

Defining quality indicators for best-practice management of inflammatory bowel disease in Canada

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BACKGROUND: There is a paucity of published data regarding the quality of care of inflammatory bowel disease (IBD) in Canada. Clinical quality indicators are quantitative end points used to guide, monitor and improve the quality of patient care. In Canada, where universal health care can vary significantly among provinces, quality indicators can be used to identify potential gaps in the delivery of IBD care and standardize the approach to interprovincial management.

METHODS: The Emerging Practice in IBD Collaborative (EPIC) group generated a shortlist of IBD quality indicators based on a comprehensive literature review. An iterative voting process was used to select quality indicators to take forward. In a face-to-face meeting with the EPIC group, available evidence to support each quality indicator was presented by the EPIC member aligned to it, followed by group discussion to agree on the wording of the statements. The selected quality indicators were then ratified in a final vote by all EPIC members.

RESULTS: Eleven quality indicators for the management of IBD within the single-payer health care system of Canada were developed. These focus on accurate diagnosis, appropriate and timely management, disease monitoring, and prevention or treatment of complications of IBD or its therapy.

CONCLUSIONS: These quality indicators are measurable, reflective of the evidence base and expert opinion, and define a standard of care that is at least a minimum that should be expected for IBD management in Canada. The next steps for the EPIC group involve conducting research to assess current practice across Canada as it pertains to these quality indicators and to measure the impact of each of these indicators on patient outcomes.

Key Words: Canada; Crohn disease; Delivery of health care; Process assessment; Quality indicators; Ulcerative colitis

The 2012 burden-of-illness report from the Crohn's and Colitis Foundation of Canada (1) estimated that the direct medical costs of inflammatory bowel disease (IBD) in Canada were \$1.2 billion, primarily funded through Canada's single-payer public health care system. The report also indicated the presence of a notable gap

Définir des indicateurs de qualité pour une gestion des maladies inflammatoires de l'intestin conforme aux pratiques exemplaires au Canada

HISTORIQUE : Il existe peu de données publiées sur la qualité des soins des maladies inflammatoires de l'intestin (MII) au Canada. Les indicateurs de qualité clinique sont des paramètres quantitatifs utilisés pour orienter, surveiller et améliorer la qualité des soins aux patients. Au Canada, où les soins universels peuvent varier considérablement entre les provinces, les indicateurs de qualité peuvent combler des lacunes dans la prestation des soins des MII et standardiser l'approche de prise en charge interprovinciale.

MÉTHODOLOGIE : Le groupe *Emerging Practice in IBD Collaborative* (EPIC) a produit une courte liste d'indicateurs de qualité en matière de MII, fondée sur une analyse bibliographique fouillée. Un processus de vote itératif a été privilégié pour sélectionner les indicateurs de qualité. Lors d'une rencontre du groupe EPIC, le membre jumelé à chaque indicateur de qualité a présenté les données probantes en appui à cet indicateur, puis des discussions ont suivi pour convenir de la formulation des énoncés. Tous les membres EPIC ont ensuite ratifié les indicateurs de qualité retenus dans le cadre d'un vote final.

RÉSULTATS : Onze indicateurs de qualité ont été établis pour la prise en charge des MII dans le système de santé à payeur unique du Canada. Ils sont axés sur un diagnostic précis, une prise en charge convenable et opportune, la surveillance de la maladie, la prévention ou le traitement des complications des MII et leur thérapie.

CONCLUSIONS : Ces indicateurs de qualité sont mesurables, reflètent les données probantes et les avis d'experts et définissent une norme de soins qui représente le minimum à atteindre dans la prise en charge des MII au Canada. Le groupe EPIC effectuera maintenant des recherches pour évaluer les pratiques en cours au Canada d'après ces indicateurs de qualité et pour en mesurer les effets sur les résultats cliniques des patients.

between the perceived ideal and actual IBD care. Moreover, there is substantial interprovincial variation in prescription drug benefit plans and access to services including elective surgery and diagnostic imaging. These disparities may threaten equitable access to optimal IBD care.

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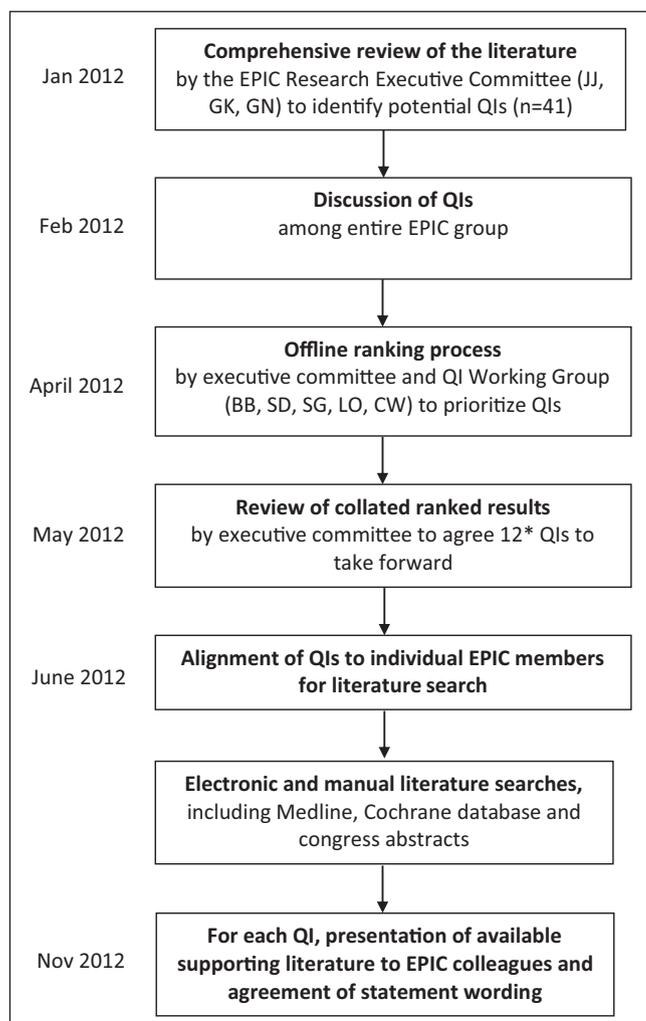


