Seminars in Arthritis and Rheumatism 64 (2024) 152342

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Exploring the complexities of pain phenotypes: OMERACT 2023 chronic pain working group workshop

Tim Pickles [a,*], Mary Cowern [b], Robin Christensen [c], Sabrina M. Nielsen [c], Lee S. Simon [d], Caitlin M.P. Jones [e,f], Lara J. Maxwell [g], Beverley Shea [h], Vibeke Strand [i], Zahi Touma [j,k], Karine Toupin-April [l,m,n,o], Philip Mease [p,1], Ernest Choy [q,1]

[a] Centre for Trials Research, Cardiff University, Cardiff, UK
[b] Versus Arthritis, UK
[c] Section for Biostatistics and Evidence-Based Research, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Research Unit of Rheumatology, Department of Clinical Research, Odense University Hospital, University of Southern Denmark, Copenhagen, Denmark
[d] SDG LLC, Cambridge, MA, USA
[e] Sydney Musculoskeletal Health, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia
[f] The Institute for Musculoskeletal Health, Sydney Local Health District, Sydney, NSW, Australia
[g] Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[h] The Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada
[i] Division of Immunology/Rheumatology, Stanford University School of Medicine, Palo Alto, CA, USA
[j] Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada
[k] Division of Rheumatology, Toronto Lupus Program, University of Toronto, Toronto, Ontario, Canada
[l] School of Rehabilitation Sciences, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
[m] Department of Pediatrics, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[n] Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
[o] Institut du Savoir Montfort, Ottawa, Ontario, Canada
[p] Seattle Rheumatology Associates and Division of Rheumatology Research, Swedish Medical Center, Seattle, WA, USA
[q] CREATE Centre, Division of Infection and Immunity, School of Medicine, Cardiff University, Cardiff, UK

ARTICLE INFO

Keywords:
OMERACT
Chronic pain
Measurement
Nociceptive
Nociplastic
Neuropathic

ABSTRACT

Objective: To educate and discuss pain mechanisms (nociceptive, neuropathic, nociplastic) illuminating its possible impact when measuring different outcomes, which may modify, confound and potentially bias the outcome measures applied across various aspects of Rheumatic Musculoskeletal Diseases (RMDs) clinical trials.
Methods: In the plenary presentations, PM lectured on different pain mechanisms and impact on disease activity assessment. Data from two data sets of RMDs patients, which assessed the prevalence and impact of nociplastic pain were presented and reviewed. Audience breakout group sessions and polling were conducted.
Results: Mixed pain etiologies may differentially influence disease activity assessment and therapeutic decision-making. Polling demonstrated a consensus on the need to assess different types of pain as a phenotype, as it constitutes an important contextual factor (a variable that is not an outcome of the trial, but needs to be recognized [and measured] to understand the study results), and to standardize across RMDs.
Conclusion: There is need for a standardized pain measure that can differentiate underlying pain mechanisms.

Introduction

Pain is the most common symptom in Rheumatic Musculoskeletal Diseases (RMDs). Chronic pain reduces physical functioning and mental well-being [1]. Patients rank pain as the most important and dominant symptom [2]. Consequently, pain is an OMERACT core domain for most RMDs [3]. Pain has typically been assessed by either a simple visual analogue scale (VAS) or a numeric rating scale (NRS) gauging pain severity and its impact.

In rheumatoid arthritis (RA), almost 80% of patient global

* Corresponding author.
E-mail address: pickleste@cardiff.ac.uk (T. Pickles).
[1] These authors have contributed equally to senior authorship.

https://doi.org/10.1016/j.semarthrit.2023.152342

Available online 15 December 2023
0049-0172/© 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

assessment is based on pain severity [4]. Despite treatment, many patients state they have clinically significant pain which impacts physical functioning even in those with low disease activity [5,6]. Chronic pain is complex and involves both peripheral and central nervous system mechanisms [7]. Accordingly, pain researchers have categorized three different types of pain; nociceptive, neuropathic, and nociplastic. People can experience these different pain mechanisms individually or together, variably over time.

OMERACT (Outcome Measures in Rheumatology) is a global, volunteer-driven, not for profit organisation committed to improving outcomes for patients with autoimmune and musculoskeletal diseases through advancing the design and quality of clinical studies. OMERACT 2023 took place at the Cheyenne Mountain Resort, Colorado Springs, Colorado, USA between May 1st and 5th, with a wide range of presentations, workshops, and interactive sessions on the topic of outcome measurement in rheumatology. The goal of the OMERACT Chronic Pain Working Group workshop was to acknowledge that pain is complex, and its assessment needs to address the relative role of different pain mechanisms to accurately measure disease activity and optimally guide therapeutic decision-making. Details on the OMERACT Chronic Pain Working Group can be found at https://omeract.org/working-groups/pain/.

