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Patient global assessment is elevated by up to 5 of 10 units in patients with inflammatory arthritis who screen positive for fibromyalgia (by FAST4) and/or depression (by MDS2) on a single MDHAQ

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ABSTRACT

Background: Patient global assessment (PATGL) is a component of rheumatoid arthritis (RA) and spondyloarthritis (SpA) activity indices, reflecting inflammation in selected clinical trial patients. In routine care, PATGL often may be elevated independently of inflammatory activity by fibromyalgia (FM) and/or depression, leading to complexities in interpretation. A feasible method to screen for FM and/or depression could help to clarify interpretation of high PATGL and index scores, including explanation of apparent limited responses to anti-inflammatory therapies.

Patients and Methods: Patients with RA or SpA in routine care in Barcelona, Chicago, and Sydney complete a 2-page multidimensional health assessment questionnaire (MDHAQ) in 5–10 min. The MDHAQ includes PATGL and three indices, RAPID3 (routine assessment of patient index data) to assess clinical status, FAST4 (0–4 fibromyalgia assessment screening tool) and MDS2 (0–2 MDHAQ depression screen). PATGL was compared for each diagnosis at each site and pooled data in FAST4 positive (+) vs negative (-) and/or MDS2+ vs MDS2- patients using medians and median regressions.

Results: Median PATGL was 5.0 in 393 RA and 175 SpA patients; 2.0–3.0 in 305 (58.9%) FAST4-,MDS2- patients, 5.5–6.0 in 71 (13.7%) FAST4-,MDS2+ patients, 7.0–7.5 in 50 (9.7%) FAST4+,MDS2- patients, and 7.0–8.0 in 92 (17.8%) FAST4+,MDS2+ patients. Positive FAST4 and/or MDS2 screens were seen in 41% of patients. Results were similar in RA and SpA at 3 settings on 3 continents.

Conclusion: Median 0–10 PATGL varied from 2-3/10 to 5.5-8/10, according to negative vs positive screening for FM and/or depression on a single MDHAQ for busy clinical settings.

Abbreviations: ASDAS, Ankylosing spondylitis disease activity score; AxSpA, axial spondyloarthropathy; CDAI, clinical disease activity index; DAPSA, Disease activity in psoriatic arthritis; DAS28, disease activity score 28; FAST4, fibromyalgia assessment screening tool; FM, Fibromyalgia; HADS-D, Hospital anxiety and depression scale - depression; MDHAQ, multidimensional health assessment questionnaire; MDS2, MDHAQ depression screen; PATGL, patient global assessment; PHQ 9, Patient health questionnaire 9; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RAPID3, routine assessment of patient index data; SpA, spondyloarthropathy.

Dr. Pincus holds a copyright and trademark on MDHAQ (multidimensional health assessment questionnaire) and RAPID3 (Routine Assessment of Patient Index Data 3), for which he receives royalties and license fees from for-profit entities but none from physicians, all of which are used to support further development of quantitative questionnaire measurements for patients and doctors in clinical rheumatology care. Dr. Gibson has received honoraria from UCB, Novartis and Janssen and grant support from Novartis. She is a part-time employee and stockholder of Eli Lilly, but no financial or other support was received from Eli Lilly in the creation of this article. Medical History Services LLC provided funding to Georgetown University for Mr. Li and Prof Luta. Dr. Schmukler and Dr. Morla do not have any financial disclosures.

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Key messages

What is already known on this topic: Patient global assessment (PATGL), a component of most indices to assess patients with inflammatory rheumatic diseases, distinguishes active from control treatments in selected clinical trial patients as significantly as any measure, but may be elevated in the presence of little or no inflammation by joint damage and comorbidities, notably fibromyalgia and/or depression. Fibromyalgia and/or depression are easily recognized in some patients but often are underrecognized, particularly when not screened for quantitatively in most long-term rheumatology databases. Elevated index scores resulting from elevated PATGL by fibromyalgia and/or depression may lead to inappropriate interpretation of index scores in certain patients.

What this study adds: Positive screening for fibromyalgia and/or depression on a multidimensional health assessment questionnaire (MDHAQ), seen in 41% of patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA), elevates median 0–10 PATGL from 2-3 to 5.5-8, half its range, as great a difference as often seen with therapeutic interventions. Recognition of these comorbidities may explain apparent poor responses to anti-inflammatory therapies and prevent possible inappropriate escalation of therapies in certain patients.

How this study might affect research, practice or policy: Quantitative screening for fibromyalgia and/or depression is difficult if multiple patient questionnaires are required, but feasible in busy routine care clinical care or research settings using the MDHAQ, which is completed by patients in 5–10 min and scored in 20–30 s. The findings may be useful toward promotion of quantitative assessment of joint damage and patient distress in routine care and long-term databases, and provide a rationale for public health and rheumatology messages toward for earlier diagnosis and treatment.

Introduction

Patient global assessment (PATGL) is a component of many indices to assess rheumatic diseases, including DAS28 (disease activity score 28), CDAI (clinical disease activity index), and RAPID3 (routine assessment of patient data index) in rheumatoid arthritis (RA) [1–4]; ASDAS (ankylosing spondylitis disease activity score) in axial spondyloarthritis (AxSpA) [5]; DAPSA (disease activity in psoriatic arthritis) [6] in psoriatic arthritis (PsA), and other indices. In RA clinical trials, PATGL distinguishes active from control treatments as efficiently as joint counts and laboratory tests [7], and is effective in AxSpA and PsA [8] disease status ascertainment. However, only 5–25% of all RA patients seen in routine care meet inclusion criteria for clinical trials (other than trials for selected patients, e.g., early arthritis) [9,10].

