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Maxwell, L.J., Jones, C., Bingham, C.O. et al. (21 more authors) (2024) Defining domains: developing consensus-based definitions for foundational domains in OMERACT core outcome sets. Seminars in Arthritis and Rheumatism, 66. 152423. ISSN 0049-0172

https://doi.org/10.1016/j.semarthrit.2024.152423

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Title: **Defining Domains: Developing Consensus-Based Definitions for Foundational Domains in OMERACT Core Outcome Sets**

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Abstract

Objective: To develop a set of detailed definitions for foundational domains commonly used in OMERACT (Outcome Measures in Rheumatology) core domain sets.

Methods: We identified candidate domain definitions from prior OMERACT publications and websites, and publications of major organizations involved in outcomes research for six domains commonly used in OMERACT Core Domain Sets: pain intensity, pain interference, physical function, fatigue, patient global assessment, and health-related quality of life. We conducted a two-round survey of OMERACT working groups, patient research partners, and then the OMERACT Technical Advisory Group to establish their preferred domain definitions. Results were presented at the OMERACT 2023 Methodology Workshop, where participants discussed their relevant lived experience and identified potential sources of variability giving the needed detail in our domain definitions.

Results: One-hundred four people responded to both rounds of the survey, and a preferred definition was established for each of the domains except for patient global assessment for which no agreement was reached. Seventy-five participants at the OMERACT 2023 Methodology Workshop provided lived experience examples, which were used to contextualise domain definition reports for each of the five domains.

Conclusion: Using a consensus-based approach, we have created a detailed definition for five of the foundational domains in OMERACT core domain sets; patient global assessment requires further research. These definitions, although not mandatory for working groups to use, may facilitate the initial domain-match assessment step of instrument selection, and reduce the time and resources required by future OMERACT groups when developing core outcome sets.

Key words: OMERACT, domains, core domain set, rheumatology

Abstract word count: 228

Introduction

Use of validated, up-to-date core outcome sets with good measurement properties is essential for conducting good clinical trials with the minimum of unnecessary duplication of research effort, time, and resources. However, development of core outcome sets can be a long process; inefficiencies can occur when multiple Working Groups replicate the same work for similar rheumatic diseases. Developing an OMERACT core outcome set requires two essential and sequential components: deciding what to measure (core domain set) and then deciding how to measure each of the endorsed domains (core outcome measurement set). The word 'domain' is similar to the words 'concept', 'attribute', and 'construct' that have also been used in the literature to describe those things that are being measured (1). Potential domains are generated through scoping reviews and qualitative work, and then a consensus process determines those that are deemed the highest priority to measure in clinical trials and longitudinal observational studies. A consensus process requires all those participating to share a common understanding of the domain under discussion. This requires a clear definition of a particular or target domain. By target domain we mean the specific concept that will be measured in a core outcome set. We use the term 'target domain' to distinguish this specific concept from one which is less specific – what we term a 'broad domain'. For example, within the broad domain of pain, different target domains such as pain intensity or pain interference can be defined (2). This target domain should be defined as simply as possible, yet not simple (i.e., it must not be vague or unclear (1, 3-4)).

OMERACT has developed an explicit method to describe target domains using a detailed, stepwise approach. The target domain is defined by detailing the breadth and depth of the important elements that are essential to capture to measure the target domain (2). This work resulted in the development of a detailed definition for each domain that is recorded on the OMERACT Domain Definition report, which OMERACT working groups complete for each of their core domains (1). The detailed target domain definition recorded on this report then becomes the "gold standard" for the critical first step in the OMERACT instrument selection process of what an instrument should capture when the concept match and content validity is evaluated in the first stage of the instrument selection process (5,6). In this paper when we use the term 'domain' we mean the target domain.

Guidance from organizations involved in core outcome set development suggest that sufficient detail about the definition of the domain is needed to communicate clearly what is being measured (7,8). Experience within OMERACT Working Groups has shown that creating and agreeing on detailed domain definitions is a challenging and time-consuming task that can present a significant barrier to making progress towards core outcome set development. Core outcome set developers are often faced with many domains, some shared across diseases. A systematic review of core outcome set development studies (9) highlighted the absence of standardized definitions for domains. This is a problem for two reasons: 1) it introduces variability in how domains are defined across different core outcome sets, and 2) it hinders efforts to evaluate and select instruments to match a domain (10, 11).

