Instruments Measuring Physical Function for Psoriatic Arthritis Endorsed at GRAPPA 2020 Annual Meeting: Updates of the GRAPPA-OMERACT Working Group

Ying Ying Leung[1] (ID), Ana-Maria Orbai[2] (ID), William Tillett[3] (ID), Alexis Ogdie[4] (ID), Lihi Eder[5] (ID), Niti Goel[6] (ID), Pil Hojgaard[7] (ID), Richard Holland[8] (ID), Ashish J. Mathew[9] (ID), Christine A. Lindsay[10], Anna Antony[11] (ID), Jeffrey Chau[12], Robin Christensen[13] (ID), Laura C. Coates[14] (ID), Philip J. Mease[15] (ID), Vibeke Strand[16] (ID), Oliver FitzGerald[17] (ID), Maarten de Wit[18] (ID), Kristina Callis Duffin[19] (ID), and Dafna D. Gladman[20] (ID)

ABSTRACT. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)–Outcome Measures in Rheumatology (OMERACT) Psoriatic Arthritis (PsA) Working Group provided updates at the 2020 GRAPPA annual meeting on its work toward developing a core outcome set for PsA. Working groups were set up for the 4 prioritized domains: enthesitis, fatigue, structural damage, and physical function. Two instruments for measurement of physical function were provisionally endorsed: (1) the Health Assessment Questionnaire–Disability Index and (2) the physical functioning domain in the Medical Outcomes Study 36-item Short Form survey.

Key Indexing Terms: OMERACT, outcome assessment, psoriatic arthritis

[1]*Y.Y. Leung, MB ChB, MD, Associate Professor, Duke-NUS Medical School, and Department of Rheumatology and Immunology, Singapore General Hospital, Singapore;* [2]*A.M. Orbai, MD, MHS, Assistant Professor of Medicine, Director, Psoriatic Arthritis Program, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA;* [3]*W. Tillett, BSc, MB ChB, PhD, MRCP, Consultant Rheumatologist, Senior Lecturer, Royal National Hospital for Rheumatic Diseases, University of Bath, Bath, UK;* [4]*A. Ogdie, MD, MSCE, Associate Professor of Medicine and Epidemiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA;* [5]*L. Eder, MD, PhD, Women's College Research Institute, Women's College Hospital, Department of Medicine, University of Toronto, Toronto, Ontario, Canada;* [6]*N. Goel, MD, Patient Research Partner, Consultant, Caduceus Biomedical Consulting, LLC, and Adjunct Assistant Professor, Duke University School of Medicine, Durham, North Carolina, USA;* [7]*P. Hojgaard, MD, PhD, Department of Rheumatology, Holbaek Hospital, Holbaek, and the Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark;* [8]*R. Holland, MBBS, Concord Repatriation General Hospital, Sydney, Australia;* [9]*A.J. Mathew, MBBS, DNB, DM, Associate Professor in Rheumatology, Christian Medical College, Vellore, India and Clinical Research Fellow, Psoriatic Arthritis Program, University Health Network, University of Toronto, Toronto, Ontario, Canada;* [10]*C.A. Lindsay, PharmD, Patient Research Partner, VP Professional and Advocacy Relations, Aurinia Pharma U.S., Inc., Rockville, Maryland, USA;* [11]*A. Antony, MBBS, Monash University School of Clinical Sciences, Monash Medical Centre, Clayton, Melbourne, Australia;* [12]*J. Chau, GRAPPA Patient Research Partner, Hong Kong;* [13]*R. Christensen, BSc, MSc, PhD, Musculoskeletal Statistics Unit, The Parker Institute, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, and Professor of Biostatistics and Clinical Epidemiology, Research Unit of Rheumatology, Department of Clinical Research, University of Southern Denmark, Odense University Hospital, Odense, Denmark;* [14]*L.C. Coates, MB ChB, PhD, Associate Professor, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK;* [15]*P.J. Mease, MD, Rheumatology Research, Swedish Medical Center/Providence St. Joseph Health, and University of Washington School of Medicine, Seattle, Washington, USA;* [16]*V. Strand, MD, Division of Immunology/Rheumatology, Stanford University School of Medicine, Palo Alto, California, USA;* [17]*O. FitzGerald, MD, FRCPI, FRCP(UK), Consultant Rheumatologist and Newman Clinical Research Professor, Conway Institute for Biomolecular Research,*

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)–Outcome Measures in Rheumatology (OMERACT) Working Group aspires to develop an outcome measurement set for important domains for clinical trials of psoriatic arthritis (PsA).[1] In this report, we summarize the updates of the Core Outcome Measures for Psoriatic Arthritis Clinical Trials (COMPACT) projects presented at the GRAPPA 2020 virtual annual meeting and trainee symposium. We focus on describing the processes leading to the endorsement of 2 outcome measures for the measurement of physical function for PsA.

