Harmonizing Pain Outcome Measures: Results of the Pre-OMERACT Meeting on Partnerships for Consensus on Patient-important Pain Outcome Domains Between the Cochrane Musculoskeletal Group and OMERACT

Kristine Phillips, Ann Taylor, Philip J. Mease, Lee S. Simon, Philip G. Conaghan, Ernest H. Choy, Jasvinder A. Singh, Vibeke Strand, Laure Gossec, Ulrike Kaiser, Marteen de Wit, Raymond Ostelo, Lara Maxwell, and Peter S. Tugwell

ABSTRACT. ***Objective.*** A variety of authorities in pain measurement and outcome methodology met prior to the Outcome Measures in Rheumatology (OMERACT) 12 meeting in May 2014 to develop partnerships for consensus on pain outcomes.

Methods. Following overview presentations, discussion centered on pain-specific and global constructs in the domain of chronic pain. Practical issues for clinical trial implementation were also discussed. Breakout sessions were completed regarding additional details of domain constructs. A nominal group process involving all workshop participants confirmed that chronic pain outcome measures encompass a broad range of constructs and that existing scales may be inadequate for assessment in clinical trials.

Results. Participants endorsed that both pain intensity and pain interference are important constructs to be measured in clinical trials of chronic pain as it pertains to rheumatologic diagnoses.

Conclusion. Further work is needed on inclusion of the patient perspective in the development of pain domains as well as Cochrane Collaboration summary of findings tables. (First Release August 1 2015; J Rheumatol 2015;42:1943–6; doi:10.3899/jrheum.141386)

Key Indexing Terms:
ARTHRITIS OUTCOME ASSESSMENT PAIN OMERACT

Musculoskeletal disorders, particularly rheumatic diseases, are major determinants of disability worldwide. Access to care for chronic pain and quality of healthcare for pain continue to vary widely even in countries with the best healthcare resources. Despite innovations in surgical and pharmacological treatments over the past decade, patients continue to experience limitations in function and unacceptable levels of pain. Variability (lack of harmonization) of outcome assessments among clinical trials has impeded the evaluation of both efficacy and effectiveness of interventions for chronic musculoskeletal and rheumatologic pain. Consensus on outcome domains and measurement instruments will facilitate comparison of results and coordination of research, and will have an effect on both personalized treatment and healthcare policy that will ultimately benefit patients.

Several groups were invited to attend a preconference meeting held in conjunction with the Outcome Measures in

From the Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA; Cardiff University, Cardiff, UK; Swedish Medical Center and University of Washington, Seattle, Washington, USA; SDG LLC, Cambridge, Massachusetts, USA; Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and National Institute for Health Research (NIHR) Leeds Musculoskeletal Biomedical Research Unit, Leeds, UK; University of Alabama at Birmingham, Birmingham, Alabama; Division of Immunology/Rheumatology, Stanford University, Palo Alto, California, USA; University Hospital Carl Gustav Carus, Dresden, Germany; Universite Pierre et Marie Curie and APHP, Department of Rheumatology, Pitie-Salpetriere Hospital, Paris, France; EMGO Institute for Health and Care Research, Department of Health Sciences, VU University, and Department of Epidemiology and Biostatistics, VU University Medical Center, VU Medical Center, Amsterdam, The Netherlands.

K. Phillips, MD, PhD, Department of Internal Medicine, University of Michigan; A. Taylor, PhD, MSc, Cardiff University; P.J. Mease, MD, Swedish Medical Center and University of Washington; L.S. Simon, MD, SDG LLC; P.G. Conaghan, MBBS, PhD, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit; E.H. Choy, MD, FRCP, Department of Medicine, Cardiff University School of Medicine; J.A. Singh, MD, MPH, University of Alabama at Birmingham; V. Strand, MD, Division of Immunology/Rheumatology, Stanford University; L. Gossec, MD, PhD, Universite Pierre et Marie Curie and APHP, Department of Rheumatology, Pitie-Salpetriere Hospital; U. Kaiser, Dr, University Hospital Carl Gustav Carus, Dresden, Germany; M. de Wit, PhD, VU Medical Center; R.W. Ostelo, MD, EMGO Institute for Health and Care Research, Department of Health Sciences, VU University; and Department of Epidemiology and Biostatistics, VU University Medical Center; L. Maxwell, MSc, University of Ottawa, Institute of Population Health; P.S. Tugwell, MD, MSc, University of Ottawa, Centre for Global Health.

Address correspondence to Dr. K. Phillips, University of Michigan, Internal Medicine, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109, USA. E-mail: kphill@umich.edu

Rheumatology (OMERACT) 12 meeting (2014). These groups are all interested in outcome measures for pain research, including the Cochrane musculoskeletal group, Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT). Three other international initiatives on outcome methodology: COMET (Core Outcome Measures in Effectiveness Trials)[1,2] and COSMIN (Consensus-based Standards for the Selection of Health Measurement Instruments)[3,4] and VAPAIN (Validation and Application of a patient relevant core outcome set to assess effectiveness of multimodal PAIN therapy) were also represented at the meeting.