Within existing OMERACT core outcome sets, certain patient-reported domains were found to be common across the different rheumatic diseases (15). Previous work had reviewed and listed all domains that are part of published OMERACT core domain sets (12), and we updated the list to capture recently endorsed core domain sets. From this list, we identified the top five most reported patient-reported life impact domains: pain, physical function, fatigue, patient global assessment, and health-related quality of life. At a prior OMERACT conference in May 2014, both pain intensity and pain interference were deemed important constructs to be measured in clinical trials of chronic pain in rheumatological conditions (13). Therefore, we decided to specify pain intensity and pain interference as two distinct domains needing detailed definitions. We termed the six domains ‘foundational domains’ due to their consistent importance across multiple OMERACT core domain sets of different rheumatological conditions. Various definitions of these foundational domains were used in the existing core domain sets.

To address the challenge of the significant amount of time and resources needed to develop a core domain set, OMERACT aims to provide working groups with the option of selecting from a set of foundational detailed target domains that have been endorsed by the OMERACT community. Working groups can review what they have found when generating domains through literature searches and qualitative work and decide whether the OMERACT-recommended definition for these foundational domains meets their needs. It is our intent that sharing these definitions and having them widely available will accelerate core outcome set development.

Methods

Study design: We conducted a targeted search for definitions of pain intensity, pain interference, physical function, fatigue, patient global assessment, and health-related quality of life from two main sources: (1) OMERACT publications of core domain sets; (2) websites and publications of major organizations in the field of outcomes research. We extracted verbatim the wording used to define the domain. We then conducted a two-round, cross-sectional survey to obtain the opinions of OMERACT patient research partners (PRPs) and experienced members of OMERACT. A final survey was conducted with the OMERACT Technical Advisory Group (TAG), a group of 16 experienced OMERACT members who provide methodological guidance.

Survey development: We drafted the survey with the definitions found in the literature and revised it in response to pilot-testing with TAG members. In the first round, for each of the six domains, we provided between three and five domain definitions and then asked respondents to rank the options from the ‘most relevant’ to ‘least relevant’. We provided an open response option for each domain and invited participants to provide another definition. We planned that the definition ranked either first or second ‘most relevant’ by 70% or more of respondents would be the recommended definition to take forward to the next round. In this second round, for those domains that resulted in a clear preference for a definition, we provided a synopsis of the results with a rationale for the recommended definitions and asked respondents whether they “agreed”, “could live with”, or “disagreed” with the recommendation. In the case where no definition reached the 70% threshold in the first round, we provided the top two ranked definitions and asked two questions: (1) whether they “agreed”, “could live with”, or “disagreed” with each of the definitions and (2) which definition they preferred. We discussed the results of this second round during a videoconference meeting of TAG members and then sent them a survey asking whether they had any significant concerns about the proposed definitions.

Administration and ethics: We used SurveyMonkey® to administer the survey. Participants could go back and change their answers to previous pages. Each round of the survey was open for 3 weeks, and we sent two reminders during each round. No incentives were provided. Ethics approval was not sought for this consensus project conducted within OMERACT since participants were selected from key members of the OMERACT community (co-chairs, patient research partners, and conference attendees).

Sample population: We sent the first and second rounds of the survey to all OMERACT working group co-chairs and OMERACT PRPs and the third round to the OMERACT TAG. The initial invitations went to 424 people including 311 patient research partners, and 113 working group co-chairs (98 researchers, and 15 clinicians).

Data analysis: Descriptive statistics were used to summarize the frequency of the domain definition options. We presented results separately by PRPs and other stakeholders to see if there was a difference in the results. We planned that a cut-off of 70% or more of those who either "agreed" or "could live with" a definition meant that it could be recommended. For the preference questions, the definition preferred by a larger percentage of participants would be selected. If there was a discrepancy in the results, we would select the definition preferred by the PRPs. For the survey of the TAG members, we pre-specified that 70% or more selecting the option of "no major concerns significant enough to override the recommendation" would mean confirmation of the recommendation.

