Core indicators of an evaluation and guidance system for quality of care in inflammatory bowel disease centers: A critical review

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Summary

The mission of the IBD Quality Care Evaluation Center (IBDQCC) is to establish indicators of quality of care (QoC), certify IBD units to generate a network of IBD quality care, and eventually improve the national level of IBD healthcare. The final list of 28 core and 13 secondary IBD QoC indicators suitable for the healthcare system in China were selected using a Delphi consensus methodology. Units that met all core indicators were qualified as "regional"; units that met all core indicators together with more than 50% of the secondary indicators received a rating of "excellence." Using the selected QoC core indicators for certifying IBD units, a network of IBD quality care units covering the majority of IBD patients in China was established.

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Keywords: Quality of care; Inflammatory bowel disease; Inflammatory bowel disease quality care evaluation center; Core indicators

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Introduction

Inflammatory bowel disease (IBD) is a chronic intestinal inflammatory disorder that includes ulcerative colitis (UC) and Crohn's disease (CD). It predominantly affects young adults and is characterized by diverse clinical manifestations, a protracted clinical course and a high incidence of complications. The common diagnostic methods for IBD include assessments of clinical history and symptoms, physical examination, laboratory assessments, imaging and endoscopy. Aminosalicylates, corticosteroids, immunosuppressants and biologics have been used to treat IBD. However, due to the lack of standardized management and precision medicine, IBD impairs patients' quality of life, and imposes a great economic burden on the patient's family and society. The incidence of IBD has significantly increased in developing areas and has become a noticeable problem in clinical practice.

Europe and America have released guidelines for the diagnosis and treatment of IBD patients in recent years.[1,2] In China, national guidelines for quality indicators for IBD were promulgated in 2016 and 2017,[3,4] which established the foundation for an evaluation and guidance system for the diagnosis and treatment of IBD. It is acknowledged that a high quality of care promotes the remission of patients with IBD, and Calvet et al. set the first consensus on quality standards for IBD care units.[5] In 2021, a certification program of evaluating the IBD integral care units was established in Spain, this study assessed 53 IBD care units through 53 quality indicators related to structure, process and results, and audited the certifications of these units as "advanced" or "excellence". The results showed that more than 90% of IBD units in Spain received the certification.[6] To establish a practical evaluation system for IBD centers, in accordance with China's present situation, the Inflammatory Bowel Disease Quality of Care Center (IBDQCC) committee, Chinese Society of IBD, and Chinese Society of Gastroenterology, Chinese Medical Association assigned IBD experts and identified

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indicators for an evaluation and guidance system for diagnostic and therapeutic quality at IBD centers.

Methods

Development of the expert committee

Experts in IBD were selected from hospitals that were capable of establishing IBDQCCs in different regions of China; to improve the international applicability of the indicators, we invited two experts from Columbia University and the University of Chicago in the United States, as well as an expert from Sheba Medical Center in Israel. All experts were from the Chinese Society of IBD (CSIBD), Chinese Society of Gastroenterology (CSG), Chinese Crohn's and Colitis Foundation (CCCF), and have published research on IBD. Finally, our expert group included 32 gastroenterologists, one surgeon, one pathologist, and one endoscopist. Further, we invited seven experts from the Chinese IBD Elite Union including seven largest IBD centers in China with >20,000 IBD patients who were committed to the IBD field and had professional statistical knowledge to form the secretariat.

Selection of quality indicators

An extensive literature search was performed on Pubmed and Chinese National Knowledge Infrastructure (CNKI) according to the following criteria: studies with full text; reviews and articles published within the last five years; search terms containing "inflammatory bowel disease," "quality," "diagnosis," "therapy," "care," "European Crohn's and Colitis Organization (ECCO)," and "China." Potential quality indicators were selected and added to the initial questionnaire. These indicators were reviewed and recollected into a comprehensive list if they complied with two requirements: (a) they can be quantified for subsequent evaluation of the results in IBDQCCs, (b) they should be accessible in most Chinese IBD centers based on the infrastructure and health care resources.

The certification process

A Delphi-style process was performed among the secretariat and panelists to rate the importance of each indicator on a three-point scale: *essential, desirable*, and *not important*.[5,7] The committee predefined the grade of indicators according to the scores: those from 7 to 9 indicated "essential" from 4 to 6 indicated "desirable" and from 1 to 3 were rated as "not important". In the first round, the secretariat gave anonymous ratings to each indicator on a scale of 1 to 9, and the indicators with a score of 7 to 9 were tentatively defined as core indicators, while those with a score of 4 to 6 were considered as secondary indicators. In the second round, 35 experts independently voted the core indicators in the previous step to determine whether they met the criteria for core indicators. The inter-rater variability with Fleiss' kappa coefficient was used to assess the consistency of experts' agreement for indicators, and the agreement was confirmed "good" with a score of 0.71, and the indicators with more than 70% pass rate were ultimately defined as core indicators. A flowchart of the process of voting and certifying regional IBD units is shown in Figure 1. The proposed manuscript meets most of the criteria for reporting, as specified in the GIN-McMaster and AGREE II checklists. Supplementary Tables 1 and 2 summarizes where each checklist domain has been covered in the manuscript.[8,9]

Search strategy and selection criteria

Search strategy and selection criteria Data for this Review were identified by searches of Pubmed, Current Contents, Chinese National Knowledge Infrastructure (CNKI), and references from relevant articles using the search terms "inflammatory bowel disease", "quality", "diagnosis," "therapy," "care," "European Crohn's and Colitis Organization (ECCO)," and "China." Abstracts and reports from meetings were included only when they related directly to previously published work. Only articles published within the last five years were included.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the article, or the decision to submit for publication.

