

Report from the OMERACT Hand Osteoarthritis Special Interest Group: Advances and Future Research Priorities

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ABSTRACT. Osteoarthritis (OA) is one of the most common musculoskeletal disorders, frequently affecting the hands. In the last decade there has been increased awareness concerning this disorder because of its clinical burden. Unfortunately, only limited treatments for symptom alleviation are available, and no effective treatment for disease modification exists. The lack of treatment is due not only to a lack of understanding of the disease process, but also to poor outcome measures to assess the condition. The OMERACT Hand OA Special Interest Group (SIG) has started to develop a core set of outcome measures for hand OA clinical trials, observational studies, and clinical record keeping. At OMERACT 11, results from a Delphi exercise were presented, and a preliminary set of core domains was discussed. The group attempted to adopt the new OMERACT Filter 2.0 in the process, and literature overviews of conventional radiographs, ultrasonography, and magnetic resonance imaging as outcome measures in hand OA were presented. Discussions that followed highlighted further suggestions for core domains, the heterogeneity of hand OA, and future research priorities. (First Release Jan 15 2014; J Rheumatol 2014;41:810–18; doi:10.3899/jrheum.131253)

Key Indexing Terms:

OUTCOME AND PROCESS ASSESSMENT

OSTEOARTHRITIS

HAND

Hand osteoarthritis (OA) is highly prevalent^{1,2,3,4}. It was long a “forgotten disease,” but during the last decade awareness has increased⁵. OA is characterized by bony enlargements and deformities⁶ and leads to symptoms such as pain or aching, stiffness, loss of mobility, decreased grip strength, esthetic damage, and disability, resulting in a considerable clinical burden with diminished quality of life (QOL)^{7,8,9,10,11,12}. Although progression in hand OA is considered a fairly slow process, deterioration of pain and disability occurs in around 50% of individuals with hand OA over 3 to 8 years^{13,14}, and radiographic progression can already be seen after 18 to 24 months of followup¹⁵. Unfortunately, its pathophysiology is incompletely understood. Currently, treatment modalities for hand OA are limited^{16,17}. Few clinical trials in hand OA have been performed, and these are generally of low quality^{18,19}. The

aim of treatment is the alleviation of symptoms, but the efficacy of different treatments is only low to moderate¹⁶. Moreover, no structure-modifying treatments exist. Therefore, recommendations for treatment of hand OA are mainly based on expert opinion¹⁶. This lack of high-quality trials not only has to do with the poor understanding of underlying disease processes — which is also the case for knee and hip OA — but is especially due to poor outcome measures preventing adequate assessment of hand OA^{18,19}.

The Outcome Measures in Rheumatology (OMERACT) Hand OA Special Interest Group (SIG) comprises health professionals and researchers with interest and experience in hand OA, whose aim is to identify a preliminary set of core domains using the OMERACT framework. A core set is the minimum number of domains and instruments needed to describe outcomes in clinical trials or clinical practice²⁰. Currently, domains are identified for phase III clinical trials following the OMERACT 3 consensus conference, which did not address hand OA specifically. Four core domains have been identified: pain, (physical) function, patient global assessment, and imaging²¹. An Osteoarthritis Research Society International (OARSI) task force for the design and conduct of clinical trials in hand OA added the following domains: mobility, deformity, inflammation, performance, stiffness, and esthetic damage²². However, the existing set of core domains has several shortcomings. Only the clinical trial setting was addressed, and in the selection process patients were not involved. Moreover, the core sets

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insufficiently incorporated the specific aspects of hand OA, such as the simultaneous involvement of multiple hand joints^{23,24,25}, and its heterogenic character. Hand OA comprises several subsets, such as interphalangeal OA, thumb base OA, and erosive and inflammatory OA^{6,15}, with different symptoms and causal underlying factors, requiring different treatments. Further, the expression of symptoms is heterogeneous between patients and depends on the setting. Symptomatic patients collected from the general population do not report a decreased health-related QOL²⁶, while patients in secondary care do^{11,12,27}. Moreover, hand OA often co-occurs with OA at other joint sites (generalized OA)⁶. These issues require careful consideration of the potential setting in which the domains will be used and of the contextual factors (e.g., 1 vs many joints, rating of pain from OA in someone with generalized OA, etc.).