At the OMERACT 2023 meeting Methodology Workshop, we presented the results of the surveys about the domain definitions and sought to obtain examples of lived experiences from the participants for the recommended definitions. We used this information to provide examples for each of the domain definition reports and to modify the definitions, if necessary.

Results

Out of 424 people, 115 responded (27% response rate) to the first round of the survey. For the domains of pain interference, pain intensity, and health-related quality of life there was a clear preference for one definition (over 70% of participants ranked it first or second in round 1). For the domains of physical function and fatigue, there was no clear preference after the first round, and we asked participants to select their preference (details below). Of four possible definitions for patient global, three were almost equally chosen as the most relevant. Across domains, comments related to issues around whether timeframe or attribution should be included in the definition. Table 1 summarizes the results for each domain for round 1. The full results are available in Supplementary materials.

Based on the results in round 1, we developed the survey questions for round 2. We received responses from 104 people (24% response rate): 66 PRPs and 38 other stakeholders. We presented a rationale for proposing recommended definitions for the three domains – pain interference, pain intensity, and health-related quality of life - where there was a clear preference for a definition in round 1 based on whether 70% or more of participants ranked it first or second. Over 95% of both PRPs and other stakeholders either agreed or 'could live with' the proposed definition for these three domains (Table 2).

For the domain of fatigue, there was not a clear preference after round 1. In round 2, respondents were asked whether they agreed or could live with the two top options from round 1 and which definition they preferred. Over 80% of both PRPs and other stakeholders either agreed or could live with each of the two definitions proposed. Both PRPs and other stakeholders preferred the PROMIS definition by approximately 10%.

For the domain of physical function, over 89% of both PRPs and other stakeholders either agreed or could live with each of the two definitions proposed. PRPs preferred the ASAS working group definition (67% vs 31%), while other stakeholders were neutral (50% vs 47%). We decided to recommend the ASAS definition as it was preferred by the PRPs.

The results for patient global were evenly split between the 3 options. PRPs ranked the definition ‘Overall evaluation of one’s physical and mental health’ slightly higher (44% ranked it first) than the other two definitions. Other stakeholders rated ‘The patient’s overall assessment of how the [disease condition] is doing’ slightly higher (40%). Given the lack of consensus on this definition, we recommend further research is needed on defining this domain.

Out of 16 TAG members, 13 responded (2 PRPs and 11 other stakeholders) to the final survey asking if they had any major concerns that are significant enough to override the recommendation (detailed results provided in the supplementary material). All definitions received 70% or higher endorsement that there were no significant concerns. During the TAG meeting to discuss the survey results we decided to make changes to two definitions in response to comments. The first was to the definition of fatigue from the Patient Reported Outcomes Measurement Information System (PROMIS): “Range of symptoms from mild subjective feelings of tiredness to an overwhelming debilitating, and sustained sense of exhaustion that likely decreases one’s ability to execute daily activities and function normally in family or social roles”. PRPs pointed out that the word ‘normal’ may be considered a problematic word as it has different connotations and may suggest there is some collective sense of normalcy or a certain value system. After discussions with the TAG, we added the following asterisk to the definition to clarify what is meant, “*Note: the term ‘normally’ is sometimes hard to define - here it relates to what is typical or usual for you as an individual.” For the definition of physical function, we removed the second sentence of the definition which included the additional concepts of physical activity and participation. We decided to use the first sentence of the definition which was clearly focused on physical functioning concepts [as shown in Table 1].

We received responses from 75 (64%) of registered participants at the OMERACT 2023 meeting in which they described their lived experience with each of the domains and commented on the proposed definitions. We revised the domain definition reports for each domain to incorporate this information into the other supporting information and the sources of variability sections of the reports to capture contextual factors that influence responses to items and scores of instruments. There were concerns expressed regarding the incorporation of ‘daily average’ and the range from no pain to worst pain imaginable in the proposed definition of pain intensity. These parts of the definition were viewed as overly precise for a domain definition and encompassed elements specific to an instrument. We revised the definition to, “The intensity of the sensation of pain, encompassing the entire spectrum from a complete absence of pain to the most extreme levels of discomfort.” The final recommended domain definitions are listed in Table 3. The domain definition report for pain interference is provided as an example in Figure 1, and the rest of the domain reports are available in the supplementary material. These reports are also available in a repository on the OMERACT website.