In routine care, PATGL may frequently be elevated by comorbidities such as joint damage as osteoarthritis [11–13], fibromyalgia (FM) [14] and depression [15], which can easily be diagnosed in some patients, but are underrecognized in many others [16,17]. Elevated PATGL in patients with little inflammatory activity may complicate interpretation of indices and a treat-to-target strategy in RA [18], AxSpA [19], and PsA [19,20]. Controversy has existed concerning apprpropriate levels of PATGL in rheumatology indices and remission criteria [21–23]; recently, PATGL was raised from 1 to 2/10.to meet ACR/EULAR Boolean criteria for remission [24].

Although elevated PATGL in patients with inflammatory rheumatic diseases and comorbid FM and depression has been described in many reports, relatively little information is available concerning the magnitude of the elevations. Furthermore, most reports have incorporated at least two questionnaires to recognize FM and depression, such as the 2011 FM criteria patient questionnaire [25], and a depression scale such as PHQ 9 (patient health questionnaire 9) [26] and/or HADS-D (hospital anxiety and depression scale – depression) [27]. It is generally not feasible for patients to complete two questionnaires in busy routine rheumatology care settings.

A multidimensional health assessment questionnaire (MDHAQ) is completed by most patients in 5–10 min, and has been incorporated in many routine care settings to be completed by all patients at all visits [28]. The MDHAQ includes PATGL and two indices, FAST4 (fibromyalgia assessment screening tool) [29,30] and MDS2 (MDHAQ depression screen) [31], which agree more than 80% with reference questionnaires [25-27,29-31], In this report, we analyze PATGL in routine care patients with RA, AxSpA and PsA according to positive or negative MDHAQ-derived FAST4 and MDS2 indices.

Patients and methods

Patients

The study is a cross-sectional retrospective analysis of data collected in routine clinical care. All patients (with all diagnoses) seen for rheumatology care at Liverpool Hospital in Sydney, NSW, Australia and at Rush University in Chicago, IL, USA are asked to complete an MDHAQ at each visit [28]. Unselected patients with primary ICD10 diagnoses of RA, AxSpA, or PsA, assigned by the treating physician, who had available PATGL, were studied retrospectively. In 2017, the revised 2011 FM criteria questionnaire [25] was added to the MDHAQ at both settings [28]). The FM questionnaire was completed only by English-language speaking patients. The HADS (hospital anxiety and depression scale) [27] was added in Liverpool in 2020.

In the Hospital Clinic of Barcelona, Spain, a study was conducted in routine care between November 2018 and February 2019 to evaluate the validity of MDHAQ depression scores compared to reference PHQ-9 [26] and HADS-D [27]. Results led to development of a cumulative 2-item MDHAQ MDS2 index [initially termed MDHAQ–Dep [31]] which agrees >80% with PHQ-9 and HADS-D, similar to agreement of PHQ-9 and HADS-D with one another [31].

Patient questionnaires

The MDHAQ [32] (Supplementary Fig. 1) is a two-page single-sheet questionnaire developed in routine care over 25 years from the Stanford health assessment questionnaire (HAQ) according to principles of continuous quality improvement [33]. The MDHAQ queries 10 physical function items on a 0–3 scale for a total of 0-30, divided by 3 for a 0-10 score [28]. Three psychological items for sleep quality, anxiety and depression are queried in the patient-friendly HAQ format [28,32]. Pain, patient global assessment (PATGL), and fatigue are assessed on 0–10 visual numeric scales (VNS), with 21 circles in increments of 0.5 units [28]. A self-report painful joint count, modified from a rheumatoid arthritis disease activity index (RADAI) [34], adds neck and back to the 16 joints in the original RADAI, for 18 joints scored 0–3 giving a total of 0–54 [35]. A 60-symptom checklist (60 symptoms) queries "Yes/No" responses to common symptoms, including depression, and can be used as a review of systems and to recognize adverse events to medications [36]. The MDHAQ also queries other medical history information as well as demographic data [28] (Supplementary Fig. 1).

Three indices within the MDHAQ are RAPID3, FAST4, and MDS2. RAPID3 is a 0–30 total of 0–10 scores for physical function, pain, and PATGL [28], and has been found informative to assess clinical status in patients with all diseases studied [36–38]. FAST4 is a composite cumulative index; one point each is assigned for pain VNS≥6, fatigue VNS≥6, RADAI≥16/54, and 60-symptoms≥16/60 [29,30]; FAST4 ≥3/4 indicates a positive FM screen [29,30]. MDS2 is a 0–2 cumulative index, reported initially as MDHAQ-Dep [31], based on a response ≥2.2/3.3 on a 0–3.3 HAQ depression query OR a positive check for depression on the 60-symptom checklist. MDS2 ≥1/2 is a positive screen; PHQ-9>10, HADS-*D* ≥ 8, and MDS2>1 agree 81.7%−83.3% with one another [31].