Imaging modalities play an increasingly important role in clinical trials and clinical practice to assess structural progression and to investigate underlying disease processes. Currently, radiographs are used mainly for this purpose. However, symptoms are not associated with structural abnormalities as depicted by radiographs²⁸. This also holds true for changes over time: no association was seen between symptomatic and radiographic progression²⁹. The dissociation between patient complaints and outcome measures underlines the need for validated outcome measures making use of new imaging methods such as ultrasound (US) or magnetic resonance imaging (MRI).

The aim of the OMERACT 11 Hand OA SIG was therefore to develop preliminary core sets of outcome measures for 4 different settings: clinical trials aiming at symptom modification, clinical trials aiming at structure modification, observational studies, and clinical record keeping.

METHODS

Literature Overviews. Literature overviews were initiated to identify available instruments: patient-reported outcomes (PRO), radiography, US, and MRI.

Delphi Exercise

A Delphi exercise of 2 rounds of voting was performed prior to the OMERACT 11 meeting. The aim was to reach consensus about the domains that should be considered either as mandatory or as optional to assess the disease course in hand OA. This was done for 4 different settings: clinical trials in hand OA investigating symptom modification, clinical trials in hand OA investigating structure modification, observational studies, and clinical record keeping.

Briefly, in round 1 of the Delphi exercise an initial list of 22 potential domains was circulated to experts in the field of hand OA, including healthcare providers and researchers experienced with OMERACT. The list of potential domains was obtained from a recent qualitative study among patients with hand OA³⁰, thus incorporating the patient perspective, extending it with potential domains previously identified as important for hand OA. Participants were explicitly encouraged to include additional domains, which were considered missing during the first Delphi round. Participants were asked to divide 100 points among the domains they considered important. In Delphi round 2 a list of domains, with the average

score assigned in the first round, were distributed. Domains with high agreement (more than an average of 10 points) were included; domains with low agreement (less than an average score of 3 points) were excluded. Invitees were again asked to divide 100 points among the remaining domains that were considered very important. At the OMERACT 11 meeting, the results of the Delphi rounds were presented and discussed.

RESULTS

Literature Reviews

There has been no selection of instruments per domain of the selected core sets. Although several instruments are available, it is at the present time impossible to recommend the use of one instrument over another²². The most often-used instruments are described below.

Clinical activity and PRO measures. In hand OA, several specific PRO measures have been developed and validated. The Functional Index of Hand OA was the first PRO measure validated for use in patients with hand OA³¹. The Australian Canadian Hand OA Index (AUSCAN) is another hand OA-specific PRO measure addressing pain, stiffness, and difficulties with daily activities³². The score for assessment and quantification of chronic rheumatic affections of the hands (SACRAH) was developed to assess patient-reported pain, stiffness, and physical function in rheumatoid arthritis (RA) and hand OA³³. The Michigan Hand Outcomes Questionnaire, an instrument developed to measure health state domains important to patients with hand disorders, has also been used in hand OA trials^{34,35,36}.

Arthritis-specific PRO measures have also been applied in hand OA trials. The Arthritis Impact Measurement Scales 2 is a multidimensional instrument initially developed for RA that has also been used for assessing function in hand OA³⁷. As an overall measure of physical function in RA, the Health Assessment Questionnaire and its modification have also been applied in hand OA^{38,39}.

Generic measures are also applied in hand OA trials; they include multidimensional health status questionnaires such as the Medical Outcome Study Short Form 36 Survey (SF-36) and visual analog scales (VAS). The SF-36 is the most commonly used generic health status questionnaire and measures 8 dimensions of health⁴⁰. The SF-36 has also been converted into a utility score: the Short Form-6D, based on 6 dimensions of health⁴¹. VAS is commonly used to assess the overall effect of hand OA, with joint pain, fatigue, and patient global assessment as the anchoring points.