The Cochrane Collaboration is a group of almost 30,000 contributors in over 100 countries who review and provide summaries of healthcare interventions that affect care at the individual and health policy level. Evidence is evaluated through a systematic review of all known published clinical trials and gives the best estimate of potential benefits in a given patient population[5]. Potential side effects are also summarized, and the systematic reviews are published and made available in the Cochrane Library. Summaries currently focus on the top 7 patient-important outcomes and include benefits and harms estimates as well as an abstract, plain-language summary, and a table of the summary of findings[6,7]. The 7 outcomes are developed by consensus with future input from the Cochrane musculoskeletal consumer group. The Cochrane summaries of evidence-based medicine help guide management of patients as well as inform policy decisions, and are critical in this regard[8]. Harmonization of outcome measures between clinical trials is problematic, because different studies use different outcome measures that may map to disparate domains and subdomains[9]. This reduces the ability to compare and make conclusions across studies, and serves as a significant barrier to progress in the field.

OMERACT has been a pioneer in the field of outcomes research, and pain has primarily been studied as a central component of rheumatic disease core domain measurement sets for many diseases[10,11,12]. Several members of OMERACT, including members of the OMERACT pain working group, have collaborations with the IMMPACT and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) groups[13,14]. IMMPACT and ACTTION are partnerships of academic researchers, regulatory groups, federal funding agencies, consumer support groups, pharmaceutical industry representatives, and others with an interest in improving outcome measures for chronic pain clinical trials. These 2 groups have led the approach to domain development for chronic pain of all etiologies, and their work has ongoing implications for the chronic pain associated with musculoskeletal and rheumatologic disease[15].

The groups were charged with defining objectives for pain research, discussing the concept of chronic pain as an independent disease, and reviewing currently recommended domains for pain research. Developing consensus in outcome measurement for pain in rheumatologic disease will benefit from further collaborations of these groups, and events such as the preconference OMERACT meeting. Translating new treatment options for patients with musculoskeletal and rheumatologic disease from basic science to the bedside and subsequently to healthcare policy will require this comprehensive approach, with consensus from all groups toward a conceptual framework and domains/subdomains of pain in these specific diseases.

MATERIALS AND METHODS

Groups with an interest in and prior history of work related to outcome measures for pain research were invited to participate. Participation was open to all members of the group with an interest in pain outcomes or pain research. Patient research partners (PRP) also participated in the sessions. In advance of the full-day preconference meeting, all participants were given access to relevant manuscripts for review and preparation. The bibliography was selected by steering committee members with additional input from all participants. Publications from representative groups were included, as well as specific publications related to outcome development for chronic pain. Examples of clinical trials using chronic pain outcomes were also included. Opening presentations reviewed the pain domains previously identified by IMMPACT. Discussion of these domains was completed prior to breakout sessions. Participants in the workshop included members of the pain working group of OMERACT and the Cochrane musculoskeletal group and Cochrane back group, as well as interested individuals with expertise in analysis of randomized controlled trial data. Patients participated in all aspects of discussion, including subgroup workshops. A modified nominal group technique fostered discussion and determination of consensus. Used for decades, the nominal group technique incorporates small group discussion with brainstorming, collection of ideas, and voting on specific items of interest to the group. It works well as a consensus effort from 2 groups because it fosters exchange of opinions among people with different perspectives, balances individual opinions, and allows prioritization of ideas.

Conference attendees were divided into several subgroups for breakout sessions, with consideration of diversity of international representation and participant category in each subgroup. Breakout sessions were led by independent researchers with experience leading breakout sessions. The sessions focused on specific, related topics including discussion of the domains of pain and a discussion of pain as a chronic disease. In Workshop A, pain domains were reviewed in dedicated presentations to develop discussion points, followed by open discussion and projected future directions. Presentation of the background for the meeting was completed prior to the breakout sessions. A survey of those invited to the preconference meeting demonstrated that the majority of attendees agree that pain intensity is an important outcome to present in summary of findings (SoF) tables for chronic conditions but that intensity alone does not capture the complexity of the effect of pain.

Consideration of different conceptual models was completed, with emphasis on the International Classification of Functioning (ICF), Disability, and Health[16] framework. Specific presentations also included an overview of physical activity and physical function instruments including performance-based measures and patient-reported outcome measures. After the breakout sessions, participants presented results of their discussion, and a list of recommendations in outline form was included. Remaining controversies were listed separately. Specific details of the discussions from the breakout groups are published separately[17].

RESULTS

Thirty-eight participants took part in workshop voting. About half the participants were clinical researchers, and the next

largest group was methodologists or statisticians. The rest were industry or other researchers, regulators, or patients. The overall participation in the workshop and subgroups was diverse and inclusive. There was wide geographical representation as well as representation from multiple perspectives including many patients, healthcare providers, and epidemiologists. One or more PRP attended each breakout group and participated equally with healthcare providers and others in all discussions and voting.

