting itself.

Overall those who responded to the questionnaire were significantly older (mean 57, SD±15) than non-responders (mean 50, SD±19, t=3.9, p<0.001) and those who joined the group (mean 50, SD±14, t=3.6, p<0.001). There was no significant difference between the mean age of non-responder non-joiners and joiners (t=0.008, p=0.9).

There was no difference in response rate between patients with Crohn's disease and ulcerative colitis (X² = 2.05, ns). However, patients with Crohn's disease were more likely to join the group than those with ulcerative colitis (X² = 5.43, p<0.01). Women were more likely to respond to the questionnaire than men (X² = 5.26, p=0.02), and also to join the self-help group (X² = 3.80, p<0.05). Patients from the Asian community were significantly less likely to reply (X² = 15.1, p<0.0001), although there was no difference between groups when it came to joining the self-help association (X²=0.01, ns). (Tables 7.1 & 7.2)

Of those who replied 138 wished to join the group (54%); this represented 7% of the inflammatory bowel disease community in Leicestershire. Most thought such groups should provide an information service (85%), an opportunity to discuss problems with fellow sufferers (77%) and should promote the needs of people with IBD in the local community (72%). Contrary to widespread belief and practice in such groups, few people were interested in social events (36%).

Additional spontaneous comments made by patients included calls for increased availability of counselling (n=5), opportunities to improve quality of life through family support and the better education of employers (n=6), improved community facilities such as toilets (n=2) and support of medical research (n=2). Less constructive comments suggested such groups
were a waste of time and money or too distant from patients' homes. Some patients (n=9) felt they were too old to join and others were too ill to consider membership (n=12).

There was an 88% (n = 159) response rate to the second questionnaire, 83 replies from joiners and 76 from non-joiners. Among those who had joined only 57% (n=47) had attended meetings. Most of those who had joined thought the group provided useful information (99%), mutual support (66%), regular updates on medical research (70%) and a place to meet people with similar or more severe problems (60%). Amongst those who had not joined 81% (n=62) thought such a group might be beneficial but gave a variety of reasons why they had not joined which are listed in table 7.3.

7.4 DISCUSSION:

This was an essentially negative study for the role of local self-help groups. Most patients with IBD in Leicester were disinterested in self-help groups, raising a question for the need for local branches in addition to national organisations. The two major functions of mutual support and problem sharing can only occur if you attend meetings and most people clearly do not, with only 4% of patients attending any one given meeting.

This disinterest is disappointing as patients with IBD clearly believe it is their right to know about their illness, as demonstrated in one Italian study which investigated what patients with IBD want to know (Martin et al 1992). In contrast, it was noted in chapter three that the medical profession believe the role of local groups to be more important than patients do. There is a need to accept that there is a problem regarding patients needs and concerns which is clearly not met by local agencies such as Leicester NACC. As 93% of patients neither responded to the questionnaire investigating the role of self-help groups nor attended the inaugural meeting other ways of reaching these patients need to be adopted. Most patients believe information regarding their illness is a priority and mediums such as educational videos could be used to teach them about their condition. A number of published leaflets already exists and are available from organisations such as NACC and some pharmaceutical companies. These should be widely available in out-patient clinics and in general practice surgeries. Access to both counsellors and nurse specialists could also be encouraged.
Only 135 (7%) patients with IBD in Leicestershire wanted to join such a local group, marginally more than reported in other studies and from national membership records (Mayberry et al 1985). These preliminary findings point to members of an IBD self-help group as being usually female and middle aged. The elderly, seriously ill and those from ethnic minorities in contrast are under represented. Nearly a third of Leicester’s population is of Indian descent. Ulcerative colitis is commoner amongst South Asians who form 11% of the IBD data base (n=223). Asian patients were less likely to respond than Europeans, but those who responded were equally likely to join. This may reflect language difficulties or cultural differences, although successive mailings in appropriate languages have failed to improve the response rates in other studies in Leicestershire (unpublished data). If the aim of such groups is to improve patients’ quality of life, they must attract the people most at need and currently these are not being effectively targeted. In particular the young, the seriously ill and members of minority groups are frequently left outside the plans of such organisations. Changes in approach and adequate assessment of such patients’ needs should be considered.

Although self-help group membership has not been shown to specifically improve quality of life several studies have alluded to a useful role. In Croatia an assessment of clubs for patients with hypertension concluded that they could increase the effectiveness of medical treatment and that clubs for patients with specific chronic illnesses should aim to encourage compliance with treatment and rehabilitation regimes, assemblance of new knowledge, better coping skills and consequently may lead to an improved quality of life (Kulcar 1991). An American study looking at the “self-help” model in patients with arthritis examined those skills which enabled some patients to overcome adversities posed by chronic illness. A small but significant contribution of self-help groups to this model was identified together with support for continued involvement of nurses in self-help education. Self-help is related to quality of life and interventions should be aimed at reducing patient dependency and uncertainty and promoting "enabling skills" or "coping skills". The study also suggested women score well on such skills and that higher income is related to greater self-help (Braden 1990).
7.5: CONCLUSION:

In conclusion, a self-help in IBD group failed to attract a significant proportion of patients in Leicestershire. Patients who do join such groups are interested in receiving more information about their illness. These findings support the overall patient view of chapter three that the role of such groups is not perceived as an important tool in learning how to live with IBD. Such support groups could, however, provide a valuable opportunity to educate both the public, employers and teachers alike about IBD both at local community meetings and by distribution of literature produced by the national organisation thereby removing some of the discrimination and stigma associated with these conditions.

Self-help groups could have a role in improving quality of life but better targeting and improved links with hospital out-patient departments could help. This could include specialist nurses, counselling, contact groups and patient education services such as videos. These services should be available to all patients and not just people who wish to join a support group. Clearly such targeting and additional services would need to be studied and show that they are effectively meeting the needs expressed by IBD patients.
TABLE 7.1: Demographics of patients who responded to the questionnaire

<table>
<thead>
<tr>
<th></th>
<th>FEMALES</th>
<th>MALES</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>European UC</td>
<td>77</td>
<td>72</td>
<td>149</td>
</tr>
<tr>
<td>Asian UC</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>European CD</td>
<td>61</td>
<td>37</td>
<td>98</td>
</tr>
<tr>
<td>Asian CD</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

The Asian community are significantly under-represented in the responder group

\(X^2=15.1, \ p<0.001\).

TABLE 7.2: Demographics of patients who joined the group

<table>
<thead>
<tr>
<th></th>
<th>FEMALES</th>
<th>MALES</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>European UC</td>
<td>49</td>
<td>24</td>
<td>73</td>
</tr>
<tr>
<td>Asian UC</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>European CD</td>
<td>38</td>
<td>23</td>
<td>61</td>
</tr>
<tr>
<td>Asian CD</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

More women than men and more patients with Crohn’s disease than ulcerative colitis joined the group.
TABLE 7.3: Reasons cited by patients (n=62) for not joining a local self-help group for IBD.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too busy</td>
<td>30 (40%)</td>
</tr>
<tr>
<td>Prefer others not to know about their illness</td>
<td>15 (20%)</td>
</tr>
<tr>
<td>Manage well enough on own</td>
<td>21 (28%)</td>
</tr>
<tr>
<td>Meetings held too far away</td>
<td>16 (23%)</td>
</tr>
</tbody>
</table>

Patients with IBD are largely disinterested in joining self-help groups and cited being "too busy" to as a one reason for not attending meetings.
CHAPTER 8: COLORECTAL CANCER RISK AND COMPLIANCE WITH TREATMENT AMONGST A TEN YEAR COHORT OF PATIENTS WITH ULCERATIVE COLITIS
8.1 INTRODUCTION:

8.1.1 Colorectal cancer screening: A review of the literature;
Colorectal cancer screening in ulcerative colitis is an emotive subject. Much has been done to promote the role of colorectal cancer screening in early detection of carcinoma but its benefits in terms of improved survival and cost-effectiveness is still controversial (Winawer, Schottenfeld, Sherlock et al 1980, Gilbertson, Mc Hugh, Schuman et al 1980 & Ranshoff & Lang 1991). In ulcerative colitis the increased risk of colorectal cancer has dictated clinical care and concerned many patients over the last twenty years. Actions have ranged from annual screening to prophylactic procto-colectomy (Mac Dougal & Lond 1964). Although clinical practice is in many centres moving away from active screening programmes and tending to support non-intervention this may be considered an inadequate response to the general failure of such programmes and open to criticism. Patients with UC are clearly concerned about their risk of developing this complication of longstanding UC and as such I felt following on from chapter three there was a need to define the size and reality of the problem amongst a cohort of longstanding colitics in Leicestershire.

