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Buchbinder, R., Page, M. J., Huang, H., Verhagen, A. P., Beaton, D., Kopkow, C., ... Shoulder Core Outcome Set Special Interest Group (2017). A Preliminary Core Domain Set for Clinical Trials of Shoulder Disorders: A Report from the OMERACT 2016 Shoulder Core Outcome Set Special Interest Group. *Journal of Rheumatology*, *44*(12), 1880-1883. [161123]. https://doi.org/10.3899/jrheum.161123

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A preliminary core domain set for clinical trials of shoulder disorders: A report from the OMERACT 2016 Shoulder Core Outcome Set Special Interest Group

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Abstract (241 words)

Background: The OMERACT Shoulder Core Outcome Set Special Interest Group was established to develop a core outcome set for clinical trials of shoulder disorders.

Methods: In preparation for OMERACT 2016, we systematically examined all outcome domains and measurement instruments reported in 409 randomised trials of interventions for shoulder disorders published between 1954 and 2015. Informed by these data we conducted an international Delphi consensus study including shoulder trial experts, clinicians and patients to identify key domains that should be included in a shoulder disorder core outcome set. Findings were discussed at a stakeholder pre-meeting of OMERACT. At OMERACT 2016 we sought consensus on a preliminary core domain set and input into next steps.

Results: There were 13 and 15 participants at the pre-meeting and OMERACT 2016 Special Interest Group meeting respectively (9 attended both meetings). Consensus was reached on a preliminary core domain set comprising an inner core of four domains: pain, physical function/activity, global perceived effect and adverse events including death. A middle core comprised three domains: emotional wellbeing, sleep and participation (recreation and work).

An outer core of research required to inform the final COS was also formulated.

Conclusion: Our next steps are to: 1) Explore whether participation (recreation and work) should be in the inner core; 2) Conduct a third Delphi round to finalise definitions and wording of domains and reach final endorsement for the domains; and 3) determine which instruments fulfil OMERACT criteria to measuring each domain.

Key Indexing Terms: Shoulder, Core outcome set, Trials, Outcome measurement

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The source(s) of support in the form of grants or industrial support

A Patient-Centered Outcomes Research Institute (PCORI) Engagement Award supported this work (#2072). RB is supported by an Australian National health and Medical Research Council (NHMRC) Senior Principal Research Fellowship (#1082138). MJP is supported by an Australian NHMRC Early Career Fellowship (#1088535). NJ is supported by funding from National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) 1K23AR059199 and 1U34AR069201.

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Short running footline of no more than 4 words

Shoulder core outcome set

WHAT IS NEW

- No core outcome set for shoulder trials currently exists
- Based upon preliminary work including a review of outcomes used in controlled trials of interventions for shoulder disorders and an international Delphi study, we reached consensus on a preliminary core domain set that should be used in all trials of shoulder disorders
- The preliminary core domain set comprises an inner core of four domains: pain, physical function/activity, global perceived effect and adverse events and a middle core comprising emotional wellbeing, sleep, and participation (recreation and work)
- Next steps will include identifying which instruments meet the OMERACT 2.0 Truth Discrimination and Feasibility (TDF) filter for measuring these domains
- Take up of the final COS will markedly improve the standardization of outcome measurement across these trials thereby enhancing our ability to compare findings from different studies and pool data in meta-analyses

Introduction

There has been exponential growth in the numbers of published trials evaluating interventions for shoulder disorders, but a lack of uniformity in measured outcomes across trials limits our ability to compare findings between studies and synthesise data in meta-analyses [e.g., 1]. A systematic examination of outcomes reported in 171 trials investigating physical therapies for adhesive capsulitis or rotator cuff disease found the median number of outcome domains

reported was 3 (range 1-6). Pain (87%), function (72%), and range of motion (67%) were most commonly reported, while adverse events (27%), patient-reported treatment success (24%), strength (18%), health-related quality of life (18%) and work disability (4%), were reported in a minority [1].