Rheumatology indices

Two hypothetical models of DAS28 [2], CDAI [3], RAPID3 [39], ASDAS [5], and DAPSA [6] results were calculated based on PATGL of 3, 5, 7: a. "extreme," i.e., all other measures except ESR and CRP were 0, b. "realistic," i.e., expected minimum levels of other index measures if PATGL=3, 5, or 7. Indices and categories were calculated arithmetically for CDAI and RAPID3, and from websites http://www.das-score.nl, https://www.asas-group.org, and https://www.mdapp.com.

Institutional approval

In Barcelona, each participant gave written consent, as approved by the Hospital Clinic Universitari de Barcelona Ethics Committee (Reg. HCB/2019/0024). In Chicago, the Rush University Institutional Review Board (IRB) waived patient consent to complete an MDHAQ, as the questionnaire is regarded as a component of quality in routine care; the IRB approved the addition of the revised 2011 FM criteria questionnaire for routine care, and approved retrospective review of deidentified routine care questionnaires (14,090,502-IRB02-AM03). In Liverpool, the study was approved by the district Human Research and Ethics Committee (LNR/13/LPOOL/370 Local project number 13/229LNR). All patients consented to the use of their anonymized data for research, including publication. The study was conducted in accordance with the Helsinki Declaration.

Patient and public involvement

There was no patient or public involvement in the study design of a retrospective cross-sectional analysis of data collected in routine clinical care

Statistical analyses

Analyses were performed separately for data from Barcelona, Chicago, and Liverpool, and for pooled data from the three settings. Descriptive statistics were computed for age, gender, and years of education in patients with primary ICD 10 diagnoses of RA, AxSpA, PsA, and pooled spondyloarthritis (All SpA = AxSpA + PsA). Medians and interquartile ranges (IQRs) for PATGL were computed for each of the three diagnoses and all SpA, separately for each setting and pooled data from the 3 settings in all patients. Medians and IQRs for PATGL were further computed according to positive (+) and/or negative (-) FM screening by FAST4 [29,30] and/or depression screening by MDS2 [31] criteria, and the proportions with positive FAST4 and MDS2. No imputation for missing data were performed. Differences between medians of PATGL with corresponding 95% confidence intervals (CI) for the comparisons between positive and negative FAST4 and/or MDS2 were estimated from median regression models; the models for the pooled analyses also included the setting.

Medians and IQRs for PATGL also were computed according to the revised 2011 FM criteria [25] in patients from Chicago and Liverpool (not available from Barcelona), and HADS-D [27] from Barcelona and Liverpool (not available from Chicago). Medians and IQRs for PATGL were computed for Liverpool data according to both positive and/or negative FM screening by the revised 2011 FM criteria [25] and depression by HADS-D criteria [27] resulting in 4 categories. Statistical analyses were performed using SAS software, version 9.4(SAS Institute Inc., Cary, NC).

Results

Patients

The study included 568 patients, 170 from Barcelona, 102 from Chicago, and 296 from Liverpool (Table 1), 393 with RA, 64 AxSpA, and 111 PsA, collectively 175 with all SpA (Table 1); all patients had PATGL data available, more than 80% of patients who had been asked to complete an MDHAQ. The patients with RA were older than those with SpA.

Table 1
Demographic data concerning patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthropathies (AxSpA) and total spondyloarthropathies (SpA) (PsA + AxSpA = SpA) from 3 settings on 3 continents, Barcelona Spain, Chicago USA, and Liverpool Australia.

Variable	Rheumatoid arthritis (RA)	Psoriatic arthritis (PsA)	Axial spondyloarthropathy (AxSpA)	Total Spondyloarthropathies (All SpA)	Total
Three settings pooled					
N (%)	393 (69.2)	111 (19.5)	64 (11.3)	175 (30.8)	568 (100)
Age (years), median (IQR)	58.9 (49.1, 68.6)	54.1 (47.3, 64.2)	49.3 (37.8, 61.1)	53.5 (42.1, 63.4)	56.9 (47.3, 67.6)
Education (years), median (IQR)	12.0 (10.0 15.0)	12.0 (10.0, 15.0)	12.5 (10.0 16.0)	12.0 (10.0, 15.0)	12.0 (10.0, 15.0)
Female, N (%)	323 (82.4)	57 (51.4)	28 (43.8)	85 (48.6)	408 (72.0)
Barcelona, Spain					
N (%)	102 (60.0)	34 (20.0)	34 (20.0)	68 (40.0)	170 (100)
Age (years), median (IQR)	57.7 (51.4, 68.1)	55.1 (48.1, 62.5)	54.0 (43.5, 66.0)	54.7 (47.2, 65.6)	56.6 (49.6, 67.5)
Education (years), median (Q1, Q3)	11.0 (8.0, 15.0)	10.0 (8.0, 14.0)	12.0 (9.0, 14.0)	10.0 (8.0, 14.0)	10.0 (8.0, 14.0)
Female, N (%)	84 (82.4)	19 (55.9)	13 (38.2)	32 (47.1)	116 (68.2)
Chicago, IL, USA					
N (%)	78 (76.5)	13 (12.7)	11 (10.8)	24 (23.5)	102 (100)
Age (years), median (Q1, Q3)	57.0 (41.0, 68.0)	48.0 (39.0, 65.5)	40.0 (32.0, 50.0)	42.0 (33.0, 64.0)	55.0 (37.0, 67.0)
Education (years), median (IQR)	15.0 (14.0, 17.0)	15.0 (12.0, 16.0)	16.0 (16.0, 18.0)	16.0 (12.0, 17.5)	16.0 (14.0, 17.0)
Female, N (%)	75 (96.2)	10 (76.9)	6 (54.5)	16 (66.7)	91 (89.2)
Liverpool, NSW, AUS					
N (%)	213 (72.0)	64 (21.6)	19 (6.4)	83 (28.0)	296 (100)
Age (years), median (IQR)	59.9 (49.2, 69.2)	54.0 (47.5, 64.5)	45.2 (34.4, 59.4)	52.1 (41.2, 61.9)	57.7 (47.6, 68.1)
Education (years), median (IQR)	11.0 (10.0, 14.0)	12.0 (10.0, 15.0)	13.0 (12.0, 16.0)	12.0 (10.0, 15.0)	12.0 (10.0, 14.0)
Female, N (%)	164 (77.4)	28 (43.8)	9 (47.4)	37 (44.6)	201 (68.1)

