Short running head: Fatigue Impact in PsA

Impact of Fatigue on Health-Related Quality of Life and Work Productivity in Psoriatic Arthritis: Findings From a Real-World Survey

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All data that support the findings of this study are the intellectual property of Adelphi Real World. All requests for access should be addressed directly to Elizabeth Holdsworth at elizabeth.holdsworth@adelphigroup.com.

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Abstract (250 words)

Objective

To evaluate fatigue frequency and severity among patients with psoriatic arthritis (PsA) and assess the impact of fatigue severity on patient-reported outcome measures (PROMs) assessing quality of life, function, and work productivity.

Methods

Data were derived from the Adelphi Disease Specific Programme, a cross-sectional survey conducted in 2018 in the United States and Europe. Patients had physician-confirmed PsA. Fatigue was collected as a binary variable and through its severity (0-10 scale, using the Psoriatic Arthritis Impact of Disease (PsAID) fatigue question) from patients; physicians also reported patient fatigue (yes/no). Other PROMs included EQ-5D-5L for health-related quality of life (HRQoL), Health Assessment Questionnaire-Disability Index (HAQ-DI), and Work Productivity and Activity Impairment (WPAI). Multivariate linear regression was used to evaluate the association between fatigue severity and other PROMs.

Results

Among the 831 included patients (mean age 47.5 years, mean disease duration 5.3 years, 46.9% female, 48.1% receiving a biologic), fatigue was reported by 78.3% of patients. Patients with greater fatigue severity had greater disease duration, PsA severity, pain levels, body surface area affected by psoriasis, and swollen and tender joint counts (all $p<0.05$). In multivariate analyses, patients with greater fatigue severity experienced worse physical functioning, HRQoL, and work productivity (all $p<0.001$). Presence of fatigue was under-reported by physicians (reported in only 32.0% of patients who self-reported fatigue).

Conclusion

Prevalence of patient-reported fatigue was high among PsA patients and under-recognized by physicians. Fatigue severity was associated with altered physical functioning, work productivity, and HRQoL.

Introduction

Psoriatic arthritis (PsA) is a chronic, heterogeneous immune-mediated inflammatory disease that occurs in approximatively 20% to 30% of individuals with psoriasis [1]. Skin and nail psoriasis, joint inflammation, axial inflammation, dactylitis, enthesitis, and fatigue are common clinical manifestations of PsA [2]. Individuals with PsA are also at risk of developing a wide range of comorbidities including diabetes, dyslipidemia, cardiovascular disease and immune-mediated affections such as uveitis and inflammatory bowel disease [3,4].

Fatigue is a common symptom of PsA and is considered a prioritized domain of PsA, in particular by outcomes research specialists [5-8] According to Husted et al, around 50% and 30% of patients with PsA experience moderate and severe fatigue, respectively [9] Several other studies confirm that fatigue is commonly experienced by patients with PsA [10,11]. While the effects of fatigue on PsA outcomes have not been widely studied, previous findings have indicated that fatigue in PsA is associated with significant burden and lower work productivity. In particular, data from a US registry revealed a higher level of presenteeism among PsA patients with high fatigue than those with low fatigue [11].

Although successful therapeutic options were once limited, novel medications combined with innovative treatment strategies such as treat-to-target have allowed individuals with PsA to achieve better outcomes overall [12,13]. Despite these advances, studies have shown that PsA continues to significantly impact physical function, mental function, work productivity, and health-related quality of life (HRQoL) [14,15].

Given the introduction of new medicines and treatment strategies for PsA over the past decade, updated research on fatigue in a real-world contemporary population of treated PsA patients will help identify the current prevalence and impact of fatigue on PsA patients and may inform strategies to manage this important symptom in PsA.

The objectives of this study were to understand the frequency and severity of fatigue in PsA, characterize patients according to their level of self-reported fatigue, and evaluate the impact of fatigue severity on HRQoL, physical functioning, health status, and work productivity using validated Patient Reported Outcome Measures (PROMs).

Methods

Study design and population

This analysis used data obtained from the Adelphi Real World Spondyloarthritis (SpA) IV Disease Specific Programme (DSP™) [16], an independent cross-sectional multinational 'real-world' survey conducted between June and August 2018 in the United States, France, Germany, Italy, Spain, and the United Kingdom. Physician-reported data were collected for each patient on demographics, current and past treatment, as well as current and past clinical symptoms and comorbidities. Patient-reported data were collected on validated PROMs which reflect patient assessment of symptom severity, physical function, HRQoL, work productivity, and treatment satisfaction.

