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MINIREVIEWS

# Quality of care in inflammatory bowel diseases: What is the best way to better outcomes?

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## Abstract

Inflammatory bowel disease (IBD) is a lifelong, progressive disease that has disabling impacts on patient's lives. Given the complex nature of the diagnosis of IBD and its management there is consequently a large economic burden seen across all health care systems. Quality indicators (QI) have been created to assess the different façades of disease management including structure, process and outcome components. Their development serves to provide a means to target and measure quality of care (QoC). Multiple different QI sets have been published in IBD, but all serve the same purpose of trying to achieve a standard of care that can be attained on a national and international level, since there is still a major variation in clinical practice. There have been many recent innovative developments that aim to improve QoC in IBD including telemedicine, home biomarker assessment and rapid access clinics. These are some of the novel advancements that have been shown to have great potential at improving QoC, while offloading some of the burden that IBD can have vis-a-vis emergency room visits and hospital admissions. The aim of the current review is to summarize and discuss available QI sets and recent developments in IBD care including telemedicine, and to give insight into how the utilization of these tools could benefit the QoC of IBD patients. Additionally, a treating-to-target structure as well as evidence surrounding aggressive management directed at tighter disease control will be presented.

**Key words:** Inflammatory bowel disease; Telemedicine; Quality indicators; Quality of care; Treat-to-target



**Core tip:** The approach to diagnosis, follow up and management of inflammatory bowel disease (IBD) has undergone a major transformation in the past decade. Many different international quality indicators that span structure, process and outcome measures have been

developed. These serve as major targets in optimizing quality of care (QoC). New developments have been designed to improve QoC including utilizing telemedicine, home biomarker testing and providing rapid access care to patients. Treating to target with proactive disease management guided by clinical history utilizing adjunctive biomarkers at the onset of IBD has been shown to improve objective outcomes. This will likely serve as the new favored treatment approach in many IBD centers across the globe.

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## INTRODUCTION

Inflammatory bowel disease (IBD) which primarily encompass ulcerative colitis (UC) and Crohn's disease (CD) are chronic, progressive and disabling inflammatory diseases of the gastrointestinal (GI) tract, that in the uncontrolled setting often have disabling effects on an individual's health and overall quality of life[1-3]. The prevalence and incidence of IBD is higher in North America and Western Europe compared to other parts of the world with data suggesting these rates are increasing[4,5]. Owing to IBD's chronicity, varying degrees of severity and lifelong presence it contributes a large economic burden in all health care systems[1,6].

The treatment approach to managing IBD has evolved in the past decade undergoing a significant paradigm shift in philosophy. With the advent of early and routine use of biological therapies the manner in which IBD is diagnosed, managed and monitored has been in constant flux. The most recent advancements have been catalyzed by evidence suggesting that targeting symptom-based outcome parameters does not largely alter the natural course of IBD[7,8]. Inspired by evidence in other specialties, notably from the rheumatoid arthritis literature, the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) devised the STRIDE recommendations with the objective of providing a treat-to-target framework for IBD[9]. In parallel, ongoing evidence was amounting in the IBD literature regarding the association of endoscopic healing with improved clinical and long-term outcomes. This supports the notion of treating-to-target in IBD patients[10]. The STRIDE recommendations include targeting improvement in clinical and endoscopic outcomes and also incorporate patient reported outcome measures (PROM). These recommendations give rise to the potential of a greater impact on IBD compared to the former symptom derived scales including the Crohn's Disease Activity Index (CDAI) or the partial Mayo Score. Virtually all newly designed and recently published clinical trials in IBD have moved towards a similar structure focusing on complex outcomes encompassing clinical, endoscopic and PROM improvements[11].

A major challenge in the field of IBD lies in the large heterogeneity in clinical practice. This variation in everyday practice is seen in many domains of IBD management such as diagnostic testing, monitoring, therapeutic interventions and knowledge of preventative care recommendations[12-14]. As a result of the apparent differences in practice, a major interest was sparked in devising a standard set of measures to assess quality and provide a means to quantify quality of care (QoC). This occurred by developing quality indicators (QIs). QIs may be related to three components in health care: Structure, process and outcome parameters of care[15]. The goal is to utilize them to develop standards by which QoC can be assessed and measured[16].

