

ULCERATIVE COLITIS AND CROHN'S DISEASE A CONFERENCE ON MORBIDITY AND MORTALITY OF INFLAMMATORY BOWEL DISEASE

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Introduction. Before discussing the findings of the Conference on Morbidity and Mortality of Inflammatory Bowel Disease (IBD), a short review is indicated of the two conditions, which are referred to under the term of IBD: ulcerative colitis and Crohn's disease. Ulcerative colitis (UC) is a mucosal disease. It is a continuous inflammation which is restricted to the colon. Crohn's disease involves the deeper layers of the bowel. It may affect any part of the gastrointestinal tract from mouth to anus. The inflammation is almost always segmental. Inflammatory bowel disease can be diagnosed only once the etiology of inflammation remains unknown after all other recognizable causes of injury such as infection, radiation, ischemic colitis, gay bowl syndrome, etc. have been excluded. In most instances, ulcerative colitis and Crohn's disease can be easily separated and appear to be the manifestations of two separate diseases. There is, however, some evidence that suggests that UC and CD may represent two extremes of the same disease. This concept is based on the observation that occasionally patients present with an intermediary form in which the two conditions cannot be clearly separated on clinical or pathologic grounds. There is also genetic evidence to support this concept: often in the same family, or even between identical twins, one individual may suffer from Crohn's disease while the other from ulcerative colitis.¹ Furthermore, the extraintestinal complications of the two diseases are similar.

Ulcerative colitis (UC) usually starts at the most distal part of the colon and may manifest as a simple proctitis involving only the rectum. Other patients may suffer from proctosigmoiditis, left-sided colitis involving the descending colon, subtotal colitis (up to the hepatic flexure) or total involvement of the large intestine.² Proctitis was considered by some as separate condition from UC but it is now becoming evident that in a considerable number of patients with proctitis the inflammation progresses to the proximal colon and in some to the entire large intestine.³ Histological findings

in ulcerative colitis show superficial ulceration of the surface epithelium, intense inflammatory infiltration of the mucosa with pus in the crypts with typical crypt abscesses. There is distortion and destruction of the glandular structure of the colon. These findings however, are not pathognomic for UC, because they occur in the presence of any severe chronic mucosal disease. As the disease becomes chronic, ulcerations may heal with flattened mucosa and the intervening normal mucosa may appear as "pseudopolyps."²

Complications of ulcerative colitis are shown in *Table 1*.

Bleeding used to be a life-threatening complication, but with better transfusion facilities, monitoring and earlier surgery, this ceased to be a major problem. Severe toxicity and dilatation of the colon, often leads to perforation. Again early and safer surgery has overcome the previous mortality associated with this complication. Healing may occur with stricture formation, but this is less common in UC than in CD. There is evidence that malignancy of the colon is more common in patients with ulcerative colitis than in the normal bowel.² However, the incidence of patients with ulcerative colitis developing malignancy has been overrated in the past and recent evidence indicates that the incidence is much lower than previously believed.³ Extraintestinal complications may involve the liver, biliary tract, joints, skin and the eyes. Because of malnutrition, fatty liver is not uncommon. Hepatitis may be due to blood transfusions and autoimmune hepatitis may accompany UC. Some of these become chronic and prolonged inflammatory changes may lead to cirrhosis. The classic biliary complication is sclerosing cholangitis with multiple intrahepatic and extrahepatic strictures of the bile ducts. Rarely this may lead to choleangiocarcinoma. Peripheral arthritis classically involves large joints in asymmetrical manner but small joints may also be involved. Development or exacerbation of this type of arthritis usually parallels intestinal disease activity, while ankylosing spondylitis and sacro-ileitis are unrelated to dis-

ease activity and may precede the development of ulcerative colitis. Several skin lesions have been observed in patients with ulcerative colitis, such as oral aphthous ulcerations, erythema nodosum, arteritis, pyoderma gangrenosum, epidermolysis bullosa, etc. Eye lesions observed in inflammatory bowel disease are episcleritis and uveitis.²

Crohn's disease (CD) may affect any part of the alimentary tract. One third of the cases are restricted to the small bowel (regional enteritis). The terminal ileum is most commonly involved. Almost half of all patients with CD have both the small and large bowel involved, and ileocolitis is the most common manifestation. Colonic Crohn's without small bowel disease occurs in approximately 20% of the cases. One of the common manifestations is perianal involvement with fistulas and perianal abscesses. This may occur in about 30% of patients.^{4,5}

The earliest visible lesions are superficial round aphthous ulcerations. These ulcers, are deeper than those in ulcerative colitis and they progress quickly to transmural inflammation. Non-caseating granulomas are often found and are considered pathognomic for Crohn's disease. However, granulomas are not always present or at least are so rare that they are not found in every biopsy. Because of the depth of the lesions, a thickening of the bowel wall is common and this may lead to strictures. Transmural inflammation is manifested by the presence of lymphoid nodules which are found at the junction of the muscularis externae and the serosa and may extend to the mesenteric side of the bowel. The presence of these nodes on the mesentery, and the multiple strictures are the classic findings of Crohn's disease at operation.⁶

The complications of Crohn's disease⁵ are shown in *Table 2*. Because of the nature of the disease, obstruction is more common than in UC. Because of the depth of the involvement, periintestinal abscesses are often found. Fistulas originating in the intestine may lead blindly into the mesentery and are the source of these abscesses. Fistulas may also connect several bowel loops. Entero-vesical and entero-cutaneous fistulas can also occur. Others may be the cause of perirectal disease. Because of the slow progression of the disease across the bowel wall, mesentery and omentum tends to adhere to the fistulas. Therefore, abscesses are common but frank perforation or massive bleeding is rare. Malignancy has been reported in long-standing Crohn's disease, and the frequency of this complication is probably less than previously believed.⁷ Because of involvement of the small bowel and frequent resection of different sections of the small intestine, malabsorption is common.⁸ As in

other situations with intestinal malabsorption, there is increased incidence of cholelithiasis and urolithiasis. If the disease is long-standing, after several years of purulent fistulas and abscesses, amyloidosis may develop. Because of the presence of chronic disease, hematologic complications, such as anemia of chronic disease or anemia due to bleeding is not uncommon.⁸ Extraintestinal manifestations of Crohn's disease are similar to those in UC.