In an effort to reduce heterogeneity in outcomes measured across clinical trials, the development of core outcome sets (COSs) in specific health conditions has been recommended [2]. A COS is defined as an agreed minimum selection of outcomes that should be measured and reported in **all** clinical trials for a particular health condition [3]. It guides and reinforces reporting of important outcomes, reduces risk of selective outcome reporting, and increases the feasibility of conducting meta-analyses. No COS for shoulder trials currently exists. The creation and up-take of a COS could markedly improve the standardization of outcome measurement across these trials thereby enhancing our ability to compare findings from different studies and pool data in meta-analyses.

The OMERACT Shoulder Core Outcome Set Special Interest Group (SIG) was established to develop a COS for clinical trials of shoulder disorders [4]. This paper outlines our preliminary work and outcomes of a pre-OMERACT meeting and SIG meeting at OMERACT 2016 which aimed to reach consensus on a preliminary core domain set and identify a research agenda to support the development of the COS.

Methods

In line with OMERACT recommendations [5], we formed a multinational, multidisciplinary Steering Committee comprising three leads (RB, AV, JG), two OMERACT fellows (MP, HH), OMERACT liaison (DB) and two patient representatives (PR and MV); and a multinational (Australia, Brazil, Canada, The Netherlands, Germany, UK and USA) and multidisciplinary (epidemiology, occupational therapy, orthopaedic surgery, physical medicine and rehabilitation, physiotherapy, primary care and rheumatology) Working Group comprising researchers and clinicians with expertise in shoulder disorders, consensus-based research procedures and measurement.

Prior to OMERACT 2016 we performed two studies. First, we systematically examined outcome domains and measurement instruments reported in randomised trials of interventions for shoulder disorders (including rotator cuff disease (e.g. tendinopathy, impingement, subacromial bursitis and tears), adhesive capsulitis, instability, glenohumeral osteoarthritis, dislocation, proximal humeral or humeral head fractures or unspecified shoulder pain) published between 1954 and 2015 [6]. We identified 409 trials reporting outcomes across 41 domains and 319 instruments. The most commonly reported outcomes were pain (90%), range of motion (78%) and physical function (71%). Adverse events were more frequently measured in dislocation/fracture trials (77% versus 20-31% for all other trials), radiographic outcomes were measured more frequently in trials of people with shoulder osteoarthritis (56%) or dislocation/fracture (50%)(versus 1-29% for all other trials), while strength was measured less frequently in trials of people with adhesive capsulitis (21%) or unspecified shoulder pain

(23%)(versus 44% to 63% for all other trials).

Second, we conducted an international Delphi consensus study including 55 shoulder trial experts and/or clinicians and 41 patients from 13 countries to identify the key domains that should be included in a shoulder COS [7]. Four domains met an a priori threshold (at least 67% of all respondents) for inclusion in the core set: pain, physical functioning, global assessment of treatment success and health-related quality of life. Two additional domains, sleep functioning and psychological functioning, met the threshold for inclusion by some but not all stakeholder groups (35% clinician/researchers unsure or preferred to exclude sleep functioning; 27% patients unsure or preferred to exclude psychological functioning).

There was consensus that number of deaths was not a core domain while no consensus could be reached for range of motion and muscle strength. It was noted that there were distinct differences in responses in the Delphi study between groups. While patients tended to rate almost all domains highly, researchers were less likely to consider measurements such as range of motion, strength and radiographic outcomes as important as other domains.

The results of these two preparatory projects were presented and discussed at a half-day meeting of the Steering and Working Groups held the morning before OMERACT 16 to optimise integration with the OMERACT process. Pre-reading included the protocol for development of the shoulder trial COS and results of the review of outcomes and Delphi studies. At this meeting we sought endorsement of our PICO (as per OMERACT, are statements used widely in studies to

define the patients/population, intervention, comparator/control and outcome), consensus on a preliminary core domain set to present to the OMERACT SIG meeting, and identified priorities for further research. In line with OMERACT guidance [5], we considered domains for the inner and middle core in the OMERACT onion format and questions related to outcome measures that need to be addressed in future research were considered for the outer core.