In the following review, an overview of the various QIs that have been developed for IBD will be provided. Additionally, emerging evidence supporting the widespread application of high QoC will be discussed along with some data on actual QI adherence at different centers and institutions. This will highlight how QIs can influence the level of care in IBD. Novel advancements which may have the potential to positively influence QoC will also be reviewed. Finally, the concept of treating-to-target along with aggressive management directed at tighter disease control will be presented.

## QUALITY INDICATORS IN IBD

In general, QIs provide specific measurable elements of care for which there is evidence or consensus that can be applied to assess the QoC provided. This, thereore has the capacity to influence and improve QoC[17,18]. In 2011 the American Gastrointestinal Association (AGA) published their clinical performance metrics that is used by federal health insurance providers to incentivize or penalize gastroenterologists managing IBD patients depending on the QoC they provide[19]. Given the limited scope of the AGA measures the Crohn's and Colitis Foundation of America (CCFA) set out to develop, *via* a robust method, a set of top process and outcome rated QIs. The CCFA came out with its top-ten highly rated process and outcome related measures with the ultimate goal of having an impact on improving QoC in IBD[16].

Outside of the Unites States of America there have been multiple other published QI sets looking at various measures. In Spain a set of structure, process and outcome measures for quality of care was published using the Delphi consensus framework[20]. In Canada a similar set of QIs was published in 2014[21]. The Spanish and Canadian QI sets had the added layer of looking at structure metrics focusing on the importance of having a medical expert, a multidisciplinary team including a dedicated IBD nurse to assist in managing these complex cases. More recently in Canada, through the development of the Promoting Access and Care through Centers of Excellence (PACE) program a new set of structure, process and outcome QIs has been

developed[22]. The PACE program's focus is to standardize QoC provided by physicians both in community hospitals and academic centers in an attempt to reduce the existing variation in practice. Unique to the process of developing these QIs was the involvement of actual IBD patients and IBD nurses in the QI selection procedure.

The British Society of Gastroenterology initially published guidelines to serve as their foundation for QoC in 2012[23]. On a similar theme with comparable components a QI set was published in Asia[24]. All these QIs have been established to accomplish the same and improve QoC. The difficulty of these approaches lies in finding the balance between a wide array of data captured and the practicality of the QI set to be used in clinical practice (Table 1).

## VARIATION IN CLINICAL PRACTICE

Despite the development of multiple clinical practice guidelines in diagnosing and managing IBD from Europe[25-28] and North America[29,30] as well as the various of published quality measures in IBD highlighted above there is substantial heterogeneity in the practice of individual physicians. Feuerstein *et al*[31] retrospectively audited medical records from practices in academic, community and private centers in the United States to assess the adherence to quality measures published by the AGA. The authors discovered poor documentation of IBD quality measures by physicians regardless of practice settings. Specifically, a low proportion of physicians evaluated vaccination status with only 16.7% of patients evaluated for pneumococcal vaccine and 28.7% of patients evaluated for influenza vaccine. Additionally, only 25% of patients were assessed for bone loss. A survey of patients with CD and UC in the United States also demonstrated a large variation in practice between gastroenterologists (GI) in academic centers (GIA) *vs* private GI and other GIs[32]. In this survey CD patients seen by a GIA compared to private GIs had less use of 5-aminosalicylates and higher rates of biologic and immunomodulator uses ($P < 0.001$ for all). Furthermore, on multivariate analysis in GIA patients with CD there was less steroid use (OR = 0.84, 95%CI: 0.567-1.06), higher rates of influenza vaccination (OR = 1.33, 95%CI: 1.15-1.53) and higher rates of clinical remission (OR = 1.18, 95%CI: 1.02-1.37). Another study from Asia using a questionnaire devised from the AGA quality metrics showed a large variety in the deliverance of performance measures, again highlighting the heterogeneity in practice[24]. The European Crohn's and Colitis Organization conducted a web based survey study of patients from 27 different European Countries also showing significant impact on quality of life (QoL)[33]. 4990 patients responded to the survey of which 52% reported corticosteroid use within 12 mo, 71% experienced at least 2 flares in a 2-year period and 44% of felt their lives were negatively impacted at times in between flares. Many reported on the negative impact the disease had with respect to work notably 44% reported losing their jobs or having to quit. Surprisingly, adequate access to care was only reported by 70% of those who responded to the survey with 53% of responders feeling they were unable to convey important information after consultation with a specialist. Clearly there are large differences in the practice of IBD between and even within a given health care system. Consequently, quality metrics and guidelines need to be reiterated and reinforced along with potential auditing measures to ensure that health professionals are upheld to appropriate standards.

