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**A core outcome set for seamless, standardized evaluation of innovative surgical procedures and devices (COHESIVE): a patient and professional stakeholder consensus study**

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**Author contributions:** KA, SP and JB conceived and initiated the study and designed the study protocol. JB developed the ideas for the NIHR Bristol BRC Surgical Innovation theme. KA and SP had joint senior oversight and co-directed the study. All named study steering group members contributed to oversight of the study, aspects of study design and/or acquisition of data and/or interpretation of data. KA wrote the first draft of this manuscript. KA, JB, CH, RM, AM, SP, NW and members of the study steering group critically revised the manuscript. All authors give final approval of the version to be published.

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**Running head:** A core outcome set for surgical innovation

## STRUCTURED ABSTRACT

**Objective:** To develop a core outcome set (COS), an agreed minimum set of outcomes to measure and report in all studies evaluating the introduction and evaluation of novel surgical techniques.

**Summary Background Data:** Agreement on the key outcomes to measure and report for safe and efficient surgical innovation is lacking, hindering transparency and risking patient harm.

**Methods:** (I) Generation of a list of outcome domains from published innovation-specific literature, policy/regulatory body documents, and surgeon interviews; (II) Prioritization of identified outcome domains using an international, multi-stakeholder Delphi survey; (III) Consensus meeting to agree the final COS. Participants were international stakeholders, including patients/public, surgeons, device manufacturers, regulators, trialists, methodologists and journal editors.

**Results:** 7,972 verbatim outcomes were identified, categorized into 32 domains, and formatted into survey items/questions. 410 international participants (220 professionals, 190 patients/public) completed at least one round 1 survey item, of which 153 (69.5%) professionals and 116 (61.1%) patients completed at least one round 2 item. 12 outcomes were scored 'consensus in' ('very important' by  $\geq 70\%$  of patients *and* professionals) and 20 'no consensus'. A consensus meeting, involving 19 professionals and 10 patient/public representatives, led to agreement on a final 8-domain COS. Six domains are specific to a surgical innovation context: modifications, unexpected disadvantages, device problems, technical procedure success, whether the overall desired effect was achieved, surgeons'/operators' experience. Two domains relate to intended benefits and expected disadvantages.

**Conclusions:** The COS is recommended for use in all studies prior to definitive RCT evaluation to promote safe, transparent, and efficient surgical innovation.

## MINI ABSTRACT

Agreement on key outcomes for evaluating the introduction of innovative surgical procedures and devices is lacking, hindering transparency and risking patient harm. This study used consensus methods to develop a core outcome set (COS). Use of the final eight-item COS is recommended to promote safe, transparent, and efficient surgical innovation.

## INTRODUCTION

Surgical innovation is essential to improving patient care(1). Optimal innovation is undertaken safely and transparently(2). Unlike the pharmaceutical industry, where rigorous regulatory pathways for new products are well-established, the introduction of novel surgical procedures is less regulated and unstandardized.

One challenge to safe and transparent innovation is consistency and transparency in the selection and reporting of relevant key outcomes. The IDEAL (Idea, Development, Exploration, Assessment, Long-term follow-up) framework describes the characteristics and recommended study designs for the stages of innovation through which new surgical procedures typically pass, describing broad outcome domains that may be measured at each stage(3). Recently-published IDEAL reporting guidelines have further emphasised the need for transparent reporting of appropriate technical, clinical and patient-reported outcomes, harms and unintended effects(4). However, consensus on which specific outcomes are essential to measure at each stage has not yet been reached, and requires a rigorous, evidence-based approach.

Inconsistency in outcome selection and reporting limits evidence synthesis and impedes efficient innovation. This may protract the introduction of promising procedures, delaying definitive evaluation in larger clinical studies or randomized controlled trials (RCT). Alternatively, it may result in ineffective or harmful procedures becoming established in routine clinical practice without a sufficient evidence base. Lack of standardized outcome reporting also provides opportunity for selective reporting that may exaggerate a procedure's benefits or underestimate its harms, compromising patient safety(5-8). These issues may be addressed through developing a core outcome set (COS); an agreed standardized set of outcomes that should be measured and reported, as a minimum, in all early phase studies of a novel invasive procedure. Core outcome sets can improve outcome measurement and reporting in effectiveness studies and RCTs(9, 10) and could have a similar benefit to improving the evaluation and quality and consistency of reporting of early phase surgical studies. Such a COS does not currently exist.

