Manuscript Doi: 10.1093/ecco-jcc/jjx161

# Developing a Standard Set of Patient-Centred Outcomes for Inflammatory Bowel Disease – an International, Cross-disciplinary Consensus (Title Page)

**Short title**: **ICHOM patient-centred outcomes for IBD**

Andrew H Kim,[1] Charlotte Roberts,[2] Brian G Feagan,[3] Rupa Banerjee,[4] Willem Bemelman,[5] Keith Bodger,[6] Marc Derieppe,[7] Axel Dignass,[8] Richard Driscoll,[9] Ray Fitzpatrick,[10] Janette Gaarentstroom-Lunt,[11], Peter D Higgins,[12] Paulo Gustavo Kotze,[13] Jillian Meissner,[14] Marian O'Connor,[15] Zhi-Hua Ran,[16] Corey A Siegel,[17] Helen Terry,[18] Welmoed K van Deen,[19] C.Janneke van der Woude,[20] Alandra Weaver,[21] Suk-Kyun Yang,[22] Bruce E Sands,[23] Séverine Vermeire,[24] and Simon PL Travis[1]

**Author Affiliations**

[1]Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, UK

[2]International Consortium for Health Outcomes Measurement, London, UK

[3]Department of Medicine, University of Western Ontario, London, Ontario, Canada

[4]Asian Institute of Gastroenterology, Hyderabad, India

© European Crohn's and Colitis Organisation (ECCO) 2017.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

[5]Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands

[6]Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, Liverpool, UK; Digestive Diseases Unit, Aintree University Hospital, Liverpool, UK

[7]Association François Aupetit, France

[8]Department of Medicine I, Agaplesion Markus Hospital, Goethe-University, Frankfurt am Main, Germany

[9]Health Quality Improvement Partnership, UK

[10]University of Oxford, Oxford, UK

[11]Department of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

[12]Department of Internal Medicine, University of Michigan Medical School, Michigan, Ann Arbor, MI 48109, USA

[13]Catholic University of Parana, Curitiba, Brazil

[14]Crohn's and Colitis Foundation of America (patient representative)

[15]St Mark's Hospital, London Northwest Healthcare NHS Trust, UK (Consultant nurse in IBD and Operational head of nursing, midwifery & allied health professionals standards)

[16]Key Laboratory of Gastroenterology & Hepatology Ministry of Health, Division of Gastroenterology and Hepatology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai Institute of Digestive Disease, Shanghai Inflammatory Bowel Disease Research Center, Shanghai, China

[17]Department of Gastroenterology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

[18]Crohn's and Colitis UK, 4 Beaumont House, Sutton Road, St Albans, Hertfordshire, AL1 5HH, UK

[19]UCLA Center for Inflammatory Bowel Diseases, Division of Digestive Diseases, David Geffen School of Medicine, University of California, Los Angeles, California, USA; USC Gehr Family Center for Implementation Science, Los Angeles, California, USA

[20]Erasmus University Medical Centre, 3015 CE, Rotterdam, The Netherlands

[21]Crohn's and Colitis Foundation of America, USA

[22]Department of Gastroenterology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

[23]Icahn School of Medicine at Mount Sinai, New York, NY, USA

[24]Department of Gastroenterology & Hepatology, University Hospitals Leuven, Leuven, Belgium

Accepted Manuscript

**Abbreviations**

AFA, Association François Aupetit; BMI, Body Mass Index; CCFA, Crohn's & Colitis Foundation of America; CCUK, Crohn's & Colitis UK; IBDQ, Inflammatory Bowel Disease Questionnaire; IBD-U, inflammatory bowel disease-undetermined; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICHOM, International Consortium for Health Outcomes Measures; MIBDI, the Manitoba IBD Index; PRO, patient-reported outcome; PROM, patient-reported outcome measure; SCQ, Self-reported Comorbidity Questionnaire

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

**Correspondence**

Professor Simon P L Travis

Translational Gastroenterology Unit

Oxford University Hospitals' Foundation Trust

Oxford OX3 9DU, UK

Tel: +44-1865 227552

Fax: +44-1865 228763

Email: simon.travis@ndm.ox.ac.uk

Accepted Manuscript

**Background and Aims**

Success in delivering value-based healthcare involves measuring outcomes that matter most to patients. Our aim was to develop a minimum Standard Set of patient-centred outcome measures for inflammatory bowel disease (IBD), for use in different healthcare settings.

**Methods**

An international working group (n=25) representing patients, patient associations, gastroenterologists, surgeons, specialist nurses, IBD registries and patient-reported outcome measure (PROM) methodologists participated in a series of teleconferences incorporating a modified Delphi process. Systematic review of existing literature, registry data, patient focus groups and open review periods were used to reach consensus on a minimum set of

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

standard outcome measures and risk adjustment variables. Similar methodology has been used in 21 other disease areas (www.ichom.org).

**Results**

A minimum Standard Set of outcomes was developed for patients (aged ≥16) with IBD. Outcome domains included survival and disease control (survival, disease activity/remission, colorectal cancer, anaemia), disutility of care (treatment-related complications), healthcare utilisation (IBD-related admissions, emergency room visits) and patient-reported outcomes (including quality of life, nutritional status and impact of fistulae) measured at baseline and at 6 or 12 month intervals. A single PROM (IBD-Control questionnaire) was recommended in the Standard Set and minimum risk adjustment data collected at baseline and annually were included: demographics, basic clinical information and treatment factors.

**Conclusions**

A Standard Set of outcome measures for IBD has been developed based on evidence, patient input and specialist consensus. It provides an international template for meaningful, comparable and easy-to-interpret measures as a step towards achieving value-based healthcare in IBD. (248 words)

**Keywords**

Inflammatory Bowel Disease, Patient Reported Outcomes, Quality Improvement

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

## INTRODUCTION

A paradigm change is happening in healthcare. Many healthcare organisations are embracing value-based healthcare,[1-4] an approach that aims to achieve the best possible health outcomes for the lowest cost.[5, 6] According to the framework presented by Porter et al,[7] the key to determining "value" is measuring outcomes that matter most to patients. When providers are asked to report outcomes, performance improves[1] even when those outcomes are not patient-defined. Outcome measurement (in contrast to more familiar measures of the care-delivery process[5, 6]) has the potential to direct resources towards strategies with the highest value, which is particularly relevant for chronic diseases that are major drivers of healthcare costs.[8] For complex conditions such as inflammatory bowel disease (IBD), the potential gain from a value-driven healthcare strategy could be even greater than conditions with defined interventions, such as cataract surgery.[9]

Crohn's disease (CD) and ulcerative colitis (UC), collectively known as IBD, disproportionately affect young adults in their educationally and economically productive years, leading to reduced quality of life, social functioning and productivity,[10-13] often requiring lifelong drug treatment or major surgery.[14, 15] This accounts for high costs to the healthcare system and society,[10, 16, 17] with annual direct healthcare costs in Europe alone estimated at 4.6 – 5.6 billion Euros, and a global rise in burden, particularly in East Asia.[12, 18-20] Despite the potential impact on the individual, no patient-reported outcome measures (PROMs) are used in routine practice, so patient-reported outcomes (PROs), other than disease-related symptoms, are rarely captured. Furthermore, there remains widespread variation in clinical practice and quality of care provided to patients with IBD.[21-23] With the exception of collaborations such as the ImproveCareNow network,[24-26] current IBD registries track different outcomes or similar outcomes with different definitions, making meaningful

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

comparisons between populations difficult.[27] Similarly, no 'core outcome sets' are currently available for IBD clinical trials to date, limiting the ability for direct comparison or combining of results.[28]

To align outcome measurement in IBD as a step towards value-driven care, the Oxford Academic Health Science Network collaborated with International Consortium for Health Outcomes Measurement (ICHOM) to form an IBD Working Group of clinical and outcome specialists, patients and their associations (Crohn's & Colitis Foundation of America, CCFA; Crohn's & Colitis UK, CCUK; and Association François Aupetit, AFA) from 12 countries. ICHOM is a non-profit organisation founded in 2012 by Michael Porter of Harvard Business School, the Boston Consulting Group and the Karolinska Institutet (www.ichom.org), that aims to drive quality improvement and reduce variation in standards between healthcare providers through outcome measurement. This has resulted (as of 2017) in 21 Standard Sets of outcomes for different medical conditions that are being implemented in practice.[29-35]. The advantage of this collective effort is that all use standardised methodology; consequently each condition becomes part of a wider whole for introducing outcome measurement into routine practice, facilitating implementation when different disease areas can learn from others.

