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ORIGINAL ARTICLE

Development of a core descriptor set for Crohn's anal fistula

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Abstract

Aim: Crohn's anal fistula (CAF) is a complex condition, with no agreement on which patient characteristics should be routinely reported in studies. The aim of this study was to develop a core descriptor set of key patient characteristics for reporting in all CAF research.

Method: Candidate descriptors were generated from published literature and stakeholder suggestions. Colorectal surgeons, gastroenterologists and specialist nurses in inflammatory bowel disease took part in three rounds of an international modified Delphi process using nine-point Likert scales to rank the importance of descriptors. Feedback was provided between rounds to allow refinement of the next ratings. Patterns in descriptor voting were assessed using principal component analysis (PCA). Resulting PCA groups were used to organize items in rounds two and three. Consensus descriptors were submitted to a patient panel for feedback. Items meeting predetermined thresholds were included in the final set and ratified at the consensus meeting.

Results: One hundred and thirty three respondents from 22 countries completed round one, of whom 67.0% completed round three. Ninety seven descriptors were rated across three rounds in 11 PCA-based groups. Forty descriptors were shortlisted. The consensus meeting ratified a core descriptor set of 37 descriptors within six domains: fistula anatomy, current disease activity and phenotype, risk factors, medical interventions for CAF, surgical interventions for CAF, and patient symptoms and impact on quality of life.

Conclusion: The core descriptor set proposed for all future CAF research reflects characteristics important to gastroenterologists and surgeons. This might aid transparent reporting in future studies.

KEYWORDS
anal fistula, consensus, Crohn's disease, methodology

INTRODUCTION

Perianal fistula affects around one in three people with Crohn's disease. Crohn's anal fistula (CAF) is associated with significant morbidity and has a negative impact on quality of life [1]. Less than a third of patients affected will achieve long-term fistula remission [2]. Current treatment guidelines advocate the use of biological drugs combined with sphincter-preserving surgical procedures where possible. Despite this, there remains a need for improvement in clinical outcomes, which is a high research priority [3].

†See Appendix 1 for collaborator names.

Recent publication of a core outcome set (COS) has highlighted significant challenges in CAF research methodology, emphasizing the importance of transparent, patient-relevant reporting to support comparable research [4]. Standardized reporting of outcomes is only one aspect of the three main challenges facing CAF researchers [5]. Other challenges include heterogeneous reporting of surgical interventions and their methods, and the variable descriptions of the patient population included in the research. Work to rectify the heterogeneity in surgical intervention reporting is already under way, beginning with a recently conducted analysis of the variation within reporting [6].

The third area of methodological challenge – the description of the sample population – is particularly relevant in CAF. CAF can range from a minimally symptomatic condition that is well controlled on medical therapy, to a debilitating, complex condition with a significant negative impact on quality of life. To understand why some patients respond well while others do not, the patients studied must be adequately described. Previous work has identified prognostic characteristics for CAF [7] that remain inconsistently reported. A standardized approach to reporting patient characteristics may reap several benefits: ensuring external validity, understanding disease phenotypes associated with varied outcomes, allowing deeper comparison in systematic review and ultimately enabling clinicians to advise patients of the most effective CAF treatment for their clinical situation.

The aim of this study was to define a standardized set of patient characteristics, known as a 'core descriptor set' (CDS), which defines the minimum patient characteristics to be reported in future research in CAF.

What does this paper add to the literature?

This study has established a consensus between gastroenterologists and colorectal surgeons on patient characteristics that should be described in future studies of Crohn's anal fistula. This may help better identification of different phenotypes and subgroups of patients.

METHOD

This study took the form of a modified Delphi consensus exercise, with the addition of principal component analysis (PCA) to interpret data structure. It was developed with reference to the COS-STAD guidelines [8] and reported using COS-STAR guidelines [9].

Scope

This CDS was developed with the intention of using it in adult cohorts or randomized trials investigating medical and/or surgical treatments in patients with CAF.

Steering group

The steering group was drawn from gastroenterologists and surgeons with a research interest in inflammatory bowel disease (IBD). The steering group was primarily drawn from the UK-based ENiGMA (CAF) research network, with international collaborators identified from the USA and Sweden. The clinical steering group included patient and public representatives.

