

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Defining Standards in Colorectal Optimisation (DiSCO): a Delphi study protocol to achieve international consensus on key standards for colorectal surgery prehabilitation
AUTHORS	Pearson, Iona; Blackwell, Sue; Fish, Rebecca; Daniels, Sarah; West, Malcolm; Mutrie, Nanette; Kelly, P; Knight, Stephen; Fearnhead, Nicola; Moug, Susan

VERSION 1 – REVIEW

REVIEWER	C.P.M. van Helsdingen Amsterdam UMC - Location AMC, The Netherlands
REVIEW RETURNED	21-Dec-2020

GENERAL COMMENTS	<p><i>Defining Standards in Colorectal Optimisation (DiSCO): study protocol to achieve international consensus on key standards for colorectal surgery prehabilitation</i></p> <p>Summary: This is a protocol for a consensus study that aims to create a core outcome set for research in the field of prehabilitation in colorectal surgery. To achieve this goal the outcomes of a systematic review and a patient and public involvement event will be combined and serve as the base of a three round Delphi study. The results of this Delphi analysis will be discussed in a stakeholder meeting to create the final standard report. Although the importance of this study is clear and the method is well thought generally, particularly the involvement of all different stakeholders, there are some concerns and questions regarding the design of the different components of the study that I explained below.</p> <p><i>Title</i></p> <p>Minor: Consider to add the type of study to the title of the manuscript.</p> <p><i>Abstract</i></p> <p>Minor:</p> <ol style="list-style-type: none">Page 6, line 16-17: Consider to mention protocol and study registrations in the ethics and dissemination section of the abstract and remove it from the introduction.Page 6, line 27-28: Consider to describe in the methods and analysis section that the participants of the Delphi process will be national <u>and</u> international stakeholders. <p><i>Introduction</i></p> <p>Minor: Page 8, line 10-13: Please consider rewriting this sentence</p>
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	<p>which is intended to emphasize the importance of this study, however in this form it lacks strength.</p> <p><i>Methods and analysis</i></p> <p>Major:</p> <ol style="list-style-type: none"> 1. The systematic review described in the methods has already been published (same PROSPERO registration ID: CRD42019120318): 'Daniels SL, Lee MJ, George J, et al. Prehabilitation in elective abdominal cancer surgery in older patients: systematic review and meta-analysis [published online ahead of print, 2020 Sep 22]. <i>BJS Open</i>. 2020;4(6):1022-1041. doi:10.1002/bjs.50347. Please add reference and remove the part describing the systematic review. 2. The systematic review that will be used to create the longlist of standards focuses on older patients with abdominal cancer, while the patients that will be selected for the PPI Event will be adults over 18 years of age and with both benign or malignant diseases. This inconsistency raises questions and can cause heterogeneity. Please explain the choice of using this systematic review in combination with the choice of criteria for the participants of the PPI Event. 3. What are the intended number of participants, for both the PPI Event and the Delphi study? Please explain what the numbers are based on and why this amount of participants is chosen. 4. Page 12, line 46-54: It is not completely clear to me which standards will be excluded in every round and why they will be excluded. And therefore it is not clear to me which standards will form the shortlist after the three round Delphi. For example, the standards which are ranked of little importance will be excluded after round 1, however that means that consensus is reached on these standards, which is an important result. So will the shortlist only contain statements that were scored to be of critical importance or also the statements that were scored to be of some importance or of little importance? Please describe more clearly which standards will be included and excluded in every round and which standards will be in the shortlist eventually. <p>Minor:</p> <ol style="list-style-type: none"> 1. Please add that the project is registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative, with registration number if available. This is now only mentioned in the abstract. 2. As stated on page 9, line 35: Please describe what is defined as "key stakeholders that have published on prehabilitation". 3. Page 11, line 43-46: Please explain how the PPI Event will take place if it is not possible to organize a face-to-face event due to COVID-19 restrictions. 4. Page 12, line 46-49: Please explain what the predetermined consensus threshold is based on or why this threshold has been chosen. Add reference if this threshold is a commonly used threshold in other Delphi studies.
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REVIEWER	Mark Coleman University Hospitals Plymouth NHS Trust
REVIEW RETURNED	25-Jan-2021

GENERAL COMMENTS	This paper is a protocol paper for an international study to achieve consensus on standards for colorectal surgery prehabilitation. The authorship represents a good representation of surgeons, other professionals including sports scientists and patients. The aims of the study are to identify key components of prehabilitation, patient
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	selection for prehabilitation, identify who should deliver prehabilitation and determine outcome measures. The study steps are clearly outlined with timelines and contributors. The Delphi process conforms to COMET criteria and accounts for limitations of Covid-19. Funding is from a charity and a multinational surgical company but there are no conflicting interests. Ethics and limitations are appropriately discussed.
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REVIEWER	Antonino Spinelli Humanitas Clinical and Research Center, IRCCS, Italy
REVIEW RETURNED	28-Jan-2021

