Impact of Multidomain Disease Presentations on Patients With Psoriatic Arthritis in the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

Alexis Ogdie, Peter Hur, Mei Liu, Sabrina Rebello, Robert R. McLean, Blessing Dube, Meghan Glynn, and Philip J. Mease

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From the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA; Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; Corrona, LLC, Waltham, MA, USA; Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, USA.

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A. Ogdie, MD, MCSE, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA; P. Hur, PharmD, MBA, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; M. Liu, PhD, S. Rebello, MPH, R.R. McLean, DSc, MPH, B. Dube, MPH, M. Glynn, MS, CPH, Corrona, LLC, Waltham, MA, USA; P.J. Mease, MD, MACR, Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, USA.

Address correspondence to: Alexis Ogdie, MD, MSCE, Hospital of the University of Pennsylvania, 3400 Spruce Street, 5 White Building, Philadelphia, PA 19104; phone: 215-662-2454; fax: 215-662-4500; E-mail: <a href="mailto:alexis.ogdie@uphs.upenn.edu">alexis.ogdie@uphs.upenn.edu</a>

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ABSTRACT (Current: 250, maximum: 250)

**Objective:** To compare disease characteristics, quality of life (QOL), and work productivity of patients with psoriatic arthritis (PsA) who had multidomain vs single-domain presentations. **Methods:** Adults with PsA enrolled in the Corrona PsA/SpA Registry (March 2013-August 2018) were included. Six PsA disease domains were evaluated: enthesitis, dactylitis, peripheral arthritis (PA), nail psoriasis, axial disease, and skin disease. Patients were classified as having multidomain (≥ 2 domains) or single-domain disease presentations; biologic initiators were characterized separately. Linear regression models evaluated the association of multidomain presentations with disease characteristics, QOL, and work productivity vs single-domain presentations.

Results: Of 2617 patients with PsA, 1698 (64.9%) had multidomain presentations, 617 (23.6%) had single-domain presentations, and 302 (11.5%) had no active disease features. Of 354 biologic initiators, 289 (81.6%) had multidomain presentations, 45 (12.7%) had single-domain presentations, and 20 (5.6%) had no active disease features. Overall, the most common single-domain and multidomain presentations, respectively, were skin disease (12.7%) and PA + skin disease (11.7%). Multidomain presenters were more likely to have fibromyalgia, depression, anxiety, and prior biologic use than single-domain presenters. Multidomain presentations were associated with significantly worse patient and physician global assessments of disease activity, pain, and fatigue; Health Assessment Questionnaire Disability Index and EQ-5D scores; and work productivity at enrollment.

**Conclusion:** In this US real-world cohort, most patients had multidomain disease presentations, which was associated with worse disease activity, QOL, and work productivity measures. This study highlights the heterogeneity of PsA and the importance of assessing all PsA domains for optimizing disease management.

### INTRODUCTION

Psoriatic arthritis (PsA) is a heterogeneous, systemic inflammatory rheumatic disease with articular and extra-articular manifestations, including axial skeleton disorders, nail and skin conditions, peripheral joint inflammation, enthesitis, and/or dactylitis (1). These manifestations can emerge either alone or in combination, resulting in pain, impaired physical function, and poor quality of life (QOL) (2-4). PsA is frequently associated with psoriasis; 10-40% of patients with psoriasis may go on to develop PsA (4-6). The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the European League Against Rheumatism (EULAR) have developed guidelines for the treatment and management of patients with PsA based on the different clinical manifestations of PsA (7-9). A PsA core set of domains for measurement in clinical trials and longitudinal observational studies was originally developed in 2006 (10) and updated in 2016 by GRAPPA with recommendations from Outcome Measures in Rheumatology (OMERACT) (2) to incorporate both physician and patient perspectives (3). The development of an updated PsA core domain set emphasizes the need to measure a wide spectrum of disease manifestations to optimize management of patients with PsA.

PsA domain presentations are often heterogeneous, ranging from single to multiple disease domains (11). Because the frequency, type, and severity of the disease domains may impact treatment effectiveness and disease outcomes, careful consideration of the disease domain by the clinician may be critical for choosing the appropriate treatment (12). There are limited real-world studies examining disease domain presentation among patients with PsA; our group has previously characterized patients with PsA affected in a single domain (13, 14). The objective of this study was to describe the epidemiology and patterns of disease domain presentations among patients with PsA and investigate the association of PsA symptoms, QOL, and work productivity among patients with PsA with single-domain vs multidomain disease presentation.