### *Aim*

To develop a COS to support standardized evaluation of all innovative invasive procedures and medical devices prior to definitive evaluation within an RCT.

## METHODS

The COHESIVE-COS study was registered on the Core Outcome Measures for Effectiveness Trials (COMET) database on 20/11/2017 (<http://comet-initiative.org/Studies/Details/1055>).

The COS was developed in the Core Outcomes for early pHasE Surgical Innovation and deVicEs (COHESIVE) study, using consensus-based methods and in accordance with the principles outlined in the COMET Handbook(11) and Core Outcome Set-STAndards for

Development (COS-STAD) guidelines(12). The full protocol has been published (13), including detailed definitions of key terminology such as ‘invasive procedures’ and ‘innovation’.

The study was registered on the Core Outcome Measures for Effectiveness Trials (COMET) database on 20/11/2017 (<http://comet-initiative.org/Studies/Details/1055>).

The study comprised three phases: 1) generation of a list of outcome domains; 2) outcome domain prioritization in a Delphi survey; 3) a consensus meeting to agree the COS.

#### *Stakeholder, patient, and public involvement*

Stakeholders, patients and public members were involved throughout study planning, design, conduct and dissemination. A steering group of 24 members, including two patient representatives, oversaw study conduct. A patient/public advisory group were consulted throughout.

#### *Phase I: generation of a list of outcome domains*

Multiple data sources of relevance to surgical innovation were selected to generate a long list of outcome domains to include in the Delphi survey: (i) focused literature reviews of purposively-selected case studies of innovative procedures/devices(13-16); (ii) review of recommendations for outcome selection and reporting in NHS trust New Procedure Committee documents(13, 17); (iii) review of recommendations for outcome selection and reporting in medical device regulatory body documents(13), and; (iv) review of transcripts of qualitative interviews with surgeons exploring their perceptions of surgical innovation(13, 18). Relevant outcomes/domains were extracted verbatim by at least two researchers independently, with discrepancies discussed with the study team.

#### *Outcome domain conceptualization*

The outcome list was used to generate a conceptual framework of outcome domains. Sections of the outcome list were categorized independently by study group members and iteratively modified ~~via group~~ through discussion. Categorization continued until no further outcome domains were identified and the framework was considered complete. The framework’s comprehensiveness was examined by mapping outcomes/outcome domains identified from a random sample of articles included in a systematic review of early phase studies of colorectal cancer surgery(19). Minor refinements were made where necessary, following discussion.

#### *Phase II: Outcome domain prioritization*

A sequential, multi-round online Delphi survey prioritized domains with stakeholders.

#### *Delphi survey questionnaire development*

Outcome domains identified were formatted into survey questionnaire items, written in plain English and piloted with two independent surgeons and two patient/public advisory group members to confirm comprehensibility and acceptability and refine terminology, layout, and formatting. Respondents scored the importance of including each item in the final COS on a 9-point Likert scale ranging from 1 (not important) to 9 (extremely important). Each item was scored for four stages of innovation, broadly consistent with the IDEAL framework(3): (i) Early phase: first few uses of the procedure/device in humans; (ii) Development stage: procedure is evolving/being refined; (iii) Comparison stage: procedure is no longer evolving/changing (stable) and ready to be compared with standard treatments; (iv) Long-term evaluation stage: long-term outcomes of procedure. While the scope of the COS was intended for evaluation of novel invasive procedures/devices prior to definitive RCT evaluation (comparison stage), this approach allowed a detailed exploration of outcome relevance across all evaluation stages. Free-text items allowed participants to propose additional outcomes, which was included in subsequent round(s) if the outcome was considered to be new and was proposed by at least two participants.

### Sampling and recruitment

Key stakeholders relevant to developing the COS and participating in the Delphi survey included surgeons, funding bodies, device industries and small and medium-sized enterprises, trialists, methodologists, journal editors, regulators, and patient representatives. Patient representatives were approached through a range of partner organisations and purposively sampled based on gender, age, geographical region, and surgical procedure to enable inclusion of a diverse range of demographics and experiences.