Discussion

When identifying and developing Core Domains Sets, it is important to define those concepts, so that all participants in a rating exercise and users of the Core set have a shared understanding of what is being measured. Because coming to consensus on the wording of definitions may be challenging for OMERACT working groups, we purposefully sought acceptable common definitions ("what you can live with") to enable them to move forward more efficiently and to reduce unnecessary duplication of research effort, time, and resources (14). Previous efforts to develop common outcome definitions across diseases had been linked to a particular platform or measurement approach (e.g., item response theory for PROMIS); whereas our intention was to create an open-source resource that could be widely used independent of measurement method or platform.

The definitions agreed upon in this effort are recommended but not mandatory. If, on the basis of qualitative studies to inform domain identification, a group feels that the OMERACT definition does not match the concepts elicited from their own work, that group may choose to develop a domain definition that meets their requirements.

An important result of this work was the lack of consensus about "patient global", with more PRPs preferring a definition angled towards "physical and mental health"; whereas other stakeholders focused more on "disease". Whilst attention is often paid to the patient global as an instrument (often a single item) this exercise pointed to the need to continue to focus on the concept or domain meaning itself. These divergent perceptions of the meaning of "patient global" require further urgent exploration of this domain with more qualitative review working towards consensus on our understanding and definition of it.

Limitations of this study included, first, the convenience sample of participants, accessed through existing OMERACT Working Groups, that may not be representative of wider groups; however, using this route of dissemination of the survey meant that participant were familiar with the principles and methods of OMERACT for reaching consensus. Secondly, the domain definitions were selected from the literature (definitions that had been used previously), but in the absence of systematic methods we could not guarantee to capture every variant of domain definition, nor were these definitions themselves necessarily rooted in qualitative research with patients with lived experience. Thirdly, the survey wording ("could live with", "any significant concerns") might have discouraged some participants from critiquing imperfect domain definitions; however, this avoided the potential problem of a multiplicity of excessively granular redefinitions of domains, that might not be applicable across the whole spectrum of rheumatic and musculoskeletal diseases within the remit of OMERACT. We thus aimed to avoid recapitulating the protracted discussions we had observed within Working Groups by establishing “good enough” definitions. We acknowledge that these definitions are a starting point and will evaluate how they are used by working groups to see if any modifications are required.

This work could be extended to identify possibly “universal” candidate instruments to measure each of these foundational domains, evaluating them through the OMERACT Filter 2.2 for their measurement properties in the contexts of interest. Our detailed definition reports with their supporting evidence will ensure that groups can revisit and refresh their knowledge of the “essential nature” of the domain. We obtained potential sources of variability in the measurement of each of the domains as this information is important for future research into the role of contextual factors as measurement-affecting factors during the instrument selection phase.

We propose domain definitions for five of the six identified foundational domains with common relevance to most rheumatic and musculoskeletal diseases within the OMERACT remit. This work will improve the efficiency of the OMERACT process, allowing Core Outcome Sets to be created and updated faster, which should reduce unnecessary duplication of research effort, time, and resources and standardize the measurement of common life impact domains. This may be of particular value for rarer or neglected rheumatic diseases, in which research capacity is still limited.

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Role of funding source

There was no funding for this quality improvement project for OMERACT.

Declarations of interest

COB, MB, RC, EC, CH, CLH, SG, FK, BJS, GAW - No conflicts

DEB: Member of Management team at OMERACT, co-chair of methods group and technical advisory group of OMERACT.

PC: Member, OMERACT Management Committee.

