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Women With Psoriatic Arthritis Experience Higher Disease Burden Than Men: Findings From a Real-World Survey in the United States and Europe

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ABSTRACT. ***Objective.*** Although psoriatic arthritis (PsA) is equally present in men and women, sex may influence clinical manifestations and the impact of disease on patients' lives. This study assessed differences in clinical characteristics, disability, quality of life (QOL), and work productivity by sex in real-world practice.

Methods. A cross-sectional survey of rheumatologists/dermatologists and their patients with PsA was conducted in France, Germany, Italy, Spain, the United Kingdom, and the United States between June and August 2018. Data collected included demographics, treatment use, clinical characteristics (tender joint count, swollen joint count, body surface area affected by psoriasis), QOL (EuroQoL 5-Dimension questionnaire [EQ-5D], Psoriatic Arthritis Impact of Disease [PsAID12]), disability (Health Assessment Questionnaire–Disability Index [HAQ-DI]), and work productivity (Work Productivity and Impairment Index [WPAI]). Outcomes were compared between men and women using parametric and nonparametric tests, as appropriate.

Results. Of 2270 patients (mean age 48.6 [SD 13.3] yrs, mean disease duration 4.9 [SD 6.0] yrs), 1047 (46.1%) were women. Disease duration, disease presentation, and biologic use (mean 54.2%) were comparable between women and men. Women reported worse QOL (EQ-5D: 0.80 [SD 0.2] vs 0.82 [SD 0.2]; $P = 0.02$), greater disability (HAQ-DI: 0.56 [SD 0.6] vs 0.41 [SD 0.5]; $P < 0.01$) and work activity impairment (WPAI: 27.9% [SD 22.0] vs 24.6% [SD 22.4]; $P < 0.01$) than men. However, women had a lower burden of comorbidities (Charlson Comorbidity Index: 1.10 [SD 0.5] vs 1.15 [SD 0.6]; $P < 0.01$).

Conclusion. In patients with similar PsA disease activity and treatment, women experienced greater disease impact than men. This represents a significant consideration for the therapeutic management of PsA.

Key Indexing Terms: psoriatic arthritis, sex

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis (PsO) and is known to affect men and women in similar proportions.[1] The presentation of PsA is heterogeneous, and includes peripheral arthritis with joint pain and stiffness, skin and nail PsO, spinal involvement, enthesitis, dactylitis, and fatigue. PsA often leads to substantial alterations in health-related quality of life (QOL), including through its social and professional consequences.[2,3]

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Sex may play an underlying role in driving the mechanisms of PsA, leading to different clinical manifestations of the disease.[1] For example, men are more affected by axial disease, whereas women suffer more from peripheral polyarticular disease.[4,5] Women with PsA may also experience greater disability and impact on their QOL than men.[1] However, there is limited research available on these differences in a real-world setting. Therefore, the aim of this study was to assess key sex differences in terms of clinical characteristics, disability, QOL, and work productivity in patients with PsA in real-world clinical practice.

METHODS

Study design and ethical considerations. Data were drawn from the Adelphi PsA Disease Specific Programme (DSP), a point-in-time survey of rheumatologists, dermatologists, and their consulting patients with PsA, conducted in France, Germany, Italy, Spain, the United Kingdom, and the United States between June and August 2018. DSPs are large, multinational, point-in-time surveys designed to investigate current disease management and patient- and physician-reported disease impact in real-world clinical practice; this study methodology has been published and validated.[6] The survey collected data using a noninterventional market research approach; no identifiable protected health information was collected. Patients and physicians gave informed consent to participate in the survey, and patients provided written informed consent for the publication of analyzed, aggregated data. The study was conducted in accordance with the relevant legislation at the time of data collection, including the US Health Insurance Portability and Accountability Act of 1996 and the Health Information Technology for Economic and Clinical Health Act of 2009. The DSP complied with all relevant market research guidelines and legal obligations according to the European Pharmaceutical Marketing Research Association guidelines. This research obtained ethics approval from the Western Institutional Review Board (study number 1183030) in the US and the Freiberg Ethics Committee (study number 02018/1077) in Europe.