Results

This system proposes 28 core indicators and 13 secondary indicators to increase the homogeneity of the diagnostic and therapeutic qualities of IBD (Table 1). The IBDQCC committee identified regional clinical centers that satisfied all core indicators and met the needs of medical treatment for IBD. In addition, we defined "excellence" for clinical centers by their adherence to all core indicators as well as at least 50% of the secondary indicators, and their ability to receive referrals of complicated patients, train physicians, and conduct clinical research.

Basic staffing and infrastructure indicators

Core indicators that reached consensus and their agreements on basic staffing and infrastructure are presented in Table 2.

Multidisciplinary teams. Although gastroenterologists are intuitively assumed to play a vital role in the

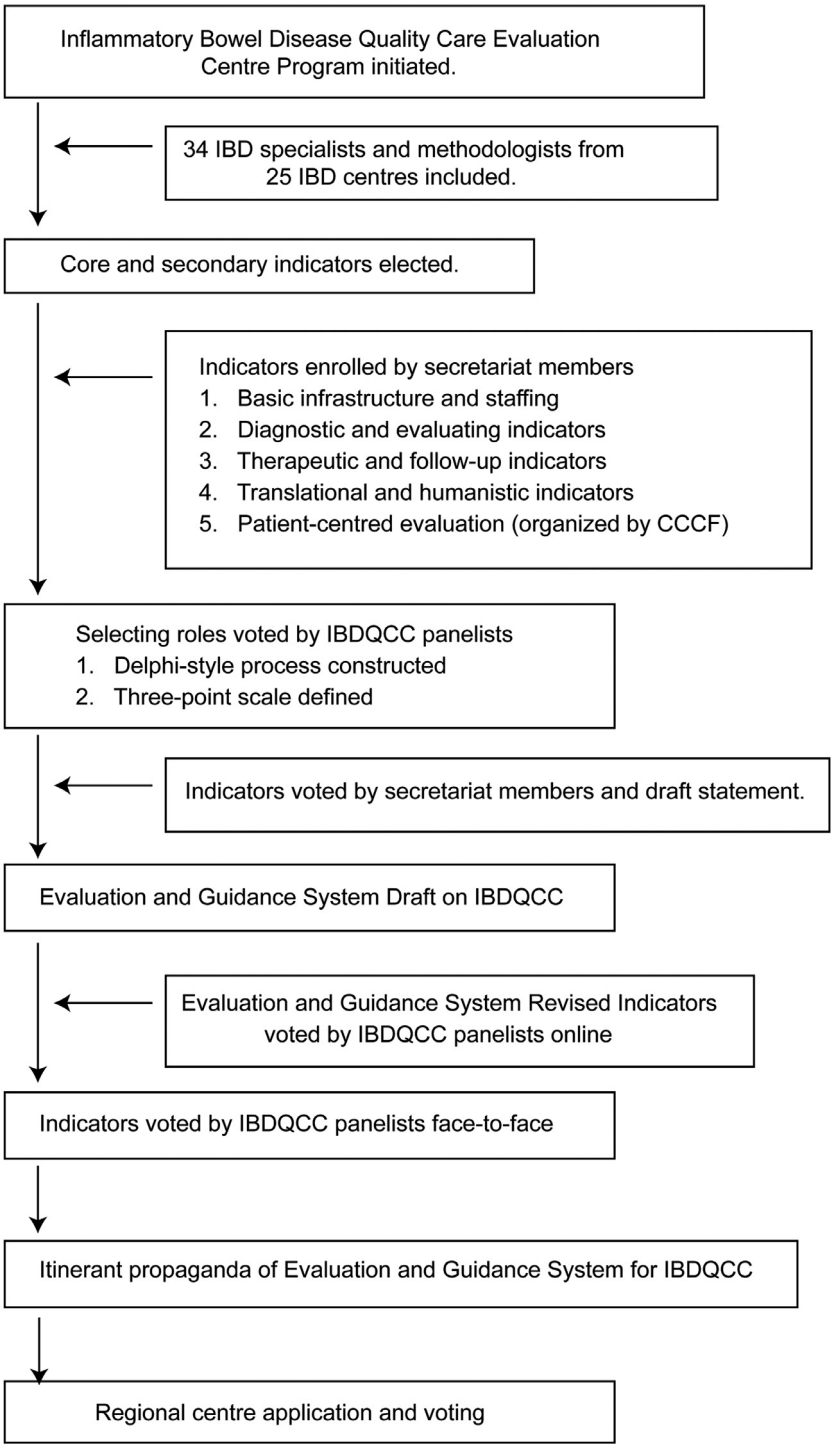

Figure 1. Flowchart of evaluation and guidance system for inflammatory bowel disease quality care evaluation centre (IBDQCC) construction and regional center application and voting created by the authors.