## EVIDENCE SURROUNDING QI APPLICATION

Intuitively one would stipulate that the more rigorously QIs are adhered to in IBD, the more one would expect to note an improvement in outcomes. Peña-Sánchez *et al*[34] conducted a retrospective population matched cohort study attempting to demonstrate a measureable outcome difference in patients exposed to a multidisciplinary IBD clinic (MIBDC) compared to controls who were not. The MIBDC accounted for some structural QIs such as having an IBD fellowship trained GI specialist, specialized IBD nurses, registered dieticians and a clinical psychologist. The goal set out by this unit was to ensure quality and continuity of care. Ultimately, what their study showed in the exposed UC group was lower rates of IBD related hospitalization (HR = 0.66, 95%CI: 0.49-0.89) and lower odds of corticosteroid dependence (OR = 0.39, 95%CI: 0.15-0.98). In the entire exposed group compared to the un-exposed matched cohort they demonstrated a lower risk of IBD-related surgeries (HR = 0.78, 95%CI: 0.61-0.99), lower rates of 5-ASA use (HR = 0.81, 95%CI: 0.69-0.95), higher rates of immunomodulatory use (HR = 1.68, 95%CI: 1.42-1.99) and higher rates of biologic use (HR = 1.85, 95%CI: 1.52-2.27). This study effectively showed that an integrated medical care model in IBD was associated with better QoC in IBD patients compared to standard practice.

Law *et al*[35] performed a cohort study focusing on the impact of having exclusively subspecialized IBD trained physicians manage IBD patients admitted to hospital on short and long term clinical outcomes. They compared a cohort whereby inpatients were managed under general gastroenterology care to ones managed under specialized IBD care. Looking at multiple in-hospital process and outcome QIs there were many similarities between the cohorts. The only statistically significant difference was that the specialized cohort ensured more objective disease assessment as evidenced by the higher rates of CRP testing at admission (82% *vs* 71%, $P = 0.05$) and discharge (25% *vs* 13%, $P = 0.05$). The cohort managed by specialized IBD care had increased frequency of high dose biologic therapy for induction (26% *vs* 9% $P = 0.04$, OR = 5.5, 95%CI: 1.3-23.17) and a higher proportion of patients in remission at 90 d (OR = 1.6, 95%CI: 0.99-2.69). Although there was no difference in rates of surgery at 90 d, early surgery (within 30 d) was more

