

European Society of Coloproctology Core Outcome Set for haemorrhoidal disease: an international Delphi study among healthcare professionals

R. R. van Tol*, M. L. Kimman†, J. Melenhorst*, L. P. S. Stassen*, C. D. Dirksen‡, S. O. Breukink* and Members of the Steering Group

*Department of Surgery and Colorectal Surgery, Maastricht University Medical Center +, Maastricht, The Netherlands, †Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, Maastricht, The Netherlands, and ‡Department of Clinical Epidemiology and Medical Technology Assessment, Care and Public Health Research Institute (CAPHRI), Maastricht University Medical Center +, Maastricht, The Netherlands

Received 29 May 2018; accepted 11 December 2018; Accepted Article Online 10 January 2019

Abstract

Aim There is considerable heterogeneity in outcomes in studies reporting on the treatment of haemorrhoidal disease (HD). The aim of this study was to develop a Core Outcome Set (COS) for HD in cooperation with the European Society of Coloproctology.

Method A Delphi study was performed according to the Outcome Measures in Rheumatology (OMERACT) methodology. In total 38 healthcare professionals and 30 patients were invited to the panel. Previously, 10 outcome domains and 59 outcomes were identified through a systematic literature review. In this study, these domains and outcomes were formed into one questionnaire for healthcare professionals and a separate questionnaire for patients. Sequential questionnaire rounds prioritizing the domains and outcomes were conducted. Panel members were asked to rate the appropriateness of each domain and outcome on a nine-point Likert scale. During a face-to-face meeting, healthcare professionals agreed on the primary and secondary end-points of the COS for HD. Finally, a short survey was sent to the healthcare professionals in order to reach consensus on how the chosen end-points should be assessed and at which time points.

Results The response rate in questionnaire round 1 for healthcare professionals was 44.7% ($n = 17$). Sixteen out of 17 healthcare professionals also completed the questionnaire in round 2. The response rate for the patient questionnaire was 60% ($n = 18$). Seventeen healthcare

professionals participated in the face-to-face meeting. The questionnaire rounds did not result in a clear-cut selection of primary and secondary end-points. Most domains and outcomes were considered important, and only three outcomes were excluded. During the face-to-face meeting, agreement was reached to select the domain 'symptoms' as primary end-point, and 'complications', 'recurrence' and 'patient satisfaction' as secondary end-points in the COS for HD. Furthermore, consensus was reached that the domain 'symptoms' should be a patient reported outcome measure and should include the outcomes 'pain' and 'prolapse', 'itching', 'soiling' and 'blood loss'. The domain 'complications' should include the outcomes 'incontinence', 'abscess', 'urinary retention', 'anal stenosis' and 'fistula'. Consensus was reached to use 'reappearance of initial symptoms' as reported by the patient to define recurrence. During an additional short survey, consensus was reached that 'incontinence' should be assessed by the Wexner Fecal Incontinence Score, 'abscess' by physical examination, 'urinary retention' by ultrasonography, 'anal stenosis' by physical examination, and 'fistula' by physical examination and MR imaging if inconclusive. During follow-up, the outcome 'symptoms' should be assessed at baseline, 7 days, 6 weeks and 1 year post-procedure. The outcomes 'abscess' and 'urinary retention' should be assessed 7 days post-procedure and 'incontinence', 'anal stenosis' and 'fistula' 1 year post-procedure.

Conclusions We developed the first European Society of Coloproctology COS for HD based on an international Delphi study among healthcare professionals. The next step is to incorporate the patients' perspective in the COS. Use of this COS may improve the quality and uniformity of future research and enhance the analysis of evidence.

Correspondence to: S. O. Breukink, MD PhD, Department of Surgery, Maastricht University Medical Centre, PO Box 5800, 6202 AZ Maastricht, The Netherlands.

E-mail: s.breukink@mumc.nl

Members of the steering group are co-authors of this study and can be found under the heading Collaborators

Keywords Outcomes, haemorrhoids, anal, surgery

What does this paper add to the literature?

This is the first study for the development of a European Core Outcome Set for haemorrhoidal disease. The rationale for its development was the heterogeneity of

outcomes in clinical studies reported by several systematic reviews. An agreed Core Outcome Set for haemorrhoidal disease to be assessed and reported as a minimum in clinical trials will enhance the ability to compare future studies in order to produce optimal treatment guidelines.

Introduction

Haemorrhoidal disease (HD) is common with a prevalence around 5% [1–4]. HD is usually classified according to the grading system of Goligher *et al.* [5–7] and therapeutic options are generally based on the HD grade. Numerous techniques are described, ranging from simple treatment including topical and medical therapies to outpatient treatments and surgical interventions.

There are several national guidelines for HD including treatment algorithms [8–10]. Nevertheless, there remains debate regarding the best treatment option for each grade of HD. Clinical trials investigating the effectiveness of interventions for HD have used a wide variety of outcomes and outcome measures. Consequently, evidence analysis within the systematic reviews is hampered and high-quality guidelines are lacking [11–13].

A solution to improve homogeneity in outcome reporting on HD is to develop and use a Core Outcome Set (COS). An agreed COS will enhance the ability to compare future studies in order to produce optimal treatment guidelines. A COS represents a consensus-derived minimum set of outcome parameters that should be reported in all studies that report on a particular condition [14]. Until now, there is no established COS for HD. Therefore, the aim of this study was to develop a COS for HD in cooperation with the European Society of Coloproctology (ESCP). This COS covers all types of treatment including simple treatment (e.g. fibre intake), outpatient treatment (i.e. rubber band ligation, sclerotherapy, infrared coagulation) and surgical procedures (i.e. Doppler-guided haemorrhoidal artery ligation, stapled haemorrhoidopexy and haemorrhoidectomy).