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# PATIENTS AND METHODS

### **Data source**

The Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry is a large, independent, prospective, observational cohort of patients diagnosed with PsA or SpA by a rheumatologist. Patients were recruited from 44 private and academic practice sites across 27 states in the United States, with 52 participating rheumatologists. As of June 30, 2019, data on approximately 3939 patients with PsA/SpA had been collected. The Corrona PsA/SpA Registry includes information on 15,806 patient visits, with approximately 8423 patient-years of follow-up, with a mean time of patient follow-up of 2.9 years (median, 2.4 years). The study protocol was approved by a central IRB (New England Independent Review board, NEIRB No. 120160070) for private practice sites and the local governing IRBs of participating academic sites. All research was conducted in compliance with the Declaration of Helsinki of 1964 and all later amendments. All registry subjects were required to provide written informed consent and authorization prior to participating.

### Study design and population

This was a cross-sectional observational study that included all adult patients with PsA enrolled in the Corrona PsA/SpA Registry between March 21, 2013, and August 1, 2018. Patients were required to meet the Classification Criteria for Psoriatic Arthritis at registry enrollment (15). Data were collected at the enrollment visit and included patient demographics, clinical characteristics, and disease activity, QOL, and Work Productivity and Activity Impairment (WPAI) measures.

### Study assessments

Patients were categorized into 6 disease domains at their enrollment visit based on the following definitions (patients may have been categorized into > 1 domain):

- Enthesitis—patients with Spondyloarthritis Research Consortium of Canada enthesitis
   count > 0
- Dactylitis—patients with peripheral dactylitis count > 0
- Peripheral arthritis (PA)—patients with tender joint counts and/or swollen joint counts > 0
- Nail psoriasis—patients with global nail psoriasis severity visual analog scale > 0
- Axial disease—patients with a physician-reported presence of spinal involvement at time
  of registry enrollment, based on clinical judgment of features thought to be
  representative of active inflammatory spondylitis and/or radiographs or magnetic
  resonance imaging (MRI) showing sacroillitis such as sacroillitis grade > 2 bilaterally or
  grades 3-4 unilaterally by X-ray, active (acute) inflammation on MRI highly suggestive of
  sacroillitis associated with SpA, definite radiographic sacroillitis according to modified
  New York criteria, and other evidence of sacroillitis on imaging
- The most common active domain presentations were characterized and the number of patients presenting with single vs multiple disease domains were examined. For each disease domain, the frequency of patients who presented with ≥ 1 active disease domain was calculated.

  Additionally, those who initiated a biologic at enrollment were examined separately for

comparison. Patients who did not meet the definition for any active disease domain were classified as having no active disease features.

Skin disease—patients with > 0% body surface area affected by psoriasis

# Statistical analysis

Categorical variables were summarized using frequency counts and percentages. Continuous variables were summarized using the number of observations, mean, and standard deviations. Within the total PsA cohort and the biologic initiator cohort, baseline demographics, clinical characteristics, and patient-reported outcome measures were compared between the

multidomain and single-domain cohorts using  $\chi^2$  tests or Fisher exact tests for categorical variables and t tests or Wilcoxon rank sum tests for continuous variables. The most common mutually exclusive disease presentations among all patients with PsA and those who initiated biologics were summarized using frequency counts and percentages. Separate univariable and multivariable linear regression models evaluated the association of the presence of multidomain presentations with selected PsA disease characteristics, QOL, and work productivity measures relative to single-domain presentations among the total PsA population. Multivariable models were adjusted for age, sex, race, body mass index, disease duration, and current and prior biologic, conventional synthetic disease-modifying antirheumatic drug (csDMARD), and prednisone use. All statistical analyses were performed using Stata, version 15 (StataCorp) (16).

### **RESULTS**

### **Epidemiology of all patients at enrollment**

A total of 2617 patients with PsA were enrolled in the Corrona PsA/SpA Registry at the time of this analysis, of whom 354 (13.5%) initiated a biologic at registry enrollment (*Supplementary Table 1*). Of the 2617 patients in the overall population, 2315 (88.5%) had  $\geq$  1 active domain presentation at enrollment; 1814 (69.3%) presented with skin disease, 1523 (58.2%) with PA, 1042 (39.8%) with nail psoriasis, 539 (20.6%) with enthesitis, 319 (12.2%) with axial disease, and 235 (9.0%) with dactylitis. Of the 354 patients who initiated a biologic at enrollment, 334 (94.4%) had  $\geq$  1 active domain presentation at enrollment; 273 (77.1%) presented with PA, 267 (75.4%) with skin disease, 159 (44.9%) with nail psoriasis, 115 (32.5%) with enthesitis, 70 (19.8%) with dactylitis, and 64 (18.1%) with axial disease. The frequency of other active disease domains present at enrollment in combination with each active disease domain among all patients with PsA who had  $\geq$  1 active domain (n = 2315) and among biologic initiators who had  $\geq$  1 active domain (n = 334) is shown in *Figure 1A* and *Figure 1B*, respectively.