Delphi design and participants

An overview of the modified Delphi method is shown in Figure 1. Three rounds of an online Delphi survey were conducted, in which participants were asked to rate a longlist of descriptors by importance, on a Likert scale of one to nine. The first round was an open internet survey distributed over social media to experts in any healthcare discipline with experience of managing patients with IBD. Email invitations were sent through professional email contacts and societies linked to the steering group. Subsequent rounds were only open to participants who had completed all previous rounds. Feedback between rounds encouraged participants to compare their responses with those from their own and other professional groups, and the overall cohort.

Longlist generation

The initial longlist for the Delphi survey was drawn from constituent studies of three systematic reviews on the topic [4,5,10] and two more recently published randomized trials [9]. Items reported in tables of baseline characteristics of CAF patients included in the studies were extracted. Where descriptors were reported with numerical cut-offs (e.g. age > 40 years, white cell count > 15×10^9/mm^3), the cut-offs were removed to retain just the main descriptor. Where scoring systems were reported, these were split into their constituent components and each component was listed separately. The longlist was reviewed by the steering group for completeness and clarity of language and meaning.

Consensus group participants

Participants who completed all three rounds of the Delphi survey were eligible to participate in the final consensus meeting to determine those descriptors to be included in the final list. Purposive sampling of interested participants ensured a global and multidisciplinary consensus group.

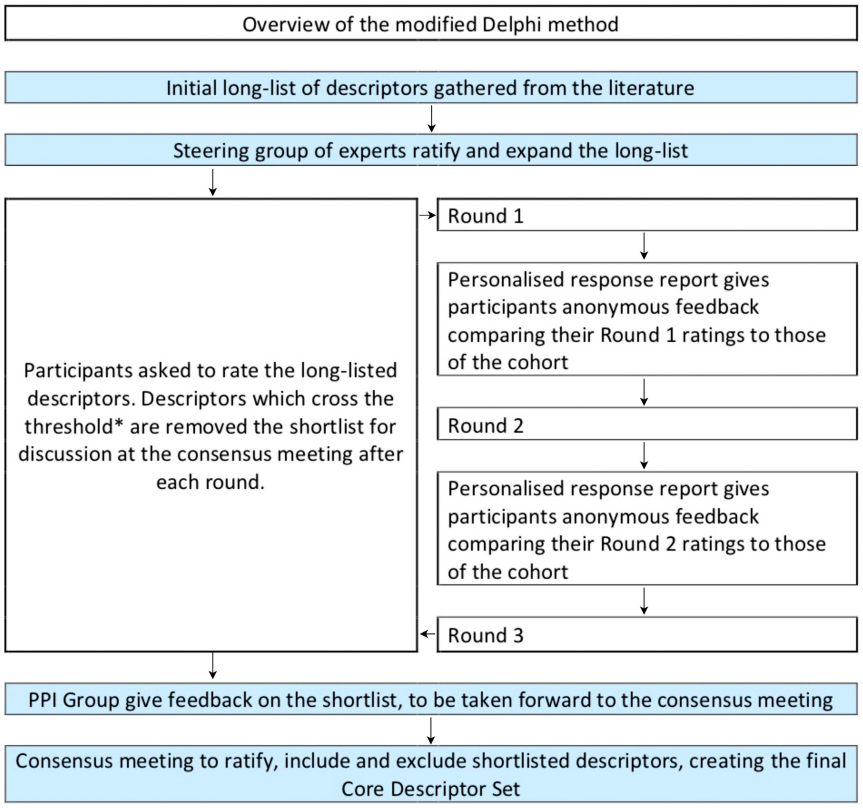

FIGURE 1 Outline of method. *Threshold for shortlisting: ≫ 70% of participants voted the descriptor as 7–9 (high importance)

Survey design

Round one presented all descriptors on one page in a random order. Participants were asked to rate descriptors by importance for inclusion in future studies on a Likert scale of one to nine: 1–3 represented 'low importance', 4–6 'neutral importance' and 7–9 'high importance'. At the end of the round one survey, participants could also propose additional descriptors for assessment in round two. These were reviewed by the steering group to ensure clarity of phrasing and avoid repetition of already assessed items.