Organization of the Conference. With this background in mind, it is now appropriate to discuss the reasons for the Conference on Morbidity and Mortality of Inflammatory Bowel Disease held in Quebec City in 1992. The Crohn's and Colitis Foundation of Canada (previously the Canadian Foundation for Ileitis and Colitis) supports medical research; education of physicians and patients; and recently it became involved in advocating for the specific needs of patients with inflammatory bowel disease (*Table 3*). The Foundation has a Lay Board and a Medical Advisory Board (MAB). There is close cooperation between the two boards. The Lay Board is involved in organizing charitable donations and the administration of finances. The MAB has three major committees, the Research Committee, the Education Committee and the Patient Advocacy Committee. The Research Committee reviews research applications and advises on the distribution of funds to support research. The Education Committee provides educational material for patients and physicians and the Patient Advocacy Committee deals with specific needs for patients such as approaching government to obtain support for the inclusion of nutrient substances into the medication list for patients with inflammatory bowel disease. For the last several years, the Lay Board received many complaints from patients about the difficulties they had obtaining insurance. Dr. Suzanne Lemire, chairman of the Patient Advocacy Committee, reported to the MAB about the medical aspects of obtaining insurance. She found that the last generally accepted text on life risk was that of "Brackenridge" which was published in 1985.⁹ A book written in 1985 could have included morbidity and mortality data published after 1982. Any report published in 1982 would deal with cases that were collected during the 1970's. Because of the many recent advances in the 1980's, the MAB of the CCFC assumed that the mortality and morbidity figures must have improved since the publication of Brackenridge's text. The major advances related to improved diagnostic techniques (*Table 4*), improved medical therapy (*Table 5*) and safer and less complex surgery (*Table 6*). The introduction of ultrasound and CT scan made it easier to differentiate an abscess from a swollen edematous inflamed bowel. The better differential diagnosis of the classic finding of a right lower quadrant mass allowed

for more appropriate therapy.¹⁰ Colonoscopy, especially because of the improved pathological recognition of dysplasia¹¹ allowed to carry out surgery before cancers have developed. *Table 4* indicates that the potentially more toxic drug Sulfasalazine can now be replaced by 5-amino-salicylic acid preparations. The conventional steroids are being replaced with steroids with first-pass kinetics. Cyclosporin and other new immunosuppressive agents have been added to Imuran and 6MP, and metranidazole has been found to be very effective, especially in perianal Crohn's disease.¹² In the past there was very little interest in nutritional support and many patients were starved on "bowel rest." Introduction of enteral nutrition and total parenteral nutrition has not only helped to induce remissions, but also allows patients to enter surgery in a better nutritional state.^{13,14} As shown in *Table 5*, surgery has become safer and much less complex.^{15,16} Avoiding exclusion of diseased bowel in blind loops resulted in a diminished incidence of small intestinal bacterial overgrowth and a lesser incidence of cancer developing in blind loops. In the past, partial colectomy was performed in Crohn's disease and this led to multiple reoperations. Presently in most centers, total colectomy is carried out even if only a segment of the colon is involved. Multiple strictures are corrected by stricturoplasty rather than by resection of large chunks of the small intestine. Better bowel preparation diminishes the chance of peritonitis.

Abscesses, if possible are evacuated by radiologic methods rather than by surgery. Post-operative surgical therapy has improved with better antibiotics and nutritional support. All these advances suggested that the morbidity and mortality must have improved during the last decade.

On the basis of these assumptions, the MAB of the Crohn and Colitis Foundation of Canada, with the support of the Lay Board, decided to organize a conference reviewing the recent data on the morbidity and mortality of inflammatory bowel disease. An organizing committee (*Table 7*) was established. In addition to the above committee, the advice of Dr. Guy Tremblay, Past President, Canadian Life Insurance Medical Officers Association, was obtained on the first meeting of this committee. A number of speakers were invited to speak on several aspects of the conference (*Table 8*). In addition to the speakers 19 Canadian gastroenterologists and surgeons were invited to participate in the conference. The total number of participants was 30. The invited guests represented a broad spectrum of individuals with specific interests, a good scattering of age and of geographic location. There was a mix of academic and non-academic physicians and surgeons. Two of the in-

vited practicing gastroenterologists were also insurance medical officers.

The organizing committee decided that before embarking on the conference, it was necessary to ascertain whether the impression of the Lay Board of the CCFC was correct in assuming that patients with inflammatory bowel disease have difficulties in obtaining insurance. Dr. Sutherland was charged to obtain data on this and to report to the conference on his findings. The conference lasted one day. In the morning lectures were given by Dr. Lloyd Sutherland on the results of the patients' survey on insurance, by Dr. Guy Tremblay on the process by which life insurance applications are evaluated, by Dr. Richard Farmer on the human cost of inflammatory bowel disease, by Mr. Rod Riley on the Canadian Experience of the morbidity and mortality of IBD. Dr. Goran Hellers reviewed the morbidity and mortality of Crohn's disease and Dr. Vibeke Binder that of ulcerative colitis. In the afternoon three group sessions were organized, each consisting of approximately ten participants. One group chaired by Dr. Desmond Leddin was charged to discuss the morbidity and mortality of ulcerative colitis and to propose recommendations which would help to improve the insurability of patients with UC. Dr. Lloyd Sutherland chaired a group that dealt with the same issues as Crohn's disease before surgery and a group chaired by Dr. Alan Thomson discussed Crohn's disease after surgery. The summary of the discussions of these small groups were reported to the reassembled plenary session by their chairmen. These were further discussed and final conclusions and recommendations were drawn.