Regarding the frequency of active PsA domain presentations by number of domains affected among all patients with PsA, 1698 patients (64.9%) had  $\geq$  2 domain presentations, 617 (23.6%) had single-domain presentations, and 302 (11.5%) had no active presentations (*Figure 2A*). The most common disease presentations were skin disease only (12.7%), PA + skin disease (11.7%), and PA + nail psoriasis + skin disease (10.3%) (*Figure 2B*); overall, 6.8% of patients were reported to have PA only. Among all 354 biologic initiators, 289 (81.6%) had  $\geq$  2 domain presentations, 45 (12.7%) had single-domain presentations, and 20 (5.6%) had no active presentations (*Figure 2C*). The most common disease presentations were PA + nail psoriasis + skin disease (11.6%), PA + skin disease (11.3%), enthesitis + PA + nail psoriasis + skin disease (8.8%), and enthesitis + PA + skin disease (5.9%) (*Figure 2D*). A total of 5.9% of biologic initiators were reported to present with PA only.

### Characterization of single-domain and multidomain disease presentations

Demographics and disease characteristics at enrollment

Among all patients with PsA manifesting single-domain vs multidomain presentations, the mean (SD) ages were 54.5 (12.9) vs 53.5 (13.2) years, and 51.5% vs 53.7% were women, respectively. Patients with multidomain presentations were more likely to have psoriasis, nail psoriasis, depression, fibromyalgia, anxiety, and a history of biologic use than were patients with single-domain presentations (all P < 0.05) (*Table 1*).

Among biologic initiators with single-domain vs multidomain presentations, the mean (SD) ages were 52.5 (12.7) vs 51.5 (13.2) years, and 47.7% and 52.2% were women, respectively. Biologic initiators with multidomain presentations were more likely to have nail psoriasis, depression, psoriasis, and current csDMARD use than were biologic initiators with single-domain presentations (all P < 0.05) (Table 1).

Disease activity, QOL, and work productivity at enrollment

As expected, patients with multidomain presentations worse overall disease activity compared with those with single-domain presentations in unadjusted comparisons both for patients with PsA overall and for biologic initiators (*Table 2*). Additionally, multidomain presenters were more likely to have worse physical function as measured by Health Assessment Questionnaire Disability Index (HAQ-DI), QOL as measured by EQ-5D and EQ visual analogue scale scores, and work and activity impairment as assessed by the WPAI questionnaire, respectively, than patients with single-domain presentations (*Figure 3*).

Unadjusted and adjusted associations of single-domain vs multidomain presentations with disease activity, QOL, and WPAI

In univariable linear models, there was an overall association between the presence of a multidomain presentation and significantly worse patient and physician global assessment of disease, patient-reported pain and fatigue, HAQ-DI and EQ-5D scores, and work productivity and activity at enrollment (all P < 0.05; data not shown). These associations remained significant after adjusting for age, sex, race, body mass index, disease duration, and current and prior biologic, csDMARD, and prednisone use (*Figure 4*). The presence of a multidomain disease presentation was associated with an increased value for all evaluated variables compared with single-domain disease presentations.

### **DISCUSSION**

Using real-world data, our results illustrate the heterogeneity and complexity of PsA. Nearly two-thirds (64.9%) of the patients with PsA enrolled in the Corrona PsA/SpA Registry had multidomain disease presentations. Approximately one-tenth of patients (11.5%) had no active disease features at time of enrollment; these patients could have been well controlled with treatment and not have had any active disease manifestations at the time of enrollment. Furthermore, a multidomain presentation was associated with worse disease activity, QOL, and

work productivity measures compared with single-domain disease presentations. We also characterized disease presentations among 354 patients who initiated a biologic at the time of enrollment. Biologic initiators may be more reflective of patients with active disease because they had a higher prevalence of multidomain disease presentations at enrollment (81.6%) than did the overall population of patients with PsA in this study. This analysis provides a unique view of the impact of single-domain vs multidomain PsA presentations from a broad geographic distribution across the United States both at the time of registry enrollment and at initiation of a biologic therapy. These results highlight the wide spectrum of disease presentations among patients with PsA. Evaluation of the active disease domains is important for the development of an effective disease management plan.

The heterogeneity of PsA can complicate diagnosis, evaluation, and management of the disease (12). Prior real-world studies have focused on characterizing patients who presented with a single active domain or 2 affected domains instead of reporting multiple disease domain presentations in individual patients with PsA (13, 14, 17). Associations between individual single-domain presentations and greater overall disease burden and poorer QOL were previously reported (13, 14, 17). Additionally, several studies have indicated a close link between nail psoriasis, dactylitis, and enthesitis (18, 19) and, in other studies, presence of PA predicted the development of erosive and deforming disease over time in prospective studies involving patients with PsA (20, 21). Taken together, these studies indicate that each of these singular core domains may have meaning for long-term outcomes. While these are important studies, ours adds to the literature the comparison of multidomain vs single-domain presentations and demonstrates that a multidomain presentation is associated with worse disease activity, QOL, and work productivity measures.