Several large studies have estimated the relative risk of developing colo-rectal carcinoma in patients with varying degrees of ulcerative colitis. Early reports include a large study from London (Mac Dougal & Lond 1964) of 1052 patients with UC which identified a thirty fold increase in risk of carcinoma in disease affecting the whole colon (35 cases of colorectal cancer). Although results vary, a consensus suggests the greatest risk is in long-standing colitis or early onset of disease (Prior, Gyde, Mc Cartney et al 1982, Lennard-Jones, Ritchie, Morson et al 1983, Rosenstock, Farmer, Petras et al 1985, Brostrum, Lofberge, Nordenvall et al 1987, Collins, Feldman & Fordtran 1987, Ekbom, Helmick, Zak et al 1990, Gyde 1990 & Nugent, Haggitt & Gilpin 1991). Three thousand one hundred and seventeen patients with ulcerative colitis diagnosed between 1922 and 1983 were reviewed in Uppsala, Sweden to re-assess this risk. The study confirmed that less extensive disease at diagnosis was associated with a lower risk (Ekbom et al 1990). Another study from Sweden of 71 patients who underwent endoscopic and histological surveillance reported the association of high grade dysplasia and/ or cancer to be almost exclusively with total colitis (Brostrum et al 1986).
Prior et al (1982) studied 676 patients with ulcerative colitis under long term review and concluded that risk of colorectal cancer was related to age at disease onset. Recent estimates of the risk of developing carcinoma of the colon in association with ulcerative colitis suggest a cumulative incidence of 5% at 20 years and 12% at 25 years in those who have not undergone surgery (Katzka, Brody, Morris et al 1983, Bostrum et al 1987, Gilat et al 1988, Gyde et al 1988 & Levin et al 1991). In contrast a recent study in Copenhagen has suggested that patients with ulcerative colitis are at no increased risk if there is an active surveillance program with effective medical and surgical interventions (Langholz et al 1992).

In a culture in which patients seek the right to informed decisions and preventive programmes must both be effective and cost effective, it is appropriate to reconsider our approach to colorectal cancer screening in ulcerative colitis and investigate if there are any other factors which would reduce the risk of developing colorectal cancer and thus improve quality of life.
8.2 COLORECTAL CANCER IN PATIENTS WITH LONG-STANDING ULCERATIVE COLITIS IN LEICESTERSHIRE:

8.2.1 Introduction:

Whilst the incidence of ulcerative colitis has been stable over recent decades, mortality from the disease appears to have declined (Langholz et al 1992, Probert et al 1993a). This may reflect improved medical management, or less likely, a change in the natural history of the condition. These developments are important in the context of patients’ anxiety about cancer risk and its effects on their quality of life.

Leicestershire provides an ideal environment to study those factors which may precipitate or prevent colorectal cancer in patients with ulcerative colitis and so offer an opportunity to favourably influence patients’ quality of life. A community based index of all patients diagnosed with the condition exists from 1972 (previously described); and this was used as the basis for this study.

8.2.2 METHOD:

Aims:

Patients are clearly concerned about the risk of developing colorectal cancer as evidenced by chapter three and other data (Godber 1989). Screening for cancer in ulcerative colitis has to date not provided any definitive evidence that it saves lives. Thus I have included an investigation of prognosis and cancer risk amongst patients with ulcerative colitis of more than ten years duration and an assessment of the impact of long-term sulphasalazine therapy on the natural course of the disease.

Cohort:

Leicestershire has a population of 950,000 served by three major teaching hospitals. All patients diagnosed as having ulcerative colitis between 1972 and 1989 in the county are recorded on a data base which has been described previously. All patients diagnosed with pancolitis (usually by a barium enema) between 1972 and 1981 were identified and their case
notes reviewed. Similarly the notes of those patients with limited ulcerative colitis who had died by 1992 were also examined. This was to identify patients where colorectal cancer may have played a part in the death of patients with less extensive disease or in case any patients with mild total colitis were missed on barium enema. This was done as colonoscopy is now known to be superior to barium enemas in detecting up mild disease.

Materials and methods:
Data on patients' age, sex, year of diagnosis, history of colectomy, history of severe dysplasia or cancer and compliance with sulphasalazine treatment were collected from their case records. Extent of disease and certainty of diagnosis were compared with endoscopy, radiology and pathology records. A 10% sample of the original biopsy and colectomy specimens were reviewed "blind" by a consultant pathologist (EH McKay) to verify the diagnosis of dysplasia or carcinoma. This was done to assess the accuracy of the original reports as well as to investigate possible inter-observer variation in the assessment of dysplasia.

Relative cancer risk was calculated as the ratio of observed to expected rates using Trent Cancer Registry data on the whole population of Leicestershire up to and including 1990. The ratio of observed to expected numbers of deaths was used as a measure of risk, and this was also based on Trent data.

Compliance with sulphasalazine therapy was assessed from case notes. Patients were recorded as non-compliant when there was clear written evidence of them not taking medication or where doctors had stopped sulphasalazine without substituting a newer 5 aminosalicylic acid compound.

When case records were missing or destroyed contact was made with the last known general practitioner to confirm diagnosis, assess compliance and check for missing cases of colorectal cancer. The NHS Central Register in Southport, Merseyside was contacted to establish the year and cause of death in those cases where data were not available.
8.2.3 RESULTS:

175 patients diagnosed between 1972 and 1981 with either total colitis (n=143) or with limited ulcerative colitis but who had died (n=32) were identified. Overall there was 98% case ascertainment and verification, (in that the incidence studies for ulcerative colitis completed by Dr CSJ Probert compare well to figures quoted both nationally and internationally and that all the suitable cases identified for this study were re-matched to pathology and radiological reports and confirmed as either CD or UC). During the case verification three patients subsequently were discovered to have Crohn’s disease and four known to be alive were untraceable either via their last known general practitioner or through case records. The details of ten deceased patients were obtained from the NHS Central Register.

Colectomy:
A total of 49 patients underwent a colectomy, 6 as emergency laparotomies, 36 for failed medical management and 7 for known colorectal cancer (including 1 for severe dysplasia which was subsequently shown to be an invasive colonic carcinoma), giving a crude colectomy rate of 23.2%. The colectomy rate was 7.2% in the year of diagnosis, decreasing in frequency over the next four years, to a steady state of approximately 1.7% per year. The cumulative colectomy rate for the total group of patients was 19% at 5 years and 25% at 10 years.

Cancer occurrence:
In the total cohort, colorectal cancer occurred in ten patients within the study period. The clinical data for these patients are shown in Table 8.1. The cumulative incidence of colorectal cancer 10 years after diagnosis was 2.1% and at 20 years 7.4% for the total group of patients excluding those with a colectomy. The mean duration of ulcerative colitis before diagnosis was 7.9 years (range 2-13). No additional cancers were identified from data made available through the Trent Cancer Registration Bureau for Leicestershire.
Compliance with treatment:

168 case records were reviewed. 26 had not been followed up either because of medical discharge (n = 16) or repeated failure to attend appointments (n = 10). Degree of compliance was assessed for each subject, keeping the subjects outcome concealed. Compliance was assessed in keeping with the recommendation that sulphasalazine treatment should be ongoing and not limited to exacerbations. Four types of outcome occurred:

1. Carcinoma of the colon.
2. The patient underwent panproctocolectomy (not for malignancy).
3. The patient died, of a cause other than from carcinoma of the colon.
4. The patient remained free of carcinoma of the colon at follow-up date.

The data were entered into the SAS routine LIFETEST which permits modelling of survival type-data. This is a computerised statistical program designed for calculating mortality data but can be used where there is a suitable identifiable end point. In this instance the event of interest or "end point" was the development of carcinoma of the colon, the other three outcomes led to censored times on the test.

For each subject, gender and ages at the relevant stages were available. Table 8.2 shows the relationship of outcome to compliance group. The crude proportions developing cancer were 5/152 (3%) in the "compliers" but 5/16 (31%) in the "non-compliers" group. This is highly significant using a simple chi-square test (X²=20.2, df=1, p < 0.001). There are slight differences in confounding factors in that the non-compliers are slightly younger at diagnosis of colitis and there is a small male preponderance. Table 8.3 gives the results of the survival analyses, where survival means remaining cancer free. Two methods were used, the log-rank technique and the generalised Wilcoxon method. Both give highly significant values for the crude effect of compliance, (p < 0.001). Adjustments for age at diagnosis and gender actually makes the chi-square values more significant. The graph 8.1 shows the clear difference in proportions remaining cancer free in non compliers (curve A) and compliers (curve B).
Inter-observer Variation:

There were no differences between the original reports and the 10% sample of histology and colectomy specimens reviewed by the pathologist.

8.2.4 DISCUSSION:

This report describes cancer risk and compliance amongst a cohort of patients diagnosed between 1972 and 1981. The development of colorectal cancer occurred more frequently in those patients who either did not comply with sulphasalazine therapy or where treatment had been stopped by a doctor without a newer prophylactic agent being substituted. This implies a protective role for sulphasalazine in the prevention of cancer in ulcerative colitis. The high relative risk of developing cancer for this cohort may reflect the lack of definitive surveillance and follow-up programmes characteristic of that era. It was also frequent clinical practice at that time to use intermittent sulphasalazine for exacerbations of colitis rather than for prophylaxis against relapse as is usual clinical practice now. This too may partly explain the higher proportion of patients developing colorectal cancer.