A geographically diverse sample of physicians were recruited from public lists of healthcare professionals to participate in the DSP™ by local field agents. Physician participation was financially incentivized, according to fair market research rates. Dermatologists and rheumatologists were eligible to participate in this survey if they were personally responsible for the treatment decisions and management of patients with PsA. Physicians that consented to participate in the survey were instructed to complete a form for their upcoming consultations with patients who had a physician-confirmed diagnosis of PsA and visited the physician for routine PsA care. Each physician was instructed to complete this form for their next 3 to 6 consecutively consulting patients, to mitigate against selection bias and to generate a representative patient sample. Patients were eligible for inclusion if they were ≥18 years old and not involved in a clinical trial at the time of the survey. Completion of the physician-reported questionnaire was undertaken through consultation of existing patient clinical records, explaining missing data for some variables.

These patients were then invited to voluntarily complete a patient-reported form, and upon agreement provide their informed consent to participate in the survey. Patients were not financially compensated for their time. Patient-reported forms were completed by the patient independently from their physician and returned in a sealed envelope, ensuring the patient's responses were kept confidential from their physician. As the data presented in this study focused on PROMs, only data from patients who had completed this self-reported questionnaire (including an assessment of fatigue) was included in this particular analysis.

This research obtained ethics approval from the Western Institutional Review Board (study number 1183030) in the US, and Freiberg Ethics Committee in Europe (study number 02018/1077). Each survey was performed in full accordance with relevant legislation, including the US Health Insurance Portability

and Accountability Act 1996 [17], and Health Information Technology for Economic and Clinical Health Act legislation [18].

Definition of key variables and outcomes

Patient characteristics

Physicians provided data on patient demographics (age, sex, gender, body mass index (BMI), ethnicity, smoking status, and employment status), total number of joints currently affected by PsA (using a 68 Tender Joint Count and 66 Swollen Joint Count), Charlson Comorbidity Index [19], physician-subjective assessments of disease severity, body surface area (BSA) affected by psoriasis, remission status, and biologic use. The survey was non-interventional - no additional tests, treatments, or investigations were performed. Therefore, physicians could only report on data they had available.

Measures of fatigue

Physicians reported the presence or absence of fatigue when asked about their patients' concomitant conditions. Specifically, the physician-reported form included the question "How else is the patient currently affected?", and fatigue was included in a prespecified list of conditions/manifestations. Physicians could answer "Yes" or "No" for each condition, and in addition a "not known" option was available. Physicians were not asked to report the degree of fatigue severity.

Patients also self-reported the presence or absence of fatigue, via an equivalent question relating to concomitant conditions experienced in the patient-reported questionnaire. In addition, patients' self-reported their degree of fatigue severity via the fatigue domain of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire [20], which was scored on a scale of 0 to 10, where 0 corresponds to no fatigue and 10 corresponds to totally exhausted (see following section for details).

PROMs

EQ-5D-5L

The EQ-5D-5L is a standardized generic measure of health status assessed using five dimensions [21]: mobility, self-care, usual activities, pain/discomfort, and anxiety. Each dimension contains five levels: no problems, slight, moderate, severe, and extreme problems. The EQ-5D results were converted into a single utility value using a mapping approach from the EQ-5D-5L to EQ-5D-3L and each country's value set. Utility values are summarized by a score on a continuous scale that is generally between 0 and 1, with 1

corresponding to perfect health and 0 corresponding to death [22]. Patients also provided an overall rating of their current health state on a 20cm Visual Analogue Scale (VAS) from 0 to 100, with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state.

Health Assessment Questionnaire-Disability Index

The Health Assessment Questionnaire-Disability Index (HAQ-DI) ranges from 0 to 3 (0=no difficulty, 3=unable to do) and assesses 20 items in 8 categories (dressing and grooming, hygiene, arising, reach, eating, grip, walking, and common daily activities) [23].

Work Productivity and Activity Impairment questionnaire

The Work Productivity and Activity Impairment (WPAI) questionnaire assesses absenteeism (work time missed), presenteeism (impairment while at work), overall impairment in work productivity (combination of absenteeism and presenteeism), and impairment in daily activities attributed to health problems [24]. The recall period for each of these questions is 7 days. All items are reported as percentage impairment, with higher scores indicating greater impairment.

