



HAL
open science

Ulcerative Colitis and Crohn's Disease Have Similar Burden and Goals for Treatment

Catherine Le Berre, Ashwin N. Ananthakrishnan, Silvio Danese, Siddharth Singh, Laurent Peyrin-Biroulet

► **To cite this version:**

Catherine Le Berre, Ashwin N. Ananthakrishnan, Silvio Danese, Siddharth Singh, Laurent Peyrin-Biroulet. Ulcerative Colitis and Crohn's Disease Have Similar Burden and Goals for Treatment. *Clinical Gastroenterology and Hepatology*, 2020, 18 (1), pp.14-23. 10.1016/j.cgh.2019.07.005 . hal-03489071

HAL Id: hal-03489071

<https://hal.science/hal-03489071v1>

Submitted on 21 Jul 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Title: Ulcerative Colitis and Crohn's Disease Have the Same Burden and Goals for Treatment

Short title: Ulcerative colitis/Crohn's disease: same goals

Catherine Le Berre^{1,2}, Ashwin N Ananthakrishnan³, Silvio Danese⁴, Siddharth Singh⁵,
Laurent Peyrin-Biroulet¹

¹ Inserm U954 and Department of Gastroenterology, Nancy University Hospital, Université de Lorraine, Vandoeuvre-lès-Nancy, France.

² Institut des Maladies de l'Appareil Digestif, Nantes University Hospital, Nantes, France.

³ Division of Gastroenterology, Massachusetts General Hospital, Boston, Massachusetts, USA.

⁴ Department of Biomedical Sciences, Humanitas University, Milan, Italy; IBD Center, Department of Gastroenterology, Humanitas Clinical and Research Center, Milan, Italy.

⁵ Division of Gastroenterology, University of California, San Diego, La Jolla, California.

Manuscript Type: Invited Narrative Review Article.

Word count: 6,031.

Grant support: None.

Abbreviations:

CD: Crohn's disease.

CDEIS: Crohn's disease endoscopic index score.

CI: Confidence interval.

CRP: C-reactive protein.

FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue.

FC: Fecal calprotectin.

IBD: Inflammatory bowel disease.

IBD-DI: Inflammatory Bowel Disease – Disability Index.

IBS: Irritable bowel syndrome.

SD: Standard deviation.

SES-CD: Simple endoscopic score for Crohn's disease.

SIBDQ: Short Inflammatory Bowel Disease Questionnaire.

STRIDE: Selecting Therapeutic Targets in Inflammatory Bowel Disease.

TNF: Tumor necrosis factor.

UC: Ulcerative colitis.

5-ASA: 5-aminosalicylic acid.

Correspondence:

Prof. Laurent Peyrin-Biroulet, MD, PhD

Inserm U954 and Department of Gastroenterology

Nancy University Hospital, Université de Lorraine

1 Allée du Morvan

54 511 Vandœuvre-lès-Nancy, France

Tel +33 3 83 15 36 61

Fax +33 3 83 15 36 33

peyrinbiroulet@gmail.com

Disclosures: The authors declare that they have no competing interests relevant to this manuscript.

Conflicts of Interest: No relevant conflicts of interest exist.

Writing assistance: None.

Author Contributions: CLB, literature review, acquisition of data and drafting of the article; LPB, study concept and design, literature review and study supervision. ANA, SD, SS, critical revision of the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

Abstract: It is unclear whether ulcerative colitis (UC) is a progressive disease like Crohn's disease (CD). Patients with UC are often undertreated, because of the possibility of curative colectomy and the perception that the disease burden is lower than that of CD. We discuss findings from studies that aimed to determine whether UC and CD have the same disease burden and should be treated in the same intensive way. We discuss the similarities between CD and UC, including effects on quality of life, long-term complications, strictures, increased risk of cancer, pseudopolyps, functional abnormalities, and anorectal dysfunction. Contrary to the generally accepted idea, surgery cannot cure UC. Post-operative complications, especially pouchitis and fecal incontinence, affect more than one-third of patients. CD and UC each pose substantial economic burdens. Monitoring, treatments, and goals of therapy are similar for all inflammatory bowel diseases. Earlier initiation of disease-modifying drugs might reduce progression of UC and reduce its burden after surgery, although UC might not cause the irreversible damage observed in patients with CD.

Key words: IBD, severity; disability; treat to target

Even though the incidence of inflammatory bowel diseases (IBD) varies across the world, both Crohn's disease (CD) and ulcerative colitis (UC) have become global diseases.

CD can affect the entire gastrointestinal tract and cause transmural lesions, and is long recognized as a disabling, progressive and destructive disease, leading to high societal costs and substantial quality-of-life burden.¹ UC causes more superficial lesions which are limited to the colon, and its progressive and disabling nature may often be underestimated. This may lead to undertreatment, because of the possibility of colectomy, that has always been traditionally considered as a cure, and the physicians' perception that disease-related burden is lower than in CD. Patients themselves often consider that CD is more severe than UC, as illustrated by their fear when the diagnosis turns out to be Crohn's rather than UC. Yet, UC and CD share the same therapeutic armamentarium, except for 5-aminosalicylic acid (5-ASA), and the same monitoring is recommended for both diseases, in order to reach the same therapeutic goal. In both CD and UC, the current trend is to move towards a personalized and more aggressive treatment, with the final aim of changing disease course and returning to a normal life.

Thus, as it has already been shown in CD, it is crucial to better highlight the disabling and progressive nature of UC, in order to act at an early stage of the disease. This review hypothesizes that UC and CD are associated with similar disease burden and aims to show to IBD physicians that both diseases should be monitored and treated in the same intensive way (Figure 1).