The goals of therapy for all patients with PsA include the achievement of the lowest possible level of disease activity in all disease domains, optimization of patient functional status, improvement in QOL, prevention of structural damage to the greatest extent possible, and

avoidance or minimization of complications, both from untreated active disease and from therapy (7). Treatment may differ depending on the PsA domains affected (7-9). Current clinical trials focus on measures of PA as the primary outcome measure, although many have included measures of skin disease as key secondary outcome measures (22-30). Most available agents also effectively treat enthesitis and dactylitis in patients with PsA (24, 25, 27, 29, 31-38). Some therapies also have demonstrated efficacy in improving nail symptoms (39-44). To date, only secukinumab has been evaluated in a large phase 3b study in patients with axial involvement in PsA (45), although in general, the tumor necrosis factor inhibitors and interleukin 17A inhibitors are effective in treating ankylosing spondylitis and are assumed to work in axial PsA as well. The optimal therapy selection is based on the domains involved and the severity of each domain (46).

Some study limitations should be noted. Because the data source was a US registry in which clinician investigators enroll their patients, results may not be generalizable to all patients with PsA. Domains were physician reported and may not reflect all PsA presentations experienced by patients. Because the Corrona registry examines patients in the course of routine clinical practice, data on domain presentation in patients who were receiving treatment may be underreported. Biologic initiators likely represent patients with an inadequate response to their previous treatment; because these patients were starting a new biologic at the time of enrollment, assessment of disease activity may not have been as confounded as in those patients who were already being treated at the time of enrollment, which may provide a more accurate reflection of the prevalence of disease domains. This was a descriptive analysis; therefore, certain factors such as treatment may not be accounted for, which may lead to the underrepresentation of the prevalence of domain presentations.

In summary, this study highlights the heterogeneity of PsA and demonstrates that the majority of patients with PsA in a US real-world setting presented with multiple active disease domains. These multidomain presentations are associated with increased clinical burden,

including worse disease activity, QOL, and work productivity measures. Future studies can build on these results to identify clusters of domains that may affect response to individual therapies.

As a first step, however, increased physician awareness of the heterogeneity of disease presentations among patients with PsA is important for optimizing disease management.

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### FIGURE LEGENDS

Figure 1. Frequency of other concurrently active disease domains in patients presenting with each active disease domain among (**A**) all patients with psoriatic arthritis (PsA) and  $\geq$  1 affected domain (n = 2315) and (**B**) biologic initiators with  $\geq$  1 affected domain (n = 334) at registry enrollment. Heat map represents the frequency of any 2 domain combinations by the range of blue shades, with the darkest blue specifying the highest frequency and the lightest blue specifying the lowest frequency of combinations. PA: peripheral arthritis.

Figure 2. Frequency of most common active psoriatic arthritis (PsA) domain presentations by number of domains affected among ( $\mathbf{A}$ ,  $\mathbf{B}$ ) all patients with PsA ( $\mathbf{n}$  = 2617) and ( $\mathbf{C}$ ,  $\mathbf{D}$ ) biologic initiators ( $\mathbf{n}$  = 354). \* "Other" presentations include axial disease, enthesitis, and dactylitis. † "Other" presentations include all other combinations of  $\geq$  2 domains not shown in the figure. ‡ "Other" presentations include nail psoriasis, enthesitis, and dactylitis.

Figure 3. Overall (**A**) physical function and quality of life and (**B**) work productivity and activity impairment at enrollment for patients with multidomain vs single-domain psoriatic arthritis (PsA) disease presentations. \* For HAQ-DI, higher scores indicate worse physical function. For EQ-5D and EQ VAS, lower scores indicate worse health status. † P < 0.05. EQ-5D: EuroQol 5 Dimensions questionnaire; EQ VAS: EuroQol visual analogue scale; HAQ-DI: Health Assessment Questionnaire Disability Index; WPAI: Work Productivity and Activity Impairment.

Figure 4. Multidomain vs single-domain impact on outcomes—multivariable regression coefficients estimating the association of presence of multidomain presentations with selected psoriatic arthritis (PsA) disease activity, quality of life, and work productivity and activity measures relative to single-domain presentations in patients with PsA. \* P < 0.05. † Analyzed using multivariable regression coefficients adjusted for age, sex, race, body mass index,

disease duration, and current and prior biologic, csDMARD, and prednisone use. csDMARD: conventional synthetic disease-modifying antirheumatic drug; EQ-5D: EuroQol 5 Dimensions questionnaire; HAQ-DI: Health Assessment Questionnaire Disability Index; WPAI: Work Productivity and Activity Impairment.