The aim of this Delphi process was to develop an international COS for HD which will recommend which minimal end-points should be assessed in future trials to assess the effectiveness of all surgical (operative and outpatient based) and non-surgical interventions.

Materials and methods

This study is registered on the COMET database (<http://www.comet-initiative.org/studies/searchresults>) and a detailed study protocol defining objectives,

the Delphi process and criteria for participant selection has been published previously [15].

Since the Outcome Measures in Rheumatology (OMERACT) Filter 2.0 resulted in successful development and implementation of COSs for many other diseases, we used their methodology [16–22]. The OMERACT Filter is a conceptual framework which encompasses the entire content of what is measurable in a study. Following this initiative, the first phase in developing the COS was a literature review [23]. Fifty-nine outcomes for HD treatment were categorized into 10 domains according to the OMERACT Filter 2.0 [24]. For example, the outcomes pain, blood loss and soiling were included in the domain ‘symptoms’.

The next step was the Delphi process to reach a consensus on the primary and secondary end-points. The Delphi process involved four phases and consisted of a panel including healthcare professionals and patients. Healthcare professionals were involved in three phases and patients in one phase of the COS development. In phase 1, the outcomes, which were identified in the literature review [23], were formed into a questionnaire for healthcare professionals with a separate questionnaire for patients. Phase 2 involved two sequential rounds of the questionnaire for healthcare professionals and one round for patients, aiming at prioritizing these outcomes [25]. Phase 3 consisted of a face-to-face consensus meeting with healthcare professionals to agree on the final end-points of the COS. In phase 4 a short survey was sent to the healthcare professionals in order to reach consensus on how the selected end-points should be assessed and at which time points pre- and post-procedure.

Ethics clearance for this study was obtained from the hospital’s ethical review board (METC 16-4-078). All participants in the Delphi study were asked to provide informed consent to have their responses included in further analysis and dissemination of the results and were informed about confidentiality of the data.

Phase I: Questionnaire development

Healthcare professionals

In the literature review, 59 outcomes were categorized into 10 domains according to the OMERACT Filter 2.0

[23]. The most frequently reported domains and outcomes were created into a web-based questionnaire. Twenty-three outcomes were used. The other 36 outcomes were reported only once or twice in the systematic reviews and were discarded. The four most commonly reported domains were ‘symptoms’, ‘complications’, ‘recurrence’ and ‘patient satisfaction’. The most commonly reported outcomes were ‘pain’, ‘prolapse’, ‘blood loss’, ‘itching’, ‘soiling’, ‘urgency’, ‘constipation’, ‘abscess’, ‘incontinence’, ‘anal stenosis’, ‘stricture’, ‘urinary retention’, ‘thrombosis’ and ‘oedema’. In the literature, the outcomes ‘prolapse’ and ‘pain’ were often used as primary end-points in studies. Therefore, ‘prolapse’ and ‘pain’ were also included as domains. In addition, the outcomes ‘fistula’, ‘nodule’ and ‘severe pain and bleeding’ were added to the domain complications based on clinical expert experience.

No agreed definition exists in the literature regarding ‘recurrence’ for HD. Therefore, we asked healthcare professionals to select one of the following options as the definition which best reflects ‘recurrence’: ‘reappearance of prolapse after symptom-free period’, ‘reappearance of initial symptoms’, ‘further intervention necessary’, ‘residual symptoms in relation to degree of satisfaction’ or ‘histological proven recurrence’.

The questionnaire included an option to add missing outcomes, because it was possible that an outcome important to patients or healthcare professionals was not reported in the literature or was previously excluded due to infrequent reporting.

The questionnaire for healthcare professionals was divided into two parts (Appendix S1). The first part consisted of the question ‘What domains should be included as the primary end-point and what domains as secondary end-points in the COS for HD?’ In the second part, healthcare professionals were asked: ‘Which outcomes should be included in these domains?’ For example, for the domain ‘complications’ the following outcomes could be selected: ‘incontinence’, ‘urinary retention’, ‘stricture’, ‘abscess’ etc.

Patients

A questionnaire was developed specifically for patients, focusing on their symptoms because some questions in the questionnaire for healthcare professionals were not relevant to patients. Patients were asked to rate the following items on a Likert-type scale: (1) suffering from symptoms (i.e. blood loss, pain, prolapse, soiling and itching), (2) distress of these symptoms in daily life, (3) treatment success (i.e. having no blood loss, no pain, no prolapse, no itching or no soiling), (4) symptom relief after treatment, (5) items to discuss during the outpatient visit (i.e. symptoms, patient satisfaction,

complications, prolapse and pain) and (6) a definition of recurrence.

The questionnaires were piloted with both healthcare professionals ($n = 2$) and patients ($n = 2$) to check understanding and acceptability. Healthcare professionals and patients were told the questionnaires were different. Healthcare professionals reviewed the patient questionnaire but not vice versa. Minor changes were made to improve the clarity and understanding of both questionnaires.

Phase 2: Questionnaire rounds

Participants

Initially we contacted the international representatives ($n = 43$) of the ESCP. However, most representatives did not treat HD. On their recommendation (i.e. snowball method) only healthcare professionals with an in-depth understanding, who have multiple cited publications in the field of proctology and/or who are familiar with the development of a COS were invited. This resulted in a smaller sample than defined in the protocol.

Dutch-speaking male and female participants (aged > 18 years) diagnosed with HD (by their general practitioner) who visited the outpatient clinic of an academic hospital (Maastricht University Medical Centre) for treatment were invited by their treating colorectal consultant (SB or JM) to participate. To ensure a variety of patients, those treated with rubber band ligation and surgical treatment were included. The colorectal consultant (SB) informed eligible patients about the study and gave them a patient information sheet. If the patient agreed, one of two researchers (RT or SK) contacted the patient explaining the purpose of the study and the procedures in depth. If the patient was willing to participate, written consent was obtained. They were not informed of the identities of other panel members. Insufficient language proficiency was an exclusion criterion.