Similar impact on patients' life

Several studies demonstrated the significant impact that IBD, including UC, can have on health-related quality of life.^{2,3} A survey confirmed that quality of life as measured by the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) could be seriously impaired in UC patients, and depended on patients' global assessment of disease activity.⁴ A recent study found a significant association between symptoms of depression and clinical disease activity in CD ($p=0.0007$) and UC ($p=0.005$) patients. This relationship was less obvious for anxiety symptoms (CD, $p=0.031$ and UC, $p=0.066$).⁵ The validation study of the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) revealed similar fatigue scores (mean \pm SD) between both diseases (UC 39.4 ± 10.6 ; CD 38.6 ± 11.3).⁶ Work productivity is also affected to a similar extent in UC and CD, with similar rates of temporary [12.6% (UC) vs. 12.2% (CD)] and permanent disability [1.6% (UC) vs. 1.7% (CD)].⁷ Moreover, the IBSEN study showed that the overall relative risk for receiving a disability pension compared with the general population was significantly increased in both UC (RR 1.80; 95% CI 1.41 to 2.27) and CD (RR 1.98; 95% CI 1.42 to 2.68).⁸ The validation study of the Inflammatory Bowel Disease – Disability Index (IBD-DI) also demonstrated that the type of IBD did not influence the IBD-DI value (mean \pm SD) (39.2 ± 23.1 in UC vs. 33.9 ± 19.5 in CD, $p=0.116$).⁹

The BIRD study was the first cross-sectional study to assess all the dimensions of patient-reported outcomes in a large, nationwide cohort of 1,185 IBD patients affiliated with the French patients' association (61% CD, 39% UC). This French cohort showed that half of patients reported poor quality of life (55.1% CD, 37.3% UC), severe fatigue (48.9% CD, 37.1% UC) and/or depression (49.9% CD, 48.5% UC). Around one-third of patients reported anxiety (31.8% CD, 28.1% UC) and/or moderate (22.1% CD, 22.7% UC) or severe disability (12.9% CD, 10.4% UC).¹⁰

Overall, these findings confirm that UC can have a high impact on patients' life and may be as disabling as CD. Table 1 gives an overview of the main studies showing similar patient-reported outcomes in patients with CD and UC.

Both diseases can lead to burdensome complications

It is well known that chronic inflammation in CD has an inexorable tendency to progress to bowel damage.¹¹ A cohort study showed that about one-fifth of patients had already experienced penetrating or stricturing complications within the first 90 days of diagnosis, increasing to half of patients 20 years after diagnosis.¹² The Lémann index has been developed to quantify cumulative bowel damage,¹ and it has been shown that early treatment with immunomodulators or anti-tumor necrosis factor (anti-TNF) within the first 2 years of CD diagnosis is associated with reduced bowel damage.¹³

Whether UC has the same progressive nature as CD and whether earlier and intensive therapy could prevent this natural history remains unknown. Proximal disease extension is common in UC, affecting between 27% and 54% of patients with proctitis or left colitis during the course of their disease.^{14,15} As UC is not solely a mucosal disease, with significant fibrosis and muscularis mucosae thickening,¹⁶ structural changes are also frequent. Among them, strictures are reported in 1.5% to 11.2% of UC patients.¹⁷⁻¹⁹ Although most colonic strictures are asymptomatic, the main problem is the risk of dysplasia or cancer. In a recent nationwide study assessing 293 patients with IBD (248 CD, 39 UC, 6 IBD unclassified) undergoing surgery for colonic strictures, 3.5% were found to have either dysplasia or cancer (2.4% CD, 10.0% UC).²⁰ Apart from strictures, pseudopolyps or post-inflammatory polyps have been described in approximately 12.5% UC patients.²¹ These pseudopolyps, especially when giant, can cause bleeding and anemia,²² colonic obstruction by bulk occlusion or intussusception,²³ or protein losing enteropathy,²⁴ but are not associated with development of any degree of

colorectal neoplasia.²⁵ However, pseudopolyps make colorectal cancer surveillance extremely challenging with lower thresholds to consider surgery just for lack of ability to adequately detect colorectal cancer. Indeed, the increased risk for colorectal cancer among IBD patients with colitis is well established. A recent meta-analysis of population based-cohorts demonstrated that UC increases the risk of colorectal cancer 2.4-fold.²⁶ Regarding CD, there is also accumulating evidence for an increased risk of both colorectal and small bowel cancer.²⁷

Functional abnormalities are common in both CD and UC. Increased colonic permeability, either measured in vitro or in vivo, has been shown to be associated with bowel symptoms in patients with quiescent IBD.^{28,29} Decreased contractility is more frequent in UC patients, with a reduction in the pressure or amplitude of segmental contractions.³⁰ Significant changes in rectal motility and compliance have been demonstrated in patients with active UC, as compared to quiescent UC and controls.³¹ This dysmotility takes part in the establishment of the so-called and historical “lead-pipe colon”, with decreased length and caliber, decreased ability to distend, absent haustra, without being necessarily related to disease activity.³² Long-standing UC can also result in anatomical changes such as rectal narrowing and widening of the pre-sacral space.³³ Both anatomical and functional alterations can be responsible for impaired anorectal function, leading to urgency, tenesmus, and fecal incontinence.³⁴ However, the causes of anorectal functional disorders during UC are not fully understood yet.

Regarding extra-intestinal complications, both diseases can be associated with bone complications, rheumatologic, hepatic, ophtalmic and cutaneous manifestations. Both UC and CD are also associated with risk of venous thromboembolism.^{35,36} Extra-intestinal manifestations in IBD are reported with frequencies ranging from 5–50%.³⁷

Taken together, these studies show that similar to CD, UC can be associated with bowel damage and impaired gastrointestinal functioning (Figure 2), even though CD complications

occur probably more frequently and at an early stage than long-term UC complications. However, at this time, by contrast to CD, there is no evidence that an early disease control will allow preventing such complications in patients with UC.

Surgery cures neither disease

In CD, it is well known that surgery is not curative, endoscopic post-operative recurrence occurs in more than half of patients at one year.³⁸ Thus, it is standard practice to favor “bowel-sparing” surgical approaches, and resection of the affected part only is preferable rather than proctocolectomy.³⁹

As regards UC, a recent meta-analysis of population-based studies observed a cumulative risk of surgery in adults of 4.4%, 10.1%, and 14.6%, respectively, 1, 5, and 10 years after UC diagnosis, with a significant decrease over time.⁴⁰ Nowadays, colectomy is still required in approximately 10% of patients within 5 years of diagnosis.⁴¹ The indications for colectomy appear to have changed over time. In a population-based cohort, among colectomies performed before 1990, 90% were performed for medically refractory disease, 5% for fulminant colitis, and 5% for colorectal neoplasia. By contrast, among surgeries performed after 1990, 56% were performed for medically refractory disease, 26% for fulminant colitis, and 12% for colorectal neoplasia.⁴²