At OMERACT 2016 we convened a 1.5-hour meeting open to all registered OMERACT participants. All participants received a pre-OMERACT report outlining the results of the preparatory projects. At this meeting we presented the background and rationale for the establishment of our group, our PICO and results of the two preparatory projects, and the preliminary core domain set endorsed at the pre-OMERACT meeting. Participants were invited to provide feedback on the preliminary core domain set and offer alternatives to the domains or the domain names. We also sought input on a research agenda. At the end of the meeting participants were asked to vote on the final preliminary core domains and their position in inner, middle and outer rings of the OMERACT onion. We considered that an acceptable level of endorsement would be at least 70% for each domain.

Results

There were 13 participants at the pre-OMERACT meeting comprising three rheumatologists, two orthopaedic shoulder surgeons, one family doctor, four epidemiologists (one individual also being a physical therapist), an occupational therapist and two patient representatives. There were 15 participants at the OMERACT SIG comprising six rheumatologists, one family

doctor, five epidemiologists, an occupational therapist and two patient representatives. There were 9 participants who attended both meetings.

Endorsement of the focus of this working group (PICO)

At both the pre-OMERACT and OMERACT meetings, there was 100% endorsement that the COS should be applicable to shoulder disorders of any duration that include rotator cuff disease (e.g. tendinopathy, impingement, subacromial bursitis and tears), adhesive capsulitis, instability, glenohumeral osteoarthritis, dislocation, proximal humeral or humeral head fractures, and unspecified shoulder pain. The primary aim of the COS would be for trials of interventions (e.g. prevention, treatment) compared with placebo, no treatment or other active interventions where the outcome/s of interest are clinical (i.e. not diagnostic accuracy of tests), although the COS may be applicable as well to observational studies (e.g. describing impact or prognosis of shoulder conditions).

Endorsement of domains and placement in the OMERACT Onion

At the pre-OMERACT meeting, participants agreed with the inclusion of pain and physical functioning as inner core domains (100% endorsement), in keeping with their endorsement by the Delphi study [7]. Global assessment of treatment success also endorsed by the Delphi study was also included in the inner core (100% endorsement), but changed to 'global perceived effect' in view of the fact that some trials include a usual care or no treatment arm where treatment success may not be a relevant concept. Health-related quality of life, endorsed by the Delphi study, was not endorsed for inclusion as an inner core domain as several of its

subdomains (pain interference, physical and psychological functioning) were already captured within other domains. Participants unanimously voted for a fourth inner core domain, 'Adverse events'. 'Deaths', expected to be rare for shoulder disorders, was not endorsed as a separate domain in keeping with the Delphi study, but it was acknowledged that it should be reported if it occurs within the domain of adverse events. Adverse events were considered as distinct from unfavorable outcomes related to the other core domains. For example, an increase in pain would not be recorded as an adverse event given it is already covered by the pain domain.

While there was discussion about whether or not subdomains of physical function such as activities of daily living (e.g. bathing, dressing), and work, sports and recreational activities, should be defined explicitly, this was not resolved. It was noted that while the ability to perform activities of daily living might be important for all shoulder disorders, ability to return to sports activities might not be equally relevant across all patients or trials. Sleep functioning was endorsed (100%) as a middle core domain as while important, it was considered a consequence of pain. Psychological functioning was also endorsed (100%) as a middle core domain.

Neither reduced range of movement nor strength was considered a core domain. The patient participants suggested that patient respondents in the Delphi study [7], were likely considering the impact that reduced range of movement and strength have on function when indicating their importance in a COS. Although OMERACT recommends inclusion of resource use as a core domain, it was noted that it was not rated highly in the Delphi study [7], and may not be relevant to all trials. Other than pain, there were also no pathophysiological manifestations

included in our preliminary core domain set. While important pathophysiological manifestations are measurable for some shoulder conditions such as fractures (fracture healing), participants noted the absence of reliable pathophysiological manifestations for all shoulder disorders.