*Table 1.* Demographics, treatment profiles, and disease activity at enrollment for patients with multidomain vs single-domain PsA disease presentations

	All Patients	With PsA (N = :	2315)	Biologic Initiators (N = 334)			
Characteristic*	Single  Domain <sup>†</sup> (n = 617)	Multidomain (n = 1698)	<i>P</i> Value <sup>‡</sup>	Single  Domain <sup>†</sup> (n = 45)	Multidomain (n = 289)	<i>P</i> Value <sup>‡</sup>	
Age, mean (SD) [n], years	54.5 (12.9) [607]	53.5 (13.2) [1678]	0.20	52.5 (12.7) [45]	51.5 (13.2) [289]	0.65	
Female, n/N (%)	314/610 (51.5)	907/1689 (53.7)	0.35	21/44 (47.7)	151/289 (52.2)	0.58	
Race, n (%) White	n = 596 572 (96.0)	n = 1655 1548 (93.5)	0.04	n = 43 42 (97.7)	n = 285 256 (89.8)	0.34	
Black Other	4 (0.7) 20 (3.4)	9 (0.5) 98 (5.9)		0 (0.0)	4 (1.4) 25 (8.8)		
BMI, mean (SD) [n], kg/m <sup>2</sup>	31.3 (7.6) [600]	32.0 (7.4) [1658]	< 0.01	33.6 (11.9) [45]	31.4 (7.3) [287]	0.69	
Symptom duration, mean (SD) [n], years	11.0 (9.7) [594]	11.3 (10.7) [1651]	0.51	7.3 (9.0) [44]	9.1 (9.9) [286]	0.12	
Disease duration, mean (SD) [n], years	8.5 (8.1) [598]	7.7 (8.8) [1662]	< 0.01	6.1 (8.9) [44]	6.0 (7.5) [285]	0.59	
History of psoriasis, n (%)	520 (84.3)	1537 (90.5)	< 0.01	33 (73.3)	247 (85.5)	0.04	
History of nail psoriasis, n (%)	81 (13.1)	602 (35.5)	< 0.01	4 (8.9)	85 (29.4)	< 0.01	

223 (36.1)	679 (40.0)	0.09	17 (37.8)	107 (37.0)	0.92
137 (22.2)	433 (25.5)	0.10	8 (17.8)	68 (23.5)	0.39
91 (14.7)	282 (16.6)	0.28	4 (8.9)	44 (15.2)	0.26
93 (15.1)	252 (14.8)	0.89	4 (8.9)	37 (12.8)	0.46
70 (11.3)	205 (16.5)	0.63	1 (2.2)	32 (11.1)	0.10
57 (9.2)	280 (16.5)	< 0.01	2 (4.4)	52 (18.0)	0.02
36 (5.8)	138 (8.1)	0.06	3 (6.7)	21 (7.3)	1.00
34 (5.5)	99 (5.8)	0.77	3 (6.7)	16 (5.5)	0.73
23 (3.7)	114 (6.7)	< 0.01	0	20 (6.9)	0.09
12 (1.9)	65 (3.8)	0.03	2 (4.4)	18 (6.2)	1.00
5 (0.8)	16 (0.9)	0.07	0	7 (2.4)	0.60
4 (0.6)	19 (1.1)	0.31	1 (2.2)	5 (1.7)	0.58
4 (0.6)	16 (0.9)	0.50	0	1 (0.3)	1.00
151 (24.5)	561 (33.0)	< 0.01	22 (48.9)	154 (53.3)	0.58
151 (24.5)	478 (28.2)	0.08	12 (26.7)	112 (38.8)	0.12
	137 (22.2) 91 (14.7) 93 (15.1) 70 (11.3) 57 (9.2) 36 (5.8) 34 (5.5) 23 (3.7) 12 (1.9) 5 (0.8) 4 (0.6) 4 (0.6) 151 (24.5)	137 (22.2)       433 (25.5)         91 (14.7)       282 (16.6)         93 (15.1)       252 (14.8)         70 (11.3)       205 (16.5)         57 (9.2)       280 (16.5)         36 (5.8)       138 (8.1)         34 (5.5)       99 (5.8)         23 (3.7)       114 (6.7)         12 (1.9)       65 (3.8)         5 (0.8)       16 (0.9)         4 (0.6)       19 (1.1)         4 (0.6)       16 (0.9)         151 (24.5)       561 (33.0)	137 (22.2)       433 (25.5)       0.10         91 (14.7)       282 (16.6)       0.28         93 (15.1)       252 (14.8)       0.89         70 (11.3)       205 (16.5)       0.63         57 (9.2)       280 (16.5)       < 0.01	137 (22.2)       433 (25.5)       0.10       8 (17.8)         91 (14.7)       282 (16.6)       0.28       4 (8.9)         93 (15.1)       252 (14.8)       0.89       4 (8.9)         70 (11.3)       205 (16.5)       0.63       1 (2.2)         57 (9.2)       280 (16.5)       < 0.01	137 (22.2)       433 (25.5)       0.10       8 (17.8)       68 (23.5)         91 (14.7)       282 (16.6)       0.28       4 (8.9)       44 (15.2)         93 (15.1)       252 (14.8)       0.89       4 (8.9)       37 (12.8)         70 (11.3)       205 (16.5)       0.63       1 (2.2)       32 (11.1)         57 (9.2)       280 (16.5)       < 0.01