The cumulative colectomy rate in the present study was similar to the rates in the Danish study of 1161 patients which reported a colectomy rate of 23.7% at 10 years (Langholz et al 1992). It was also similar to the complete Leicester cohort colectomy rate of 17.6% (Probert et al 1993a). The cumulative colectomy rate was much higher in Scandinavian countries in the 1970's when a rigorous policy of prophylactic colectomy after 10 years of disease was practised, but it has remained relatively stable in other countries (Katzka et al 1983, Bostrum et al 1986). Cancer developed after a mean of 7.9 years compared to the 11.5 years reported in the Danish and recent Swedish studies (Ekbom et al 1990, Langholz et al 1992). The cumulative cancer incidence at 10 and 20 years is similar to data from early studies including one from Birmingham in the early 1980's where 676 patients under long-term follow-up were reviewed and found to have a cumulative risk of 8% at 25 years (Prior et al 1982). These figures are substantially higher than the Danish data which suggested a cumulative incidence of 1.8% in patients with extensive disease (Langholz et al 1992).
It is accepted that patients with longstanding left sided disease are also at risk of colorectal cancer although the risks are generally thought to be much less than with more extensive disease (Gilbertson et al 1980, Lennard-Jones et al 1983). To address this problem I sought to identify patients with less extensive ulcerative colitis who had died by 1992 in order to pick up any missed cases of cancer although the cancer rate in my study was already higher than expected. It is still possible that one or two cases of cancer in very longstanding disease may have been alive and missed although studies such as this tend to detect an increased number of cancers because of the pre-existing, although hap-hazard, screening programmes. Older age at diagnosis confounds those patients presenting in their later decades as cancer is more common in the "normal" population with advanced age anyway. In the present study there were 6 cancers occurring in patients over the age of 70 and some of these may have represented the increased risk of colon cancer seen with advancing age in the population in general, however, 3 of these patients had had their colitis for more than 10 years. Older age also partly explains the observed higher proportion of distal cancers in our study.

There were no statistical differences between the original histology reports and the 10% of specimens reviewed. Failure to detect dysplasia has been suggested to be a major problem in screening programmes, with figures of between 4-8% inter-observer variation quoted amongst experienced pathologists and somewhat higher figures in the less experienced (Collins et al 1987). This was not apparent in our study. There is also disagreement amongst pathologists and clinicians over the interpretation of the different grades of dysplasia, their relationship to cancer risk and their most appropriate management (Collins et al 1987). A retrospective study cannot address these issues satisfactorily; moderate dysplasia early in a series of biopsies spanning twenty years is bound to bias the report towards a "mild" classification whereas moderate dysplasia in a series prior to colectomy for carcinoma would more likely be graded as severe.

This is one of the first studies to demonstrate that patients with ulcerative colitis who do not comply with sulphasalazine therapy are significantly more likely to develop colorectal cancer than their compliant counterparts. In Sweden (Langholz et al 1992) 102 cases of colorectal cancer amongst a cohort of 3112 patients with ulcerative colitis were examined in a case note study. The 102 cases of cancer were compared with 196 matched controls and the authors
found that pharmacological treatment, especially sulphasalazine, for a period more than three months conferred a cancer protective effect which was independent of disease activity (RR = 0.28). Non-steroidal anti-inflammatory drugs are known to inhibit the synthesis of prostaglandins which play a role in cell proliferation, neoplasia and immune responses (Rosenberg, Palmer, Zauber et al 1991). These drugs reduce levels of prostaglandins and inhibit tumour growth in the colons of rodents treated with carcinogens (Jaffe 1974, Lupulescu 1978, Lynch, Castes & Astoin 1978). This effect is likely to be reversed by discontinuation of treatment.

Interest in the role of aspirin in prevention of colorectal cancer has suggested that patients with negative faecal occult bloods (true negatives) consume more aspirin (and related compounds) than age matched controls with positive faecal occult bloods (true positives), (Logan, Little, Hawthin et al 1993). This confirms an earlier study in rats which suggested aspirin reduced the risk of developing fatal colorectal cancer (Davis, Patterson & Crouch 1992). Others have shown that sulindac can cause regression of rectal polyps in familial adenomatous polyposis (Waddell & Loughry 1983). Another large study investigated NSAID use among patients with large bowel cancer (n=1326) and two hospital control groups; group one were patients with cancers thought to be unrelated to NSAID use including pancreas and prostate (n=1011), and group two were other patients admitted with trauma or infection (n=3880). Regular use was defined as NSAIDS taken for four days per week for at least three months. The authors concluded that regular NSAID use reduced the incidence of human large bowel cancer (Rosenberg et al 1991).

There are important implications of an association between regular sulphasalazine use and relative risk of cancer in ulcerative colitis. Encouraging patients to comply with treatment may reduce the incidence of cancer and would be substantially cheaper than techniques such as aneuploidy, flow cytometry and immunochemical markers which have been suggested as useful adjuncts to screening. Such techniques could allow the identification of high risk patients and so encourage better targeting of surveillance programmes.
8.3 Conclusion:

Patients in chapter three were clearly concerned about their risk of developing colorectal cancer. Although the risk of developing this complication seems less than was first thought patients in our cohort developed more cancers than would be expected compared to national data - in our study there was a high relative risk of cancer amongst patients diagnosed as having pan-colitis between 1972 and 1981. The cumulative colectomy risk has not changed over the past few decades despite advances in treatment and the advent of "screening". Thus the concerns expressed by our patients are real and must be addressed.

Patients who comply with sulphasalazine treatment are less likely to develop colorectal cancer than non-compliers who may also be the type of patients who default from follow-up. The benefits from lifelong sulphasalazine therapy are likely to apply to the active component of the drug and so to the newer 5 amino-salicylic compounds although prospective trials are needed.

Although the results should be interpreted with caution as the cancers detected in this study may have been overrepresented by patients who were older with coincidental cancers. The message from this study is a positive one which will encourage the medical profession to allay patients' real fears about developing colorectal cancer. Compliance with treatment is likely to be more effective in saving lives as well as resources when compared to national screening campaigns and could lead to a clear improvement in patients' quality of life. In addition these benefits of sulphasalazine therapy need to be emphasized in the context of patients fears about the safety of medications.
Table 8.1: Clinical data on patients ulcerative colitis in Leicestershire diagnosed between 1972 and 1981 who subsequently developed colorectal cancer.

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
<th>8</th>
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<td>Sex</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>F</td>
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<td>M</td>
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<td>M</td>
</tr>
<tr>
<td>Age at Diagnosis of UC</td>
<td>47</td>
<td>34</td>
<td>27</td>
<td>65</td>
<td>71</td>
<td>80</td>
<td>78</td>
<td>65</td>
<td>59</td>
<td>58</td>
</tr>
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<td>Age at diagnosis of cancer</td>
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<td>70</td>
<td>81</td>
<td>87</td>
<td>80</td>
<td>75</td>
<td>67</td>
<td>71</td>
</tr>
<tr>
<td>Year of onset of UC</td>
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<td>'81</td>
<td>'72</td>
<td>'79</td>
<td>'74</td>
<td>'72</td>
<td>'72</td>
<td>'75</td>
<td>'72</td>
<td>'71</td>
</tr>
<tr>
<td>Year of diagnosis of cancer</td>
<td>'92</td>
<td>'91</td>
<td>'79</td>
<td>'84</td>
<td>'84</td>
<td>'78</td>
<td>'74</td>
<td>'85</td>
<td>'80</td>
<td>'90</td>
</tr>
<tr>
<td>Cancer locat(^a)</td>
<td>SF</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>TC</td>
<td>AC</td>
<td>DC</td>
<td>R</td>
<td>DC</td>
<td>TC</td>
</tr>
<tr>
<td>Extent of UC</td>
<td>T</td>
<td>T</td>
<td>T</td>
<td>D</td>
<td>T</td>
<td>T</td>
<td>ST</td>
<td>D</td>
<td>ST</td>
<td>T</td>
</tr>
<tr>
<td>Years of F/U</td>
<td>13</td>
<td>10</td>
<td>20</td>
<td>5</td>
<td>10</td>
<td>7</td>
<td>2</td>
<td>10</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Status</td>
<td>A</td>
<td>D</td>
<td>A</td>
<td>D</td>
<td>D</td>
<td>D</td>
<td>D</td>
<td>D</td>
<td>D</td>
<td>A</td>
</tr>
</tbody>
</table>

Key: M = male, F = female.
SF = splenic flexure, R = rectum, TC = transverse colon,
AC = ascending colon, DC = descending colon, T = total, ST = subtotal, D = distal;
A = alive, D = dead.