Participants at the OMERACT SIG meeting recommended several changes to the OMERACT onion. For the inner core, physical functioning was altered to 'physical function/activity'. For the middle core, 'psychological functioning' was changed to 'emotional wellbeing' as it was considered to more clearly convey the intended concept, and 'sleep functioning' was changed to 'sleep'. Further work was considered necessary to define the physical function/activity and emotional wellbeing domains. There was also consensus for removing work and recreation/leisure activities from physical function to a new domain - participation (recreation and work). While patient representatives suggested locating this domain in the inner core, after discussion it was agreed that further research was needed before it could be considered for the inner core set and it was therefore placed in the middle core.

There was wide support for explicitly including death as part of the adverse events domain rather than a domain in its own right. It was also considered worthwhile to perform a review of qualitative studies that had explored the lived experience of having shoulder pain to ensure that all relevant domains have been considered. Finally, there was consensus that we need not try to force our core domains into the OMERACT framework. Future updates and research will revisit this latter point.

Figure 1 presents the final preliminary core domain set – each domain and its location in the OMERACT onion received 100% endorsement by SIG participants. Table 1 provides current definitions for each domain [7].

Conclusion

There was unanimous agreement at the 2016 OMERACT Shoulder Core Outcome Set SIG meeting that the preliminary core domain set for shoulder disorder trials comprise an inner core of pain, physical function/activity, global perceived effect and adverse events including death, a middle core of emotional wellbeing, sleep and participation (recreation and work), and an outer core of research required to inform the final COS.

Our next steps will be to 1) Explore whether participation (recreation and work) should be in the inner core; 2) Perform a review of qualitative studies that had explored the lived experience of having shoulder pain; 3) Conduct a third Delphi round to finalise definitions and wording of domains and reach final endorsement for the domains from Delphi participants; and 4) Determine which instruments can be endorsed after having passed the OMERACT 2.0 Truth Discrimination and Feasibility (TDF) filter [7]. Results of this work will inform the final COS which we plan to present to OMERACT for endorsement.

Acknowledgements

We gratefully acknowledge the participation and insights of OMERACT 2016 attendees who attended our SIG session.