The aim was to include as many panel members and patients as possible [18,20], since this increases the reliability of the group judgement [24,26]. All 43 representatives of the ESCP and a total of 30 patients were approached.

Questionnaires

Healthcare professionals and patients were invited by email to complete the web-based questionnaire using the online software Survey Monkey (SurveyMonkey, Palo Alto, California, USA). Healthcare professionals were invited to complete two Delphi rounds. Patients received only one questionnaire parallel to the first round of the healthcare professionals.

The survey was kept online for 5 weeks and reminder emails were sent 2 and 4 weeks after the initial invitation. The first questionnaire round ran from 13 June to 27 July 2016. Healthcare professionals who completed the first questionnaire were invited to the subsequent round, unless they decided to opt out. The second questionnaire round for healthcare professionals ran from 25 August to 8 September 2016. Healthcare professionals were not informed of the identities of other panel members.

Both healthcare professionals and patients were asked to rate the questionnaire items on a nine-point Likert scale. All items rated as 'appropriate' and/or 'unsure' (median score ≥ 4) were carried forward to the second round including additional items suggested by the participants. Items rated as 'inappropriate' (i.e. medium score ≤ 4) were omitted. In the second round, healthcare professionals were also shown their first scores and the distribution of the scores for these outcomes per participant. Participants were invited to re-score the domains and outcomes. All domains and outcomes that had a median score of ≥ 4 were carried forward to the face-to-face meeting including additional items suggested by the participants. There were no agreed methods to remove criteria and therefore the criteria were chosen according to other consensus studies [27,28].

Phase 3: Face-to-face meeting

The third phase involved a face-to-face meeting during the 11th annual meeting of the ESCP in September 2016 with the aim of agreeing on a final COS. Healthcare professionals who had completed at least one questionnaire round were invited to attend this meeting. Two independent facilitators (SB, RT), who did not participate in the questionnaire rounds, were informed of the results and chaired the meeting.

First, the results of the patient questionnaire, presented in a Powerpoint presentation, were discussed extensively. Then the retained items (i.e. domains and outcomes) of the second questionnaire from the healthcare professionals were presented. There was opportunity for an open discussion regarding the remaining items and dissenting views were actively sought. Thereafter, healthcare professionals were asked to vote on both primary and secondary end-points as 'yes' or 'no' for inclusion in the final COS. A domain or outcome was included in the COS when $\geq 70\%$ of healthcare professionals voted 'yes' in this final vote [29]. After all domains and outcomes had been voted on, and the total COS had been reviewed, the healthcare professionals were given another opportunity to comment on included items. After being sent a summary of the meeting by email, healthcare

professionals believed the COS was comprehensive. They were asked if they had additional comments.

Phase 4: Short survey

After reaching consensus on the end-points during the face-to-face meeting we discussed how we should measure these end-points. We first checked which instruments were most commonly reported in the literature. This showed that for some outcomes several instruments were used, e.g. the St Marks or Wexner Fecal Incontinence Scale for the outcome 'incontinence'. However, for most outcomes there was a gold standard, e.g. MR imaging for fistula [30,31]. Based on a literature review, we were able to make a short list of the selected outcomes for the COS and the evidence-based instruments currently used to assess these outcomes. This list was sent to the healthcare professionals and they were asked to vote 'yes' or 'no' for the proposed instrument. We also asked the group to fill in at what time points the outcomes should be assessed.

Results

The response rate in the first round for healthcare professionals was 44.7% ($n = 17$). Sixteen out of 17 healthcare professionals also completed the second questionnaire (Fig. 1). The group consisted of colorectal residents with an in-depth understanding of outcomes relevant for the treatment of HD and experience with the development of a COS. The following countries were represented: Germany ($n = 4$), Denmark ($n = 3$), England ($n = 2$), Italy ($n = 3$), The Netherlands ($n = 2$), Greece, ($n = 3$) Israel ($n = 1$) and Austria ($n = 3$).

First questionnaire

In the first part of the questionnaire regarding the question 'What domains should we use as primary and secondary end-points in the COS for HD', the domains (in order of level of appropriateness) 'symptoms', 'patient satisfaction', 'recurrence', 'complications', 'prolapse' and 'pain' were rated appropriate as primary end-point options. As secondary end-points, the domains 'patient satisfaction', 'complications' and 'recurrence' were rated as appropriate and 'symptoms', 'prolapse' and 'pain' were rated as unsure.

In the second part of the questionnaire, regarding the question 'Which outcomes should be included in the domains', most outcomes (i.e. 'pain', 'prolapse', 'itching', 'soiling', 'blood loss', 'abscess', 'incontinence', 'anal stenosis', 'stricture', 'fistula', 'severe bleeding', 'severe pain', 'urinary retention', 'thrombosis') were rated as