Clinical data including extent of disease and duration of follow-up on those patients who developed colorectal cancer are shown.
**TABLE 8.2: Outcome by compliance with sulphasalazine therapy amongst 152 patients with pancolitis in Leicestershire.**

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>% who were Men</th>
<th>Mean age at diagnosis of UC</th>
<th>Mean age at diagnosis of cancer or at follow up</th>
<th>Mean duration of follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compliers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>152</td>
<td>53</td>
<td>41.1</td>
<td>51.3</td>
<td>10.2</td>
</tr>
<tr>
<td>Cancer</td>
<td>5</td>
<td>60</td>
<td>58.6</td>
<td>67.4</td>
<td>8.8</td>
</tr>
<tr>
<td>No cancer</td>
<td>147</td>
<td>52</td>
<td>40.5</td>
<td>50.7</td>
<td>10.2</td>
</tr>
<tr>
<td>PPC*</td>
<td>43</td>
<td>53</td>
<td>36.2</td>
<td>39.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Unrelated death</td>
<td>36</td>
<td>53</td>
<td>59.4</td>
<td>69.5</td>
<td>10.1</td>
</tr>
<tr>
<td>Still unaffected</td>
<td>68</td>
<td>51</td>
<td>33.2</td>
<td>48.2</td>
<td>15.0</td>
</tr>
<tr>
<td><strong>Non-compliers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>16</td>
<td>63</td>
<td>39.2</td>
<td>50.3</td>
<td>11.1</td>
</tr>
<tr>
<td>Cancer</td>
<td>5</td>
<td>40</td>
<td>56.8</td>
<td>63.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Still unaffected</td>
<td>11</td>
<td>73</td>
<td>31.3</td>
<td>44.4</td>
<td>13.1</td>
</tr>
</tbody>
</table>

Mean ages at diagnosis of UC and diagnosis of carcinoma of the colon or last follow-up if unaffected, and mean duration of resulting follow-up are also shown.

* ppc = panproctocolectomy.
TABLE 8.3: Survival analyses modelling outcome on age at diagnosis, gender and compliance.

<table>
<thead>
<tr>
<th>Factors incorporated in model</th>
<th>df</th>
<th>$X^2$ (logrank)</th>
<th>$X^2$ (Wilcoxon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance only</td>
<td>1</td>
<td>15.14 *</td>
<td>14.34 *</td>
</tr>
<tr>
<td>Age at diagnosis and gender</td>
<td>2</td>
<td>10.64 *</td>
<td>10.25 *</td>
</tr>
<tr>
<td>Age at diagnosis, gender and compliance</td>
<td>3</td>
<td>28.29 *</td>
<td>25.92 *</td>
</tr>
<tr>
<td>Effect of compliance adjusted for age at diagnosis and gender</td>
<td>1</td>
<td>17.64 *</td>
<td>15.67 *</td>
</tr>
</tbody>
</table>

Survival analyses (remaining cancer free) using logrank and generalised wilcoxon methods for crude effect of compliance and adjusted for the confounding variables of age at diagnosis and gender. * All values were highly significant (p<0.001).
Compliance with sulphasalazine therapy significantly decreased the risk of developing colorectal cancer.
Survival Distribution Function

Sulphasalazine Compliance Survival Function Estimates

- Without sulphasalazine
- With sulphasalazine

Years of Follow Up
CHAPTER 9: THE DEVELOPMENT AND VALIDATION OF A QUALITY OF LIFE MEASURE IN INFLAMMATORY BOWEL DISEASE
9.1: INTRODUCTION:

Chronic disease can affect many aspects of a patient's life, as well as that of his or her carers. Ill health can affect employment, family life, leisure time and education. Concerns about the consequences of the disease and its treatment may be profound, even if based upon misconceptions.

This thesis has attempted to explore the extent and nature of these fears and concerns of patients with IBD. In order to assess fears and concerns in the broader sense it is necessary to have an effective measure of quality of life to identify and quantify individual fears so that they may be dealt with. A comprehensive quality of life evaluation must assess the impact that a disease and its treatment have on these dimensions and must include measures of psychological, social, occupational and physical well-being (Fallowfield 1990). Such indices must include aspects of education, employment and family life and help to pinpoint areas of need. They should include assessments of depression, anxiety, sleep and eating patterns, mobility and pain. Good assessment tools must also contain positive aspects. This is especially important for chronic conditions with a relapsing course as this will ensure that such assessments can be equally applied to "normal" controls. Clinical interventions may then be directed at areas of need and could include counselling, access to self-help groups and information booklets as well as conventional medical treatment. Identifying particular needs will enable us to better educate employers, teachers and insurance companies who are so often ignorant of patients' strengths and weaknesses (Mc Neil et al 1978, Probert & Mayberry 1991).

Until recently the literature was largely devoid of any reference to the long-term prognosis of patients with inflammatory bowel disease (IBD) although some investigators suggested an optimistic future with a normal "quality of life" but with limited data on which to base these comments (Gazzard et al 1978, Hendriksen et al 1980 & Binder et al 1985). Whilst the impact of IBD has largely been based on clinical disease parameters, in recent years investigators have recognised the failure of such clinical measures to assess functional disability, psychosocial functioning and drug toxicity. A general health assessment of quality
of life in IBD is needed so that patients can be encouraged to involve themselves in the management of their disease, promote understanding of its natural history and guide their future expectations (Farmer et al 1992). A Canadian measure, the IBDQ, initially developed by Guyatt et al (1989) and more recently by Irvine et al (1994) has been used in clinical trials and is raising the profile of this approach in everyday practice and in the context of drug trials and surgical interventions. The IBDQ was specifically designed to complement traditional measures of outcome in clinical trials and so does not necessarily address the day to day needs of individual patients. Thus a general health measure to explain an individual’s illness experience and health outcomes may still be needed (Garrett & Drossman 1990). Ideally it should also be easy and rapid to complete.

This chapter details the development, testing and subsequent use of a concise questionnaire designed in collaboration with patients to measure quality of life amongst those with inflammatory bowel disease (IBD) in Britain taking into account the anxieties identified in earlier chapters. It encompasses patient concerns expressed during open discussion groups in a non-clinical setting and follows the established format of including details on the four domains of life thought necessary to investigate quality of life namely social, psychological, occupational and physical functioning (Fallowfield 1990, Bowling 1990). The need for a concise measure was adhered to and a weighting scheme was not tested as they do not offer any advantage over a simple scoring system (Jenkinson, Ziebland, Fitzpatrick et al 1991). Quality of life and its relationship to either a problem or emotional based approach to dealing with illness was also investigated.

9.2: METHOD:

20 patients with IBD attended a series of 3 discussion groups with an experienced gastroenterologist (JFM) and a psychologist (CG). The purpose of these meetings was to ascertain a core of problems specific to IBD together with possible solutions or methods of coping which patients had identified and used. A draft questionnaire was developed to further investigate these problems and this was subsequently piloted on these 20 patients and a common questionnaire agreed. The problems identified by this technique were fitted into the four domains essential for measuring quality of life. The final questionnaire - the Quality
Index in Crohn's and Colitis (QuICC) was further tested on members of the committee of a local self help organisation for people with IBD. A separate questionnaire which investigated the coping strategies identified by the group was also piloted on this group and subsequently modified to fit with a previously validated American measure developed by Billings and Moos (1981). This questionnaire divides coping strategies for dealing with illness behaviour into either emotionally focused or problem/behaviourally focused data sets and had many overlaps with the strategies suggested by our patients who attended the discussion groups. The methods proposed by our patients were thus divided into these two categories.

The QuICC questionnaire (appendix 9.1) consists of 37 statements, which are divided between 4 sections. The first section investigates psychological aspects of the disease; the next assesses social functioning of the patient, section three deals with occupational issues and section four with physical well-being. Each statement is divided into three possible responses; always, sometimes or never, each of which scores either 3, 2 or 1 respectively. Patients are invited to decide to which extent IBD causes them to experience each of the statements. The best score (ie no effect on quality of life) is 37 and the worst score (ie a profound effect on quality of life) is 111. A demographic section includes general questions about which type of inflammatory bowel disease the patient has and any major surgical procedures such as an ileostomy or a pouch they have undergone, but this is not part of the scoring system. The whole questionnaire takes less than 5 minutes to complete with minimal instruction necessary.

The coping strategy questionnaire (appendix 9.2) consisted of 28 items and was administered in the same format as the QuICC score. Each of the 28 items were coded as either an emotional method of coping (of which there were 13) or a physical or problem based method of coping (of which there were 15). In the analysis further coding of the coping stratagems took place including dividing them up into behaviour thought to be maladaptive or adaptive and analyzing which of these stratagems aggregated together.

50 patients were selected by choosing every fiftieth name on the Leicester IBD data base (previously described). They were invited to attend a series of special out-patients clinics at
which several measures of health and disease activity were assessed. These included;

i) Disease activity using the Simple Index of Crohn’s Disease Activity described by Harvey and Bradshaw (1980).

ii) The Grogono Health Score (Grogono & Woodgate 1971).

iii) The Sickness Impact Profile (SIP) (Bergner, Bobbitt, Kressels et al 1976).

iv) The Quality Index in Crohn’s and Colitis (QuICC score).