Median PATGL and proportion of FAST4 positive or MDS2 positive patients according to diagnosis

Median PATGL in the 3 diagnosis categories in the 3 settings and the pooled data was 5.0 (Table 2). Median PATGL in RA was 4.8 in Barcelona, 5.0 in Chicago, 5.0 in Liverpool. Median PATGL in all SpA (pooled AxSpA + PsA) was 6.0 in Barcelona, 3.0 in Chicago, 4.5 in Liverpool (Table 2).

Among these 568 patients, 518 (91.2%) with complete data for calculation of FAST4 and MDS2, included 169 (99.4%) from Barcelona, 92 (90.2%) from Chicago, and 257 (86.8%) from Liverpool (Table 3). The proportion of patients with RA or SpA, respectively, who were positive for FAST4 was 26.6% and 29.1% in the pooled data, similar at 3 sites (Table 2). The proportion with RA or SpA, respectively, who were positive for MDS2 was 29.4% and 34.9% in the pooled data, again similar at 3 sites (Table 2). Results according to 2011 revised FM criteria, PHQ-9 or HADS-D, each available in only 2 of the 3 settings, were quite similar to results according to FAST4 and MDS2, respectively (Table 2).

Median PATGL according to whether patients screened positive for fibromyalgia and/or depression

Median PATGL in 376 patients who were FAST4 negative was 3.0 in RA, 3.0 in PSA, 3.5 in AxSpA, and 3.0 in all SpA (Table 3). By contrast, median PATGL in 142 FAST4 positive patients was 8.0 in RA, 8.0 in PsA, 7.0 in AxSpA, and 8.0 in all SpA. Median PATGL in 355 MDS2 negative patients was 3.5 in RA, 3.0 in PSA, 3.5 in AxSpA, and 3.0 in all SpA (Table 3). By contrast, median PATGL in 163 MDS2 positive patients was 7.0 in RA, 7.0 in PsA, 6.5 in AxSpA, and 6.8 in all SpA (Table 3). Patterns were similar at the 3 settings (chi-square=5.15, $p = 0.52$), with variation explained in part by small numbers of patients.

Median PATGL in 305 patients (58.9%) who were both FAST4 and MDS2 negative was 3.0 in RA, 2.0 in PsA, 3.0 in AxSpA, and 2.5 in all SpA (Table 3). Median PATGL in 71 patients (13.7%) who were FAST4 negative and MDS2 positive was 5.5 in RA, 6.0 in PSA, 6.0 in AxSpA and 6.0 in all SpA. Median PATGL in 50 patients (9.7%) who were FAST4 positive and MDS2 negative was 7.5 in RA, 7.5 in PsA, 7.0 in AxSpA, and 7.3 in all SpA. Median PATGL in 92 patients (17.8%) who were FAST4 positive and MDS2 positive was 8.0 in RA, 8.0 and PSA, 7.0 in AxSpA, and 8.0 in all SpA (Table 3). Among all 213 patients who were either FAST4 or MDS2 positive, 33.3% were positive for only MDS2, 23.5% for only FAST4, and 43.2% for both FAST4 and MDS2 (Table 3).

Analyses also were performed according to the reference revised 2011 FM criteria and HADS-D for comparisons with the FAST4 and MDS2 indices, respectively, in a subset of 114 RA and 62 SpA in patients from Liverpool (Table 4). Median PATGL was 3.0 and 2.3 in 60.2% of RA or SpA patients, respectively, who were negative for both reference questionnaires (Table 4), compared to 3.0 and 2.5, respectively, in 60.3% of patients according to FAST4 and MDS2 (Table 3). Levels of PATGL appeared similar according to positive or negative FAST4 (Table 3) or revised 2011 FM criteria (Table 4), or positive or negative MDS2 (Table 3) or HADS-D (Table 4).

Discussion

Data in this report indicate that median values of PATGL are substantially elevated from 2-3/10 to 5.5-8/10 (or 20-30/100 to 55-80/100) in patients with RA, PsA, AxSpA, and all SpA, who screened negative vs positive for FM and/or depression. This observation is not new, but the report provides three possible advances: a. The MDHAQ provides a feasible, pragmatic single questionnaire to screen for FM according to FAST4 [29,30] which agrees >90% with reference revised 2011 FM criteria [25,29,30], and for depression according to MDS2 [31], which agrees >80% with PHQ9 [26] and HADS-D [27,31], (as well as to assess clinical status by RAPID3) in patients with any rheumatic disease. The MDHAQ is completed by patients in 5–10 minutes and scored by clinicians in 20–30 seconds, and obviates a need for multiple questionnaires in each patient and different questionnaires for different diseases, which are not feasible in busy clinical settings. b. The impact of FM or depression on 0–10 PATGL is documented quantitatively, with 0–10 PATGL 2–3-fold higher (up to 5 units, half the range of the 0–10 scale) in patients who screen negative vs positive for FM and/or depression, a profound difference generally as great or greater than seen with most therapeutic interventions. c. Positive quantitative screening for FM and depression on the MDHAQ was seen in 41.2% of patients, 10–15% for either index and 15–20% positive for both indices, without additional questionnaires.