For evaluation of performance, grip-strength measurement is often used⁴². The Doyle Index is a measurement of tenderness by palpation of the hand joints and is validated for use in hand OA⁴³.

Imaging. There are few clinical trials investigating structure modification in hand OA. More studies have been performed in knee and hip OA, and joint space narrowing on conventional radiography (CR) as reflection of cartilage loss was the outcome measure most frequently used in clinical

trials. Nonetheless, the role of CR measures of joint space width has been debated because of its variable association to PRO measures such as pain and the importance of joint positioning⁴⁴.

Studies have revealed that joint inflammation is frequent in hand OA, although the role of synovitis in the pathophysiology of OA is still not well understood⁴⁵. The hypothesis concerning the potential effect of an inflammatory component in OA is strengthened by a study showing an association between US-detected inflammation and patient-reported pain in patients with hand OA⁴⁶. To investigate new, effective treatments for hand OA in clinical trials, we need to define outcome measures that can be assessed by valid, reliable, responsive, and feasible instruments.

Outcome measures for conventional radiography. CR is used mostly to assess structural damage in hand OA, because it is widely available, cheap, and reproducible. Radiography allows visualization of osteophytes, joint space narrowing (JSN), subchondral cysts, sclerosis, and central erosions (bone damage).

Several standardized scoring systems are available such as the Kellgren-Lawrence (KL)⁴⁷, Kessler⁴⁸, and Kallman grading scales⁴⁹, the OARSI scoring atlas^{50,51}, and the Verbruggen-Veys anatomical phase score (VV)⁵². Table 1 provides a summary of the joints and type of scores applied as well as the ranges of the scoring methods.

The KL grading scale is a global score where osteophytes are required to define OA. Joints are graded 0–4, as described in the atlas (0 = no OA; 1 = doubtful OA; 2 = definite minimal OA; 3 = moderate OA; 4 = severe OA). Kessler, *et al* suggested a global hand scale for OA, where JSN is crucial in defining OA. Osteophytes and sclerosis are less important, unless seen in conjunction with JSN. Joints are scored dichotomously for the presence of OA. The Kallmann Radiographic Scale grades 6 individual features: osteophytes (range 0–3), JSN (range 0–3), subchondral sclerosis (range 0–1), subchondral cysts (range 0–1), lateral deformity ($\geq 15^\circ$; range 0–1), and collapse of central joint cortical bone (range 0–1). Distal interphalangeal joints (DIP), proximal interphalangeal (PIP), and first IP are

assessed for all of these features. First carpometacarpal (CMC) is scored for all but cortical collapse and trapezioscapoid joint is scored for JSN, subcondral sclerosis, and cysts. The OARSI atlas grades individual radiographic features as well. Osteophytes and JSN (range 0–3), and subchondral erosions, sclerosis, and malalignment (range 0–1) are assessed in the DIP, PIP, first IP-1, and first CMC. Pseudowidening (range 0–1) is assessed in the DIP joints, and cysts (range 0–1) are assessed in the PIP and first CMC joints. The VV anatomical phase score comprises 5 phases with a numerical value representing the evolution of erosive hand OA: N phase = normal joint; S phase = stationary OA with osteophytes and JSN; J phase = complete loss of joint space in the whole or part of the joint; E phase = subchondral erosion; R phase = remodeling of subchondral plate. In addition to the VV score, the Ghent University Scoring System (GUSS) focuses on progression in erosive IP OA. Within the J, E, and R phases of the VV score, changes in proportions of the subchondral bone showing osteolytic areas, the relative amount of the resorbed subchondral bony plate and the disappearance of the normal joint space are graded on an 11-point rating scale (range 0–100 with 10 unit increases)⁵³.

