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Interventions and targets aimed at improving quality in inflammatory bowel disease ambulatory care

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Core tip: Over the past decade, there has been increasing focus on improving quality in healthcare. This has led to the reinvigoration of the quality improvement movement. Inflammatory bowel disease is a complex, chronic condition with associated morbidity, health care costs, and reductions in quality of life. The condition is managed primarily in the outpatient setting. The delivery of high quality care is suboptimal in several ambulatory IBD domains. This review outlines current gaps in performance in IBD outpatient care and provides potential initiatives aimed at improvement.

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Abstract

Over the past decade, there has been increasing focus on improving the quality of healthcare delivered to patients with chronic diseases, including inflammatory bowel disease. Inflammatory bowel disease is a complex, chronic condition with associated morbidity, health care costs, and reductions in quality of life. The condition is managed primarily in the outpatient setting. The delivery of high quality of care is suboptimal in several ambulatory inflammatory bowel disease domains including objective assessments of disease activity, the use of steroid-sparing agents, screening prior to anti-tumor necrosis factor therapy, and monitoring thiopurine therapy. This review outlines these gaps in performance and provides potential initiatives aimed at improvement including reimbursement programs, quality improvement frameworks, collaborative efforts in quality improvement, and the use of healthcare information technology.

INTRODUCTION

Over the past decade, there has been increasing focus on improving the quality of healthcare. Much of this interest was inspired through the publication of *To Err is Human* by the Institute of Medicine (IOM) in 2000, that painted a portrait of a health care system full of preventable morbidity and mortality in desperate need for change^[1]. This has led to the reinvigoration of the quality improvement (QI) movement, the foundation of which had developed over the last century.

QI is defined by the IOM as "the degree to which health services for individuals and populations increase

the likelihood of desired health outcomes and are consistent with current professional knowledge^[2]. Fundamental principles of the study of QI include reflection on individual and peer performance in delivering high quality care, transparency in reporting performance, and implementing changes to improve deficiencies with the ability to measure successes and failures. Variation in practices may also be a marker of suboptimal performance. This had led to the resurrection and refinement of measures, study designs, and statistical analyses that are uniquely suited to QI.

Chronic disease management has become a significant focus of QI initiatives given their associated morbidity and cost. Some of this may be due to gaps in delivering evidence-based care. This was demonstrated in a landmark trial that showed that only 57% of outpatients regularly receive recommended standard of care for a variety of conditions^[3]. As a result, there has been significant focus on improving delivery of evidence based care and preventative measures to patients with chronic disease in order to decrease complications, hospitalizations, and death. Moreover, quality indicators are increasingly becoming incorporated in the accreditation and funding models of healthcare institutions. Inflammatory bowel disease (IBD) is a chronic gastrointestinal condition characterized by relapsing inflammation. Crohn's disease (CD) and ulcerative colitis (UC) are the major subtypes of IBD. In North America, the incidence of CD ranges from 3.1-20.2 cases per 100000 population and 2.2-19.2 cases per 100000 population for UC^[4,5]. While the incidence is less in Asia and the Middle East, the incidence and prevalence have been noted to be rising in many different regions of the world^[5]. As in other chronic diseases, IBD patients are at increased risk of morbidity due to symptoms, hospitalizations, and complications of disease or therapy^[6]. Moreover, there are significant health care costs and reduction in quality of life associated with IBD^[7,8]. The economic burden of IBD is significant, with high disability rates among this young cohort of patients^[9] and one cost analysis of eight European cohorts showing a mean total health care cost of 1871 euros per patient-year over 10 years^[10]. Patients requiring hospitalization had 10 fold higher costs. Most patients with IBD are managed in the outpatient setting. However as disease severity progresses and complications of disease or therapy arise, hospitalization is often required. Unlike some other chronic conditions, IBD is a heterogeneous disease with a wide spectrum of disease phenotypes and management strategies. This makes disease wide QI strategies particularly challenging. Nonetheless, there are several areas of IBD care that are amenable to QI study and change. This review outlines current gaps in quality in a number of outpatient domains and provides potential initiatives aimed at improvement.