The Meeting. The first lecture was by Dr. Lloyd Sutherland on the results of the patient survey on insurability.¹⁷ Drs. Beck, Leddin, Prokipchuk, Thomson and Sutherland sent questionnaires to 50 cases each, and Dr. Lemire; whose cases represented the experience of the French-Canadian population sent questionnaire to 70 patients with IBD. A total of 320 questionnaires were sent out and 206 responded providing a 66% response rate. The results for straight life insurance are shown in *Figure 1* indicating a high rejection rate for both disease. Rejection and special rating for disability insurance showed similar results. Interestingly, group life was refused in 35% of patients with ulcerative colitis and 17% of patients with Crohn's disease.

Thus there appears to be reasonable evidence indicating that patients with IBD has considerable difficulties in obtaining insurance.

The next and most exciting lecture was given by Dr. Guy Tremblay on the process by which life insurance appli-

cations are evaluated/rated.¹⁸ He explained how insurance companies work. Most clinicians were unaware of the fact that for the first 7 to 8 years after obtaining an insurance, the life expectancy of the insured population is half to one-third lower than that of the general population. This is because individuals who have recognizable diseases have been already excluded. Because the insurance business is competitive and companies want to sell insurance, patients with IBD have a better chance to obtain insurance at a lower additional rate if they shop around among several insurance companies. He pointed out that the insurability of patients improves after periods of good health and suggested that we should encourage patients to reapply after periods of remission. He pointed out that patients will do better if a clinician helps the medical director to evaluate the risk. Dr. Tremblay advised that clinicians should write a letter, rather than just fill out a form, and that if applicable, clinicians should mention the period of remission, the fact that the patient is reliable and is under ongoing follow-up. Medications used should be mentioned, especially if the patient is not on steroids or immunosuppressive agents. An important factor is the patient's ability to function, i.e. if he/she is back to work and has held the same job for a certain length of time. He also suggested that patients have group insurance coverage at their work, should be advised not to change their jobs.

Dr. Richard Farmer, previously physician in chief of the Division of Medicine and director of the Department of Gastroenterology at the Cleveland Clinic, reviewed the human cost of inflammatory bowel disease.¹⁹ He investigated 164 patients with IBD whose disease onset started around the age of 20. Only those patients were included in the study whose follow-up was over 10 years. A questionnaire was designed to assess their (a) ability to function, (b) social and recreational activities, (c) attitude towards life and health and their (d) medical status. The findings of the study indicates that ulcerative colitis patients have a better quality of life than patients with Crohn's disease and patients with both diseases enjoy a better quality of life before than after surgery. Most importantly, IBD patients have a close to normal life-style, with 44% functioning well and being able to work, 50% functioning 11 well but sub-optimally, the majority of whom still can work and only 6% had severe disabling symptoms.

A review of the Canadian morbidity and mortality data based on hospital discharges between 1971 and 1989 was presented by Rod Riley, MA from the Canadian Center of Health Information, Statistics Canada.²⁰ Discharge diagnosis are filled out in every Canadian hospital. These forms are submitted to the Provincial

Ministries of Health and then forwarded annually to the Canadian Center for Health Information. As patients may be admitted several times a year, the statistics presented by Mr. Riley do not provide incidence for prevalence. They are, however, useful to assess the general trends and provide accurate mortality statistics. The data indicated that between 1971 and 1989, in Canada, similar to the observations in other Western countries, Crohn's disease was on the rise, while the rate of discharge for ulcerative colitis remained unchanged (*Figure 2*). There was a greater increase in the numbers of hospitalizations of the elderly patients with IBD. Unfortunately, it is impossible to tell how many of the older patients with atherosclerotic vessels suffered from ischemic bowel disease rather than IBD. The mortality rate was steadily decreasing since 1971 and in 1989, mortality due to ulcerative colitis was 1.5/million and for Crohn's disease 2/million (*Figure 3*). Mortality was extremely low in the young and somewhat higher in the elderly. Some patients of the later group may have had multisystem diseases and may not be suffering from IBD but from ischemic or other types of bowel disease.

The literature on the morbidity and mortality of Crohn's disease was reviewed by Dr. Goran Hellers.⁷ Mortality rate in early studies was considerably higher than the expected mortality rate of the general population (*Figure 4*)²¹ but was equal to the expected in the study of Dr. Vibeke Binder²² which included patients up to the year of 1985 (*Figure 5*). Dr. Heller also reported on standard incidence ratio of cancer in Crohn's disease. There appears to be an increased excess mortality due to cancer in younger patients but not in the older population. After the age of 30, the ratio falls to 1.5 and this is not significantly different from that of the general population.

Dr. Vibeke Binder reported on the morbidity and mortality of ulcerative colitis, in Copenhagen County between 1962 and 1987.³ The median observation time was 11.7 years (range 1 to 25 years). Dr. Binder found that in the first year after diagnosis, there was a slight increase in mortality, but once the patient survived the first year of illness, the mortality rate became that of the background population. To study the incidence of cancer, she selected only those patients who were followed for over 7 years. She found that the calculated lifetime cancer risk of the Danish population was 3.7%, while that for ulcerative colitis was 3.6%. Thus in the Copenhagen study, it appears that patients with ulcerative colitis do not have an increased risk of malignancy. She also studied the quality of life of patients with ulcerative colitis and found that their working capacity, professional life, private, family and sexual adjustment was similar of that of the general population.