Studies have shown that the KL, Kallman, OARSI, and VV systems are reliable instruments for the assessment of hand OA structural damage^{54,55}. Regarding the ability to measure change of structural OA damage, the GUSS has been shown to be a reliable and sensitive method⁵³. Further, 2 comparative studies showed that KL, VV, and the OARSI scoring systems were reliable and sensitive to change over a 2-year period⁵⁴, and Kallman and VV scores were sensitive to change already over a 1-year period⁵⁵.

However, the knowledge of associations between PRO measures and radiological findings is still limited^{29,56}. Current results show poor association between CR pathologies and PRO measures and warrant further study, especially addressing assessment of followup.

Outcome measures for ultrasonography. US enables a dynamic image of the joints without radiation and allows visualization not only of osteophytes, but also marginal erosions and synovitis. Demonstration of the articular

Table 1. Radiographic scoring systems for hand osteoarthritis.

Scoring Method	No. of Joints	DIP	PIP	1st IP	MCP	1st CMC	TS	Type of Score	Range of Total Score
Kellgren-Lawrence	30	+	+	+	+	+	–	Global	0–120
Kessler	18	+	+	–	–	+	–	Global	0–16
Kallman	22	+	+	+	–	+	+	Individual features	0–208
OARSI	20	+	+	+	–	+	–	Individual features	0–198
Verbruggen-Veys	28	+	+	+	+	+	–	Anatomical phases	0–218.4
GUSS	18	+	+	+	–	–	–	Progression erosions	10–300

DIP: distal interphalangeal joint; PIP: proximal interphalangeal joint; IP: interphalangeal joint; MCP: metacarpophalangeal joint; CMC: carpometacarpal joint; TS: trapezioscapoid joint; GUSS: Ghent University Scoring System; OARSI: Osteoarthritis Research Society International.

cartilage and bone damage is mostly restricted to the peripheral parts of the joint⁵⁷, because of the acoustic window, although studies have shown reliable assessment of articular cartilage in the PIP and metacarpophalangeal (MCP)⁵⁸. Large overlying osteophytes disturbing the acoustic window may complicate the joint evaluation.

Most US studies of patients with hand OA have reported high prevalence of greyscale synovitis^{59,60,61,62}, while power Doppler activity is less frequently seen^{59,61,62}. However, some studies have demonstrated similar prevalence^{60,63} of these 2 features. This variation across studies may be due to differences in study populations or US techniques. A comparative study of hand OA patients and healthy controls found that effusion and power Doppler activity, but not greyscale synovitis, were more common in the patients with hand OA⁶⁴. Higher power Doppler activity, synovial hypertrophy, and joint effusion have been found in patients with radiographic erosive OA joints compared with patients with radiographic nonerosive OA⁶³. Synovitis seems to be most prevalent in joints with active erosions, while the prevalence is lower in joints that are remodeled⁶⁵. One preliminary US scoring system has been developed for hand OA including assessment of synovitis (greyscale hypertrophy/effusion and power Doppler) and osteophytes on semiquantitative scales⁶⁶. Lately, a US atlas for assessment of osteophytes was proposed, and the authors found excellent intra- and inter-reader reliability for evaluation of osteophytes using the proposed atlas⁶⁷.

Erosions, cartilage assessment, or JSN were not included in the scoring system owing to concerns about reliable definitions, acquisition, current available US technology, and feasibility related to duration of scanning. Divergent reliability results of the proposed scoring system were found in a large reliability exercise, but the system was considered as a good basis for further development of an US outcome tool⁶⁶.