General discussion of conceptual frameworks included the observation that there is no ideal framework that can serve as a comprehensive tool for identifying all pain subdomains. The ICF framework was felt to be a good starting point by many participants; however, many also said that this framework is focused on disease mechanism and is not comprehensive. Previous OMERACT groups have also identified these limitations[18]. Subsequent discussion about specific pain domains included discussion of published IMMPACT identified domains (i.e., pain intensity, pain interference) for generalized chronic pain clinical trials. These were said to not fully explore all the domains or subdomains relevant for chronic musculoskeletal pain, such as participation. Other practical issues discussed during the general overview included characteristics, response to each instrument, instrument quality, and reliability of diary data. Participants agreed that identification of an appropriate conceptual framework and consensus on domains and subdomains should precede identification of measures that have demonstrated appropriate psychometric or other measurement properties with the lowest participant burden.

Most of the general discussion also included identification of results that are important from the perspective of each participant. Including an OMERACT approach with significant and meaningful input from patients into SoF tables was considered an important contribution from ongoing collaborations between the participating groups. Questions arose regarding limitations on the number of rows in the SoF table and the effect this may have on information shared. Some participants recommended consideration of different SoF tables for different participants. Regarding identification of different pain subdomains, the effect of different pain thresholds and derivation of categories was discussed.

After reviewing previously identified subdomains of pain, participants endorsed additional subdomains of pain for inclusion in musculoskeletal pain clinical trials (see Table 1).

Voting by all participants including PRP confirmed that both pain intensity and pain interference should be included in any clinical trial of chronic musculoskeletal or rheumatologic pain. Eighty-seven percent of participants voted yes to including both.

Table 1. Musculoskeletal and rheumatology-specific domain constructs from participants' discussion.

Pain-specific Constructs	Global Constructs (Global Impact of Pain)
Duration	Physical activity
Intensity	Physical function
Mechanism	Pain interference
Peripheral nociception	
Central sensitization	
Variability (experience/consistency)	Others
Flare	
Emotional outcomes	
Time anchor	
Contextual factors	
Others	

DISCUSSION

This meeting represents the first unique international gathering of representative groups with interest in outcome measures of chronic pain. This report describes preparations, general overview, and outline of the composition of the meeting. Topics for discussion at the breakout sessions are described separately. Harmonization of outcome measures in chronic pain will improve comparisons between studies and allow for more meaningful summary reporting, including summary of findings tables from the Cochrane group. Prior to harmonization of specific instruments, consensus on the domains and subdomains must occur, and should include patient involvement in their development at the earliest stage. Current core sets of measurement are disease-focused and may not completely classify all constructs and complexities of chronic pain. Identification of domains and subdomains of musculoskeletal pain and consensus on their use in clinical trials will allow development of instruments that cover all patient-important constructs and facilitate comparison and integration of data among studies.

Previous OMERACT meetings developed a filter through which selected measures must pass. To be applicable in its intended setting, a measure must be truthful (free from bias, with construct and face validity), discriminative, and feasible[19]. In 2012, the OMERACT Filter was updated (Filter 2.0) to include broader assessments of core areas of measurement[20,21]. Core areas of measurement include a conceptual structure of health conditions, and consensus on which areas (generic or specific) are part of the core. For any disease state, the overall effect of health conditions on resource use and life impact are considered. Life impact measures directly related to chronic pain include activity, participation, quality of life, perception of health, and loss of ability to work. Secondary impact on family and caregivers is also included in this rubric. The OMERACT Filter 2.0 provides a framework to evaluate pain using an approach that can address these different aspects of a complex experience, and may benefit the implementation of new methods of summarizing data being developed by the Cochrane Collaboration.

Future Directions

Research in this area will need to confirm consensus on the following domains and subdomains of chronic musculoskeletal and rheumatologic pain:

- Hierarchy of subdomains
- Clinimetrics within subdomains
- Practical clinical trial design aspects such as
  - Implementation considerations
  - Time anchors
  - Responsiveness to change

Complex issues arising from reporting accurately from the patient perspective were also discussed, including issues such as adaptation and frame shifting. Contextual factors such as genetic or epigenetic background and social determinants of health were also considered. Consensus was reached, with the majority of participants endorsing future involvement of PRP in development of all future chronic pain outcome measures, including harmonization.

Patient involvement has been cited by others as critical for healthcare improvement — "It has been said that healthcare won't get better until patients play a leading role in fixing it; we agree and look forward to helping drive the patient revolution on."[22]

The Cochrane Collaboration, COMET, COSMIN, and OMERACT share common interests in the area of pain domains. The membership and activities of all participating groups are complementary, and will combine well with ongoing efforts in the ACTTION/IMMPACT network. OMERACT brings the unique and sometimes overlooked importance of patient perspective in the development and harmonization of outcome measurement instrument for clinical trials. Future directions of research in the area of pain outcomes will benefit from expertise and coordination from all these groups.

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