Descriptors included in rounds two and three were presented in groups based upon PCA components from round one ratings. This approach is described below. New descriptors added to the longlist following round one were assigned to a group generated by PCA by the steering group. Random order of the descriptors in each group was used in rounds two and three of the survey.

Principal component analysis

Principal component analysis is a dimension reduction technique that gathers items into conceptual groups known as components, as identified by patterns in item ratings [7]. This means that items which have similar rating patterns across raters will be grouped together, suggesting a relationship or common idea underpinning them. For example, in a study one might find that procalcitonin, C-reactive protein, white cell count and interleukin-6 all showed correlations (rated consistently high or low). Using PCA, these could be grouped into a component called 'inflammation'. Utilizing this approach in a Delphi scheme could allow researchers to group items which measure different aspects of the same idea into a single group. If surveys group items according to PCA component, participants can rate them by comparison with other items in the area. Secondly, the identification of these groups might allow researchers to identify underlying theories of disease and prognosis which are implicit in the descriptors.

Principal component analysis was performed in SPSS v.26 (IBM). Likert ratings of each item were included in the assessment, which was performed using a varimax rotation approach. Appropriateness of data for PCA was determined using Bartlett's test for sphericity and the Kaiser–Meier–Olkin test for sampling adequacy. As all items in round one were mandatory, there were no missing data points. Components were identified using the eigenvalue method, where the eigenvalue of the component was greater than or equal to one. PCA is a reactive statistical technique, therefore the loading threshold which generates components was set postanalysis. Items which were loaded across more than one component were allocated to the component with the greatest loading value after review by the steering group.

Inclusion criteria

Criteria for inclusion and exclusion of descriptors was defined a priori. Descriptors were included if they were unique, concerning CAF or Crohn's disease, and presumed a confirmed diagnosis of CAF. Descriptors were excluded if they were duplicates, over-ambiguous and undefinable, or if they described characteristics related to the diagnostic process of CAF. Descriptors could be sourced from the literature or be

the suggestions of the steering group and participants. New descriptors could not be included after commencement of round two of the survey.

Shortlisted descriptors

Thresholds for inclusion were set a priori; descriptors rated as 7–9 'high importance' by over 70% of each professional group were set aside after each round and automatically shortlisted for the consensus meeting. Three rounds were planned to ensure that any items proposed in round one had two opportunities to reach consensus for inclusion or exclusion. The descriptors shortlisted over the three rounds were grouped for presentation to the Patient and Public Involvement Group and consensus meeting. Descriptor groups were generated by the steering group, based on the grouping of concepts in the underlying data elicited by PCA. Borderline descriptors were identified in round three, defined as those descriptors rated 7–9 'high importance' by 65%–69% of each professional group.

Patient and public involvement

Patient representation was included in the steering group and provided feedback on the development of the CDS, and is reported in line with GRIPP-2 SF [11]. The aim of patient involvement was to inform the steering group about the burden and acceptability of recording of items in the descriptor set. Feedback was conducted via multiple virtual discussions about the shortlisted descriptors and their groups, and how they might be measured. This involved sharing the longlist prior to the meeting and then discussion of each item on the list. Patient representatives were asked about their overall impression of the shortlist, borderline descriptors and grouping of individual descriptors. The potential added patient burden of having a minimum standard for descriptors measured was also discussed.

Consensus meeting

A virtual consensus meeting was convened to discuss and vote upon each change to the proposed final set as defined by the Delphi surveys. Changes which were voted 'yes' by 80% or more of voting participants were finalized. Planned votes included the inclusion of borderline descriptors, combination and rewording of descriptors as proposed by the steering group. Spontaneous votes could include the renaming and rearrangement of groups, and the combination and rewording of descriptors.

RESULTS

Longlist of descriptors

Ninety six descriptors were eligible for the longlist, and the most common reason for removal was duplication of concept. Of these, 83 descriptors were longlisted (Appendix 2) and rated in round one. An additional 14 descriptors were generated from the comments submitted in round one and rated in subsequent rounds (Figure 2).