Figure 1 Methodology for identification and agreement of quality indicators (QI). *Only 11 QIs have been included in the final Emerging Practice in Inflammatory Bowel Disease (IBD) Collaborative (EPIC) set because it was conceded that there was insufficient evidence to support the 12th QI. Jan January; Feb February; Nov November

Clinical quality indicators (QIs) are quantitative end points used to guide, monitor and improve the quality of patient care (2). In particular, QIs that assess performance or process make it possible to document quality of care, set goals for appropriate standards of care, make comparisons over time among health care settings, make judgments and set priorities, and support accountability and quality improvement (3). Such indicators are becoming increasingly recognized in all areas of medicine and have been particularly well established in areas such as cardiology (4) and cystic fibrosis (5).

The use of QIs in IBD is relatively nascent; however, it is becoming increasingly recognized that such measures are important in improving quality of care in these chronic diseases. The American Gastroenterological Association (AGA) recently developed a physician performance measures set for adults with IBD (6). These measures were primarily designed to be used for accountability and performance management, rather than quality improvement as such. In parallel, the Crohn's and Colitis Foundation of America developed a set of process and outcome QIs for IBD based on reviews of guidelines, position papers and input from a multidisciplinary panel (7). It is important to understand that these QIs are not meant to reflect ideal care, but rather a minimum acceptable standard of care that should be expected based on the evidence currently available.

The Emerging Practice in IBD Collaborative (EPIC) is a network for Canadian IBD-focused gastroenterologists that aims to improve and standardize IBD management across Canada. A current objective of the EPIC group is to define a set of clinical QIs in the management of IBD patients ≥18 years of age in Canada. These QIs are measurable, reflective of the evidence base and expert opinion, and define a standard of care that is at least the minimum that should be expected for IBD management (8).

METHODS

The methodology is illustrated in Figure 1. The EPIC Research Executive Committee (JJ, GK and GN) generated an initial list of 41 QIs relating to the management of IBD patients ≥18 years of age, based on a comprehensive review of the literature, which was then presented to the entire group in February 2012. EPIC members were asked to consider the QIs and rank up to 14 statements. The EPIC Research Executive Committee made a final decision on 12 QIs to take forward (Table 1) and each EPIC member was asked to align themselves with a QI. EPIC members conducted comprehensive literature searches for each QI, collected full articles for review and, based on these data, prepared a summary of evidence for each QI. In a

TABLE 1
Quality indicators for inflammatory bowel disease (IBD) care, defined by the Emerging Practice in IBD Collaborative (EPIC)*

1. Patients who are hospitalized for the treatment of acute IBD (flare) should be offered pharmacological prophylaxis against venous thromboembolism or mechanical prophylaxis when the former is contraindicated.
2. Hospitalized IBD patients with diarrheal symptoms should undergo testing for *Clostridium difficile*.
3. CD patients who smoke should be informed about the poor clinical outcomes associated with ongoing smoking and, where available, they should be offered specialized counselling to improve smoking cessation rates.
4. To accurately diagnose, treat and prognosticate, clinicians performing colonoscopy in patients with IBD should document the following: diagnosis (CD versus UC); disease location; and disease severity.
5. In patients with corticosteroid-dependent IBD, an efficacious steroid-sparing therapy should be recommended.
6. Patients with IBD should be assessed for tuberculosis and hepatitis B before initiation of tumour necrosis factor antagonists.
7. In patients hospitalized for acute severe UC who have not responded to intravenous steroid therapy, implementation of salvage therapy should not be delayed beyond seven days from the start of intravenous corticosteroids[†].
8. All IBD patients with risk factors for metabolic bone disease, including prolonged steroid use, should be assessed for bone loss and treated if indicated.
9. Patients with long-standing UC and Crohn's colitis should undergo routine surveillance colonoscopy to detect dysplasia. IBD patients with concomitant primary sclerosing cholangitis should undergo surveillance at the time of primary sclerosing cholangitis diagnosis and annually thereafter.
10. CD patients who have undergone resection should have objective assessment for disease recurrence within six to 12 months, regardless of current therapy.
11. Pneumococcal vaccination and annual influenza vaccination should be administered to IBD patients, especially those on immunosuppressive therapies. Pneumococcal vaccination should be administered as early as possible after diagnosis.