Although surgery theoretically cures UC by removing the entire colon and rectum, the patient may still be left with significant new problems. A recent systematic review based on studies reporting outcomes from colectomies conducted between 2002 and 2015 (20,801 patients) demonstrated that post-operative complications occur in more than one-third of patients.⁴³ Early complications (≤ 30 days) occurred in 9–65% of patients and included infectious complications (20%), ileus (18%), pouch-related complications (8%), small bowel obstruction (8%), fistula (4%), pelvic abscess (3%), anastomotic leakage (2%), and mortality (1%). Late

complications (>30 days) occurred in 17–55% of patients and included pouchitis (29%), fecal incontinence (21%), small bowel obstruction (17%), ileus (11%), fistula (6%), pouch failure (5%), and mortality (0.2%).⁴³

A recent meta-analysis of population-based studies included 67,057 patients with UC and 75,971 patients with CD and showed that post-operative mortality was higher after emergent (5.3% in UC, 3.6% in CD), but not elective (0.7% in UC, 0.6% in CD), intestinal resection in patients with IBD. Post-operative mortality did not differ for elective or emergent surgery when comparing UC and CD patients.⁴⁴

Thus, even though surgery is an adequate and effective approach in patients with chronic active UC refractory to medical treatment, and even a potentially lifesaving procedure in acute severe colitis, post-operative consequences must not be underestimated (Figure 3).

Similar monitoring

Until recently, therapeutic strategies targeted control of IBD-related symptoms and were based on a step-wise approach according to clinical response. Such strategies did not appear to significantly change the natural course of any type of IBD.^{45,46} This may be related to the poor correlation that exists between symptoms and endoscopic disease activity. The “treat-to-target” paradigm has been developed in this context, first for CD patients, based on regular assessment of disease activity and subsequent therapeutic adjustment.⁴⁷ Discrepancies between patient-reported outcomes and endoscopic appearance also exist in UC, as complete normalization of stool frequency is rarely encountered in patients with mucosal healing, even though absence of rectal bleeding is more accurate.⁴⁸ Although several clinical and biological markers have been reported to predict the risk of colectomy in patients with acute severe UC,^{49,50} a recent study involving patients with moderate-to-severe UC who were treated with golimumab has found no factors predicting endoscopic remission at 14 weeks.⁵¹ Yet, several

studies demonstrated that early mucosal healing during induction therapy was associated with favorable long-term outcomes.^{51,52} Thus, the “treat-to-target” strategy has been extrapolated to UC patients (Figure 4). In 2015, the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) consensus recommended to assess clinical remission at 3 months and endoscopic remission at 6- to 9-month intervals during the active phase of CD, and at 3-month intervals in UC.⁵³ However, a recent real-world study showed that the uptake of STRIDE recommendations is limited in clinical practice, as illustrated by the fact that physicians used CRP more frequently than endoscopy as a marker for disease activity.⁵⁴ This is a challenge to the implementation of the STRIDE guidelines, especially as there has been no assessment of the efficacy of this consensus since 2015. For both CD and UC, trials comparing symptom-driven with endoscopy-driven decisions are eagerly awaited to investigate whether these recommendations have the potential to change disease course.

Apart from endoscopy, the STRIDE consensus also suggested to use C-reactive protein (CRP) and fecal calprotectin (FC) as adjunctive measures to monitor residual intestinal inflammation. In CD, there is now accumulating evidence supporting the efficacy of the use of objective biomarkers in making therapeutic decisions. In 2017, the CALM study showed that a treatment algorithm based on FC and CRP concentrations and clinical symptoms led to faster treatment optimization and a higher rate of mucosal healing than symptom-driven decisions alone.⁵⁵ Regarding UC, a study demonstrated that FC levels at 3 months after initiating treatment could predict recurrence within 3 years in patients with new onset of UC.⁵⁶ Two recent randomized controlled trials showed that dose-escalation of 5-ASA was associated with decreased FC levels,⁵⁷ and when guided by FC >300 µg/g, active dose-escalation decreased risk of relapse.⁵⁸ However, there is no CALM-like study in patients with moderate-to-severe UC. Based on an expert opinion, FC is a valuable tool to optimize the care for IBD patients, although major therapeutic changes should not be based on FC alone as long

as dedicated trials comparing symptom-driven decisions alone to a treatment algorithm based on FC/CRP concentrations and clinical symptoms are pending.⁵⁹ Moreover, adherence to fecal tests remains low, mostly due to forgetfulness, thus there is a need for better patient education.⁶⁰

Finally, it should be noted that therapeutic drug monitoring is increasingly used to guide treatment adjustment in IBD patients treated with biologics, and the type of IBD does not influence the suggested target trough concentrations.

Similar treatment goals

In the last decade, treatment goals in both CD and UC have moved from exclusively controlling symptoms to “deep remission”, encompassing both clinical remission and mucosal healing, with the final aim of preventing disease progression and disability. The STRIDE evidence-based consensus aimed to define appropriately the concept of “deep remission”⁵³ (Figure 4).

In CD patients, endoscopic remission is defined as resolution of ulceration at ileocolonoscopy (or of inflammation findings on cross-sectional imaging). A French study demonstrated that the use of a strict definition of mucosal healing (Crohn’s disease endoscopic index score CDEIS = 0) was associated with a lower risk of clinical relapse and intestinal resection.⁶¹ However, a CDEIS score of zero may be hard to achieve, as shown in the CALM trial where the percentage of patients achieving this score was lower (18%) than those who achieved a CDEIS <4 with absence of deep ulcers (46%).⁵⁵ Finally, it seems that during the induction phase of treatment, endoscopic response defined as >50% decrease in CDEIS or Simple endoscopic score for Crohn’s disease (SES-CD) should be the treatment goal, while the goal of endoscopic remission defined as a SES-CD score of 0-2 may be more important during the maintenance phase.⁶²

In UC, endoscopic remission is defined as resolution of friability and ulceration at flexible sigmoidoscopy or colonoscopy. The STRIDE consensus stated that a Mayo subscore of 0–1 should be the minimum treatment goal to reach. Since 2015, several studies demonstrated that a Mayo subscore of 0 is associated with lower risk of relapse⁶³ and colectomy,⁶⁴ as compared to a Mayo subscore of 1, even though further randomized controlled trials are required before the implementation of this strict definition of endoscopic remission in clinical practice. Indeed, the nature of the disease in UC may lend itself more readily to a ‘treat-to-target’ strategy given the superior correlation of symptoms with objective disease activity compared to CD, relative ease of assessment of endoscopic healing through sigmoidoscopy rather than need for an ileocolonoscopy, more uniform distribution of histologic activity, and better correlation of biochemical markers.

