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

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*ABSTRACT.* ***Objective.*** To evaluate fatigue frequency and severity among patients with psoriatic arthritis (PsA) and assess the effect 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 12-item Psoriatic Arthritis Impact of Disease fatigue question) from patients; physicians also reported patient fatigue (yes/no). Other PROMs included the 5-level EuroQol 5-dimension questionnaire (EQ-5D-5L) for health-related quality of life (HRQOL), Health Assessment Questionnaire–Disability Index, and Work Productivity and Activity Impairment Questionnaire. 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 yrs, mean disease duration 5.3 yrs, 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 underreported by physicians (reported in only 32% of patients who self-reported fatigue).

***Conclusion.*** Prevalence of patient-reported fatigue was high among patients with PsA and underrecognized by physicians. Fatigue severity was associated with altered physical functioning, work productivity, and HRQOL.

*Key Indexing Terms:* fatigue, health-related quality of life, patient-reported outcomes, psoriatic arthritis, real-world data, work productivity

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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 diseases 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, approximately 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 patients with PsA 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 affect 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 effect of fatigue on these 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 effect 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 using validated PROMs that 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 the survey if they were personally responsible for the treatment decisions and management of patients with PsA. Physicians who 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 aged ≥ 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) were 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 (study number 02018/1077) in Europe. 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, 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 noninterventional—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 an additional "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, through an equivalent question relating to concomitant conditions experienced in the patient-reported questionnaire. In addition, patients self-reported their degree of fatigue severity through 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 the following section for details).

- *PROMs.*

1. *EQ-5D-5L.* The 5-level EuroQol 5-dimension questionnaire (EQ-5D-5L) is a standardized generic measure of health status assessed using 5 dimensions[21]: mobility, self-care, usual activities, pain/discomfort, and anxiety. Each dimension contains 5 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 20 cm visual analog scale (VAS) from 0 to 100, with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state.

2. *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]

3. *Work Productivity and Activity Impairment Questionnaire*. The Work Productivity and Activity Impairment Questionnaire (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.

4. *PsAID-12*. The PsAID-12 questionnaire is a disease-specific instrument that assesses the general effect of PsA on life[20] 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 SD 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 compared using a Kruskall-Wallis test, and categorical variables 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, sex/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.

Patient-physician concordance regarding the presence of fatigue was analyzed and reported using a $\kappa$ statistic.[25] The significance level for all analyses was set at 5%, and all tests were 2-sided. All analyses were conducted using Stata v16.0.[26]

## 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, 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%, 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 who were on long-term sick leave, retired, unemployed, or homemakers.

Patients with higher fatigue scores generally had a longer 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% 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 7.8 and 1.6, 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%, 24.6%, and 39.3% 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 ($P = 0.06$).

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 ($P < 0.001$; data not shown).

*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; Figures 1A,B). 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 (presenteeism), 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% (fatigue score = 0) to 58.5% (fatigue score > 7; Figure 1D). Greater PsAID fatigue scores were 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 6.56 for patients with a PsAID fatigue score of 0, 1 to 3, 4 to 7, and

*Table 1.* Demographic characteristics by severity of fatigue.

| | Fatigue Score | | | | | |
|---|---|---|---|---|---|---|
| | Total, n = 831 | 0[a], n = 180 | 1-3[a], n = 445 | 4-7[a], n = 142 | > 7[a], n = 64 | *P* |
| Age, yrs | | | | | | < 0.001* |
| Mean (SD) | 47.5 (13.4) | 45.3 (13.0) | 46.5 (13.7) | 51.2 (12.6) | 52.5 (12.2) | |
| Median (range) | 46.0 (18.0-87.0) | 45.0 (18.0-82.0) | 45.0 (18.0-83.0) | 51.5 (24.0-87.0) | 54.5 (23.0-81.0) | |
| Female sex, n (%) | 390 (46.9) | 62 (34.4) | 213 (47.9) | 78 (54.9) | 37 (57.8) | < 0.001** |
| BMI, kg/m$^2$ | | | | | | 0.53* |
| 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 (%) | | | | | | 0.23** |
| 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) | 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) | 3 (1.7) | 4 (0.9) | 0 (0) | 1 (1.6) | |
| Hispanic/Latino | 14 (1.7) | 4 (2.2) | 7 (1.6) | 3 (2.1) | 0 (0) | |
| Other[b] | 23 (2.8) | 4 (2.2) | 13 (2.9) | 4 (2.8) | 2 (3.1) | |
| Smoking status, n (%) | | | | | | 0.003** |
| n | 751 | 160 | 398 | 135 | 58 | |
| Current smoker | 153 (20.4) | 30 (18.8) | 81 (20.4) | 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** |
| n | 812 | 176 | 436 | 140 | 60 | |
| Working full-time | 489 (60.2) | 125 (71) | 280 (64.2) | 61 (43.6) | 23 (38.3) | |
| Working part-time | 66 (8.1) | 11 (6.3) | 40 (9.2) | 14 (10) | 1 (1.7) | |
| On long-term 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) | |
| Student | 21 (2.6) | 7 (4) | 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) | 7 (11.7) | |