ASSESSMENT OF DISEASE ACTIVITY

A challenging management issue in patients with IBD is how to best assess disease activity. This assessment has

traditionally been based on clinical symptoms. However, with the increasing number of more objective tools to assess disease activity now available, such as serum inflammatory markers and fecal calprotectin, the use of symptoms alone may no longer be the best approach to follow these patients. Reliance solely on symptoms can potentially miss ongoing inflammation that may not be clinically apparent. In a Groupe d'Etudes Therapeutiques des Affections Inflammatoires Digestives (GETAID) study of 121 patients with CD, there was weak correlation between clinical symptoms and endoscopic activity^[11]. This puts patients at risk of disease complications and may make treatment more difficult once symptoms ultimately develop. Alternatively, active inflammation may not always be the cause of persistent gastrointestinal symptoms in patients with IBD. A meta-analysis of 13 studies containing 1703 IBD patients found the pooled prevalence for symptoms meeting criteria for IBS was 39%, with an OR compared to healthy controls of 4.89 (95%CI: 3.43-6.98)^[12]. Similarly, a pediatric study found significant overlap between functional abdominal pain and CD, with almost half of the patients meeting criteria for functional pain classified as having active IBD according to the Pediatric CD activity index^[13]. This often leads to patients being inappropriately treated with immunosuppressants, with a low likelihood of improvement in symptoms and exposure to unnecessary risk. Therefore, there is a clear need for routine objective assessments of patients with IBD both at diagnosis and during follow up. While regular endoscopic evaluation, the gold standard to assess disease activity, has well established barriers such as cost and invasiveness, incorporating other objective tools such as erythrocyte sedimentation rate, C-reactive protein, and fecal calprotectin may facilitate more accurate and targeted approaches to managing these patients. A recent comparison of these tools noted a sensitivity and specificity of C-reactive protein > 6 mg/L of 68% and 72%, respectively as compared to a sensitivity and specificity of fecal calprotectin of 91% and 90%, respectively for the detection of endoscopically active disease^[14]. More studies such as this are needed to provide more insight on the most valuable and cost-effective non-invasive approach to monitor disease activity in patients.

STERIODS SPARING AGENTS

Corticosteroids are effective in inducing remission among patients with CD and UC^[15]. However, they have not been shown to be helpful in long-term maintenance^[16]. Moreover, their poor safety profile and tolerability makes avoidance of prolonged use a priority. Nonetheless, a significant proportion of patients treated with corticosteroids remain on extended courses. A retrospective review of patients referred to a tertiary IBD center in the United States found that over 75% of patients had been on corticosteroids for over 3 mo, including patients classified as having "mild" disease^[17]. There was no attempt to consider steroid sparing medications, such as immunomod-

lators, in almost 60% of patients. Similarly, in a study of time trends in therapy among 16 medical centers between the years 1998 and 2005, there was a 27% increase in prolonged corticosteroid use (defined as > 120 d) among patients with UC^[18]. Significant variation in the use of steroid-sparing agents was noted among centers. This was also demonstrated among 10 North American pediatric centers whereby the use of immunomodulators as a steroid sparing-agent varied significantly, ranging from 30%-95% of patients followed at the center^[19]. Corticosteroids are a well-established risk factor for osteoporosis and as such, patients on extended courses should undergo bone density measurement. Despite this recommendation, a practice audit at a large tertiary IBD center found that almost 80% of patients referred had not received the appropriate screening for metabolic bone disease^[17]. Clearly there is significant variation in practice patterns regarding the recognition of the need to minimize steroid exposure and highlights the underuse of steroid-sparing agent such as immunomodulators and anti-TNF therapy.