**Table 1 Available quality indicators-set to assess the quality of care in inflammatory bowel disease**

| | AGA | CCFA | PACE[1] | Spanish[1] | Asia |
|---|---|---|---|---|---|
| Structural QIs | | | | | |
| IBD unit/clinic | | | | | |
| Has access to healthcare professionals: pharmacist, ophthalmologist, rheumatologist, obstetrician and dermatologist | | | √ | | |
| Has access to all of the following healthcare professionals: Dieticians, mental health worker/psychologist, stoma therapist | | | √ | | |
| Has a dedicated IBD nurse. | | | √ | √ | |
| Has at least one gastroenterologist with specialized IBD training | | | √ | | |
| Has timely access to an Endoscopy Unit | | | √ | √ | |
| Has access to CT and MRI with at least one modality with enterography | | | √ | √ | |
| Has access to a GI radiologist and a GI histopathologist | | | √ | √ | |
| Has access to a surgical program that performs at least 10 Ileoanal pouch operations a year | | | √ | | |
| Has access to a fellowship trained colorectal surgeon | | | √ | √ | |
| Should be integrated in a hospital with an Emergency Department | | | √ | √ | |
| Process QIs | | | | | |
| IBD type documented including disease location and severity | √ | √ | √ | | √ |
| Latent tuberculosis and Hepatitis B testing before anti-TNF therapy | √ | √ | √ | √ | √ |
| Appropriate initiation of steroid-sparing therapy | √ | √ | √ | √ | √ |
| *Clostridium difficile* testing during acute flares | √ | √ | √ | √ | √ |
| Venous thromboembolism prophylaxis is administered to patients according to national guidelines | √ | √ | √ | √ | √ |
| Cytomegalovirus testing *via* flexible sigmoidoscopy in steroid-refractory UC | | √ | √ | √ | |
| TPMT testing prior to thiopurine therapy | | √ | √ | | |
| Colectomy or close surveillance for low-grade dysplasia | | √ | √ | √ | |
| Surveillance colonoscopy for patients with colonic disease | | √ | √ | √ | |
| Screening and counseling for smoking cessation | √ | √ | √ | √ | √ |
| Vaccine education including pneumococcal and influenza | √ | √ | √ | √ | √ |
| Each IBD patient should be assigned one identifiable IBD specialist in charge of their care | | | √ | √ | |
| In patients with corticosteroid refractory IBD other induction therapies are recommended | | | √ | | |
| Medical salvage therapy and surgery are offered in UC inpatients failing to respond to intravenous corticosteroids within 5 d | | | √ | | |
| The IBD Unit/clinic has a mechanism to screen for mental health issues | | | √ | | |
| Patients with IBD receiving maintenance immunosuppressive therapy are monitored with a blood count and liver profile every three months | | | √ | √ | |
| Disease activity assessment is performed after initiating induction therapy | | | √ | | |
| The IBD Unit/clinic has a formal process for transfer of care from pediatric to adult | | | √ | | |
| IBD patients at risk for metabolic bone disease are assessed managed accordingly | √ | √ | √ | | √ |
| Calcium and Vitamin D are recommended in conjunction with systemic corticosteroids | | | √ | | |
| All HBsAg+ IBD patients should receive antiviral drugs while being treated with an anti-TNF drug | | | √ | √ | |
| Outcomes QIs | | | | | |
| Proportion of patients with steroid-free clinical remission (CR) for > 12-mo period | | √ | √ | | |
| Proportion of patients currently taking prednisone (excluding those diagnosed within 112 d) | | √ | | | |
| Number of days per month/year lost from school/work attributable to IBD | | √ | | | |
| Number of days per year in the hospital attributable to IBD | | √ | √ | | |
| Number of emergency room visits per year for IBD | | √ | √ | | |
| Proportion of patients with malnutrition | | √ | | | |
| Proportion of patients with anemia | | √ | | | |
| Proportion of patients with normal disease-targeted health-related quality of life | | √ | | | |
| Proportion of patients currently taking narcotic analgesics | | √ | | | |
| Proportion of patients with nighttime BM's or leakage | | √ | | | |
| Proportion of patients with incontinence in the last month | | √ | | | |
| Number of IBD-related surgeries per patient-year | | | √ | | |
| Validated assessment of patient adherence to management plan | | | √ | | |

[1]Only selected QIs included. AGA: American Gastrointestinal Association; CCFA: Crohn's and Colitis Foundation of America; MRI: Magnetic resonance imaging; PACE: Promoting access and care through centers of excellence; QI: Quality indicators; IBD: Inflammatory bowel disease; CT: Computed tomography; GI: Gastrointestinal; UC: Ulcerative colitis.

commonly seen in the subspecialized IBD care group (OR = 2.73, 95%CI: 1.22-6.12). While both retrospective in nature these two studies support the notion that providing resources and specialized care geared at focusing on optimizing and maximizing QoC is associated with better outcomes in IBD patients.

There is a scarcity of published data in the literature of IBD centers reporting on their performances with respect to the various published QIs. Recently, a study from Hungary was one of the first of its kind to report on its center's performance with respect to well accepted structure, process and outcome QIs. Gonczi *et al*[36] vigorously evaluated whether or not their center was meeting the targeted QIs. In addition, they demonstrated effective implementation of a fast track open clinic concept centered on IBD care. This func-

tioned by providing immediate access for outpatient consultation within a median of 1 d following request. This fast track resource coupled with the IBD center applying and self-assessing adherence to QIs has a large potential on positively effecting QoC, optimizing resource utilization and possibly impacting disease outcomes. An important shortcoming to highlight while assessing QIs is that certain outcome QIs may differ depending on center type. For instance, the outcomes at subspecialized referral centers for complex, refractory IBD cases are certainly different than community GI centers.