GENERAL COMMENTS	<p>The authors are presenting a study protocol to achieve international consensus on multimodal prehabilitation in elective colorectal surgery, involving patients and stakeholders in a multi-step process that includes an initial review of the literature, an online survey, and a three-round Delphi consensus.</p> <p>The authors address a topic of great interest in colorectal surgery and provide a robust conceptual design. In general, the study is well designed, well-written, and well-presented.</p> <p>I have only a few minor concerns/suggestions:</p> <ul style="list-style-type: none"> • Reference 7: the reference dates 2017, I would suggest also cite the more recent meta-analysis from Hegers et al. (PMID: 31228083), which is extended to low-risk patients and reported similar results compared with Barberan-Garcia. • There is limited evidence in the literature of the effectiveness of prehabilitation in IBD patients, compared with colorectal cancer patients. However, IBD patients would particularly benefit from preoperative nutritional and functional improvement interventions. I would suggest the authors add few details in the background about the current practice on IBD prehabilitation. • I know that the method section is already complex, but the authors should add some additional details on the systematic review methods: I think that the databases screened and the interval period of search would be informative enough. • It is unclear whether the opinion leaders involved in the Delphi process are the same involved in the PPI coordination. The author should clarify the expertise and number of participants in the Delphi process, as this may influence the outcome of the voting. • Among the stakeholders involved in the PPI process there are colorectal surgeons; colorectal anesthetists; colorectal nurse specialists; colorectal oncologist (medical or clinical); exercise oncologists; exercise physiologists; sports scientists; sports medicine specialists; physical exercise/ activity specialists; nutritionists/ dieticians; psychologists; geriatricians, pharmacists, General practitioners. Since the prehabilitation is intended to include also IBD patients, I would add to the stakeholders list also gastroenterologists and IBD experts.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Minor: Consider to add the type of study to the title of the manuscript.

This has been changed as requested in the title. Defining Standards in Colorectal Optimisation (DiSCO): a Delphi study protocol to achieve international consensus on key standards for colorectal surgery prehabilitation.

Abstract

Minor:

1. Page 6, line 16-17: Consider to mention protocol and study registrations in the ethics and dissemination section of the abstract and remove it from the introduction.

This has been removed from the introduction section changing the last sentence of the introduction to: The DiSCO Study (Defining Standards in Colorectal Optimisation) aims to achieve international consensus from all stakeholders on key standards to provide a framework for reporting future prehabilitation research.

And we have added to the ethics section: The University of Glasgow College of Medical, Veterinary & Life Sciences Ethics Committee has approved this protocol which is registered as a study (200190120) with the Core Outcome Measures in Effectiveness Trials (COMET) initiative

2. Page 6, line 27-28: Consider to describe in the methods and analysis section that the participants of the Delphi process will be national <u>and</u> international stakeholders.

Thank you. This line has been modified in the Methods section of the abstract as requested. This will engage all stakeholders (healthcare professionals and patients) both nationally and internationally.

Introduction

Minor: Page 8, line 10-13: Please consider rewriting this sentence which is intended to emphasize the importance of this study, however in this form it lacks strength.

Thank you for your comment. We are uncertain what sentence you mean but would be happy to strengthen as requested. We suspect our page numbers are different to yours as page 8 is the methods section not introduction.

Methods and analysis

Major:

1. The systematic review described in the methods has already been published (same PROSPERO registration ID: CRD42019120318): 'Daniels SL, Lee MJ, George J, et al. Prehabilitation in elective abdominal cancer surgery in older patients: systematic review and meta-analysis [published online ahead of print, 2020 Sep 22]. *BJS Open*. 2020;4(6):1022-1041. doi:10.1002/bjs5.50347. Please add reference and remove the part describing the systematic review.

Thank you - you are correct in that the review has been published since our submission to BMJ Open. We have included this reference [16] in the systematic review section, removed the description also and added the full reference as follows in the reference list.

*Daniels SL, Lee MJ, George J, et al. Prehabilitation in elective abdominal cancer surgery in older patients: systematic review and meta-analysis. *BJS Open*. 2020; 4(6):1022.*

2. The systematic review that will be used to create the longlist of standards focuses on older patients with abdominal cancer, while the patients that will be selected for the PPI Event will be adults over 18 years of age and with both benign or malignant diseases. This inconsistency raises questions and can cause heterogeneity. Please explain the choice of using this systematic review in combination with the choice of criteria for the participants of the PPI Event.