Core indicators	
Statement 1	1. IBD center should have a fixed MDT including gastroenterologists, surgeons, radiologists, pathologists, pharmacists, psychologists, obstetricians, gynecologists, and pediatricians to handle special cases. The team holds multidisciplinary case discussion regularly at least twice a month
Statement 2	2. IBD center has a fixed clinical dietitian.
Statement 3	3. IBD center should have specialized nurses.
Statement 4	4. Specialized outpatient unit is necessary in IBD center.
Statement 5	5. IBD centers require a relatively fixed and reasonable number of hospital beds or specialized wards for IBD patients.
Statement 6	6. All centers should have an electronic database.
Statement 7	7. In these evaluation centers, standard operating procedure (SOP), including standardized screening, biological agent infusion process is necessary.
Statement 8	8. Capsule endoscopy and enteroscopy should be the regular routine examination items.
Statement 9	9. IBD centers should make computed tomography enterography (CTE), magnetic resonance enterograghy (MRE), and MR on the pelvic and fistula as routine examinations.
Statement 10	10. The examination of stool routine and stool incubation is essential before the diagnosis of initial UC.
Statement 11	11. IBD evaluation centers should have a system of diagnosis and treatment to exclude ITB, including tuberculin skin test (TST), mixed lymphocyte culture (MLC) + T-Spot, chest CT, acid-fast staining technique for diseased tissues.
Statement 12	12. IBD centers should have the detection technology of Clostridium difficile infection (CDI).
Statement 13	13. IBD centers perform routine screening for hepatitis virus infection, including hepatitis B virus surface marker and HBV DNA detection, hepatitis C virus (HCV) antibody assay.
Statement 14	14. IBD centers should have an ability to perform blood cytomegalovirus (CMV) DNA test and immune histochemistry (IHC) of cytomegalovirus in tissue routinely.
Statement 15	15. All the patients signed the informed consent before using immunoregulatory drugs.
Statement 16	16. Detection of TPMT and/or NUDTI5 polymorphism is required in IBD centers.
Statement 17	17. Patients with latent tuberculosis (TB) should receive anti-tuberculosis treatment routinely, combined with glucocorticoids, immunosuppressants and biological reagents therapy.
Statement 18	18. Patients with hepatitis B surface antigen (HBsAg) positive should be given anti-virus therapy before treating with glucocorticoids, immunosuppressants and biological reagents.
Statement 19	19. The use and withdraw of glucocorticoids should according to guidelines, do not use glucocorticoids for maintenance treatment.
Statement 20	20. Immunosuppressants and biological reagents should be used in steroid-dependent (SD) and steroid-resistant (SR) patients, and all IBD centers have an experience with second-line immunosuppressants or biologics.
Statement 21	21. IBD centers should have an ability to handle pregnancy in patients with IBD, including the experience with glucocorticoids, immunosuppressants or biologics.
Statement 22	22. IBD centers should have an ability to perform the endoscopic treatment of IBD, such as the dilatation of stricture, stricturotomy and the setting of ileus tube.
Statement 23	23. IBD centers have to be capable of evaluating the surgical indications and complications, as well as the experience on perioperative managements of patients with IBD.
Statement 24	24. There must be a special person responsible for stoma and nutrition tube care, and IBD centers should have an ability to formulate and use biological agents.
Statement 25	25. IBD centers should have a continuous follow-up plan and each patient has follow-up paper materials or electronic documents.
Statement 26	26. IBD centers should have plans and operation procedures of cancer surveillance according to related guidelines.
Statement 27	27. IBD centers should have a capacity of training for junior hospital and specialists in IBD: regional centers require the ability of training for specialists in IBD; excellent centers should not only offer guidance to the junior centers or hospitals of diagnosis and treatment of IBD, but carry out training for novel knowledge and skills.
Statement 28	28. IBD centers should carry out patient education activities regularly, establish reasonable contact information and online communication channels, in addition, provide the patients with popular science information and cards with the address, telephone number and visit time of IBD centers.
Secondary indicators	
Statement 1	1. The diagnosis and treatment center of IBD covers at least one province or municipality.
Statement 2	2. The IBD center has two kinds of doctors among clinical pharmacists, psychologists, pediatricians and gynecologists.
Statement 3	3. There are standardized assessment scales used to evaluate the quality of life, mental state and nutritional status.
Statement 4	4. Skilled in the remedial treatments after the failure of intravenous glucocorticoid of acute severe UC, including cyclosporine, biologics, and surgery.
Statement 5	

Table 1 *(Continued)*

Core indicators	
	5. Carry out parenteral nutrition (PN), enteral nutrition (EN), intravenous iron, anticoagulant therapy, prevention of osteoporosis, and leukocyte adsorption therapy routinely.
Statement 6	6. IBD centers should have a routine determination of drug concentration and surveillance of adverse drug events based on the standardization system.
Statement 7	7. Two years surgery rate of neither narrow nor penetrating patients at their first visit should be less than 20%.
Statement 8	8. The mortality of acute severe UC should be below 5% in regional IBD centers, while lower than 2% in excellent centers.
Statement 9	9. The postoperative recurrence rate in CD of anastomotic stoma under endoscope should be below 10%.
Statement 10	10. The reoperation rate in patients with CD should lower than 10% within 1 year after surgery.
Statement 11	11. The missing rate of follow-ups should be below 10% after one year.
Statement 12	12. The missing rate of follow-ups should be below 20% after two years.
Statement 13	13. Newly diagnosed patients should have a routine screening of Mold, syphilis, human immunodeficiency virus combined with endoscopic performance.

***Table 1*: Core indicators and secondary indicators created by the authors.**

Statements	Agreement rate, 100%
1. IBD center should have a fixed MDT that including gastroenterologists and surgeons, radiologists, pathologist, pharmacist, psychologist, obstetricians and gynecologist, and pediatrician to handle special cases. The team holds multidisciplinary case discussion regularly at least twice a month.	100
2. IBD center has a fixed clinical dietitian.	77
3. IBD center should have specialized nurses.	80
4. Specialized outpatient unit is necessary in IBD center.	100
5. IBD centers require a relatively fixed and reasonable number of hospital beds or specialized wards for IBD patients.	71
6. All centers should have an electronic database.	91
7. In these evaluation centers, standard operating procedure (SOP), including standardized screening, biological agent infusion process is necessary.	100
8. Capsule endoscopy and enteroscopy should be the regular routine examination items.	100
9. IBD centers should make computed tomography enterography (CTE), magnetic resonance enterograghy (MRE), and MR on the pelvic and fistula as routine examinations.	86