Objectives: The objectives of the OMERACT 2023 Chronic Pain Working Group workshop were:

1. to educate OMERACT attendees about the complexity and experience of pain mechanisms in RMDs;
2. to assess the potential need for standardization of pain assessments across these conditions.
3. to review and evaluate the influence of different pain mechanisms on disease activity assessments;
4. to poll attendees about the importance of development of reliable pain measures which address this complexity.

Methods

The OMERACT 2023 Chronic Pain Working Group workshop was held on Thursday 4th of May 2023 in Colorado Springs, Colorado, United States. The workshop included an educational lecture, a breakout group session, and polling. The agenda was planned to describe the importance of understanding pain from the patients' perspective and classification of different forms of human pain phenotypes, including nociceptive, neuropathic, and nociplastic pain, present real-world data sets which distinguish the prevalence and impact of mixed etiology pain experience in RMDs, explore the challenges in assessing and characterizing these different pain phenotypes as a possible contextual factor and discuss methodologies for achieving accurate pain assessments and characterization.

Educational lecture: The educational lecture was initiated by MC, a patient research partner (PRP), presenting a patient's perspective. PM presented an overview of the neurobiology of pain, the differentiation of nociceptive, neuropathic, and nociplastic pain, the definition of fibromyalgia (FM), and the impact of these differing pain mechanisms on disease assessment in RMDs. Two new studies since the last OMERACT Chronic Pain Working Group workshop were presented. PM presented an analysis of psoriatic arthritis (PsA) patients from the CorEvitas registry assessing FM and chronic widespread pain using the American College of Rheumatology 2016 FM questionnaire to determine prevalence of these conditions and their impact on disease activity assessments.

The OMERACT fellow (TP) presented data from a cross-sectional study on chronic pain phenotypes in inflammatory arthritis. Patients with inflammatory arthritis treated at the Rheumatology Department of the University Hospital of Wales, UK, were invited to take part when attending routine outpatient appointments. Pain assessments included Brief Pain Inventory (BPI), Widespread Pain Index (WPI) Symptom Severity Scale (SSS), and painDETECT questionnaires and pressure pain threshold (PPT) was assessed by algometer. The painDETECT questionnaire was used to categorize patients as 'nociceptive, 'unclear' or 'neuropathic' groups. The Health Assessment Questionnaire Disability Index (HAQ-DI) was also collected.

Breakout groups and Polling: Breakout groups discussed four questions and reported at a final plenary session before the questions were polled; all related to the overarching question of whether pain mechanism - as a phenotype - should be perceived as a possible contextual factor in RMDs clinical trials (i.e., a variable that is not an outcome of the study, but needs to be recognized [and measured] to understand the study results). The questions were:

- Do the types of pain affect the sensitivity (the extent of the change) of the instruments that measure the efficacy of a treatment in a RMDs clinical trial?
- Do the types of pain affect the validity (truth) of the instruments (e.g., tender and swollen joint counts, pain Severity, pain Interference and remission)?
- Do we need to assess and/or select patients by the types of pain in RMDs clinical trials?
- Do you believe using a single pain measurement scale (e.g., NRS or VAS) is sufficient to assess nociceptive, neuropathic, and nociplastic pain, or should we combine general pain intensity scales with more specific and multidimensional assessment tools for a comprehensive evaluation?

Results

MC, a PRP, emphasized the individualized nature of the patient's pain experience. Each patient brings their own unique state to the disease experience: age, gender, immunobiologic, psychologic, sociocultural, and disease activity, all of which influence pain severity and interference.

PM provided an overview of pain neurobiology and classification. The International Association for the Study of Pain (IASP) classifies three types of pain; nociceptive, neuropathic, and nociplastic, which may present in a mixed fashion [8]. Pain cannot be inferred solely from activity in sensory neurons. This is particularly relevant in patients with RMDs as healthcare professionals often assume that pain arises only from sites of disease.

Nociceptive pain is a common form of pain arising from tissue damage or inflammation. Examples include the pain signalling arising from active synovitis in RA patients or mechanical irritation in osteoarthritis (OA). A common measure of this type of pain is a VAS or NRS scale of pain severity.