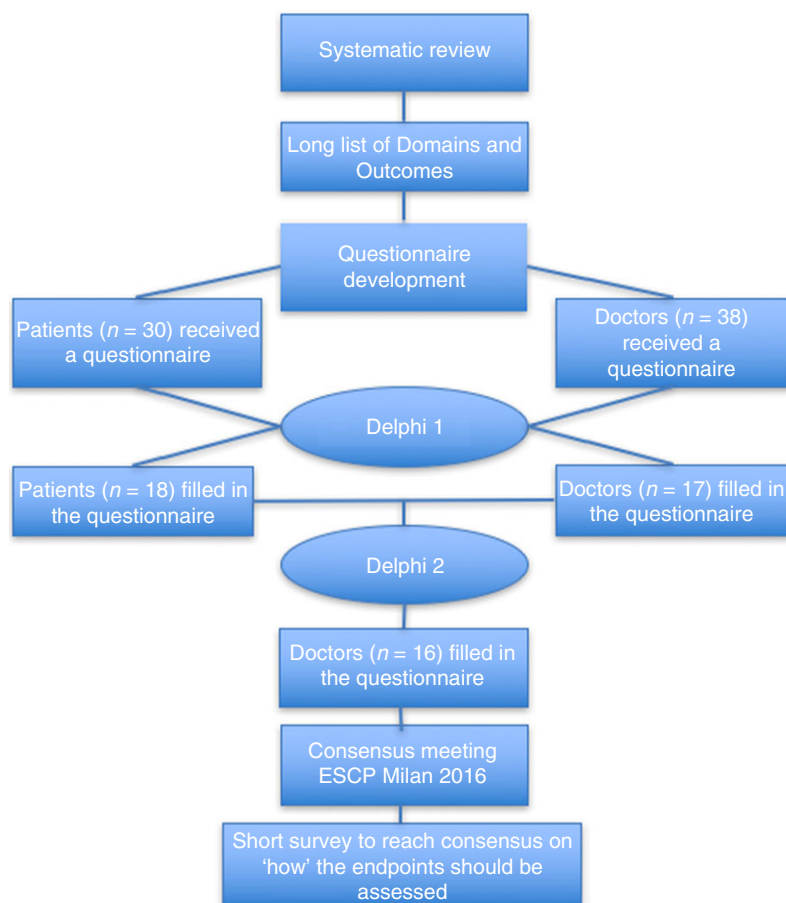


Figure 1 Delphi process.

appropriate. The outcomes ‘urgency’ and ‘constipation’ were rated as unsure. The outcomes ‘oedema’ and ‘nodule’ were rated as inappropriate and were omitted.

The following definitions of recurrence were rated as appropriate: ‘recurrent prolapse after a symptom-free period’, ‘reappearance of initial symptoms’ and ‘further intervention necessary’. The definition ‘residual symptoms in relation to degree of satisfaction’ was rated as unsure. ‘Histological proven recurrence’ was rated as inappropriate.

Second questionnaire

In the second questionnaire healthcare professionals rated (in order of level of appropriateness) ‘symptoms’, ‘patient satisfaction’, ‘recurrence’ and ‘complications’ as appropriate primary end-point options and ‘prolapse’ and ‘pain’ as unsure. As secondary end-point options, ‘patient satisfaction’, ‘recurrence’, ‘prolapse’, ‘complications’, ‘symptoms’ and ‘pain’ were all rated as appropriate.

Regarding the question ‘Which outcomes should be included in the domains’, ‘constipation’, ‘urgency’,

‘urinary retention’ and ‘thrombosis’ were rated as unsure. ‘Pain’, ‘prolapse’, ‘itching’, ‘soiling’, ‘blood loss’, ‘abscess’, ‘incontinence’, ‘anal stenosis’, ‘fistula’, ‘stricture’, ‘severe pain’ and ‘severe bleeding’ were rated as appropriate outcomes (Appendix S2).

To define recurrence the following options were rated as appropriate: ‘further intervention necessary’, ‘recurrent prolapse after symptom-free period’, ‘reappearance of initial symptoms’ and ‘residual symptoms in relation to degree of satisfaction’.

In conclusion, based on the two questionnaire rounds, no obvious selection emerged regarding the primary and secondary outcomes. Some domains which were rated as appropriate in the first questionnaire were rated as unsure in the second questionnaire, and vice versa. Only two outcomes and one definition of recurrence were excluded based on the questionnaire rounds.

Patient questionnaire

The response rate for patients was 60% ($n = 18$) with a mean age of 55 (35–77) of whom seven were females.

Regarding prior treatment, 70% of the patients had received rubber band ligation and the remaining 30% a mucopexy.

In response to the first question, 'How much do you suffer from the following symptoms on a scale from 0 (not at all) to 9 (a lot)', they rated as medium 'a lump near your anus (prolapse)', 'pain' and 'blood loss' (score between 4 and 7) and as less or not at all 'itching' and 'soiling' (mean score < 2) (Fig. 2). In response to the second question, 'How much do these symptoms bother you in daily life from 0 (no bother at all) to 9 (very bothersome)', 'a lump near your anus' was rated as moderately bothersome (mean score 5.5) and 'pain', 'blood loss', 'itching' and 'soiling' as little or no bother in daily life (mean score < 3) (Fig. 3). In response to the third question, 'When is treatment successful from 0 (not successful at all) to 9 (very successful)', they rated 'no blood loss', 'no pain' and 'no lump' as a successful outcome (mean score between 7 and 9) and 'no itching' and 'no soiling' as reasonably successful (mean score < 7) (Fig. 4). In response to the fourth question, 'What should have been treated by a surgical intervention on a scale from 0 (not important) to 9 (very important)', patients rated 'blood loss' and 'a lump near your anus' as very important (mean score > 8), 'pain'

and 'itching' as unsure and 'soiling' less important (mean < 6). In response to the fifth question, 'What is important to be discussed by your clinician during the outpatient visit – 0 (not important) and 9 (very important)', patients rated 'symptoms', 'patient satisfaction', 'complications', 'a lump near your anus' and 'pain' as important (mean > 7). In response to the final question, 'How would you describe the term recurrence', 'reappearance of initial symptoms' was rated as the most appropriate definition (mean of 7) and 'reappearance of prolapse after a symptom-free period' and 're-intervention necessary' as moderately appropriate (mean of 5) (Appendix S3).

Face-to-face meeting

Seventeen healthcare professionals attended the meeting, of whom 16 had responded to both questionnaires.

The patient questionnaires were discussed extensively. The following complaints were reported: 'pain', 'prolapse', 'itching', 'soiling' and 'blood loss'. These symptoms were the most important to be discussed during the outpatient clinic.