Psoriatic Arthritis Impact of Disease questionnaire

The PsAID-12 questionnaire is a disease-specific instrument that assesses the general impact of PsA on life [25]. and more specifically 12 domains of health relevant to patients, including pain, fatigue, skin problems, work/leisure activities, functional capacity, discomfort, sleep, coping, anxiety, embarrassment, social participation, and depression. Each domain is scored from 0 to 10 on a numerical rating scale. A summary score between 0 and 10 was calculated, with higher scores indicating greater disease impact.

Statistical analyses

Descriptive statistics were reported for patient characteristics, biologic use, and PROMs, stratified by fatigue severity based on the PsAID-12 fatigue domain scores, which were grouped using the following categories: 0, 1 to 3, 4 to 7, or >7, for the purposes of analysis. Patients who did not report a PsAID-12 fatigue score were excluded from the analyses. The mean and standard deviation were reported for continuous variables, and frequency counts and percentages were reported for categorical variables. Bivariate analysis was conducted with numeric variables compared using an ANOVA; ordered categorical variables were compared using a Kruskall-Wallis test, and categorical variables were compared using a chi-squared test.

Multivariate linear regression was performed to evaluate the association between patient-reported fatigue severity and key outcomes based on the PROMs. Model coefficients and associated p-values were reported.

Each model was adjusted for the following confounding factors: age, gender, BMI, percent BSA affected by psoriasis, number of joints affected (as reported by the physician), current pain, and the Charlson Comorbidity Index score [19], all taken from the physician-reported form. Missing data were not imputed; therefore, the base of patients for analysis could vary from variable to variable and was reported separately for each analysis. Patients with missing values were excluded from this analysis. Thus, the full models could be run on a reduced population ranging from 386 to 716 patients depending on the availability of PROM data.

Descriptive statistics were also reported to evaluate patient characteristics stratified by the presence of anxiety/depression. Multivariate linear models were then developed to evaluate the association between anxiety/depression and the PROMs. Further information on the methodology for these analyses is provided in Appendix A.

Patient-physician concordance regarding the presence of fatigue was analyzed and reported using a kappa (κ) statistic [26]. The significance level for all analyses was set at 5%, and all tests were two-sided. All analyses were conducted using Stata v16.0 [27].

Results

Patient demographic and clinical characteristics

A total of 831 patients who completed the self-reported questionnaire with PROMs were included in this analysis. The mean patient age was 47.5 years and the mean disease duration was 5.3 years, 46.9% of patients were female and 48.1% were receiving a biologic (Tables 1 and 2).

Among the included patients, 180 (21.7%), 445 (53.5%), 142 (17.1%) and 64 (7.7%) reported fatigue severity scores of 0, 1 to 3, 4 to 7, and >7, respectively (Table 1). Patients with greater fatigue severity were older on average ($p<0.001$). The proportion of females ranged from 34.4% (fatigue score=0) to 57.8% (fatigue score>7) ($p<0.001$). The proportion of patients working full time was 71.0%, 64.2%, 43.6%, and 38.3% among patients with a PsAID fatigue score of 0, 1 to 3, 4 to 7, and >7, respectively ($p<0.001$). Patients with greater PsAID fatigue severity scores were less likely to be in full-time employment, with a greater number of patients on long-term sick leave, retired, unemployed and homemakers.

Patients with higher fatigue scores generally had a greater time since diagnosis and onset of symptoms, more severe disease, greater pain levels, a higher percent BSA affected by psoriasis, higher number of

swollen and tender joints, and anxiety/depression was more commonly present (all p<0.001, Table 2). Moderate-to-severe PsA was reported among 59.4% of patients with a PsAID fatigue score >7, compared with only 5.0% of patients with a fatigue score of 0. The mean PsAID pain score was nearly 5 times higher among patients with a fatigue score >7 than those with a PsAID fatigue score of 0, at 7.83 and 1.61, respectively. Percent BSA affected by psoriasis ranged from 2.2% (PsAID fatigue score=0) to 9.2% (PsAID fatigue score of 4-7). Physician-reported anxiety/depression affected 6.1%, 12.4%, 24.7%, and 47.5% of patients reporting a PsAID fatigue score of 0, 1 to 3, 4 to 7, and >7, respectively. Biologic use was not significantly different among the fatigue score groups, with an average of 48.1% of patients receiving biologics overall (p=0.059).