Neuropathic pain represents damage or dysfunction of nerve tissue. This type of pain is often described as burning, shooting, or tingling. Examples of neuropathic pain include diabetic neuropathy and carpal tunnel syndrome. A commonly used tool to screen for neuropathic pain is the multi-question painDETECT questionnaire [9].

Nociplastic pain is defined as 'pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain' [10]. This replaces the term 'central sensitization' or 'central pain' in which severity of pain is attributed to amplification of neural signalling within the central nervous system. The pain aspect of FM is typically nociplastic [11]. FM is common and affects 2-8% of the general population [12]. Patients with FM often report chronic widespread pain, fatigue, non-refreshed sleep and cognitive impairment (i.e., brain fog). In patients with inflammatory arthritis, including RA, PsA and axial spondyloarthritis (axSpA), 10-25% of patients have concomitant FM [13,14]. When FM coexists with RMDs, patients demonstrate higher disease activity scores. This finding has been highlighted by the European Alliance of Associations for Rheumatology (EULAR) as a factor that is associated

with difficult to treat RA, as patients may have pain but little inflammation [15]. EULAR has published management recommendations for FM [16]. The potential mechanisms whereby patients with RA develop FM have been reviewed [17]. The prevalence and impact of FM on disease activity assessment in the spondyloarthritides, including PsA, have been similarly reviewed [14]. A variety of validated questionnaires to assess nociplastic pain and FM were described, including the WPI and SSS, which together constitute the 2016 American College of Rheumatology criteria for FM, the FiRST questionnaire, and the Central Sensitization Inventory.

RMDs patients often experience a combination of nociceptive, neuropathic, and nociplastic pain, all of which contribute to pain severity and interference (Fig. 1). The complexity of assessing different forms of pain in RMDs patients lies in the diverse and often overlapping nature of their pain experiences. When attempting to achieve a state of remission or low disease activity, if FM is present and confounds the ability to accurately assess disease activity, inappropriate therapeutic decision-making may occur. Accurate and reliable characterization of these complex pain types is crucial for tailoring appropriate treatment strategies and improving patient outcomes. However, using a simple methodology to assess this complexity can be challenging.

PM presented a study which analyzed 1823 PsA patients in the CorEvitas PsA/axSpA registry. All patients were administered the American College of Rheumatology 2016 WPI and SSS. The two measures are used together, and high scores denote the presence of FM. High scores on the WPI denote the presence of Widespread Pain (WP). FM was noted in 11.2% and WP in 13.4%. Patients with FM had twice as severe disease activity scores: cDAPSA, patient global, patient pain, and tender joint counts.

The fellow (TP) presented a study to characterize chronic pain phenotypes in inflammatory arthritis. 166 patients (53 RA and 113 PsA) were recruited. 54.8% were female. Their mean age was 53.8 (SD 15.54) and mean disease duration was 12.3 years (SD 11.09). 47 patients (28.3%) fulfilled the ACR2010 criteria for FM. Patients with concomitant FM, had higher BPI Severity (7.4 vs 2.0, $p<0.001$) and BPI Interference scores (6.8 vs 3.0, $p<0.001$). They were more likely to be classified as having neuropathic-like pain by the painDECTECT questionnaire (75%). There was no statistically significant difference in PPT. BPI Severity correlated highly with BPI Interference ($\rho = 0.833$; Table 1). Correlations between BPI Severity and Interference with WPI and SSS were moderate ($0.579 \leq \rho \leq 0.744$), with low correlations with PPT.

Breakout Groups: PRPs (between three and five in each breakout group) shared their experiences of suffering from chronic pain. Pain varied from day-to-day in intensity and was experienced in different ways. Chronic low-grade pain is what many have learned to live with but may experience flare that can be debilitating and stressful. Most did not realize there are different types of pain, although some PRPs with two or more diseases, such as RA and osteoarthritis, felt they could distinguish pain from each. Many PRPs felt the information in the educational lecture was helpful and supported developing better ways of assessing different types of pain in RMDs clinical trials.

Polling: The final plenary session polling results (Table 2) showed that more than 80% of the attendees agreed that different types of pain can affect the validity and sensitivity of the instruments that are used to assess treatment effect. Among those who voted (23.5% were PRPs), it was felt that stratification of patients, based on pain phenotype, in RMDs clinical trials would be desirable. For assessing pain, only a few attendees (4%) felt a single pain measurement scale is sufficient to assess nociceptive, neuropathic, and nociplastic pain and many felt combining general pain severity scales with specific and multidimensional assessment tools is desirable (60%). The remaining 36% of attendees felt there was insufficient information to understand and answer the question.