With these results healthcare professionals rated the domain 'symptoms' as the most appropriate primary

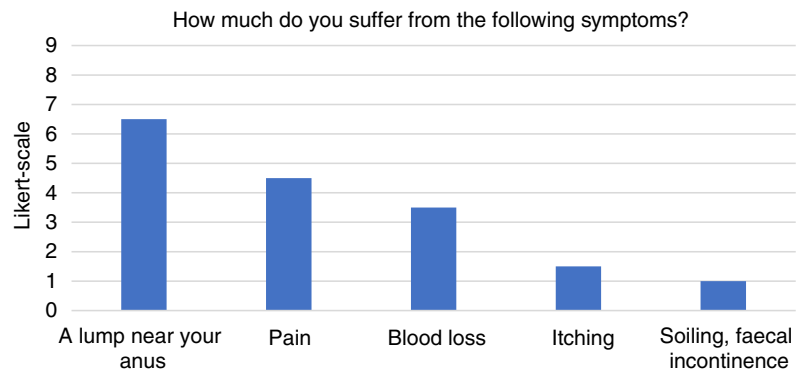


Figure 2 Results, patient questionnaire.

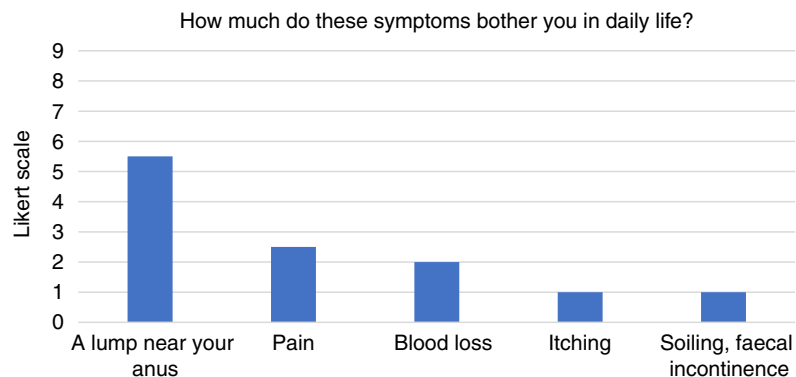


Figure 3 Results, patient questionnaire.

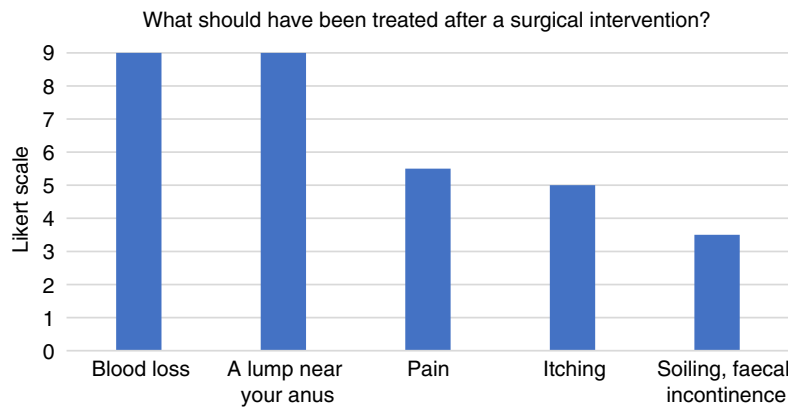


Figure 4 Results, patient questionnaire.

end-point in the COS. Further, healthcare professionals reached consensus that the domains ‘complications’, ‘recurrence’ and ‘patient satisfaction’ should all be used as secondary end-points in the COS for HD (Table 1).

Healthcare professionals agreed that the domain ‘symptoms’ should be a patient reported outcome measure (PROM) and should include the outcomes ‘pain’, ‘prolapse’, ‘itching’, ‘soiling’ and ‘blood loss’.

The domain ‘complications’ should include the outcomes ‘incontinence’, ‘abscess’, ‘urinary retention’, ‘anal stenosis’ and ‘fistula’.

During the face-to-face meeting the definition of recurrence was discussed extensively. Consensus was reached to use ‘reappearance of initial symptoms’ as reported by the patient to define recurrence.

Short survey

In total 15 healthcare professionals completed the short survey. Consensus was reached that ‘incontinence’ should be assessed by the Wexner Fecal Incontinence Score [32], ‘abscess’ by physical examination, ‘urinary retention’ by ultrasonography, ‘anal stenosis’ by physical examination and ‘fistula’ by MR imaging after inconclusive physical examination. During follow-up, the outcome ‘symptoms’ should be assessed at baseline (i.e. before the procedure) and 7 days, 6 weeks (possibly by telephone) and at 1 year post-procedure. The outcomes ‘abscess’ and ‘urinary retention’ should be assessed 7 days post-procedure, and ‘rectal stenosis’, ‘incontinence’ and ‘fistula’ at 1 year post-procedure (Table 2).

Discussion

This consensus study presents the first ESCP COS for HD based on a systematic review of the literature and an international Delphi study among healthcare

professionals. As the primary end-point, the domain ‘symptoms’ was selected. The three domains ‘complications’, ‘recurrence’ and ‘patient satisfaction’ were chosen as secondary end-points. Eventually healthcare professionals agreed that the domain ‘symptoms’ should be a PROM and should include the outcomes ‘pain’ and ‘prolapse’, ‘blood loss’, ‘itching’ and ‘soiling’. The domain ‘complications’ should include the outcomes ‘incontinence’, ‘abscess’, ‘urinary retention’, ‘anal stenosis’ and ‘fistula’. Consensus was also reached on how the primary and secondary outcomes should be measured and at which time points pre- and post-procedure.