The Simple Index of Crohn’s Disease Activity (SICDA) was used both in Crohn’s disease and ulcerative colitis. Many of the available indices including the Crohn’s Disease Activity Index (CDAI), (Sandler, Jordan & Kupper 1988) require the use of several biochemical parameters which are often not routinely measured. There are also several studies which suggest that disease activity does not consistently mirror patients’ symptomatology (Hyams, Mandel, Ferry et al 1992, Rao, Holdsworth & Read 1988). Some investigators have also used modified versions of both the CDAI, the SICDA as well as Truelove and Witt’s index in ulcerative colitis and they have concluded that such measures are applicable to ulcerative colitis as scores for all measures correlate well (Seo, Okada, Yao et al 1992). The SICDA was used in this study as it reflects the needs of British patients with IBD and is easy to complete. A score above 5 was considered representative of active disease in both groups. The Grogono health score was used to measure general health because it too is simple to apply. It was also used to assess differences between different physicians rating of disease activity. The SIP was used as a comparative gold standard of general health measures and has rather a behavioral slant to it (Bergner et al 1976).

Both disease activity and the Grogono health score were assessed twice by two different physicians (AH & JFM) to measure inter-observer variation in assessing disease activity, general health and quality of life. Following appropriate training (as per SIP instructions) a consultant clinical psychologist (CG) administered the Sickness Impact Profile (SIP) to each patient. Afterwards each patient was given brief instructions and asked to complete the QuICC and the Coping Strategies Questionnaires. The QuICC Index was re-administered by direct interview over the telephone four months later as a measure of the questionnaires.
reliability.

The QuICC index was also administered to two different control groups to assess content and face validity. It was completed by 47 unselected patients with asthma attending a respiratory clinic and by 41 employees of a local firm in Leicester.

Results were analyzed using SPSS statistical software incorporating analysis of variance and multiple regression analysis. To allow comparison between SIP and QuICC the QuICC scores are quoted as a percentage throughout this report, although the data were analyzed in their raw format.

9.3: RESULTS:

1: PATIENTS:

General health assessments:

There was good correlation between the two physicians measuring both disease activity, \( r=0.97 \), \( p<0.001 \), the Grogono health score, \( r=0.84 \), \( p<0.001 \) and the QuICC score \( r=0.85 \), \( p<0.001 \). The QuICC score correlated significantly with both disease activity and the Grogono Score, \( r=0.4 \), \( p<0.01 \), \( r=0.4 \), \( p<0.01 \) respectively. The total QuICC score also correlated significantly with the total SIP score, \( r=0.4 \), \( p<0.001 \).

In particular the score for occupational function correlated with disease activity and also with the Grogono score, \( r=0.4 \), \( p<0.01 \), \( r=0.4 \), \( p<0.001 \) respectively. The sub set scores of the QuICC correlated with sub set scores for the SIP (Table 9.1) and the total score of the SIP correlated well with each of the four sub sets of the QuICC: Psychological function, \( r=0.4, p<0.001 \); social function, \( r=0.6, p<0.001 \); occupational function, \( r=0.4, p<0.001 \) and physical function, \( r=0.7, p<0.001 \).

26 male and 24 female patients participated of whom 23 had Crohn’s disease (CD) and 27 ulcerative colitis (UC). 9 patients with UC had an ileostomy. Patients with ulcerative colitis and Crohn’s disease were of a similar mean age and had similar mean SIP and QuICC scores (Table 9.2) as did those with an ileostomy.
SIP is scored from 0 to 100 and in this study values between 0 to 39.1 were obtained, with a range of means of the SIP score from 8.8 to 11.5. The QuICC is scored from between 37 and 111, in this study the range was 54 to 81. To allow comparison with the SIP scores these were converted to percentages; 48.7 to 72.6. The range of means of the QuICC score was 55.7 to 57.8. There were no significant differences in scores if groups were compared by age, disease or sex.

Those patients who perceived they had an impaired quality of life (having answered "yes" to the appropriate question at the end of the assessment) had significantly worse total QuICC scores, \( t = -2.55, \ p < 0.01 \) as well as worse physical function scores, \( t = -2.2, \ p < 0.03 \).

If disease activity scores for all patients are split into active and inactive, high levels of disease activity in both UC and CD correlated with poor quality of life scores, in UC; \( t = -2.3, \ p < 0.05 \) and in CD; \( t = -2.6, \ p < 0.02 \). Poor sub set scores in occupational and physical function also correlated well with impaired quality of life (Table 9.3).

Coping strategies:

The coping strategies questionnaire divides coping into categories of emotion and physical (problem) focused methods. There were very few significant correlations between either methods of coping and quality of life. Patients who exhibited high levels of problem orientated coping had correspondingly poor physical function scores (ie active disease), \( t = -2.2, \ p < 0.03 \). A number of recurrent strategies were associated with the sub scores for QuICC, (Table 9.4). The strategies that correlated with occupational function were grouped together and labelled occupational coping, those that correlated with physical functioning were labelled physical coping and those with psychological functioning psychological coping. The sum of these three categories was called total coping (Table 9.5).

Overall QuICC score correlated with occupational coping, \( r = 0.5, \ p < 0.001 \), with physical coping, \( r = 0.6, \ p < 0.001 \) and with total coping, \( r = 0.5, \ p < 0.001 \). The constituents of these sub divisions of coping include: increased smoking; become depressed; become angry and alter diet. Poor quality of life scores were significantly associated with: occupational coping,
t=-3.86, p<0.001; with physical coping, t=-4.29, p=0.000; and with total coping, t=-3.86, p<0.001. These strategies associated with poor quality of life are predominantly negative or unhelpful strategies. A more useful way of analyzing the relationship was to divide coping into "adaptive" strategies, which are more likely to produce a positive outcome and "maladaptive" mechanisms which are likely to be unhelpful. The maladaptive strategies included increased smoking, being passive, becoming depressed and submitting to the illness. Patients with CD were much more likely to use maladaptive strategies than patients with UC, t=-2.3, p<0.03. Thus patients with CD are more likely to use strategies which may be perceived as unhelpful in dealing with their disease (eg smoking which is associated with increased risk of relapse).

Multiple regression analysis:
Multiple regression analysis were performed on all the parameters which affected quality of life in order to obtain an equation which could predict quality of life. This was done by imputting all variables into SPSS - the following two equations gave significant results and suggest that those with active disease employing physical, occupational or "maladaptative" strategies to cope with their disease tend to have poor quality of life.

1. physical coping + occupational coping + disease activity + disease = poor quality of life.
   Multiple r = 0.65, SE = 5.8, analysis of variance, F = 8.2, significant f = 0.000

2. maladaptive coping + disease + disease activity = poor quality of life.
   Multiple r = 0.43, SE = 6.8, analysis of variance, F = 3.5, significant F = 0.02.

2. CONTROLS:
(i) Asthma patients:
47 unselected asthma patients attending a respiratory clinic completed the QuICC index. 25 male and 22 female patients participated, they had had asthma for a mean of 9.8±5.5 years. There were no statistical differences between male and female patients in both their mean ages or mean QuICC scores.
(ii) Local employees

41 apparently healthy employees from a local company also completed the index. 22 female and 19 male employees participated, the mean age of males was $35.9 \pm 12.8$ and females $34.1 \pm 13.8$, the mean QuICC score for men was $38.2 \pm 4.8$ and for women $37.9 \pm 5.3$. There were no differences between asthma and healthy controls for either age or QuICC score.

There was no statistical difference in the ages of the patients and the asthma control group, for males, $t=0.9$, ns and for females, $t=0.5$, ns. However patients with IBD had significantly higher QuICC scores, for males, $t=10.5$, $p<0.0001$ and for females, $t=9.8$, $p<0.0001$.

The QuICC score takes less than 5 minutes to complete. There were no significant changes in the QuICC scores in the 10% of medically stable patients re-interviewed at four months. All patients were current out-patients at the time of the study.

9.4: DISCUSSION:

The QuICC index is a concise, reliable and valid measure of quality of life in patients with IBD. It exhibits test-retest reliability and measures the impact of having IBD on quality of life and not just general ill health. Although in the context of a chronic relapsing and remitting illness reliability is often difficult to measure, the group of stable patients re-interviewed had not changed significantly. Unless issues such as fear of colorectal cancer are addressed the score is also unlikely to improve with repeated administration in stable patients. This emphasises the overall concerns expressed by patients with IBD. Despite this the score correlated well with disease activity and although on face value the lack of change of scores on re-interview 3 months later may seem surprising all patients were in fact out-patients and their treatments were largely unchanged in keeping with stable chronic IBD. Another criticism may be the use of a telephone survey for the re-test instead of self-completion of the QuICC. Self completion would have been preferred but I felt the patients had co-operated extensively with all my studies and I did not want to cause them any further inconvenience by arranging further hospital attendance. Many studies have shown that it is the level of personal interest of the questions and not the method or length of questionnaires that
influences response (Janssens et al 1980 & Herzog et al 1981). QuICC also correlates with general measures of health such as the SIP and the Grogono health score and reflects disease activity well. The QuICC index is specific as suggested by the significantly higher scores compared to asthma and healthy community controls.