## NOVEL ADVANCEMENTS WITH POTENTIAL TO INFLUENCE QOC

Optimizing patient care in IBD is a challenging process owing to the fact that achieving tight disease control and adequately monitoring patients requires substantial resource utilization, while requiring a significant commitment from patients with respect to their time. This, coupled with the current demand to incorporate PROMs and assessing quality metrics to optimize QoC has sparked initiatives for reorganization of how care is delivered. Telemedicine, generally referred to as medicine practiced at a distance, has been present in healthcare in a variety of chronic diseases for nearly two decades[37] [Wootton, 2012 #61]. It provides a means to incorporate patient self-management by allowing patients to relay information to health care providers and to receive feedback[37]. Given the constraints and high resource usage in active IBD care, incorporating telemedicine appears promising. A systematic review and meta-analysis published in 2014 looked at all the published randomized control trials (RCTs) found that distance management significantly decreased clinic visits (mean difference of -1.08, 95%CI: -1.6 to -0.55) but did not affect relapse or hospital admission rates[38]. One of the main limitations of this analysis was the heterogeneity in the type of distance management or forms of telemedicine used in the included trials.

Many platforms for telemedicine in IBD exist but are limited to specific subsets of IBD patients[39]. A group from the Netherlands recognized this limitation which provided the foundation for the development of MyIBDcoach[40]. MyIBDcoach is the first telemedicine system that enables home monitoring for all subtypes of IBD. The platform may be used in academic and non-academic settings and looks at IBD facets, non-IBD related aspects as well as other features including PROMS and quality metrics. De Jong *et al*[40] showed in their inception study that myIBDcoach was practical and well received by patients and health care providers. The same group then conducted a multicenter randomized control trial (RCT) to investigate the effect on care that their system may have compared to standard of care[41]. In the trial, they sought to compare outpatient visits; patient reported quality care and PROMs between the two groups. Overall the group that incorporated telemedicine *via* myIBDcoach had fewer outpatient visits, fewer telephone consultations, fewer admissions to hospital as well as an increased adherence to medication. Importantly there were no significant differences in flare rates, rates of surgeries, emergency room visits or rates of corticosteroid use. Effectively *via* the well-designed myIBDcoach system the authors showed improved QoC, decreased resource utilization in terms of outpatient visits without demonstrating negative outcomes with respect to flares or complications of active disease.

Another major challenge with a large economic burden in the management of IBD relates to frequent emergency room (ER) visits. In a study from Manitoba, Canada, over a three-year period 76% of newly diagnosed IBD cases and 49% of patients already known to have IBD had at least 1 ER visit[42]. Many strategies have been utilized to decrease this burden in the ER and provide rapid access to the appropriate clinical care needed in times of active IBD. A pediatric study showed that increasing the availability of IBD specialists and specialized nurses *via* an electronic platform can decrease the frequency of ER visits[43]. Although in its infancy, a tertiary IBD center at McGill University in Montreal aimed to demonstrate improved quality of care by implementing a rapid access clinic (RAC)[44]. The RAC was structured by providing IBD patients followed at the clinic with an emergency contact email address, with a specific document explaining the pertinent symptoms that merit utilization of this access avenue. Each email was read and reviewed by a specialized IBD nurse or physician and depending on the situation a RAC visit was booked and the patient was seen. The preliminary data demonstrated a more optimized resource utilization including frequent use of proactive biomarker measurements such as therapeutic drug monitoring, fecal calprotectin and C-reactive protein levels. The preliminary data also revealed that there was less need for computed tomography (CT), magnetic resonance imaging (MRI) and endoscopy. Notably, only a few patients in the RAC cohort required an ER visit within 30-90 d after accessing care. Clearly at high volume IBD centers this model of implementing a RAC may have significant potential to optimize resource utilization, decrease ER visits and improve QoC.

IBD has a large psychosocial impact on patients with respect to their careers, productivity and social and intimate lives dramatically affecting their QoL[45,46]. The European Federation of Crohn's and Ulcerative Colitis Associations published the results of a large survey to assess the impact of IBD from the patient's perspective[45]. In total 4670 patients responded to a questionnaire that spanned 6 categories and contained 52 questions. 48% of respondents felt that their life was significantly impacted by IBD even in times in remission. With respect to work, 60% of surveyed patients felt stresses or pressured about taking time off when sick with 20% reporting being discriminated at workplace due to IBD. 56% of people felt that IBD had affected their career

paths with 31% of individuals stating they either lost a job or quit a job due to their illness. 35% felt that their disease had prevented them from pursuing intimate relationships. These negative impact patient centered measures on QoL were not incorporated into outcome metrics in many of the landmark IBD clinical trials. More recently however, this has changed and incorporating PROMs are an integral component in newly designed trials[11].