Patients also provided their own assessment of the severity of their joint and skin symptoms. Severe joint symptoms were reported by 0%, 1%, 11% and 25% of patients with PsAID fatigue scores of 0, 1 to 3, 4 to 7, and >7, respectively (p<0.001), and severe skin symptoms were reported by 0%, 1%, 6% and 11% of patients with fatigue severity of 0, 1 to 3, 4 to 7, and >7, respectively (p<0.001).

PROMs

The EQ-5D-5L health utility values ranged from 0.52 (fatigue score>7) to 0.95 (fatigue score=0), and the VAS score ranged from 52.9% (fatigue score>7) to 87.4% (fatigue score=0) (Figure 1a and 1b). Results from the multivariate linear regression demonstrated increased PsAID fatigue scores were significantly associated with lower utility values and VAS scores (p<0.001 for both, Table 3).

Physical functioning based on HAQ-DI scores ranged from 0.09 among patients with a fatigue score of 0 to 1.35 among patients with a fatigue score >7 (Figure 1c). Greater HAQ-DI scores were significantly associated with greater fatigue severity scores in the multivariate linear model (p<0.001, Table 3).

Patients with a PsAID fatigue score of 0 reported 6.2% productivity loss, whereas patients with a PsAID fatigue score >7 reported a productivity loss of 40.4%. Overall work impairment ranged from 9.1% (fatigue score=0) to 42.5% (fatigue score>7), and total activity impairment ranged from 8.0% (fatigue score=0) to 58.5% (fatigue score>7) (Figure 1d). Greater PsAID fatigue scores was significantly associated with increased work presenteeism, overall work impairment, and total activity impairment (p<0.001, Table 3).

PsAID-12 summary scores were 0.39, 1.85, 4.76, and 6.6 for patients with a PsAID fatigue score of 0, 1 to 3, 4 to 7, and >7, respectively (p<0.001, Figure 1e). Greater fatigue severity scores were significantly associated with higher PsAID-12 summary scores, after adjusting for confounding factors in the multivariate linear model (p<0.001, Table 3). In particular, greater pain levels, as reported in the PsAID,

were associated with greater PsAID fatigue scores, after adjusting for confounding factors (coefficient=0.475, 95% confidence intervals [CI]=0.399, 0.552; p<0.001).

The association of anxiety/depression with patient characteristics and PROMs was also evaluated, in order to assess its similarity in outcomes when compared with fatigue. Similarly, to fatigue, anxiety/depression was associated with worse HRQoL, physical functioning, and overall work and total activity impairment. Patients experiencing anxiety/depression also had a higher mean PsAID-12 summary score.

Patient-physician concordance on the presence of fatigue

Of the 831 patients with complete information, 651 (78.3%) patients reported to have fatigue, whereas physicians reported fatigue as a manifestation in 208 patients, i.e., 25.0% of the 831 patients and 32.0% of the 651 patients who self-reported fatigue; leading to a low agreement (kappa, 0.13, Supplementary Table 1).

Discussion

In this cross-sectional survey of patients with PsA and their physicians, greater PsAID fatigue severity scores were significantly associated with lower patient-reported health status, physical functioning, work productivity, and HRQoL. Patient characteristics also differed significantly based on the level of PsAID fatigue severity; patients with greater fatigue severity were generally older on average, experienced greater PsA disease severity and pain levels, had a longer time since diagnosis and symptom onset, and anxiety/depression was more commonly reported.

A number of previous studies have evaluated the association between fatigue in PsA and patient characteristics, health status, physical functioning, and HRQoL; overall, findings were similar to this study though different PROMs were used. In a Brazilian cross-sectional observational study of 101 patients with PsA, fatigue (assessed via the Functional Assessment of Chronic Illness Therapy – Fatigue Scale, FACIT-F) was observed to correlate with physical functioning (assessed via the HAQ-DI) and HRQoL (assessed via the SF-36) [28]. A Turkish multicenter study of 1028 patients with PsA reported a correlation between fatigue (assessed via a 10-point VAS) and HRQoL (assessed via the PsAQoL) [29-31]. Linear regression analysis of cross-sectional data from 499 patients attending a Canadian PsA clinic showed **f**atigue (assessed using the modified Fatigue Severity Scale) to be associated with female gender, physical functioning (assessed using the HAQ-DI), poorer psychological functioning (assessed using the SF-36), and pain (assessed using the SF-36) [9,32]. Furthermore, in a study by Walsh et al that analyzed data for 107 patients

from a US registry, presenteeism (assessed using the Work Limitations Questionnaire) was significantly associated with fatigue (as measured by PsAQoL and Bath Ankylosing Spondylitis Disease Activity Index), after adjusting for disease activity and depression [5].