His	story of						
pre	ednisone use, n	83 (13.5)	(61.3) 980 (57.7) 0.13 45 (100.0) 289 (100.0) — (54.9) 859 (50.6) 0.06 24 (53.3) 104 (36.0) 0.03 (6.8) 122 (7.2) 0.75 9 (20.0) 30 (10.4) 0.06 (csDMARD: conventional synthetic disease-modifying antirheumatic noma skin cancer; PsA, psoriatic arthritis.				
(%	b)						
4	urrent biologic use,	378 (61.3)	980 (57.7) 0.13 45 (100.0) 289 (100.0) —  859 (50.6) 0.06 24 (53.3) 104 (36.0) 0.03  122 (7.2) 0.75 9 (20.0) 30 (10.4) 0.06  D: conventional synthetic disease-modifying antirheumatic cancer; PsA, psoriatic arthritis.  d on available data. For continuous variables, [n] represents available.  tions for PsA overall (N = 617) included skin disease (53.8%), soriasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and isease presentations for biologic initiators (N = 45) included				
n (	(%)		1.3) 980 (57.7) 0.13 45 (100.0) 289 (100.0) —  4.9) 859 (50.6) 0.06 24 (53.3) 104 (36.0) 0.03  8) 122 (7.2) 0.75 9 (20.0) 30 (10.4) 0.06  DMARD: conventional synthetic disease-modifying antirheumatic na skin cancer; PsA, psoriatic arthritis.  d based on available data. For continuous variables, [n] represents in data available.  resentations for PsA overall (N = 617) included skin disease (53.8%),				
	urrent csDMARD	339 (54.9)	859 (50.6)	280 (57.7) 0.13 45 (100.0) 289 (100.0) — 359 (50.6) 0.06 24 (53.3) 104 (36.0) 0.03  122 (7.2) 0.75 9 (20.0) 30 (10.4) 0.06  conventional synthetic disease-modifying antirheumatic acer; PsA, psoriatic arthritis.  In available data. For continuous variables, [n] represents itable.  In serior PsA overall (N = 617) included skin disease (53.8%), itasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and ase presentations for biologic initiators (N = 45) included			
use	e, n (%)						
Cu	urrent prednisone	42 (6.8)	122 (7.2)	0.75	9 (20 0)	30 (10 4)	0.06
use	e, n (%)	339 (54.9) 859 (50.6) 0.06 24 (53.3) 104 (36.0) 0.03 ne					
6	BMI: body mass	index; csDMARI	D: conventional s	ynthetic di	isease-modifying	g antirheumatic	
+	drug; NMSC: no	nmelanoma skin	cancer; PsA, pso	oriatic arth	ritis.		
	* All values were	e calculated base	d on available da	ata. For co	ntinuous variabl	es, [n] represents	
	the number of pa	atients with data	available.				
0	† Single-domain	disease presenta	ations for PsA ov	erall (N = 0	617) included sk	in disease (53.8%	ώ),
(1)	peripheral arthrit	tis (29.0%), nail p	soriasis (10.9%)	, axial dise	ease (3.4%), ent	hesitis (1.8%), an	d
	dactylitis (1.1%)	. Single-domain o	lisease presenta	tions for bi	iologic initiators	(N = 45) included	
	peripheral arthrit	tis (46.7%), skin (	disease (35.6%),	axial dise	ase (6.7%), nail	psoriasis (4.4%),	

- \* All values were calculated based on available data. For continuous variables, [n] represents the number of patients with data available.
- † Single-domain disease presentations for PsA overall (N = 617) included skin disease (53.8%), peripheral arthritis (29.0%), nail psoriasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and dactylitis (1.1%). Single-domain disease presentations for biologic initiators (N = 45) included peripheral arthritis (46.7%), skin disease (35.6%), axial disease (6.7%), nail psoriasis (4.4%), enthesitis (4.4%), and dactylitis (2.2%).
- $^{\ddagger}$  t test or Wilcoxon rank sum test for continuous variables and  $\chi^2$  or Fisher exact test for categorical variables.