Professional participants were purposively sampled to include international representation and a range of professional backgrounds (e.g. surgeons, speciality professional associations, industry collaborators, device manufacturers). Identification and sampling of professionals was informed by: (i) expert knowledge of study team and study steering group members and their colleagues; (ii) contact lists held by the Centre for Surgical Research (University of Bristol) of attendees at surgical-related academic events (e.g. attendees at relevant conferences/workshops); (iii) review of public websites and other public resources; and (iv) specialty professional associations directly circulating the survey to their membership via email.

Additional patient and professional participants were recruited by advertising on social platforms (e.g. twitter: @CohesiveStudy) and/or participants opting-in to complete the Delphi survey via the open-access COHESIVE study website(20).

### Delphi survey rounds

Participants completed two sequential survey rounds (1: July-September 2019; October-November 2019). Survey questionnaires were administered online, facilitated by secure REDCap (Research Electronic Data Capture) electronic data capture software(21) and in

accordance with the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines(22). A paper-based survey was available for postal administration, if requested. All round 1 respondents were invited to complete round 2. All items were retained between rounds 1 and 2, providing opportunity for participants to re-score items taking into consideration feedback from their own and the other stakeholder group (11, 23, 24). Anonymized feedback from round 1, including the respondent's own score and the median score from each stakeholder group (patients and professionals, displayed separately) for each item was included next to each item. This enabled each stakeholder group to see the other's results before re-scoring each item, to encourage prioritization. In round 2, participants re-scored each item's importance. It was agreed *a priori* that a third round may be considered if insufficient consensus to proceed to the consensus meeting was not reached after round 2.

A definition of consensus was outlined *a priori* (Table 1). Following discussion within the study steering group a *post hoc* decision was made to use a stricter definition of consensus after round 2 due to the high proportion of items scored as 'extremely important', as it was felt unlikely that a third survey round would result in any further prioritization. Data was analysed in Stata(25). Only items/domains relevant to the 'early phase' or 'development stage' of innovation were taken to the consensus meeting.

#### Attrition

Participant attrition between rounds was monitored. Automatic reminder emails were sent to participants who had started but not completed the survey.

#### *Phase III: consensus meeting*

The consensus meeting was held in Bristol, UK, in February 2020. Participants were purposively sampled to include representation from all key stakeholder groups. The meeting was facilitated by an independent chair who had not been involved in the study's design/conduct. The chair encouraged discussion and ensured that all participants were able to freely express their views.

A summary of the survey results was presented. Participants were asked to ratify the inclusion or exclusion of outcome domains categorized as 'consensus in' or 'consensus out' following Phase II. Discussion and voting were undertaken for outcome domains/items where objections were raised and for items where no consensus was reached during the Delphi survey. Participants were asked to vote items 'In' or 'Out' of the COS. Items voted 'In' by  $\geq 70\%$  of participants were included in the final COS. Decisions to group items were made following moderated discussion and further voting. All other items were discarded. Voting was conducted anonymously, using electronic polling software (TurningPoint). Participants unable to attend in person were offered an option to listen (though not contribute) to the discussion via teleconference and vote remotely. The consensus meeting concluded with asking participants to vote to ratify the final COS.



### *Sample size*

In the absence of formal guidance for sample size calculations for COS development, consideration is given to achieving representation from all key stakeholder groups(11). A target sample of 150 professional and 50 patient survey participants and 20-25 consensus meeting participants from all stakeholder groups was agreed, in line with similar research(11). A 3:1 ratio of professionals to patients was considered appropriate to sample multiple sub-groups of professional stakeholders.

### *Ethics and dissemination*

Ethical approval was granted by North East - Newcastle and North Tyneside 1 Health Research Authority Research Ethics Committee (18/NE/0378). Written informed consent was obtained from participating patients separately for the Delphi survey and consensus meeting. Written consent was obtained from professional participants prior to the consensus meeting.

## **RESULTS**

### *Phase I: generation of a list of outcome domains*

A final long list comprising 7,972 verbatim outcomes was identified from all data sources included in Phase I(13-16, 18). Following de-duplication and categorization, 32 outcome domains were included in the long list/conceptual framework. Of these, 22 were considered conceptually specific to evaluating innovation and 10 conceptually similar to outcomes measured in effectiveness studies. Some 2,073 verbatim outcomes extracted from 51 studies identified from the systematic review of early phase studies of colorectal cancer surgery were successfully mapped to confirm the comprehensiveness of the conceptual framework, with some minor refinements(19).