Patients with IBD lead an impaired life reflected in the high scores obtained from the QuICC score. Occupational functioning is an accurate reflection of overall well being, patients unable to attend work have correspondingly poor QuICC scores. Patients with poor QuICC scores exhibited high levels of "maladaptive strategies", in particular those with CD. The reasons for this are likely to be complex and further confuses the issue regarding personality, stress and illness behaviour in relation to IBD. Some investigators believe patients with CD exhibit a higher incidence of depression and anxiety than either patients with UC or other chronic medical controls (Gerbert 1980, Robertson, Ray, Diamond et al 1989 & Drossman 1986). The longer an illness is present the more adjustments are required to advance through these phases (Drossman 1992). Limited psychological abilities or severely incapacitating disease may lead to maladjustment (Drossman 1992). This could explain why patients with CD were more "maladaptive" than patients with UC.

The QuICC score was not developed for use in clinical trials but for use by patients and their doctors to plan treatment regimes and provide a background to educate patients about their prognosis and as a guide to their future expectations. However further studies (unpublished data) examining the sensitivity of the QuICC to change using a three point scoring system in comparison with the IBDQ have shown it not to meet the sensitivity criteria recently set out by Streiner and Norman (1995). It performs better with a five point scoring system and a seven point scoring system is currently being evaluated (unpublished data). These higher scoring systems may make the QuICC useful in British clinical trials. However elements of the score relating to justified fears about colorectal cancer and risks to family members will not change from one clinic visit to the next unless these issues are addressed in the patients for whom these concerns are a problem. The use of the QuICC index in clinical trials could provide valuable information about the impact of new therapeutic procedures on day to day aspects of patients' lives more accurately than clinical and biochemical improvements alone.
The QuICC index encompasses many of the criteria necessary for a useful measure of quality of life. Its application in clinical practice could identify treatments that not only improve inflammatory, biochemical and histological markers but that also enable patients with IBD to lead useful and optimistic lives. Because it is concise, its use in busy out-patient clinics could provide "an easy to see" picture of each patient's progress, especially if completed by patients before each clinic visit or in the out-patient waiting area.

9.5: Conclusion

There is a clear need for a tool to measure the impact of IBD and its treatment on patients' quality of life. The QuICC index attempts to incorporate some of the fears and concerns expressed by patients in chapter three into such a measure together with the accepted ingredients that should comprise a reliable and valid quality of life measure. The QuICC meets many of the criteria necessary to be a useful measure although its sensitivity to change could be questioned. Further studies are ongoing comparing the QuICC with the IBDQ (Irvine et al 1994) and moving to a weighted scoring system with 5 possible answers may improve the questionnaire's sensitivity. Appropriate use of the QuICC will identify areas of concern in individual patients and thus facilitate a better quality of life through education and treatment in such patients.
**TABLE 9.1:** *Quality Index in Crohn’s and Colitis (QuICC) score and Sickness Impact Profile score (SIP): Correlation between scores in a group of patients with inflammatory bowel disease.*

<table>
<thead>
<tr>
<th>QuICC score</th>
<th>SIP score</th>
<th>SIP social functioning score</th>
<th>SIP physical functioning score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>QuICC score</strong></td>
<td>r=0.4 **</td>
<td>r=0.4 *</td>
<td>r=0.3</td>
</tr>
<tr>
<td>QuICC social</td>
<td>r=0.6 **</td>
<td>r=0.5 **</td>
<td>r=0.4 **</td>
</tr>
<tr>
<td>functioning score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QuICC occupational</td>
<td>r=0.7 **</td>
<td>r=0.7 **</td>
<td>r=0.5 **</td>
</tr>
<tr>
<td>score</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**  p < 0.001  
*  p < 0.01

The SIP score includes elements for social and emotional functioning and also physical functioning. QuICC is a total quality of life score which also contains social and occupational functioning. These sub-set scores were compared.

The QuICC score correlates significantly with the total SIP score. The sub-set scores of the QuICC correlate with sub-set scores of the SIP.
TABLE 9.2: The effect of age, sex and type of inflammatory bowel disease on SIP and QuICC scores in 50 patients.

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>CD</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>33.3±10.7</td>
<td>35.2±11.0</td>
<td>33.9±10.9</td>
<td>34.3±10.9</td>
</tr>
<tr>
<td>SIP total</td>
<td>9.1±12.8</td>
<td>11.1±16.8</td>
<td>11.5±17.6</td>
<td>8.8±12.0</td>
</tr>
<tr>
<td>QuICC total</td>
<td>56.9±7.4</td>
<td>56.4±7.5</td>
<td>57.8±7.4</td>
<td>55.7±7.3</td>
</tr>
<tr>
<td>age t=# SIP</td>
<td>0.7 ns</td>
<td>0.5 ns</td>
<td>0.1 ns</td>
<td>0.6 ns</td>
</tr>
<tr>
<td>QuICC</td>
<td>0.2 ns</td>
<td></td>
<td>1.0 ns</td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>26</td>
<td>24</td>
<td>23</td>
<td>27</td>
</tr>
</tbody>
</table>

# = t test

There were no significant differences in the age, SIP or QuICC scores between either sexes or Crohn's disease and ulcerative colitis.
TABLE 9.3: The relationship between disease activity, type of disease and QuICC scores in 50 patients with inflammatory bowel disease.

<table>
<thead>
<tr>
<th></th>
<th>N =</th>
<th>Mean</th>
<th>SD</th>
<th>t=</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>QuICC score *</td>
<td>G1 = 26</td>
<td>54.0</td>
<td>7.2</td>
<td>-2.8</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>G2 = 19</td>
<td>60</td>
<td>7.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>physical functioning</td>
<td>G1 = 26</td>
<td>58.3</td>
<td>8.2</td>
<td>-2.4</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>G2 = 19</td>
<td>64.0</td>
<td>7.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>occupational</td>
<td>G1 = 26</td>
<td>45.4</td>
<td>12.3</td>
<td>-2.4</td>
<td>0.02</td>
</tr>
<tr>
<td>functioning #</td>
<td>G2 = 19</td>
<td>56.1</td>
<td>18.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD</td>
<td>G1 = 7</td>
<td>2.8</td>
<td>2.5</td>
<td>-2.6</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>G2 = 7</td>
<td>8</td>
<td>4.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UC</td>
<td>G1 = 7</td>
<td>1.4</td>
<td>2.3</td>
<td>-2.3</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>G2 = 5</td>
<td>6.3</td>
<td>4.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The total QuICC score was split at the 25th (Group 1, best quality of life scores) and 75th (Group 2, worst quality of life scores) centiles. The means and standard deviations were compared for these two groups. Disease activity scores were also divided at the 25th (Group 1, lowest disease activity) and 75th (Group 2, highest disease activity) centiles and their means and standard deviations compared.

G Group.
# Disease activity split at 25th and 75th centiles, HBI < 4 & HBI > 5.
## QuICC score split at 25th and 75th centiles, QuICC < 51.8 and QuICC > 62.

Poor quality of life (poor overall QuICC score), poor physical and occupational functioning scores were associated with active disease. Active disease was associated with poor quality of life (poor overall QuICC score) both in patients with CD and UC.
**TABLE 9.4: Relationship between quality of life and coping strategies in 50 patients with inflammatory bowel disease**

<table>
<thead>
<tr>
<th></th>
<th>Passive activity</th>
<th>Become angry</th>
<th>Become depressed</th>
<th>Submit</th>
<th>Increase smoking</th>
<th>Alter diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational function</td>
<td></td>
<td>0.4*</td>
<td>0.4*</td>
<td>0.4**</td>
<td>0.4*</td>
<td></td>
</tr>
<tr>
<td>physical function</td>
<td>0.4*</td>
<td>0.4*</td>
<td></td>
<td>0.5**</td>
<td>0.4*</td>
<td></td>
</tr>
<tr>
<td>psychological function</td>
<td>0.5**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.4*</td>
</tr>
</tbody>
</table>

Items which correlated with occupational, physical and psychological functioning.

**TABLE 9.5: relationship between coping strategies and quality of life in 50 patients with IBD**

<table>
<thead>
<tr>
<th>Coping scores</th>
<th>QuICC scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational coping</td>
<td>0.5**</td>
</tr>
<tr>
<td>Physical coping</td>
<td>0.6**</td>
</tr>
<tr>
<td>Psychological coping</td>
<td>0.5**</td>
</tr>
</tbody>
</table>

The new groups of items were termed occupational coping, physical coping and psychological coping. These groups correlated well with the overall QuICC score.