SCREENING PRIOR TO ANTI-TUMOR NECROSIS FACTOR THERAPY

Anti-tumor necrosis factor therapy (anti-TNF) has emerged as an effective treatment for IBD^[20-23]. It, however, carries risk of infection due to immunosuppression. The incidence of reactivation of latent tuberculosis infection (LTBI) has been shown to be increased among individuals treated with anti-TNF. A review of the United States Food and Drug Administration Adverse Event Reporting System found an incidence of 24 cases of tuberculosis per 100000 per year among those treated with anti-TNF, which translates into a 4 fold increased risk^[24]. Similarly, the incidence of hepatitis B virus (HBV) reactivation is also increased among these patients^[25-27].

In order to minimize this risk, screening measures have been recommended prior to initiating anti-TNF therapy. Screening for LTBI and HBV prior to treatment has been recommended by the United States Food and Drug Administration, Health Canada, and all gastrointestinal societies^[28-31]. Screening is effective in reducing infections complications, is easy to perform, and has minimal risks to patients^[32-34]. This involves tuberculin skin testing and chest-X-ray for LTBI and a panel of three serological blood tests for HBV (HBsAg, HBsAb, HBcAb). Adherence to screening with tuberculin skin testing and chest x-ray has been shown to reduce the risk of tuberculosis by 78%-90%^[32,33]. Screening for HBV with subsequent vaccination or chemoprophylaxis if indicated has also been shown to be effective^[34].

Despite these recommendations, cases of severe and sometimes fatal infection with tuberculosis or hepatitis B have been described, and many of these can be attributed to lack of screening^[34-36]. A retrospective review of over 200 patients followed at a large United States academic IBD center revealed only 65% of patients were appropriately screened for tuberculosis and 25% screened for

hepatitis B^[37]. Similarly, a study from Australia showed that only 50% of gastroenterologists were routinely screening for HBV prior to starting anti-TNF^[38]. This underscores the problem in provider's adherence to screening. The development of tuberculosis or hepatitis B while on anti-TNF has the potential for high morbidity and mortality. Given the ease and effectiveness of screening and the consequences of lack of screening, one can argue that anti-TNF screening rates less than 100% are unacceptable.

There is growing literature exploring contributors to this safety problem. In their review of 287 IBD patients starting anti-TNF, Vaughn *et al.*^[37] identified factors most often associated with lack of screening for tuberculosis: previous exposure to anti-TNF [OR = 5.3 (95%CI: 2.8-10.3)], health care providers in practice for more than 10 years [2.5 (95%CI: 1.4-4.5) and treatment at a non-IBD center [1.9 (95%CI: 1-3.4)]. The factors contributing to lack of HBV screening were the same. These reasons highlight the role of lack of knowledge, as physicians in practice longer or those at a non-IBD center may be less likely to be up to date with current guidelines. Previous exposure to anti-TNF may falsely reassure the prescribing physician that the appropriate work up had already been completed. This highlights the contribution of confusion as to who is responsible for screening. Uncertainty as to how and when to screen is also an important contributor, as evident in a gastroenterology practice audit that showed that while most knew that screening was indicated, there was significant heterogeneity in the type and timing of screening^[38]. Thus, knowledge gaps as to the need for screening, confusion surrounding responsibility for screening, and details regarding how to screen appear to be major contributors to this problem.

MONITORING THIOPURINE THERAPY

Thiopurines, including azathioprine and 6-mercaptopurine, are commonly used in patients with IBD. While most patients tolerate these medications with minimal side effects, ongoing monitoring is required once therapy commences. Regular complete blood counts (CBC) are recommended by all published guidelines to monitor for myelosuppression^[39-42], for example weekly CBC within the first month of therapy, every other week for the following two months, and every 3 mo thereafter. While the routine checking of thiopurine S-methyltransferase (TPMT) genotype and phenotype status prior to therapy remains controversial, it is strongly recommended by the United States Food and Drug Administration and has recently been listed as a quality indicator^[31,43]. Regular monitoring of liver chemistries is also recommended by some, although the frequency of which is less clear^[42]. Despite tremendous experience with this class of medication that has been available for over 5 decades, variation in monitoring patients while on this medication is significant and lapses in many best-practice recommendations are noted. A survey of members of the Canadian Association of Gastro-