[a] Score for the fatigue domain of the PsAID-12. [b] Includes African, Chinese, Middle Eastern, mixed race. * ANOVA. ** Chi-square test. PsAID-12: 12-item Psoriatic Arthritis Impact of Disease.

> 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 = 0.48, 95% CI 0.40-0.55, $P < 0.001$).

The association of anxiety/depression with patient characteristics and PROMs was also evaluated, 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 higher mean PsAID-12 summary scores.

*Patient-physician concordance on the presence of fatigue.* Of the 831 patients with complete information, 651 (78.3%) patients self-reported as having fatigue, whereas physicians reported fatigue as a manifestation in 208 patients (ie, 25% of the 831 patients and 32% of the 651 patients who self-reported fatigue). This led to a low agreement (κ 0.13, Supplementary Table S1, available with the online version of this article).

## 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 using the Functional Assessment of Chronic Illness Therapy – Fatigue Scale [FACIT-F]) was observed to correlate with physical functioning (assessed using the HAQ-DI) and HRQOL (assessed using the 36-item Short Form Health Survey [SF-36]).[27] A Turkish multicenter study of 1028 patients with PsA reported a correlation between fatigue

*Table 2.* Clinical characteristics by severity of fatigue.

| | Total, n = 831 | Fatigue Score 0[a], n = 180 | 1-3[a], n = 445 | 4-7[a], n = 142 | > 7[a], n = 64 | *P* |
|---|---|---|---|---|---|---|
| Time since symptom onset, yrs | | | | | | < 0.001* |
| 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 (0.0-45.3) | 5.1 (0.0-45.3) | 2.2 (0.0-39.4) | 9.3 (0.0-35.9) | 8.3 (0.5-43.7) | |
| Time since diagnosis, yrs | | | | | | < 0.001* |
| 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** |
| n | 831 | 180 | 445 | 142 | 64 | |
| Mild | 623 (75) | 171 (95) | 350 (78.7) | 76 (53.5) | 26 (40.6) | |
| Moderate | 189 (22.7) | 9 (5) | 89 (20) | 59 (41.6) | 32 (50) | |
| Severe | 19 (2.3) | 0 (0) | 6 (1.4) | 7 (4.9) | 6 (9.4) | |
| Overall pain level[b,c] | | | | | | < 0.001* |
| 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-12 pain score | | | | | | < 0.001* |
| n | 830 | 180 | 445 | 142 | 63 | |
| Mean (SD) | 3.7 (2.3) | 1.6 (1.3) | 3.2 (1.3) | 5.98 (1.8) | 7.8 (2.0) | |
| Median (range) | 3 (1-11) | 1 (1-11) | 3 (1-9) | 6 (1-11) | 8 (2-11) | |
| Current BSA, % | | | | | | < 0.001* |
| 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-joint swollen joint count | | | | | | < 0.001* |
| 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-joint tender joint count | | | | | | < 0.001* |
| 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*** |
| n | 785 | 170 | 418 | 135 | 62 | |
| Yes | 322 (41) | 121 (71.2) | 149 (35.7) | 33 (24.4) | 19 (30.7) | |
| Anxiety/depression[b], n (%) | | | | | | < 0.001*** |
| n | 831 | 180 | 445 | 142 | 64 | |
| Yes | 125 (15) | 11 (6.1) | 55 (12.4) | 35 (24.7) | 24 (37.5) | |
| Biologic use, n (%) | 400 (48.1) | 91 (50.6) | 196 (44) | 76 (53.5) | 37 (57.8) | 0.06*** |

[a] Score for the fatigue domain of the PsAID-12. [b] In the physician's opinion. [c] From a numerical rating scale, on which 1 = no pain and 10 = worst possible pain. * ANOVA. ** Kruskall-Wallis test. *** Chi-square test. BSA: body surface area; PsAID-12: 12-item Psoriatic Arthritis Impact of Disease.