***Table 2*: Consensus indicators about the basic staffing and infrastructure.**

diagnosis and treatment of IBD, an IBD team should ideally also involve radiologists, pathologists, and surgeons to optimize disease management.[10] European expert recommendations suggest the development of MDTs with specifically defined specialist expertise in IBD, to implement processes that facilitate cross-functional communication and to invest in shared care models of IBD management.[2] A retrospective review of 166 MDT cases found that they may facilitate complex decision-making in the management of IBD and that the success of MDTs in shaping oncological practice could be used to push for their adoption in the realm of IBD.[11] MDTs are considered to provide the best care for patients with IBD, and the IBD MDT meeting allows for multidisciplinary consideration of complex cases and/or diagnostic dilemmas to create a clear care plan, as well as appropriate correspondence regarding clinical decisions to general practitioners and patients.[12] Although MDTs can improve the quality of care for IBD, different care models may be required in different healthcare settings, and these models may work differently based on arrangements with payer(s) within a given region.[13,14]

Fixed clinical nutritionists. Malnutrition has proven to be a common complication of IBD as a result of inflammation, diarrhea, anorexia, corticosteroid use or previous intestinal resection.[15] Approximately, half of the patients with IBD show malnutrition, including high prevalence of inadequate iron, vitamin D, vitamin E, vitamin A, calcium, folate, and vitamin C consumption. Malnutrition leads to poor quality of life and higher health care costs.[16–18] In one survey, although most patients reported problems with food and nutrition, less than half had seen a dietitian for tailored nutritional advice to address these problems, highlighting the need for clinical nutritionists in IBD centers.[19] Several

studies have verified the validity of dietary therapy in the management of IBD.[20,21] Levine et al. confirmed the effect of the Crohn's disease exclusion diet with or without partial enteral nutrition in children and adults with mild-to-moderate CD.[22,23] However, many patients adopt restrictive diets that increase the risk of micronutrient deficiencies, and a routine dietitian review can prevent this occurrence.[24] ECCO has identified the role of diet and nutrition in the etiology and management of IBD, and suggested that nutritionists are integral members of MDTs for IBD.[25] We consider that clinical dietitians play an important role in IBD centers, and require the ability to apply and publish subjects.

Specialist nurses. Specialized nursing for IBD has emerged recently because IBD management is increasingly being concentrated in units with expertise in the condition leading to substantial improvement in outcomes. Nurses are the first point of contact for patients as they accompany the patient and provide advice, support, and education to the patients and their families to help them develop an understanding of the pathophysiology and treatment strategies for IBD. The N-ECCO consensus stated that IBD nurses should not only have a good conceptual understanding of IBD, but also an awareness of other patients' requirements, including fistulous IBD, diet and nutrition, incontinence, sexuality, fatigue, and pain management.[26] Two retrospective studies identified the effects of IBD nurses on the quality of delivered care, and the results showed that IBD nurses reduced presentations to the emergency rooms and clinic visits, and improved patient compliance by providing advice and psychosocial support. Furthermore, IBD nurses play an important role in therapeutic monitoring and association with other departments, and also provide efficient triaging of those who show aggravation by either phone management with a rapid clinic review if required, or by streamlining admission, which helps save doctors' time.[27,28] An international survey of IBD health professionals showed that the majority of respondents considered IBD nurses as providers of direct patient care, the first point of contact for patients, educators, administrators of biologics, and providers of social support.[29] Therefore, we recognized the need for specialist nurses in IBD centers.

Specialist IBD clinics. Specialist clinics are outpatient services that are divided according to specific diseases or symptoms, and constitute a new medical service mode centered on patients' disease demands. A British systematic search showed that despite the increase in the incidence of IBD only 29.9% of all patients were definitively under specialist care.[30] A retrospective control study compared specialist IBD clinics with general gastroenterology clinics using six criteria. The results showed that a specialist IBD clinic could provide more timely blood tests during the management of IBD, and patients in specialist IBD clinics had better outcomes, suggesting that specialist IBD clinics provided better care than non-specialist general gastroenterology clinics.[31] We recommend establishing more efficient and scientific specialist IBD clinics, that can integrate multiple related departments, and provide patients with a "one-stop "service and individualized treatment.

Specialized wards or units with electronic databases. The IBD center of excellence may require more than 1200 IBD hospital admissions per year, as well as relatively independent wards or medical teams. The IBDQCC committee believes that IBD wards or IBD patients account for more than 80% of all patients.

All centers should have an electronic database built with IBD as a single disease, independent of the hospital system, such as the HIS and PACS. In addition, this database in excellence centers should allow tracing of the physical locations of biological samples, such as blood, tissue, and stool. The IBD database can facilitate standardized and systematic management of various case characteristics, promote clinical retrospective studies, and provide assistance for clinical diagnosis and treatment.

Standard operating procedures, checklist systems and screening. Standard operating procedures (SOPs), including standardized processes for screening and biological agent infusion, are essential for IBD centers. Moreover, excellence centers also require at least one standardized checklist system, which may include a clinical index checklist, an imaging checklist, and a pathological diagnosis checklist.