Our goal was to develop a minimum Standard Set of patient-centred outcomes for IBD to provide a common language for outcomes that can be tracked systematically.

## MATERIALS AND METHODS

### Context and overview

The Standard Set for patients with IBD (age ≥16y) aims to provide a template with meaningful, comparable and easy-to-interpret measures that can be implemented in any

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

healthcare setting to track and compare outcomes. It represents a 'minimum' standard to cover the cycle of care for both CD and UC and tracks health status (Figure 1[5]), while not precluding collection of additional measures.

Selection principles for outcomes were:

(1) feasible to capture in routine clinical practice;

(2) the end results of care, not the process of care;

(3) important to patients with IBD; and

(4) responsive to change.

Four domains (Survival and Disease Control; Symptoms, Function, and Quality of Life; Disutility of Care; and Healthcare Utilisation) were pre-specified, but not the number of measures. For PROMs, considerations included domain coverage and psychometric properties.[36, 37] In the selection of the PROM tool, we aimed to capture health status and impact on quality of life beyond specific disease-related symptoms using a validated instrument applicable to both CD and UC. Time points for data collection were determined by considering these principles and the burden of data capture on the patient or provider.

Case-mix variables for risk adjustment were selected by: (1) the relevance (strength of causal linkage between the characteristic and the outcome); (2) independency; (3) practicality; and (4) comparability at a global level.

**The Project Team and Working Group**

The Project Team comprised a Chair (ST), an ICHOM Project Leader (CR), and a Research Fellow (AK) responsible for co-ordinating a series of teleconferences and consensus process. Material for discussion at each call was jointly prepared by the Project Leader and

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

the Research Fellow who reviewed available registry data and evidence from scientific literature. The Project Team invited patient associations to recommend patients or representatives and identified internationally recognised specialists. In accordance with standard ICHOM criteria, final selection of Working Group members considered 1) expertise, as evidenced by publications on patient outcomes, invitation to speak at international conferences, or national-level leader status, 2) representation of different geographical areas and areas of expertise, 3) availability in terms of being able to participate in discussions during teleconferences, and 4) having no conflict of interest that could compromise the neutrality of the Standard Set. The resulting Working Group (n=25, see author list) represented seven specialties or interest groups (patients, gastroenterologists, surgeons, specialist nurses, IBD registries, PROM methodology specialists and representatives of large patient organisations) from 12 countries (Australia, Belgium, Brazil, Canada, China, France, Germany, India, Netherlands, South Korea, UK and USA).

**Consensus Process**

A *systematic literature review* to identify IBD-related outcomes, relevant definitions and measurement tools of electronic databases (Medline, EMBASE, PsychInfo, Cumulative Index to Nursing and Allied Health Literature, Allied and Complementary Medicine, University of Oxford PROM bibliography database – to 2005, the Cochrane Library) was undertaken. The search strategy was deliberately chosen to capture all studies that reported on any clinical or patient-reported outcomes (including instruments used to measure them) for IBD, without restricting the search to specific domains or time frame, although it was limited to randomised controlled trials, reviews, and meta-analyses published in English (see Supplementary Material 1, available as Supplementary Data at ECCO-JCC online).This was supplemented by manual searching of references from key journals that included published IBD guidelines and reviews of IBD-related outcomes. The group convened 8 *teleconferences*

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

and 7 *online surveys* incorporating a modified two-round Delphi process[38] to reach consensus based on evidence and specialist opinion between October 2015 and July 2016. Before each teleconference, the Project Team circulated an agenda, list of key proposals and relevant evidence from the literature for review where relevant outcomes and metrics were organised into summary tables using a defined hierarchy – these were then used to generate the discussions with all participants at each call contributing to key decisions.

Each teleconference was followed by minutes and an online survey for feedback and voting (from all Working Group members including non-participants of the call). *Key decision areas* included: (1) the scope to be covered by the Standard Set (Calls 1 and 2, 1 survey); (2) items to be included in the Standard outcome set including definition, response options, data source, and timing of collection (Calls 2-5, 3 surveys); and (3) case-mix factors required for risk adjustment including definition, response options, data source, and timing of collection (Calls 5-8, 3 surveys). '*Consensus*' was predefined as greater than 70% of the voting Working Group members rating the item as very important (score of 7-9 on a 9-point Likert scale) in either voting round. The Project Team was excluded from voting, giving a maximum of 22 possible votes for each item. Results as percentage agreement were then made available to all Working Group members. Any items where consensus was not reached but ranked 7-9 by at least 50-70% of respondents were further discussed, followed by a second survey. Items ranked 7-9 by less than 50% of respondents were excluded from further surveys. Similarly, any newly introduced items, change in definition or timing of collection were subject to further surveys to reach consensus. All voted items were reviewed at the subsequent teleconference, whether voted in or out as per pre-defined consensus definition, to provide an additional opportunity for any of the Working Group members to challenge or confirm their inclusion.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

A *patient focus group* including six IBD patients and two *1:1 patient interviews* were conducted[39] by CR after the Working Group launch, to obtain patients' perspectives on outcomes that matter most to them, using a structured interview and open-ended questions. Participants, nominated by CCUK and Crohn's & Colitis Australia, discussed which outcomes were of greatest importance to them. The focus groups represented a mix of patients with CD or UC who had received a variety of surgical and/or medical treatments with different healthcare utilisation experiences. Additional 1:1 interviews were undertaken for one man and one pregnant woman. Representatives of patient associations and other Working Group members shared their experience with other patient focus groups[22, 40-42] during teleconferences to confirm that the most important patient-reported outcome domains and patient concerns were represented in the Standard Set.

The resulting Standard Set was approved unanimously by the Working Group before being subject to *patient validation surveys* and a period of *open review* by interested clinicians before finalisation. The patient validation surveys involved circulation of the Standard Set to geographically and culturally diverse group of patients with the aid of multiple patient organisations, including CCUK and Crohn's & Colitis Australia as well as local patient groups invited by Working Group members from Brazil, India, and China (PK, RB, ZhR). The survey was translated into French, Hindi, Brazilian Portuguese, and simplified Chinese. It was completed by 318 patients representing a diverse age group and geographical location, with 83% indicating that they felt that the current Standard Set captured the most important outcomes that matter or have mattered to them (see Supplementary Material 2, available as Supplementary Data at ECCO-JCC online). A web-based draft version of the Standard Set was made available to interested clinicians, ICHOM website registrants and other stakeholders for comment on the Standard Set before finalisation.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

## RESULTS

### Scope: Patients with Inflammatory Bowel Disease

The agreed focus (75%, n=16/20) was all patients (age ≥16y) with IBD defined by International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes K50 (CD), K51 (UC) and K52.3 (IBD-Undetermined [IBD-U]). Children (age <16y) were excluded because PROMs derived for adults were potentially inapplicable and the Montreal classification of IBD[43] uses this threshold, recognising that transitional care for young people with IBD can begin as early as age 14[44-46] Other non-infective causes of colitis in ICD-10 code K52 were excluded.

### Systematic Review of IBD-related Outcomes and Measures

Using a defined hierarchy,[5] outcomes and metrics were selected from 565 papers and abstracts for the Working Group, which was further informed by registry databases and input from patient focus groups. In the four domains, 239 preliminary outcome measures were identified, from which 14 measures and their instruments were selected (see Supplementary Material 3 and 4, available as Supplementary Data at ECCO-JCC online).