Group Discussions. With this background information, the Conference broke up into three groups of 10 participants. Each group was requested to review the literature on morbidity and mortality of the area designated to them. They were also asked to come up with recommendations to the CCFC and the profession to educate patients and physicians on the workings of insurance companies. The chairman of each session summarized the discussion and reported to the general session which reconvened immediately after the small groups finished their sessions.

Dr. Leddin reported on ulcerative colitis. The group reviewed the appropriate section of the volume "Medical Selection of Life Risks, A Comprehensive Guide to Life Expectancy for Underwriters and Clinicians" by R. D. C. Brackenridge, 1985.⁹ They agreed with the classification and the approach used in "Brackenridge" to divide ulcerative colitis into mild, moderate and severe. However, according to their opinion, the data were out of date on mortality. This group like the other two came up with important suggestions regarding the patient's and physician's approach to insurance companies. The recommendations of this group will be incorporated below with those of the two other groups.

The second group discussed Crohn's disease before surgery. Dr. Sutherland summarized the data. Since most patients eventually go to surgery, the group found that there is very little known about the morbidity and mortality of those patients with Crohn's disease who do not end up with an operation. Nor did they find any specific predictors as to when patients will have surgery. Dr. Don Daly, a gastroenterologist, who is also a medical officer of Prudential of England, brought with him the text "M & G Underwriting." They reviewed the criteria used by Prudential of England to assess insurability of patients with CD. Apparently, the highest premium was paid by patients with ileocecal involvement. Astonishingly, patients with jejunitis were rejected irrespective of the severity of the disease. The group wondered whether the involvement of the jejunum with Crohn's disease was confused with the more severe condition "ulcerative jejunitis." Interestingly, the type of therapy had no effect on rating. This group like the other two came up with recommendations to the CCFC and the Canadian Association of Gastroenterology (CAG).

The third group dealt with Crohn's disease after surgery. This section was chaired by Dr. A.B.R. Thomson. Dr. Goran Hellers was a member of this group providing surgical expertise. Dr. Thomson reported that evidence exists that, morbidity and mortality after surgery in Crohn's disease has recently improved. This is due to

the modern surgical and post surgical techniques, reviewed in Table 6, and because of the excellent surgical results patients are sent earlier and in a better condition to surgery. Dr. Heller stated that the operation for Crohn's disease is not more risky than an operation for any other cause and that there is no additional surgical mortality related to Crohn's disease. The reoperation rate is 4% per year.

Accordingly, previous surgery should not be a consideration for extra rating for life insurance. However, based on the report by Dr. Farmer and personal experience of the group indicated that previous surgery may be a factor in disability insurance. This group's recommendations to the CCFC and GAG are incorporated with those of the other two groups and is discussed below.

Recommendations. All three groups indicated that the CCFC should develop an educational booklet for patients. This pamphlet should explain how insurance companies rate applicants. Patients should be encouraged to reapply after a period of remission. Most importantly, patients should understand that they should try to stay in the same job to maintain their group insurance. Patients should be advised that if they maintain their regular follow-up, they may get better insurance ratings. It was felt that the CCFC should develop a form providing the information that is important to convey to the insurance companies in order to obtain a more favorable rating. When a patient applies for insurance, they could take this form to their physician as a guideline. It was also suggested that the CCFC should identify insurance brokers in different communities who have an understanding of IBD.

The recommendations to the Canadian Association of Gastroenterology suggested that this organization should embark on an educational campaign to physicians to enlighten them about insurance companies and their method of ratings. Specifically, it was felt that clinicians should be more open in their interaction with the medical officers of insurance companies, and may even communicate directly with them. Rather than filling out a form, physicians should be encouraged to write a letter about their patients and, if applicable, they should point out that the patient has lost little time from work, has constant careful follow-up, is on maintenance therapy, has no jejunal disease, is not sufficiently ill to require TPN or long-term steroid therapy. Since jejunitis is a cause for complete rejection by at least one insurance underwriting text, it would be of interest to investigate why jejunal disease is considered so deleterious that it excludes patients from insurance.

Conclusion. Patients with IBD have considerable difficulty in obtaining straight life and disability insurance. This, in spite of the fact that the quality of life of most patients with IBD is not very different from that of the general population and the mortality rate of patients with IBD is decreasing and presently is not different from that of the general population. However, members of the Conference learned from representatives of the insurance industry that the mortality rate of general population is higher during the first seven years than that of insured population. Members of the Conference learned that patients with IBD had a better chance to obtain insurance if there is a close cooperation between the treating physician and the medical officer of the insurance company.

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TABLE 1.
Complications of Ulcerative Colitis

Gastrointestinal

- Bleeding
- Toxic Megacolon Perforation
- Stricture
- Malignancy

Extra Intestinal

- | | |
|----------------|---|
| Liver Disease: | Fatty Liver, Hepatitis, Cirrhosis |
| Biliary Tract: | Sclerosing Cholangitis, Cholangiocarcinoma |
| Arthritis : | Peripheral, Ankylosing Spondylitis, Sacro-ileitis |
| Skin Lesions: | Erythema nodosum, Arteritis, Pyoderma Gangrenosum |
| Eye Lesions: | Episcleritis, Uveitis |

TABLE 2
Complications of Crohn's Disease

Gastrointestinal

- Intestinal
 - Obstruction Abscess
 - Fistulas
 - Enteric
 - Mesenteric
 - Perirectal
 - Vesical
 - Cutaneous
 - Perforation (Rare)
 - Bleeding (Rare)
 - Malignancy
- Metabolic
 - Malabsorption - (Cholelithiasis, Urolithiasis)
 - Amyloidosis
 - Hematologic

Extra Intestinal

- Liver and Biliary Tract Disease - Same as in ulcerative colitis
- Joint , Skin and Eye Lesions - Same as in ulcerative colitis