*Following a comprehensive literature review, it was agreed that there is insufficient evidence at present to support the inclusion of quality indicator 12: "There should be objective measurement of response to medical therapy for IBD patients on maintenance therapy"; [†]Consideration should be given to shortening the time frame for salvage treatment implementation to three days in patients with a more fulminant presentation. CD Crohn disease; UC Ulcerative colitis

TABLE 2
Summary of society guidelines for venous thromboembolism (VTE) prophylaxis in hospitalized inflammatory bowel disease (IBD) patients

Society guideline (reference), year	Recommendations
ACCP (19), 2012	Thromboprophylaxis with low molecular weight heparin, low-dose unfractionated heparin or fondaparinux in acutely ill hospitalized medical patients at increased risk for thrombosis (Grade 1B). Mechanical thromboprophylaxis for acutely ill, hospitalized medical patients at increased risk of thrombosis who are bleeding or at high risk for major bleeding (Grade 2C), with the substitution of pharmacological thromboprophylaxis once bleeding risk decreases if VTE risk persists (Grade 2B). In contrast to the previous iteration of the guidelines, there were no specific recommendations for IBD.
ECCO (20), 2012	Consider mechanical thromboprophylaxis and heparin (low molecular weight heparin or unfractionated heparin) in UC patients at risk of VTE. Treatment of VTE in IBD should follow established antithrombotic therapy options taking into account the potentially increased risk of bleeding.
CAG (21), 2012	VTE prophylaxis for individuals with severe UC.
BSG (22), 2011	Pharmacological VTE prophylaxis for hospitalized patients with severe UC.
ACG (23), 2010	Consideration of VTE prophylaxis with heparin for individuals with severe UC flares who require hospitalization.
ECCO (24), 2010	Consider VTE prophylaxis in all hospitalized patients with CD. Treatment of VTE in IBD should follow established antithrombotic therapy options, taking into account the potentially increased risk of bleeding.

ACCP American College of Chest Physicians; ACG American College of Gastroenterology; BSG British Society of Gastroenterology; CAG Canadian Association of Gastroenterology; CD Crohn disease; ECCO European Crohn's and Colitis Organisation; UC Ulcerative colitis

face-to-face consensus meeting in Toronto (Ontario) on November 2, 2012, available evidence to support each QI was presented by the EPIC member(s) aligned to it, followed by group discussion to modify and ultimately agree on the wording of the QI statement. The selected QIs were then ratified in a final vote by all EPIC members. Following the consensus meeting, there was unanimous agreement that there was insufficient evidence at present to support the inclusion of the following QI: "There should be objective measurement of response to medical therapy for IBD patients on maintenance therapy." Therefore, only 11 QIs have been included in the final set.

Medical writers from Leading Edge (Buckinghamshire, United Kingdom) integrated the summaries of evidence for each QI written by EPIC members and discussions and presentations slides from the consensus meeting in Toronto to draft the full manuscript outlining QIs recommended by EPIC for best practice in IBD.

DESIGNATED QIs IN IBD AND SUPPORTING EVIDENCE

QI 1. Patients who are hospitalized for the treatment of acute IBD (flare) should be offered pharmacological prophylaxis against venous thromboembolism or mechanical prophylaxis when the former is contraindicated

Numerous population- and hospital-based studies have demonstrated an approximately twofold increased risk of venous thromboembolism (VTE) in individuals with IBD compared with the general population, as summarized in a recent meta-analysis (9). Moderate-to-severe disease activity has been recently shown to be a provoking factor for VTE, with individuals incurring an approximately eightfold higher risk during ambulatory IBD flares compared with periods of remission (10). The absolute risk for VTE was highest during IBD flares that required hospital admission (37.5 per 1000 person-years), which was nearly 27 times higher than during periods of remission (1.4 per 1000 person-years) (10). However, even IBD patients who were in clinical remission and admitted to hospital for another indication had an elevated risk for VTE compared with hospitalized non-IBD controls (HR 1.7 [95% CI 1.1 to 2.9]). Hospital-based studies from the United States and Canada have confirmed the increased risk for VTE among hospitalized IBD patients compared with non-IBD inpatients (11,12). Moreover, a recently developed model established IBD as a dominant risk factor for VTE in hospitalized medical patients (13). IBD patients who develop VTE during hospitalization have a 2.5-fold higher risk of in-hospital mortality compared with those who do not have VTE (11).

Although the absolute risk for VTE increases with age, it should be noted that the relative risk of VTE in IBD patients compared with those without IBD is highest among adults <40 years of age (11). Consequently, young adults with IBD should be considered

for VTE prophylaxis. Because hospitalized IBD patients who have undergone major surgery have a twofold increased risk of VTE, prophylaxis should also be administered in the postoperative setting (14,15).

Despite evidence supporting an increased risk for VTE and its associated morbidity and mortality in IBD patients, there is significant variation in practice for VTE prophylaxis among gastroenterologists (16,17). A recent United States medical and drug insurance claims database review indicated that fewer than one-third of hospitalized IBD patients receive prophylactic anticoagulants (18). Current guidelines provide a range of recommendations for VTE prophylaxis in hospitalized patients with IBD (19-24) (Table 2). Although the risk of bleeding while on anticoagulants can be an issue of concern in IBD inpatients given the commonality of gastrointestinal (GI) bleeding during active disease, a large retrospective study suggests that pharmacological VTE prophylaxis is safe in this population (25). Moreover, a meta-analysis of studies in which unfractionated and low molecular weight heparin were used as primary therapy in ulcerative colitis (UC) did not show any increased risk for major bleeding in the presence of active disease among those who received therapeutic doses of heparin compared with those who did not receive anticoagulation (26). Pharmacological prophylaxis is, however, contraindicated in individuals with hemodynamically significant GI bleeding. These individuals should instead receive mechanical prophylaxis, preferably intermittent pneumatic compression. When bleeding is no longer hemodynamically significant, consideration should be given to switching from mechanical to pharmacological prophylaxis (27). Initiatives to measure and optimize VTE prophylaxis rates in IBD patients would likely have a beneficial impact on morbidity, mortality and hospital costs.