Updates on the 4 Prioritized Domains

Within the COMPACT projects, 4 PsA domains were prioritized[2] in 2019 and working groups were established for each of the domains to evaluate and standardize the outcome measures set. These 4 domains are (1) enthesitis (under musculoskeletal disease activity), (2) fatigue, (3) structural damage, and (4) physical function. Each working group was led by a team leader and engaged members across the globe, including at least 2 patient research partners (PRPs).[3] The progress by each working group is summarized in Table 1. The enthesitis and fatigue working groups are working on "domain match" and "feasibility" of instruments. Domain match concerns whether stakeholders consider the outcome measures to be a good match with the domain they are supposed to measure. Feasibility addresses whether the outcome measure instruments can be used in randomized controlled trials (RCTs) and longitudinal observational studies. The structural damage working group is completing a systematic literature review (SLR) for radiographic outcomes for PsA and starting the work stream, selecting outcome measures for magnetic resonance imaging. The work on the domain of physical function was the focus at GRAPPA 2020. The physical function working group has completed the necessary evaluation for 2 outcome candidate measures: the Health Assessment Questionnaire–Disability Index (HAQ-DI) and the physical functioning domain in the Medical Outcomes Study 36-item Short Form survey (SF-36 PF).

Physical Function Domain

Physical function is 1 of the 4 common core domains used in clinical trials to measure severity and outcomes for PsA[4] and is widely used in RCTs of PsA.[5,6,7] A physical function working group composed of 15 members was set up in June 2018.[3] The

University College Dublin, Dublin, Ireland; [18]M. de Wit, PhD, Patient Research Partner, Amsterdam, The Netherlands; [19]K. Callis Duffin, MD, MS, Department of Dermatology, University of Utah, Salt Lake City, Utah, USA; [20]D.D. Gladman, MD, FRCPC, Professor of Medicine, University of Toronto, Senior Scientist, Krembil Research Institute, and Director, Psoriatic Arthritis Program, University Health Network, Toronto Western Hospital, Toronto, Ontario, Canada.

members in the working group represent 3 continents (America, Asia, and Europe) and include 11 rheumatologists, 3 PRPs, and 1 methodologist. The working group discussed and preselected 6 patient-reported outcome measures (PROMs) to undergo vigorous appraisal using the OMERACT Filter 2.1[8]: HAQ and its 4 modifications (HAQ-DI, HAQ-Spondyloarthritis, modified HAQ, multidimensional HAQ), SF-36 PF, and the Patient-Reported Outcomes Measurement Information System physical functioning module (PROMIS PF).[3] From 2019–2020, the working group completed the OMERACT instrument selection workbook for HAQ-DI and SF-36 PF.

The OMERACT Methodology

The OMERACT Framework Instrument Selection Algorithm (OFISA) is the methodology OMERACT developed to guide the selection of outcome measures/instruments[8] and is based on the 3 pillars of OMERACT: Truth, Discrimination, and Feasibility. The 3 pillars used 4 signalling questions to help evaluate the existing evidence for each measure/instrument: (1) Is it a match with target domain (Truth)? (2) Is it practical to use (Feasibility)? (3) Do numeric scores make sense (Truth)? (4) Can it discriminate between groups of interest (Discrimination)?

Each instrument undergoes evaluation of 7 measurement properties: truth (domain match, construct validity), discrimination (test-retest reliability, longitudinal construct validity [responsiveness], clinical trial discrimination, thresholds of meaning), and feasibility. For each of these properties, it is necessary to answer the question of whether there is adequate evidence to support the instrument in clinical research.

The evidence supporting all 7 measurement properties for each instrument are presented in the summary of measurement property (SOMP) table.[8] The ratings for each of the 7 measurement properties are classified as: GREEN (good to go), AMBER (some cautions, but still can use), RED (stop, do not use this), or WHITE (no data). A final rating for whether the instrument has adequate evidence to support its use in clinical research is proposed. The complete appraisal for each instrument is documented in a selection workbook that requires approval by the OMERACT Technical Advisory Group (TAG), to be endorsed as a recommended core instrument.

Evidence Supporting Measurement Properties for HAQ-DI and SF-36 PF

Domain match and feasibility. The assessment of domain match and feasibility requires a consensus from experts and PRPs. Through discussions by webinars and email correspondence, the working group members selected 6 PROMs for physical function.[3] The working group members participated in a Delphi exercise to achieve a consensus for domain match and feasibility for all 6 PROMs.

