A Protocol for the Development of Core Outcome Sets in Pelvic Organ Prolapse Research

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Study protocol

Keywords: core outcome sets, outcome measures, pelvic organ prolapse, Delphi survey, randomized trials

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Abstract

Background The high prevalence of symptomatic pelvic organ prolapse (POP) and the women's lifetime risk of requiring surgery, as well as the significant impact of POP on women's health related quality of life has resulted in a variety of studies on POP interventions. A wide variety of outcomes have been reported across randomized trials evaluating interventions for POP and various outcome measures have been used. Such variation leads to a limited value of research to provide reliable evidence-based data for clinical practice guidance. The development and use of a core outcome set (COS) would help to address these issues ensuring outcomes important to all stakeholders, primarily women with POP. We aim to produce, disseminate and implement a COS for POP. Methods A steering group within the CHORUS, an International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health will guide the development of this COS. Systematic reviews of trials that reported outcomes and outcome measures on interventions for POP will form the basis for the creation of an outcome inventory. Core outcome selection process will be performed using an international, multi-perspective, online Delphi survey. The modified Delphi method encourages stakeholder group agreement towards consensus core outcomes through repeated reflection and rescoring of items. Discussion Dissemination and implementation of the resulting COS within an international context will be promoted. An embedded COS for POP within future studies will most likely be reflected by an increased value of research that provides guidance for clinical practice. The paradigm of the COS development could further inform research priorities in POP treatments, and support clinical guidelines development and better patient care. KEYWORDS: core outcome sets, outcome measures, pelvic organ prolapse, Delphi survey, randomized trials.

Background

Patient centered high-quality care should be based on the best available research evidence. However, research quality and outcomes are highly variable. It has been estimated that most research findings are false (1). Furthermore 85% of research funding is wasted in the design and reporting of clinical trials as well as other types of research (2). Waste is evident in all stages of production and reporting and is related to the inclusion of low priority outcomes, inappropriate study design that may lack consideration of existing evidence, selective reporting, publication bias and concealment of planned study outcomes (3–4). Although this mainly refers to clinical trials, such issues are expected to feature in other types of research as well.

In POP research, several issues around quality of evidence have been highlighted, particularly by Cochrane reviews. For example, in surgery for women with posterior compartment prolapse, evidence quality was found to range from very low to moderate (5). Similar findings were reported by another Cochrane review on POP interventions (6).

As 1 in 5–10 women will undergo surgery for prolapse or urinary incontinence (7) in their lifetime, this health burden is considerable and treatment methods are constantly being developed and require robust

evaluation. Although randomized trials have been a research priority, the collection and reporting of outcomes and the selection of outcome measures has been largely overlooked. The consequence of this is a variety of different outcomes that make drawing conclusions across a group of studies through systematic reviews and meta-analyses difficult or impossible. For example, the majority of POP trials have not evaluated the safety of potential treatments, particularly over the long term. Evidence synthesis can be limited by the use of different definitions and measurement instruments. The development and use of a minimum set of outcomes, termed a core outcome set (COS), would help to address these issues. COS are data sets that can be measured in a standardized manner and reported consistently (8).

CHORUS is an International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health with representatives from different geographical areas and academic institutions. Specific projects undertaken by CHORUS aim to tackle limitations in research evidence and current standards. Among other initiatives, a number of systematic reviews on surgical interventions for anterior compartment vaginal prolapse, synthetic mesh procedures for POP, childbirth trauma and apical prolapse surgery has been completed and published (9–12). The aim of CHORUS is to develop and sustain a robust research culture and clinical excellence by promoting, conducting and implementing research that not only contributes to improvements in knowledge base and patient care, but also informs the development of clinical standards and aims to improve clinical services. Commitment to delivering a research agenda that is focused on enhancing clinical and cost-effectiveness and on systematic measures to monitor and improve quality is a priority.

Our work is based on the paradigm of the Outcome Measures in Rheumatology (OMERACT) initiative (13). This initiative has developed COS for many different conditions. For example, successful implementation of the rheumatoid arthritis COS has resulted in a significant change in the quality and relevance of research and enriched clinical practice by identifying consensus outcomes which are now routinely monitored by healthcare professionals and patients around the world.