Table 2. Disease activity at enrollment for patients with multidomain vs single-domain PsA disease presentations

	All Patien	ts With PsA	Biologic Initiators			
	(N =	2315)	(N = 334)			
	Single		Single			
	Domain†	Multidomain	Domain†	Multidomain		
Characteristic*	(n = 617)	(n = 1698)	(n = 45)	(n = 289)		
Enthesitis, n (%)	11 (1.8)	528 (31.1)	2 (4.4)	113 (39.1)		
SPARCC Enthesitis Index	2.1 (1.5) [11]	3.8 (2.9) [528]	1.5 (0.7) [2]	3.6 (3.0) [113]		
(1-16)						
Dactylitis, n (%)	7 (1.1)	228 (13.4)	1 (2.2)	69 (23.9)		
Dactylitis count (1-20)	1.3 (0.5) [7]	2.4 (2.1) [228]	2.0 (NA) [1]	2.5 (1.9) [69]		
Tender joint count (1-68)	5.7 (6.9) [155]	8.7 (10.2) [1226]	6.8 (7.4) [20]	9.1 (9.5) [240]		
Swollen joint count (1-66)	4.0 (4.0) [127]	4.8 (4.9) [966]	4.5 (4.5) [18]	6.2 (5.4) [199]		
Nail psoriasis VAS (1-100)	13.3 (18.8) [67]	19.1 (22.5) [975]	26.0 (33.9) [2]	27.3 (26.2)		
				[157]		
DAPSA	11.6 (10.1)	22.3 (17.5) [950]	16.8 (13.0) [31]	26.8 (19.2)		
	[337]			[189]		
DAPSA group, n (%)	n = 337	n = 950	n = 31	n = 189		
Remission	79 (23.4)	53 (5.6)	3 (9.7)	6 (3.2)		
Low	165 (49.0)	292 (30.7)	15 (48.4)	44 (23.3)		
Moderate	69 (20.5)	359 (37.8)	9 (29.0)	69 (36.5)		
High	24 (7.1)	246 (25.9)	4 (12.9)	70 (37.0)		
PASDAS	2.8 (1.2) [325]	4.1 (1.4) [923]	3.7 (1.0) [32]	4.7 (1.4) [185]		
PASDAS group, n (%)	n = 325	n = 923	n = 32	n = 185		

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Inactive	198 (60.9)	258 (28.0)	9 (28.1)	27 (14.6)
Moderate	80 (24.6)	215 (23.3)	12 (37.5)	33 (17.8)
Active	45 (13.8)	375 (40.6)	10 (31.3)	98 (53.0)
Very active	2 (0.6)	75 (8.1)	1 (3.1)	27 (14.6)
Physician global assessment	10.9 (15.0)	24.3 (21.4)	22.6 (19.4) [45]	36.4 (21.5)
(VAS 0-100)	[612]	[1686]		[287]
Physician global assessment of	12.9 (15.0)	28.0 (22.6)	24.9 (20.6) [42]	41.6 (22.0)
psoriasis (VAS 0-100)	[594]	[1661]		[284]

DAPSA: Disease Activity in PSoriatic Arthritis; NA: not available; PASDAS: Psoriatic Arthritis

Disease Activity Score; PsA: psoriatic arthritis; SPARCC: Spondyloarthritis Research

Consortium of Canada; VAS: visual analog scale.

- \* All values were calculated based on available data and are presented as mean (SD) [n] unless otherwise stated; [n] represents the number of patients with data available.
- <sup>†</sup> Single-domain disease presentations for PsA overall (N = 617) included skin disease (53.8%), peripheral arthritis (29.0%), nail psoriasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and dactylitis (1.1%). Single-domain disease presentations for biologic initiators (N = 45) included peripheral arthritis (46.7%), skin disease (35.6%), axial disease (6.7%), nail psoriasis (4.4%), enthesitis (4.4%), and dactylitis (2.2%).

Concurrent	Active PsA Disease Domain							
Active Domains, n (%)	Enthesitis (n = 539)	Dactylitis (n = 235)	PA (n = 1523)	Nail Psoriasis (n = 1042)	Axial Disease (n = 319)	Skin Disease (n = 1814)		
Enthesitis	539 (100)	66 (28.1)	465 (30.5)	285 (27.4)	110 (34.5)	423 (23.3)		
Dactylitis	66 (12.2)	235 (100)	210 (13.8)	125 (12.0)	26 (8.2)	195 (10.7)		
PA	465 (86.3)	210 (89.4)	1523 (100)	699 (67.1)	214 (67.1)	1150 (63.4)		
Nail Psoriasis	285 (52.9)	125 (53.2)	699 (45.9)	1042 (100)	160 (50.2)	848 (46.7)		
Axial Disease	110 (20.4)	26 (11.1)	214 (14.1)	160 (15.4)	319 (100)	233 (12.8)		
Skin Disease	423 (78.5)	195 (83.0)	1150 (75.5)	848 (81.4)	233 (73.0)	1814 (100)		