Patients and methods. Data were collected from physician-completed patient record forms and patient self-reported questionnaires, with the main patient inclusion criterion being a physician-confirmed diagnosis of PsA. Physicians were instructed to complete a patient record form for the next 3 to 6 consecutive patients with active PsA who visited for diagnosis or routine care. These physician-completed patient record forms included patient demographics, clinical characteristics including prevalence of enthesitis, dactylitis, inflammatory back pain and sacroiliitis, as well as medication use and treatment history. The 68-tender joint count (TJC68) and 66-swollen joint count (SJC66) scores were calculated. Body surface area (BSA) affected by PsO and a Charlson Comorbidity Index score were also determined.

These same patients were then invited to voluntarily complete a self-reported questionnaire, which collected a range of patient-reported outcome measures (PROs). These included the EuroQoL 5-Dimension questionnaire (EQ-5D), which is an instrument for measuring generic health status, with a maximum score of 1 indicating the best health state, as well as the EQ-5D visual analog scale, which ranges from 0 to 100, with 100 indicating the best health status.[7] The Health Assessment Questionnaire–Disability Index (HAQ-DI) was included as an assessment of disability; scores range from 0 to 3, with 3 representing the most severe disability. Further, PROs encompassed the 12-item Psoriatic Arthritis Impact of Disease (PsAID12), which assesses 12 different numerical rating scales and gives an overall score in the range 0 to 10, where a higher figure indicates worse status,[8] and the Work Productivity and Impairment questionnaire (WPAI), which ranges from 0 to100%, where a greater percentage represents greater work impairment and reduced productivity.

Data analysis. Bivariate analysis comparing outcomes between women and men were conducted using parametric tests (t test) and nonparametric tests (Wilcoxon rank-sum, Fisher exact, chi-square test), as appropriate. To determine the effect of sex on PROs, a series of ordinary least squares linear regression models were employed. In separate models, each PRO (outcome) was compared among men vs women (exposure) and adjusted for intragroup correlation across physicians, as well as patient age, BMI, time since diagnosis, employment (except in the WPAI model), and advanced therapy use (targeted synthetic disease-modifying antirheumatic drugs [DMARDs] and biologic DMARDs). The coefficients and associated P values outputted in the regressions indicated the effect of sex on each PRO and its significance within the model, with the coefficient interpreted as the difference in men compared to women (ie, negative score meaning score lower in men than women). Statistical significance in all cases was set to $P < 0.05$. Analyses were conducted using Stata version 15 (StataCorp).

RESULTS

Patient demographics and clinical characteristics. In total, data were collected for 2270 patients (USA, n = 595; Spain, n = 369; Italy, n = 360; Germany, n = 360; UK, n = 309; France; n = 277), recruited by 382 rheumatologists and 190 dermatologists.

Of these patients, 1223 were men (53.9%) and 1047 women (46.1%). Overall patient demographics and clinical characteristics were comparable between men and women (Table 1). The mean age was 48.6 years and 90.4% of patients were White. The mean BMI was 26.8 kg/m^2, with 24.2% of patients classified as obese (BMI > 29). The mean PsA duration time was 4.9 years, with a mean time from first symptoms to diagnosis of 1.3 years.

There were no significant sex differences in the reported frequencies of PsA manifestations such as BSA PsO involvement, enthesitis, dactylitis, inflammatory back pain, and sacroiliitis. No significant differences were observed between men and women regarding TJC68. Men had a higher mean SJC66 than women (4.5 vs 4.1, $P = 0.03$; Table 1 and Figure 1), but more male patients experienced ≤ 1 swollen joint. A higher proportion of men than women were in full-time employment (68.6% vs 49.4%, $P < 0.01$).

PRO measures. A number of differences in PROs were observed (Table 2). Women reported worse QOL than men as defined by their EQ-5D utility score (0.80 vs 0.82, respectively; $P = 0.02$). Women also reported a greater level of disability and impaired physical functioning than men as defined by their HAQ-DI score (0.56 vs 0.41, respectively; $P < 0.01$); this is also demonstrated by the differences in the proportion of women and men classified with mild (78.7% vs 87.0%) and moderate (20.1% vs 12%) disease according to the HAQ-DI ($P < 0.01$).