Table 1 American Gastroenterology Association Physician Quality Reporting System inflammatory bowel disease measures

1	IBD type, location and activity all documented
2	Corticosteroid sparing therapy after 60 d
3	Bone loss assessment
4	Influenza immunization
5	Pneumococcal immunization
6	Testing for latent tuberculosis before initiating anti-TNF therapy
7	Assessment of Hepatitis B status before initiating anti-TNF therapy
8	Tobacco use: screening and cessation intervention

IBD: Inflammatory bowel disease; TNF: Tumor necrosis factor.

enterology revealed that while all providers acknowledged the need to monitor blood counts, there were differences in the frequencies of monitoring^[44]. Forty-two percent of those surveyed checked CBC weekly after starting therapy while 26% said they checked monthly and 23% biweekly during the initial period of treatment. Moreover, only 62% of respondents routinely monitored liver chemistries. In terms of routine TPMT testing, an international questionnaire sent to experts in the use of thiopurines in IBD found that only 30% and 43% routinely ordered genotype and phenotype testing, respectively^[45]. Lack of reimbursement for testing was the most important predictor of not ordering the test, and almost half of respondents felt that they would incorporate routine testing into their practice if it was reimbursed.

More recently, an association with thiopurine use and non-melanoma skin cancer (NMSC) has been noted. In a review of over 1000 South African IBD patients, a strong association was noted between thiopurine exposure and NMSC (OR = 5.0, 95%CI 1.1-22.8)^[46]. This was similar to the association noted by Peyrin-Biroulet *et al*^[47] in which ongoing thiopurine use had a hazard ratio for NMSC development of 5.9 (95%CI: 2.1-16.4). Lifelong, regular dermatologic screening has therefore been recommended^[48]. Nonetheless, a recent survey of dermatologists and gastroenterologist found that only 46% of gastroenterologists were aware of the association between NMSC and immunosuppression^[49]. This implies that at least half of IBD patients are not receiving the recommended screening.

INTERVENTIONS AIMED AT IMPROVEMENT

In order to adequately address gaps in care, an understanding of the contributing factors to the target problem is essential. While the evidence in support of a potential intervention is often regarded as the most important factor when choosing between potential initiatives focused on improving care, there is often limited supporting research available. As a result, other factors also need to be considered when choosing QI interventions including the prevalence and severity of the problem, the potential for undesirable outcomes as a result of the intervention, cost, complexity, and the ability to generate momentum

for future related initiatives^[50]. Moreover, once an intervention has been selected, continuous measurement is essential in order to know if an observed change represents an improvement. Thus, prior to implementing an initiative, well defined measures need to be developed and measured continuously. This will provide support that the initiative is responsible for any observed improvements in performance or alternatively, negative outcomes and unattended consequences.

Reimbursement programs

Guidelines have outlined algorithmic approaches for following this complex group of patients. However, the uptake of IBD guidelines by gastroenterologists has been shown to variable^[51,52]. Therefore, other improvement approaches are necessary. In 2006, the American Gastroenterology Association began to develop quality indicators that would be eligible for reimbursement through the Physician Quality Reporting System (PQRS)^[53]. Recently, IBD specific measures have been added to this growing list of indicators, and documentation of disease activity was the first such IBD indicator implemented. Other IBD indicators eligible for reimbursement through this program include recommending steroid-sparing therapy after 60 d of corticosteroid, assessment of tuberculosis and hepatitis B status prior to anti-TNF therapy, vaccinations, bone loss assessment, and addressing tobacco cessation (Table 1). While the impact of the PQRS on increasing objective assessment of disease activity is not yet known, data extrapolated from other disease states shows promise for the potential beneficial impact of similar reimbursement programs^[54]. Nonetheless, prior to implementing such an intervention, careful study is required as the literature showing the benefits of reimbursement programs on quality are conflicting and some studies identifying unintended consequences, such as providers avoiding the most severely ill patients, a phenomenon known as “adverse selection”^[54-57].