В	Concurrent	Active PsA Disease Domain							
	Active Domains, n (%)	Enthesitis (n = 115)	Dactylitis (n = 70)	PA (n = 273)	Nail Psoriasis (n = 159)	Axial Disease (n = 64)	Skin Disease (n = 267)		
	Enthesitis	115 (100)	25 (35.7)	104 (38.1)	62 (39.0)	27 (42.2)	95 (35.6)		
	Dactylitis	25 (21.7)	70 (100)	64 (23.4)	33 (20.8)	10 (15.6)	57 (21.3)		
	PA	104 (90.4)	64 (91.4)	273 (100)	131 (82.4)	48 (75.0)	217 (81.3)		
	Nail Psoriasis	62 (53.9)	33 (47.1)	131 (48.0)	159 (100)	33 (51.6)	141 (52.8)		
	Axial Disease	27 (23.5)	10 (14.3)	48 (17.6)	33 (20.8)	64 (100)	50 (18.7)		
	Skin Disease	95 (82.6)	57 (81.4)	217 (79.5)	141 (88.7)	50 (78.1)	267 (100)		

Figure 1. Frequency of other concurrently active disease domains in patients presenting with each active disease domain among (A) all patients with psoriatic arthritis (PsA) and  $\geq 1$  affected domain (n = 2315) and (B) biologic initiators with  $\geq 1$  affected domain (n = 334) at registry enrollment. Heat map represents the frequency of any 2 domain combinations by the range of blue shades, with the darkest blue specifying the highest frequency and the lightest blue specifying the lowest frequency of combinations. PA: peripheral arthritis.

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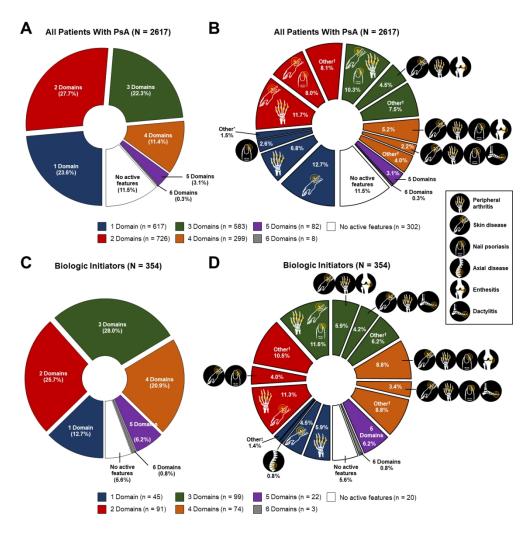
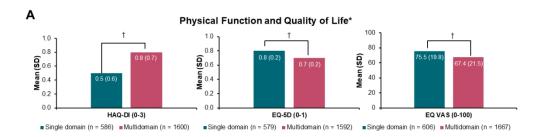


Figure 2. Frequency of most common active psoriatic arthritis (PsA) domain presentations by number of domains affected among (A, B) all patients with PsA (n = 2617) and (C, D) biologic initiators (n = 354). \* "Other" presentations include axial disease, enthesitis, and dactylitis.  $\dagger$  "Other" presentations include all other combinations of  $\geq$  2 domains not shown in the figure.  $\dagger$  "Other" presentations include nail psoriasis, enthesitis, and dactylitis.

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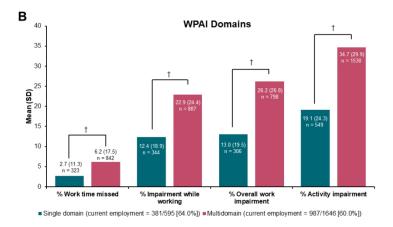


Figure 3. Overall (A) physical function and quality of life and (B) work productivity and activity impairment at enrollment for patients with multidomain vs single-domain psoriatic arthritis (PsA) disease presentations. 
\* For HAQ-DI, higher scores indicate worse physical function. For EQ-5D and EQ VAS, lower scores indicate worse health status. † P < 0.05. EQ-5D: EuroQol 5 Dimensions questionnaire; EQ VAS: EuroQol visual analogue scale; HAQ-DI: Health Assessment Questionnaire Disability Index; WPAI: Work Productivity and Activity Impairment.

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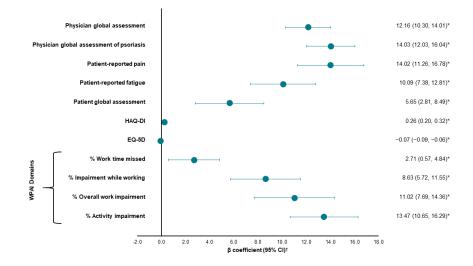


Figure 4. Multidomain vs single-domain impact on outcomes—multivariable regression coefficients estimating the association of presence of multidomain presentations with selected psoriatic arthritis (PsA) disease activity, quality of life, and work productivity and activity measures relative to single-domain presentations in patients with PsA. \* P < 0.05. † Analyzed using multivariable regression coefficients adjusted for age, sex, race, body mass index, disease duration, and current and prior biologic, csDMARD, and prednisone use. csDMARD: conventional synthetic disease-modifying antirheumatic drug; EQ-5D: EuroQol 5 Dimensions questionnaire; HAQ-DI: Health Assessment Questionnaire Disability Index; WPAI: Work Productivity and Activity Impairment.

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