To engage the broader GRAPPA membership audience, a video showing detailed information on the 6 PROMs was developed by the team lead and 2 PRPs in the working group (NG and JC; https://youtu.be/Qd86PwzgvQI). All GRAPPA PRPs were then invited to participate in a separate Delphi exercise on domain match and feasibility for all 6 PROMs.

Table 1. Working groups and progress of the 4 prioritized domains for PsA.

Prioritized PsA Domain	Workstream Progress
1. Physical function	· Completed evaluation HAQ-DI, SF-36 PF
2. MSK disease activity: enthesitis	· Domain match/ feasibility
3. Fatigue	· Prioritizing PROMs
	· Domain match/ feasibility
4. Structural damage	· Completed systematic literature review for radiographic scoring
	· Working group for MRI in development

HAQ-DI: Health Assessment Questionnaire–Disability Index; MRI: magnetic resonance imaging; MSK: musculoskeletal; PROM: patient-reported outcome measure; PsA: psoriatic arthritis; SF-36 PF: Medical Outcomes Study 36-item Short Form survey physical functioning domain.

Combining results from both Delphi exercises for working group members and PRPs, the final voting for domain match and feasibility were AMBER and GREEN, respectively, for HAQ-DI. As for SF-36 PF, the final ratings were AMBER for both domain match and feasibility.

Systematic literature review and final ratings. The working group has conducted 2 SLRs on the PROMs for physical function. One SLR included articles with a primary aim to evaluate measurement properties of all PROMs in PsA (PROSPERO ID: CRD42016032546),[9] and the second SLR was to evaluate data of the physical function PROMs from RCTs (PROSPERO ID: CRD42019129557).[10] The first SLR identified 10 relevant articles for HAQ-DI and 6 articles for SF-36 PF. Subsequently, new evidence was generated by working group members to bridge the gap of knowledge for HAQ-DI (n = 4 studies) and SF-36 PF (n = 1 study). For the second SLR, relevant RCTs were reviewed for data on HAQ-DI (n = 31) and for SF-36 PF (n = 4), as shown in Table 2. At least 2 working group members evaluated each article and reached a consensus on the quality of each measurement property using the OMERACT good method checklist.[8] For those articles that passed this assessment, study findings and characteristics supporting each measurement property were reviewed and summarized in the instrument selection workbook. Then, the evidence supporting HAQ-DI and SF-36 PF was summarized in the final SOMP tables. Extracts of the SOMP tables are presented in Table 2. At the GRAPPA 2020 annual meeting, the working group proposed a provisional endorsement for both HAQ-DI and SF-36 PF. Further evidence on test-retest reliability, RCT discrimination, and development of threshold of meaning for SF-36 PF should be collected to ensure full endorsement of both instruments.

Endorsement
After presenting the relevant data, live polling was conducted at the GRAPPA 2020 annual meeting to endorse the final ratings for both instruments. Two questions were asked: "Given the evidence, do you agree with the working group to endorse HAQ-DI as provisional core instrument for the measurement of physical function in PsA studies?" The same question was asked for the SF-36 PF. Forty-nine GRAPPA members participated in the live polling, with 93.9% and 86.7% voting positively for HAQ-DI and SF-36 PF, respectively (Table 3). The 2 instrument selection workbooks were then reviewed by the OMERACT TAG, who suggested minor updates, though the final ratings

Table 2. Number of articles from literature review or new evidence and ratings to support HAQ-DI and SF-36 PF domains for measurement of physical function in PsA.

PROMs for Physical Function	Domain Match	Feasibility	Truth Construct Validity	Test-retest Reliability	Discrimination Longitudinal Construct Validity	Clinical Trial Discrimination	Thresholds of Meaning	Final Rating
HAQ-DI · No. articles from SLR (new)	NA	NA	6 (+2)	None (+2)	2 (+2)	31	3 (+1)	Provisionally endorsed
· Rating	AMBER from WG votes	GREEN from WG votes	GREEN	GREEN	GREEN	GREEN	AMBER	
SF-36 PF · No. articles from SLR (new)	NA	NA	4	None (+1)	2	4	1	Provisionally endorsed
· Rating	AMBER from WG votes	AMBER from WG votes	GREEN	AMBER	AMBER	AMBER	AMBER	

The rating for each of the 7 measurement properties is given as GREEN (good to go), AMBER (some cautions, but still can use), or RED (stop, do not use this). Number of articles found in literature searches and new evidence derived from WG members (in parenthesis). HAQ-DI: Health Assessment Questionnaire–Disability Index; PROM: patient-reported outcome measure; PsA: psoriatic arthritis; SF-36 PF: Medical Outcomes Study 36-item Short Form Survey physical functioning domain; SLR: systematic literature review; WG: working group.

Table 3. Endorsement of HAQ-DI and SF-36 PF for measurement of physical function in PsA trials.