### *Phase II: Outcome domain prioritization*

The 32 outcome domains were formatted into Delphi survey questionnaire items, each with four components to distinguish the four pre-specified stages of evaluation.

#### Round 1

Some 410 participants, including 220 professionals and 190 patients/public, completed at least one questionnaire item (Supplemental Table 1, <http://links.lww.com/SLA/D152>). Most (n=168, 76%) professionals were male and aged 30-60 years (n=188, 85%). Around half (108, 49%) were from the UK, with the remainder from Europe (45, 21%), the Americas (n=34, 16%), Asia (n=17, 8%), Australasia (n=8), Africa (n=6) and the Middle East (n=2). Over half of professionals identified as consultant surgeons/attending physicians (n=131, 60%) or trainee/resident surgeons (n=36, 16%). One quarter (n=58, 26%) of professionals identified as researchers/academics/trialists/methodologists. Professional participants also included journal editors (n=10, 5%), industry representatives (n=6), regulatory

representatives (n=5), allied healthcare professionals (n=2) and an anaesthetist (n=1). Professionals represented all major surgical specialties, including general (n=38, 17%), neurological (n=37, 17%), colorectal (n=35, 16%), orthopaedic (n=29, 13%) and emergency (n=21, 10%) surgery. Over half of patients were female (n=115, 61%) and most were aged 50 and over (n=148, 78%). Most (n=180, 95%) were from the UK, with the remainder from Europe, Asia, North America, Australasia and the Middle East. All patients had previous experience of undergoing surgery of varying types and severity. Round 1 outcome domain scores are shown in Supplemental Table 2, <http://links.lww.com/SLA/D153>. No new items were proposed by more than one participant.

## Round 2

Some 153 (69.5%) professionals and 116 (61.1%) patients who scored at least one round 1 item participated in round 2 (and completed at least one round 2 item). Participant demographic characteristics were similar between rounds (Supplemental Table 1, <http://links.lww.com/SLA/D152>). Twelve of the 32 outcome domains were scored 'consensus in' ('very important' by  $\geq 70\%$  of patients *and* professionals) and were carried forward to the consensus meeting to ratify their inclusion in the final COS (Supplemental Table 2, <http://links.lww.com/SLA/D153>). Of the remaining 20 domains, seven were scored 'very important' by  $\geq 70\%$  of only either patients *or* professionals and nine 'very important' by 50-70% of either patients *or* professionals, and were carried forward for further discussion and voting at the consensus meeting. The remaining four domains were scored 'very important' by  $\leq 50\%$  of either patients *and* professionals and were carried forward to the consensus meeting to ratify their exclusion.

### *Phase III: consensus meeting*

Ten patient/public representatives attended the consensus meeting (7 male, 3 female). Nine were from the UK and one from Europe. All had experience of undergoing at least one invasive procedure. Nineteen professionals (10 female, 9 male) attended, including 10 surgeons/ or attending physicians, 6 researchers/academics/trialists/methodologists, 2 members of hospital trust or National Institute for Health Research clinical research organisations and 1 industry representative. Seventeen professionals were from the UK, one from the USA and one from Europe.

Participants agreed to include 24 of the 32 Delphi survey outcome domains in the final COS (Supplemental Table 3, <http://links.lww.com/SLA/D154>). Of these 24 included domains, 12 were scored 'consensus in' during the Delphi survey and 12 were included following additional discussion and voting during the consensus meeting. Eight domains were excluded.

During consensus meeting discussion, participants proposed collapsing 18 items into four broader outcome domains due to similarities and overlap in concepts across the 24 included outcome domains. These related to intended benefits of the procedure (6 items),

disadvantages of the procedure (6 items), completion of planned technical steps either with/without modifications (3 items), and patients' experiences (3 items). This resulted in a proposed COS comprising 10 items. All but one participant endorsed the proposed final COS at the end of the meeting (96% agreement). Participants agreed, however, that the terminology of some domains would need refinement by the study team after the meeting for clarity and consistency. Refinement resulted in a final COS comprising eight domains, of which six are specific to the context of surgical innovation (Table 2).