QI 2. Hospitalized IBD patients with diarrheal symptoms should undergo testing for *Clostridium difficile*

IBD has emerged as an important independent risk factor for *C. difficile* infection (CDI). An analysis of hospital discharges between 1998 and 2004 using the United States Nationwide Inpatient Sample found that hospitalized patients with UC had an absolute prevalence of CDI that was eightfold higher than that of non-IBD patients admitted with a GI indication (37.3 cases per 1000 discharges versus 4.8 cases per 1000 discharges; $P < 0.00001$) (28). Rates of CDI were also significantly higher in Crohn disease (CD) patients than non-IBD GI patients (10.9 cases per 1000 discharges; $P < 0.00001$). Furthermore, the elevated prevalence of this infection in individuals with IBD does not appear to be limited to hospitalized patients (29,30) and has increased over the past decade, particularly in patients with UC (28,29,31,32).

CDI has been shown to significantly increase length of hospital stay and hospitalization costs among IBD patients (28,33). Furthermore, there is mounting evidence that CDI confers poor outcomes in IBD. A recent retrospective cohort study from Ontario showed that CDI in patients with UC impacted mortality during the index hospitalization (adjusted OR 8.90 [95% CI 2.80 to 28.3]) and mortality over five years following hospital discharge risk (adjusted HR 2.40 [95% CI 1.37 to 4.20]) (34). Other studies have also shown increased in-hospital mortality among IBD patients with CDI compared with noninfected IBD patients (31,33). However, the impact of CDI on the risk of in-hospital colectomy (28,33) and long-term colectomy (34-36) in UC patients is not clear.

Routine testing for *C difficile* in patients presenting with an exacerbation of IBD is an important intervention given the high incidence and potentially poor outcomes associated with CDI. While more evidence evaluating the benefits of routine testing is indicated, the literature to date supports its use and designation as a QI in the Canadian context.

QI 3. CD patients who smoke should be informed about the poor clinical outcomes associated with ongoing smoking and, where available, they should be offered specialized counselling to improve smoking cessation rates

Smoking is independently associated with early development of stricture and penetrating CD (37-39), postsurgical recurrence of ileal CD (40,41) and the need for maintenance treatment, specifically with biological therapy (39). Higher tobacco load, as assessed according to pack-years, increases the risk of adverse outcomes (39).

In contrast, CD patients who stop smoking fare better than those who continue to smoke (41-43), suggesting that strategies for smoking cessation for CD patients are warranted. Recommendations for smoking cessation in CD patients have been published, based on reviews of guidelines for the general population (44). These include asking CD patients about their smoking habits at each outpatient visit and advising current smokers to stop. Motivated individuals should be provided with written information and considered for counselling, nicotine replacement therapy or pharmacological smoking cessation therapy.

QI 4. To accurately diagnose, treat and prognosticate, clinicians performing colonoscopy in patients with IBD should document the following: diagnosis (CD versus UC); disease location; and disease severity

Colonoscopy is currently considered to be the gold standard for the diagnosis and management of IBD. Despite the intuitive importance of accurate, reproducible and meaningful endoscopic documentation of disease (45), there is a paucity of data and direct evidence to support this QI in IBD. Furthermore, minimum terminology has not been standardized across centres (46).

Guidelines on the use of endoscopy in IBD have been produced by the American Society for Gastrointestinal Endoscopy; however, these do not discuss appropriate documentation of endoscopic findings (47). While the Canadian Association of Gastroenterology (CAG) has also recently published consensus guidelines on QIs in GI endoscopy (48,49), it is important that specific QIs be implemented for IBD endoscopy. Endoscopic reporting in IBD should be held to the same standards as those applied to colon cancer screening. Standardization of IBD endoscopic reporting is a fundamental objective and applies to all clinicians who perform IBD endoscopy (gastroenterologists, surgeons, internists and family physicians). This is particularly relevant in Canada because many nongastroenterologists perform IBD endoscopy. In addition, there is a need to maximize appropriate access to endoscopy – a resource that is managed differently across provinces and is limited by excessive wait times (50). Additional data are required to further delineate what comprises a minimum standard for appropriate reporting of an endoscopic procedure for IBD and then to evaluate the impact that appropriate documenting of endoscopic evidence of

disease has on quality of care, resource utilization and disease-related outcomes in patients with IBD.

QI 5. In patients with corticosteroid-dependent IBD, an efficacious steroid-sparing therapy should be recommended

In Canada, the steroid-sparing agents most commonly used for the management of IBD include the purine antimetabolites azathioprine (AZA) and 6-mercaptopurine (6-MP), as well as methotrexate (MTX) and the tumour necrosis factor (TNF) antagonists infliximab and adalimumab. The quality of the evidence supporting the efficacy of these drugs as steroid-sparing agents varies between CD and UC.