	Live Polling at GRAPPA 2020	Online Voting for All GRAPPA Members (Oct–Nov 2020)
Participants, n (%)	49 (100)	119 (100)
Rheumatologist	21 (42.9)	94 (79.0)
Dermatologist	3 (6.1)	13 (10.9)
Clinician (other specialities)	1 (2.0)	0
Methodologist or other researchers	1 (2.0)	4 (3.4)
Patient research partners	8 (16.3)	6 (4.4)
Industry	13 (26.5)	0
Regulatory/government/administrator	0	0
Missing	2 (4.1)	2 (1.7)
Endorsement votes, %		
HAQ-DI	93.9	97.5
SF-36 PF	86.7	77.3

Online votes consistent with live polling results. HAQ-DI: Health Assessment Questionnaire–Disability Index; PsA: psoriatic arthritis; SF-36 PF: Medical Outcomes Study 36-item Short Form Survey physical functioning domain.

remained unchanged. Both instrument selection workbooks and ratings were endorsed by the OMERACT TAG in September 2020. A subsequent online poll of all GRAPPA members was conducted from October 20, 2020, to November 16, 2020. The original data, updates, and results of the live poll at the GRAPPA 2020 annual meeting were presented. The identical voting questions were used in both polls. GRAPPA members participated (n = 119) and voted for provisional endorsement of HAQ-DI (97.5% positive) and SF-36 PF (77.3% positive) as core instruments for the measurement of physical function in PsA studies.

Future plans for this working group include comparing discrimination in RCTs for the selected instruments using meta-analysis, further evaluation of thresholds of meaning for both the HAQ-DI and SF-36 PF, and appraisal of 4 other preselected PROMs for physical function using OFISA.

Conclusion
This report provides an update for the workstream involved in select core outcome instruments for 4 prioritized domains in PsA. The measurement properties of HAQ-DI and SF-36 PF for measurement of physical function in PsA were evaluated using the OFISA of the OMERACT Filter 2.1. Provisional endorsement for both instruments was obtained from the GRAPPA community.

REFERENCES
1. Tillett W, Orbai AM, Ogdie A, Leung YY, Strand V, Gladman DD, et al; GRAPPA OMERACT Psoriatic Arthritis Working Group. GRAPPA-OMERACT initiative to standardise outcomes in psoriatic arthritis clinical trials and longitudinal observational studies. Ann Rheum Dis 2018;77:e23.
2. Leung YY, Tillett W, Orbai AM, Ogdie A, Eder L, Coates LC, et al. The GRAPPA-OMERACT Working Group: 4 prioritized domains for completing the Core Outcome Measurement Set for Psoriatic Arthritis 2019 updates. J Rheumatol Suppl 2020;96:46-9.
3. Leung YY, Orbai AM, Ogdie A, Hojgaard P, Holland R, Goel N, et al. Appraisal of candidate instruments for assessment of the physical function domain in patients with psoriatic arthritis. J Rheumatol 2020;48:58-66.
4. Orbai AM, de Wit M, Mease P, Shea JA, Gossec L, Leung YY, et al. International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Ann Rheum Dis 2017;76:673-80.
5. Stamm TA, Nell V, Mathis M, Coenen M, Aletaha D, Cieza A, et al. Concepts important to patients with psoriatic arthritis are not adequately covered by standard measures of functioning. Arthritis Rheum 2007;57:487-94.
6. Orbai AM, de Wit M, Mease PJ, Callis Duffin K, Elmamoun M, Tillett W, et al. Updating the psoriatic arthritis (PsA) core domain set: a report from the PsA workshop at OMERACT 2016. J Rheumatol 2017;44:1522-8.
7. Dures E, Hewlett S, Lord J, Bowen C, McHugh N; PROMPT Study Group, et al. Important treatment outcomes for patients with psoriatic arthritis: a multisite qualitative study. Patient 2017; 10:455-62.
8. Beaton DE, Maxwell LJ, Shea BJ, Wells GA, Boers M, Grosskleg S, et al. Instrument selection using the OMERACT filter 2.1: the OMERACT methodology. J Rheumatol 2019;46:1028-35.
9. Højgaard P, Klokker L, Orbai AM, Holmsted K, Bartels EM, Leung YY, et al. A systematic review of measurement properties of patient reported outcome measures in psoriatic arthritis: a GRAPPA-OMERACT initiative. Semin Arthritis Rheum 2018;47:654-65.
10. Leung YY, Holland R, Mathew AJ, Lindsay C, Goel N, Ogdie A, et al. Clinical trial discrimination of physical function instruments for psoriatic arthritis: a systematic review. Semin Arthritis Rheum 2020;50:1158-81.