## DISCUSSION

The COHESIVE study has developed a COS to support the introduction and standardized evaluation and reporting of innovative invasive procedures and medical devices. Multiple data sources with specific relevance to innovation identified a comprehensive list of outcomes to inform a conceptual framework, including innovation-specific outcome domains. Consensus methods, involving key stakeholders in a large international survey and consensus meeting, then prioritized items for COS inclusion. The final COS comprises eight outcome domains to measure and report and is recommended for use in all early-phase studies of innovative surgical procedures to optimise learning, minimise risk and inform full evaluation in later phase studies. Ultimately, this will protect patients, surgeons, and healthcare providers.

Standard COS that specify the outcomes that should be measured and reported, as a minimum, in all effectiveness trials of specific conditions or interventions focus on traditional clinical outcomes, such as complications and quality of life, of specific relevance to that area (11). The COS developed here is intentionally generic to be applicable to the full breadth of surgical innovation. This will enable consistent, rigorous evaluation of key outcomes from the earliest stages of evaluation. An independent safety review of medical devices has recently highlighted substantial flaws with current mechanisms for spotting trends in harm outcomes(26). The IDEAL framework describes broad outcome domains to measure that may vary across the stages of evaluation, including technical achievement, disasters and dramatic successes (stage 1: Idea), technical and procedural success (2a: Development) and clinical outcomes (2b: Exploration)(3). Regulatory guidance for introducing new devices from the US Food and Drug Administration and UK Medicines and Healthcare products Regulatory Agency (MHRA) focus primarily on evaluation of safety and efficacy(27-29), overlooking outcomes that this study shows are important to evaluating the process of innovation. The COS will facilitate surgeon innovators, methodologists and device manufacturers in the practical application of the IDEAL framework by clarifying the essential outcomes to measure throughout the innovation life cycle(4). While the COS includes some outcome domains characteristic of effectiveness studies (e.g. the intended benefit of the procedure, expected disadvantages), most are specific to innovation. These innovation-specific domains, including technical procedure success, modifications, and surgeon/operator experience, may not traditionally be recognised as outcomes but their measurement is key to

driving safe and efficient innovation. Consistently measuring and reporting these outcomes may streamline innovation; enabling rapid identification of promising interventions for definitive RCT evaluation while allowing ineffective or potentially harmful interventions to be confidently abandoned before becoming established

The COS was developed in accordance with the principles outlined by the COMET Initiative(11), though standard methods for identifying potential outcomes were modified to include data sources of specifically relevance to innovation. Rigorous consensus methods, including a large survey of a diverse group of patients and professionals, ensured that the chosen outcomes are relevant and meaningful to key stakeholders. An international survey enabled the views of stakeholders with experience of different global healthcare and research systems to be included. Such inclusive stakeholder engagement is vital if the COS is to be adopted and used in practice.

Various COS development methods are available(11). Alternative data sources may have identified outcomes not included in the long list. While frameworks exist to structure the categorization of outcomes into domains, these reflect conceptualizations relevant predominantly to the context of effectiveness trials or particular outcomes(30). It was considered important to deductively derive a conceptual framework to categorize outcomes from data sources that were selected for their specific relevance to surgical innovation. This involved outcome categorization by multiple study group members and iterative modifications following group discussion. Comprehensiveness of the long list and suitability of the conceptual framework was assessed by mapping outcomes onto those from an independent systematic review of early phase surgical studies(19). Survey participants could also propose the inclusion of additional outcomes, though did not identify any new outcomes. While sampling was designed to include international representation from a wide range of key stakeholder groups, around two thirds of survey participants were from the UK and Europe. This may have influenced item prioritization. Regulatory processes, for example, vary internationally and it is possible that including more international regulatory representatives may have altered the findings, though this is considered unlikely. While most patients and professionals completed both survey rounds, the survey was long ~~survey~~ and this may have increased attrition, introducing bias. A *post-hoc* decision to use a stricter consensus definitions after round 2 was made due to the high proportion of items still scored as extremely important. This may have influenced discussion and voting during the consensus meeting. While a third survey round could have been held, this was considered unlikely to encourage any further consensus on prioritisation.