The first report comparing US and CR found that CR was more sensitive than US in detection of erosions⁶⁸. However, later reports have shown that US is more sensitive in detection of erosions^{60,69}, as well as osteophytes and JSN^{60,69,70}. Estimation of JSN by US may be problematic because only the peripheral inter-bone distance can be documented, and overlying osteophytes may further disturb the acoustic window⁷⁰. However, significant associations have been found between US-defined cartilage thickness (quantitative scale) and radiographic severity, radiographic JSN (semiquantitative scale), and radiographic JSW (quantitative scale)^{58,63}. So far, few studies have compared the findings by US and MRI, but the current results support the use of US as a valid instrument^{69,71}. Wittoek, *et al* found good agreement for both structural features and inflammation⁶⁹.

Several studies have reported that US pathological features such as greyscale synovitis, power Doppler signal,

and osteophytes are significantly associated with pain in the same joint^{59,62,72}. However, studies are less likely to show significant associations to pain, stiffness, or physical disabilities when the analyses are performed on patient level instead of individual joint level^{59,62,73}.

Currently, we have very limited knowledge about US findings over time in hand OA.

Outcome measures for magnetic resonance imaging (MRI). MRI provides a multiplanar image of all joint components including structural features such as osteophytes, cartilage, erosions/cysts, malalignment, collateral ligaments, and inflammatory features such as synovitis and tenosynovitis. MRI is the only imaging modality that is able to show bone marrow lesions (BML). Tan, *et al* imaged OA using high-resolution MRI and showed that virtually all structures were affected in both chronic and early OA⁷⁴. BML, erosions, and synovitis were common features in this small study. Remarkably, collateral ligament abnormalities were universal in both chronic and early disease, and they demonstrated close anatomic relation between ligaments and erosions, BML, and bone formation. However, it should be noted that collateral ligament pathology was also frequent in the elderly controls, and whether these changes are only age-related or play a role in the pathogenesis of the disease is currently not clear.

The prevalence of MRI pathology in patients with hand OA has been investigated in several cohorts^{69,75,76}. All studies demonstrated high prevalence of synovitis based on enhancement of gadolinium^{69,75,76}. The frequency of BML varied across studies, possibly as a result of differences between study participants, as well as differences in field strength and resolution of the MRI scanners. Patients with radiographic erosive hand OA usually demonstrated more joint pathology compared to those with nonerosive hand OA, and MRI-defined erosions, synovitis, and BML were more frequent in patients with radiographic erosive disease than in patients with radiographic nonerosive disease⁶⁹. Haugen, *et al* proposed a preliminary MRI scoring system with an accompanying atlas for hand OA, which includes assessment of osteophytes, JSN, erosions, cysts, malalignment, synovitis, flexor tenosynovitis, BML, collateral ligament pathology such as absence/discontinuity, and BML at insertion sites⁷⁷. The score was developed for the IP joints and showed good intra- and inter-reader reliability. Future studies must confirm whether the score can be applied for MCP and first CMC. Good reliability of the scoring system has also been confirmed in another cohort⁷⁵.

Currently we have limited knowledge about the validity of MRI features in hand OA against histology^{78,79}, or computed tomography, and future studies are needed. Grainger, *et al* have reported that high-resolution MRI was more sensitive than CR in detection of erosions⁸⁰. These findings have later been confirmed by studies using conventional MRI^{69,75,76}. MRI was able to visualize more joints

with erosions in patients with radiographic erosive hand OA, but was also able to detect joints with erosions in patients with radiographic nonerosive disease. MRI is also more sensitive than CR in detecting osteophytes^{75,76}, which is probably due to the multiplanar demonstration of the joint, but the results are not consistent across all studies.

We have limited knowledge about the association between MRI features and symptoms. Haugen, *et al* found that synovitis, BML, and bone damage were associated with tenderness in the same joint⁸¹, and the results were confirmed by Kwok, *et al*⁷⁵. The associations between MRI features and disability were inconsistent and weak⁸¹.

Delphi Exercise

Forty-eight experts on hand OA were invited for voting (participation rate 65% in first round and 62% in the second round). Of the invited OMERACT experts, 7 responded in the first round and 3 in the second round. Because the number of OMERACT experts was far lower than the number of hand OA experts, the calculations were based on the voting of the hand OA experts only. Comments and proposals of OMERACT experts have been included.