We thank you for raising this point. We chose to do this review on these populations because the majority of prehabilitation is published in the area of colorectal cancer which has an older adult population. We thought that this would allow parameters/ standards to be taken forward into the Delphi, whereas if we used younger/benign population there would be almost no published work to combine and analyse as prehab remains relatively unexplored in those areas (as stated by reviewer 3)..

Whilst we acknowledge this is a limitation you can see from our aims that we are striving to include overlooked prehab populations and voices to achieve consensus. In particular our PPI group will include younger and IBD/ benign populations.

3. What are the intended number of participants, for both the PPI Event and the Delphi study? Please explain what the numbers are based on and why this amount of participants is chosen.

Thank you – we have added the following to the PPI section A target of 20 participants will be sought, with a minimum of 10 of these being patients.

And have added the following to the Stage 2: Creating standards shortlist in the analysis section A target of 100 or above respondents will be sought.

4. Page 12, line 46-54: It is not completely clear to me which standards will be excluded in every round and why they will be excluded. And therefore it is not clear to me which standards will form the shortlist after the three round Delphi. For example, the standards which are ranked of little importance will be excluded after round 1, however that means that consensus is reached on these standards, which is an important result. So will the shortlist only contain statements that were scored to be of critical importance or also the statements that were scored to be of some importance or of little importance? Please describe more clearly which standards will be included and excluded in every round and which standards will be in the shortlist eventually.

We have modified the paragraphs to be clearer as follows:

Stage 2: Creating standards shortlist

...To reduce bias, a predetermined consensus threshold will be used: Standards which are ranked of critical importance (7-9) by >70% or of little importance (1-3) by <15% of each stakeholder group will be deemed to have reached the threshold for consensus for inclusion in the shortlist of key standards. After round 1 of the Delphi, standards reaching the threshold of consensus for inclusion will be directly added to the shortlist and not included in subsequent rounds. All items not reaching this threshold will be taken forward to round 2. The same criteria will be used after round 2 to select items to take forward into round 3. After round 3 any additional items reaching the threshold for consensus for inclusion will be added to the shortlist. Any items which are ranked of critical importance (7-9) by <50% of each stakeholder group, or of little importance (1-3) by >50% of each stakeholder group after round 3 will be excluded from the final shortlist. Standards that do not meet the criteria for inclusion or exclusion will be considered borderline. The final shortlist and borderline items will be taken forward for discussion at the final consensus meeting.

Stage 3: Finalising the standards set

...The shortlist of standards that met the threshold for consensus after each round of the Delphi will be presented and ratified by vote. The borderline standards will be discussed and voted on individually. For each standard, the group will anonymously rank its importance on the same 9-point scale used in the Delphi study to establish a group baseline. Following this, there will be a group discussion of the standard with arguments for and against its inclusion in the final standards set. A further round of anonymous voting will follow discussion. A result of at least 70% ranking the standard as critically important, and fewer than 15% ranking it of little importance will be required for inclusion in the final standards set. There are no universally agreed consensus criteria and the criteria used here follow published recommendations [20].

Minor:

1. Please add that the project is registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative, with registration number if available. This is now only mentioned in the abstract.

Thank you – we have added the following comment to the last sentence of Methods and Analysis. (registered as a study; 200190120).

2. As stated on page 9, line 35: Please describe what is defined as “key stakeholders that have published on prehabilitation”.

There is an extensive list of what the key stakeholders are (listed below). We feel that this is one of the largest and varied stakeholder groups to be asked about prehab, but would be happy to hear if the reviewer feels we have overlooked any groups.

“will identify key stakeholders that have published on prehabilitation. This is likely to include: colorectal surgeons; colorectal anaesthetists; colorectal nurse specialists; colorectal oncologist (medical or clinical); exercise oncologists; exercise physiologists; sports scientists; sports medicine specialists; physical exercise/ activity specialists; nutritionists/ dieticians; psychologists; geriatricians, pharmacists, General practitioners (GP). To ensure inclusivity, specialist associations related to these stakeholders will be approached: American College of Sports Medicine (ACSM), International Society of Behavioural, Nutrition and Physical Activity (ISBNPA), Scottish Physical Activity Research Collaborative (SPARC), Macmillan, Royal College of Anaesthetists (RCoA); Association of Surgeons of Great Britain and Ireland (ASGBI); Association of Coloproctology of Great Britain and Ireland (ACPGBI); TriPOM (Trainees with an interest in Perioperative Medicine); ERAS (Enhanced Recovery After Surgery) Association’.

3. Page 11, line 43-46: Please explain how the PPI Event will take place if it is not possible to organize a face-to-face event due to COVID-19 restrictions.