AB: Received research grants for Abbvie and Lilly and fees for lectures or consultations from Abbvie, UCB, Novartis, Galapagos and Pfizer, all to her department and unrelated to the topic of this manuscript

AD has the following relationships unrelated to the conduct of this study: Chair of the International Myositis Assessment & Clinical Studies Group (not for profit) Chair of the Radiological Society of North America (RSNA) Annual Planning Committee for Pediatric Radiology (not for profit), Co-Chair of the American College of Radiology (ACR) Pediatric Imaging Research Committee (not for profit), Chair of the Bias in Recruitment, Hiring, Promotion, Awards Committee of the Canadian Association of Radiology (not for profit), and PI of research grants from Novo Nordisk, the Terry Fox Foundation, the PSI Foundation, the Society of Pediatric Radiology, and the Garron Family Cancer Centre, unrelated to the topic of this manuscript.

MADA: Grants from Abbvie, Amgen, Pfizer. Royalties or licenses from Elsevier. Consulting fees from Abbvie, Amgen, BMS, Galapagos, Novartis, Lilly, Janssen, UCB. Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Abbvie, Amgen, BMS, Galapagos, Novartis, Lilly, Janssen, UCB. Support for attending meetings and/or travel from Janssen, Novartis.

BH: OMERACT 2023 conference in Colorado Springs. Paid by OMERACT to support my role a Patient Research Partner.

CJ: Seed funding grants for unrelated project (pilot trial of opioids used after total joint replacement surgery) from ANZMUSC ($19,956), Arthritis Australia ($20,000) and Wiser Healthcare ($4,000). Casual payments from OMERACT for hours spent creating an unrelated e-learning series (technician role) in 2022-2023. Registration, flight and accommodation costs covered by OMERACT for attendance at OMERACT Colorado Springs 2023. Current member of ECR committee of ANZMUSC

SLM reports: Consultancy on behalf of her institution for Roche/Chugai, Sanofi, AbbVie, AstraZeneca, Pfizer; Investigator on clinical trials for Sanofi, GSK, Sparrow; speaking/lecturing on behalf of her institution for Roche/Chugai, Vifor, Pfizer, UCB, Novartis and AbbVie; chief investigator on STERLING-

PMR trial, funded by NIHR; patron of the charity PMRGCAuk. No personal remuneration was received for any of the above activities. Support from Roche/Chugai to attend EULAR2019 in person and from Pfizer to attend ACR Convergence 2021 virtually. SLM is supported in part by the NIHR Leeds Biomedical Research Centre. The views expressed in this article are those of the authors and not necessarily those of the NIHR, the NIHR Leeds Biomedical Research Centre, the National Health Service or the UK Department of Health and Social Care.

AM: Consulting fees from Sanofi, Abbvie, Amgen. Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Sobi, Sanofi, Abbvie. Registration, flight and accommodation costs covered by OMERACT for attendance at OMERACT Colorado Springs 2023.

LJM is a paid staff member of OMERACT.

LSS is on the Management Committee of OMERACT and is Chair, Finance Committee of OMERACT.

YY (Katy)L is supported by National Medical Research Council of Singapore. AbbVie, DKSH, Janssen, Novartis and Pfizer- Speaker fee and honorarium paid to me. AbbVie, DKSH, Janssen, Novartis and Pfizer - Research sponsorship paid to institution. APLAR: Travel and accommodation to APLAR congresses. GRAPPA: Travel and accommodation to GRAPPA congresses. Co-Chair of Scientific Committee of Asia Pacific League of Associations of Rheumatology, APLAR - No payment. Education committee of Group for Research and Assessment for Psoriasis and Psoriatic Arthritis, GRAPPA -No payment.

PT: Consulting Fees from Reformulary Group. An independent Committee Member for clinical trial Data Safety Monitoring Boards for FDA approved trials being conducted by: UCB Biopharma GmbH & SPRL, Parexel International, Prahealth Sciences. I am [unpaid] Chair of the Management Group of a registered non-profit independent medical research organization, OMERACT, whose goal is to improve and advance the health outcomes for patients suffering from musculoskeletal conditions. OMERACT receives arms-length funding from 11 companies: Abbvie, Astra Zenaca, Aurinia, BMS, Centrexion, GSK, Horizon Pharma Inc , Janssen, Novartis, Pfizer & Sparrow.

ZT: Leadership or fiduciary role in other board, society, committee or advocacy group: Co-chair American College of Rheumatology Criteria development subcommittee.