To address the issue of incorporating PROMs the IBD Disability index (IBD-DI) was developed as a tool that physicians can administer to evaluate the functional status of IBD patients[47]. The IBD-DI was validated for use in clinical trials showing high internal consistency, inter-observer reliability and construct validity[48]. The limitations of such a tool are its length and the fact that it was designed to be administered by health care professionals in the setting of clinical trials. Given the importance of QoL in managing IBD a recently developed tool known as the IBD-Disk was developed[49]. It is a self-administered shortened adaptation of key components integrated in the IBD-DI tool. There are 10 items within the questionnaire with explanatory statements for each item. These are scored in a disc-shaped visual analog scale from 0 (absolutely disagree) to 10 (absolutely agree). This shortened IBD-Disk has the potential to be an integral PROM that can be used in day-to-day practice. Further work is needed to assess the tool's operating characteristics and should compare the tool to the IBD-DI.

Within the realm of IBD management a major limitation that exists in many heath care systems is the challenge in objectively determining disease activity. Endoscopy is ubiquitously considered the gold standard[50] but is expensive, invasive and utilizes significant health care resources thus imposing limitations when assessing IBD disease response during time of disease activity. Non-invasive markers biochemical and fecal markers such as CRP and FC are therefore often used in adjunct with clinical parameters in assessing disease response to therapy[51,52]. FC physiologically representing gut specific inflammation, has become more commonly implemented as it has been shown to more accurately reflect endoscopic activity compared to CRP[51]. The drawback of conventionally available FC testing is that the test is enzyme-linked immunosorbent assay (ELISA) based and often is run in batches in hospitals. Consequently, there are often delays from obtaining the test and acting on the results which may result in unnecessary therapy escalation or utilizing endoscopy, which is more immediately available and reliable while waiting on the results of FC[53]. This limitation sparked the development of more rapidly available ELISA testing with the caveat that these tests also need to be performed in the hospital as point of care testing[54, 55]. Recognizing this drawback, a group out of Norway (CALPRO, Inc., Oslo, Norway) set out to develop a test that would allow FC testing directly by the patient as opposed to the point of care model which was simultaneously being developed[56]. The same group developed the CalproSmart that allows FC testing to be performed by the patients themselves at home with the results available within minutes[53]. Vinding *et al*[53] compared the performance of the CalproSmart tool to conventional FC ELISA testing with exciting results. The correlation coefficient was 0.685 with sensitivity, specificity, positive predictive value and negative predictive values of 82%, 85%, 47% and 97% respectively using a cut-off of 150 μg/g. The positive likelihood ratio (LR+) at this cut-off was 5.51 while the negative likelihood ratio (LR-) was 0.21. Extrapolating from the performance of the CalproSmart home assessment at the cut-off used (150 μg/g) it appears to be more suitable in correlating the absence of disease activity rather than predicting disease activity. Nevertheless, this kind of tool empowers the patient, can be integrated in eHealth and telemedicine systems and provides a means of potentially identifying early relapse in IBD.

## TREATING TO TARGET IN IBD

There has been a major shift in the management of IBD in the past decade. Classically, IBD was managed in a step-up approach escalating therapy if it were felt to be indicated based primarily on symptom driven scores[57]. However, the step-up paradigm of management has many limitations. Firstly, it puts individuals at a higher risk of prolonged corticosteroid exposure and the associated increased adverse events[58]. Secondly, due to time constraints inherent in a step-up framework there is a delay in delivering more effective therapy in high risk patients[59]. Lastly, this model depends on symptom derived scales for disease activity which poorly correlate to endoscopic disease activity[59]. Evidence has been conclusive in the rheumatoid arthritis (RA) literature whereby treatment strategies that utilize aggressive upfront strategies treating-to-target, as opposed to conventional step up therapy have resulted in better outcomes[60]. In RA management strategies are employed that modify treatments aggressively and proactively in response to changes in validated outcome measures indicative of active disease[61].