Novel endoscopic imaging techniques have emerged in recent years, including capsule endoscopy (CE) and enteroscopy, which can facilitate both the diagnosis and characterization of IBD, detection of dysplasia, and assessment of mucosal healing.[32,33] Capsule endoscopy (CE) enables excellent visualization of the small bowel mucosa, and is a valuable tool for the diagnosis of obscure CD, monitoring of disease activity, and detection of complications.[34] Furthermore, CE plays an important role in the evaluation of treatment and the recurrence of IBD.[35,36] A multicenter retrospective study in the United States evaluated the use of double-balloon enteroscopy (DBE) in the diagnosis and its impact on patient management in known and suspected CD, and found that DBE can be more effective than radiology studies for diagnosing IBD.[37] ACG clinical guidelines recommend that video CE is a useful adjunct in the diagnosis of small-bowel CD in patients with a high index of suspicion of disease. Deep enteroscopy is not a part of routine diagnostic testing in patients with

Statements	Agreement rate, 100%
1. The examination of stool routine and stool incubation is essential before the diagnosis of initial UC.	100
2. IBD evaluation centers should have a system of diagnosis and treatment to exclude ITB, including tuberculin skin test (TST), mixed lymphocyte culture (MLC) + T-Spot, chest CT, acid-fast staining technique for diseased tissues.	100
3. IBD centers should have the detection technology of Clostridium difficile infection (CDI).	86
4. Routine screening for hepatitis virus infection, including hepatitis B virus surface marker and HBV DNA detection, hepatitis C virus (HCV) antibody assay.	89
5. IBD centers should have an ability to perform blood cytomegalovirus (CMV) DNA test and immune histochemistry (IHC) of cytomegalovirus in tissue routinely.	83

***Table 3*: Consensus indicators about the diagnosis and evaluation of IBD.**

suspected CD, but may provide additional information in patients who require biopsy/sampling of small bowel tissue for diagnosis.[38] Therefore, we suggest that CE and enteroscopy should be regular routine examination items in IBD centers.

Two prospective studies showed that MRE and CTE have similar sensitivities for detecting active small-bowel inflammation.[39,40] A systematic review with meta-analysis identified that MRE had high sensitivity and specificity for the signs of intestinal inflammation and damage, such as mucosal lesions, abscess and fistula.[41] Researchers also found several risk factors for high radiation exposure, including young age, upper gastrointestinal tract involvement, ileo-colonic disease, corticosteroid use and IBD-related surgery.[42,43] As the potentially carcinogenic impact of high radiation may be relevant to patients with IBD, who are at increased risk of developing gastrointestinal carcinoma and tumors of the liver or biliary tract, and carry a significant excess risk of developing small bowel lymphoma, MRE should be used preferentially in these patients.[38] Perianal diseases such as fistulas and perirectal abscesses are common complications of IBD, and some studies have proven that perianal MRI could provide accurate information on the activity of perianal diseases.[44,45] Thus, we recommend that all IBD centers should include CTE, MRE, and perianal MRI as routine examinations, especially at the time of initial differential diagnosis.

Diagnosis and evaluation indicators

The core indicators that reached consensus and their agreement about the diagnosis and evaluation of IBD are presented in Table 3.

Routine stool examination and fecal pathogen culture. IBD shares clinical symptoms with irritable bowel syndrome (IBS) and infectious enteritis, such as abdominal pain, diarrhea and altered bowel habits.[46] For accurate and prompt diagnosis of IBD, routine examination of stool and stool cultures is essential, especially in cases with initial UC. Several studies have shown that fecal calprotein (FC) and lactoferrin are highly sensitive for distinguishing IBD and IBS, and that the levels of FC and lactoferrin were significantly higher in patients with IBD than in those with IBS or healthy people.[47,48] However, as indicators of inflammation, the levels of these markers may also be increased in infectious enteritis and colitis. The most common pathogen in enteric infections is *Clostridium difficile* followed by *Escherichia. coli*.[49] To exclude infections, fecal pathogen culture should be obtained at the first visit. In some potential high-risk areas, it is a routine test to screen certain parasites such as schistosomes and endemic amebiasis. To improve the accuracy of diagnosis, routine examination of stool and stool culture is essential before the diagnosis of initial UC.

Exclusion of intestinal tuberculosis and clostridium difficile and virus infections. IBD and intestinal tuberculosis (ITB) have similar clinical, radiological, endoscopic, and pathological features, such as abdominal pain, diarrhea, and intestinal ulcerations. However, their treatments are quite different; the commonly used therapeutic agents for IBD are immunosuppressants, which can exacerbate ITB; misdiagnosing IBD as ITB may delay the treatment, which could have serious consequences such as intestinal obstruction and toxic megacolon.[50–52] To avoid these outcomes, IBD centers should have the ability to differentiate between ITB and IBD. Chest radiography is insufficient for high-risk areas because of its low detection rate.

Surveys have shown that the prevalence of Clostridium difficile infection (CDI) is higher in patients with IBD than in those without IBD, especially in those with UC.[53] CDI is associated with increased hospitalization, morbidity, and mortality in IBD; additionally, it may necessitate escalation of therapy and colectomy.[54,55] The increasing incidence of CDI in IBD may be due to an imbalance of intestinal bacteria and a loss of colonization resistance against *C. difficile*.[56] Due to the poor outcomes of CDI in IBD, it should be detected early, and

treated with escalation or de-escalation of immunosuppressants along with appropriate antibiotics, such as vancomycin.[57] We suggest that all IBD centers should test patients who present with an aggravation of underlying IBD for CDI and patients should be tested for recurrent CDI if diarrhea or other symptoms of colitis persist or return after antibiotic treatment.

Previous studies in Europe and America showed that patients with IBD had a higher risk of HBV and HCV infections than those without IBD.[58–60] The prevalence of HBV and HCV infection is high in China. A retrospective study showed that the incidence of HBV and HCV infections in China was significantly higher than that reported previously in some cohorts of patients with IBD from Europe and America.[61] Blood transfusions have been proven to increase the risk of HBV and HCV infection, while the influence of surgical procedures, colonoscopies, and intravenous drug abuse has remained obscure.[59] Remarkably, one study showed that infliximab treatment may be associated with HBV reactivation and could be followed by a flare or exacerbation of disease when therapy is discontinued, suggesting that patients with IBD should be tested for HBV serological markers before treatment.[62] A retrospective study in China revealed that the incidence of HBV infection in patients with IBD was higher than that in patients without IBD, and that the prevalence of HCV infection in IBD patients was slightly increased; however, only a small proportion of IBD patients received effective vaccinations.[61] The American College of Gastroenterology (ACG) guidelines also recommend that every IBD patient lacking HBV immunity should be immunized with hepatitis B vaccine, especially before the start of anti-tumor necrosis factor (anti-TNF) therapy, and should undergo regular evaluations of the anti-HBs titer to confirm immunity.[63] We recommend routine HBV and HCV testing in all IBD centers to detect and treat HBV and HCV infections early.