Analyses in this report indicated considerable similarity in patients with 3 inflammatory arthritides at 3 settings on 3 continents, including

Table 2
Median patient global assessment scores (PATGL) and proportion of patients positive for FAST4 (fibromyalgia assessment screening tool), MDS2 (MDHAQ depression screen), revised 2011 fibromyalgia criteria, and HADS-D (hospital anxiety and depression scale –depression).

Primary diagnosis according to physician	Total (%) *	Median PATGL (IQR)	FAST4 FM Positive N (%)	MDS2 Positive N (%)	FM 2011 Criteria Positive N (%)	HADS-D or PHQ-9 Positive N (%)[#]
Three settings pooled	***n* = 568**					
Rheumatoid arthritis	393 (69.2%)	5.0 (2.0, 7.0)	95 (26.6%)	115 (29.4%)	66 (22.7%)	71 (32.9%)
Psoriatic arthritis	111 (19.5%)	5.0 (1.8, 7.0)	34 (32.7%)	40 (36.7%)	21 (27.3%)	28 (31.8%)
Axial spondyloarthropathy	64 (11.3%)	5.0 (2.5, 7.0)	14 (23.0%)	20 (31.7%)	7 (23.3%)	18 (42.9%)
Total Spondyloarthropathies	175 (30.8%)	5.0 (2.0, 7.0)	48 (29.1%)	60 (34.9%)	28 (26.2%)	46 (35.4%)
Barcelona, Spain	***n* = 170**					
Rheumatoid arthritis	102 (60.0%)	4.8 (2.0, 6.5)	27 (26.5%)	33 (32.7%)	NA	34 (33.3%)
Psoriatic arthritis	34 (20.0%)	6.3 (3.0, 7.0)	14 (41.2%)	15 (44.1%)	NA	13 (38.2%)
Axial spondyloarthropathy	34 (20.0%)	5.8 (3.0, 7.0)	11 (32.4%)	13 (38.2%)	NA	16 (47.1%)
Total Spondyloarthropathies	68 (40.0%)	6.0 (3.0, 7.0)	25 (36.8%)	28 (41.2%)	NA	29 (42.6%)
Chicago, IL, USA	***n* = 102**					
Rheumatoid arthritis	78 (76.5%)	5.0 (2.0, 7.0)	18 (25.0%)	18 (23.1%)	11 (14.1%)	NA
Psoriatic arthritis	13 (12.7%)	3.0 (1.0, 6.0)	4 (33.3%)	4 (33.3%)	4 (30.8%)	NA
Axial spondyloarthropathy	11 (10.8%)	3.0 (2.0, 5.5)	2 (22.2%)	2 (18.2%)	3 (27.3%)	NA
Total Spondyloarthropathies	24 (23.5%)	3.0 (1.5, 5.8)	6 (28.6%)	6 (26.1%)	7 (29.2%)	NA
Liverpool, NSW, AUS	***n* = 296**					
Rheumatoid arthritis	213 (72.0%)	5.0 (2.0, 7.5)	50 (27.3%)	64 (30.2%)	55 (25.8%)	37 (32.5%)
Psoriatic arthritis	64 (21.6%)	4.5 (1.0, 7.0)	16 (27.6%)	21 (33.3%)	17 (26.6%)	15 (27.8%)
Axial spondyloarthropathy	19 (6.4%)	4.0 (2.0, 6.5)	1 (5.6%)	5 (27.8%)	4 (21.1%)	2 (25.0%)
Total Spondyloarthropathies	83 (28.0%)	4.5 (2.0, 7.0)	17 (22.4%)	26 (32.1%)	21 (25.3%)	17 (27.4%)

NA indicates that data on the item was not collected at the specific setting.
[#] Barcelona has data for PHQ-9 and Liverpool for HADS-D.

Table 3
Median patient global assessment scores (PATGL) and (interquartile ranges) according to positive or negative FAST4 (fibromyalgia assessment screening tool) or MDS2 (MDHAQ depression screen).