### The Standard Set: Outcome Domains and Measures

*Survival and Disease Control*

Four measures were selected (Figure 2). Although death attributable to IBD is infrequent, it is of overriding relevance to patients, highlighted by patient focus groups. Capturing overall survival allows the ultimate impact of care to be assessed. Recognising the limitations of

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

death registries and reporting in many countries, the Working Group voted (82%, n=14/17) to include both *overall and IBD-specific survival*. The Working Group recommends tracking survival each year.

Control of *disease activity and remission* is one of the major goals of treatment. Defining remission, however, is not straightforward and no agreed tool currently exists to capture disease activity, which in itself can be defined in many ways. There is often discrepancy between the patient's symptoms and their state of biological remission, so the Working Group considered these separately. The consensus (100%, n=17/17) was to use the Manitoba IBD index (MIBDI)[47] (Table 2) for both UC and CD at baseline and 6-monthly intervals. The MIBDI is a single-item, patient-defined disease activity measure reported on a 6-point Likert scale allowing a 6-month recall period. It has been validated against Harvey-Bradshaw Index, Powell-Tuck Index, and the Inflammatory Bowel Disease Questionnaire (IBDQ).[48] The Working Group decided (88%, n=16/18; 94%, n=17/18) that the clinician should separately report clinical remission and biological remission, and document how biological remission was determined (biochemical, endoscopic, imaging).

*Colorectal cancer*, although infrequently complicating IBD,[49] was important to patient focus groups. The Working Group agreed (94%, n=16/17), since treatment may alter this outcome. Annual tracking of a definitive diagnosis was recommended, and for affected patients, reporting whether colorectal dysplasia had previously been diagnosed, and whether they had been participating in colorectal cancer surveillance. Surveillance details were considered to be beyond the scope of minimum standards.

*Anaemia*, defined by the World Health Organisation (WHO),[50] was recommended (71%, n=12/17) as an independent marker of disease activity and potentially modifiable outcome, tracked at baseline and at 6-monthly intervals.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

*Healthcare Utilisation*

Two measures were selected (Figure 2). Unplanned admissions or Emergency Department visits concern patients with IBD, since they can imply suboptimal disease control, non-specialist care, or increased use of ionising radiation (CT scans).[22] To achieve a practical measure, the Working Group recommended (71%, n=12/17) recording *the total number of emergency room visits every 12 months* and *all IBD-related admissions requiring at least an overnight stay*, defined as planned or unplanned, and recording the total length of stay in days over a 12-month period.

*Disutility of Care*

Two measures were selected (Figure 2). *Complications resulting from IBD-related treatment* are a central concern for patients that informs their choices about management. Attribution to disease or therapy is contentious and determining severity is difficult. The Working Group recommended (76%, n=14/18) documenting a complication that occurred during or within 3 months of any treatment (medical, endoscopic, radiological, or surgical), separately recording the outcome (further intervention, unplanned admission, or prolonged hospitalisation).

Steroid dependency is a cause of morbidity in IBD, is a concern to patients and may reflect quality of care.[51, 52] The Working Group recommended (82%, n=14/17) documenting any systemic *steroid use* within the previous 12 months and whether the duration exceeded 3 months.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

*Symptoms, Function, and Quality of Life (Patient-Reported Outcomes [35])*

One tool was selected to cover five measures that matter to patients (*change in bowel symptoms, pain & discomfort, normal activities, energy & fatigue, and depression & anxiety*) (Figure 2). The tool recommended (100%, n=20/20) was the IBD-Control Questionnaire,[42] applied every 6 months. All IBD-specific PROMs were examined by specialists within the Working Group (RF, WvD) for their conceptual and measurement designs, domain coverage and psychometric properties using ISOQOL criteria (Table 3).[36] Although the best established PROM in IBD is the Inflammatory Bowel Disease Questionnaire (IBDQ),[48] it has failed to embed itself in clinical practice because of its length and need for a licence. The IBD-Control questionnaire[42] captures disease control from the patient's perspective using generic language and measuring themes with which all patients with IBD can identify. It can be administered in less than a minute and has shown strong validity against EQ-5D,[53] UK-IBDQ,[54] Harvey-Bradshaw Index[55] / Simple Clinical Colitis Activity Index,[56] and Physician Global Assessment. For the purpose of the Standard Set, the Working Group selected Questions 1, 2, and 3 of the IBD Control Questionnaire to be included (Table 4) which adequately covered the five measures of interest.

*Nutritional status* and impact of *fistulae* (for patients with CD) were considered separately. No simple, responsive measure for either could be identified. The Working Group recommended (100%, n=19/19) recording *height and weight* at baseline as a surrogate marker for nutritional status, from which the Body Mass Index (BMI) can be calculated, then the change in weight at 6 monthly intervals. For fistulae, a single question on presence or absence of a fistula (none, perianal, rectovaginal, enterocutaneous, or other) was added, to be completed at baseline and 6-monthly intervals.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

**Case-mix Variables for Risk Adjustment**

The Working Group defined a minimum set of patients' baseline characteristics (Table 5) to enable comparisons of outcomes between centres, regions or countries to be placed in context. Selection had to be practical to capture in routine care, balancing the burden with the need for accurate comparisons. The categories of case-mix variables included: *demographics* (year and sex at birth, education level, smoking status), baseline *clinical factors* (Self-reported Comorbidity Questionnaire, SCQ,[57] with specific inclusion of autoimmune conditions and previous infections with Human Immunodeficiency Virus, hepatitis B virus, or tuberculosis), baseline *condition factors* (diagnosis, date of diagnosis, disease phenotype using Montreal Classification,[43] and presence of extra-intestinal manifestations categorised as eye, skin, joint, hepatobiliary or other), and *treatment factors* (current medication: no IBD drugs, steroids, biologics, immunomodulators, other; type of IBD-related surgery). Demographics and baseline clinical factors will be patient-reported, whilst baseline condition and treatment factors will be clinician-reported at baseline, and tracked annually as appropriate for smoking status, disease location/behaviour and treatment.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

## DISCUSSION

A 'minimum' set of standardised outcome measures represents a common language that can be used across healthcare jurisdictions as a step towards value-driven care in IBD. Value-driven care relies on reporting and systematic tracking of patient-centred outcomes, allowing providers to compare meaningful outcomes for patients and to adopt strategies that achieve the best 'value' for participating stakeholders. This work represents a first step. The performance characteristics of the measures need evaluating in real world practice. If adopted and implemented, such an approach has the potential to reduce variations in practice and improve standards of care on a global scale.

Existing studies show wide variations in the quality and delivery of care in IBD and suggest significant potential for improvement. National audit in the UK in 2006 led to the development of a set of IBD Standards that defined key performance indicators and recommendations for quality, patient-centred care.[23] In the United States, a collaborative of paediatric IBD centres formed the ImproveCareNow network to develop an outcomes registry using a shared, prospective database between nearly 50 centres. Over the years, remission rates within the participating centres have increased from 55% to 75%, using physician's global assessment.[24] This highlights what can be achieved when the provision of care is driven by outcomes.

The Standard Set presented here is the first coordinated international, multidisciplinary effort to reach a precisely defined core set of outcomes for all adult patients with IBD. The development process has followed reporting guidelines for core outcome sets.[58] This is an advantage, because IBD becomes just one of many (21 diseases as of 2017, www.ichom.org) diseases subject to the same process. The final Standard Set (Figure 2)

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

tracks 14 outcome measures that encompass the full cycle of care for both CD and UC, as well as health status beyond completion of care. The selection process was guided by careful consideration of the hierarchy of outcome measures and pre-specified domains. Each of the selected outcome measures was subject to voting on definition, response options and data source in a formal consensus process. Practicality in terms of burden on the patient and/or the provider, and feasibility in a broad range of healthcare settings were additional considerations.