Cytomegalovirus (CMV) is an opportunistic infectious agent in patients with IBD, and several studies have been conducted to identify the prevalence of CMV infection in IBD in recent years, with reported incidence rates ranging from 4.5% to 16.6%.[64–69] Notably, CMV has been verified to be linked to the severity and activity of IBD, and CMV infection may exacerbate the course of IBD. Moreover, CMV reactivation should be considered in patients with refractory IBD who either fail to respond to immunosuppressive therapy or experience worsening of symptoms despite therapy.[70,71] Due to the similarity of clinical symptoms and endoscopic features between CMV-induced colitis and CMV infection in UC patients, a gold standard for diagnosis is required.[72] Immunohistochemistry (IHC) performed on colon biopsy specimens with monoclonal antibodies directed against CMV immediate early antigen is considered the current gold standard for diagnosis.[73] As the prevalence of CMV has been recognized to be related to IBD, the outcome for patients with CMV appears worse during steroid and immunosuppressive therapy.[74] We suggest that IHC and CMV DNA detection should be performed regularly.

Statements	Agreement rate, 100%
1. All the patients signed the informed consent before using immunoregulatory drugs.	100
2. Detection of TPMT and/or NUDTI5 polymorphism is required in IBD centers.	86
3. Patients with latent tuberculosis (TB) should receive anti-tuberculosis treatment routinely, combined with glucocorticoids, immunosuppressants and biological reagents therapy.	91
4. Patients with hepatitis B surface antigen (HBsAg) positive should be given anti-virus therapy before treating with glucocorticoids, immunosuppressants and biological reagents. Adult patients with IBD should receive HBV vaccination before anti-TNF therapy.	100
5. The use and withdraw of glucocorticoids should according to guidelines, do not use glucocorticoids for maintenance treatment.	100
6. Immunosuppressants and biological reagents should be used in steroid-dependent (SD) and steroid-resistant (SR) patients, and all IBD centers have an experience with second-line immunosuppressants or biologics.	94
7. IBD centers should have an ability to handle pregnancy in patients with IBD, including the experience with glucocorticoids, immunosuppressants or biologics.	91
8. IBD centers should have an ability to perform the endoscopic treatment of IBD, such as the dilatation of stricture, stricturotomy and the setting of ileus tube.	100
9. IBD centers have to be capable of evaluating the surgical indications and complications, as well as the experience on perioperative managements of patients with IBD.	94
10. There must be a special person responsible for stoma and nutrition tube care, and IBD centers should have an ability to formulate and use biological agents.	71

***Table 4*: Consensus indicators about the treatment of IBD.**

Statements	Agreement rate, 100%
1. Having a continuous follow-up plan and each patient has follow-up paper materials or electronic documents.	86
2. Having plans and operation procedures of cancer surveillance according to related guidelines.	80
3. Having a capacity of training for junior hospital and specialists in IBD: regional centers require the ability of training for specialists in IBD; excellent centers should not only offer guidance to the junior centers or hospitals of diagnosis and treatment of IBD, but carry out training for novel knowledge and skills.	77
4. Patient education and communication: carry out patient education activities regularly, establish reasonable contact information and online communication channels, in addition, provide the patients with popular science information and cards with the address, telephone number and visit time of IBD centers.	89

***Table 5*: Consensus indicators about follow-up and humanities management.**

Evaluation indicators of treatment: standardization of treatment

Consensus statements regarding the treatment of IBD and agreement rates are shown in Table 4.

Ethical issues. Although immunoregulatory drugs including azathioprine or 6-mercaptopurine, methotrexate, cyclosporine, tacrolimus, thalidomide, and biological agents show therapeutic effects against IBD, they also have certain side effects.[75] The adverse effects of azathioprine and 6-mercaptopurine include allergic reactions, pancreatitis, myelosuppression, nausea, infections, hepatotoxicity, and malignancy, especially non-melanoma skin cancer and lymphoma, and methotrexate has similar adverse effects including nausea and vomiting, hepatotoxicity, pulmonary toxicity, bone marrow suppression, skin cancer, and lymphoma.[76,77] The common adverse effects of tacrolimus include tremors, paresthesia, and headache. More rarely, nephrotoxicity can be a serious adverse effect of tacrolimus and cyclosporine.[78,79] As the preferred drugs for IBD, biological agents such as anti-TNF may increase the potential risk of infection and malignancy.[75] Considering these adverse effects, we suggest that all patients should sign informed consent forms before treatment in IBD centers.

Detection of genetic variations of thiopurine. Thiopurines containing azathioprine and its active metabolite, mercaptopurine are widely used in the treatment of IBD, and their efficiency in remission maintenance is unclear. However, some common adverse events may still preclude further administration or be life-threatening.[80] Some studies have shown that the incidence of side effects of thiopurine, especially thiopurine-induced leukopenia, ranged from 23.8% to 35.4% in Asian countries.[81–83] As a result, the potential risks should be detected before thiopurine therapy. Genetic variations in thiopurine s-methyltransferase (TPMT) and nudix hydrolase 15 (NUDT15) have already been linked to myelotoxicity by regulating enzyme activity.[82,84] The American Gastroenterological Association Institute suggested that the TPMT genotype or enzyme activity should be detected routinely before initiation of therapy with either AZA or 6-MP.[85] Recent studies in our country have shown that the NUDT15 polymorphism is a better predictor of thiopurine-induced myelotoxicity than TPMT.[83,86] Therefore, we propose that polymorphisms of TPMT and/or NUDT15 should be routinely monitored in all IBD centers.