Responses and respondents

Round one received 133 unique responses from three healthcare professional roles (gastroenterologist, colorectal surgeon, IBD nurse specialist) and 22 countries (Table 1). Top-responding countries

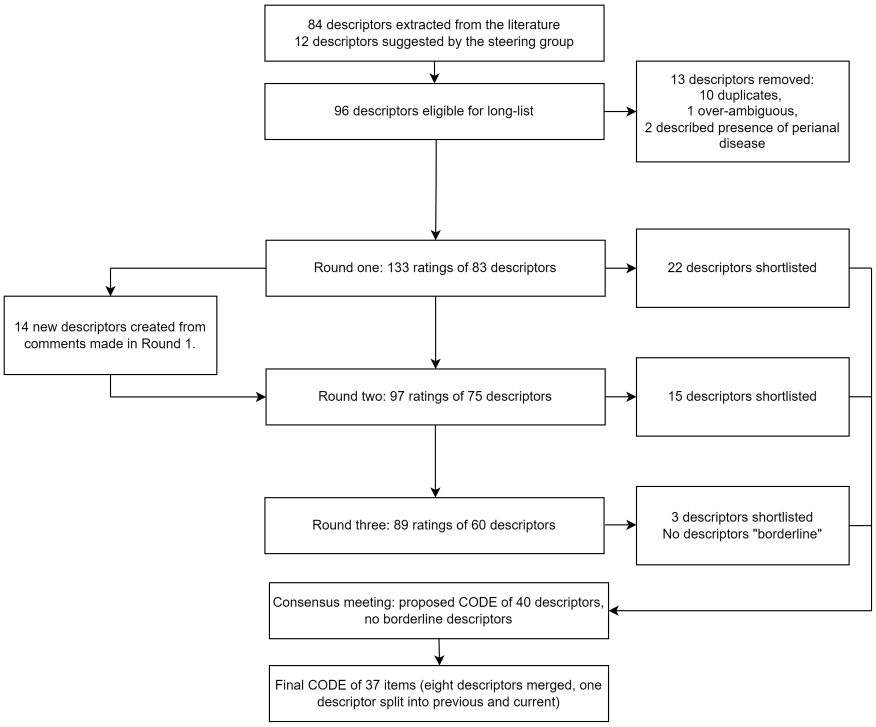

FIGURE 2 Flow of items through Delphi

TABLE 1 Respondent characteristics from each round number (percentage of that characteristic in each round)

	Round 1	Round 2	Round 3
Healthcare professional role			
Colorectal surgeon	73 (54.9)	53 (54.6)	49 (55.1)
Gastroenterologist	54 (40.6)	40 (41.2)	37 (41.6)
IBD specialist nurse	6 (4.5)	4 (4.1)	3 (3.4)
Country			
UK	51 (38.3)	35 (36.1)	31 (34.8)
USA	28 (21.1)	18 (18.6)	16 (18.0)
Sweden	16 (12.0)	15 (15.5)	15 (15.6)
Italy	9 (6.8)	6 (6.2)	5 (5.6)
Slovenia	4 (3.0)	2 (2.1)	2 (2.2)
Spain	4 (3.0)	3 (3.1)	3 (3.4)
Greece	3 (2.3)	3 (3.1)	3 (3.4)
Australia	2 (1.5)	2 (2.1)	1 (1.1)
Ireland	2 (1.5)	1 (1.0)	1 (1.1)
Israel	2 (1.5)	2 (2.1)	2 (2.2)
Other (12 Countries)	12 (9.6)	10 (10.0)	10 (11.0)
Total respondents	133	97	89

included the UK, USA and Sweden. The majority of responses were received from colorectal surgeons and gastroenterologists. These trends continued through all three rounds.

Round two received 97 unique responses, and round three received 89 unique responses, from 20 countries. The response rate between rounds one and three was 67.0%, and between rounds two and three was 91.8%. No strong attrition trends were identified.