Almost 80% of patients reported some level of fatigue in this study, with 25% reporting a PsAID fatigue of level ≥4 and 8% a PsAID fatigue of level >7 for the PsAID fatigue domain [20]. Previous studies have also identified a high prevalence of fatigue in PsA, with estimates ranging from 49% to 60% [5,9,33]. Differences in these estimates are in part due to the different definitions and measurements used to identify fatigue, as these studies used measures based on moderate fatigue [9], high fatigue [5], and clinically important fatigue [33].

A lack of concordance between physicians and patients in their evaluation of the presence of fatigue was also observed, with physicians under-reporting fatigue compared with patients (25% vs. 78%, respectively). It is however noteworthy that the questions on fatigue for patients and physicians were not symmetrical, with physicians reporting fatigue (yes/no) as a concomitant condition, which may explain partly this lack of concordance. A previous study by Orbai et al used international patient and physician focus groups to identify the importance of fatigue, among other domains, in PsA; 78% of patients and 63% of physicians reported that fatigue was important to measure in all studies [34]. Desthieux et al applied the PsAID-12 questionnaire to evaluate the discordance in patient and physician-reported fatigue, and similarly found higher fatigue levels when reported by patients than physicians [35]. The consequences of patient and physician misalignment have been previously documented in other disease areas, but this research merits further investigation in PsA [36-38].

Anxiety/depression was more common among patients with greater fatigue severity. A review by Mathew et al highlighted the mental health burden associated with PsA, showing that a large number of patients with PsA also suffer from depression and anxiety, both of which are commonly associated with fatigue. Other studies have found that the relationship between fatigue and anxiety/depression is highly correlated [8,9,28]. A multidisciplinary European working group concluded that the interdependence of fatigue and anxiety, together with pain, may form a "vicious cycle" with negative effects on PsA symptoms [39]. As such, anxiety/depression was not considered a confounding factor in our multivariate linear models because, given the strong correlation, adjustment for these variables could impair the ability to accurately evaluate the relationship between fatigue and the outcomes measured, a concept known as collinearity. This illustrates the concept that fatigue is multifactorial. In patients with anxiety and depression, addressing these factors could potentially improve some of the fatigue as well (Figure 2).

This study has several limitations. First, the DSP™ is not based on a true random sample of physicians or patients; while certain inclusion criteria governed the selection of the participating physicians, participation was influenced by their willingness to complete the survey. Identification of the target patient group was also based on the clinical judgement of the corresponding physician and not a formalized diagnostic checklist; however, this was representative of physicians' classification of the patient. Physicians were asked to provide data for a consecutive series of patients to avoid selection bias, but no formal patient selection verification procedures were used. As patient recruitment was based on successive physician consultations with PsA patients, patients recruited may be those who visited their physician frequently and therefore more severely affected than those who consulted their physician less frequently. The cross-sectional design of this study also prevents any conclusions about causal relationships; however, identification of significant associations is possible. While confounding factors were adjusted for in the multivariate linear models, the lack of certain data reduced the sample size for the multivariate analyses; and furthermore, certain underlying confounding factors could not be accounted for. For example, information on fibromyalgia, enthesitis, dactylitis, and axial disease were not collected in this study. Recall bias might also have affected the responses of both patients and physicians to the record forms, which is a common limitation of surveys. However, the data for these analyses were collected at the time of each patient's appointment, which helps limit the impact of recall bias. While the study design included methods to ensure that physicians and staff were unaware of patient responses on the patient-reported forms, it was not possible to confirm that no information exchange occurred between physicians and their patients. This has the potential to influence patient responses to the PROMs.

This study demonstrated the substantial impact fatigue severity has on health status, physical function, work productivity, and HRQoL in a real-world setting. Despite many patients receiving advanced therapy, fatigue is still highly prevalent among patients with PsA and under-recognized by physicians. These findings highlight the importance of prioritizing fatigue in the research and management of PsA. Additional research that evaluates the causes and potential interventions to improve fatigue in PsA are needed.