Similar therapeutic management... except for biologic use

Both UC and CD share the same therapeutic armamentarium, except for 5-ASA. Biologics are used in moderate-to-severe UC, defined as patients with >4–6 bowel movements per day, moderate-to-severe rectal bleeding, constitutional symptoms, and high overall inflammatory burden. However, several criteria, even in patients who present initially with mild-to-moderate disease activity, may predict an aggressive disease course, including age <40 years at diagnosis, extensive disease, severe endoscopic activity, extra-intestinal manifestations, and elevated inflammatory markers.⁶⁵ Majority of patients have a mild-to-moderate activity at diagnosis, but 10-15% of patients experience an aggressive course with a cumulative risk of relapse of 70-80% at 10 years.³⁶ However, as regards the use of biologics, a cross-sectional study analyzing US health care utilization in 964,633 IBD patients between 2010 and 2012 demonstrated that UC patients were much less frequently treated with biologics than CD patients (3.5% vs. 16.8%, respectively).⁶⁶ Another study led in the US including more than

400,000 IBD patients showed that the proportion of patients using biologics increased for both diseases during a 9-year period (2007-2015), but to a much higher extent in patients with CD (from 21.8% to 43.8%) than in patients with UC (from 5.1% to 16.2%),⁶⁷ although lower use does not necessarily indicate "under-use". It should also be noted that the use of anti-TNFs for CD was established earlier than for UC and this might represent a lag time in changes in physician practice.

Although biological prescriptions significantly increased in the last ten years, there was no significant decrease in corticosteroid or narcotic prescriptions.⁶⁸ In the aforementioned cross-sectional study, systemic corticosteroids were used to a similar extent in patients with CD (47.0%) and UC (44.4%), including for a long-term period (8.3% and 8.4% of CD and UC patients, respectively).⁶⁶ In a retrospective study including 117 IBD patients, outpatient narcotic use was not statistically different between CD and UC patients (36.9% vs. 21.2%, respectively, $p=0.10$), even though this may be due to false negatives as CD patients were more likely to be treated with narcotics during hospitalization.⁶⁹

As regards hospitalization rates after the introduction of anti-TNF therapy, the risk for IBD-related hospitalization decreased only in CD (65.6/100 vs. 41.2/100 patient-years, $p<0.001$) but not UC (48.8/100 vs. 54.3/100 patient-years).⁷⁰ A recent study investigated the trends in IBD-related emergency department visits and hospitalization rates, showing that the proportion of emergency department visits decreased from 2007 to 2014, but there was no significant change in hospitalization rates. The hospitalization rate following emergency visits was 47.2% in CD patients and 55.6% in UC patients ($p=0.100$).⁷¹

Similar economic burden

A recent retrospective analysis of commercial US insurance claims between 2006 and 2010 demonstrated broadly similar costs related to suboptimal therapy in both diseases, even

though the disparity in CD patients was greater than in UC patients (\$18,736 vs. \$10,878 in CD patients with vs. without suboptimal therapy, $p < 0.001$; \$12,679 vs. \$9,653 in UC patients with vs. without suboptimal therapy, $p < 0.001$).⁷²

A systematic review showed that surgical complications also represent a substantial economic burden in UC patients, as additional mean costs of postoperative complications ranged from \$18,650 per patient with complications at a 6-month follow-up to \$34,714 over a 5-year period. Pouchitis, pouch failure and small bowel obstruction carried the greatest economic burden.⁷³

Taken together, these findings reinforce the idea that UC-related burden should not be underestimated as compared to CD.

Future Directions

One of the classical differences that differentiates UC from CD relies on the superficial nature of lesions which are limited to the colon. Disease-related burden is often underestimated and colectomy is usually considered as a cure for UC. This is reflected by the low exposure to biologics of UC patients as compared to CD patients. Yet, other medications are often not sufficient to control the disease. Unmet medical needs remain and there is still plenty of room for improvement in the therapeutic management of UC patients.

By reviewing available evidence and direct or indirect comparison between CD and UC, we could highlight the similarities between both diseases, in terms of impact on patients' life, disease complications, especially post-operative complications, and economic burden, although the irreversible damage that occurs in CD is less certain in UC. Monitoring rules and treatment goals are similar whatever the type of IBD (Figure 1).

It is time to be more ambitious regarding the therapeutic targets to reach in IBD patients. Likewise the growing concept of transmural healing in CD, histological healing may be the ultimate therapeutic goal in UC.⁷⁴ Patients with histological remission or healing are more likely to be symptom-free than patients with inflammation,⁷⁵ have reduced risks of relapse,⁷⁶ hospitalization,⁷⁷ and colorectal cancer.⁷⁸ A recent study demonstrated that the cumulative burden of endoscopic and microscopic inflammation is strongly associated with the risk of developing colorectal cancer in patients with UC.⁷⁹ Early intervention with the aim of achieving mucosal healing might reduce the incidence of UC-related colorectal cancer. Intervention studies addressing these issues are eagerly awaited.

In conclusion, disease-modifying drugs should not be used anymore as a rescue therapy in UC but rather included in a rapid step-up strategy based on a tight monitoring of objective signs of inflammation similar to CD. This will be the only way to change disease course and patients' life, even though large disease-modification trials supporting these recommendations

are not yet available. In contrast to CD, there is no evidence at the moment that early intervention is associated with reduced disease-related burden in UC. Another unanswered question is how to quantify irreversible bowel damage in UC. There is a need for a quantitative tool to assess bowel damage in UC similar to the Lémann index in CD.

Table 1. Key studies showing similar patient-reported outcomes in patients with Crohn's disease and ulcerative colitis.