Prospective registration

This project has been prospectively registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative (registration number 981) (14). The Core Outcomes in Women's Health (CROWN) initiative [www.crown-initiative.org] will support the dissemination and implementation of a COS for POP to increase the value of primary research by encouraging future POP trials to report core outcomes and therefore, contribute data to high quality meta-analyses (8).

Methodology

Creating a group for the development of a COS for POP

A group of healthcare professionals, researchers and women with POP will guide the development of a COS that will be applicable to clinical studies evaluating therapeutic interventions for women with POP.

This group will consider the urgent need for development of effective interventions to reduce the impact of POP on women's quality of life given the flaws and weaknesses of current evidence documented in Cochrane reviews (15–18).

Study management

The project for developing a COS for POP will be supervised by a management team and a steering committee. The management team will meet monthly and organize day-to-day tasks and overall work progress. The management team will include different research partners. The steering committee will meet every 6 months and will include an independent chairperson and two other independent expert members who can provide advice on methodology and POP-related issues. There will also be representatives from the management team. The purpose of the steering committee will be to provide support and guidance. Two women with POP will be invited to participate as key contributors in the study management process.

Outcome and outcome measure selection in clinical trials on POP interventions

We aim to expand our previous work on studying the variation of outcomes and outcome measures in POP trials (9–10)(12), in order to create a comprehensive inventory of potential outcomes through literature reviews and group discussions.

Selection of appropriate outcomes is an essential step of study design. Clinical trials that evaluate interventions for POP must select outcomes of relevance to key stakeholders and measure them using adequate instruments. The main issues that arise throughout this process are inconsistent selection, measurement and reporting of outcomes. Measuring the outcomes of interventions for POP in a variety of ways leads to outcome reporting bias. Therefore, the barrier to compare and synthesize clinical trials' findings has an inevitable negative impact on the quality of evidence produced by meta-analyses and embedding of poor-quality evidence into clinical practice.

One way to address these issues is a process illustrated by figure 1 and recommended by Core Outcome Measures in Effectiveness Trials (COMET) Initiative (19). This process has been successfully applied in several disciplines in order to develop, disseminate, and implement different COS.

Figure 1. The COS for POP development process

Our protocol is based on the COMET Initiative Handbook guidelines and other COS development research relevant to women's health, including preeclampsia, endometriosis and fetal growth restriction (20–22).

Step 1

Potential outcomes selection

The “Standard Protocol Items Recommendations for Interventional Trials” (SPIRIT) statement, supported by funders of health research, provides specific recommendations and supports the use of COS where they exist (23). Mapping all outcomes reported in clinical trials on interventions for POP will provide the basis for the development of COS. All outcomes and outcome measures reported within published trials will be classified into domains and themes.

Outcome inventory

A comprehensive inventory of outcomes identified by the systematic review and analysis of the qualitative interviews will be developed. Outcome domains will be listed in a database and coded according to the taxonomy proposed by the COMET Initiative.

If there is uncertainty as to how to classify or present an outcome, consensus of the steering group will be sought. Following the steering group’s agreement, the outcome inventory will be entered into the modified Delphi method.

Step 2

Core outcomes selection process

The core outcomes will be determined using a modified Delphi method (24), where several surveys are delivered over a series of rounds. The modified Delphi method facilitates repeated reflection and rescoring of items. This promotes whole and individual stakeholder group consensus on core outcomes and has advantages over less structured methods. Online Delphi surveys are considered, efficient and acceptable (25–26).

Key stakeholders involved in POP interventions will be invited to participate. Urogynaecologists, gynaecologists, colorectal surgeons, urologists, general practitioners, researchers, policy makers, industry representatives, professional societies representatives and women with POP will be involved in the development of the COS.

Round 1

Participants will be invited to register online, provide demographic details and commit to all rounds. They will be allocated a unique identifier, which will anonymise their responses. A list of outcomes to be scored will be arranged alphabetically, by domains. The list of outcomes will include the option to display a more detailed plain language description. This option is meant to increase stakeholder's adherence to the study protocol. Participants will be invited to score individual outcomes using a 7-point Likert Scale anchored between one (not important) to seven (critically important). This scale was created by the Grading of Recommendations Assessment, Development and Evaluation working group and it has been widely adopted by COS developers (27). There will be provision for an option for participants to suggest additional outcomes.