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Figure Legend

Figure 1. PROMs by severity of fatigue (as defined by PsAID fatigue score) for (a) EQ-5D-5L health utility index, (b) EQ-5D-5L VAS, (c) HAQ-DI, (d) WPAI, and (e) PsAID-12 summary score

EQ-5D-5L, EuroQol 5 Dimension questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; PsAID, Psoriatic Arthritis Impact of Disease questionnaire; SD, standard deviation; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire

Means and standard deviations are reported. P values were generated using analysis of variance.

Figure 2. Inter-relationship of patient characteristics and symptoms/comorbidities with humanistic and economic endpoints in PsA

Table 1. Demographic characteristics by severity of fatigue

	Total (N=831)	Fatigue score 0[a] (N=180)	Fatigue score 1–3[a] (N=445)	Fatigue score 4–7[a] (N=142)	Fatigue score >7[a] (N=64)	P-value
Age, years						<0.001[c]
Mean (SD)	47.5 (13.4)	45.3 (13.0)	46.5 (13.7)	51.2 (12.6)	52.5 (12.2)	
Median [range]	46 [18, 87]	45 [18, 82]	45 [18, 83]	51.5 [24, 87]	54.5 [23, 81]	
Sex, n (%) female	390 (46.9)	62 (34.4)	213 (47.9)	78 (54.9)	37 (57.8)	<0.001001[d]
BMI, kg/m2						0.530[c]
N	830	180	445	142	63	
Mean (SD)	26.6 (4.9)	26.8 (5.4)	26.4 (4.8)	27.1 (4.7)	26.9 (4.7)	
Median [range]	26.0 [15.6, 64.0]	25.9 [18.7, 57.6]	25.9 [17.4, 64.0]	26.3 [17.6, 46.4]	26.4 [15.6, 41.4]	
Race/Ethnicity, n (%)						0.229[d]
White	768 (92.4)	167 (92.8)	412 (92.6)	130 (91.6)	59 (92.2)	
African American/Afro-Caribbean	11 (1.3)	0 (0.0)	6 (1.4)	4 (2.8)	1 (1.6)	
Asian – Indian subcontinent	7 (0.8)	2 (1.1)	3 (0.7)	1 (0.7)	1 (1.6)	
Asian – other	8 (1.0)	3 (1.7)	4 (0.9)	0 (0.0)	1 (1.6)	
Hispanic/Latino	14 (1.7)	4 (2.2)	7 (1.6)	3 (2.1)	0 (0.0)	
Other[b]	23 (2.8)	4 (2.2)	13 (2.9)	4 (2.8)	2 (3.1)	
Smoking status, n (%)						0.003[d]
N	751	160	398	135	58	
Current smoker	153 (20.4)	30 (18.8)	81 (29.4)	22 (16.3)	20 (34.5)	
Ex-smoker	206 (27.4)	59 (36.9)	93 (23.4)	42 (31.1)	12 (20.7)	
Never smoked	392 (52.2)	71 (44.4)	224 (56.3)	71 (52.6)	26 (44.8)	

Employment status, n (%)						<0.001[d]
N	812	176	436	140	60	
Working full-time	489 (60.2)	125 (71.0)	280 (64.2)	61 (43.6)	23 (38.3)	
Working part-time	66 (8.13)	11 (6.3)	40 (9.2)	14 (10.0)	1 (1.7)	
On long-time sick leave	19 (2.3)	2 (1.1)	5 (1.2)	4 (2.9)	8 (13.3)	
Homemaker	66 (8.1)	10 (5.7)	28 (6.4)	19 (13.6)	9 (15.0)	
Student	21 (2.6)	7 (4.0)	11 (2.5)	1 (0.7)	2 (3.3)	
Retired	108 (13.3)	16 (9.1)	55 (12.6)	27 (19.3)	10 (16.7)	
Unemployed	43 (5.3)	5 (2.8)	17 (3.9)	14 (10.0)	7 (11.7)	

[a]Score for the fatigue domain of the PsAID-12

[b]Includes African, Chinese, Middle Eastern, Mixed race, and Other

[c]Analysis of variance

[d]Chi-squared test

BMI, body mass index.