Use of a COS does not mean that outcomes in a specific study should be restricted to the COS(11), and we recommend additional outcomes be collected where relevant. Use of the COS is intended to complement reporting guidelines developed for authors to report studies accurately and comprehensively. For example, stage-specific checklists have recently been published to improve standards of reporting in publications of IDEAL format studies(4). These checklists recommend that authors declare important contextual information that may be omitted, such as sources of funding and conflicts of interest. A COS specifies *what*

outcomes should be measured. Important next steps to improve the quality and consistency of evaluation of surgical innovation is to reach consensus on *how* the COS outcomes should be measured(31) and to evaluate COS uptake in future evaluations. Development of a core measurement set, a set of instruments to measure the COS domains(31), including identifying a measure of surgeons' experience, is underway. This involves mapping the COHESIVE COS to COS developed for effectiveness trials to identify outcomes of relevance throughout the innovation lifecycle. In parallel, work with key stakeholders has commenced to co-create a real-time reporting platform to optimize the utility and effective incremental sharing of surgical innovation and outcome data. Future work will consider implementation of the COS in surgical registries and its application to governance processes. Previous research has, for example, explored the benefits of novel methods to improve quality and safety processes for surgical innovation without impeding efficiency(32) and optimal ethical regulation (33), and the COS is considered complementary to this work. Engagement with the surgical community essential to ensure uptake of the COS and implementation of real-time outcome sharing, and this work is ongoing. If successful, these measures will promote the safe, transparent, and efficient introduction and evaluation of surgical innovation to benefit patients and the wider healthcare community.

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## **CONTRIBUTIONS**

KA, SP and JB conceived and initiated the study and designed the study protocol. JB developed the ideas for the NIHR Bristol BRC Surgical Innovation theme. KA and SP had joint senior oversight and co-directed the study. All named study steering group members contributed to oversight of the study, aspects of study design and/or acquisition of data and/or interpretation of data. KA wrote the first draft of this manuscript. KA, JB, CH, RM, AM, SP, NW and members of the study steering group critically revised the manuscript. All authors give final approval of the version to be published.

## **COMPETING INTERESTS STATEMENT**

PW and JB are members of the Core Outcome Measures for Effectiveness Trials (COMET) Initiative Management Group.

## REFERENCES

1. Gani F, Ford DE, Pawlik TM. Potential Barriers to the Diffusion of Surgical Innovation. *JAMA Surg.* 2016;151(5):403-404.
2. Birchley G, Ives J, Huxtable R, et al. Conceptualising Surgical Innovation: An Eliminativist Proposal. *Health Care Anal.* 2020;28(1):73-97.
3. McCulloch P, Altman DG, Campbell WB, et al. No surgical innovation without evaluation: the IDEAL recommendations. *Lancet.* 2009;374(9695):1105-1112.
4. Bilbro NA, Hirst A, Paez A, et al. The IDEAL Reporting Guidelines: A Delphi Consensus Statement Stage specific recommendations for reporting the evaluation of surgical innovation. *Ann Surg.* 2020. DOI: 10.1097/SLA.0000000000004180.
5. Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials.* 2012;13:132.
6. Chan AW, Song F, Vickers A, et al. Increasing value and reducing waste: addressing inaccessible research. *Lancet.* 2014;383(9913):257-266.
7. Dyer C. Robot assisted surgery is blamed for heart patient's death. *BMJ.* 2018;363:k4791.
8. Cohen D. How safe are metal-on-metal hip implants? *BMJ.* 2012;344:e1410.
9. Kirkham JJ, Boers M, Tugwell P, et al. Outcome measures in rheumatoid arthritis randomised trials over the last 50 years. *Trials.* 2013;14:324.
10. Wuytack F, Smith V, Clarke M, et al. Towards core outcome set (COS) development: a follow-up descriptive survey of outcomes in Cochrane reviews. *Syst Rev.* 2015;4:73.
11. Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: version 1.0. *Trials.* 2017;18(Suppl 3):280.
12. Kirkham JJ, Davis K, Altman DG, et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. *PLoS Med.* 2017;14(11):e1002447.
13. Avery K, Blazeby J, Wilson N, et al. Development of reporting guidance and core outcome sets for seamless, standardised evaluation of innovative surgical procedures and devices: a study protocol for content generation and a Delphi consensus process (COHESIVE study). *BMJ Open.* 2019;9(9):e029574.