Discussion

The key goals of the OMERACT 2023 Chronic Pain Working Group workshop were to educate OMERACT attendees about the complexity of pain mechanisms and experience in RMDs, address the need for standardization of pain assessment across RMDs, demonstrate the influence of different pain mechanisms on assessments of disease activity, and poll attendees about the importance of development of reliable pain measures which address this complexity.

It was agreed that pain is a cardinal feature of RMDs, impacting function and quality of life. The neurobiology of chronic pain is complex involving both peripheral and central nociception, influenced by genetic and environmental/socio-cultural factors. Concomitant nociplastic pain/FM influences assessment and outcomes and should be considered in shared decision making about treatment. Although pain is complex and may need a complex instrument to capture its full dimensions, a standardized approach across all RMDs may be feasible and desirable.

There was a consensus on the need to improve assessment of pain as a standalone phenotype since it potentially could represent an important contextual factor that can either: (i) effect modify the endpoint of a RMDs clinical trial, (ii) be outcome influencing in cohorts, or (iii) impact (distort or bias) the measurement properties of the core outcome measures [18]. Attendees agreed that different types of pain could affect response to treatment e.g., nociplastic pain not responding to advanced immunomodulatory medications. Therefore, different types of pain can affect the validity and sensitivity to change of current instruments used to assess disease activity. The future objective of the OMERACT Chronic Pain Working Group will be to systematically review the available instruments and determine their ability to assess different types of pain in patients with RMDs in line with the OMERACT Filter 2.2 methodology [19,20,21,22]. If necessary, the OMERACT Chronic Pain Working Group will look to develop a pain assessment instrument, or instruments, to

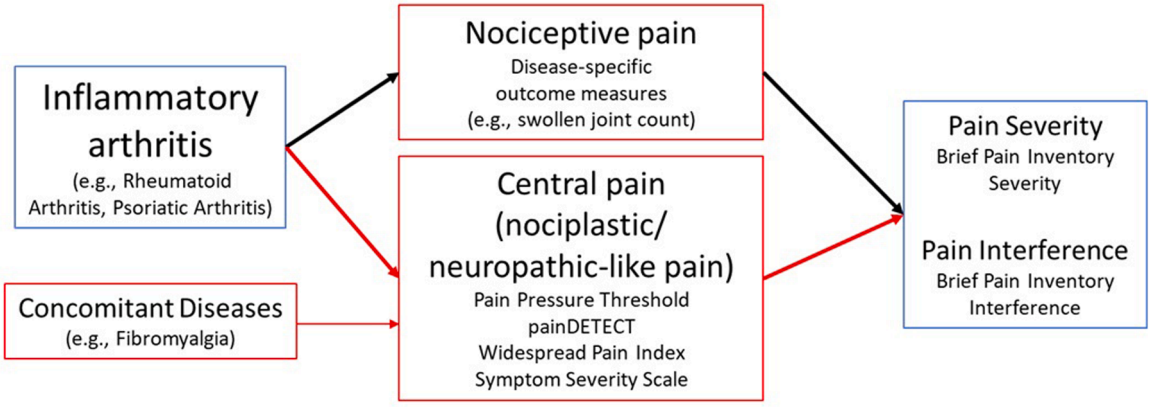

Fig. 1. Nociceptive, neuropathic, and nociplastic pain contribution to pain severity and interference.

Table 1
Spearman's correlation coefficients between different pain measures.

	HAQ-DI	painDETECT	BPI Severity	BPI Interference	Widespread Pain Index	Symptom Severity Scale
painDETECT	0.608					
BPI Severity	0.700	0.556				
BPI Interference	0.783	0.653	0.833			
Widespread Pain Index	0.551	0.508	0.579	0.593		
Symptom Severity Score	0.672	0.643	0.621	0.744	0.551	
Pressure Pain Threshold	-0.330	-0.246	-0.317	-0.247	-0.227	-0.219

HAQ-DI: health assessment questionnaire disability index
BPI: brief pain inventory

Table 2
Results of Polling.