The impact of disease, as defined by PsAID12 score, was also greater in women than men (2.66 vs 2.27, respectively; $P < 0.01$). Both fatigue and pain were greater in women than men as well ($P < 0.01$). Differences were observed in the proportion of women and men classified with an acceptable PsAID12 score (0-4; 77.6% vs 84.0%). Women also reported a greater degree of overall activity impairment than men, as measured by the WPAI questionnaire (27.9% vs 24.6%, respectively; $P < 0.01$). However, no differences were observed for work time missed in respondents who reported that they were in paid employment (Table 2).

When controlled for age, BMI, time since diagnosis, employment (excluding the WPAI model), and targeted advanced treatment use, regression models indicated that men had significantly

Table 1. Patient demographics and clinical characteristics (N = 2270).

	Women [a]		Men [a]		*P*
	n (%)	Outcome	n (%)	Outcome	
Age, yrs	1047 (46.1)	48.3 (13.7) [b]	1223 (53.9)	48.8 (12.8) [b]	0.42
Employment					
Working full-time [c]	417	206 (49.4) [d]	510	350 (68.6) [d]	< 0.01
Working part-time	417	36 (8.6) [d]	510	26 (5.1) [d]	–
On long-term sick leave	417	6 (1.4) [d]	510	18 (3.5) [d]	–
Homemaker	417	78 (18.7) [d]	510	8 (1.6) [d]	–
Student	417	12 (2.9) [d]	510	12 (2.4) [d]	–
Unemployed	417	24 (5.8) [d]	510	24 (4.7) [d]	–
Retired	417	55 (13.2) [d]	510	72 (14.1) [d]	–
CCI score	1047	1.10 (0.5) [b]	1223	1.15 (0.6) [b]	< 0.01
Time from first symptoms to diagnosis, yrs	634	1.48 (3.5) [b]	707	1.14 (2.5) [b]	0.76
PsA duration, yrs	832	4.87 (6.2) [b]	972	4.95 (5.8) [b]	0.42
Currently receiving biologic treatment	1047	557 (53.2) [d]	1223	674 (55.1) [d]	0.38
BSA psoriasis involvement	819	5.5 (8.4) [b]	973	5.5 (8.1) [b]	0.87
TJC68	243	3.2 (7.0) [b]	276	3.5 (6.9) [b]	0.39
SJC66	243	4.1 (5.2) [b]	256	4.5 (8.0) [b]	0.03
Enthesitis	1047	59 (5.6) [d]	1223	72 (5.9) [d]	0.86
Dactylitis	1047	79 (7.5) [d]	1223	75 (6.1) [d]	0.21
IBP	1047	101 (9.6) [d]	1223	127 (10.4) [d]	0.58
Sacroiliitis	1047	34 (3.2) [d]	1223	49 (4.0) [d]	0.37

[a] Percentages calculated on available data. [b] Values are mean (SD). [c] In paid employment outside home. [d] Values are n (%). BSA: body surface area; CCI: Charlson Comorbidity Index; IBP: inflammatory back pain; PsA: psoriatic arthritis; SJC66: 66-swollen joint count; TJC68: 68-tender joint count.