Acknowledgements

Thank you to Mohamad Babiker for entering the responses from OMERACT 2023 Methods Workshop participants into a database for analysis.

SLM and PGC are supported in part by the NIHR Leeds Biomedical Research Centre. RC is via Section for Biostatistics and Evidence-Based Research, the Parker Institute, Bispebjerg and Frederiksberg Hospital is supported by a core grant from the Oak Foundation (OCAY-18-774-OFIL). The views expressed in this article are those of the authors and not necessarily those of the NIHR, the NIHR Leeds Biomedical Research Centre, the National Health Service or the UK Department of Health and Social Care.

Table 1. Preferred domain definitions, ranked by proportion of participants in survey round 1

Pain interference (N=115)	**%**
1. Consequences of pain on relevant aspects of one's life. This includes the extent to which pain hinders engagement with social, cognitive, emotional, physical, and recreational activities. [PROMIS] 2. The degree to which there are consequences of pain on aspects of a participant's life. [INTEGRATE-Pain] 3. The degree to which there are consequences of pain on aspects of a participant's life (in the past 24 hours or past week for acute or chronic pain, respectively). [INTEGRATE-Pain]	PRP 66 Other 58 PRP 23 Other 18 PRP 10 Other 25
Pain intensity (N=111)	
1. The daily average of the intensity of the sensation of pain expressed on a range from no pain to worst pain imaginable. [OMERACT Lessons from Imaging. D'Agostino et al]	PRP 50 Other 40
2. Reflects the overall magnitude of the pain. [IMMPACT]	PRP 12 Other 42
3. Magnitude of the pain. [INTEGRATE-Pain]	PRP 19 Other 19
4. How much a person hurts. [PROMIS]	PRP 19 Other 0
Health-related quality of life (N=109)	
1. A term referring to the health aspects of quality of life, generally considered to reflect the impact of disease and treatment on disability and daily functioning; it has also been considered to reflect the impact of perceived health on an individual's ability to live a fulfilling life. [ISOQOL]	PRP 58 Other 76
2. At an individual level, HRQOL includes physical and mental health perceptions, (e.g., energy level, mood) and their correlates—including health risks and conditions, functional status, social support, and socioeconomic status**.** [WHOQoL]	PRP 22Other 19
3. Broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life. [CDC]	PRP 10 Other 2
4. Subjective evaluations of both positive and negative aspects of physical life (i.e., Pain and discomfort, Energy and fatigue, Sexual activity, Sleep and rest, Sensory functions). [WHOQoL]	PRP 9 Other 2
Fatigue (N=110)	
1. Range of symptoms, from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely	PRP 33 Other 47

decreases one's ability to execute daily activities and function normally in family or social roles.$^+$[PROMIS]	
2. A feeling of extreme tiredness or exhaustion attributable to [disease condition], limiting someone to perform his/her usual and meaningful daily activities.$^+$ [OMERACT Myositis]	PRP 27 Other 21
3. Fatigue describes the overall feeling of tiredness and/or lack of energy; inability to optimally use mental or physical capacity. [ASAS-OMERACT]	PRP 13 Other 26
4. Is a clinically relevant symptom characterized by difficulty in initiation or sustaining voluntary activities and is distinguished from the lay notion of tiredness. [ISOQOL]	PRP 12Other 7
5. Fatigue is overwhelming and different from normal tiredness; it permeates every sphere of life [OMERACT Fatigue]	PRP 15 Other 0
Physical function (N=109)	
1. Physical functioning is defined as one's ability to carry out various activities that require physical capability, ranging from self-care (activities of daily living) to more vigorous activities that require increasing degrees of mobility, strength, or endurance. An important aspect in this domain is physical difficulty: any problems with physical activity resulting from impairment, any activity limitations and participation restrictions; and the ability to transfer oneself from one place to another (i.e., walking, cycling). $^+$ [ASAS-OMERACT]	PRP 45 Other 55
2. A person's ability to carry out daily physical activities, ranging from self-care. (e.g., bathing, combing hair) to more complex activities that require a combination of skills (e.g., driving a car). $^+$ [OMERACT Shoulder]	PRP 37Other 33
3. The ability to perform basic and desired activities of daily living that is affected by limited functioning of muscles, mobility and instrumental acts of daily living, due to "[disease condition]". [OMERACT Myositis]	PRP 13 Other 5
4. Self-reported capability rather than actual performance of physical activities. This includes the functioning of one's upper extremities (dexterity), lower extremities (walking or mobility), and central regions (neck, back), as well as instrumental activities of daily living, such as running errands.[PROMIS]	PRP 5 Other 7
Patient global (N=106)	
1. Overall evaluation of one's physical and mental health. [PROMIS]	PRP 39 Other 21
2. The patient's overall assessment of how the [disease condition] is doing. [ACR RA core set]	PRP 16 Other 44
3. Considering the ways that the health condition affects the individual on a given day. [Integrate-Pain]	PRP 27 Other 21
4. Patient-reported disease-related health status. [OMERACT Psoriatic Arthritis]	