With respect to AZA/6-MP in CD, a meta-analysis of five randomized placebo-controlled trials in patients with active disease demonstrated a reduction in prednisone use to <10 mg/day while maintaining remission in 65% of AZA recipients compared with 36% of placebo recipients (Peto OR 3.69 [95% CI 2.12 to 6.42]) (51). In two very small randomized placebo-controlled trials (including 30 patients in total) evaluating the steroid-sparing effect of AZA in quiescent CD, 87% of AZA recipients were able to reduce or discontinue steroids compared with 50% of placebo recipients (Peto OR 5.22 [95% CI 1.06 to 25.68]) (52).

MTX has been evaluated as induction and maintenance therapy for CD. Feagan et al (53) examined the effect of intramuscular MTX (25 mg/week) compared with placebo for induction in patients with chronically active CD despite a minimum of three months of prednisone therapy. At study entry, all patients received oral prednisone (20 mg/day), which was tapered over a 10-week period. After 16 weeks, 39% of MTX recipients had discontinued prednisone therapy and remained in remission compared with 19% of placebo recipients (P=0.025), with the effects most pronounced in patients who had been receiving higher dosages of steroids (>20 mg/week) before study entry (39% versus 10%, respectively; P=0.003). Furthermore, the cumulative dose of steroid used by patients in the MTX group was significantly less than that of the placebo-treated patients. In a second study by the same group (54), MTX was evaluated as a maintenance agent for patients who had responded to induction therapy. Patients in remission were randomly assigned to weekly intramuscular MTX 15 mg or placebo. Over the 40-week follow-up period, fewer patients in the MTX group required prednisone for relapse (28%) than those in the placebo group (58%; P=0.01). However, the cumulative dose and total duration of steroid treatment were similar between groups. Therefore, adequate doses of both AZA and MTX are reasonably efficacious in active CD and exert a steroid-sparing effect, although their exact roles as monotherapy continue to be debated. Similarly, these agents appear to demonstrate a steroid-sparing effect in patients with quiescent disease.

The clinical efficacy of infliximab and adalimumab has been studied extensively in active CD (55-60). However, the primary end point and the use of corticosteroids in these studies has varied, making it challenging to ascertain the overall steroid-sparing effect. A recent systematic review examined all published studies that fully described the degree of corticosteroid withdrawal in infliximab- and adalimumab-treated CD patients versus those in control groups (61). Only three infliximab studies (55,57,62) and one adalimumab study (59) met the inclusion criteria. This analysis found that 30% of adults treated with corticosteroids at baseline successfully tapered and remained steroid and surgery free from week 30 through week 54. In actual practice, the rate of steroid-free remission will vary due to the heterogeneity of clinical factors. Nevertheless, these published rates illustrate two points. First, TNF antagonists can be effective as steroid-sparing therapy for active CD. Second, there is considerable room for improvement in terms of the efficacy of steroid-sparing therapies. The recent Study of Immunomodulator Naive Patients in Crohn's Disease (SONIC) trial evaluating infliximab, with or without AZA, versus AZA monotherapy clearly demonstrated the superiority of infliximab over AZA in all clinical and endoscopic end points, including steroid-free remission (60). However, it is important to recognize that patients included in this trial had active disease requiring corticosteroids but were not necessarily corticosteroid dependent.

The steroid-sparing effect of AZA/6-MP in patients with active UC is less clear. Three early small studies of varying designs failed to demonstrate a convincing steroid-sparing effect (63-65). Other studies with varied treatment duration, designs and end points suggest some efficacy and steroid-sparing effect (66-69). The largest study evaluating AZA in UC (UC-SUCCESS) compared AZA and infliximab as monotherapy and in combination in adult patients with active UC with an inadequate response to corticosteroids (70). In this study, only 24% of AZA monotherapy patients were in steroid-free remission at 16 weeks. Furthermore, a single randomized, placebo-controlled trial showed no benefit of MTX as a steroid-sparing agent in active UC, albeit at a low oral dose (71).

Infliximab has been demonstrated to be an effective induction and maintenance agent for active UC, with a significant steroid-sparing effect compared with placebo (72). In the UC-SUCCESS trial, 40% of patients receiving infliximab plus AZA combination therapy were in corticosteroid-free remission at 16 weeks compared with 22% of patients receiving infliximab monotherapy ($P < 0.05$ versus combination therapy) and 24% of patients receiving AZA monotherapy ($P < 0.05$ versus combination therapy) (70). The efficacy of adalimumab in adults with active UC has been evaluated in two large randomized controlled trials (73,74), leading to its approval in Europe and the United States, although it is not currently approved by Health Canada. A recent post hoc analysis of one of these trials demonstrated that approximately 20% of patients who responded to adalimumab induction therapy were in steroid-free remission at one year versus approximately 6% of placebo-treated patients (75).

There is a lack of consistent, convincing evidence that AZA is efficacious as a steroid-sparing agent for active UC and its role continues to be debated. MTX cannot currently be advocated for this role. There is good evidence that infliximab is an efficacious steroid-sparing therapy in adults with active UC. Data are evolving for adalimumab; however, no firm recommendation can yet be made. As in CD, there is considerable room for progress in achieving this challenging end point. However, given the significant toxicity of prolonged corticosteroid use, there is sufficient evidence to warrant that these non-steroidal agents be recommended.

QI 6. Patients with IBD should be assessed for tuberculosis and hepatitis B before initiation of TNF antagonists

Given the higher rate of reactivation of latent tuberculosis (TB) in unselected IBD patients exposed to TNF antagonists (76-78), it is important to actively identify patients with latent TB before initiating TNF antagonists. However, while screening levels have improved over time, rates remain suboptimal (79).