Table 2. Clinical characteristics by severity of fatigue

	Total (N=831)	Fatigue score 0[a] (N=180)	Fatigue score 1–3[a] (N=445)	Fatigue score 4–7[a] (N=142)	Fatigue score >7[a] (N=64)	P-value
Time since symptom onset, years						<0.001[d]
N	505	98	267	87	53	
Mean (SD)	7.3 (8.2)	7.2 (7.9)	5.4 (6.9)	10.8 (9.1)	11.2 (10.3)	
Median [Range]	4.1 [0, 45.3]	5.1 [0, 45.3]	2.2 [0, 39.4]	9.3 [0.0, 35.9]	8.3 [0.5, 43.7]	
Time since diagnosis, years						<0.001[d]
N	683	149	369	109	56	
Mean (SD)	5.3 (6.6)	4.8 (5.9)	4.5 (6.0)	6.9 (7.6)	8.0 (8.7)	
Median [Range]	2.8 [0.0, 43.2]	2.3 [0.0, 35.3]	2.2 [0.0, 39.4]	4.1 [0.0, 34.5]	5.6 [0.0, 43.2]	
Current overall PsA severity[b], n (%)						<0.001[e]
N	831	180	445	142	64	
Mild	623 (75.0)	171 (95.0)	350 (78.7)	76 (53.5)	26 (40.6)	
Moderate	189 (22.7)	9 (5.0)	89 (20.0)	59 (41.6)	32 (50.0)	
Severe	19 (2.3)	0 (0.0)	6 (1.4)	7 (4.9)	6 (9.4)	
Overall pain level[b,c]						<0.001[d]
N	831	180	445	142	64	
Mean (SD)	2.8 (1.7)	1.6 (1.0)	2.6 (1.3)	4.0 (1.8)	4.6 (2.1)	
Median [Range]	2 [1, 9]	1 [1, 7]	2, [1, 8]	4 [1, 9]	5 [1, 9]	
PsAID pain score						<0.001[d]
N	830	180	445	142	63	
Mean (SD)	3.67 (2.32)	1.61 (1.30)	3.18 (1.29)	5.98 (1.83)	7.83 (2.00)	
Median [Range]	3 [1, 11]	1 [1, 11]	3 [1, 9]	6 [1, 11]	8 [2, 11]	
Current BSA, %						<0.001[d]
N	664	154	343	119	48	
Mean (SD)	5.9 (8.1)	2.2 (3.7)	6.2 (7.7)	9.2 (10.2)	7.6 (10.8)	
Median [Range]	2.9 [0.0, 53.6]	0.7 [0.0, 24.4]	3.6 [0.0, 53.6]	5.4 [0.0, 50.6]	3.0 [0.0, 49.8]	
66 swollen joint count						<0.001[d]
N	206	44	91	38	33	
Mean (SD)	3.1 (6.2)	0.6 (1.8)	2.3 (3.9)	7.1 (11.3)	4.2 (4.8)	
Median [Range]	1 [0, 59]	0 [0, 10]	0 [0, 20]	3.5 [0, 59]	3 [0, 20]	

68 tender joint count						<0.001[d]
N	197	39	93	33	32	
Mean (SD)	3.8 (5.1)	1.1 (3.2)	2.8 (3.5)	7.6 (7.8)	6.2 (4.3)	
Median [Range]	2 [0, 42]	0 [0, 19]	2 [0, 20]	6 [0, 42]	5.5 [0, 22]	
Patient in remission[b], n (%)						<0.001[f]
N	785	170	418	135	62	
Yes	322 (41.0)	121 (71.2)	149 (35.7)	33 (24.4)	19 (30.7)	
Anxiety/depression[b], n (%)						<0.001[f]
N	831	180	445	142	61	
Yes	125 (15.0)	11 (6.1)	55 (12.4)	35 (24.7)	24 (37.5)	
Biologic use, n (%)	400 (48.1)	91 (50.6)	196 (44.0)	76 (53.5)	37 (57.8)	0.059[f]

[a]Score for the fatigue domain of the PsAID-12

[b]In the physician's opinion

[c]From a numeric rating scale, on which 1 = no pain and 10 = worst possible pain

[d] Analysis of variance

[e]Kruskall-Wallis test

[f]Chi-squared test

BSA, body surface area; PsAID, Psoriatic Arthritis Impact of Disease questionnaire