Primary diagnosis according to physician	FAST4 Neg	MDS2 Neg	FAST4 Pos	MDS2 Pos	FAST4 Neg MDS2 Neg	FAST4 Neg MDS2 Pos	FAST4 Pos MDS2 Neg	FAST4 Pos MDS2 Pos
Three settings pooled	***n* = 376**	***n* = 355**	***n* = 142**	***n* = 163**	***n* = 305 (58.9%)**	***n* = 71 (13.7%)**	***n* = 50 (9.7%)**	***n* = 92 (17.8%)**
Rheumatoid arthritis	3.0 (1.3, 5.5)	3.5 (1.3, 6.0)	8.0 (7.0, 9.0)	7.0 (5.0, 8.5)	3.0 (1.0, 5.0)	5.5 (3.6, 6.5)	7.5 (6.5, 8.5)	8.0 (7.0, 9.0)
Psoriatic arthritis	3.0 (1.0, 5.5)	3.0 (1.0, 6.0)	8.0 (6.5, 9.0)	7.0 (5.3, 8.5)	2.0 (1.0, 4.5)	6.0 (4.5, 6.5)	7.5 (6.5, 9.0)	8.0 (6.8, 9.5)
Axial spondyloarthropathy	3.5 (2.0, 6.0)	3.5 (2.0, 5.8)	7.0 (6.5, 8.0)	6.5 (4.8, 8.3)	3.0 (2.0, 5.0)	6.0 (2.5, 7.0)	7.0 (7.0, 8.0)	7.0 (6.5, 10.0)
Total Spondyloarthropathies	3.0 (1.0, 5.5)	3.0 (1.0, 6.0)	8.0 (6.5, 9.0)	6.8 (5.0, 8.5)	2.5 (1.0, 5.0)	6.0 (4.0, 6.5)	7.3 (6.8, 8.5)	8.0 (6.5, 10.0)
Barcelona, Spain	***n* = 117**	***n* = 108**	***n* = 52**	***n* = 61**	***n* = 90 (53.3%)**	***n* = 27 (16.0%)**	***n* = 18 (10.7%)**	***n* = 34 (20.1%)**
Rheumatoid arthritis	3.3 (1.5, 5.0)	3.5 (1.5, 5.5)	8.0 (6.0, 8.5)	7.5 (5.0, 8.5)	3.0 (1.0, 4.5)	5.5 (3.6, 6.8)	6.0 (5.5, 7.0)	8.5 (8.0, 8.5)
Psoriatic arthritis	4.3 (1.4, 6.3)	4.0 (1.0, 6.5)	7.8 (6.5, 9.0)	6.5 (6.0, 8.5)	2.0 (0.5, 4.0)	6.0 (6.0, 6.5)	7.0 (6.5, 8.0)	8.5 (5.8, 9.5)
Axial spondyloarthropathy	3.5 (2.0, 6.5)	3.5 (2.0, 6.0)	7.0 (6.5, 10.0)	7.0 (6.5, 9.0)	3.0 (1.0, 5.5)	6.8 (6.3, 8.0)	7.5 (7.0, 8.0)	7.0 (6.5, 10.0)
Total Spondyloarthropathies	4.0 (1.8, 6.5)	3.5 (1.4, 6.5)	7.5 (6.5, 9.0)	6.5 (6.0, 8.8)	3.0 (0.8, 5.0)	6.5 (6.0, 7.0)	7.3 (6.5, 8.0)	7.5 (6.5, 10.0)
Chicago, IL, USA	***n* = 69**	***n* = 70**	***n* = 23**	***n* = 22**	***n* = 60 (65.2%)**	***n* = 9 (9.8%)**	***n* = 10 (10.9%)**	***n* = 13 (14.1%)**
Rheumatoid arthritis	3.3 (1.0, 6.0)	4.0 (1.3, 7.0)	8.3 (7.0, 9.5)	7.0 (5.5, 7.8)	3.0 (1.0, 6.0)	6.0 (3.5, 7.0)	8.5 (8.0, 9.5)	7.0 (7.0, 9.0)
Psoriatic arthritis	2.5 (1.0, 3.8)	2.0 (1.0, 4.5)	10.0 (4.0, 10.0)	7.0 (3.5, 10.0)	2.0 (1.0, 4.5)	3.0 (3.0, 3.0)*	NA	10.0 (4.0, 10.0)
Axial spondyloarthropathy	2.0 (1.0, 5.0)	3.0 (2.0, 5.5)	7.0 (7.0, 7.0)*	4.0 (1.0, 7.0)	2.5 (2.0, 5.0)	1.0 (1.0, 1.0)*	7.0 (7.0, 7.0)*	7.0 (7.0, 7.0)*
Total Spondyloarthropathies	2.0 (1.0, 4.5)	2.5 (1.0, 5.0)	7.0 (7.0, 10.0)	5.5 (3.0, 10.0)	2.0 (1.0, 4.5)	2.0 (1.0, 3.0)	7.0 (7.0, 7.0)*	8.5 (5.5, 10.0)
Liverpool, NSW, AUS	***n* = 190**	***n* = 177**	***n* = 67**	***n* = 80**	***n* = 155 (60.3%)**	***n* = 35 (13.6%)**	***n* = 22 (8.6%)**	***n* = 45 (17.5%)**
Rheumatoid arthritis	3.0 (1.0, 5.5)	3.5 (1.0, 6.5)	8.0 (7.0, 9.0)	7.0 (5.0, 8.5)	3.0 (1.0, 5.0)	5.5 (4.5, 6.5)	7.5 (7.0, 8.0)	8.0 (7.0, 9.0)
Psoriatic arthritis	2.8 (1.0, 5.0)	2.5 (1.0, 5.0)	8.0 (7.5, 9.0)	8.0 (5.5, 8.0)	2.0 (0.5, 5.0)	5.3 (2.8, 6.8)	9.0 (7.0, 9.5)	8.0 (8.0, 8.5)
Axial spondyloarthropathy	4.0 (2.0, 5.5)	4.0 (2.0, 5.5)	6.5 (6.5, 6.5)*	4.0 (2.5, 6.5)	4.0 (2.0, 5.5)	3.3 (1.5, 6.5)	NA	6.5 (6.5, 6.5)*
Total Spondyloarthropathies	3.0 (1.0, 5.0)	3.0 (1.0, 5.0)	8.0 (7.0, 9.0)	7.0 (4.5, 8.0)	2.5 (1.0, 5.0)	4.5 (2.0, 6.8)	9.0 (7.0, 9.5)	8.0 (7.0, 8.5)

Neg = Negative, Pos = Positive.
* Only one patient available in this category.
Values were rounded to one decimal place.