The high incidence of anergy in patients who are already receiving immunosuppressants limits the precision of the purified protein derivative tuberculin skin test (TST) to rule out latent TB before commencing TNF antagonists (80). It has been suggested that the interferon-gamma release assay (IGRA) be used to test for latent TB in patients with IBD in regions with a general population that has low endemic TB and high proportions of Bacillus Calmette-Guérin vaccination because this assay has higher specificity than the TST (81). However, the precision of the IGRA is also negatively affected by immunosuppressants (82). Furthermore, there is growing evidence that a TST can prime the immune response and boost subsequent IGRA results, potentially yielding a false positive (83). Current Canadian guidelines for TB testing recommend a two-step approach of TST followed by IGRA. To prevent boosting and false positives, it is recommended that blood for the IGRA be drawn before or within 72 h of the TST being performed (84).

A range of guidelines recommend that a comprehensive patient history be obtained with a TST and chest x-ray in IBD patients being considered for TNF antagonists (85-88). Based on current evidence, then authors recommend that candidates for TNF antagonists should be screened for latent TB with a comprehensive history, TST and/or IGRA if available (preferably on the same day), and a chest x-ray if possible.

Therapy with TNF antagonists also increases the risk of reactivation of chronic hepatitis B virus (HBV) infection (89). However, as with TB, the frequency of screening for HBV infection is currently suboptimal in candidates for TNF antagonists (79). The American College of Gastroenterology guidelines for UC currently recommend screening all patients for HBV before treatment with infliximab (23), while the CAG recommends screening for HBV before treatment with TNF antagonists in patients with risk factors for acquiring HBV infection (88). Given the possibility of reactivation and the ease of obtaining the test, the authors recommend that all patients with IBD be tested for latent or active HBV (hepatitis B surface antigen and antibody, and hepatitis B core antibody) to rule out infection before commencing TNF antagonists.

QI 7. In patients hospitalized for acute severe UC who have not responded to intravenous steroid therapy, implementation of salvage therapy should not be delayed beyond seven days from the start of intravenous corticosteroids

Intravenous corticosteroids are the mainstay of treatment for patients hospitalized with acute severe UC (90). However, approximately 27% of patients ultimately fail to respond to corticosteroids and require colectomy (91). Cyclosporin and TNF antagonists (generally infliximab in Canada) are often initiated as salvage therapy in an attempt to prevent colectomy for patients who have not responded to intravenous corticosteroids. However, it is essential that the decision to proceed with salvage therapy be made in a timely manner such that colectomy, if required, is not unnecessarily delayed because this may significantly increase postoperative morbidity and mortality (92-94). In addition, patients in hospitals with high colectomy volumes have been shown to have better postoperative outcomes (92); therefore, it is important that deferring colectomy does not preclude the patient from being transferred to a centre with colectomy experience should surgery ultimately be required.

Several predictive rules have been developed to identify patients with acute severe UC requiring colectomy. These studies are not based on prospective data, however, and have not been externally validated. In the era before biologic therapy, Travis et al (95) found that patients with > 8 stools/day, or three to eight stools/day and C-reactive protein > 45 mg/L after three days of intensive corticosteroid treatment, had an 85% chance of requiring colectomy during the same hospital admission. Subsequently, a Spanish group developed a decision tree to identify predictors of rapid response to systemic corticosteroids in moderate-to-severe UC flares (96). The absence of rectal bleeding, C-reactive protein < 43 mg/L, platelet count $< 318 \times 10^9/L$ and < 3 bowel motions per day at day 3 after initiation of intravenous prednisone at a dose of 1 mg/kg/day was predictive of a response to steroids at day 7.

No published rules have been identified for predicting which severe UC patients are likely to require an escalation of medical therapy or on the appropriate timing of referral of patients to tertiary care centres with expertise in managing severe UC. Until such data are available, we propose that implementation of salvage therapy should not be delayed beyond seven days from the start of intravenous corticosteroids to ensure timely colectomy if required. In keeping with the Toronto consensus statements from the CAG for patients hospitalized with severe UC (21), treatment response should be assessed by day 3 and consideration should be given to shortening the time frame for treatment implementation to three days in patients with a more fulminant presentation (97).

QI 8. All IBD patients with risk factors for metabolic bone disease, including prolonged steroid use, should be assessed for bone loss and treated if indicated

The prevalence of osteoporosis in adults with IBD ranges from 18% to 42% (98-103), and may be more pronounced in CD than UC (104). A comprehensive analysis of literature published by the American Gastroenterological Association Clinical Practice Committee (105) found grade A evidence supporting the premise that IBD has only a

TABLE 3
Summary of guidelines for surveillance of dysplasia in patients with long-standing ulcerative or Crohn's colitis