Patient-reported outcomes	Main studies (related questionnaire)	Country	Ulcerative colitis	Crohn's disease
Disease-specific quality of life	Iglesias-Rey <i>et al.</i> , ⁸⁰ 2013 (IBDQ), mean [95% CI]	Spain	198 [195–202]	192 [188–196]
	Huppertz-Hauss <i>et al.</i> , ⁸¹ 2016 (IBDQ), mean [SD]	Norway	183 [26]	178 [26]
	Williet <i>et al.</i> , ¹⁰ 2017 (SIBDQ), median [IQR]	France	44 [40–48]	44 [39–47]
Anxiety/Depression				
• Depression	Nordin <i>et al.</i> , ⁸² 2002 (HADS), mean [SD]	Sweden	3.3 [3.2]	4.2 [3.4]
	Iglesias-Rey <i>et al.</i> , ⁸⁰ 2013 (IBDQ), mean [95% CI]	Spain	7.4 [7.0–7.9]	7.3 [6.8–7.7]
	Mikocka-Walus <i>et al.</i> , ⁸³ 2016 (HADS-D>7), %	Switzerland	18.5	21.5
	Williet <i>et al.</i> , ¹⁰ 2017 (HADS), median [IQR]	France	7 [5–10]	7 [5–11]
• Anxiety	Nordin <i>et al.</i> , ⁸² 2002 (HADS), mean [SD]	Sweden	5.2 [4.3]	6.3 [4.4]
	Iglesias-Rey <i>et al.</i> , ⁸⁰ 2013 (IBDQ), mean [95% CI]	Spain	4.9 [4.5–5.3]	4.8 [4.4–5.3]
	Mikocka-Walus <i>et al.</i> , ⁸³ 2016 (HADS-A>7), %	Switzerland	34.9	39.5
	Williet <i>et al.</i> , ¹⁰ 2017 (HADS), median [IQR]	France	5 [3–8]	5 [3–8]
Fatigue	Tinsley <i>et al.</i> , ⁸⁴ 2011 (FACIT-F), mean [SD]	USA	39.4 [10.6]	38.6 [11.3]
	Williet <i>et al.</i> , ¹⁰ 2017 (FACIT-F), median [IQR]	France	31 [23–40]	30 [21–39]
Work disability				
• Disability rate	Høivik <i>et al.</i> , ⁸ 2013, %	Norway	18.5	19.4
	Williet <i>et al.</i> , ¹⁰ 2017 (WPAI:1), median [IQR]	France	0.0 [0.0–0.0]	0.0 [0.0–0.0]
• Absenteeism	Gonczi <i>et al.</i> , ⁸⁵ 2019 (WPAI :1), mean % of total work time	Canada	9.5	6.1
	Williet <i>et al.</i> , ¹⁰ 2017 (WPAI:2), median [IQR]	France	10.0 [0.0–30.0]	20.0 [0.0–40.0]
• Presenteeism	Gonczi <i>et al.</i> , ⁸⁵ 2019 (WPAI :2), mean % of total work time	Canada	15.8	15.9
	Williet <i>et al.</i> , ¹⁰ 2017 (WPAI:3), median [IQR]	France	17.5 [0.0–34.7]	20.0 [0.0–40.0]
• Work productivity loss	Gonczi <i>et al.</i> , ⁸⁵ 2019 (WPAI :3), mean % of total work time	Canada	25.3	22.0

• Activity impairment	Williet <i>et al.</i> , ¹⁰ 2017 (WPAI:4), median [IQR]	France	30.0 [0.0–50.0]	30.0 [10.0–60.0]
Disability	Gower-Rousseau <i>et al.</i> , ⁸⁶ 2017 (IBD-DI), mean [SD]	France	39.2 [23.1]	33.9 [19.5]
	Williet <i>et al.</i> , ¹⁰ 2017 (IBD-DI), median [IQR]	France	26.8 [14.3–38.5]	26.9 [16.1–41.1]

Abbreviations: CI, Confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HADS, Hospital Anxiety and Depression Score (-A: Anxiety; -D: Depression); IBD-DI, Inflammatory Bowel Disease Disability Index; IBDQ, Inflammatory Bowel Disease Questionnaire; IQR, Interquartile range; SD, Standard deviation; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; USA, United States of America; WPAI, Work Productivity and Activity Impairment.

Figure legends

Figure 1. Schematic representation of the comparison between Crohn's disease and ulcerative colitis.

Figure 2. Potential complications occurring in the natural course of Crohn's disease and ulcerative colitis.

Abbreviations: CD, Crohn's disease; UC, Ulcerative colitis.

Figure 3. Key features of main post-operative long-term complications in Crohn's disease and ulcerative colitis.

Abbreviations: SB, Small bowel.

Figure 4. Schematic representation of treat-to-target strategy for Crohn’s disease and ulcerative colitis. Adapted from “Treat to Target: A Proposed New Paradigm for the Management of Crohn’s Disease”, *Clinical Gastroenterology and Hepatology*, 2015.

According to risk stratification, disease-modifying therapy should be administered to high-risk patients. Treatments should then be monitored and adjusted by using a predefined objective target which is “deep remission” in both CD and UC, encompassing clinical remission and mucosal healing.

*: Or resolution of inflammation (MRI) when endoscopy cannot adequately evaluate inflammation; §: Transmural healing may be the ultimate therapeutic goal in CD; ¥: Histological healing may be the ultimate therapeutic goal in UC; ¤: Treatment adjustment according to therapeutic drug monitoring: optimize ongoing drug, or switch intra/other class, or add drugs; £: Available biomarkers are not targets but adjunctive measures to monitor residual inflammation. At this time, major therapeutic changes should not be based on biomarkers alone, and dedicated trials comparing symptom-driven decisions alone to a treatment algorithm based on FC/CRP and clinical symptoms are awaited.

Abbreviations: CD, Crohn’s disease; CRP, C-reactive protein; FC, Fecal calprotectin; MRI, Magnetic resonance imaging; UC, Ulcerative colitis.