The scores for individual outcomes will be calculated and represented graphically. Only complete responses will be considered. Additional outcomes listed by participants will be reviewed by the outcome committee and, if novel, listed in the next round. This round will close after a four-week window.

Key stakeholders will be invited to participate in the Delphi survey. There are no clear recommendations, to our best knowledge, for calculating the optimal sample size (28); based upon previous studies, we will aim to include 20 participants from each stakeholder group.

The number of participants in each stakeholder group who respond to round one will be assessed following the end of round 1. Results will be presented as total number and / or percentage of:

•survey registrations

•respondents who have completed the survey

•respondents who completed the round

•respondents in each stakeholder group

•respondents versus potential respondents

•new respondents who joined the survey after its beginning.

Round 2

Participants will be informed regarding the outcome scores from the previous round. After revealing their own score, participants will be invited to rescore each outcome. Any changes in the score from round-to-round will be noted and analysed. The round will close after a four-week window.

The modified Delphi method promotes agreement towards consensus core outcomes (29). This round's results will enable individual outcomes to be classified as shown in table 1 (28). These definitions and criteria have been proposed by previous COS developers (30).

Table 1. Consensus status based on core outcome criteria

The round's 2 results will be reviewed by the steering group to consider the need for a further Delphi survey round.

Consensus meeting

During this final phase, a meeting led by an independent coordinator will be organized with the purpose of deciding which outcomes will be validated and included in the COS. In addition, outcomes that do not meet core outcome criteria will be discussed and analysed. This meeting will purposefully include various points of views from participants who have completed all rounds of the Delphi survey. During the consensus meeting, the results from each round of the Delphi survey will be presented. To avoid biased consensus within a group of participants, the steering committee will consider all opinions (8)(31) in an interactive meeting. Potential conflicts of interests generated by a particular interest in a specific outcome will be addressed. To facilitate dissemination and implementation, editors from key journals and funders of POP research will be invited to participate.

Discussion

Ethical aspects and dissemination

As with previous COS development projects, this project is considered a service evaluation not directly influencing patient safety (21)(32–33) and therefore, ethics approval is not required. Consent will be obtained from all participants involved before participating in either stakeholder interviews or the Delphi survey. The protocol will comply to the Declaration of Helsinki (33). A "no-response" option will be allowed both for the survey and interactive parts of the research to ensure responder's right to withhold information. A specific timeframe of the Delphi process will be provided and information concerning the interval of data storage and handling will be made available to participants.

As dissemination is the pivotal step in the effective application of trial outcomes, this will be planned in detail, drawing on the necessary expertise, at the outset of any research undertaking. The full academic

publication will be constructed with reference to the COS—Standards for Reporting (COS-STAP) statement and checklist (34).

The National Institute for Health and Care Excellence supports the use of COS when selecting outcomes during evidence scoping and synthesis (19). As this activity forms the basis of updating guideline recommendations, the COS could have a direct impact in improving healthcare of women with POP.

Abbreviations

POP—pelvic organ prolapse

COS—core outcome set(s)

CHORUS - International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health

COS–STAP—Core Outcome Set-STAndardised Protocol Items

OMERACT - Outcome Measures in Rheumatology

Declarations

•*Ethics approval and consent to participate:* As with previous COS development projects, this project is considered a service evaluation not directly influencing patient care or safety, therefore ethics committee approval was not required. All participants involved will be asked for their consent before participating in either stakeholder meetings or the Delphi survey. Medical Research Council's decision tool was used to determine whether this research required approval from an NHS Research Ethics Committee (appendix 1).

•*Consent for publication:* Not applicable.

•*Availability of data and material:* Not applicable.

•*Competing interests:* The authors declare no competing interests.

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•*Authors' contributions:* SKD led the development of the protocol. SKD and MPR drafted the manuscript. VP, GF, JMH, and CB reviewed and finalised the protocol. All authors contributed and take responsibility for the protocol concept and design.