Importantly, the Standard Set emphasises outcomes that matter most to patients. The US Food and Drugs Administration has advocated routine inclusion of PROs as co-primary endpoints in clinical trials.[59] Although improving quality of life is a common secondary endpoint in clinical trials, it has been the primary endpoint in only one trial in IBD[60] and is rarely captured in routine practice. Whilst the IBDQ has been widely used in trials, it has failed to embed itself in routine practice because of its length, and pragmatic reasons of cost and administrative burden. A shorter version,[61] and other more recent variations of the IBDQ such as the UK version of the IBDQ[54] and Crohn's and Ulcerative Colitis Questionnaire[62] have similarly failed to gain popularity. The IBD-Control Questionnaire,[42] unanimously recommended by the Working Group, is a PROM tool developed with the primary aim of supporting patient-centred care in practice. It captures the patient's perspective on disease control using a simple set of generic items applicable to all patients with IBD. It is freely available without a licence and takes less than 60 seconds to complete, which gives it great potential in routine practice. Strong psychometric properties have led to its selection for the UK IBD registry although it is yet to be validated in other languages apart from Spanish. The Standard Set of outcomes defined here are designed for clinical practice and would only be adaptable to clinical trials once performance characteristics are defined by prospective measurement.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Parallel efforts to define PROMs in IBD have been driven by the CCFA within the United States whose 10 most highly rated process and outcome measures were published in 2013.[22] The current Working Group took advantage of this work by including key patient, association and clinical specialist representatives involved in the CCFA process. Similarly, the National Institutes of Health Patient-Reported Outcomes Measurement Information System metrics were developed for gastrointestinal symptoms in 2014.[63] The development process and selected measures of both these initiatives reassuringly have much in common with ICHOM, but challenges remain with standardisation of these measures. Strengths of the ICHOM Standard Set include international representation of patients and clinicians' perspectives (including low income countries), precise definitions of outcome measures and data sources for implementation, as well as recommended timelines for data collection. A minimum set of baseline characteristics (case-mix variables) has been determined to allow meaningful comparisons between populations via risk adjustment. The IBD Standard Set was further subject to patient validation surveys in several languages for global implementation and open review for comment by interested clinicians before finalisation. Standard Sets remain open to modification by international agreement.

Nevertheless, the Standard Set has limitations. Patient numbers involved in focus groups and face to face interviews were few: however, unlike evidence-based science, the methodology of qualitative research and quality improvement depends not on numbers but the extent to which concepts reflect the opinions of representative groups. There is no standard for determining an adequate group size[64] and work in other fields has considered groups of 5-10 patients to be optimal.[39, 65] Symptom domains of importance and concerns identified by our focus groups reflected those of earlier work by patient associations and others.[23, 40, 41, 66-68] Patient representatives on the Working Group (MD, JM, HT, AW) present for the discussions and final decisions represented large patient organisations (CCFA, CCUK, and AFA). More patients, groups and a wider validation survey might have been

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

involved, but a balance had to be struck between resources and delivery within a 12 month timeframe.

Despite the Working Group's best efforts to develop consensus definitions that were unambiguous, cultural characteristics and infrastructural differences will inevitably influence local data. For some measures, this meant that a broad definition had to be adopted. For example, although readmission and unexpected admission were identified as important outcomes for the domain Healthcare Utilisation, the Working Group recognised the variation in thresholds for admission that exists between healthcare providers. It therefore chose to measure total length of stay and separately to track ED visits. The Standard Set also includes outcome measures that rely on pre-existing registry or administrative data. This is relevant for the Survival domain. Inaccurate or inconsistent information with respect to cause of death is well-recognised. However, death is a central concern to patients, so could not reasonably be excluded as an outcome. The Working Group chose to include "unknown" as a response option for cause of death. Furthermore, not all outcome measures had practical definitions or validated tools available. This was the case for nutrition. Existing tools such as the Malnutrition Universal Screening Tool[69] act as a screening tool for referral (process measure) rather than monitoring. Tools requiring anthropometrics or incorporating biochemical measures were considered impractical. The Working Group chose to measure height and weight at baseline for BMI calculation and then change in weight as a surrogate marker of nutritional status and an outcome of care, because this is a universally-available, objective measure in low income countries where access to more costly assessments may be difficult. We used a modified two round Delphi process to reach consensus on each of the selected outcome measures and case-mix variables including *how* and *when* these should be captured. The level of consensus deemed necessary in the Delphi process remains ambiguous in the literature, and there are no agreed norms for size of consensus, with practice varying from basic majority to more stringent proportions. The level of agreement

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

used in our work was pragmatic, based on other successfully conducted international consensus processes for outcomes, including those used by ICHOM in other published Standard Sets. Notably, the Core Outcome Measures in Effectiveness Trials initiative used this cutoff.[70] The minimum denominator for all votes was 17, representing 77-81% of the Working Group members (excluding the Project Team). It should be noted that whilst numbers formally participating in any given vote varied, all Working Group members were subsequently prompted for feedback and had the opportunity to confirm or challenge the results. The final Standard Set was approved unanimously by the Working Group.

This international, multidisciplinary IBD Working Group has developed a minimum set of patient-centred outcomes, tools and PROMs for collection in patients with IBD. Data collection needs to be piloted and a standardised collection platform developed before data quality and outcomes can be compared in different settings. ICHOM is committed to facilitating broad adoption of this set and has made the full recommendations freely available on its website (www.ichom.org/medical-conditions/inflammatory-bowel-disease), along with a reference guide to assist with technical aspects of implementation. The near-term goal will be to implement the set and to use this as a proof of concept towards broader adoption or endorsement by payors and governments. A steering committee will oversee revisions to the Standard Set to reflect changes in data collection capacity, to clarify outcome or baseline characteristics definitions as needed and respond to improvements in outcome measurement tools. In this way, the international IBD community can move towards the ultimate goal of acquiring internationally comparable data on patient-centred outcomes and improve the value of care.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

## Funding

This work was supported through sponsorship from the Oxford Academic Health Science Network (AHSN). The Oxford AHSN's contribution to this work was funded in part via an independent grant from AbbVie. Oxford AHSN funding paid for the time of the Research Fellow, ICHOM Project Leader, Research Associate and ICHOM supervision, but individual contributions from the Chair, or members of the working group were not remunerated.

## Acknowledgements

The authors gratefully acknowledge the contributions from patients, patient organisations, registries and all those who participated in the surveys and open review to provide feedback towards improving the final Standard Set. Summary of the Delphi rounds for presentation as Supplementary Material was prepared with assistance from Matt Salt, a research associate from ICHOM. A special tribute is for the contribution by Janette Gaarentstroom-Lunt, who sadly passed away on May 4, 2016 during this work.

## Authors' Contributions

AK: study design, literature review, acquisition of data, analysis and interpretation of data, material support, drafting of manuscript, preparation of figures and tables, critical revision of the manuscript for important intellectual content, and approval of final work. CR: study design, material and technical support, acquisition of data, analysis and interpretation of data, preparation of figures and tables, critical revision of the manuscript for important intellectual content, and approval of final work. ST: study concept and design, obtained funding, study supervision, acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and approval of final work. MD,

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

JG, JM, HT: acquisition of data, interpretation of data. BF, RB, WB, KB, AD, RD, RF, PH, PK, MoC, ZhR, CS, WvD, JvdW, AW, SkY, BS, SV: acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and approval of final work.

## Conflicts of Interest

Andrew H Kim (AK) declares no conflicts of interest.

Charlotte Roberts (CR) declares no conflicts of interest.