Prevention of concomitant infections. Latent TB should be considered in patients with a history of recent exposure to the disease, positive initial tuberculin skin test (TST), positive booster TST or IGRA test and no radiological evidence of active TB.[87,88] As effective therapeutic agents for IBD, glucocorticoids, immunosuppressants, and biological agents may increase the risk of TB infection, decrease the positive rate of diagnosis, and cause more severe outcomes due to their effects on immune function.[89,90] Therefore, ECCO suggested that patients should be screened for TB before treatment for IBD, and serial tuberculin skin tests (TST) may improve the detection of latent TB infection in patients with IBD.[91,92] TB chemoprophylaxis regimens are based on treatment with isoniazid (INH) for 6–9 months.[93–95] In conclusion, we recommend that patients should be screened for TB, and treated for latent TB before the initial therapy for IBD.

Researchers have also proposed that HBV treatment should be administered before the initiation of immunosuppressive therapies.[96] Recently, studies have shownthat the immunosuppressants used for IBD including corticosteroids, immunomodulators, and/or anti-TNF might increase the risk of HBV infection and reactivation. In addition, immunosuppressants are independent predictors of liver dysfunction and result in liver failure and even death in patients with IBD and HBVsAg (+).[97,98] To avoid poor outcomes, HBVsAg (+) IBD patients should be treated in a timely manner. ECCO proposed that before, during and for at least 12 months after immunomodulator treatment has ceased, patients who are HBsAg-positive (chronic HBV

infection) should receive potent antiviral agents, and antiviral therapy should be continued until HBV DNA ≤ 2000 IU/mL.[91] Nucleotide/nucleoside analogs are considered the first-choice agents for antiviral treatment in HBsAg (+) patients.[99,100] Entecavir and tenofovir have been shown to be the preferred drugs because of their rapid onset of action, high antiviral potency, and low incidence of resistance.[101,102] We suggest that HBsAg-positive patients should be administered antiviral therapy before immunosuppressive treatment and antiviral therapy should continue for at least 12 months after the cessation of immunosuppressants. Furthermore, adult patients with IBD should receive HBV nonlive vaccines before anti-TNF therapy according to the guidelines of the American College of Gastroenterology.[63]

Use and withdraw glucocorticoid regimens. Glucocorticoids play a vital role in the induction of remission in moderate-to-severe IBD.[103] However, glucocorticoid-related side effects are common and range from cosmetic to life-threatening.[104] At present, the recommended treatment strategy for traditional steroids is 1 mg/kg/day of prednisone equivalents (max 60 mg/day) followed by tapering, which involves reducing dosages above 30 mg daily in 10 mg steps per week and reducing dosages of 30 mg daily and below in 5 mg steps per week for 12–16 weeks.[85,105,106] Glucocorticoids are not recommended as maintenance treatment for IBD; a Cochrane review demonstrated that they are no better than placebo in preventing relapse.[85,107] Therefore, we do not recommend the use of glucocorticoids as maintenance therapy.

Immunosuppressants or biologics. A steroid-dependent (SD) status is defined as the inability to discontinue corticosteroids without experiencing a symptomatic relapse, while patients whose disease remains uncontrolled on 1 mg/kg prednisolone daily and who require additional immunosuppressive agents to adequately control disease activity or patients who do not respond to immunosuppressive drugs should be considered as steroid-resistant (SR).[108] Purine analogs, such as azathioprine, mercaptopurine, and methotrexate, have been shown to be effective and preferred in SD/SR patients with IBD. Additionally, cyclosporine and anti-TNF can be considered as second-line therapies.[75,109–111] ECCO proposed that patients who are steroid-dependent or steroid-resistant should be treated with azathioprine/mercaptopurine as first-line therapy, and methotrexate can be considered if purine analogs are ineffective or the patients cannot tolerate them, as a second-line treatment, biologics such as infliximab may be administered when the above treatments fail and the patients do not show septic complications.[112,113] In order to improve the effects of treatment, we recommend that IBD centers should be able to promptly identify and manage patients with steroid-dependent or steroid-resistant IBD.

Management of pregnant patients with IBD. Epidemiological information shows notable variations in the incidence of IBD between sexes, and most women are diagnosed with IBD during the reproductive years.[114,115] Pregnancy may increase the risk of adverse outcomes in patients with IBD, including prematurity, low birth weight, cesarean section, and congenital abnormalities.[116] A recent study also found that pregnancy was associated with an increased risk of new-onset psychiatric disorders.[117] Proper management of IBD is important for improving the poor prognosis of pregnancy, and remission of IBD has been verified to be beneficial to pregnancy outcomes.[118] Various studies have been conducted on the safety and effectiveness of drugs in pregnant patients, and the results identified biologics and azathioprine as the preferred therapeutic agents. With the exception of methotrexate and thalidomide, most medications used to treat IBD are considered low-risk and may continue during pregnancy.[114,119–121] Although novel drugs such as vedolizumab have emerged their safety requires confirmation.[122]

Endoscopic and surgical treatment. A majority of IBD patients may show common complications, such as stricture, fistula, abscess, and some may even develop obstruction and colitis-associated neoplasia (CAN). Endoscopic therapy has emerged as an effective, feasible, and well-tolerated treatment for these complications.[123,124] Endoscopic therapy plays a vital role in stricture, while endoscopic balloon dilation showed high rates of short-term and long-term technical and clinical efficacies in comparison with surgery; however, this treatment requires experienced endoscopists.[125,126] Endoscopic therapy can be used not only for strictures, but also for fistulas, and ileus.[127] CAN may develop in patients with longstanding IBD, and the SCENIC consensus suggests that lesions can be ablated through endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD).[128] As a result, it is important for IBD centers to master endoscopic technology.