14. Macefield R, Wilson N, Hoffmann C, et al. Outcome selection, measurement and reporting for new surgical procedures and devices: a systematic review of IDEAL/IDEAL-D studies to inform development of a core outcome set. *BJS Open*. 2020;4:1072In Press.
15. Main BG, Blencowe NS, Howes N, et al. Protocol for the systematic review of the reporting of transoral robotic surgery. *BMJ Open*. 2018;8(1):e019198.
16. Kirkham EN, Main BG, Jones KJB, et al. Systematic review of the introduction and evaluation of magnetic augmentation of the lower oesophageal sphincter for gastro-oesophageal reflux disease. *Br J Surg*. 2020;107(1):44-55.
17. Cousins S, Richards H, Zahra J, et al. Introduction and adoption of innovative invasive procedures and devices in the NHS: an in-depth analysis of written policies and qualitative interviews (the INTRODUCE study protocol). *BMJ Open*. 2019;9(8):e029963.
18. Zahra J, Paramasivan S, Blencowe N, et al. Discussing surgical innovation with patients: A qualitative study of surgeons' and governance representatives' views. *BMJ Open*. 2020;In press.
19. Hoffmann C, Wilson N, Blencowe N, et al. A systematic review and in-depth analysis of early phase studies of colorectal surgical innovation. *Colorectal Disease*. 2019;21(S3 Special Issue: Abstracts of the 14th Scientific and Annual Meeting of the European Society of Coloproctology, Austria Centre, 25-27 September 2019):33-128.
20. McCulloch P, Cook JA, Altman DG, et al. IDEAL framework for surgical innovation 1: the idea and development stages. *BMJ*. 2013;346:f3012.
21. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381.
22. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J Med Internet Res*. 2004;6(3):e34.
23. van 't Hooft J, Duffy JM, Daly M, et al. A Core Outcome Set for Evaluation of Interventions to Prevent Preterm Birth. *Obstet Gynecol*. 2016;127(1):49-58.
24. Harman NL, Bruce IA, Callery P, et al. MOMENT--Management of Otitis Media with Effusion in Cleft Palate: protocol for a systematic review of the literature and identification of a core outcome set using a Delphi survey. *Trials*. 2013;14:70.
25. Stata [computer program]: Release 16. College Station, TX: StataCorp LLC; 2019.



26. Cumberlege J. First do no harm: The report of the Independent Medicines and Medical Devices Safety Review. 2020 08/07/2020. Report No.: ISBN 978-1-5272-6567-7.
27. US Food and Drug Administration. Device Advice. Comprehensive Regulatory Assistance [US FDA website]. 2020. Available at <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>. Accessed September 11, 2020.
28. Medicines and Healthcare products Regulatory Agency. Guidance - Medical devices: how to comply with the legal requirements [Gov.UK MHRA website]. 2014. Available at <https://www.gov.uk/guidance/medical-devices-how-to-comply-with-the-legal-requirements>. Accessed September 11, 2020.
29. European Union Commission. The Medical Devices Directive 93/42/EEC. EU Commission; 1993.
30. Dodd S, Clarke M, Becker L, et al. A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol*. 2018; 96:84.
3031. Prinsen CA, Vohra S, Rose MR, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. *Trials*. 2016;17(1):449.
32. Marcus RK, Lillemoe HA, Caudle AS, et al. Facilitation of surgical innovation. Is it possible to speed the introduction of new technology while simultaneously improving patient safety? *Ann Surg*. 2019;270:937.
33. McKneally MR and Daar AS. Introducing New Technologies: Protecting Subjects of Surgical Innovation and Research. *World J Surg*. 2003;27:930.

**Table 1. Definition of consensus**

Category	Original (rounds 1 and 2)		Revised (round 2 only)		Consensus meeting	
	Definition	Action	Definition	Action	Definition	Action
Consensus in	Scored as very important (7–9) by $\geq 70\%$ <i>and</i> not important (1–3) by $< 15\%$ of either patients <b>or</b> professionals	Domain retained for next survey round/consensus meeting	Scored as very important (8–9) by $\geq 70\%$ <i>and</i> not important (1–3) by $< 15\%$ of patients <b>and</b> professionals	Domain retained for ratification at consensus meeting	Same as round 2	Domain included in final COS, following ratification <sup>a</sup>
Consensus out	Scored as not important (1-3) by $\geq 70\%$ <i>and</i> very important (7-9) by $< 15\%$ of either patients <b>or</b> professionals <b>or</b> both	Domain discarded after round 2 (to be ratified at consensus meeting)	Same as original	Same as original	Same as original	Domain not included in final COS, following ratification
No consensus	Neither criteria above are met	Domain retained for next survey round/consensus meeting	Neither above criteria are met	Domain sub-categorized:		
				(i) scored ‘very important’ (median 8-9) by $\geq 70\%$ of either patients <i>or</i> professionals	Same as round 2	Iterative rounds of discussion and voting until consensus achieved