In the first round, the participants proposed new domains: for the setting clinical trials investigating symptom modification 6, clinical trials investigating structure modification 3, clinical record keeping 8, and observational studies 8. Further, proposals were prepared for instruments (standardized questionnaires, imaging procedures, scoring methods), trial design (treatments, adverse events), and contextual factors (such as demographics, smoking, hypermobility, association between seasonal temperature and symptoms, handedness, history, duration of symptoms, erosive disease, thumb base OA vs interphalangeal OA).

In Delphi round 1 the domains pain and physical function got an average score of more than 10 points for all settings and were included after the first round. The domain structural damage got an average score of more than 10 points for the setting clinical trials aiming at structure modification and observational studies, and were therefore also included after the first round.

In the second round comments were given on instruments, contextual factors (such as various hand OA subsets, generalized OA, occupation, ethnicity, leisure activities) and on the potential overlap between domains. Potential domains that got more than an average of 10 points were included in the final list. Patient global assessment was included for all settings. Several domains were included for different settings as is shown in Table 2.

Discussions and development of the preliminary core set for outcome measures. The results of the Delphi exercise were openly discussed during OMERACT 11 in the SIG. Around 30 to 40 health professionals with expertise in clinical care for patients with hand OA, hand OA researchers, OMERACT experts, and patient experts, including a patient with hand OA, have attended the meeting. Pain, physical function, and patient global were included domains for all study settings. Although patient global was included as a core domain, it was felt that the patient perspective was not sufficiently taken into account. Therefore efforts should be made to improve this. There was an overlap between proposed domains, which could have influenced the results. The suggestion was made to pool similar domains. Therefore, different measures of structural damage, being bony joint swellings, esthetic damage, and deformity, were combined into 1 domain, whereas tender and swollen joint were combined into another domain, joint activity. The final proposal for core domains in hand OA is presented in Figure 1.

Table 2. The average score (maximal 100 points) for the endorsed potential core domains for hand osteoarthritis in 4 settings after Delphi exercise 1 and 2.

	Clinical Trials			
	Symptom Modification	Structural Modification	Clinical Record Keeping	Observational Studies
Esthetic damage	7.3	11.9	5.5	3.8
Bony joint swellings	NA	19.3	7.4	9.7
Deformity	NA	13.0	6.2	6.2
Pain	26.3	10.5	17.0	15.6
Pain medication	9.9	NA	13.5	14.3
Patient global assessment	24.4	13.21	12.6	15.4
Physical function	16.3	10.6	13.0	12.1
Quality of life	13.6	7.8	7.3	9.9
Reduced mobility	5.0	10.3	5.2	6.3
Reduced strength	10.9	9.0	7.7	10.5
Soft joint swellings	8.4	14.0	10.1	10.9
Structural damage	NA	34.0	12.5	10.7
Tender joints	14.5	8.9	9.7	9.2

Areas included after the initial Delphi exercise. Areas included after the second Delphi exercise. NA: not applicable.

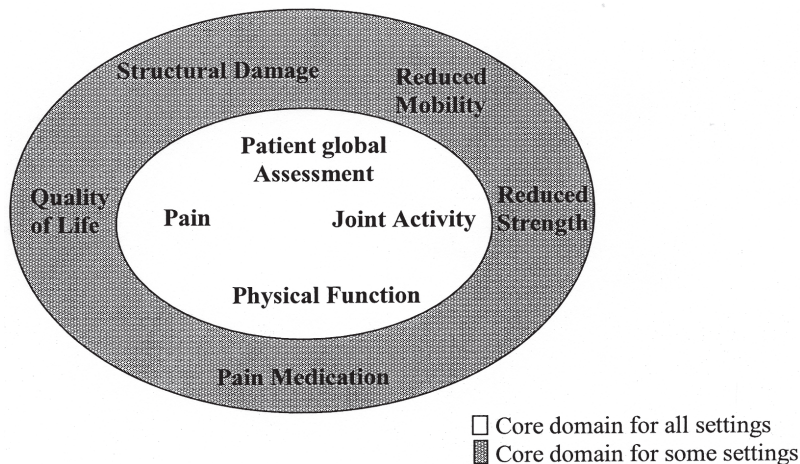


Figure 1. Proposed core domains for different settings of hand osteoarthritis.