Brian G Feagan (BF) has received financial support for research from Abbott/AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Janssen Biotech (Centocor), JnJ/Janssen, Millennium, Pfizer, Receptos, Roche/Genentech, Sanofi, Santarus, Tillotts, UCB Pharma; has received lecture fees from Abbott/AbbVie, JnJ/Janssen, Takeda, UCB Pharma, Warner Chilcott; has served as a consultant for Abbott/AbbVie, Actogenix, Albireo Pharma, Amgen, AstraZeneca, Avaxia Biologics Inc, Avir Pharma, Axcan, Baxter Healthcare Corp, Biogen Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Calypso Biotech, Celgene, Elan/Biogen, EnGene, Ferring Pharmaceuticals, GiCare Pharma, Gilead, Given Imaging Inc, GSK, Ironwood Pharmaceuticals, Janssen Biotech (Centocor), JnJ/Janssen, Kyowa Hakko Kirin Co, Ltd, Lexicon, Lilly, Merck, Millennium, Nektar, Novo Nordisk, Pfizer, Prometheus Therapeutics and Diagnostics, Protagonist, Receptos, Roche/Genentech, Salix Pharmaceuticals, Serono, Shire, Sigmoid Pharma, Synergy Pharmaceuticals Inc, Takeda, Teva, TiGenix, Tillotts, UCB Pharma, Vertex Pharmaceuticals, Warner Chilcott, Wyeth, Zealand, Zyngenia; has served on advisory boards for Abbott/AbbVie, Amgen, AstraZeneca, Avaxia Biologics Inc, Bristol-Myers Squibb, Celgene, Centocor Inc, Elan/Biogen, Ferring Pharmaceuticals, JnJ/Janssen, Merck, Novartis, Novo Nordisk, Pfizer, Prometheus Laboratories, Protagonist, Salix Pharmaceuticals, Takeda, Teva, TiGenix, Tillotts, UCB

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Pharma; and holds a directorship as CEO and Senior Scientific Director at Robarts Clinical Trials Inc, Western University, London, Ontario.

Rupa Banerjee (RB) declares no conflicts of interest.

Willem Bemelman (WB) declares no conflicts of interest.

Keith Bodger (KB) has received unrestricted research grant from AbbVie to develop IBD-Control PROM; and received speaker fees from Boston Scientific.

Marc Derieppe (MD) declares no conflicts of interest.

Axel Dignass (AD) has served as a consultant for Abbott, MSD, Ferring, UCD, Otsuka Roche/Genetech, Takeda, Pharmacosmos, Holystone Biotech, Falk, Takeda, Sandoz, Hospita, Munipharma; received grants from Institut für Gemeinwohl, Stiftung Leben mit Krebs; has received lecture fees including service on speakers bureaus from Falk Foundation, Ferring, MSD, Abbott, Otsuka, Vifor, Immunodiagnostik, Kompetenetz CED, Takeda, Pharmacosmos, Mundipharma; has received payment for manuscript preparation from Falk Foundation; and has received payment for development of educational presentation from Abbott, Pharmacosmos, Falk Foundation, and Ferring.

Richard Driscoll (RD) declares no conflicts of interest.

Ray Fitzpatrick (RF) declares no conflicts of interest.

Janette Gaarentstroom-Lunt (JG) has received consultant fees from AbbVie and Takeda.

Peter Higgins (PH) has received consulting fees from AbbVie, PRIME Medical Education, UCB; received grants from Lycera; and is currently involved in the development of PRO instruments for UC and CD being reviewed by the FDA.

Paulo Gustavo Kotze (PK) has received lecture fees and served on advisory boards for AbbVie, Janssen, Ferring, and Takeda.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Jillian Meissner (JM) declares no conflicts of interest.

Marian O'Connor (MoC) has received speaker fees from AbbVie Pharmaceuticals, Actavis Pharma, MSD, Otsuka, Takeda Pharma, Vifor Pharma; has served on advisory boards for AbbVie Pharmaceuticals, MSD, Takeda Pharma, Vifor Pharma; and received financial support to attend educational meetings from AbbVie Pharmaceuticals and MSD.

Zhi-Hua Ran (ZhR) declares no conflicts of interest.

Corey A Siegel (CS) has served as a consultant for AbbVie, Amgen, Janssen, Lilly, Pfizer, Prometheus, Salix, Takeda; has received speaker fees from AbbVie, Janssen, Takeda; has received grant support from AbbVie, Janssen, Salix, Takeda; and is the co-chair of the CCFA quality of care program.

Helen Terry (HT) declares no conflicts of interest.

Welmoed van Deen (WvD) has received consulting fees from AbbVie paid to UCLA.

C.Janneke van der Woude (JvdW) has received lecture fees including service on speakers bureaus from AbbVie, Falk, Ferring, Janssen, Celtrion; and has received consulting fees paid to institution from AbbVie, Falk, Ferring, MSD, Mundipharma, Pfizer, Tramedico, and Janssen.

Alandra Weaver (AW) declares no conflicts of interest.

Suk-Kyun Yang (SkY) has received grants from Janssen Korea.

Bruce E Sands (BS) has received fees for consulting, advising, and speaking from AbbVie, Amgen, AstraZeneca, Avaxia Biologics, Bristol-Myers Squibb, Curatio CME Institute, Focus Medical Communications, Janssen Biotech, Millennium Pharmaceuticals/Takeda, Pfizer, Prometheus Laboratories, Puretech Ventures, LLC, Salix, Shire, Topivert Pharma, Luitpold Pharmaceuticals, MedImmune, Immune Pharmaceuticals, IMEDEX, Vindico Medical

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Education, Akros Pharma, Rockpointe, Strategic Consultants International, TiGenix, Celgene; has received research support from AbbVie, Amgen, AstraZeneca, Centers for Disease Control and Prevention, Crohn's & Colitis Foundation of America, Janssen Biotech, Millennium Pharmaceuticals/Takeda, Celgene, Pfizer, Prometheus Laboratories; and owns non-publicly traded stock from Avaxia Biologic and ETX Pharma.

Séverine Vermeire (SV) has received grant support from AbbVie, MSD, and Takeda; has received speaker fees from AbbVie, MSD, Takeda, Ferring, Dr. Falk Pharma, Hospira, Pfizer Inc and Tillots; and served as a consultant for AbbVie, MSD, Takeda, Ferring, Genentech/Roche, Shire, Pfizer Inc, Galapagos, Mundipharma, Hospira, Celgene, Second Genome, and Janssen.

Simon PL Travis (ST) has served as a consultant for AbbVie, Amgen, Asahi, Biogen, Bristol Myers Squibb, Celgene, Centocor, Chemocentryx, Cosmo Technologies, Enterome, Genentech, Giuliani, Glenmark Pharma, Elan Pharma, Lilly, Merck and co, Novartis, Novo Nordisk, NPS, Otsuka Pharmaceuticals, PDL Biopharma, Pfizer, Procter & Gamble, Proximagen, Santarus Inc, Schering-Plough, Shire Pharma, Synthon Pharma, Takeda, Tillotts Pharma, Topivert, VHsquared, Vifor, Warner Chilcott; has received grants from Ferring, AbbVie, Schering-Plough, MSD, Warner Chilcott, IOIBD, Lilly, Norman Collisson Foundation, UCB, Vifor; has received lecture fees including service on speakers bureaus from AbbVie, Ferring Pharmaceuticals, Schering-Plough, Centocor, Merck and co, Given Imaging, UCB Pharma, Tillotts Laboratories, Shire, Sanofi Aventis, Vifor, Takeda; has received payment for development of educational presentations from Abbot Laboratories, Procter & Gamble, Warner Chilcott; has received support for travel, accommodation, and expenses from AbbVie, and UEG; and has developed the UCEIS.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

## SUPPLEMENTARY DATA

Supplementary data are available at *ECCO-JCC* online.

## REFERENCES


1. Larsson S, Lawyer P, Garellick G, et al. Use of 13 disease registries in 5 countries demonstrates the potential to use outcome data to improve health care's value. Health Aff (Millwood) 2012;31:220-7.
2. Porter ME. Value-based health care delivery. Ann Surg 2008;248:503-9.
3. Porter ME. A strategy for health care reform--toward a value-based system. N Engl J Med 2009;361:109-12.
4. Porter ME, Teisberg EO. Redefining competition in health care. Harv Bus Rev 2004;82:64-76, 136.
5. Porter ME. What is value in health care? N Engl J Med 2010;363:2477-81.
6. Porter ME, Teisberg EO. How physicians can change the future of health care. JAMA 2007;297:1103-11.
7. Porter ME, Larsson S, Lee TH. Standardizing Patient Outcomes Measurement. N Engl J Med 2016;374:504-6.
8. Muka T, Imo D, Jaspers L, et al. The global impact of non-communicable diseases on healthcare spending and national income: a systematic review. Eur J Epidemiol 2015;30:251-77.
9. Mahmud I, Kelley T, Stowell C, et al. A Proposed Minimum Standard Set of Outcome Measures for Cataract Surgery. JAMA Ophthalmol 2015;133:1247-52.


Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

10. Burisch J, Jess T, Martinato M, et al. The burden of inflammatory bowel disease in Europe. J Crohns Colitis 2013;7:322-37.
11. Huppertz-Hauss G, Lie Hoivik M, Jelsness-Jorgensen LP, et al. Health-related Quality of Life in Patients with Inflammatory Bowel Disease 20 Years After Diagnosis: Results from the IBSEN Study. Inflamm Bowel Dis 2016;22:1679-87.
12. Kaplan GG. The global burden of IBD: from 2015 to 2025. Nat Rev Gastroenterol Hepatol 2015;12:720-7.
13. Nurmi E, Haapamaki J, Paavilainen E, et al. The burden of inflammatory bowel disease on health care utilization and quality of life. Scand J Gastroenterol 2013;48:51-7.
14. Bouguen G, Peyrin-Biroulet L. Surgery for adult Crohn's disease: what is the actual risk? Gut 2011;60:1178-81.
15. Hancock L, Mortensen NJ. How often do IBD patients require resection of their intestine? Inflamm Bowel Dis 2008;14 Suppl 2:S68-9.
16. Kappelman MD, Moore KR, Allen JK, et al. Recent trends in the prevalence of Crohn's disease and ulcerative colitis in a commercially insured US population. Dig Dis Sci 2013;58:519-25.
17. Kappelman MD, Porter CQ, Galanko JA, et al. Utilization of healthcare resources by U.S. children and adults with inflammatory bowel disease. Inflamm Bowel Dis 2011;17:62-8.
18. Loftus EV, Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology 2004;126:1504-17.
19. Molodecky NA, Soon IS, Rabi DM, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology 2012;142:46-54 e42; quiz e30.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

20. Ng SC, Tang W, Ching JY, et al. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. Gastroenterology 2013;145:158-165 e2.

21. Siegel CA, Allen JI, Melmed GY. Translating improved quality of care into an improved quality of life for patients with inflammatory bowel disease. Clin Gastroenterol Hepatol 2013;11:908-12.

22. Melmed GY, Siegel CA, Spiegel BM, et al. Quality indicators for inflammatory bowel disease: development of process and outcome measures. Inflamm Bowel Dis 2013;19:662-8.

23. The IBD Standards Group. Standards for the Healthcare of People who have Inflammatory Bowel Disease (IBD) - IBD Standards 2013 Update. Available at: htttp://ibdstandards.org.uk. Accessed August 8, 2016.

24. Crandall WV, Margolis PA, Kappelman MD, et al. Improved outcomes in a quality improvement collaborative for pediatric inflammatory bowel disease. Pediatrics 2012;129:e1030-41.

25. Crandall WV, Boyle BM, Colletti RB, et al. Development of process and outcome measures for improvement: lessons learned in a quality improvement collaborative for pediatric inflammatory bowel disease. Inflamm Bowel Dis 2011;17:2184-91.

26. Crandall W, Kappelman MD, Colletti RB, et al. ImproveCareNow: The development of a pediatric inflammatory bowel disease improvement network. Inflamm Bowel Dis 2011;17:450-7.

27. Nelson EC, Dixon-Woods M, Batalden PB, et al. Patient focused registries can improve health, care, and science. BMJ 2016;354:i3319.

28. The COMET (Core Outcome Measures in Effectiveness Trials) Initiative. Available at: www.comet-initiative.org. Accessed September 23, 2016.

29. ICHOM - International Consortium for Health Outcomes Measurement. Available at: www.ichom.org. Accessed July 9, 2016.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

30. de Roos P, Bloem BR, Kelley TA, et al. A Consensus Set of Outcomes for Parkinson's Disease from the International Consortium for Health Outcomes Measurement. J Parkinsons Dis 2017.

31. Zerillo JA, Schouwenburg MG, van Bommel ACM, et al. An International Collaborative Standardizing a Comprehensive Patient-Centered Outcomes Measurement Set for Colorectal Cancer. JAMA Oncol 2017;3:686-694.

32. Ong WL, Schouwenburg MG, van Bommel ACM, et al. A Standard Set of Value-Based Patient-Centered Outcomes for Breast Cancer: The International Consortium for Health Outcomes Measurement (ICHOM) Initiative. JAMA Oncol 2017;3:677-685.

33. Mak KS, van Bommel AC, Stowell C, et al. Defining a standard set of patient-centred outcomes for lung cancer. Eur Respir J 2016;48:852-60.

34. McNamara RL, Spatz ES, Kelley TA, et al. Standardized Outcome Measurement for Patients With Coronary Artery Disease: Consensus From the International Consortium for Health Outcomes Measurement (ICHOM). J Am Heart Assoc 2015;4.

35. Morgans AK, van Bommel AC, Stowell C, et al. Development of a Standardized Set of Patient-centered Outcomes for Advanced Prostate Cancer: An International Effort for a Unified Approach. Eur Urol 2015;68:891-8.

36. Reeve BB, Wyrwich KW, Wu AW, et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. Qual Life Res 2013;22:1889-905.

37. Fitzpatrick R, Davey C, Buxton MJ, et al. Evaluating patient-based outcome measures for use in clinical trials. Health Technol Assess 1998;2:i-iv, 1-74.

38. Murphy MK, Black NA, Lamping DL, et al. Consensus development methods, and their use in clinical guideline development. Health Technol Assess 1998;2:i-iv, 1-88.

39. Krueger RA. Designing and Conducting Focus Group Interviews, 2002. Available at: http://www.eiu.edu/ihec/Krueger-FocusGroupInterviews.pdf. Accessed December 14, 2015.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

40. Joyce JC, Waljee AK, Khan T, et al. Identification of symptom domains in ulcerative colitis that occur frequently during flares and are responsive to changes in disease activity. Health Qual Life Outcomes 2008;6:69.

41. Waljee AK, Joyce JC, Wren PA, et al. Patient reported symptoms during an ulcerative colitis flare: a Qualitative Focus Group Study. Eur J Gastroenterol Hepatol 2009;21:558-64.

42. Bodger K, Ormerod C, Shackcloth D, et al. Development and validation of a rapid, generic measure of disease control from the patient's perspective: the IBD-control questionnaire. Gut 2014;63:1092-102.

43. Silverberg MS, Satsangi J, Ahmad T, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol 2005;19 Suppl A:5A-36A.

44. Bennett AL, Moore D, Bampton PA, et al. Outcomes and patients' perspectives of transition from paediatric to adult care in inflammatory bowel disease. World J Gastroenterol 2016;22:2611-20.

45. Leung Y, Heyman MB, Mahadevan U. Transitioning the adolescent inflammatory bowel disease patient: guidelines for the adult and pediatric gastroenterologist. Inflamm Bowel Dis 2011;17:2169-73.

46. Baldassano R, Ferry G, Griffiths A, et al. Transition of the patient with inflammatory bowel disease from pediatric to adult care: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 2002;34:245-8.

47. Clara I, Lix LM, Walker JR, et al. The Manitoba IBD Index: evidence for a new and simple indicator of IBD activity. Am J Gastroenterol 2009;104:1754-63.

48. Guyatt G, Mitchell A, Irvine EJ, et al. A new measure of health status for clinical trials in inflammatory bowel disease. Gastroenterology 1989;96:804-10.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

49. Jess T, Simonsen J, Jorgensen KT, et al. Decreasing risk of colorectal cancer in patients with inflammatory bowel disease over 30 years. Gastroenterology 2012;143:375-81 e1; quiz e13-4.

50. WHO. Haemoglobin concentrations for the diagosis of anaemia ad assessment of severity. World Health Organization: Geneva, 2011.

51. Van Assche G, Dignass A, Panes J, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Definitions and diagnosis. J Crohns Colitis 2010;4:7-27.

52. Dignass A, Eliakim R, Magro F, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis. J Crohns Colitis 2012;6:965-90.

53. EuroQol G. EuroQol--a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199-208.

54. Cheung WY, Garratt AM, Russell IT, et al. The UK IBDQ-a British version of the inflammatory bowel disease questionnaire. development and validation. J Clin Epidemiol 2000;53:297-306.

55. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980;1:514.

56. Walmsley RS, Ayres RC, Pounder RE, et al. A simple clinical colitis activity index. Gut 1998;43:29-32.

57. Sangha O, Stucki G, Liang MH, et al. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum 2003;49:156-63.

58. Kirkham JJ, Gorst S, Altman DG, et al. Core Outcome Set-STAndards for Reporting: The COS-STAR Statement. PLoS Med 2016;13:e1002148.


Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

59. U. S. Department of Health. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Health Qual Life Outcomes 2006;4:79.

60. Williams JG, Alam MF, Alrubaiy L, et al. Infliximab versus ciclosporin for steroid-resistant acute severe ulcerative colitis (CONSTRUCT): a mixed methods, open-label, pragmatic randomised trial. Lancet Gastroenterol Hepatol 2016;1:15-24.

61. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. Am J Gastroenterol 1996;91:1571-8.

62. Alrubaiy L, Cheung WY, Dodds P, et al. Development of a short questionnaire to assess the quality of life in Crohn's disease and ulcerative colitis. J Crohns Colitis 2015;9:66-76.

63. Spiegel BM, Hays RD, Bolus R, et al. Development of the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) gastrointestinal symptom scales. Am J Gastroenterol 2014;109:1804-14.

64. Carlsen B, Glenton C. What about N? A methodological study of sample-size reporting in focus group studies. BMC Med Res Methodol 2011;11:26.

65. Halcomb EJ, Gholizadeh L, DiGiacomo M, et al. Literature review: considerations in undertaking focus group research with culturally and linguistically diverse groups. J Clin Nurs 2007;16:1000-11.

66. Long MD, Kappelman MD, Martin CF, et al. Development of an internet-based cohort of patients with inflammatory bowel diseases (CCFA Partners): methodology and initial results. Inflamm Bowel Dis 2012;18:2099-106.

67. Kappelman MD, Long MD, Martin C, et al. Evaluation of the patient-reported outcomes measurement information system in a large cohort of patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol 2014;12:1315-23 e2.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

68. Chung AE, Sandler RS, Long MD, et al. Harnessing person-generated health data to accelerate patient-centered outcomes research: the Crohn's and Colitis Foundation of America PCORnet Patient Powered Research Network (CCFA Partners). J Am Med Inform Assoc 2016;23:485-90.

69. BAPEN Malnutrition Advisory Group. The 'MUST' Report: Nutritional screening of adults: a multidisciplinary responsibility - Executive Summary. Available at: http://www.bapen.org.uk. Accessed August 28, 2016.

70. Prinsen CA, Vohra S, Rose MR, et al. Core Outcome Measures in Effectiveness Trials (COMET) initiative: protocol for an international Delphi study to achieve consensus on how to select outcome measurement instruments for outcomes included in a 'core outcome set'. Trials 2014;15:247.

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

## LIST OF FIGURES AND TABLES

Figure 1. Michael Porter's hierarchy of outcome measures

Figure 2. ICHOM Standard Set for Inflammatory Bowel Disease

[1] IBD-Control Questionnaire (Q1-3)

[2] The Manitoba IBD Index

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

Table 1. ICHOM Standard Set for Inflammatory Bowel Disease

| Patient Population | Measure | Supporting Information | Timing | Suggested Data Sources |
|---|---|---|---|---|
| **Symptoms, Function, and Quality of Life** | | | | |
| All patients | Change in bowel symptoms | Tracked via the IBD-Control | Baseline and 6-monthly | Patient-reported |
| | Missing planned activities | | | |
| | Night symptoms | | | |
| | Pain or discomfort | | | |
| | Energy and fatigue | | | |
| | Feel anxious or depressed | | | |
| | Overall control over IBD | | | |
| | Weight | | | |
| All patients with Crohn's Disease | Fistula symptoms | N/A | | |
| **Disutility of Care** | | | | |
| All patients | Steroid use | Use of any systemic steroids within the previous 12 months | Baseline and annual follow-up | Clinician-reported |
| | Occurrence and | Including whether a | | |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

| | | | | |
|---|---|---|---|---|
| | impact of complication from an IBD intervention | complication occurred and the outcome of the complication | | |
| **Healthcare Utilisation** | | | | |
| All patients | Time spent in hospital | Including all IBD-related admissions requiring an overnight stay and emergency department visits | Baseline and annual follow-up | Clinician-reported |
| **Survival and Disease Control** | | | | |
| All patients | Presence of anaemia | Using WHO definitions | Baseline and 6-monthly | Clinician-reported |
| | Disease activity and remission | Tracked via the Manitoba IBD Index and additional clinician report | | Patient and Clinician-reported |
| | Colorectal cancer | Diagnosis of colorectal cancer and preceding colorectal dysplasia | Baseline and annual follow-up | Clinician-reported |
| | Overall survival | Date of death | | |
| | Cause of death | Death attributable to IBD or to an intervention for IBD | | |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

Table 2. The Manitoba IBD Index[47]

| In the last 6 months, my disease has been |
| --- |
| 0 = Constantly active giving me symptoms every day |
| 1 = Often active, giving me symptoms most days |
| 2 = Sometimes active, giving me symptoms on some days (for instance 1-2 days/week) |
| 3 = Occasionally active, giving me symptoms 1-2 days/month |
| 4 = Rarely active, giving me symptoms on a few days in the past 6 months |
| 5 = I was well in the past 6 months, what I consider a remission or absence of symptoms |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

Table 3. Domain coverage and psychometric properties of IBD specific PROMs

| | Domain Coverage by IBD specific PROMs | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Outcome Domains*** | **IBDQ** | **SIBDQ** | **IBDQ-9** | **UK-IBDQ** | **CUCQ-32** | **CUCQ-8** | **IBD-Control** | **RFIPC** | **IBD-DI** |
| **Overall change in symptom status** | Partially | No | Partially | No | No | No | Yes | No | No |
| **Abdominal pain / discomfort** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Bowel habit** | Yes | No | Yes | Yes | Yes | No | Indirectly | No | Yes |
| **Rectal bleeding** | Yes | No | No | Yes | Yes | No | Indirectly | No | Yes |
| **Tenesmus** | Yes | Yes | No | Yes | Yes | No | Indirectly | No | No |
| **Night time bowel movement / leakage** | Indirectly | No | No | No | Yes | Yes | Yes | No | Indirectly |
| **Faecal incontinence** | Yes | No | No | Yes | Yes | No | Indirectly | Yes | No |
| **Perianal fistula / discharge / pain** | No | No | No | No | No | No | Indirectly | No | No |
| **Unintentional weight change** | Yes | Yes | No | No | No | No | No | No | No |
| **Health related QoL** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Fatigue and energy** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Emotional health** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Limitations to usual ADL** | No | No | No | Yes | Yes | No | Indirectly | No | Yes |
| **Work / education productivity** | Yes | No | No | Yes | Yes | No | Yes | Partially | Yes |

*Outcomes preliminarily selected by Working Group for inclusion within the Symptoms, Function, and Quality of Life domain

| | **Psychometric Properties by IBD specific PROMs** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Psychometric Properties** | **IBDQ** | **SIBDQ** | **IBDQ-9** | **UK-IBDQ** | **CUCQ-32** | **CUCQ-8** | **IBD Control** | **RFIPC** | **IBD-DI** |
| **Test-retest Reliability (= reproducibility)** | High | High | High | High | High | High | High | High | Med |
| **Reliability - Internal Consistency** | Med | Med | Med | Med | High | High | High | High | High |
| **Content Validity** | High | High | High | High | High | High | High | High | High |
| **Construct Validity** | Med | Med | Med | Med | High | High | High | High | High |
| **Responsiveness (Ability to detect change)** | Med | Low | Low | Med | Unknown | Unknown | High | Low | Unknown |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