ECCO recommends that surgery should always be considered as an option for localized disease, and emergency surgery should be performed for life-threatening complications, such as intestinal perforation, refractory bleeding, or toxic megacolon, while elective surgery is indicated for patients with dysplasia or malignancy, a refractory disease course, or intolerance to long-term immunosuppression or other pharmacological therapies. Laparoscopy should be the preferred option when

necessary.[129] Several risk factors have been proposed to be associated with postoperative complications, such as nutritional status, medication use, disease behavior, duration of disease, prior operations and perioperative bleeding.[130–132] The nutritional status should be optimized disease locations should be assessed before surgery, and the principles of enhanced recovery should be applied in postoperative care.[129,133]

Evaluation indicators of follow-up and humanities management

Consensus statements and agreement rates regarding follow-up and humanities management are shown in Table 5.

Follow-up plans. Consecutive follow-up can prevent the incidence of complications, change patients' behavior and promote their quality of life, and close follow-up may yield good results by improving the quality of healthcare and establishing a harmonious doctor-patient relationship. However, the current status of follow-up in our country is not encouraging due to the insufficient understanding of the importance of follow-up, low compliance of patients, and poor quality of follow-up. We advise IBD centers to establish a consecutive, complete, and standardized follow-up plan.

IBD has been linked to an increased risk of colorectal cancer (CRC) through dysplasia, which is the best marker of CRC in IBD.[134] Multiple studies have shown that colonoscopy is the first choice for CRC surveillance because of its safety and efficiency. The consensus of the Crohn's & Colitis Foundation of America has recommended criteria and intervals for colonoscopy in patients with IBD.[135] Subsequently, the AGA guidelines proposed the management of dysplasia discovered on surveillance colonoscopy for IBD.[134,136,137] We suggest that IBD doctors can refer to these guidelines and appropriately address cancer surveillance in IBD patients.

Training and education. Doctors in junior hospitals should receive training and knowledge updates at least twice a year, to meet the follow-up and medical consultation needs of patients at these hospitals. Training of these doctors and IBD specialists can not only improve medical quality, but also save significant healthcare resources. The existing systems for continuing medical education in IBD need to be transferred from tertiary hospitals or local medical centers to professional clinics and communities. Increasing diversity and a rapidly changing landscape for providers delivering care, treatment, and comprehensive quality care in IBD are emerging.[138] The main contents of training should cover everything from diagnosis and treatment, follow-up, and medical consultation, with the provision of an examination system after training.

At all IBD centers, patient education should be conducted more than four times a year, and the educational objectives: patient education should include patients and relatives, and establishment of effective contacts and online communication channels. Special attention should be given to measures that guide patients to deal with adverse drug reactions, and contact the core teams of the IBD centers in time. Excellence centers should provide patients with informative and accessible popular science handbooks, which clarify the characteristics of the centers, as well as cards with the center's address, phone number, and consultation hours. Patient education can improve compliance, relieve patients' negative mental states, reduce the fear of drugs and surgery, change unhealthy behaviors associated with IBD, and improve the physician-patient relationship.

Assessment of certification in IBDQCCs

To assess the implementation of this nationwide evaluation and guidance system for IBDQCCs, we audited 39 IBDQCCs in December2021. The results showed that there were 15 (38.34%) centers defined as "excellence center" which achieved all the core indicators and more than 50% of the secondary indicators, and 18 (46.15%) IBD units approached a certification grade of regional, while other 6 (15.38%) IBD center could not pass the assessment. The completion of each quality indicator revealed that all 28 core indicators were reached by more than 80% of the IBDQCCs. Only three secondary indicators were achieved in less than 50% centers; one was the coverage of IBDQCCs; two additional were related to the standardized assessment scales and anastomotic endoscopic recurrence rate, respectively.

Discussion

The incidence of IBD in China has increased significantly in recent years. Although many medical institutions have established IBD centers, the diagnosis and treatment process infrastructure, and humanized management are still not standardized.

The IBDQCC committee conducted the IBDQCC program with a steering committee to identify the QoC indicators. The 28 core and 13 secondary indicators covered various aspects. The first part focuses on basic staffing and infrastructure. The second area mainly concerns diagnostic indicators and the third aspect is related to the establishment of therapeutic indicators to standardize treatment; indicators of follow-up and human management are also crucial parts of this evaluation and guidance system, and all centers should have reasonable plans for follow-up and cancer surveillance. Training of doctors in junior hospitals and IBD

specialists, and patient education is necessary for all IBD centers.

Although this evaluation and guidance system will facilitate the homogeneity of IBD care assistance in China, there are some limitations to our study. First, these indicators were based on China's national situation, and our system may be difficult to extrapolate to other countries with different public health care systems. Second, the expert panelists were dominated by gastroenterologists, given their expertise in IBD and their central position in managing IBDQCC. In further studies, we aimed to develop a more comprehensive system based on a multidisciplinary team including surgeons, radiologists, and nurses in the IBD area. Furthermore, the assessment result of this system in 39 IBDQCCs was examined by the Chinese Health Promotion Foundation; hence, the specific completion of each indicator for each IBDQCC was unavailable. The last limitation was the lack of evaluation of patients with IBD.

This evaluation and guidance system provides operable evaluation indicators for the construction, management and evaluation of IBD centers and forms the standard operating process for the diagnosis and treatment of IBD in China. The indicators should help to improve the quality of care for patients with IBD and should be reconsidered and updated as appropriate when prospective long-term studies emerge.

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

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