TABLE 3.
Crohn's and Colitis Foundation Of Canada*

Supports Medical Research
Provides Education
Supports Specific Needs of Patient with IBD

Lay Board — Medical Advisory Board

MAB Committees
Research Committee
Education Committee
Patient Advocacy Committee

*Canadian Foundation for Ileitis and Colitis

TABLE 4.
Improved Diagnostic Methods

Ultrasound
CT Scan
Colonoscopy
Improved Pathologic Interpretations — Dysplasia

TABLE 5.
Improved Medical Therapy

Therapy available in the 1970's	Recent useful additions
Drugs	
Sulfasalazine	5-ASA
Steroids (Conventional)	With First-Pass Kinetics
Imuran - 6MP	Cyclosporine
	Metronidazole
Nutrition	
Little Interest	Enteral Nutrition
Bowel Rest	Total Parenteral Nutrition

TABLE 6.
Safer and Less Complex Surgery

- Avoidance of Blind Loops
- Avoidance of Partial Colectomy for Crohn's Disease Strictureplasty
- Better Bowel Preparation
- Invasive Radiology
- Better Post-Surgical Care
- Better Antibiotics
- Nutritional Support

TABLE 7.
Organizing Committee of the Conference

- Ivan T. Beck, Kingston (Chair)
- Desmond D. Leddin, Halifax
- Suzanne E. Lemire, Quebec
- Eldon A. Shaffer, Calgary
- Lloyd R. Sutherland, Calgary
- Alan B. R. Thomson, Edmonton
- Raymond J. Van Berkel, Toronto

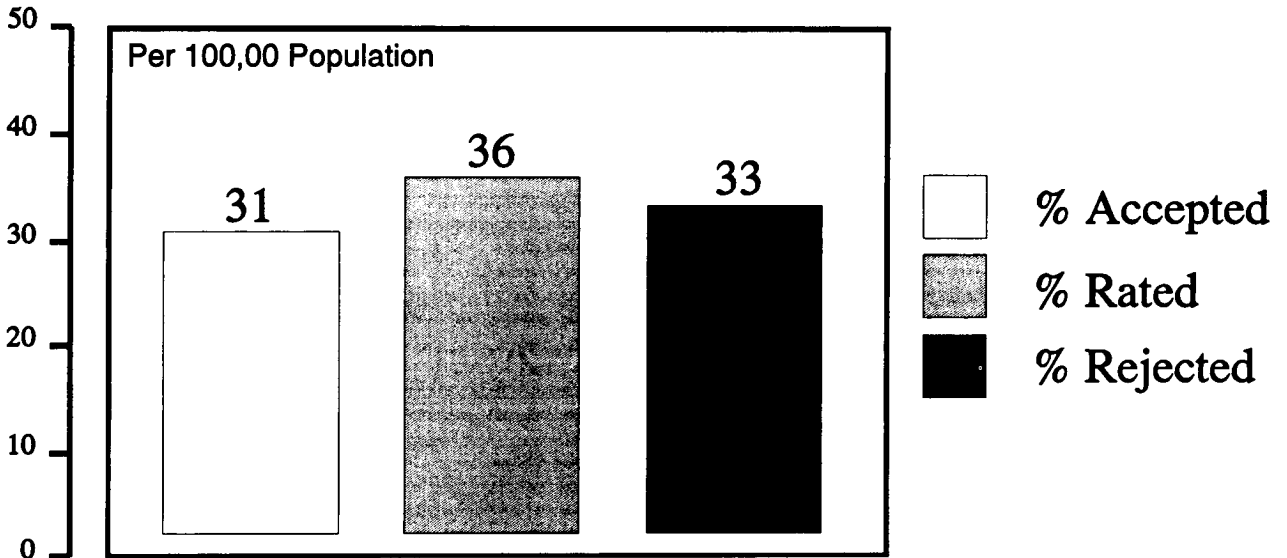
TABLE 8.
Guest Speakers of the Conference

- Guy Tremblay, Quebec, Quebec
Past President/Canadian Life Insurance Medical Officers Association
- Richard G. Farmer, Washington, D. C.
Medical Advisor, Agency for International Development
- Rod Riley, Ottawa
Canadian Center for Health Information Statistics Canada
- Goran Hellers, Huddinge, Sweden
Department of Surgery, Karolinska Institute
- Vibeke Binder, Copenhagen, Denmark
Department of Gastroenterology, Helev Hospital

FIGURE 1.
Straight Life Insurance

Percent acceptance, rating and rejection for straight life insurance of Canadian patients with IBD

Crohn's Disease:



Ulcerative Colitis:

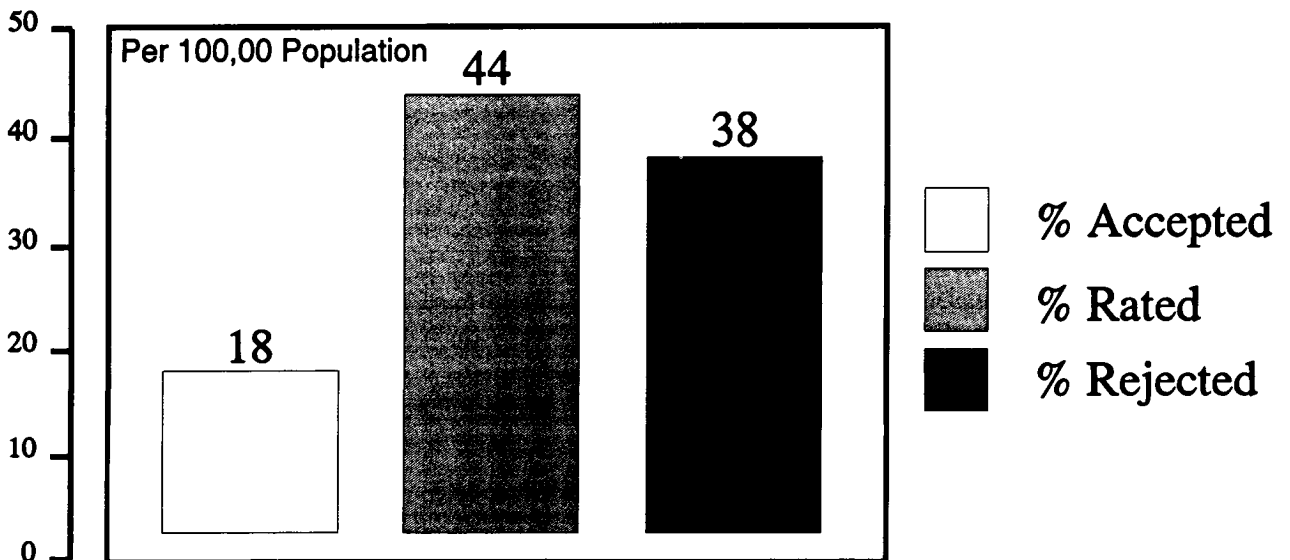
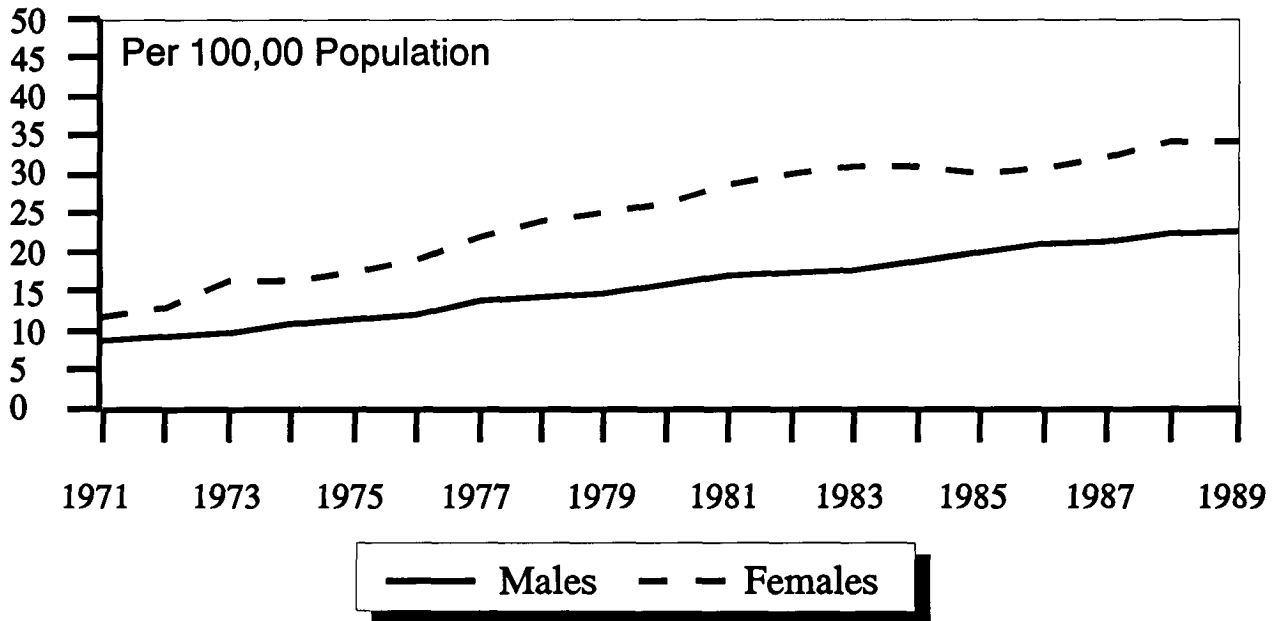


FIGURE 2.
Hospital Discharge Rates

Changes in Canadian hospital discharge rates with patients with IBD between 1971 and 1989
(reproduced from ref.20)