Principal component analysis

Bartlett's test of sphericity and the Kaiser–Meier–Olkin value validated the PCA conducted after round one. PCA produced 19 components with an eigenvalue of more than one, and a positive loading threshold of 0.45 was applied. Eight components contained four or more descriptors, and another 10 contained three or fewer descriptors. Of 83 descriptors rated in round one, 61 were included in a component. The eight largest components were categorized by the steering committee as fistula complexity, extraintestinal manifestations and demographics, general health, immunomodulation and biological therapy, quality of life, background health, timeline and infection-related descriptors.

Shortlisted descriptors

Most shortlisted descriptors (22 out of 40 submitted to consensus) were extracted in round one, and the fewest were extracted in round three (Table 2). Of the 40 descriptors shortlisted, 31 were included in a PCA component, and five were not included in any PCA component group as they were generated after round one. Descriptors tended to belong in the fistula complexity, immunomodulation and biological therapy, quality of life, and infection-related or smaller components. The six proposed groups for the CDS were loosely based on these components: fistula anatomy, disease activity, risk factors, medical interventions for CAF, surgical interventions for CAF and quality of life.

Public and patient involvement

Public and patient involvement included detailed consultations with three patient representatives. Lay-person explanations were provided for descriptors where required. Patients felt their own disease characteristics were well represented within the CDS and agreed that it was not appropriate for patients to vote in the Delphi rounds as this would have introduced bias due to differences in patients' disease course and uncertainty about future prognosis. It was recommended that patients were included throughout to potentially add descriptors to the longlist and ensure fuller representation. The overriding theme of these consultations reinforced the importance of descriptions of quality of life and particularly the psychological impact of CAF. Patient representatives also felt that pain, while not explicitly included in the CDS, should be measured as part of the descriptors covering quality of life. The number of descriptors and of quality-of-life measures was not considered a barrier to research participation by any of the patient representatives.

Consensus meeting

Six consultant gastroenterologists, five consultant colorectal surgeons and two IBD nurse specialists were invited to attend and vote at the consensus meeting. Changes were made to five of the six proposed groups, including two renamed groups, one descriptor regrouped, eight descriptors combined, one descriptor split into 'previous' and 'current' and four descriptors reworded. Discussion emphasized the importance of future-proofing and measurement of quality of life.

Final core descriptor set

The finalized CDS for CAF contained 37 descriptors within six groups (Table 3). 'Best' methods of measurement for each descriptor cannot currently be described. Group F, 'Patient symptoms and impact on quality of life' measures six descriptors and the Group F methods of measurement should also explicitly assess pain, impact on sitting down and ability to defaecate.

DISCUSSION

This study has completed an international consensus process to agree key patient and disease descriptors to be reported in

TABLE 2 Shortlisted descriptors sorted by round and principal component analysis status

Round 1	Round 2	Round 3
Associated enterocutaneous fistula	Crohn's disease-specific quality of life descriptor	General quality of life descriptor
Complex fistula	Duration of current course of biological drug therapy	Current small bowel disease
Current defunctioning stoma	Fistula (symptom-specific) quality of life descriptor	Distribution of Crohn's disease
Current proctitis	Presence of discharge from fistula	
History of proctitis	Previous defunctioning stoma	
Current recto-urogenital fistula	Previous drainage of perianal abscess	
History of recto-urogenital fistula	Previous loss of response to biological drug therapy	
Location of tracts in relation to the sphincter	Previous treatment with immunomodulation	
Number of current fistulas	Previous treatment with biological drug therapy	
Number of previous fistula interventions	Simple fistula	
Number of primary tracts	Degree of inflammatory changes seen on imaging	
Number of secondary tracts	Faecal incontinence	
Presence of anorectal stenosis	Previous attempted definitive repair(s)	
Presence of perianal abscess	Psychological impact of living with CAF	
Previous seton drainage	Previous response to biological treatments	
Recurrent fistulas		
Severity of stenosis		
Smoking status		
Total number of external openings		
Total number of internal openings		
Endoscopic severity of disease		
Measure of perianal disease severity		

Note: Table of shortlisted descriptors, indicating both round and PCA inclusion (blue indicates inclusion in a component, white exclusion from a component and yellow exclusion from analysis).

future studies of CAF treatments. It has identified 37 descriptive items across six key domains. This work should complement previously published studies on outcomes [12] and may provide more granular detail for other phenotype/treatment-driven classifications [13].