Society guideline (reference), year	Start/intervals	Method
BSG (135), 2002 / CAG/CDHF (136), 2004	UC or CD pancolitis: 0–10 years after onset; begin colonoscopies at 8 years after onset. 11–20 years after onset: every 3 years 21–30 years after onset: every 2 years 31–40 years after onset: every year Left sided: Start at 15 years after onset Primary sclerosing cholangitis: Every year from diagnosis onward	2–4 random biopsies every 10 cm with additional biopsies of suspicious regions
ASGE (137), 2006 / AGA (138), 2010	UC or extensive CD (>1/3 colon): Begin colonoscopies 8–10 years after onset and repeat every 1–2 years.	Four quadrant biopsies, every 10 cm, at least 32 biopsies, microscopically involved segments if less extensive disease
CCFA (139), 2005	Pancolitis or left-sided: 0–10 years after onset; begin colonoscopies at 8–10 years after onset and repeat every 1–2 years Revert to 1–3 years if two assessments are negative ≥20 years after onset; revert to assessing every 1–2 years	At least 33 biopsies, every 5 cm in the lower sigmoid and rectum

AGA American Gastroenterological Association; ASGE American Society for Gastrointestinal Endoscopy; BSG British Society of Gastroenterology; CAG Canadian Association of Gastroenterology; CCFA Crohn's and Colitis Foundation of America; CDHF Canadian Digestive Health Foundation; CD Crohn disease; UC Ulcerative colitis

modest effect on bone mineral density, with corticosteroid use being the predictive factor most strongly associated with osteoporosis. Other risk factors include older age, family history of osteoporosis, previous fractures, tobacco use, excessive alcohol use, low body mass index, malnutrition and hypogonadism (105-107).

Several practice guidelines have been developed with respect to the diagnosis and treatment of bone loss in patients with IBD (20,24,105,107,108). In general, it is recommended that all patients with IBD be educated on basic preventive measures for bone loss, such as minimizing corticosteroid use, ensuring adequate vitamin D and calcium, weight-bearing exercise, smoking cessation and avoiding excess alcohol. All major guidelines recommend dual x-ray absorptiometry scan as the standard of practice when assessing bone density. The decision to screen IBD patients for bone loss should be based on the presence of one or more of the following risk factors: male >50 years or age or postmenopausal female; >3 months or recurrent corticosteroid use; history of low-trauma fracture; or hypogonadism (105). As per practice guidelines, bisphosphonates should be considered in postmenopausal women and males >50 years of age with osteoporosis (T-score ≤-2.5) or patients with a history of low-trauma vertebral fracture (20,24,105,107,108). In all other IBD patients with significant bone loss (Z-score ≤-2.0) or those who will be exposed to prolonged corticosteroids, referral to an endocrinologist or osteoporosis clinic for assessment of bisphosphonate therapy should be considered. In patients with significantly low bone mineral density (T-score ≤-2.5 or Z-score ≤-2.0), assessment for other causes of bone loss should be performed (complete blood count, serum calcium, alkaline phosphatase, creatinine, 25-hydroxyvitamin D, protein electrophoresis and testosterone in males).

QI 9. Patients with longstanding UC and Crohn's colitis should undergo routine surveillance colonoscopy to detect dysplasia. IBD patients with concomitant primary sclerosing cholangitis should undergo surveillance at the time of primary sclerosing cholangitis diagnosis and annually thereafter

Long-standing UC and Crohn's colitis are associated with an increased risk for colon cancer, with an incidence rate ratio of 2.75 for UC and 2.64 for Crohn's colitis (109). Cohort studies have shown that the risk for colon cancer increases with extent of disease (110-112) and with disease duration, reaching 30% at 40 years (113-115). The severity of colonic inflammation also influences the risk of developing colon cancer (112). Interestingly, a recently published cohort study including

47,374 Danish patients with IBD followed over a 30-year period found a decreasing risk for colon cancer from 1979 to 2008, possibly because of improved therapies that target mucosal inflammation (116).

Primary sclerosing cholangitis (PSC) is an extraintestinal manifestation of IBD characterized by progressive inflammation and scarring of hepatobiliary ducts. Several population-based cohort studies have indicated that colonic dysplasia (neoplasm confined to the epithelium) and/or advanced neoplasia occurs more often in UC patients with PSC than those without (117-120). However, other studies have not found any association between PSC and the development of dysplasia (121,122). Colon cancer typically appears early after a diagnosis of PSC in IBD, with a mean time from diagnosis of PSC to dysplasia/cancer of 2.9 years (118,123).

Surveillance for dysplasia in IBD involves colonoscopy with biopsy samples taken along the length of the colon. The sensitivity of testing for detecting dysplasia is increased with a greater number of biopsies taken. Longstanding UC and Crohn's colitis patients who undergo surveillance have a significantly lower cumulative incidence of colon cancer (10.8% at 40 years), resulting in a reduced need for prophylactic colectomy (124-127). Furthermore, earlier detection of dysplasia or cancer may result in better prognosis, with indirect evidence suggesting that surveillance improves survival (128-133).

The cost effectiveness of surveillance colonoscopy in patients with UC decreases as the regularity of surveillance increases (134). However, because the risk of cancer also increases exponentially over time, a reduced screening interval should be considered in patients with longer disease duration. Guidelines recommend that surveillance generally begins eight to 10 years after diagnosis, with increased frequency with longer duration of disease (135-139) (Table 3).

The evidence base needs to be further augmented by evaluating the most effective method of surveillance, including additional modalities such as chromoendoscopy, narrow band imaging and confocal endomicroscopy, as well as determining the role of chemoprophylaxis in patients at increased risk for colorectal cancer. Nevertheless, adopting routine surveillance for dysplasia in patients with longstanding UC or Crohn's colitis as a QI should be of value in improving the detection of dysplasia.