	PRP 18 Other 14

+These definitions were presented as the top two preferred options for round 2

CDC: Centres for Disease Control and Prevention
INTEGRATE-Pain: IMI-NIH Transatlantic Emphasis Group on Research and Translation-to-care Efforts for Pain
ISOQOL: International Society for Quality of Life Research
PROMIS: Patient-Reported Outcomes Measurement Information System
WHOQOL: World Health Organization Quality of Life Assessment

Table 2: Survey results round 2

Domain	**Recommended definition**	**2nd round results, %:**	
		agreed	**‘can live with’***
Pain interference	“Consequences of pain on relevant aspects of one’s life. This includes the extent to which pain hinders engagement with social, cognitive, emotional, physical and recreational activities”. (source: PROMIS)	PRP 82 Other 84	PRP 17 Other 16
Pain intensity	“The daily average of the intensity of the sensation of pain expressed on a range from no pain to worse pain imaginable.” (source: OMERACT Lessons learned from Imaging. D’Agostino et al. 2021) **Note:** The wording of this definition was modified after the OMERACT meeting to address concerns. See Table 3 and the Domain Definition Report: ‘Pain intensity’ for the final wording (supplemental material)	PRP 55 Other 68	PRP 41 Other 32
Health-related quality of life	“A term referring to the health aspects of quality of life, generally considered to reflect the impact of disease and treatment on disability and daily functioning. It has also been considered to reflect the impact of perceived health on an individual’s ability to live a fulfilling life.” (source: ISOQOL)	PRP 95 Other 82	PRP 5 Other 18
Fatigue	“Range of symptoms from mild subjective feelings of tiredness to an overwhelming debilitating, and sustained sense of exhaustion that likely decreases one’s ability to execute daily activities and function normally in family or social roles” (source: PROMIS) *Note: The wording of this definition was modified after the TAG meeting to address concerns. We specified with an asterisk: the term ‘normally’ is sometimes hard to define - here it relates to what is typical or usual for you as an individual.	> 80% of PRPs and other stakeholders either agreed or could live with the top two preferred definitions. However, both groups preferred this definition by approximately 10%.	
Physical function	“Physical functioning is defined as one’s ability to carry out various activities that require physical capability, ranging from self-care (activities of daily living) to more vigorous activities that require increasing degrees of mobility, strength or endurance.” (source: ASAS-OMERACT Working Group)	> 89% of PRPs and other stakeholders either agreed or could live with each of the two definitions proposed. PRPs preferred this definition to the second option (67% vs 31%), while in the other stakeholders preferences were neutral (50% vs 47%).	

Patient global assessment	No clear preference after round 2, therefore no definition recommended. Further research is needed.	44% PRPs preferred the first definition; 40% other stakeholders preferred the second definition.