Although not designed for the purposes of a reimbursement program, the Crohn's and Colitis Foundation of American have recently sponsored the publication of a set of quality indicators^[43]. Both process and outcome indicators were developed that encompass a variety of domains in IBD care including treatment, surveillance, and health care maintenance. A number of corticosteroid related indicators are defined such as “IF a patient with IBD requires at least 10 mg prednisone (or equivalent) for 16 wk or longer, THEN an appropriately dosed steroid-sparing agent or operation should be recommended” and steroid related outcomes measures including; (1) proportion of patients with steroid-free clinical remission for a 12 mo period; and (2) the proportion of patients currently taking prednisone. Screening for latent tuberculosis and hepatitis B prior to therapy with anti-TNFs and TPMT testing prior to thiopurine therapy are also included. As more quality indicators develop and become increasingly incorporated into the accreditation processes of health care institutions, it is likely that more reimbursement models, or alternatively citations and pen-

alties for under performance, can be expected over the coming years.

Quality improvement frameworks

It does not appear that knowledge gaps are solely responsible for barriers in delivering high quality, evidence-based care. In terms of the underuse of steroid sparing agents, for example, the avoidance of prolonged corticosteroid and the importance of transitioning to steroid-sparing agents are not new concepts, have been endorsed by all gastrointestinal societies, and have been highlighted in guidelines for many years. This was borne out in a survey of gastroenterologists from 36 countries whereby 100% of those surveyed agreed that there is minimal evidence for continuing high dose corticosteroids for more than 3 wk and that steroid-sparing agents should begin to be considered after 2-4 wk of therapy^[58]. Therefore other contributors beyond physician knowledge base need to be addressed. Patients often initiate or modify steroid doses on their own without consultation with their health care provider. This may be due to poor access to a timely visit to a gastroenterologist when symptoms first present or when disease activity flares. Early referral to a specialist has been shown to improve IBD outcomes and initiatives aimed at improving access to gastroenterology have been shown to reduce steroid use and increase the use of early steroid-sparing therapy^[59]. A Swedish gastroenterology unit implemented a quality improvement framework whereby a registry of quality metrics was established and performance tracked^[60]. All routine visits were initiated by the clinic, rather than the patients and regular reminders to contact a designated IBD nurse for problems was provided. The program resulted in 98% of patients receiving regular IBD follow up visits, less than 3 wk between primary care referral and specialist visit, and less than 2 d to schedule an acute patient visit during disease flares. This experience highlights that implementing well designed frameworks, which are common place in other chronic diseases, has the potential to improve quality of care in IBD^[61]. Frameworks need to be developed with the appropriate local context in mind with and some have argued that frameworks do nothing to improve quality but rather improve documentation alone^[62]. This underscores the importance of continuous measurement after implantation to ensure the effort and costs associated are translating to improvements.

Collaborative efforts in quality improvement

Another potential motivator for change is collaborative efforts between institutions. These involve multiple sites working together towards a common improvement goal through receiving training in quality improvement methods, defining QI metrics, tracking performance, and transparency in reporting^[63]. While the use of improvement collaboratives in inflammatory bowel disease lags behind other chronic diseases, early outcomes of such initiatives have been promising. The ImproveCareNow Network consists of 51 pediatric hospitals across the United States and Europe that adopted the Chronic Ill-

ness Care Model and developed standardized practices and measures^[64,65]. Process and outcomes measures were prospectively collected and shared between sites. Early data has shown significant improvements in processes of care and patient outcomes in a variety of care areas. The use of a classification bundles to assess disease location, phenotype, activity, and nutritional/growth parameters at every visits has allowed for standardization between sites. Not only does this improve care, but also allows for collaborative clinical research efforts. Other outcomes already reported by the network include a decrease in the number of patients with CD on corticosteroids and an increase in the number of patients starting thiopurines with TPMT activity measured. These improvements in process measures are likely responsible for the increased remission rates noted in the participating sites. While more data on the efficacy of this and other such collaboratives are needed, given that an overarching theme of QI is to improve care delivery throughout the entire health care system, more widespread adoption of such broad, multi-site quality improvement initiatives should be considered.