OMERACT is currently revising the OMERACT filter and the new hand OA core domains should follow the new filter. Although the final format of the new filter must be awaited, the current work of the hand OA group was debated with this renewed methodology in mind. It was proposed that a separate Delphi exercise should be performed to define contextual factors. Potential contextual factors are: number of joint replacements in the hand joints, different hand OA subsets, and generalized OA.

Future Research Agenda

During OMERACT 11, discussions led to the following research agenda:

- The patient perspective should be extended in the selection of core domain for outcome measures
- For definition of contextual factors, a Delphi exercise should be performed. Potential contextual factors are number of joint replacements in the hand joints, different hand OA subsets, and generalized OA
- All 3 imaging modalities should be further elaborated on as possible instruments to assess structural damage in hand OA
- There is a need of further validation of all imaging modalities
- The number and selection of assessed joints should be elaborated. Whether this has an effect on the different imaging scoring methods should also be studied
- CR: Studies to agree upon preferred scoring system(s) are needed. Issues, such as individual features versus global scoring, joint level versus total hand analyses, and standardization of acquisition would be taken into account
- MRI: Use of MRI to assess joint activity should also be further elaborated. There will be collaboration with the MRI in Inflammatory Arthritis Group for validation of an MRI scoring system for PIP and DIP hand OA

- US: Use of US to assess joint activity should also be further elaborated. This will be performed in collaboration with the US group on scoring system validation. Patient-based exercises testing the reliability of US in grading cartilage abnormalities and osteophytes in hand OA will be performed in Oslo, September 2012

Hand OA is a prevalent disorder with high unmet needs in patients. At the moment, therapeutic options are limited. To establish progress in the field of hand OA further definition of core sets for various settings including the selection of the instruments for the various domains is warranted. Further, to be prepared for evaluation of potential disease-modifying OA drugs in future trials, it is especially important to select a valid scoring system for the various imaging modalities.

ACKNOWLEDGMENT

The authors acknowledge all the participants of the OMERACT 11 Hand Osteoarthritis Special Interest Group for their contributions. We also thank all the hand osteoarthritis experts for their contributions to this work, especially for their participation and valuable comments in the Delphi exercises: K.D. Allen, R. Altman, N.K. Arden, F. Berenbaum, S. Bierma-Zeinstra, J.W.J. Bijlsma, F. Birrell, P.G. Conaghan, M. Doherty, M. Dougados, K.S. Dziedzic, C.H. van den Ende, M. Englund, D. Felson, L. Gossec, H.B. Hammer, G. Hawker, D. Hunter, M. Ishimori, H. Jonsson, L. Kalichman, M.C. Kortekaas, T.K. Kvien, B. Leeb, E. Maheu, M. Marshall, D. McGonagle, K. Pavelka, S. Poiraudau, L. Punzi, R. Ramonda, F. Rannou, B. Slatkowsky-Christensen, J.S. Smolen, T. Spector, T. Stamm, A.L. Tan, P. Taylor, C. Thorstensson, G. Verbruggen, M. Vlychou, I. Watt, R. Wittoek, and T. Woodworth.

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Correction

Report from the OMERACT Hand OA Special Interest Group: Advances and Future Research Priorities

Kloppenburg M, Bøyesen P, Smeets W, Haugen IK, Liu R, Visser W, van der Heijde DM. J Rheumatol 2014;41:810-18. Dr. Haugen's name should appear as Ida K. Haugen. Her middle initial was omitted. We regret the omission.

doi:10.3899/jrheum.131253.C1