This is an excellent point – thank you. We have removed ‘Unable to physically attend the PPI event’ from the exclusion criteria. We have added in the following line to cover COVID-19 restrictions. If the event occurs during the COVID-19 pandemic then the format will be moved to a secure online NHS-approved virtual platform.

4. Page 12, line 46-49: Please explain what the predetermined consensus threshold is based on or why this threshold has been chosen. Add reference if this threshold is a commonly used threshold in other Delphi studies.

*This is a commonly used threshold and for clarity we have added in a reference. Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012; 13:132.*

Reviewer: 2

There are no issues or comments to address. Thank you.

Reviewer: 3

- Reference 7: the reference dates 2017, I would suggest also cite the more recent meta-analysis from Hegers et al. (PMID: 31228083), which is extended to low-risk patients and reported similar results compared with Barberan-Garcia.

We thank you for your kind suggestion. We have included this as reference 7 and modified the other references accordingly.

*Heger P, Probst P, Wiskemann J, Steindorf K, Diener MK, Mihaljevic A. A Systematic Review and Meta-analysis of Physical Exercise Prehabilitation in Major Abdominal Surgery. *Journal of Gastrointestinal Surgery*. 2020; 24. 1385.*

- There is limited evidence in the literature of the effectiveness of prehabilitation in IBD patients, compared with colorectal cancer patients. However, IBD patients would particularly benefit from preoperative nutritional and functional improvement interventions. I would suggest the authors add few details in the background about the current practice on IBD prehabilitation.

We understand exactly what this reviewer is asking. To incorporate their comment and highlight other overlooked patient populations we have done the following: Introduction we have added: predominately. And added into the next paragraph: One major shortcoming is the lack of

research performed in non-cancer populations, including inflammatory bowel disease (IBD), pelvic floor and diverticular disease.

- I know that the method section is already complex, but the authors should add some additional details on the systematic review methods: I think that the databases screened and the interval period of search would be informative enough.

As per the Editor request we have changed this section to show that the systematic review has been published since our BMJ Open submission. We have provided the full reference to allow the reader to access any additional details needed.

- It is unclear whether the opinion leaders involved in the Delphi process are the same involved in the PPI coordination. The author should clarify the expertise and number of participants in the Delphi process, as this may influence the outcome of the voting.

The PPI will be performed prior to the Delphi process as results from the PPI will drive the long-listing for the Delphi. PPI work with the systematic review comes under Stage 1. Stage 2 is the Delphi as stated in the methods.

The online Delphi will be sent out to key stakeholders and advertised on Twitter. This is to allow equity of access to as many people involved with prehab as possible. Overall numbers will be reported and each participant is asked their job/ specialist role at the start of the Delphi that will allow reporting of the participants.

- Among the stakeholders involved in the PPI process there are colorectal surgeons; colorectal anesthetists; colorectal nurse specialists; colorectal oncologist (medical or clinical); exercise oncologists; exercise physiologists; sports scientists; sports medicine specialists; physical exercise/ activity specialists; nutritionists/ dieticians; psychologists; geriatricians, pharmacists, General practitioners. Since the prehabilitation is intended to include also IBD patients, I would add to the stakeholders list also gastroenterologists and IBD experts.

We have chosen not to include medical gastroenterologists as many will not be involved in the pre-surgical pathway. We have included surgeons and nurse specialists that will be experts in IBD which allows IBD experts to have their say in defining prehabilitation standards in this body of work. In addition, the support from groups such as International Society of Behavioural Nutrition and Physical Activity should ensure nutrition experts to have their input and Ileostomy and Internal Pouch Association will allow IBD patients access to the survey.

VERSION 2 – REVIEW

REVIEWER	Claire P.M. van Helsdingen Amsterdam UMC, the Netherlands
REVIEW RETURNED	19-Feb-2021

GENERAL COMMENTS	<p>Thank you for the revised manuscript and your response to the comments.</p> <p>I have one last minor comment on the Methods and Analysis section, page 7 and 8.</p> <p>Please have a look at references 16 and 17.</p> <p>Page 7, "Stakeholders" line 38/39-40 you mention both the systematic review and the recently published guideline, however only the reference of the systematic review [16] is in the text, please add the reference of the guideline [17].</p> <p>And on page 8, "Systematic review" line 45/46-47 the systematic review is described, however the reference of the guideline is in the text [17] and not [16] of the systematic review.</p>
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REVIEWER	Antonino Spinelli IRCCS Humanitas Research Hospital, Italy
REVIEW RETURNED	17-Feb-2021

GENERAL COMMENTS	The authors provided exhaustive information according to the first revision.
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