Table 4. The IBD Control Questionnaire[42] (Questions 1-3)

| | |
|---|---|
| 1. Do you believe that: | |
| a. Your IBD has been well controlled in the past 2 weeks? | Yes/No/Not sure |
| b. Your current treatment is useful in controlling your IBD? | |
| 2. Over the past 2 weeks, have your bowel symptoms been getting worse, getting better or not changed? | Better/No change/Worse |
| 3. In the past 2 weeks, did you: | |
| a. Miss any planned activities because of IBD? (e.g. attending school/college, going to work or a social event) | Yes/No/Not sure |
| b. Wake up at night because of symptoms of IBD? | Yes/No/Not sure |
| c. Suffer from significant pain or discomfort? | Yes/No/Not sure |
| d. Often feel lacking in energy (fatigued) (by 'often' we mean more than half of the time) | Yes/No/Not sure |
| e. Feel anxious or depressed because of your IBD? | Yes/No/Not sure |
| f. Think you needed a change to your treatment? | Yes/No/Not sure |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

Table 5. ICHOM Standard Set for Inflammatory Bowel Disease: Case-Mix and Treatment Variables

| Patient Population | Measure | Supporting Information | Timing | Suggested Data Sources |
|---|---|---|---|---|
| **Demographics** | | | | |
| All patients | Year of birth | N/A | | Patient-reported |
| | Male or female | | | |
| | Education level | Highest level of schooling completed using the International Standard Classification of Education | Baseline | |
| | Smoking status | (of cigarettes, cigars or tobacco) | Baseline and annual follow-up | |
| | Patient height | To calculate BMI | Baseline | |
| | Patient weight | | | |
| **Baseline Clinical Factors** | | | | |
| All patients | Comorbidities including autoimmune | N/A | Baseline and annual follow-up | Patient-reported |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

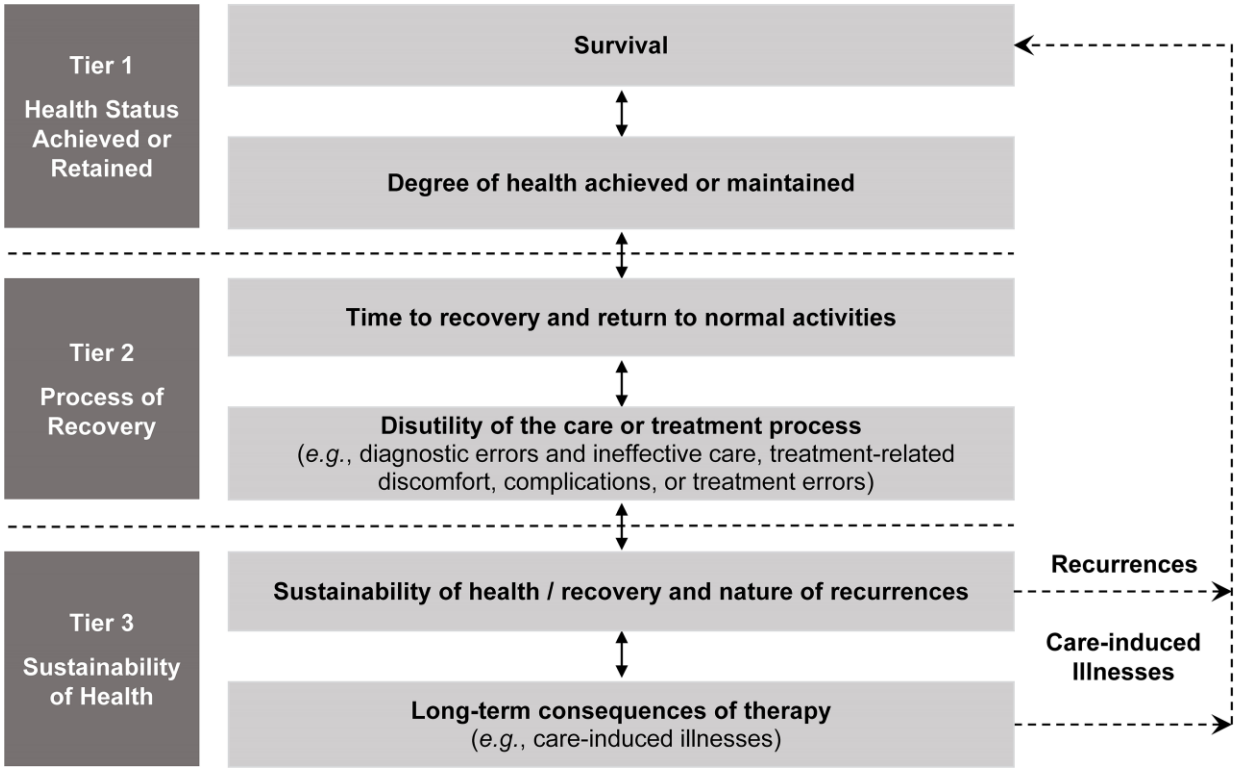
| | | | | |
|---|---|---|---|---|
| | conditions | | | |
| | Previous infection | HIV, HBV or TB | | |
| **Baseline Condition Factors** | | | | |
| All patients | Diagnosis | Crohn's disease, ulcerative colitis, indeterminate IBD or colitis unclassified | Baseline | Clinician-reported |
| | Date of diagnosis | N/A | | |
| | Disease phenotype | Tracked via Montreal Classification | | |
| | Presence of extra-intestinal manifestations | Eye, skin, joint, hepatobiliary or other | Baseline and annual follow-up | |
| **Treatment Factors** | | | | |
| Surgical patients | Type of IBD-related surgery | Including method of surgical procedure, date of surgery, and type of colectomy | Baseline and annual follow-up | Clinician-reported |
| Medical patients | Current medication | | | |
| Patients diagnosed with colorectal cancer | Participation in a colorectal cancer surveillance programme | N/A | | |

Accepted Manuscript

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

Manuscript Doi: 10.1093/ecco-jcc/jjx161

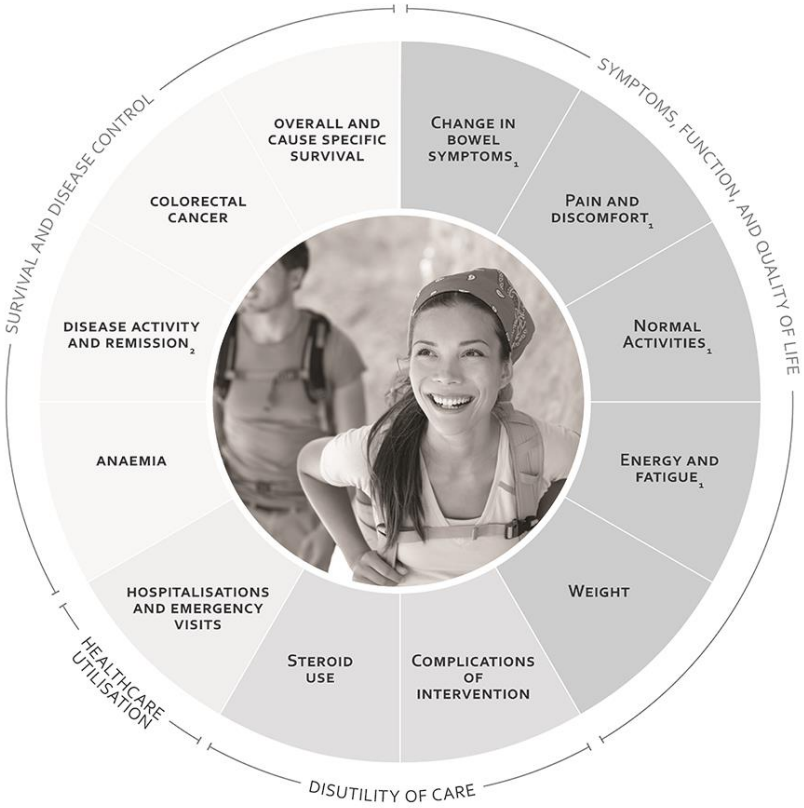
**Figure 1.**




Accep

Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017

**Figure 2.**




Downloaded from https://academic.oup.com/ecco-jcc/advance-article-abstract/doi/10.1093/ecco-jcc/jjx161/4694039
by University of Liverpool user
on 18 December 2017