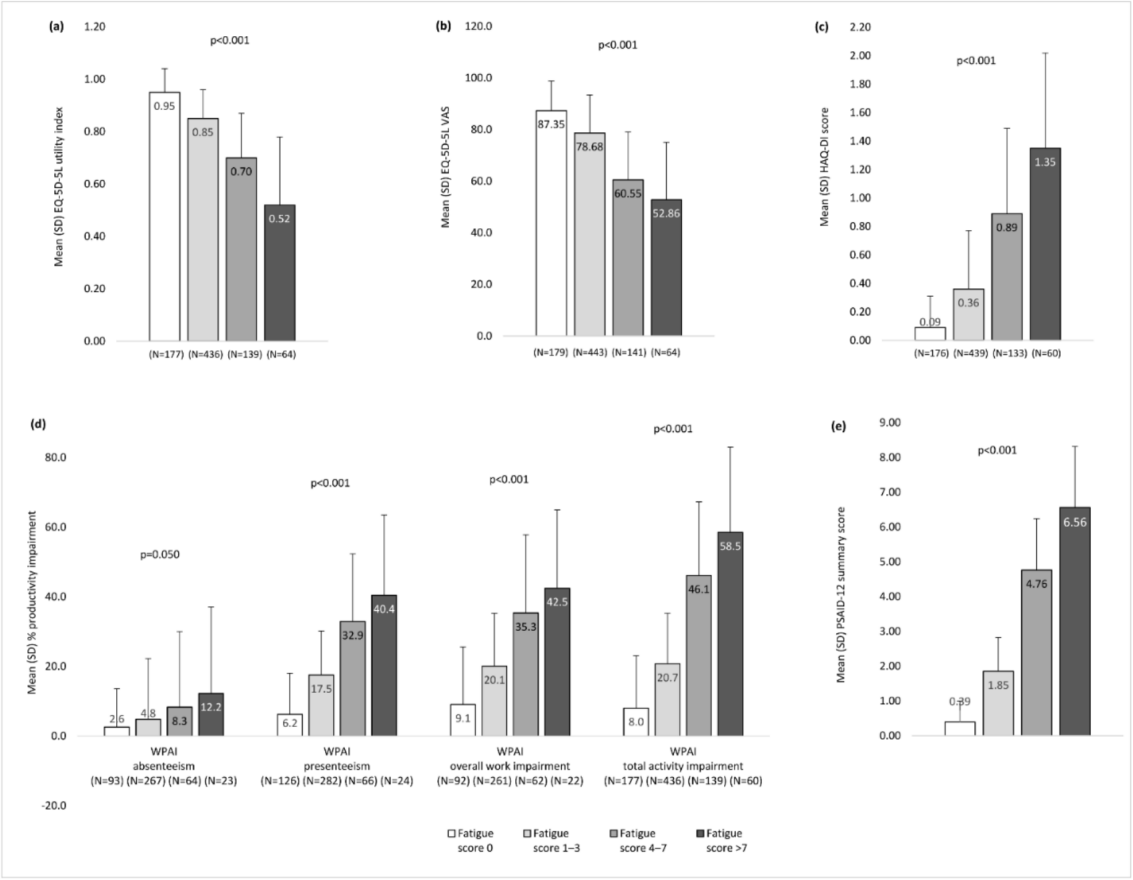
Table 3. Linear regression analysis of PROMs by fatigue score

	Coefficient	95% CI	P-value
EQ-5D-5L health utility index	-0.028	-0.036, -0.021	<0.001
EQ-5D-5L VAS	-2.23	-3.08, -1.37	<0.001
HAQ-DI score	0.098	0.075, 0.121	<0.001
WPAI absenteeism, %	0.740	-0.149, 1.63	0.102
WPAI presenteeism, %	2.69	1.67, 3.71	<0.001
WPAI overall work impairment, %	2.81	1.51, 4.11	<0.001
WPAI total activity impairment, %	4.03	3.13, 4.93	<0.001
PsAID-12 summary score	0.573	0.509, 0.636	<0.001

CI, confidence interval; EQ-5D-5L, EuroQol 5 Dimension questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; PROMs, patient reported outcome measures; PsAID, Psoriatic Arthritis Impact of Disease questionnaire; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire

Confounding factors controlled in the models were age, gender, body mass index, percent body surface area (BSA) affected by psoriasis, number of joints affected, current pain, and Charlson Comorbidity Index score

Figure 1. PROMs by severity of fatigue for (a) EQ–5D–5L health utility index, (b) EQ–5D–5L VAS, (c) HAQ-DI, (d) WPAI, and (e) PsAID–12 summary score



EQ–5D–5L, EuroQol 5 Dimension questionnaire; HAQ-DI, Health Assessment Questionnaire–Disability Index; PsAID, Psoriatic Arthritis Impact of Disease questionnaire; SD, standard deviation; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire

Means and standard deviations reported. P values were generated using analysis of variance.