Table 4
Median and interquartile ranges for patient global assessment scores (PATGL) and (interquartile ranges) according to positive or negative revised 2011 fibromyalgia criteria and/or HADS-D (hospital anxiety and depression scale–depression) in patients with rheumatoid arthritis (RA) and total spondyloarthropathies (all SpA) in patients from Liverpool, Sydney, Australia.

Primary diagnosis according to physician	All non-missing FM2011 and HADS-D	FM2011 Neg HADS-D Neg	FM2011 Neg HADS-D Pos	FM2011 Pos HADS-D Neg	FM2011 Pos HADS-D Pos
Liverpool, NSW, AUS	***n* = 176**	***n* = 106 (60.2%)**	***n* = 26 (14.8%)**	***n* = 16 (9.1%)**	***n* = 28 (15.9%)**
Rheumatoid arthritis	114	3.0 (1.0, 5.0)	6.0 (3.5, 7.3)	7.5 (7.5, 8.0)	7.5 (6.0, 8.5)
Total Spondyloarthropathies	62	2.3 (1.0, 5.5)	6.0 (3.5, 8.5)	7.0 (2.5, 8.0)	8.5 (5.5, 10.0)
Primary diagnosis according to physician	**All non-missing FM2011 and HADS-D**	**FM2011 Neg**	**HADS-D Neg**	**FM2011 Pos**	**HADS-D Pos**
Liverpool, NSW, AUS	***n* = 176**	***n* = 132**	***n* = 122**	***n* = 44**	***n* = 54**
Rheumatoid arthritis	114	3.5 (1.5, 6.0)	3.5 (1.5, 6.0)	7.5 (6.0, 8.5)	7.0 (5.0, 8.0)
Total Spondyloarthropathies	62	3.0 (1.0, 5.8)	3.0 (1.0, 6.0)	7.5 (5.5, 8.5)	8.0 (4.5, 8.5)

Neg = Negative, Pos = Positive.

identical median PATGL for all diagnoses of 5.0 (Table 2). Differences between diagnoses and settings were neither clinically important nor statistically significant. Agreement of FAST4 with the 2011 FM criteria questionnaire and MDS2 to PHQ-9 and HADS-D (Table 4) adds further evidence of validity of the MDHAQ indices.

A possible impact of elevated PATGL scores on rheumatology index scores was analyzed according to two hypothetical models of minimum DAS28, CDAI, RAPID3, ASDAS, and DAPSA, with categories calculated based on PATGL of 3, the median in FAST4-,MDS2- patients; 5, the median in all patients; or 7, the median of FAST4+,MDS2+ patients, in two categories: a. "extreme," i.e., all other index measures except ESR/CRP were 0, b. "realistic," i.e., minimum expected clinical levels of other

index measures if PATGL=3, 5 or 7 (Table 5). If PATGL=3, remission was possible in the "extreme" models for DAS28, RAPID3 and DAPSA, low for CDAI and ASDAS3; in the "realistic" models, minimum activity/severity was "low" or "moderate." If PATGL=5, minimum activity/severity was "low" for all indices in the "extreme" models, and "moderate" for all but CDAI in the "realistic" models. If PATGL=7, "low" activity/severity was seen in the "extreme" models for all indices other than RAPID3, and "moderate activity/severity" in the "realistic" models for all indices (Table 5).

Patient global assessment is as efficient as swollen joint count (SJC) or tender joint count (TJC) to distinguish active from control treatments in RA clinical trials [7]. However, eligibility for clinical trials generally includes only a small fraction of all RA patients [9,10]. Furthermore, clinical trial patients typically are selected for high inflammatory activity and the absence of comorbidities; overall, fewer than 25%, and sometimes fewer than 10%, meet inclusion criteria [9,10].

Patients seen in routine care generally are more likely to have joint damage, fibromyalgia and/or depression than clinical trial patients [40]. As with any clinical measure, PATGL requires interpretation by a knowledgeable physician or other health professional in formulating clinical decisions, as all clinical measures may be impacted (or not) by comorbidities. For example, ESR may be elevated by neoplasms or infections, in addition to inflammatory activity. The capacity to recognize FM and/or depression on a single 2-page MDHAQ may enhance interpretation of PATGL in clinical care.

It may appear disappointing that median PATGL remains 5.0 in recent years. PATGL may have reflected primarily inflammatory activity in the past, particularly in patients selected for clinical trials [9], while joint and other organ damage and distress due to FM and/or depression, remain common in patients seen in routine care [40]. Perhaps new strategies, including public health and clinical messages toward earlier treatment [41] and awareness of comorbidities, are needed for optimal treatment of RA.