There are a number of explanations for heterogeneity in reporting of characteristics. Researchers are not always consistent in how they categorize continuous data, such as age, into bands. They may disagree on how a construct breaks down into different dimensions. Studies may use different instruments to measure the same underlying construct, an example being quality of life. The CDS list represents the items that should be reported but, to encourage researchers to be responsive to contextual needs and emerging information on instrument validity/reliability, does not proscribe how this should be undertaken. Where resources allow, researchers should select descriptors which are reliable and valid, using COSMIN principles where possible [14]. This process can help in reduction of initial longlists of candidate instruments.

The treatment of CAF often follows a complex pathway, with many opportunities for tailoring or personalizing care [15]. The items included in the CDS reflect a range of factors that inform clinical decision-making surrounding the range and timing of treatments offered to patients with CAF [16,17]. The CDS covers some of the key descriptors seen in current clinical guidelines [16,17] and in previous research which identifies prognostic factors [7]. Many of these items are covered in moderate detail in the CDS, including

TABLE 3 Core descriptor set for reporting on studies in Crohn's anal fistula

Domain name	Descriptors to be included	
Domain A: fistula anatomy	1. Simple or complex fistula	
	2. Location of tracts in relation to the sphincter	
	3. Total number of external openings	
	4. Total number of internal openings	
	5. Number of current fistulas/primary tracts	
	6. Number of secondary tracts	
Domain B: current disease activity and phenotype	Previous	Current
	7. Perianal abscess drainage	8. Perianal abscess
	9. Recto-urogenital fistula	10. Recto-urogenital fistula
	11. Proctitis	12. Proctitis
	13. Distribution of Crohn's disease (including small bowel disease)	14. Distribution of Crohn's disease (including small bowel disease)
	15. Measure of perianal disease severity	
	16. Endoscopic severity of disease	
	17. Degree of inflammatory changes seen on imaging	
	18. Presence and severity of anorectal stenosis	
	19. Recurrent fistulas	
	20. Concurrent enterocutaneous fistulas	
Domain C: risk factors	21. Smoking status	
Domain D: medical interventions for CAF	22. Previous and/or current treatment with immunomodulation	
	23. Previous response to biological therapy	
	24. Previous loss of response to biological therapy	
	25. Previous treatment with biological therapy	
	26. Duration and type of current course of biological therapy	
Domain E: surgical interventions for CAF	27. Number of previous fistula interventions	
	28. Previous and/or current seton drainage	
	29. Previous surgical attempt(s) at fistula closure	
	30. Previous defunctioning stoma	
	31. Current defunctioning stoma	
Domain F: patient symptoms and impact on quality of life	32. Fistula (symptom-specific) quality of life descriptor	
	33. Crohn's disease-specific quality of life descriptor	
	34. General quality of life descriptor	
	35. Psychological impact of living with CAF	
	36. Presence of discharge from fistula	
	37. Faecal incontinence	

descriptors of fistula anatomy, the presence of sepsis, presence of proctitis and other active luminal disease. The longlisted descriptors were assessed after round one using PCA, and these concept-based groupings are broadly carried through to the final CDS. In this study, PCA helped the research team to understand the shape and structure of the items, and how they relate to each other. It has been used to inform the presentation of items as unnamed groups in rounds two and three. This was to allow participants to see the items they were voting on in the context of other related ideas, and hopefully will have improved discrimination between them. Where PCA identified variance and a component with only two items, this might reflect an area where there is underrepresentation of descriptors. Finally, using PCA as a guide, it was possible to construct a framework for the descriptors which appears to have face validity. The concepts elicited by PCA suggest consideration of underlying theories of disease or prognosis, including fistula complexity

and exposure to biological drugs. This assessment supports the face validity of the process to the steering group. Additionally, aspects of the CDS are reflected in existing tools to describe severity of CAF [18,19].