References

1. Pariente B, Mary J-Y, Danese S, et al. Development of the Lémann index to assess digestive tract damage in patients with Crohn's disease. *Gastroenterology* 2015;148:52-63.e3.
2. Love JR, Irvine EJ, Fedorak RN. Quality of life in inflammatory bowel disease. *J Clin Gastroenterol* 1992;14:15-19.
3. Casellas F, López-Vivancos J, Vergara M, et al. Impact of inflammatory bowel disease on health-related quality of life. *Dig Dis* 1999;17:208-218.
4. Van Assche G, Peyrin-Biroulet L, Sturm A, et al. Burden of disease and patient-reported outcomes in patients with moderate to severe ulcerative colitis in the last 12 months - Multicenter European cohort study. *Dig Liver Dis* 2016;48:592-600.
5. Mikocka-Walus A, Pittet V, Rossel J-B, et al. Symptoms of Depression and Anxiety Are Independently Associated With Clinical Recurrence of Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol* 2016;14:829-835.e1.
6. Tinsley A, Macklin EA, Korzenik JR, et al. Validation of the functional assessment of chronic illness therapy-fatigue (FACIT-F) in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2011;34:1328-1336.
7. Siebert U, Wurm J, Gothe RM, et al. Predictors of temporary and permanent work disability in patients with inflammatory bowel disease: results of the swiss inflammatory bowel disease cohort study. *Inflamm Bowel Dis* 2013;19:847-855.
8. Høivik ML, Moum B, Solberg IC, et al. Work disability in inflammatory bowel disease patients 10 years after disease onset: results from the IBSEN Study. *Gut* 2013;62:368-375.
9. Gower-Rousseau C, Sarter H, Savoye G, et al. Validation of the Inflammatory Bowel Disease Disability Index in a population-based cohort. *Gut* 2017;66:588-596.
10. Williet N, Sarter H, Gower-Rousseau C, et al. Patient-reported Outcomes in a French

Nationwide Survey of Inflammatory Bowel Disease Patients. *J Crohns Colitis* 2017;11:165-174.

11. Fiorino G, Bonifacio C, Peyrin-Biroulet L, et al. Preventing Collateral Damage in Crohn's Disease: The Lémann Index. *J Crohns Colitis* 2016;10:495-500.

12. Thia KT, Sandborn WJ, Harmsen WS, et al. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. *Gastroenterology* 2010;139:1147-1155.

13. Fiorino G, Bonifacio C, Allocca M, et al. Bowel Damage as Assessed by the Lémann Index is Reversible on Anti-TNF Therapy for Crohn's Disease. *J Crohns Colitis* 2015;9:633-639.

14. Meucci G, Vecchi M, Astegiano M, et al. The natural history of ulcerative proctitis: a multicenter, retrospective study. Gruppo di Studio per le Malattie Infiammatorie Intestinali (GSMII). *Am J Gastroenterol* 2000;95:469-473.

15. Solberg IC, Lygren I, Jahnsen J, et al. Clinical course during the first 10 years of ulcerative colitis: results from a population-based inception cohort (IBSEN Study). *Scand J Gastroenterol* 2009;44:431-440.

16. Gordon IO, Agrawal N, Willis E, et al. Fibrosis in ulcerative colitis is directly linked to severity and chronicity of mucosal inflammation. *Aliment Pharmacol Ther* 2018;47:922-939.

17. De Dombal FT, Watts JM, Watkinson G, et al. Local complications of ulcerative colitis: stricture, pseudopolyposis, and carcinoma of colon and rectum. *Br Med J* 1966;1:1442-1447.

18. Gumaste V, Sachar DB, Greenstein AJ. Benign and malignant colorectal strictures in ulcerative colitis. *Gut* 1992;33:938-941.

19. Yamagata M, Mikami T, Tsuruta T, et al. Submucosal fibrosis and basic-fibroblast

growth factor-positive neutrophils correlate with colonic stenosis in cases of ulcerative colitis. *Digestion* 2011;84:12-21.

20. Fumery M, Pineton de Chambrun G, Stefanescu C, et al. Detection of Dysplasia or Cancer in 3.5% of Patients With Inflammatory Bowel Disease and Colonic Strictures. *Clin Gastroenterol Hepatol* 2015;13:1770-1775.

21. Goldgraber MB. Pseudopolyps in ulcerative colitis. *Dis Colon Rectum* 1965;8:355-363.

22. Maggs JRL, Browning LC, Warren BF, et al. Obstructing giant post-inflammatory polyposis in ulcerative colitis: Case report and review of the literature. *J Crohns Colitis* 2008;2:170-180.

23. Maldonado TS, Firoozi B, Stone D, et al. Colocolonic intussusception of a giant pseudopolyp in a patient with ulcerative colitis: a case report and review of the literature. *Inflamm Bowel Dis* 2004;10:41-44.

24. Koga H, Iida M, Aoyagi K, et al. Generalized giant inflammatory polyposis in a patient with ulcerative colitis presenting with protein-losing enteropathy. *Am J Gastroenterol* 1995;90:829-831.

25. Mahmoud R, Shah SC, Ten Hove JR, et al. No Association Between Pseudopolyps and Colorectal Neoplasia in Patients With Inflammatory Bowel Diseases. *Gastroenterology* December 2018.

26. Jess T, Rungoe C, Peyrin-Biroulet L. Risk of colorectal cancer in patients with ulcerative colitis: a meta-analysis of population-based cohort studies. *Clin Gastroenterol Hepatol* 2012;10:639-645.

27. Jess T, Gamborg M, Matzen P, et al. Increased risk of intestinal cancer in Crohn's disease: a meta-analysis of population-based cohort studies. *Am J Gastroenterol* 2005;100:2724-2729.

28. Vivinus-Nébot M, Frin-Mathy G, Bziouche H, et al. Functional bowel symptoms in quiescent inflammatory bowel diseases: role of epithelial barrier disruption and low-grade inflammation. *Gut* 2014;63:744-752.
29. Chang J, Leong RW, Wasinger VC, et al. Impaired Intestinal Permeability Contributes to Ongoing Bowel Symptoms in Patients With Inflammatory Bowel Disease and Mucosal Healing. *Gastroenterology* 2017;153:723-731.e1.
30. Loening-Baucke V, Metcalf AM, Shirazi S. Rectosigmoid motility in patients with quiescent and active ulcerative colitis. *Am J Gastroenterol* 1989;84:34-39.
31. Rao SS, Read NW, Davison PA, et al. Anorectal sensitivity and responses to rectal distention in patients with ulcerative colitis. *Gastroenterology* 1987;93:1270-1275.
32. De Dombal FT, Geffen N, Darnborough A, et al. Radiological appearances of ulcerative colitis: an evaluation of their clinical significance. *Gut* 1968;9:157-163.
33. Alp MH, Sage MR, Grant AK. The significance of widening of the presacral space at contrast radiography in inflammatory bowel disease. *Aust N Z J Surg* 1978;48:175-177.
34. Torres J, Billioud V, Sachar DB, et al. Ulcerative colitis as a progressive disease: the forgotten evidence. *Inflamm Bowel Dis* 2012;18:1356-1363.
35. Peyrin-Biroulet L, Loftus EV, Colombel J-F, et al. Long-term complications, extraintestinal manifestations, and mortality in adult Crohn's disease in population-based cohorts. *Inflamm Bowel Dis* 2011;17:471-478.
36. Fumery M, Singh S, Dulai PS, et al. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. *Clinical Gastroenterology and Hepatology* 2018;16:343-356.e3.
37. Vavricka SR, Schoepfer A, Scharl M, et al. Extraintestinal Manifestations of Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2015;21:1982-1992.
38. Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course

of Crohn's disease. *Gastroenterology* 1990;99:956-963.