* $p<0.01$, ** $p<0.001$

All the coping items that correlated with sub-set scores of the QuICC index were grouped together. Certain unhelpful strategies, such as smoking, were associated with poor quality of life.
CHAPTER 10: CONCLUSIONS
The original hypothesis under investigation in this thesis was that quality of life was impaired for patients with inflammatory bowel disease and that if so it should be capable of measurement. In chapter one the clinical course of both ulcerative colitis and Crohn's disease as well as an overview of their epidemiology and aetiology were reviewed. This has provided an insight into the type of symptoms and treatments such patients may experience. Chapter two reviews the current state of quality of life research both in general terms and more specifically in relation to inflammatory bowel disease. The next few chapters investigated the reality of patients' experiences in their daily life.

In chapter 3 the fears and concerns of patients with IBD were investigated and compared with the views of physicians and surgeons caring for them. Doctors maybe interested in these topics but too few responded to the questionnaire to draw meaningful conclusions. However, those that did respond to the questionnaire had very different views to patients. People with IBD were concerned about the risk of colorectal cancer, the risk to family members, dependence on drugs and their side-effects and faecal incontinence. These issues were examined in detail to confirm their reality or otherwise whilst developing a concise quality of life measurement for use in IBD.

Chapter 4 investigated the attitude of employers and insurance companies to people with IBD. Companies employed significantly fewer people with IBD than would be expected. Some patients appear to hide the fact that they have IBD from prospective employers. However, many companies suggest that paid leave to attend hospital out-patients is widely available, but acknowledge the fact that chronic disease can affect opportunities for promotion. There is now evidence that patients with IBD experience discrimination by leading insurance companies, few offering premiums at standard rates despite the normal life expectancy of patients with IBD. Insurance companies also advised professional enquirers of different rates than those offered in practice to prospective clients.

Chapter 5 investigated the sexual function of patients with IBD. Women with CD have sexual intercourse less frequently than age matched controls because of dyspareunia, abdominal
pain, disabling diarrhoea, fatigue and fear of faecal incontinence. Other patients with IBD believe they encounter the same problems but in our study they did not exhibit a reduced frequency of sexual intercourse.

In chapter 6 the effect of having IBD on fertility and fetal outcome was examined. Both patients with CD and UC have a reduced fertility rate after diagnosis. Women with CD also had more miscarriages, caesarian sections and forceps procedures than controls. Drug side effects were reported as a major concern by patients with IBD. Whilst the overall number of children with congenital malformations born to parents with IBD was similar to that found in other Leicestershire families, malformations were significantly associated with men and women taking sulphasalazine during conception.

Chapter 7 describes the limited role of a newly formed self-help group for IBD in Leicestershire. In contrast to the medical profession who believe self-help organisations are invaluable, patients with IBD were largely disinterested in joining a new branch of a national self-help organisation. Those who did join tended to be older women with CD. Patients who were disinterested suggested they were too busy to join or that they did not want others to know of their illness and associated problems. It therefore unlikely that such a group will be able to significantly influence the concerns of the majority of patients and so improve quality of life.

In chapter 8 the prognosis and cancer risk of a cohort of patients with ulcerative colitis was investigated to address the fear patients have of developing this often fatal complication. Patients are rightly concerned about the risk of developing colorectal cancer as the relative risk in our cohort of patients at 20 years was 7.4. However, patients who did not comply with sulphasalazine therapy were significantly more likely to develop colorectal cancer than those who did, and this represents an important avenue for dealing with patients concerns in this emotive area. Persuading patients to comply with treatment could substantially reduce the risk of developing cancer.

These findings confirm my original hypothesis that patients with IBD lead an impaired quality of life in that they suffer significant sexual problems, have a reduced fertility rate,
are at increased risk of developing colorectal cancer and are discriminated against by insurance companies and employers alike.

In chapter 9 all of these issues were incorporated into the QuICC index. The QuICC index is a concise, reliable and valid measure of quality of life in patients with IBD. It measures the impact of IBD on quality of life and not just general ill health. It also exhibits test-retest reliability. Patients with IBD lead an impaired life and this is reflected in the high scores obtained with the QuICC score. Occupational functioning is an accurate reflection of overall well being, patients unable to attend work have correspondingly poor QuICC scores. The development of the QuICC score again supports my hypothesis that there is an impaired quality of life in IBD.

Unlike the IBDQ (Irvine et al 1994) my measure was not developed specifically for use in clinical trials but for use by patients and their doctors to plan treatment regimes and provide a background to educate patients regarding their prognosis and guide their future expectations. Some parameters will not change upon re-administration unless efforts at addressing issues such as patients fear of developing colorectal cancer are dealt with. Further studies (unpublished data) examining the sensitivity of the QuICC using the three point scoring system in comparison with the IBDQ have shown it not to meet the sensitivity criteria set out by Streiner and Norman (1995). It performs better with a five point scoring system and a seven point scoring system is currently being evaluated (unpublished data). These higher scoring systems may make the QuICC a more useful tool. Future research will be targeted at measuring improvements when investigating educational and counselling strategies, new therapies or surgical procedures.

The application of the QuICC score to clinical practice would allow individual patients needs and concerns to be identified and a programme to both educate the patient and help manage their chronic illness could be developed. Quality of life indices could be used routinely in IBD clinics to assess the month to month and year to year changes in individual patients. A nurse specialist or trained counsellor could be available to encourage patients to discuss the more difficult areas of sexual dysfunction or discrimination in the work place or by insurance companies. If these concerns are identified and addressed it is likely that such an approach
could have profound effects on patients’ perception of their quality of life.

Some of the studies reported in this thesis are retrospective which inevitably attracts criticism. Problems encountered in retrospective studies include:

(i) Selection bias:
Most of the patients were chosen at random from a community data base. However those patients who chose not to respond may introduce some bias in the analysis of results which is difficult to control.

(ii) Representativeness:
Non-responders may hold different views and have had other experiences than responders.

(iii) Bias in obtaining information:
The design of the questionnaires used in the studies was as simple as possible, often requiring "yes" or "no" answers. The reliability of the questionnaire was tested by re-interviewing a random 10% of the responders several months later. The absence of any significant changes probably reflects the simplicity of the questionnaires. All patients studied were current outpatients and as such had relatively stable disease. The consistency of replies also indicates the test-retest reliability of the questionnaires.

The problems highlighted in this thesis need urgent attention. Patients have a growing concern with the quality of their care as well as its effectiveness. Empowered by the principles of the Patient’s Charter, they have the right to know more about treatment and prognosis. However, such concepts have traditionally been difficult to measure with the precision of laboratory based tests but can now be measured using well developed and reliable tools. The QuICC index is an example of this approach. It is based on patients’ perceptions of their needs and anxieties. It has been developed for use in the ongoing management of patients so that appropriate help can be sought. It could be completed easily by patients themselves prior to a clinic assessment or review by a nurse counsellor and so has potential as a clinically useful tool.
In conclusion patients with inflammatory bowel disease do have an impaired quality of life as evidenced by this thesis. The areas of concern call for better education of doctors and patients in the management of their condition. Recognition by patients and doctors alike that some of these problems will not be alleviated by current treatment regimes is also needed. Other avenues such as nurse based counselling, the role of clinical psychologists and organisations such as Relate (marriage guidance organisation) and SPOD (Sexual and Personal Problems of the Disabled) need to be considered.
APPENDICES:

APPENDIX 3.1: Questionnaire investigating relative importance of various issues to people with IBD

Please score the following issues and ways of coping in terms of their importance to your Crohn’s disease or ulcerative colitis with a number from 1 to 5 where 5 equals extremely important, 4 equals very important, 3 equals quite important, 2 equals not so important and 1 equals not important at all.

A: issues:
1. Public ignorance

2. Attitude of employers

3. Risk of cancer

4. Fear of incontinence

5. Effects on social life

6. Risk to family members

7. Attitude of insurance companies

8. Drug side-effects

9. Tiredness

10. Dependence on tablets
APPENDIX 3.2: Questionnaire investigating relative importance of various coping strategies to people with IBD

B: coping strategies

1. Keep fit

2. Keep relaxed/ keep serene

3. Keep occupied

4. Join a self-help group

5. Find out the truth

6. Counselling

7. Grin and bear it
APPENDIX 4.1: Questionnaire investigating the attitude employers to people with IBD

1. How many people do you employ?

2. How many people are known to have
   i) ulcerative colitis?
   ii) Crohn’s disease?

3. Do you keep any information on your files about inflammatory bowel disease? (ulcerative colitis and Crohn’s disease).
   if yes, to whom is this information available.

4. Would you reject an application from someone who had inflammatory bowel disease?

5. Would having inflammatory bowel disease affect the types of duties performed?

6. Would paid leave be available to your employees to attend
   i) out-patients?
   ii) for surgery?

7. Would having inflammatory bowel disease prevent promotion to a more responsible job?

8. What illnesses might jeopardise promotion prospects at your company?
   Please list below.

9. Do you offer any health promotion or general health screening at your company?
   If yes, what is available.
APPENDIX 4.2: Letters and questionnaires investigating the attitude of insurance companies to people with IBD.