It is notable that genetic markers have not been included in the final CDS, despite studies demonstrating their prognostic relevance [5,20]. As genetic markers are not routinely used in practice, or may be some way off full validation for a prognostic role, their presence may not directly inform management. Therefore, they may not currently be considered a useful descriptor by clinicians. This reflects the wider challenge as we move towards precision medicine in IBD – having access to prognostic markers that might predict the natural disease course, identifying the risk of specific presentations or complications of disease or responsiveness to specific treatments [21].

This study has several strengths. It followed recommendations set out for the development of COSs [8], and mirrored standards for defining disease [22], which are comparable to this study design. In addition, the methodology was validated by PCA to define the structure and theories underlying participant rating behaviour. Participants were drawn from several countries, continents, healthcare systems and clinical specialties, which we believe will improve the external validity of this study.

While every effort was made to identify and extract patient descriptors from previous studies, it is possible that some descriptors were not identified at longlisting or at the later opportunities to add items. Some descriptors alone, for example fistula-related quality of life, might not be considered sufficiently descriptive. The integration of patients into this work highlighted the need to focus on subdomains or aspects of these descriptors, such as pain and incontinence. Future iterations of the method ensure patient participation during longlisting, with a focus on identifying key baseline symptoms. In this case, pain was felt to be a key baseline descriptor driving patient and clinician decisions. However, this is inconsistently recorded clearly in the literature. There was a drop-out in participation over the study, mostly between rounds one and two. This rate and pattern of drop-out broadly matches that seen in other Delphi studies [22,23]. This does introduce the risk of an attrition/selection bias into the dataset. Most participants were from Europe or the USA, with smaller numbers from other countries that may have moderate to high levels of IBD. It is not known whether clinicians from other geographical areas might have differing views on key characteristics. It might be argued that this represents a weakness of this Delphi process.

This is one of the first attempts to develop a CDS, and the methodology is developing as the research team learns from the process. Key considerations so far include:

-Generation of a comprehensive list of descriptors from the literature might be achieved with a 'saturation'-based approach (no new descriptors identified in five or ten papers), rather than a comprehensive systematic review. This could reduce the set-up workload.

-Engagement of interested parties from different disciplines, and from a range of countries, is needed to ensure external validity and potential wide uptake of the descriptor set.

-There should be regular reminders to participants and the steering group that the aim is to develop a list of 'what' to measure not 'how' to measure it.

The final longlist may be lengthy, particularly in complex chronic conditions or those treated by a range of clinicians. There may be value in considering how the number of included items might be limited and if this would still provide adequate characterization.

Patient involvement in longlist generation may aid in the identification of key baseline symptoms that may not be considered by clinicians.

Development of this international multidisciplinary CDS for CAF research paves the way for meaningful comparison within and between studies when evaluating the potential efficacy of any clinical intervention, including identifying obscure subgroups and phenotypes. It ensures that the patient populations in which treatments are being considered are clearly defined and encourages applicability of research findings to clinical practice. There are some potential barriers to implementation of this work in the design of future research. The patient representatives did not feel that the recommended level of description was burdensome to them as patients, as the information collected was all integral to optimizing their care. However, clinicians may baulk at the list of items. It should be considered that the likely tools used to collect these data are already in use. For example, items in domain F might easily be captured using the CAF-QOL tool [24]. Other domains may equally be covered by commonly used tools. Likewise, research funders will undoubtedly recognize the need for inter-study comparisons and overcoming barriers to implementation of research findings. Descriptors relevant to both surgical and medical treatment feature, as a reflection of the interdisciplinary collaboration. Given that most patients are treated with a combination of medical and surgical therapy [25], these descriptors will be relevant to most studies and should be reported, regardless of which primary outcome from the agreed COS is chosen by CAF researchers [12]. Additionally, in studies with multiple follow-up stages, and in observational studies, it may be useful to report aspects of the CDS throughout as a record of changing disease characteristics. It would be expected that the presence or absence of all items in the CDS should be recorded. It is conceivable that statements in the inclusion or exclusion criteria might address these in the methods, for example 'patients with rectovaginal fistula were not included in this study'.