Several important limitations are seen in this study. First, only 3 settings are studied, although similar variation in PATGL according to positive and/or negative screening for FM and/or depression in patients with different diagnoses in 3 different settings in 3 continents suggest possible generalizability. Second, data concerning physical examination, laboratory variables, and imaging were not available, and only hypothetical model scores are presented to characterize a possible impact of these variables on indices. Nonetheless, several reports indicate that DAS28 is substantially elevated in patients with joint damage [12], FM [14], or depression [42], and a PATGL of 5 precludes "remission" according to most indices, and even "low disease activity" if any other measure is minimally elevated (Table 5). Third, some patients did not complete all items on the MDHAQ to analyze complete data; however, about 80% provided complete data, and that seems preferable to no quantitative data in routine care concerning possible FM and/or depression. Fourth, the FAST4 and MDS2 indices studied are validated for screening rather than diagnosis, although the reference questionnaires with which they agree strongly are correlated with diagnosis [25–27]. Fifth, the PATGL query concerned global health for which responses may differ from an arthritis-specific query [43–46]. French el al describe a mean score of 41.4 in a general health format and 43.0 in an arthritis-specific format; the 2 queries were correlated significantly at $r = 0.74$ [44], in the range of test retest reliability of core data set measures [46]. Khan et al. noted that the two formats "are individually not equivalent [but] can be used interchangeably for calculating composite indices for RA activity and assessment [with] excellent concordance in DAS28, CDAI and RAPID3 indices and greater than a 80% absolute agreement (kappa 0.75–0.84)" [45]. Differences of 3–5 fold (30–50% of the scale) described in the current report are considerably greater than differences described between the 2 formats of PATGL, but it would be of interest to examine the magnitude of differences using an arthritis-specific PATGL.

In summary, quantitative 2–3-fold elevations of PATGL according to

Table 5
Minimum level of DAS28-ESR, CDAI, RAPID3 ASDAS-ESR and DAPSA according to PATGL of 3, 5 and 7 in patients with inflammatory arthritis and extreme (all other measures 0 or normal) or (somewhat) more realistic scores with minimal scores of other measures and indices if PATGL is 3.

Measures	Indices for RA DAS28-ESR		CDAI		RAPID3		Index for AxSpA ASDAS-ESR		Index for PsA DAPSA	
	Extr	Real	Extr	Real	Extr	Real	Extr	Real	Extr	Real
SJC	0	1	0	1	–	–	–	–	0	2
TJC	0	2	0	2	–	–	–	–	0	4
DOCGL	–	–	0	2	–	–	–	–	–	–
ESR	20	20	–	–	–	–	20	20	–	–
CRP	–	–	–	–	–	–	–	–	0.5	0.5
FN	–	–	–	–	0	1	–	–	–	–
Pain VNS	–	–	–	–	0	4	–	–	0	3
Back pain	–	–	–	–	–	–	0	3	–	–
Peripheral pain	–	–	–	–	–	–	0	1	–	–
Morning Stiffness	–	–	–	–	–	–	0	1	–	–
PATGL: 3/10	**2.52L**	**3.59M**	**3 M**	**8L**	**3 R**	**8 M**	**1.6L**	**2.0L**	**4 R**	**13L**
PATGL: 5/10	**2.80L**	**3.87M**	**5 L**	**10L**	**5 L**	**10M**	**1.8L**	**2.2M**	**6 L**	**15M**
PATGL: 7/10	**3.08L**	**4.15M**	**7 L**	**12M**	**7 M**	**12 H**	**2.1 L**	**2.4M**	**8 L**	**17H**
Indices	Levels of…									
Categories:	DAS28-ESR		CDAI		RAPID3		ASDAS-ESR*		DAPSA	
Remission	**≤2.6**		**≤2.8**		**≤3**		**<1.3**		**0–4**	
Low	**2.6–3.2**		**2.9–10**		**3.1–6**		**1.3–2.1**		**5–14**	
Moderate	**3.2–5.1**		**10.1–22**		**6.1–12**		**2.2–3.5***		**15–28**	
High	**>5.1**		**>22**		**>12**		**>3.5***		**>28**	

Abbreviations: PATGL= patient global assessment (L = low, M = median, H = high, R = remission), RA = rheumatoid arthritis, AxSpA = axial spondyloarthropathy, PsA= psoriatic arthritis, DAS28-ESR = disease activity score 28 erythrocyte sedimentation rate, CDAI = clinical disease activity index, RAPID3 = routine assessment of patient index data, ASDAS = ankylosing spondylitis disease activity score, DAPSA = disease activity in psoriatic arthritis, Extr = extreme hypothetical index score - all other measures 0 except ESR and CRP, Real = More realistic hypothetical index score of minimum values of other measures if PATGL is 5, NA = Not applicable, i.e., not included in the index, SJC = swollen joint count, TJC = tender joint count, DOCGL = physician global assessment, CRP = C-reactive protein, FN = physical function, PN = Pain, to distinguish active from control treatments in RA.

* =ASDAS categories are remission, low, high, and very high.

– = Individual measure is not included in the index

Categories of indices are also coded by color: high, moderate, low, remission.

positive screening for FM and/or depression was documented in patients with RA or SpA. Availability of PATGL, RAPID3 and screens for FM and depression within a single MDHAQ completed by most patients in 5–10 min provides a feasible approach for busy clinical settings. The capacity to screen easily and quantitatively for FM and depression could enhance interpretation of PATGL for improved clinical decisions and patient outcomes.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2022.152151.

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