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Table

Table 1. Consensus status based on core outcome criteria

Consensus status	Description	Criteria
Consensus achieved	Classify as a core outcome	Over 70% of participants in each stakeholder group score this outcome domain 'critical' AND
		Less than 15% of participants in each stakeholder group score outcome domain 'not important'.
Consensus not achieved	Do not classify as a core outcome	Over 70% of participants in each stakeholder group score outcome domain 'not important' AND Less than 15% of participants in each stakeholder group score outcome domain 'critical'.
No consensus	Do not classify as a core outcome	Anything else

Figures

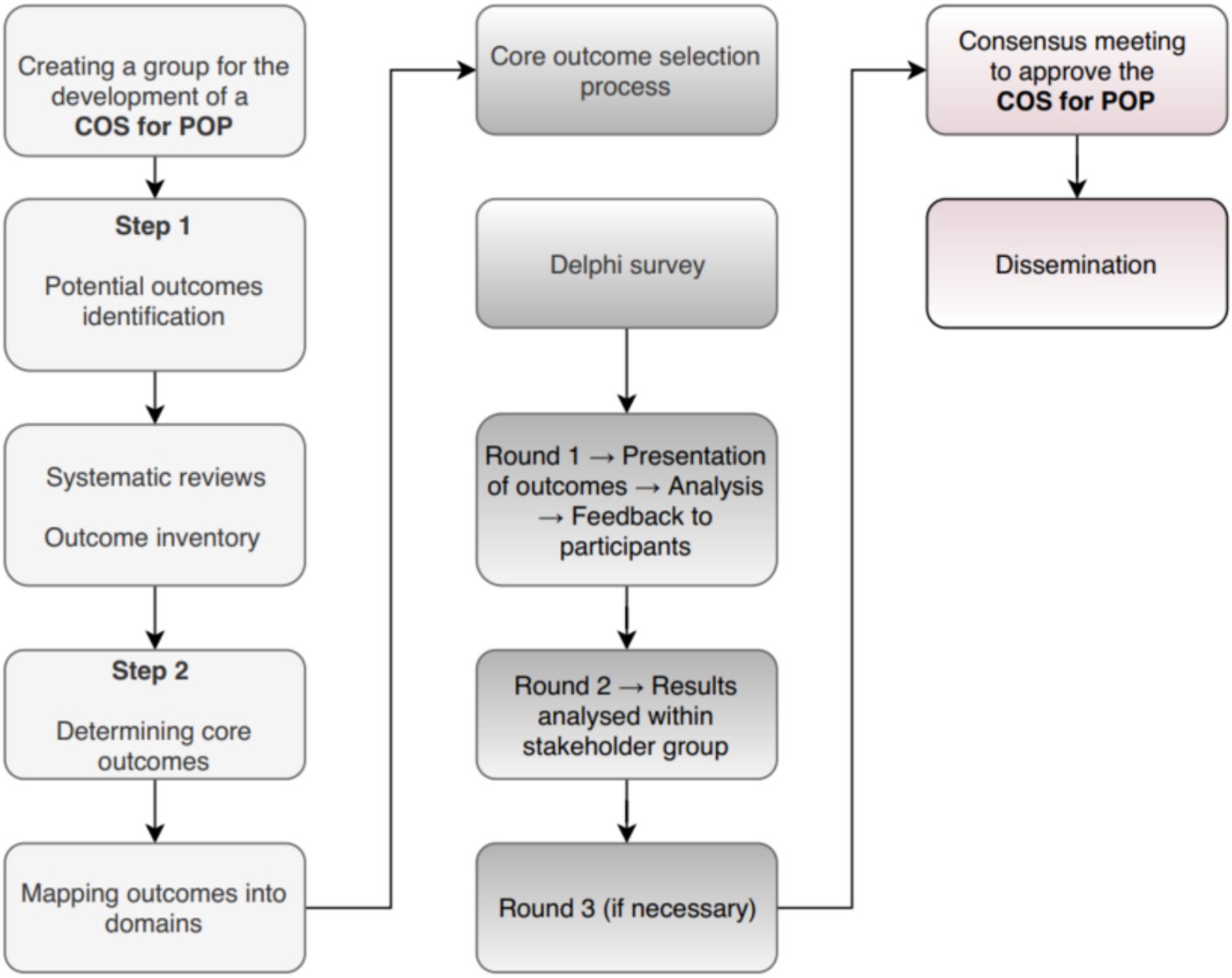

Figure 1

The COS for POP development process

Supplementary Files

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