Poll questions		All	PRPs
Do the types of pain affect the sensitivity (the extent of the change) of the instruments that measure the efficacy of a treatment in a clinical trial?	Yes	63 (97%)	16 (100%)
	No	2 (3%)	0 (0%)
Do the types of pain affect the validity (truth) of the instruments (e.g., tender and swollen joint count, pain Severity, pain Interference and remission)?	Yes	58 (85%)	13 (81%)
	No	10 (15%)	3 (19%)
Do we need to assess and/or select patients by the types of pain in clinical trials?	Yes	57 (89%)	15 (94%)
	No	7 (11%)	1 (6%)
Do you believe using a single pain measurement scale (e.g., NRS or VAS) is sufficient to assess nociceptive, neuropathic, and nociplastic pain, or should we combine general pain intensity scales with more specific and multidimensional assessment tools for a comprehensive evaluation?	Yes	3 (4%)	0 (0%)
	Combine general pain intensity scales with specific and multidimensional assessment tools	40 (60%)	12 (75%)
	Insufficient information to understand	24 (36%)	4 (25%)

PRP: patient research partner.

assess different types of pain in patients with RMDs.

Funding

The Parker Institute is grateful for the financial support received from public and private foundations, companies, and private individuals over the years. The Parker Institute, Bispebjerg and Frederiksberg Hospital is supported by a core grant from the Oak Foundation (OCAY-18–774-OFIL).

CRediT authorship contribution statement

Tim Pickles: Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Mary Cowern:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Robin Christensen:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Sabrina M. Nielsen:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Lee S. Simon:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Caitlin M.P. Jones:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Lara J. Maxwell:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Beverley Shea:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Vibeke Strand:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Zahi Touma:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Karine Toupin-April:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Philip Mease:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing. **Ernest Choy:** Conceptualization, Formal analysis, Investigation, Project administration, Software, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Mary Cowern

Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid - Leadership role - Head of Nations at Versus Arthritis - Paid role

Lee S Simon

Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid - Chair of OMERACT Finance Committee

Caitlin M P Jones

Grants or contracts from any entity - Awarded seed funding grants for unrelated projects from Arthritis Australia, ANZBACK and Wiser healthcare

Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events - Contractor to OMERACT for casual research work (not related to this project)

Support for attending meetings and/or travel - OMERACT supported me to attend OMERACT 2023 in Colorado USA (economy class flights, accommodation and conference registration)

Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid - Member of the ANZMUSC ECR committee, Member of the Sydney University School of Public Health EMCR committee

Lara J Maxwell

Other financial or non-financial interests - LJM is a paid staff member of OMERACT

Beverley Shea

Other financial or non-financial interests - OMERACT Senior Methodologist

Vibeke Strand

All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) - I am a founding member of the executive committee of Outcome Measures in Rheumatology (OMERACT) [1992 – present], an international consensus organization that develops and validates outcome measures in rheumatology randomized controlled trials and longitudinal observational studies and has received arms-length funding from as many as 36 sponsors.

Grants or contracts from any entity - I am a founding member of the executive committee of Outcome Measures in Rheumatology (OMERACT) [1992 – present], an international consensus organization that develops and validates outcome measures in rheumatology randomized controlled trials and longitudinal observational studies and has received arms-length funding from as many as 36 sponsors.

Karine Toupin-April

Support for attending meetings and/or travel - OMERACT travel award given to the Shared decision making group to help attend the OMERACT 2023 meeting

Philip Mease

Grants or contracts from any entity - Acelyrin, Amgen, Bristol Myers Squib, Eli Lilly, Janssen, Novartis,

Pfizer, UCB

Consulting fees - Acelyrin, Aclaris, Amgen, Bristol Myers Squib, CorEvitas, Eli Lilly, Inmagene, Janssen, Moonlake Pharma, Novartis, Pfizer, UCB, Ventyx

Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events - Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB

Participation on a Data Safety Monitoring Board or Advisory Board - Genascence – DSMB

Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid - Group for Research and Assessment of Psoriasis and Psoriatic Arthritis – Executive board, Spondyloarthritis Research and Therapy Network

Ernest Choy

Grants or contracts from any entity - Bio-Cancer, Biogen, Novartis, Pfizer, Sanofi

Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events - Abbvie, Amgen, Asofarma, Biogen, Bristol Myer Squibbs, Chugai Pharma, Eli Lilly, Fresenius Kabi, Galapagos, Janssen, Novartis, Pfizer, Sanofi, UCB

Support for attending meetings and/or travel - Galapagos, Janssen, UCB

Stock or stock options – Inmedix

Receipt of equipment, materials, drugs, medical writing, gifts or other services - Inmedix

References

[1] Hadi MA, McHugh GA, Closs SJ. Impact of chronic pain on patients' quality of life: a comparative mixed-methods study. J Patient Exp 2019;6(2):133–41.