Further, consensus was reached to define ‘recurrence’ as ‘reappearance of initial symptoms’.

With the continuing evolution of different treatments for HD, the effectiveness of treatments needs to be analysed in a systematic way. Reviews of the published literature highlighted the lack of uniformity of outcome definition, measurement and reporting [11–13]. This resulted in wide variation in outcomes between studies using the same techniques but which used different definitions for the same outcomes and/or various outcomes for the same treatment modalities. As a result, HD studies cannot inform directly an optimal treatment algorithm. This may hamper efficient use of healthcare resources [33]. The standardization of outcomes and outcome measurement in HD studies is mandatory to support the development of effective patient care.

Besides uniformity in reporting, this Delphi study underlined the need to integrate PROMs with traditional clinical outcomes. PROMs have become an increasingly important component of assessing treatment response [34]. Several HD-specific symptom scores and quality of life outcomes are developed for use in clinical practice. Examples include the Symptom-based Severity Score [35] and the Haemorrhoid Severity Score [36].

Table 1 Summary of the core domains for haemorrhoidal disease

Core outcome set	
Primary outcome	
Patient reported symptoms	Patient reported outcome measure (PROM)
Blood loss	
Pain	
Prolapse	
Itching	
Soiling	
Secondary outcome	
Complications	
Incontinence	Wexner Fecal Incontinence Score
Abscess	Physical examination
Fistula	MR imaging after inconclusive physical examination
Urinary retention	Ultrasonography
Anal stenosis	Physical examination
Recurrence	The reappearance of initial symptoms
Patient satisfaction	This end-point will be included in the PROM

Table 2 Follow-up scheme.

	Outcomes	Baseline	7 days	6 weeks	1 year
Primary end-point	Symptoms (PROM)	×	×	×	×
Secondary end-points	Abscess		×		
	Urinary retention		×		
	Anal stenosis				×
	Incontinence				×
	Fistula				×

These symptom scores offer a potential solution to simplify the various symptoms of haemorrhoids. However, the lack of fully validated instruments is a limitation to incorporating them in future HD studies.

At the moment, we are developing a disease-specific PROM for haemorrhoids that will be based on the results of this Delphi study. We will also incorporate the results of a qualitative study with patients in this PROM. We recently conducted individual interviews with 15 patients to obtain a more in-depth understanding of patients' experiences with HD, impact on daily life and results of treatment.

We suggest that future studies evaluating interventions for HD should assess and report the primary and secondary end-points of the COS reported here. Additional outcomes may be included if appropriate for the specific intervention or setting. Furthermore, especially for research purposes, it is advisable that the primary outcome 'symptoms' is also measured at baseline, i.e. before the procedure.

To our knowledge, our project is the first Delphi process to develop a COS for HD. We started with an in-depth literature review which identified 10 domains, 59 outcomes and several different instruments. Subsequently, as described in this paper, the minimum COS was compiled from the perspectives of 17 healthcare professionals and 18 patients with HD using a Delphi process. The extensive process following OMERACT and the broad consensus reached are the main strengths of this study.

However, several limitations remain present. First, although Delphi processes have been recommended as an ideal approach to identify which outcomes to measure in clinical trials [26], they have also been criticized. One of the major critiques is assuring methodological rigour which is often cited as a weakness, because there are 10 different types of Delphi methods [37]. We chose to follow OMERACT Filter 2.0 since their guideline resulted in successful development and implementation of COSs for many other diseases.

A second limitation of this study was that patients were only partially involved in the development of this COS. Patients received a modified questionnaire, because some questions posed to the healthcare professional were deemed irrelevant for patients. The modified questionnaire focused on symptoms they experienced in daily life and how much they were bothered by them. As a result, patients were not asked specifically what outcomes they consider most important in a research setting. For example, the question ‘What domains should be included as the primary end-point and what domains as secondary end-points in the COS for HD?’ was not posed to patients. However, patient input regarding the most important symptoms of HD resulted in the selection of the five symptoms that make up the primary outcome in the COS. Furthermore, while we conducted qualitative interviews to get more input from the patients’ point of view to be able to develop a PROM, these interviews should have been performed prior to the Delphi study to ensure patient views were adequately represented in the Delphi surveys. Patients also did not participate in the face-to-face meeting. However, the results and comments on the patient questionnaire were presented to the healthcare professionals. These results were discussed extensively during the meeting. There was opportunity for open discussion and dissenting views regarding the patients’ results were actively sought.

A third limitation was that the questionnaires used in the Delphi rounds were not validated. It is therefore possible that some outcomes may have been missed. Further, we made a selection of the domains and outcomes that were identified in the literature review, based on the frequency of reporting, because we felt that 59 outcomes were too many to present to the panel in a Delphi survey. However, by doing so we may have overlooked outcomes that may be important to patients. It would have been better to organize a consensus meeting to reduce the outcomes to a manageable number for the Delphi questionnaire.

Fourth, while we contacted all 43 representatives of the ESCP, most representatives did not treat HD regularly and could not therefore take part in the Delphi survey. This resulted in fewer healthcare professionals on the panel than was initially planned (and stated in the protocol) [38]. Finally, there may be a concern that 18 Dutch patients may not represent fully the views of HD patients across Europe. Unfortunately, our resources were limited and we were unable to conduct patient interviews in other countries. However, by testing the COS and validating the PROM (that has been developed based on patient views) in an international setting, we expect that, if present, diverging views will

emerge and it will be possible to adapt them. It is important to emphasize that a COS is dynamic and can (and should) be reviewed regularly. Future work should ensure a more prominent role of the patient in COS development.

In conclusion, this study presents the first ESCP COS for HD based on an international Delphi study among healthcare professionals. This COS will be useful for future intervention trials in this condition, encouraging a more coordinated approach than currently exists to interventional research in the future and facilitating more meaningful analysis of research findings.