Advancing healthcare information technology

The widespread incorporation for healthcare information technology (HIT) has been identified as essential in order to improve quality, safety, efficiency, and coordination of care by many leaders in the field of QI and patient safety^[66]. Many of the organizations regarded as leaders in the field of QI, such as the Veterans Affairs (VA) system in the United States or the Intermountain Healthcare Network in Utah attribute their success to the early adoption of electronic medical records and ongoing refinement of HIT resources^[67]. Providers delivering care to IBD patients have the potential to benefit from a variety of HIT related interventions including an electronic health record, computerized provider order entry (CPOE), and clinical decision support. If designed well and appropriately adapted to the context of a given institution, an electronic health record has the potential to improve efficiency, safety, and communication. It also has the potential to engage patients as platforms in which patients are able to access their own health record are increasingly being developed^[66]. This is important in IBD as patients are often young and may travel or move frequently for school and work. An electronic record also lends well to automated reminders which could address many areas of care that have been shown to have suboptimal performance such as monitoring blood work on thiopurines and bone density assessments^[63]. CPOE is another HIT intervention that in addition to decreasing medication errors, has the potential to enable drug interaction warnings, monitoring tests, and linkage to decision support systems^[66]. For example, order sets involve a collection of orders or investigations at one location that when designed well, are effective through improving efficiency, decreasing variation, enhancing workflow, and improving communication of evidence based practices^[68,69]. Traditionally, order sets have been paper-based, but

electronic order sets have become increasingly popular and have already been evaluated extensively in the patient safety literature. Compared to traditional paper order sets, electronic order sets have been shown to be more readily accessible, easier to link with other relevant order sets, and can be updated in real time^[70]. A number of areas within IBD patient care may be improved with electronic order sets, such as pre anti-TNF screening. While the evidence for order sets improving anti-TNF screening is lacking, examples in other fields support their utility. A pediatric study showed that an order set improved adherence to evidenced based asthma medication behaviors by almost 25%^[71]. While these results are encouraging, the quality of most studies evaluating order sets is not high and often employ simple before and after designs with poor control of biases^[72]. Moreover, some studies have shown unintended consequences of HIT. For example, one study aimed at using an electronic reminder to improve adherence to colon cancer found that following the intervention was unveiled, colon cancer screening adherence actually declined as a result of ineffective reminders and increased fecal occult blood screening rather than colonoscopy^[73]. Nonetheless, the theory behind order set effectiveness is sound and addressed several of the contributors to the anti-TNF safety problem identified above including knowledge gaps and confusion with details as to how to screen.

CONCLUSION

Caring for patients with IBD can be challenging due to the heterogeneous nature of the disease and the lack of consensus in many areas of practice. Variation in practice is therefore unavoidable and does not necessarily imply deficiencies in quality. Nonetheless, there are several aspects of IBD care whereby suboptimal performance has been documented and may be amenable to quality improvement initiatives including regular objective assessments of disease activity, recommending steroid sparing therapy, and appropriate monitoring of patients initiating and ongoing immunomodulator and anti-TNF therapy. Reimbursement programs, chronic disease frameworks, QI collaboratives, and health information technology resources are several potential interventions that may benefit IBD patient care. Quality performance indicators are expected to increasingly become incorporated into accreditation and funding models and it is therefore important that gastroenterologists become familiar with QI concepts and consider implementing initiatives where warranted.

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