[2] Heiberg T, Finset A, Uhlig T, Kvien TK. Seven year changes in health status and priorities for improvement of health in patients with rheumatoid arthritis. Ann Rheum Dis 2005;64(2):191–5.

[3] Beaton DE, Boers M, Tugwell P, Ch ML. Assessment of health outcomes. Firestein & Kelley's textbook of rheumatology, 36. Elsevier, Inc.; 2021. Eleventh Edition.

[4] Studenic P, Radner H, Smolen JS, Aletaha D. Discrepancies between patients and physicians in their perceptions of rheumatoid arthritis disease activity. Arthritis Rheum 2012;64(9):2814–23.

[5] Lee YC, Cui J, Lu B, Frits ML, Iannaccone CK, Shadick NA, et al. Pain persists in DAS28 rheumatoid arthritis remission but not in ACR/EULAR remission: a longitudinal observational study. Arthritis Res Ther 2011;13(3):R83.

[6] Ferreira RJO, Dougados M, Kirwan JR, Duarte C, de Wit M, Soubrier M, et al. CoimbRA investigators, RAID investigators and COMEDRA investigators. Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients. Rheumatology 2017;56(9):1573–8. Oxford.

[7] Crofford LJ. Chronic pain: where the body meets the brain. Trans Am Clin Climatol Assoc 2015;126:167–83.

[8] Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain 2020;161(9):1976–82.

[9] Rifbjerg-Madsen S, Christensen AW, Boesen M, Christensen R, Danneskiold-Samsøe B, Bliddal H, et al. The course of pain hypersensitivity according to painDETECT in patients with rheumatoid arthritis initiating treatment: results from the prospective FRAME-cohort study. Arthritis Res Ther 2018;20(1):105.

[10] Nijs J, Lahousse A, Kapreli E, Bilika P, Saraçoğlu İ, Malfliet A, et al. Nociplastic pain criteria or recognition of central sensitization? pain phenotyping in the past, present and future. J Clin Med 2021;10(15):3203.

[11] Fitzcharles MA, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Häuser W. Nociplastic pain: towards an understanding of prevalent pain conditions. Lancet 2021;397 (10289):2098–110.

[12] Clauw DJ. Fibromyalgia: a clinical review. JAMA 2014;311(15):1547–55.

[13] Duffield SJ, Miller N, Zhao S, Goodson NJ. Concomitant fibromyalgia complicating chronic inflammatory arthritis: a systematic review and meta-analysis. Rheumatology 2018;57:1453–60.

[14] Mease PJ. Fibromyalgia, a missed comorbidity in spondyloarthritis: prevalence and impact on assessment and treatment. Curr Opin Rheumatol 2017;29(4):304–10.

[15] Nagy G, Roodenrijs NMT, Welsing PMJ, Kedves M, Hamar A, van der Goes MC, et al. EULAR points to consider for the management of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis 2022;81(1):20–33.

[16] Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76(2):318–28.

[17] Das D, Choy E. Non-inflammatory pain in inflammatory arthritis. Rheumatology 2023;62(7):2360–5. Oxford.

[18] Nielsen SM, Tugwell P, de Wit MPT, Boers M, Beaton DE, Woodworth TG, et al. Contextual factors working group. identifying provisional generic contextual factor domains for clinical trials in rheumatology: results from an OMERACT initiative. J Rheumatol 2019;46(9):1159–63.

[19] Boers M, Beaton DE, Shea BJ, Maxwell LJ, Bartlett SJ, et al. OMERACT filter 2.1: elaboration of the conceptual framework for outcome measurement in health intervention studies. J Rheumatol 2019;46(8):1021–7.

[20] Maxwell LJ, Beaton DE, Shea BJ, Wells GA, Boers M, Grosskleg S, et al. Core domain set selection according to OMERACT filter 2.1: the OMERACT methodology. J Rheumatol 2019;46(8):1014–20.

[21] Maxwell LJ, Beaton DE, Boers M, D'Agostino MA, Conaghan PG, Grosskleg S, et al. The evolution of instrument selection for inclusion in core outcome sets at OMERACT: Filter 2.2. Semin Arthritis Rheum 2021;51(6):1320–30.

[22] Beaton D., Maxwell L., Grosskleg S., Shea B., Tugwell B. (editors). Chapter 5. Instrument selection for core outcome sets. The OMERACT Handbook, version 2.1 updated April 1st 2021; Available from: https://omeract.org/handbook/.