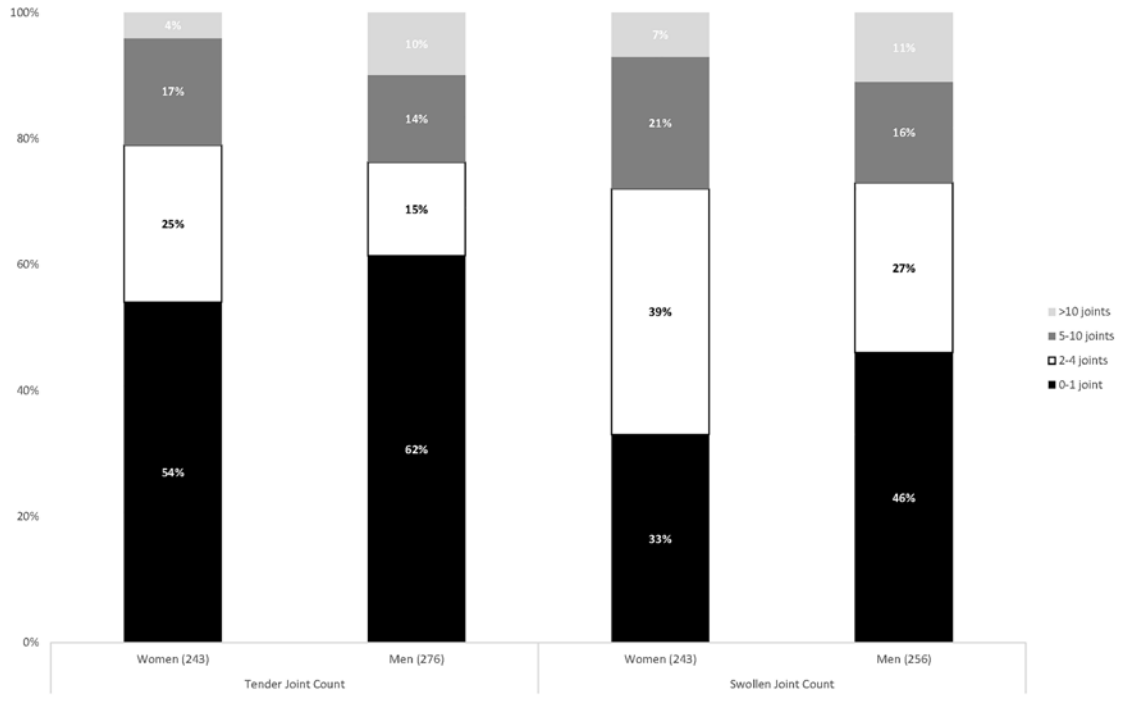

Figure 1. Joint score distributions.

better HAQ-DI scores (coefficient −0.15; $P < 0.01$) and experienced significantly less overall activity impairment than women (coefficient −3.08; $P = 0.05$; data not shown). There were no statistical differences in EQ-5D, physical functioning as defined by PsAID12, and work time missed.

DISCUSSION

In this point-in-time survey of physicians and their patients with PsA, despite women and men presenting with similar levels of disease activity and receiving comparable levels of biologic treatments, women reported reduced QOL, a greater level of

Table 2. Quality of life, disability, and work productivity compared between men and women with PsA.

	Women		Men		*P*
	n	Outcome	n	Outcome	
EQ-5D utility score	435	0.80 (0.2) [a]	508	0.82 (0.2) [a]	0.02
Pain domain, no pain	440	120 (27.3) [b]	515	158 (30.7) [b]	0.12
EQ-5D utility score,					
Low (< 0.65)		64 (14.7) [b]		59 (11.6) [b]	0.02
Medium (0.65-0.85)		203 (46.7) [b]		216 (42.5) [b]	–
High (> 0.85)		168 (38.6) [b]		233 (45.9) [b]	–
HAQ-DI score	422	0.56 (0.6) [a]	493	0.41 (0.5) [a]	< 0.01
HAQ-DI score					
Mild (0-1)		332 (78.7) [b]		429 (87.0) [b]	< 0.01
Moderate (1-2)		85 (20.1) [b]		59 (12.0) [b]	–
Severe (> 2)		5 (1.2) [b]		5 (1.0) [b]	–
PsAID12 score	419	2.66 (2.1) [a]	500	2.27 (1.98) [a]	< 0.01
Pain NRS		2.97 (2.3) [a]		2.53 (2.2) [a]	< 0.01
Fatigue NRS		3.17 (2.5) [a]		2.58 (2.4) [a]	< 0.01
PsAID12 score					
Acceptable (0-4)		325 (77.6) [b]		420 (84.0) [b]	0.01
Not acceptable (> 4)		94 (22.4) [b]		80 (16.0) [b]	–
WPAI, % of activity impairment	423	27.9 (22.0) [a]	511	24.6 (22.4) [a]	< 0.01
WPAI, % of work time missed	210	4.0 (14.0) [a]	302	5.8 (19.2) [a]	0.62

[a] Values are mean (SD). [b] Values are n (%). EQ-5D: EuroQoL 5-Dimension questionnaire; HAQ-DI: Health Assessment Questionnaire–Disability Index; NRS: numerical rating scale; PsA: psoriatic arthritis; PsAID12: 12-item Psoriatic Arthritis Impact of Disease; WPAI: Work Productivity and Activity Impairment questionnaire.

disability, and higher work impairment than men, while experiencing a lower number of comorbidities. Other factors not assessed in the study are likely to be contributing to disease burden, and these unmeasured factors may affect men and women differently.