Acknowledgements

This work was undertaken with support of the European Society of Coloproctology. The project received no funding.

Conflicts of interest

No conflicts of interest.

Collaborators

National representatives of the European Society of Coloproctology are collaborators in the study: Andreas Salat¹, Andreas Ommer², Pasquale Giordano³, Lilli Lundby⁴, Paola de Nardi⁵, Raimund Strouhal⁶, Martina Lemmerer⁷, Konstantinos M. Stamou⁸, Georgius Pechliivanidis⁹, Nikolaos Gouvas¹⁰, Evaghelos Xynos¹¹, Alexander Herold¹², Ingo Alldinger¹³, Faramarz Pakravan¹³, Corrado R. Asteria¹⁴, Dimitri Christoforidis¹⁵, Niels Qvist¹⁶, Gunnar Baatrup¹⁶, Nir Wasserberg¹⁷.

1. Department of Surgery, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria

2. End- und Dickdarm-Zentrum Essen, Rüttenscheider Strasse 66, 45130 Essen, Germany

3. Barts Health NHS Trust, Whitechapel, Turner St, Whitechapel, London E1 1BB, UK

4. Department of Surgery P, Aarhus University Hospital, Tage-Hansens Gade 2, 8000 Aarhus C, Denmark

5. Department of Surgery, San Raffaele Scientific Institute, Milan, Italy

6. General Surgery, Krankenhaus Oberndorf, Paracelsusstrasse 37, 5110 Oberndorf bei Salzburg, Austria

7. Department of General and Visceral Surgery, Medical University Clinic Graz, Auenbruggerplatz 29, A-8036 Graz, Austria

8. Department of Colorectal Surgery, Peritoneal Surface Malignancy Program, Bioclinic, Athens, Greece

9. General Surgery, Metropolitan Hospital of Piraeus, Ethnarchou Makariou 9, Pireas 185 47, Greece
10. Worcestershire Acute Hospitals NHS Trust, Charles Hastings Way, Worcester WR5 1DD, UK
11. Creta Inter-Clinic Hospital, Heraklion, Crete, Greece
12. End- und Dickdarm-Zentrum Mannheim, Bismarckpl. 1, 68165 Mannheim, Germany
13. CPZ-Coloproktologisches Zentrum Düsseldorf, Schadowstraße 11B, 40212 Düsseldorf, Germany
14. Department of Surgery and Orthopaedics, ASST, Mantova, Str Lago Paiolo, 10 I-46100 Mantova, Italy
15. Ospedale Regionale di Lugano, Via Tesserete 46, 6900 Lugano, Italy
16. University of Southern Denmark, Campusvej 55, 5230 Odense M, Danmark
17. Department of Surgery, Herzliya Medical Centre, 7 Ramat Yam St Herzliya, Israel

References

- 1 Yang J, Cui PJ, Han HZ, Tong DN. Meta-analysis of stapled hemorrhoidopexy vs LigaSure hemorrhoidectomy. *World J Gastroenterol* 2013; **19**: 4799–807.
- 2 Burkitt DP. Varicose veins, deep vein thrombosis, and haemorrhoids: epidemiology and suggested aetiology. *Br Med J* 1972; **2**: 556–61.
- 3 Alonso-Coello P, Zhou Q, Martinez-Zapata MJ *et al*. Meta-analysis of flavonoids for the treatment of haemorrhoids. *Br J Surg* 2006; **93**: 909–20.
- 4 Gencosmanoglu R, Sad O, Koç D, Inceoğlu R. Hemorrhoidectomy: open or closed technique? A prospective, randomized clinical trial. *Dis Colon Rectum* 2002; **45**: 70–5.
- 5 Banov L Jr, Knoepf LF Jr, Erdman LH, Alia RT. Management of hemorrhoidal disease. *J S C Med Assoc* 1985; **81**: 398–401.
- 6 Gaj F, Trecca A, Busotti A, Brugiotti C, Carboni M. The new classification of hemorrhoids: PATE 2000-Sorrento. History of the scientific debate. *Minerva Chir*, 2002; **57**: 331–9.
- 7 Elbetti C, Giani I, Novelli E, Fucini C, Martellucci J. The single pile classification: a new tool for the classification of haemorrhoidal disease and the comparison of treatment results. *Updates Surg* 2015; **67**: 421–6.
- 8 Rivadeneira DE, Steele SR, Ternent C, Chalasani S, Buie WD, Rafferty JL; Standards Practice Task Force of the American Society of Colon and Rectal Surgeons. Practice parameters for the management of hemorrhoids (revised 2010). *Dis Colon Rectum* 2011; **54**: 1059–64.
- 9 Higuero T, Abramowitz L, Castinel A *et al*. Guidelines for the treatment of hemorrhoids (short report). *J Visc Surg* 2016; **153**: 213–8.
- 10 Altomare DF, Roveran A, Pecorella G, Gaj F, Stortini E. The treatment of hemorrhoids: guidelines of the Italian Society of Colorectal Surgery. *Tech Coloproctol* 2006; **10**: 181–6.
- 11 Shanmugam V, Thaha MA, Rabindranath KS, Campbell KL, Steele RJ, Loudon MA. Systematic review of randomized trials comparing rubber band ligation with excisional hemorrhoidectomy. *Br J Surg* 2005; **92**: 1481–7.
- 12 Shao WJ, Li GC, Zhang ZH, Yang BL, Sun GD, Chen YQ. Systematic review and meta-analysis of randomized controlled trials comparing stapled hemorrhoidopexy with conventional hemorrhoidectomy. *Br J Surg* 2008; **95**: 147–60.
- 13 Simillis C, Thoukididou SN, Slessor AA, Rasheed S, Tan E, Tekkis PP. Systematic review and network meta-analysis comparing clinical outcomes and effectiveness of surgical treatments for haemorrhoids. *Br J Surg*, 2015; **102**: 1603–18.
- 14 Klokker L, Tugwell P, Furst DE *et al*. Developing an OMERACT Core Outcome Set for assessing safety components in rheumatology trials: the OMERACT Safety Working Group. *J Rheumatol* 2017; **44**: 1916–9.
- 15 van Tol RR, Melenhorst J, Dirksen CD, Stassen LPS, Breukink SO. Protocol for the development of a Core Outcome Set (COS) for hemorrhoidal disease: an international Delphi study. *Int J Colorectal Dis* 2017; **32**(7): 1091–1094.
- 16 Hall NJ, Kapadia MZ, Eaton S *et al*. Outcome reporting in randomised controlled trials and meta-analyses of appendicitis treatments in children: a systematic review. *Trials* 2015; **16**: 275.
- 17 Schmitt J, Spuls PI, Thomas KS *et al*. The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. *J Allergy Clin Immunol* 2014; **134**: 800–7.
- 18 Mackie SL, Twohig H, Neill LM *et al*. The OMERACT core domain set for outcome measures for clinical trials in polymyalgia rheumatica. *J Rheumatol* 2017; **44**: 1515–21.
- 19 Toupin-April K, Barton J, Fraenkel L *et al*. Toward the development of a core set of outcome domains to assess shared decision-making interventions in rheumatology: results from an OMERACT Delphi survey and consensus meeting. *J Rheumatol* 2017; **44**: 1544–50.
- 20 Hatemi G, Meara A, Ozguler Y *et al*. Developing a core set of outcome measures for Behcet disease: report from OMERACT 2016. *J Rheumatol* 2017; **44**: 1750–3.
- 21 Singh JA, Dowsey M, Choong PF. Patient endorsement of the Outcome Measures in Rheumatology (OMERACT) Total Joint Replacement (TJR) clinical trial draft core domain set. *BMC Musculoskelet Disord* 2017; **18**: 111.
- 22 Singh JA, Dowsey MM, Dohm M *et al*. Achieving consensus on total joint replacement trial outcome reporting using the OMERACT filter: endorsement of the final core domain set for total hip and total knee replacement trials for endstage arthritis. *J Rheumatol* 2017; **44**: 1723–6.
- 23 van Tol RR, van Zwietering E, Kleijnen J *et al*. Towards a core outcome set for hemorrhoidal disease – a systematic review of outcomes reported in literature. *Int J Colorectal Dis* 2018; **33**: 849–56.
- 24 Boers M, Kirwan JR, Wells G. *J Clin Epidemiol*, 2014; **67**: 745–53.
- 25 Steurer J. The Delphi method: an efficient procedure to generate knowledge. *Skeletal Radiol* 2011; **40**: 959–61.