(assessed using a 10-point VAS) and HRQOL (assessed using the PsAQoL).[28-30] Linear regression analysis of cross-sectional data from 499 patients attending a Canadian PsA clinic showed fatigue (assessed using the modified Fatigue Severity Scale) to be associated with female sex, physical functioning (assessed using the HAQ-DI), poorer psychological functioning (assessed using the SF-36), and pain (assessed using the SF-36).[9,31] Further, 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 the present 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%.[5,9,32] 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.[32]

A lack of concordance between physicians and patients in their evaluation of the presence of fatigue was also observed, with physicians underreporting fatigue compared with patients

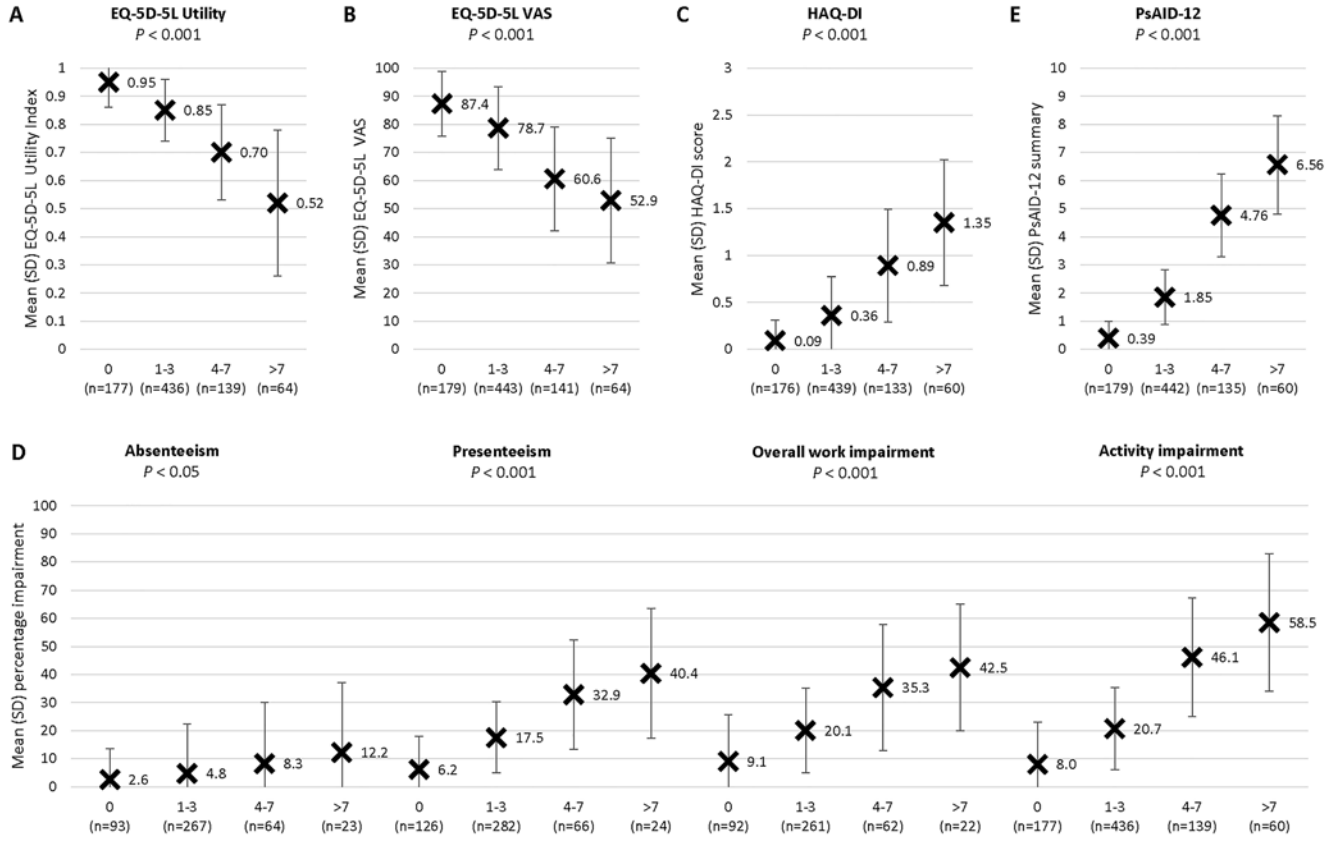


*Figure 1.* PROMs by severity of fatigue (as defined by PsAID fatigue score) for (A) EQ-5D-5L health utility index, (B) EQ-5D-5L VAS, (C) HAQ-DI, (D) WPAI, and (E) PsAID-12 summary score. Means and SDs are reported. *P* values were generated using ANOVA. EQ-5D-5L: 5-level EuroQol 5-dimension questionnaire; HAQ-DI: Health Assessment Questionnaire–Disability Index; PROMs: patient-reported outcome measures; PsAID: Psoriatic Arthritis Impact of Disease; VAS: visual analog scale; WPAI: Work Productivity and Activity Impairment questionnaire.