QOL in patients with PsA is affected both by the physical and the psychological impact of the disease.[2] Previous studies have shown that, while the extent of physician's assessment of disease activity was similar between sexes, women reported worse functional performance, lower complement levels, more frequent erosive disease, higher SJC66 and HAQ-DI scores, as well as more aggressive peripheral disease than men.[5] Men are more affected by axial disease, while women suffer more from peripheral polyarticular disease.[4,5] Our study demonstrated the finding that the mean SJC66 in male patients with PsA was greater than that observed in their female counterparts, with the distribution of joint count scores favoring the extreme categories in male patients (≤ 1 or > 10 joints); this finding warrants further investigation in future research.

In another study of patients with PsA, disease activity, physical disability, functional limitation, depression, and anxiety scores were all higher in female patients, whereas QOL was better and Psoriasis Area and Severity Index scores were higher in male patients.[9] This was further quantified in studies assessing the differences in work disability between sexes, where female patients experienced increased work disability.[10,11]

There are also differences in treatment outcomes between male and female patients with PsA. In this study, biologic use was similar between male and female patients; however, other literature suggests biologic use is more frequent in women than men.[11] In a large observational cohort study that assessed outcomes of new tumor necrosis factor inhibitor (TNFi) treatments, women had worse PRO scores and higher frequencies of hospital-diagnosed anxiety or depression and chronic pulmonary disease than men. Male sex was also associated with greater treatment effectiveness and higher odds of achieving response after 3 and 6 months from treatment initiation.[12] Female patients more frequently reported side effects with TNFi and discontinued treatments earlier. Women less frequently achieved the treatment target than men, and had a greater life impact, including worse pain and fatigue.[13] In another study, female patients showed a statistically lower response to TNFi in rheumatoid arthritis, spondyloarthritis, and PsA.[14] It is evident, therefore, that there is an unmet need in the female PsA patient population for effective treatments to improve disease burden, and that life impact needs to be taken into consideration alongside physician-assessed disease activity measures when planning treat-to-target approaches.

Biological factors, including the effect of sex hormones, gene expression, or differences in patient-reported perceptions of pain are thought to play a role in these sex differences.[1] For example, the HLA-B27 antigen has been identified as a genetic risk factor for PsA; however, this may be more relevant in male patients.[5] Additionally, there may be differences in the way patients self-reported the impact of their disease. A cross-sectional study indicated that sex did not make a difference in Composite Psoriatic Disease Activity Index scores in patients with PsA; however, subjective disease scores were higher in female patients.[15] Further research into the pathophysiologic difference between male and female patients could help to

define the differing impact of disease male and female patients experience.

This study had some limitations. The survey design resulted in a geographically diverse sample of the PsA population; however, those presenting to their physician more frequently may have been overrepresented in this sample. The completion of patient self-reported questionnaires was voluntary; therefore, PROs were based solely on patients who agreed to participate. Recall bias is a common limitation of surveys; however, data in the study were collected at the time of the patient visit and thus recall bias was limited. Also, test scores were collected only if the physicians carried out the test at the visit; they were not required to do so. Hence, base sizes fluctuated across different variables. Another limitation is that we did not collect data on fibromyalgia (FM) using a validated score, but rather from a list of comorbidities. The prevalence observed in the present study for FM (2.1%) is much lower than what has been reported in other studies.[16,17] The effect of FM and the difference between male and female patients has not been examined in this study, nor have other factors such as sleep disturbance, anxiety, and joint erosion, which could be examined in more detail in future studies.

In conclusion, despite women and men having similar levels of physician-assessed disease activity and receiving similar treatment regimens, women reported a reduced QOL and greater levels of disability and work impairment than men, while experiencing a lower comorbidity burden. Further research is needed to explore the additional burden experienced by women with PsA, and whether alternative treatment regimens would alleviate some of these differences.

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 Nicola Booth at nicola.booth@adelphigroup.com.

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