Motivated by the rheumatology field and other chronic diseases such as diabetes mellitus that use a model that actively guide therapy based on specific targets, a treat-to-target paradigm was devised for IBD. Initially Bouguen *et al*[59] proposed a framework to guide treating-to-target in Crohn's disease. In this model during the initial treatment phase, disease response should be actively followed using clinical symptoms, biochemical markers adjunctively and ultimately targeting mucosal healing. If there is a lack of response, initial therapy should be optimized accordingly with consideration of adding adjunctive medication. If, despite this, treatment targets are not achieved then a class switch should be considered. While the CD specific framework was developed IOIBD were simultaneously working on developing IBD related treat-to-target recommendations. The IOIBD published the STRIDE recommendations

encompassing targets to strive for in both UC and CD[9]. These recommendations encompassed specific targets that should be the main focus when managing IBD.

## EVIDENCE SUPPORTING TIGHTER CONTROL LEADING TO BETTER OUTCOME

Prior to the innovation and development of treating-to-target, the concept of early combined immunosuppression (ECI) emerged. This treatment strategy was conceived due to the evidence of shortcomings in how IBD was being managed at the time using a step-up approach. Both the TOP-DOWN[62] [D'Haens, 2008 #78] and SONIC[63] were well designed RCTs for treatment naïve Crohn's patients that showed superiority in the ECI group compared to conventional therapy. Note that both these trials utilized symptoms derived primary outcome measures: Harvey Bradshaw Index (HBI) $\leqslant$ 4 for SONIC and Crohn's disease activity index (CDAI) < 150 in TOP-DOWN. Despite the results of these two landmark trials, the common practice at the time remained limited to the step-up model. Subsequently the REACT trial was designed to validate the generalizability of algorithm-based therapy notably in the practice of community GIs in existing IBD patients[64]. The REACT trial randomized two groups to either the algorithm-based or conventional therapy. Disease activity was assessed at 4 or 12 wk post initial corticosteroid therapy with remission being defined by a HBI $\leqslant$ 4. In the algorithm-based group disease was reassessed every 12 wk and therapy was optimized if clinical remission was not attained. Ultimately, although the study did not demonstrate statistically different rates of corticosteroid free clinical remission at 12 mo, the trial did show that at 24 mo the composite outcome rate of surgery, hospital admissions and or serious disease related complications was lower in the algorithm-based group while no differences in serious drug related adverse events was noted.

Novel concepts of treating-to-target combined with a top-down approach were the inspirations for designing the CALM study[65]. This study was a RCT aimed at investigating the efficacy and safety of two treatment algorithms in achieving mucosal healing in early CD. One arm, the tight control group, was modelled on a treat-to-target framework with therapy decisions determined on the basis of pre-specified treatment failure criteria compromised of clinical symptoms (CDAI) and biomarkers of inflammation (CRP and FC). Comparatively, the clinical management group's treatment plan was solely based on clinical symptoms (CDAI). A few of the exclusion criteria included current or previous biologic or immunomodulator exposure, fibrostenotic disease and fistulizing disease (only perianal fistula not draining at enrolment were included). The primary endpoint was the proportion of patients with mucosal healing, defined by a Crohn's disease endoscopic index of severity (CDEIS) < 4 and no deep ulcers 48 wk after randomization. With respect to the primary outcome 46% of patients in the tight control group achieved mucosal healing compared to 30% in the clinical management group ($P$ = 0.01). In terms of secondary outcomes, statistically significant differences were observed between the two groups in deep remission, biological remission and steroid-free remission at every follow up visit. There were no significant differences in adverse events nor serious adverse events between the two arms. The CALM study is a pivotal trial in IBD as it is the first to show superiority of incorporating objective markers of inflammation in addition to clinical symptoms in a treat-to-target framework that leads to better outcomes in IBD compared to conventional clinical management approaches.

## CONCLUSION

The field of IBD is rapidly changing with major shifts in the philosophy of management. Meeting structure, process and outcome QIs and keeping the patient at the center of focus is key in achieving good QoC. Much advancement in the diagnosis, follow-up and access to care are being made with promising results.

It is becoming increasingly clear, particularly looking at the CALM and REACT trials, aggressive and proactive management guided by treating-to-target and actively reassessing a patient's evolution is a promising path to improve long term related IBD disease outcomes. Measuring multiple QIs and adjusting the treatment plan accordingly will help to improve the level of care and optimize patient access, monitoring and outcomes of patients with IBD.

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