39. Gionchetti P, Dignass A, Danese S, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 2: Surgical Management and Special Situations. *J Crohns Colitis* 2017;11:135-149.

40. Frolkis AD, Dykeman J, Negrón ME, et al. Risk of surgery for inflammatory bowel diseases has decreased over time: a systematic review and meta-analysis of population-based studies. *Gastroenterology* 2013;145:996-1006.

41. Williet N, Pillot C, Oussalah A, et al. Incidence of and impact of medications on colectomy in newly diagnosed ulcerative colitis in the era of biologics. *Inflamm Bowel Dis* 2012;18:1641-1646.

42. Samuel S, Ingle SB, Dhillon S, et al. Cumulative Incidence and Risk Factors for Hospitalization and Surgery in a Population-based Cohort of Ulcerative Colitis. *Inflammatory Bowel Diseases* May 2013:1-.

43. Peyrin-Biroulet L, Germain A, Patel AS, et al. Systematic review: outcomes and post-operative complications following colectomy for ulcerative colitis. *Aliment Pharmacol Ther* 2016;44:807-816.

44. Singh S, Al-Darmaki A, Frolkis AD, et al. Postoperative Mortality Among Patients With Inflammatory Bowel Diseases: A Systematic Review and Meta-analysis of Population-Based Studies. *Gastroenterology* 2015;149:928-937.

45. Magro F, Rodrigues A, Vieira AI, et al. Review of the disease course among adult ulcerative colitis population-based longitudinal cohorts. *Inflamm Bowel Dis* 2012;18:573-583.

46. Peyrin-Biroulet L, Loftus EV, Colombel J-F, et al. The natural history of adult Crohn's disease in population-based cohorts. *Am J Gastroenterol* 2010;105:289-297.

47. Bouguen G, Levesque BG, Feagan BG, et al. Treat to Target: A Proposed New

Paradigm for the Management of Crohn's Disease. *Clinical Gastroenterology and Hepatology* 2015;13:1042-1050.e2.

48. Colombel J-F, Keir ME, Scherl A, et al. Discrepancies between patient-reported outcomes, and endoscopic and histological appearance in UC. *Gut* 2017;66:2063-2068.

49. Ho GT, Lee HM, Brydon G, et al. Fecal calprotectin predicts the clinical course of acute severe ulcerative colitis. *Am J Gastroenterol* 2009;104:673-678.

50. Choy MC, Seah D, Gorelik A, et al. Predicting response after infliximab salvage in acute severe ulcerative colitis. *J Gastroenterol Hepatol* 2018;33:1347-1352.

51. Bossuyt P, Baert F, D'Heygere F, et al. Early Mucosal Healing Predicts Favorable Outcomes in Patients With Moderate to Severe Ulcerative Colitis Treated With Golimumab: Data From the Real-life BE-SMART Cohort. *Inflammatory Bowel Diseases* 2019;25:156-162.

52. Colombel JF, Rutgeerts P, Reinisch W, et al. Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis. *Gastroenterology* 2011;141:1194-1201.

53. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): Determining Therapeutic Goals for Treat-to-Target. *Am J Gastroenterol* 2015;110:1324-1338.

54. Bryant RV, Costello SP, Schoeman S, et al. Limited uptake of ulcerative colitis "treat-to-target" recommendations in real-world practice. *J Gastroenterol Hepatol* 2018;33:599-607.

55. Colombel J-F, Panaccione R, Bossuyt P, et al. Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. *Lancet* 2018;390:2779-2789.

56. Lasso A, Simrén M, Stotzer P-O, et al. Fecal Calprotectin Levels Predict the Clinical Course in Patients With New Onset of Ulcerative Colitis: *Inflammatory Bowel Diseases*

2013;19:576-581.

57. Osterman MT, Aberra FN, Cross R, et al. Mesalamine dose escalation reduces fecal calprotectin in patients with quiescent ulcerative colitis. *Clin Gastroenterol Hepatol* 2014;12:1887-1893.e3.

58. Lassin A, Öhman L, Stotzer P-O, et al. Pharmacological intervention based on fecal calprotectin levels in patients with ulcerative colitis at high risk of a relapse: A prospective, randomized, controlled study. *United European Gastroenterol J* 2015;3:72-79.

59. Reenaers C, Bossuyt P, Hindryckx P, et al. Expert opinion for use of faecal calprotectin in diagnosis and monitoring of inflammatory bowel disease in daily clinical practice. *United European Gastroenterology Journal* 2018;6:1117.

60. Maréchal C, Aimone-Gastin I, Baumann C, et al. Compliance with the faecal calprotectin test in patients with inflammatory bowel disease. *United European Gastroenterol J* 2017;5:702-707.

61. Yzet C, Loreau J, Lemouel J-P, et al. What is the Best definition of Mucosal Healing in Crohn Disease? *Gastroenterology* 2017;152:S210.

62. Vuitton L, Marteau P, Sandborn WJ, et al. IOIBD technical review on endoscopic indices for Crohn's disease clinical trials. *Gut* 2016;65:1447-1455.

63. Barreiro-de Acosta M, Vallejo N, de la Iglesia D, et al. Evaluation of the Risk of Relapse in Ulcerative Colitis According to the Degree of Mucosal Healing (Mayo 0 vs 1): A Longitudinal Cohort Study. *J Crohns Colitis* 2016;10:13-19.

64. Manginot C, Baumann C, Peyrin-Biroulet L. An endoscopic Mayo score of 0 is associated with a lower risk of colectomy than a score of 1 in ulcerative colitis. *Gut* 2015;64:1181-1182.

65. Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. *Gastroenterology* 2019;156:748-764.