A. Letter from fictitious patient

I am a 31 year old electrician and am currently considering buying a house with my wife. I was diagnosed as having Crohn’s disease 5 years ago following an emergency operation when they removed some of my small bowel. However since then I have been very well requiring no treatment. Will I automatically receive an additional loading on any life insurance or mortgage policy? I would be grateful for any information you could provide me with,

yours sincerely.

B: Letter from consultant gastroenterologist

I am a consultant gastroenterologist with a special interest in inflammatory bowel disease. Many of my patients ask me for advice regarding applying for insurance policies and little information is available regarding this area. I would be grateful if you could send me your guidelines for people with inflammatory bowel disease both for those with active and inactive disease so that I can pass accurate information on to my patients,

Yours sincerely.
C: Insurance Questionnaire to patients with IBD

1. How old are you?
2. Are you male or female?
3. Have you ever applied for any of the following?
   i) Low cost endowment?
   ii) Flexible whole life?
   iii) Term assurance?
   iv) Mortgage protection?
4. Where either your family doctor or hospital specialist required to provide a medical report? If so, which one?
5. Did you have to pay an extra premium because of your inflammatory bowel disease? If yes, what form did this take?
6. Did anyone recommend a company that specialises in insuring people with inflammatory bowel disease?
APPENDIX 5.1: Questionnaire investigating sexual dysfunction:

A. GENERAL:
1. Age
2. Ethnic origin and religion
3. Marital status / partner
4. Number of years with present partner/husband
5. Patients and partners occupation and earnings
6. Smoker / non smoker
7. Alcohol consumption
8. Any other medical problems.

B. ABOUT INFLAMMATORY BOWEL DISEASE
1. How long they have the disease and whether it is Crohn’s disease or ulcerative colitis.
2. Site affected
3. Frequency of exacerbations
4. Severity of exacerbations ( admission, off work etc. ).
5. Any perianal fistulae / abscesses
6. Any surgery

C: ABOUT MENSTRUAL CYCLE:
1. Age at menarche
2. Length of cycle
3. Duration of menstrual bleed

D: PAST OBSTETRIC HISTORY:
1. Total number of pregnancies
2. Any miscarriages or terminations
3. Any complications ( caesarians, forceps )
4. Number of children and their ages
5. Length of time elapsed for each conception
6. Contraceptive practices
7. Ever sought medical advice about trying to conceive
E: SEXUAL AND PERSONAL PROBLEMS:

1. Frequency of sexual intercourse per week?
2. Any dyspareunia - does it interfere with the relationship?
3. Is there anything else which interferes with your sex life?
4. Have you ever had thrush?
5. Have you ever had any sexually transmitted disease?
6. Have you ever received any form of gynaecological treatment?
7. Is your partner / husband understanding about these problems?
CONFIDENTIAL QUESTIONNAIRE:

1. Age?
2. Male or female?
3. Marital status?
   Single
   Cohabiting
   Married
   Divorced
   Widowed
   If you are married or cohabiting please state how long for?
4. Do you have any children?
   If yes how many?
5. How many times have you/your partner been pregnant?
6. Did any of the pregnancies take longer than one year to conceive?
   If so, please give details.
7. Have you/your partner ever had a
   i) miscarriage
   ii) stillbirth
   iii) termination
   If yes, please give details.
8. Have you/your partner ever had any of the following
   i) caesarian section
   ii) forceps procedure
   If yes, please give details.
9. Do any of your children have any serious illnesses or where they born with a mental
   or physical disability?
   If yes, please give details.
10. Did you take sulphasalazine during any of your pregnancies or during the time
    you/your partner became pregnant?
    If so please give details.
Appendix 7.1: which services are important to patients with IBD joining a local self help group. Should such a group provide

1. information resources, eg information booklets, videos etc.
2. social events, eg discos etc.
3. opportunities to discuss problems with fellow sufferers
4. promotion of the needs of IBD sufferers in the local community

Appendix 7.2: Follow up questionnaire to joiners and non joiners of the local NACC

If you joined Leicester NACC following its inauguration

1. Have you attended any meetings?
2. Did they provide
   i) useful information
   ii) mutual support
   iii) regular updates on medical research
   iv) a place to meet other people with similar problems

If you did not join Leicester NACC was this because

   i) meetings are held too far away
   ii) you are too busy
   iii) you manage well on your own
   iv) you do not wish others to know your business
Appendix 9.1 Quality of life assessment in IBD

In relation to your Crohn’s disease or ulcerative colitis

1. PSYCHOLOGICAL PROFILE:

<table>
<thead>
<tr>
<th>Question</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Do you feel frustrated?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you feel anxious?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you feel depressed?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you feel worried?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you usually sleep well?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you feel good about yourself?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you feel hopeful?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do you have a sense of humour?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Are you afraid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- of surgery?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- of having an ostomy (&quot;bag&quot;)?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- of developing cancer?</td>
<td></td>
<td></td>
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<tr>
<td>- of the future?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- of investigations?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- of out-patients?</td>
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</table>

2. SOCIAL ACTIVITIES:

<table>
<thead>
<tr>
<th>Question</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Do you have regular partner?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Do people close to you understand you?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>* Do you have friends or relations to discuss problems with?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Question</td>
<td>Always</td>
<td>Sometimes</td>
<td>Never</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Do you argue with your partner/spouse?</td>
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<td></td>
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<tr>
<td>- with others?</td>
<td></td>
<td></td>
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<tr>
<td>Do you receive enough affection?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Are you concerned about going out because of urgency or frequency of bowels?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Do you ever have to cancel social engagements?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Do you worry about going on holiday?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does IBD ever interfere with sexual intercourse?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you manage to go out every week?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you have visitors every week?</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

3. RELATED TO OCCUPATION:

<table>
<thead>
<tr>
<th>Question</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you able to perform your current major daily activity (i.e. work, housewife etc)?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you need help to perform your current major daily activity?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
* Are you ever discriminated against by employers or insurance agencies because of your illness? [ ] [ ] [ ]

4. **PHYSICAL WELL-BEING:**

<table>
<thead>
<tr>
<th>Question</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Do you have bleeding from the back passage?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Do you feel bloated?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Do you suffer with flatulence?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Do you worry that you produce offensive odours?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Do you have noisy bowel sounds?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Are you ever incontinent?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Do you ever feel lethargic?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>* Do you get indigestion?</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
5. GENERAL:

* Do you have Crohn’s disease?
* Do you have ulcerative colitis?
* Have you got an ileostomy or colostomy?
* Do you think your quality of life been significantly impaired by your illness?

6. ADDITIONAL COMMENTS:

........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
### 9.2 COPING STRATEGIES:

Have you ever done any of the following to help your ulcerative colitis or Crohn's disease?

<table>
<thead>
<tr>
<th></th>
<th>always</th>
<th>sometimes</th>
<th>never</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Keep fit / exercise more</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>2. Kept busy</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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<tr>
<td></td>
<td>Eg: knitting</td>
<td>[ ]</td>
<td>[ ]</td>
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<tr>
<td></td>
<td>reading</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>listening to music</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>3. Prepare for the worst</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>4. Grin and bear it, not worry</td>
<td>[ ]</td>
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<tr>
<td>5. Tried to find out more about it</td>
<td>[ ]</td>
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<tr>
<td>6. Took positive action</td>
<td>[ ]</td>
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<tr>
<td></td>
<td>Eg: homeopathy</td>
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<tr>
<td></td>
<td>relaxation therapy</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>breathing exercises</td>
<td>[ ]</td>
<td>[ ]</td>
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<tr>
<td></td>
<td>health shops</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>joined a self-help group</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>7. Tried to see positive side</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>8. Altered diet</td>
<td>[ ]</td>
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<tr>
<td>9. Talked to friends about it</td>
<td>[ ]</td>
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<tr>
<td>10. Talked to spouse / relative</td>
<td>[ ]</td>
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<tr>
<td>11. Considered several options</td>
<td>[ ]</td>
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<tr>
<td>12. Talked with professional persons Eg: doctor</td>
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<tr>
<td></td>
<td>nurse</td>
<td>[ ]</td>
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<tr>
<td></td>
<td>Reduce stress by increased smoking [ ] [ ] [ ]</td>
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<tr>
<td>13</td>
<td>Reduced stress by increased drinking [ ] [ ] [ ]</td>
<td></td>
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<tr>
<td>14</td>
<td>Draw on past experiences [ ] [ ] [ ]</td>
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<tr>
<td>15</td>
<td>Become angry depressed [ ] [ ] [ ]</td>
<td></td>
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<tr>
<td>16</td>
<td>resentful [ ] [ ] [ ]</td>
<td></td>
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<td></td>
<td>submissive [ ] [ ] [ ]</td>
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<td>17</td>
<td>Take one step at a time [ ] [ ] [ ]</td>
<td></td>
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<tr>
<td>18</td>
<td>Denied you were ill [ ] [ ] [ ]</td>
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