The CDS methodology is new and evolving. It demonstrates strengths including drawing all interested parties together to ensure the relevance of cross-disciplinary conditions. The added strength of PCA allows us to explore underlying theories of disease and prognosis, which can be converted to testable hypotheses. Time is required to assess whether it becomes a broadly acceptable approach to the challenge of variable descriptions of patients and disease. Future developments will include assessment of how longlists are generated and defining a pragmatic number of descriptors for a condition.

Work to improve standardized description of patients with CAF is ongoing, and recent studies have used higher-level phenotypes for classification [13]. Further work is required to define included

descriptors in a way that is clinically and prognostically relevant [26]. We also recognize that the field continues to evolve, and the descriptor set will need to be reviewed in the future. Such a revision may include reassessment of clinical descriptors, refined imaging parameters and inclusion of genetic markers or other personalized treatment stratifiers [27,28]. The implementation of a CDS into routine clinical practice will take time, and require the engagement of researchers, funders and journal editors.

In conclusion, this study has achieved agreement on a 'core' list of patient descriptors to be reported in all clinical studies of CAF. Use of this in conjunction with an appropriate COS [12] might provide a strong foundation for studies. Future work might include the use of this CDS in CAF registries and adequately powered cohort studies, to evaluate current classification strategies [29] and to identify a range of key phenotypes, allowing more precise treatment strategies and predictors of success and failure of potential treatments [30].

FUNDING INFORMATION

None.

CONFLICT OF INTEREST

No conflicts of interest to declare.

ETHICAL STATEMENT

This study was approved by the University of Sheffield Research Ethics Committee (Ref: 034049).

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article

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APPENDIX 1

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APPENDIX 2

Longlist of items prior to round one

Age
Sex
Body mass index
Smoking status
Diagnosis of diabetes mellitus
Race (physical and inherited traits)
Self-identified ethnicity
Socioeconomic status
Country where the studied group(s) live
Time since Crohn's disease diagnosis
Time since diagnosis of first fistula
Age at diagnosis of Crohn's disease
Current small bowel disease
History of small bowel disease
Current proctitis
History of proctitis
Extraintestinal manifestations
Associated enterocutaneous fistulas
Time between Crohn's disease diagnosis and onset of current fistula
Time between Crohn's disease diagnosis and onset of first fistula
Previous drainage of perianal abscess
Number of current fistulas
Simple fistula
Complex fistula
Number of setons
Duration of seton drainage
Current recto-urogenital fistula
History of recto-urogenital fistula
Presence of anorectal stenosis
Severity of stenosis
Presence of ulcers
Presence of fissures
Number of previous bowel resections
Previous seton drainage
Previous defunctioning stoma
Current defunctioning stoma.
Age at first biological drug therapy
Previous treatment with biological drug therapy
Previous treatment with immunomodulation
Previous treatment with antibiotics
Recent treatment with steroids
Duration of current course of biological drug therapy
Previous loss of response to biological drug therapy
Pretreatment C-reactive protein
Pretreatment albumin
Degree of inflammatory changes seen on imaging
Presence of discharge from fistula
Presence of pain from fistula
Presence of restriction of intimacy due to fistula
Degree of induration
Frequency of liquid stools
Frequency of abdominal pain
General wellbeing
Diagnosis of arthritis/arthralgia
Diagnosis of uveitis/iritis
Presence of skin/mouth lesions
Recent fever
Taking medication for faecal incontinence
Presence of an abdominal mass
Pretreatment haematocrit
Current weight
Recent weight loss or gain
Disease-specific quality of life descriptor
Previous loss of response to immunomodulation
Crohn's disease-specific activity measure
Measure of perianal disease severity
Total number of external openings
Total number of internal openings
Pretreatment haemoglobin
Recurrent fistulas
Number of previous fistula interventions
Location of tracts in relation to the sphincter
Presence of perianal abscess
Duration of current fistula
Fistula (symptom-specific) quality of life descriptor
General quality of life descriptor
Total fistula volume as defined on imaging
Degree of perianal skin damage
Number of primary tracts
Number of secondary tracts
Pretreatment faecal calprotectin
Previous stem cell treatment
Endoscopic severity of disease