66. van Deen WK, van Oijen MGH, Myers KD, et al. A nationwide 2010-2012 analysis of U.S. health care utilization in inflammatory bowel diseases. *Inflamm Bowel Dis* 2014;20:1747-1753.
67. Yu H, MacIsaac D, Wong JJ, et al. Market share and costs of biologic therapies for inflammatory bowel disease in the USA. *Alimentary Pharmacology & Therapeutics* 2018;47:364-370.
68. Narula N, Borges L, Steinhart AH, et al. Trends in Narcotic and Corticosteroid Prescriptions in Patients with Inflammatory Bowel Disease in the United States Ambulatory Care Setting from 2003 to 2011. *Inflamm Bowel Dis* 2017;23:868-874.
69. Long MD, Barnes EL, Herfarth HH, et al. Narcotic use for inflammatory bowel disease and risk factors during hospitalization. *Inflamm Bowel Dis* 2012;18:869-876.
70. Mandel MD, Balint A, Golovics PA, et al. Decreasing trends in hospitalizations during anti-TNF therapy are associated with time to anti-TNF therapy: Results from two referral centres. *Digestive and Liver Disease* 2014;46:985-990.
71. Huh G, Yoon H, Choi YJ, et al. Trends in emergency department visits and hospitalization rates for inflammatory bowel disease in the era of biologics. de Zoeten EF, ed. *PLOS ONE* 2019;14:e0210703.
72. Rubin DT, Mody R, Davis KL, et al. Real-world assessment of therapy changes, suboptimal treatment and associated costs in patients with ulcerative colitis or Crohn's disease. *Aliment Pharmacol Ther* 2014;39:1143-1155.
73. Lindsay JO, Bergman A, Patel AS, et al. Systematic review: the financial burden of surgical complications in patients with ulcerative colitis. *Aliment Pharmacol Ther* 2015;41:1066-1078.
74. Peyrin-Biroulet L, Bressenot A, Kampman W. Histologic remission: the ultimate therapeutic goal in ulcerative colitis? *Clin Gastroenterol Hepatol* 2014;12:929-934.e2.

75. Isaacs KL. How rapidly should remission be achieved? *Dig Dis* 2010;28:548-555.
76. Riley SA, Mani V, Goodman MJ, et al. Microscopic activity in ulcerative colitis: what does it mean? *Gut* 1991;32:174-178.
77. Travis SPL, Higgins PDR, Orchard T, et al. Review article: defining remission in ulcerative colitis. *Aliment Pharmacol Ther* 2011;34:113-124.
78. Gupta RB, Harpaz N, Itzkowitz S, et al. Histologic inflammation is a risk factor for progression to colorectal neoplasia in ulcerative colitis: a cohort study. *Gastroenterology* 2007;133:1099-1105; quiz 1340-1341.
79. Choi C-HR, Bakir IA, Ding N-S (John), et al. Cumulative burden of inflammation predicts colorectal neoplasia risk in ulcerative colitis: a large single-centre study. *Gut* 2019;68:414-422.
80. Iglesias-Rey M, Barreiro-de Acosta M, Caamaño-Isorna F, et al. Psychological Factors Are Associated with Changes in the Health-related Quality of Life in Inflammatory Bowel Disease: *Inflammatory Bowel Diseases* November 2013:1.
81. Huppertz-Hauss G, Lie Høivik M, Jelsness-Jørgensen L-P, et al. Health-related Quality of Life in Patients with Inflammatory Bowel Disease 20 Years After Diagnosis: Results from the IBSEN Study. *Inflammatory Bowel Diseases* 2016;22:1679-1687.
82. Nordin K, Pählman L, Larsson K, et al. Health-Related Quality of Life and Psychological Distress in a Population-based Sample of Swedish Patients with Inflammatory Bowel Disease. *Scandinavian Journal of Gastroenterology* 2002;37:450-457.
83. Mikocka-Walus A, Pittet V, Rossel J-B, et al. Symptoms of Depression and Anxiety Are Independently Associated With Clinical Recurrence of Inflammatory Bowel Disease. *Clinical Gastroenterology and Hepatology* 2016;14:829-835.e1.
84. Tinsley A, Macklin EA, Korzenik JR, et al. Validation of the functional assessment of chronic illness therapy-fatigue (FACIT-F) in patients with inflammatory bowel disease.

Aliment Pharmacol Ther 2011;34:1328-1336.

85. Gonczi L, Kurti Z, Verdon C, et al. Perceived Quality of Care is Associated with Disease Activity, Quality of Life, Work Productivity, and Gender, but not Disease Phenotype: A Prospective Study in a High-volume IBD Centre. *J Crohns Colitis*.
86. Gower-Rousseau C, Sarter H, Savoye G, et al. Validation of the Inflammatory Bowel Disease Disability Index in a population-based cohort. *Gut* 2017;66:588-596.



Similar impact on patient's life

Similar economic burden

Both diseases can lead to burdensome complications

Surgery cures neither disease

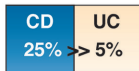
Similar monitoring

Similar treatment goals

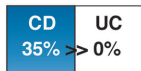
Similar therapeutic armamentarium

Bowel damage

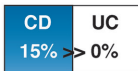
Stricture



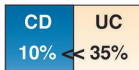
Fistula



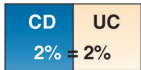
Abscess



Disease extension



Colorectal cancer



Rectal narrowing, widening of presacral space



Impaired gastrointestinal functioning

Increased colonic permeability



Decreased contractility



Mixed mechanism

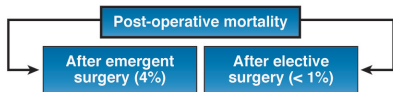
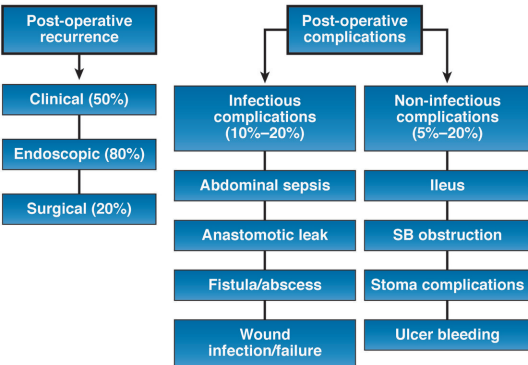
Anorectal dysfunction



Lead pipe colon



Crohn's disease



Ulcerative colitis