- 26 Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. *PLoS Med* 2011; **8**: e1000393.
- 27 McNair AG, Whistance RN, Forsythe RO *et al.* Core outcomes for colorectal cancer surgery: a consensus study. *PLoS Med* 2016; **13**: e1002071.
- 28 Potter S, Holcombe C, Ward JA, Blazeby JM; BRAVO Steering Group. Development of a core outcome set for research and audit studies in reconstructive breast surgery. *Br J Surg*, 2015; **102**: 1360–71.
- 29 Moossdorff M, van Roozendaal LM, Strobbe LJ *et al.* Maastricht Delphi consensus on event definitions for classification of recurrence in breast cancer research. *J Natl Cancer Inst* 2014; <https://doi.org/10.1093/jnci/dju288>.
- 30 Sudol-Szopinska I, Kucharczyk A, Kołodziejczak M, Warczyńska A, Pracon G, Wiączek A. Endosonography and magnetic resonance imaging in the diagnosis of high anal fistulae – a comparison. *J Ultrason* 2014; **14**: 142–51.
- 31 Lunniss PJ, Armstrong P, Barker PG, Reznick RH, Phillips RK. Magnetic resonance imaging of anal fistulae. *Lancet* 1992; **340**: 394–6.
- 32 Seong MK, Jung SI, Kim TW, Joh HK. Comparative analysis of summary scoring systems in measuring fecal incontinence. *J Korean Surg Soc* 2011; **81**: 326–31.
- 33 NICE (National Institute for Health and Care Excellence). Process and methods [PMG19] in Guide to the Processes of Technology Appraisal. 2014: London.
- 34 Speight J, Barendse SM. FDA guidance on patient reported outcomes. *BMJ* 2010; **340**: c2921.
- 35 Pucher PH, Qurashi M, Howell AM *et al.* Development and validation of a symptom-based severity score for haemorrhoidal disease: the Sodergren score. *Colorectal Dis* 2015; **17**: 612–8.
- 36 Brown S, Tiernan J, Biggs K *et al.* The HubBLc Trial: haemorrhoidal artery ligation (HAL) versus rubber band ligation (RBL) for symptomatic second- and third-degree haemorrhoids: a multicentre randomised controlled trial and health-economic evaluation. *Health Technol Assess* 2016; **20**: 1–150.
- 37 Beretta R. A critical review of the Delphi technique. *Nurse Res* 1996; **3**: 79–89.
- 38 van Tol RR, Melenhorst J, Dirksen CD, Stassen LPS, Breukink SO. Protocol for the development of a Core Outcome Set (COS) for hemorrhoidal disease: an international Delphi study. *Int J Colorectal Dis* 2017; **32**: 1091–4.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Questionnaire 1: Healthcare professionals.

Appendix S2. Healthcare professionals scoring the domains and outcomes on a nine-point scale, where 1–3 equals ‘inappropriate’ (out) and 4–6 equals ‘unsure’ (vote again).

Appendix S3. Translated patient questionnaire.