Ulcerative Colitis



Crohn's Disease

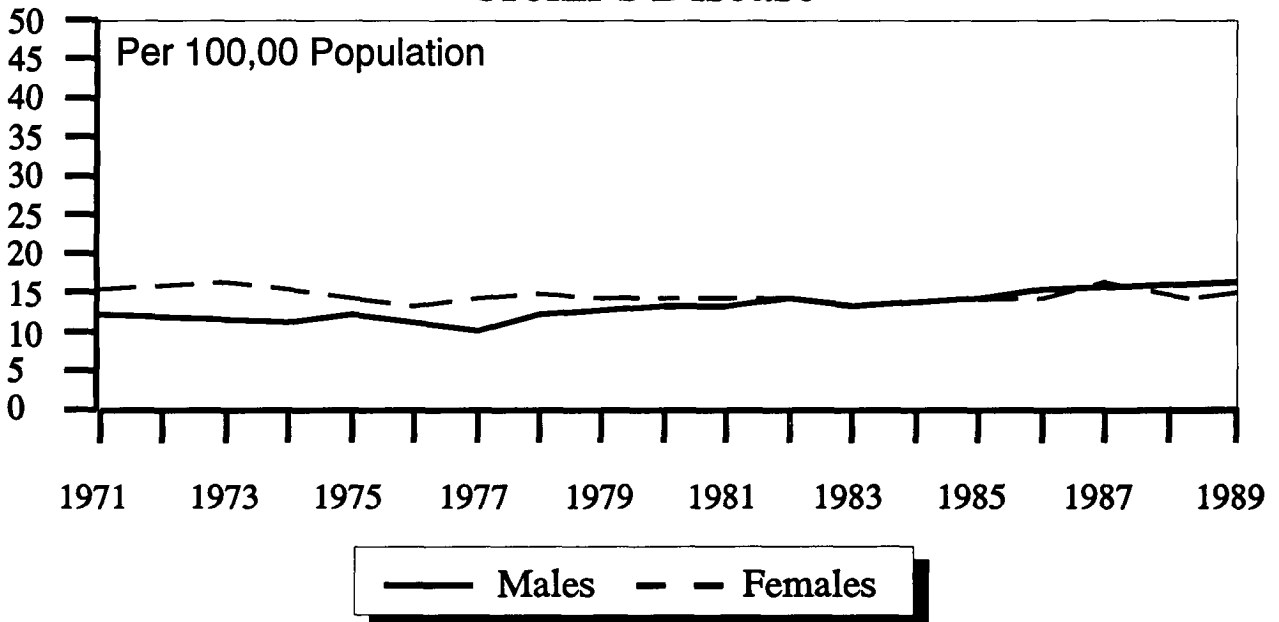


FIGURE 3.
Mortality Rates

Changes in Canadian mortality rates of IBD patients between 1971 and 1989 (reproduced from ref.20)

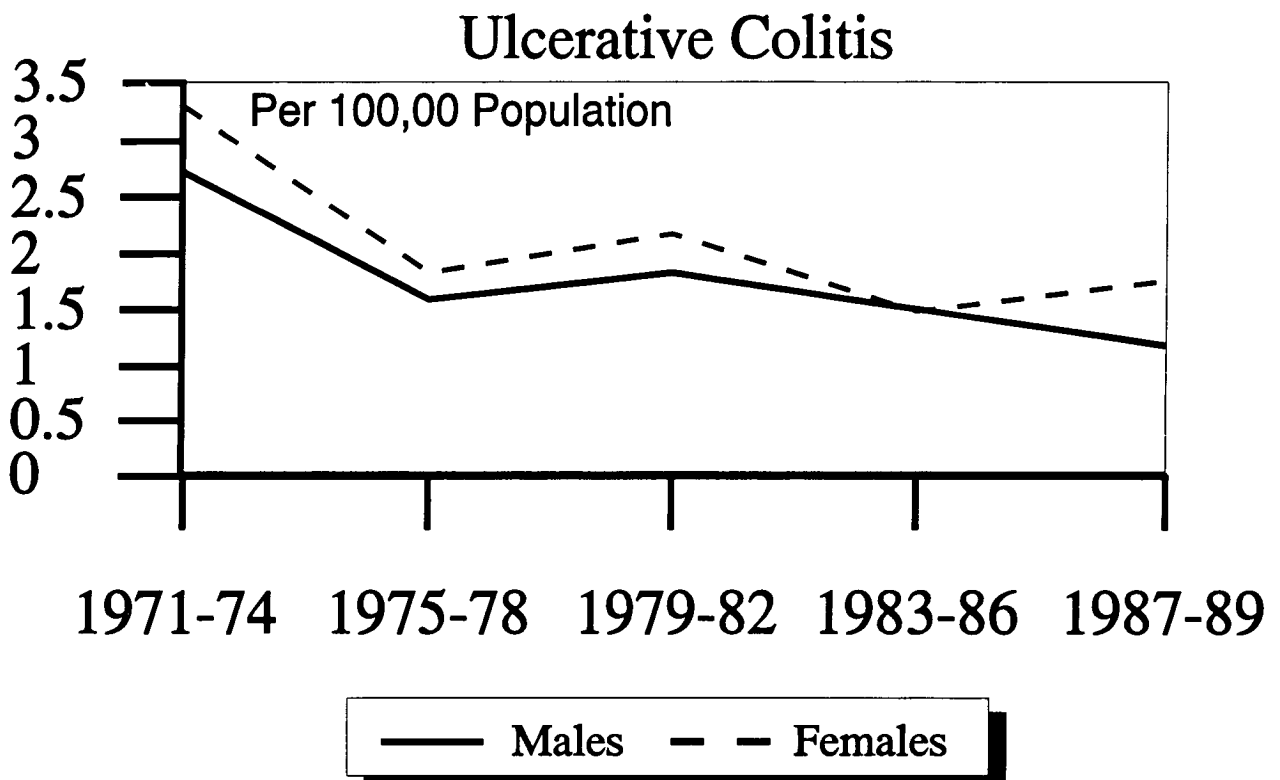
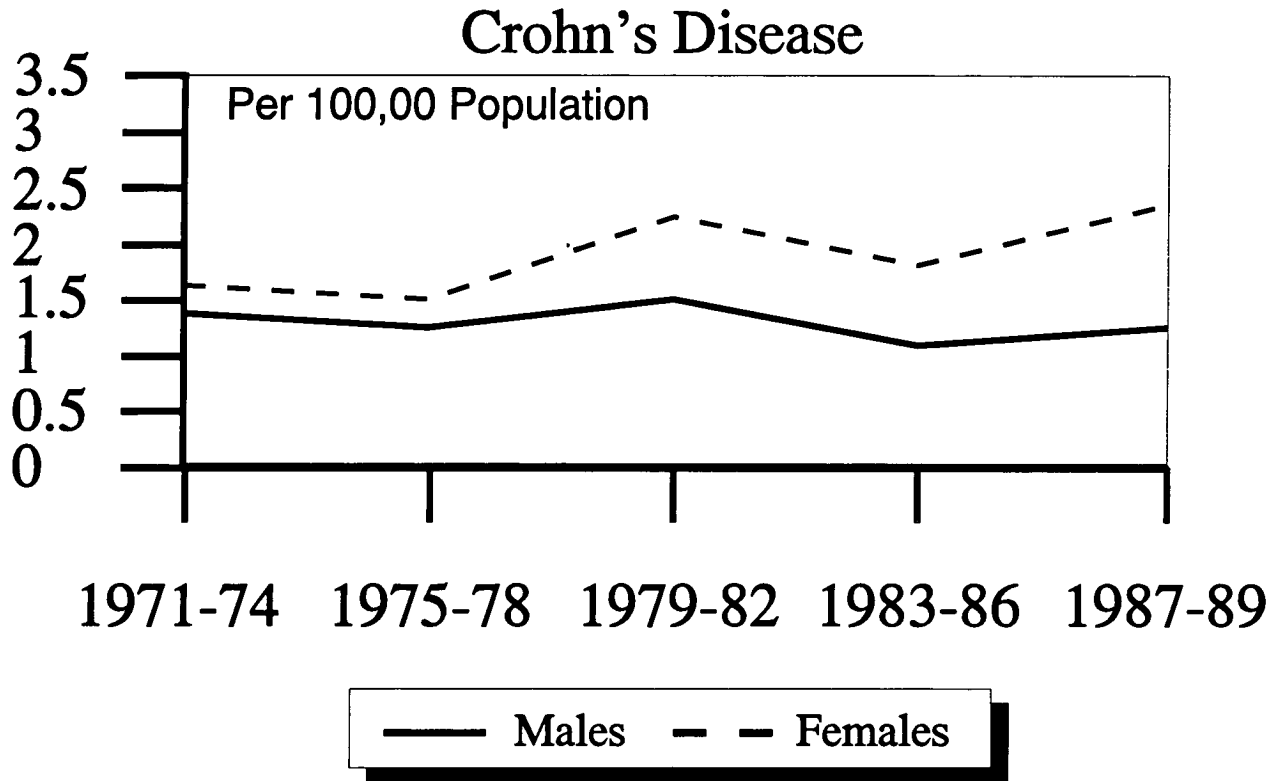
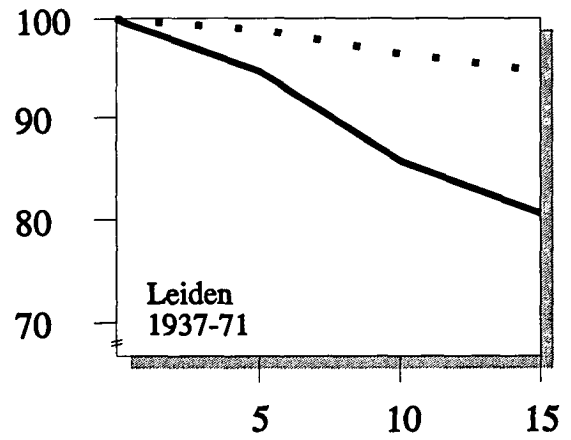
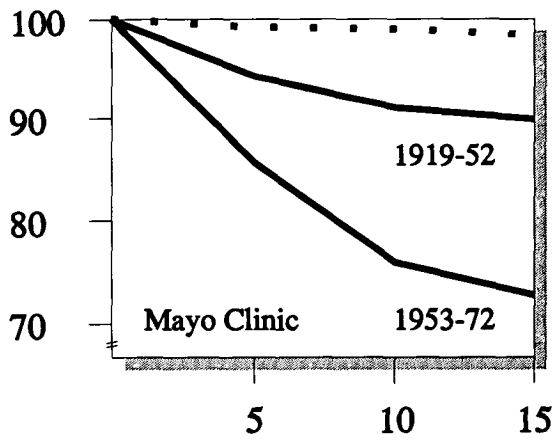


