Making a Case for Patient-Reported Outcomes in Clinical Inflammatory Bowel Disease Practice

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Patients seek medical care when they perceive a deterioration in their health. Gastroenterologists and health care providers are trained to seek out clinical, laboratory, radiologic, and endoscopic evidence of pathology. Conventional endpoints in inflammatory bowel disease (IBD) clinical trials and clinical care may fail to capture the full health status and disease experience from the patient perspective. The Food and Drug Administration (FDA) has called for the development of coprimary endpoints in research trials to include an objective measure of inflammation in conjunction with patient-reported outcomes (PROs). The objective is to support labelling claims and improve safety and effectiveness in the drug approval process.[1] There is also growing recognition that high-value care includes management of biologic and psychosocial factors to enable patients with chronic diseases to regain their health. Clinicians might follow suit by incorporating valid, reliable PRO measures to usual IBD care in order better to achieve patient-centered care, inform decision making, and improve the quality of the care provided.

What Are Patient-Reported Outcomes?

The FDA defines a PRO as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else."[2] PROs are used to measure various aspects of health including physical, emotional, or social domains. PROs have emerged as tools that may foster a better understanding of the patient's condition, which may go beyond disease activity or symptoms. In effect, incorporating PROs into clinical practice enables a model of "coproduction" of health care, and may contribute to a more reciprocal patient-provider interaction where the needs of the patient may be more fully understood and incorporated into decision-making that may lead to improved patient satisfaction and outcomes.[3,4]

There are hundreds of available PROs in gastroenterology,[5] ranging from simple (characterizing pain with a basic numeric rating scale) to complex multidomain, multi-item instruments. PROs may cover symptom assessment, health-related quality of life, adherence to and satisfaction with treatment, and may be generic or disease-specific. Numerous PROs have been developed for patients with IBD to better understand the varied ways health can be affected by the disease. Commonly used PROs in IBD include severity scales for pain, defecatory urgency, and bloody stool, and several disease-specific and generic instruments assessing different health-related quality-of-life domains have been used in research studies for patients with IBD.

The Current Approach to Patient-Centered Care for Inflammatory Bowel Disease Is Limited

IBD is a difficult disease to manage in-part because there is no known biomarker that accurately reflects the full spectrum of disease activity. Numerous indices have been developed to better quantify disease activity, measure response to treatment, and identify remission. Among the most frequently used indices in clinical trials are the Crohn's Disease Activity Index (CDAI) and (for ulcerative colitis [UC]) the Mayo Clinic Score. These endpoints incorporate signs and symptoms, laboratory findings (in the CDAI), and endoscopic assessments. The CDAI is a suboptimal instrument because of a lack of correlation with endoscopic inflammation and potential confounding with concomitant gastrointestinal illnesses, such as irritable bowel syndrome.[6] The Mayo Clinic Score is difficult to interpret because of some subjective elements (what is considered a normal number of stools

Abbreviations used in this paper: **CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; FDA, Food and Drug Administration; IBD, inflammatory bowel disease; PRO, patient-reported outcomes; PROMIS, Patient-Reported Outcomes Measurement Information System; UC, ulcerative colitis.**

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1542-3565/$36.00
https://doi.org/10.1016/j.cgh.2017.12.027

per day?); vagueness (mostly bloody stools more than half the time?); and it requires a physician assessment, which often does not correspond with the patient's perception of their disease.[7] From a research perspective, this disconnect can compromise the quality of trial data. Clinically, it can negatively impact patients' satisfaction of care and impair the patient-provider relationship.[8]

To that end, regulatory agencies, scientific bodies, and healthcare payors are shifting toward a more "patient-centered" approach with an emphasis on PROs. However, although the FDA is incorporating the patient perspective in its trials, measuring meaningful outcomes in day-to-day clinical care is challenging. In the absence of active inflammation, more than 30% of patients with IBD still suffer from gastrointestinal symptoms because of a myriad of reasons.[9] Furthermore, physicians frequently underestimate the impact of depression, anxiety, fatigue, and sleep on patient health. Likewise, some patients with active small bowel Crohn's disease (CD) may experience few gastrointestinal symptoms but have profound fatigue, weight loss, and impaired quality of life. A focused assessment for disease activity may fail to identify aspects of health most relevant or important to individual patient well-being. There is a need for effective, efficient, and standardized strategies to better understand the concerns of the individual seeking help.

Although there are several PROs that measure disease activity primarily for clinical research trials,[10] their prevalence in gastroenterology practices has not been systematically assessed. Most likely few clinical practices currently integrate standardized PROs in routine patient care. This may be because of several reasons, including lack of awareness of newly developed PROs, administrative burden including time and resources to collect PROs, potentially complex interpretation of results, and perhaps a reluctance among physicians to alter tried- and true traditional patient interview methods of obtaining information about the health status of their patients. For effective use in clinical care, PROs require simple and relevant interpretation to add value to the clinician's practice, and must minimally impact clinical flow and resources. The use of Internet-enabled tablets has been shown to be a feasible, efficient, and effective means of PRO assessment in gastroenterology practices, with good levels of patient satisfaction.[11]

Reaping Potential Benefits of Patient-Reported Outcomes

The National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS) is an initiative developed to investigate and promote implementation of PRO measures among patients with chronic diseases. The collection of PROMIS measures has been shown to be feasible at a tertiary care IBD center, enabling a biopsychosocial model of care.[12] Likewise, implementation of PROs in other clinical areas including oncology, orthopedics, and rheumatology has been robust.

In an innovative orthopedic study, PROMIS measures collected and linked to the electronic medical record predicted the likelihood of a clinically meaningful benefit from foot and ankle surgery.[13] This has facilitated tailored patient-specific preoperative discussions about the expected benefit of surgery. In a study at a rheumatology clinic patients with rheumatoid arthritis were asked to identify their highest priority treatment targets using PROMIS domains (fatigue, pain, depression, social function). The highest priority domain was tracked over time as a patient-centered marker of health, essentially personalizing measures of success for the individual patient.[14]

PROs have the unique potential to affect multiple levels of health care. At the patient level, PRO data can identify specific concerns, manage expectations of recovery, and tailor treatment decisions to personal preference. At the population level, PRO data can be used to standardize aspects of care, to understand comparative health and disease among all patients in a practice or relative to outside practices, identify outliers, and drive improvement. PROs can thus offer an expanded armamentarium of clinical measurements in IBD care to facilitate personalized approaches to care.

Optimizing Patient-Reported Outcomes for Use in Clinical Trials: Crohn's Disease–Patient-Reported Outcomes and Ulcerative Colitis–Patient-Reported Outcomes

Developing standardized, validated instruments according to FDA guidance is a complex process. The lack of an FDA-approved PRO has resulted in substantial variability in the definitions of clinical response or remission in clinical trials to date.[15] As a result, IBD-specific PROs (UC-PRO and CD-PRO) are being developed under FDA guidance for use in clinical trials.[16] Having achieved prequalification for open use, UC-PRO and CD-PRO will cover 5 IBD-specific outcomes domains or modules: (1) bowel signs and symptoms, (2) systemic symptoms, (3) emotional impact, (4) coping behaviors, and (5) IBD impact on daily life. The bowel