QI 10. CD patients who have undergone resection should undergo objective assessment for disease recurrence within six to 12 months, regardless of current therapy

Up to 55% of patients with CD require surgery for their disease within 10 years of diagnosis (140). Because medical therapy in the postoperative setting may prevent recurrence in high-risk individuals (141,142), it is important to identify patients at risk for postoperative recurrence to allow prophylactic treatment. Although studies have suggested that certain clinical features, such as disease behaviour (143) and smoking status (41), are associated with higher risk for recurrent disease, these are usually not sufficient to predict recurrence in the individual patient. Almost three decades ago, Rutgeerts et al (144) found that 72% of patients with CD treated with an ileocolonic resection had endoscopic recurrence within one year of therapy, primarily confined to the neoterminal ileum. The recurrence rate did not increase substantially after the first year, although endoscopic lesions did become progressively more severe. Importantly, clinical manifestations of recurrence were not usually present in the earlier stages of endoscopic recurrence. In a subsequent study, it was found that the best predictor of symptomatic recurrence was endoscopic recurrence within the first year after resection, leading to the development of a prognostic scoring system (145). Similar findings were reported in a study involving 30 CD patients who underwent an ileocolic resection (146).

Based on these observations, objective disease activity assessment within one year of ileocolonic resection is recommended. Although ileocolonoscopy currently remains the test of choice because of its well-described prognostic score and availability, the advent and validation of less invasive procedures for detection of early disease recurrence (such as computed tomography and magnetic resonance enterography, transabdominal bowel ultrasound and fecal calprotectin assays) may further increase access to this QI process given the limited resources available for endoscopy in Canada.

QI 11. Pneumococcal vaccination and annual influenza vaccination should be administered to IBD patients, especially those on immunosuppressive therapies. Pneumococcal vaccination should be administered as early as possible after diagnosis

There is a higher risk for respiratory infections in patients with IBD than the general population, particularly those treated with immunosuppressants or TNF antagonists (147). Despite current guidelines recommending pneumococcal and influenza vaccination for individuals at risk, including those with chronic disease or those who are immunosuppressed (148,149), adherence to recommendations is poor (150,151). It has also been demonstrated that patients and their physicians often lack awareness of the need for vaccination in IBD (150).

While no disease flare has been reported as a result of pneumococcal vaccination (PSV23 vaccine) in IBD patients (152), current use of immunosuppressants may predict a low response to vaccination (152-155). This suggests that pneumococcal vaccination should ideally be administered in IBD patients soon after diagnosis and before initiation of immunosuppressive therapy. However, because it is an inactivated vaccine, it is permissible to administer while on immunosuppressive therapy, with this strategy likely being preferable to no vaccination whatsoever in this context. Further studies are needed to ascertain whether the lower responses obtained in immunocompromised patients remain protective against infection and whether patients with a poor response or those with waning serological responses should be revaccinated.

There are very limited data regarding the immunogenic effects of influenza vaccination in adult patients with IBD, with knowledge mostly extrapolated from pediatric studies. In general, influenza vaccination induces adequate immunogenic responses in immunosuppressed IBD patients, with seroprotection rates similar to that in healthy controls and nonsuppressed IBD patients (156-159). No unexpected safety concerns or IBD reactivation were noted. Overall, responses to influenza A strains were similar in immunosuppressed and nonimmunosuppressed IBD patients and in controls. However, IBD patients were less likely than controls to respond to B strains (158,159). Patients on immunosuppressants may also have an inadequate or a delayed response to vaccination (159).

The immune response to the adjuvant 2009 A/H1N1 pandemic (pH1N1) vaccine has been evaluated in adult IBD patients treated with maintenance TNF antagonists with or without immunomodulators (160). Comparisons were made with a control group of healthy subjects. There was a similar seroprotection rate in all groups at four weeks postimmunization; however, a lower immunogenic response was reported in IBD patients compared with controls ($P=0.009$). None of the patients experienced a disease flare.

Collectively, these studies show that pneumococcal and influenza vaccines are safe and reasonably immunogenic in immunocompromised IBD patients. More data regarding the impact of individual immunomodulators on risk of infection are required, as well as the influence of age and comorbidities on vaccine response rates. In addition, there may be a delay in optimal response to vaccination in immunosuppressed patients.

FUTURE DIRECTIONS

The introduction of process QIs for IBD patients in Canada, as described in the present document, is an important step toward delivery of consistent, evidence-based, high-quality care that meets, at least, a specific minimum standard. The present position paper addresses some of the key parameters of IBD management, based on current available evidence. While the development of the QIs described above has stemmed from the current evidence base, it has also revealed that there is a significant lack of published data that supports best practice in many areas of the field of IBD.

QIs are of limited use if they measure only change in practice rather than actual improvement in health outcomes. It is not yet known whether adherence to these QIs will improve outcomes. This is an area of research that will evolve over time; however, results demonstrating improved outcomes in the United States with the ImproveCareNow initiative undertaken in the arena of pediatric IBD are encouraging (161).

The next steps for the EPIC group involve conducting research to assess current practice across Canada as it pertains to these QIs and to measure the impact of each of these indicators on IBD patient outcomes. Evaluation of the clinical outcomes that are driven by the adoption of these QIs is likely to require collaboration among gastroenterologists, quality improvement leaders, hospital administrators and patients themselves. Robust reporting systems will need to be implemented to allow QIs to be measured in an accurate and timely manner, with appropriate outputs to inform decisions on the effectiveness of the QIs.

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