				(ii) scored 'very important' (median 8-9) by 50-70% of either patients <i>or</i> professionals	Same as round 2	Iterative rounds of discussion and voting until consensus achieved
				(iii) scored 'very important' (median 8-9) by $\leq 50\%$ of both patients <i>and</i> professionals	Same as round 2	Domain excluded from final COS, following ratification

<sup>a</sup> Either as an individual or grouped with another domain(s)

**Table 2. Final core outcome set**

	<b>Domain discussed during consensus meeting<sup>1</sup></b>	<b>Domain decided at consensus meeting<sup>1</sup> (n=10)</b>	<b>Final COS domain (n=8)</b>
9	Anticipated advantages during	Intended benefits before, during or after the procedure	*Intended benefit(s) of the procedure, including (i) before, (ii) during or (iii) after the procedure (e.g. fewer tests needed before surgery, less operative time, better recovery)
10	Unanticipated advantages during		
11	Anticipated short-term advantages following		
12	Unanticipated short-term advantages following		
13	Anticipated long-term advantages following		
14	Unanticipated long-term advantages following		
5	Whether any accompanying intervention of the innovative procedure required modifications	Whether any accompanying intervention of the innovative procedure required modifications	#Modifications to the (i) procedure, (ii) concomitant interventions or (iii) which patients were offered the procedure during the study. <i>NB: excludes abandoning or changing to another procedure at any point (e.g. laparoscopic approach converted to open)</i>
30	Whether changes were made to which patients were offered the innovative procedure	Whether changes were made to which patients were offered the innovative procedure	
2	Whether the planned innovative procedure was abandoned or changed	Whether the planned innovative procedure was abandoned or changed	#Procedure completion success, either with/without modifications
1	Whether all the technical steps of the innovative procedure were completed as planned	Technical steps completed as planned, either with/without modifications, details of what and why	
3	Whether any individual technical steps of the planned innovative procedure required modifications		
4	Details of any modifications		
7	DEVICES: Whether the new device mechanically/technically did not function as intended	DEVICES: Whether the new device mechanically/technically did not function as intended	#Problems with the device working (e.g. new stapler misfired), if applicable

15	Anticipated disadvantages during	Expected and unexpected disadvantages before, during and after the procedure	*a) Expected disadvantages, including (i) before, (ii) during or (iii) after the procedure  (e.g. more tests needed before surgery, longer operative time, more patients required intensive care)
16	Unanticipated disadvantages during		
17	Anticipated short-term disadvantages after		
18	Unanticipated short-term disadvantages after		#b) Unexpected disadvantages, including (i) before, (ii) during or (iii) after the procedure (e.g. unexpected instrument clashing, inadvertent injury to nearby tissue and/or organs)
19	Anticipated long-term disadvantages		
20	Unanticipated long-term disadvantages		
6	Whether the innovative procedure was completed (as planned or with modifications) and the overall desired effect of the procedure was achieved	Whether the overall desired effect of the procedure was achieved	*Overall desired effect (overall aim) of the procedure/device achieved (e.g. tumour successfully excised)
8	Operators'* perceptions/ experiences	Surgeons'/operators' perceptions/experiences of performing the innovative procedure (before, during and after)	#Surgeons'/operators' emotional, psychological, or physical experience of the procedure (e.g. ergonomic comfort during the operation)
27	Patients' physical experiences during	Patients' experience (multidomain) before, during and after the procedure	#Patients' emotional, psychological, or physical experience relating to the procedure being innovative (e.g. anxiety because of the procedure being new)
28	Patients' psychological or emotional experiences		
29	Patients' experiences following		

COS: core outcome set; <sup>1</sup>Abbreviated description; \*shared with effectiveness studies; #innovation-specific