* Patient research partner (PRP): n=66; other stakeholders: n=38

Table 3: Final recommended domain definitions

Domain	**Recommended definition***
Pain interference	Consequences of pain on relevant aspects of one's life. This includes the extent to which pain hinders engagement with social, cognitive, emotional, physical and recreational activities. (source: PROMIS)
Pain intensity	The intensity of the sensation of pain, encompassing the entire spectrum from a complete absence of pain to the most extreme levels of discomfort. (source: OMERACT)
Health-related quality of life	A term referring to the health aspects of quality of life, generally considered to reflect the impact of disease and treatment on disability and daily functioning. It has also been considered to reflect the impact of perceived health on an individual's ability to live a fulfilling life. (source: ISOQOL)
Fatigue	Range of symptoms from mild subjective feelings of tiredness to an overwhelming debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally[#] in family or social roles (source: PROMIS) [#] the term 'normally' is sometimes hard to define - here it relates to what is typical or usual for you as an individual.
Physical function	Physical functioning is defined as one's ability to carry out various activities that require physical capability, ranging from self-care (activities of daily living) to more vigorous activities that require increasing degrees of mobility, strength or endurance. (source: ASAS-OMERACT Working Group)

*the complete definition report for each domain is available in the supplementary material.

Figure 1: Domain Definition Report: Pain interference

<table>
<tr><td colspan="3">**Working Group:** Generic</td><td colspan="2">**Date completed:**</td></tr>
<tr><td>**Population:**
People with musculoskeletal conditions</td><td>**Intervention(s):**</td><td colspan="2">**Control(s):**</td><td>**Context: (target type of study)**</td></tr>
<tr><td>**What is the name that you give to your target domain?**</td><td>Pain interference</td><td>**Is this part of a broader domain?**</td><td colspan="2">☐ **No**
☒ **Yes ….If yes, which one: Pain**</td></tr>
<tr><td>**Tell us more about that domain** –this is your domain definition. what is the breadth, depth – what do you want to be able to see.</td><td colspan="4">Consequences of pain on relevant aspects of one's life. This includes the extent to which pain hinders engagement with social, cognitive, emotional, physical and recreational activities.</td></tr>
<tr><td>Which of the **core areas** does this fall into? (check one)</td><td colspan="4">☐ Pathophysiological manifestations
☒ Life impact
☐ Death/Lifespan
☐ Resource use (i.e., costs)</td></tr>
<tr><td colspan="5"></td></tr>
<tr><td colspan="5">**Tracking for future reference…. (we suggest you track these now while you are thinking about it, but they are not mandatory. You (or your successors) will need them later in instrument selection)**</td></tr>
<tr><td>***…How did you come to understand this target domain well?***</td><td colspan="4">*Other supporting information that helps to understand the domain (i.e., add relevant quotes from patients & other stakeholders or references to literature that aid in understanding of what this is….and what it is not)*
"Modify activity and participation to avoid pain intensity - particularly for predictable pain. Plan to avoid. Lack of enjoyment."
"Impact of pain on concentration, and emotional well-being. Intervenes on multiple levels: work, family, avoidance / management strategies."
"Pain interferes with joy in life. This is a consequence of decreased anticipation. There is a psychological aspect due to unpredictable nature."
"Living life to the fullest except when pain makes it completely stop. Usually temporary. Will to live through pain. Dismissed for having pain. Family-relationships. Frustrating loss of employment."
"Knee pain - dancing (social), limited activity with grandchildren (emotional,) limited in running (physical). Fear of having pain. Afraid of being involved with social & work."
"Painful ankles and not being able to get coffee. Not being able to go running."
"Different types of pain also can be different/impact differently for me at the</td></tr>
</table>

	same intensity – for example, I find neuropathic pain more disruptive than some of my chronic nociplastic pain.” “Different types of pain interfere differently. Pain causes triage of life – there are levels of interference that require even more expenditure of energy to decide “need” vs “want” vs “critical”. “Some days pain interferes with socialization I wish to do, other days interference is as “deep” as disrupting my ability to brush my teeth. Many of these are also interlinked – I may be experiencing cognitive difficulties and feel frustration due to pain, which in turn influences so many things – overall mood, physical function, etc.” “This is much more important to patients than pain intensity.”
	Other available definitions, frameworks used (i.e., did you take definition from another framework, or another working group – both are great if they work for you – cite here) Source: PROMIS https://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis/list-of-adult-measures
….Are there any “it all depends” type factors. Factors that make a difference in the number/score obtained?	*Examples: +/- use of assistive device, type of imaging machine, technician variability, time of day…* Different types of pain (e.g., nociplastic, nociceptive)