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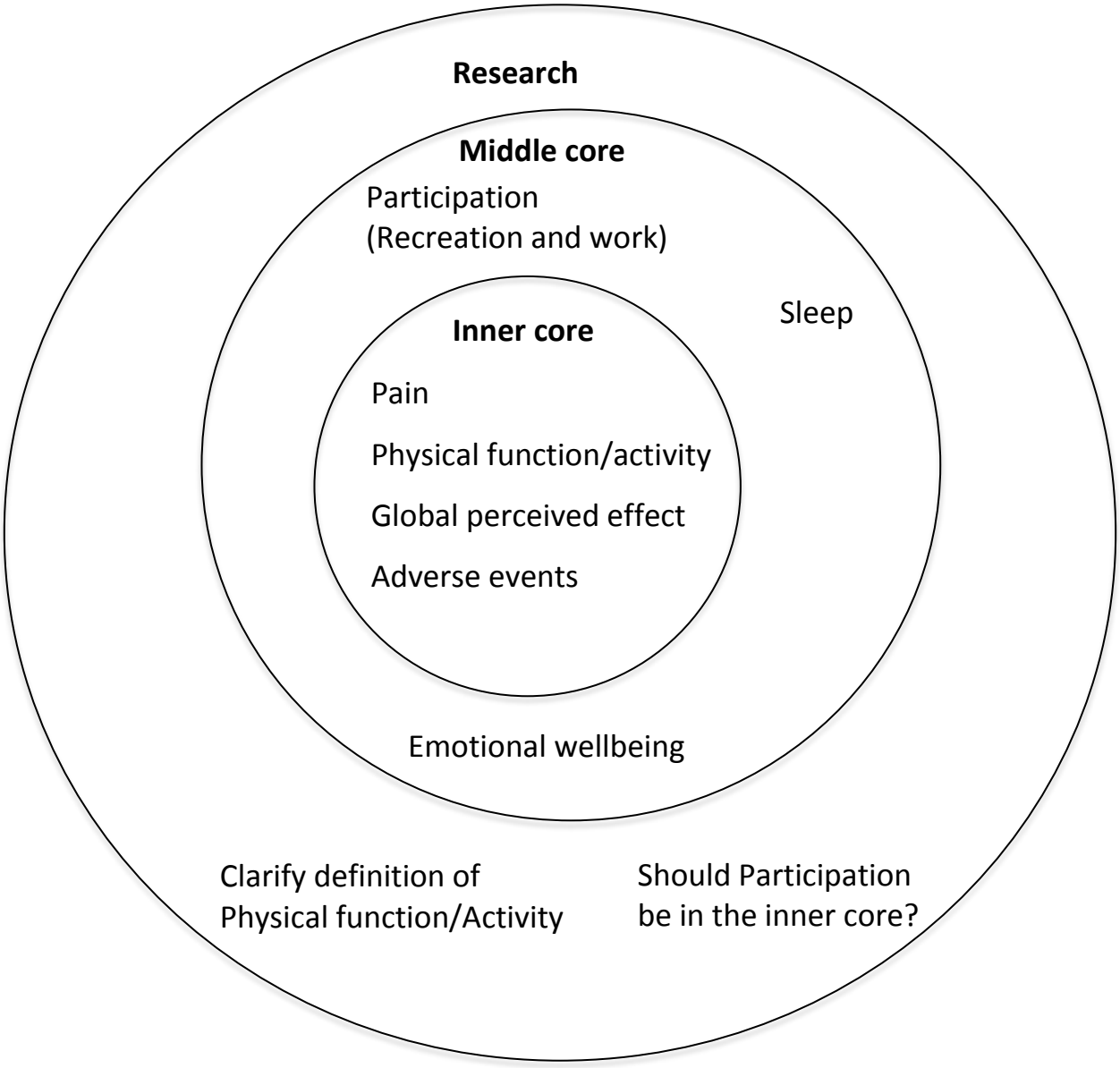
Table 1: Definitions of proposed preliminary core domain set for trials of people with shoulder disorders

Domain	Definition
INNER CORE	
Pain	How much a person's shoulder hurts, reflecting the overall magnitude of the pain experience (i.e. at rest, during and after activity, at night)
Physical function/activity	A person's ability to carry out daily physical activities required to meet basic needs, ranging from self-care (e.g. bathing, combing hair) to more complex activities that require a combination of skills (e.g. driving a car)
Global perceived effect	A person's assessment of their recovery or degree of improvement
Adverse events	Any major or minor adverse event that occurs during the course of the trial including any deaths
MIDDLE CORE	
Participation (recreation/work)	A person's ability to engage in any form of play, recreational or leisure activity acts (e.g. sports of any kind or levels), and the ability to meet physical and/or psychological demands of work (for people who work)
Sleep	Sleep functions like onset, maintenance, quality, amount of sleep, and functions involving the sleep cycle. This domain also includes the impact on perceptions of alertness and sleepiness during usual

	waking hours
Emotional wellbeing	Impact on person's emotions, including levels of depression, anxiety, or other types of psychological distress. Depression refers to negative mood, loss of self-confidence, loss of motivation and enjoyment. Anxiety refers to fear, extreme worrying and hyper-arousal symptoms

Figure 1 **Final proposed preliminary core domain set for trials in people with shoulder disorders* at OMERACT 16**



*Shoulder disorders include rotator cuff disease (e.g. tendinopathy, impingement, subacromial bursitis and tears), adhesive capsulitis, instability, glenohumeral osteoarthritis, dislocation, proximal humeral or humeral head fractures or unspecified shoulder pain