*Table 3.* Linear regression analysis of PROMs by fatigue score.

| | Coefficient | 95% CI | *P* |
|---|---|---|---|
| EQ-5D-5L health utility index | −0.03 | −0.04 to −0.02 | < 0.001 |
| EQ-5D-5L VAS | −2.23 | −3.08 to −1.37 | < 0.001 |
| HAQ-DI score | 0.098 | 0.08 to 0.12 | < 0.001 |
| WPAI absenteeism, % | 0.74 | −0.15 to 1.63 | 0.10 |
| WPAI presenteeism, % | 2.69 | 1.67 to 3.71 | < 0.001 |
| WPAI overall work impairment, % | 2.81 | 1.51 to 4.11 | < 0.001 |
| WPAI total activity impairment, % | 4.03 | 3.13 to 4.93 | < 0.001 |
| PsAID-12 summary score | 0.57 | 0.51 to 0.64 | < 0.001 |

Confounding factors controlled in the models were age, sex/gender, BMI, percent BSA affected by psoriasis, number of joints affected, current pain, and Charlson Comorbidity Index score. BSA: body surface area; EQ-5D-5L: 5-level EuroQol 5-dimension questionnaire; HAQ-DI: Health Assessment Questionnaire–Disability Index; PROMs: patient-reported outcome measures; PsAID: Psoriatic Arthritis Impact of Disease; VAS: visual analog scale; WPAI: Work Productivity and Activity Impairment questionnaire.

(25% vs 78%). It is worth noting, however, 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.[33] 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.[34] The consequences of patient and physician misalignment have been previously documented in other disease areas, but this research merits further investigation in PsA.[35-37]

Anxiety/depression was more common among patients with greater fatigue severity. A review by Mathew and Chandran 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.[38] Other studies have found that the relationship between fatigue and anxiety/depression is highly correlated.[8,9,27] 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

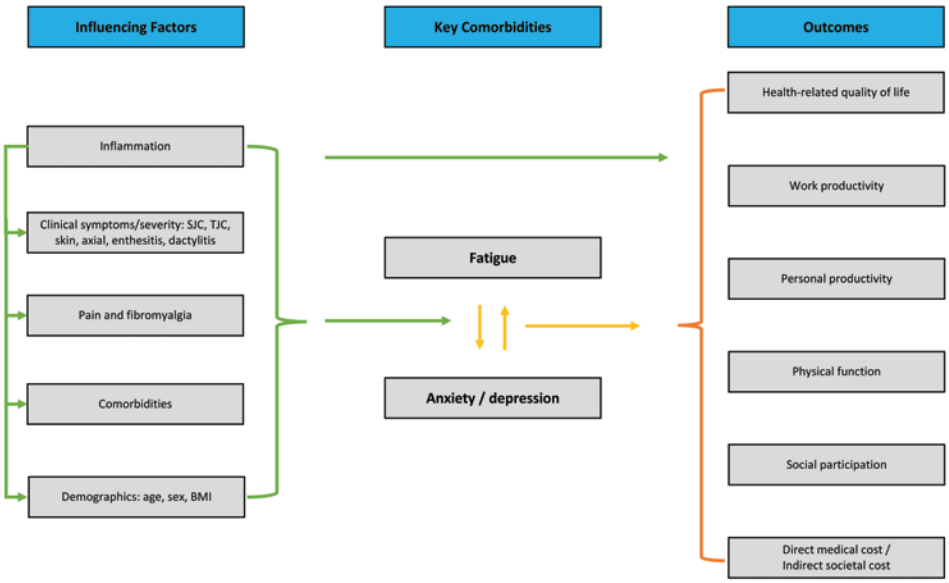


*Figure 2.* Interrelationship of patient characteristics and symptoms/comorbidities with humanistic and economic endpoints in PsA. PsA: psoriatic arthritis; SJC: swollen joint count; TJC: tender joint count.

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 their 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 judgment 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 patients with PsA, 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. Further, 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 effect 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 underrecognized 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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## DATA AVAILABILITY

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.

## ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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