FIGURE 4.
Mortality in Crohn's Disease — Early Studies

The expected and observed (continuous line) mortality in studies from different time periods (The Mayo Clinic 1919-52, Leiden 1937-71, Oxford 1938-70, and Stockholm 1955-74). Early studies on mortality in Crohn's disease (reproduced from ref. 7 and 21)



..... Observed
 ————— Expected

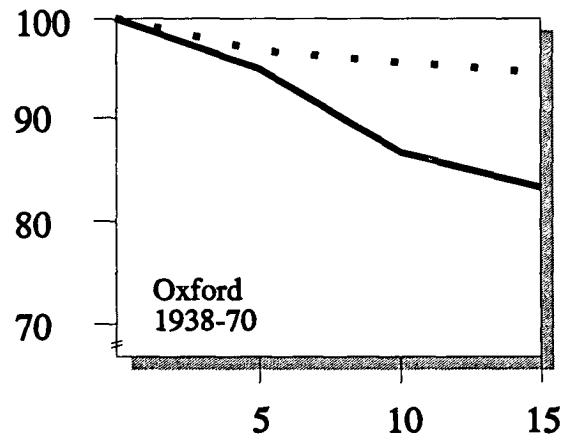
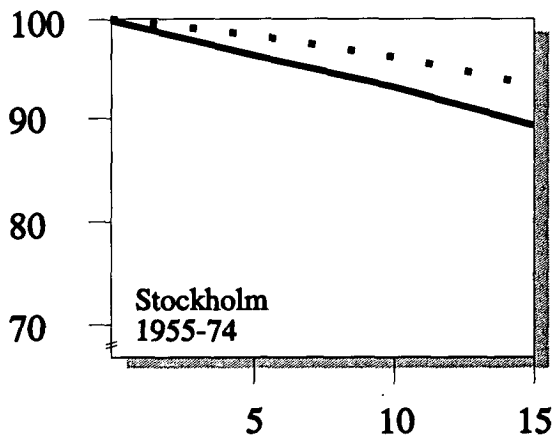


FIGURE 5.
Later Study
Survival, Crohn's Disease - Males and Females

Survival of patients with Crohn's disease compared with the age- and sex-matched background population.
A later study on mortality in Crohn's disease (reproduced from ref. 22)

