



# Prevalence of Musculoskeletal Symptoms in Patients with Psoriasis and Predictors Associated with the Development of Psoriatic Arthritis: Retrospective Analysis of a US Claims Database

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## ABSTRACT

**Introduction:** Psoriasis (PsO) is associated with the development of psoriatic arthritis (PsA). Patients with PsO often experience pre-PsA musculoskeletal (MSK) symptoms, leading to potential structural damage and substantial disease burden with impact on function. The objective of this study is to describe prevalence rates and evidence of MSK symptoms, including incidence of comorbid PsA diagnosis, in patients newly diagnosed with PsO and identify factors associated with PsA diagnosis.

**Methods:** This retrospective analysis included administrative claims from the Optum Research Database for adult patients with a new PsO

diagnosis between January 2008 and February 2019. Eligible patients had  $\geq 2$  claims for PsO on unique dates, were aged  $\geq 18$  years at the date of the first claim with a diagnosis of PsO (index date), and had continuous enrollment with medical and pharmacy coverage for 12 months before (baseline period) and  $\geq 12$  months following the index date. Primary outcomes were incidence of comorbid PsA diagnosis, prevalence of MSK symptoms other than PsA, and evidence of MSK symptoms collected at baseline and assessed in 12-month intervals through 60 months.

**Results:** Of the 116,203 patients with newly diagnosed PsO, 110,118 were without baseline comorbid PsA. High prevalence rates of MSK symptoms among patients with only PsO were seen at baseline (47.1%), 12 months (48.2%), and 60 months (82.1%). Patient age, baseline MSK symptoms, and baseline MSK symptom-related healthcare utilization were associated with increased hazard of a PsA diagnosis.

**Conclusion:** Increased prevalence rates of MSK symptoms and burden are experienced by patients newly diagnosed with PsO through 60 months of follow-up. Several baseline factors were associated with increased risk of PsA diagnosis.

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## PLAIN LANGUAGE SUMMARY

### A Study to Look at Symptoms of Muscles, Joints, and Bones in Patients with Psoriasis and Whether They Can Predict a Diagnosis of Psoriatic Arthritis

Psoriasis is an inflammatory skin disease that results in areas of significant itchiness, pain, and scaling, and ultimately decreases patient quality of life. Psoriasis affects approximately 2–4% of the general US population and 1.3–2.2% of the UK population. Some patients with psoriasis may experience musculoskeletal symptoms and may go on to develop psoriatic arthritis. The goal of this study was to determine the frequency of patients with psoriasis who experienced complaints of musculoskeletal pain prior to and/or following their psoriasis diagnosis, and whether these were associated with further probability of developing psoriatic arthritis.

Using a large US-based database with data from approximately 115,000 patients with newly diagnosed psoriasis, we determined the percentage of newly diagnosed psoriasis patients with existing musculoskeletal pain complaints within 12 months of their initial diagnosis. We found that 47% of newly diagnosed patients had previous musculoskeletal pain complaints, with joint pain, back pain, and overall fatigue representing the most common forms. Notably, psoriasis patients with previous joint pain were approximately 50% more likely to develop psoriatic arthritis compared with patients with no previous joint pain. Furthermore, patients with previous other forms of arthritis were nearly twice as likely to develop psoriatic arthritis.

This study provides additional support that existing musculoskeletal pain in patients with newly diagnosed psoriasis may predict the potential future onset of psoriatic arthritis. These findings will help guide primary care physicians, dermatologists, and rheumatologists in understanding the importance of earlier detection of psoriatic arthritis to provide more appropriate care.

**Keywords:** Claims analysis; Early disease; Musculoskeletal symptoms; Psoriasis; Psoriatic arthritis

### Key Summary Points

#### *Why carry out this study?*

Limited data exist on prevalence of musculoskeletal symptoms in patients newly diagnosed with psoriasis and patient factors that are predictors of psoriatic arthritis diagnosis in early psoriasis.

This study aimed to describe the prevalence rates of musculoskeletal symptoms in patients with newly diagnosed psoriasis.

#### *What was learned from this study?*

Musculoskeletal symptoms were increasingly prevalent in patients with psoriasis through 60 months; baseline symptoms were associated with higher risk of psoriatic arthritis diagnosis.

These findings highlight that physicians should be asking their patients with psoriasis about musculoskeletal complaints and presents an opportunity for primary care providers and dermatologists to collaborate with rheumatologists in the management and care of patients with psoriasis who have musculoskeletal complaints.

## INTRODUCTION

Psoriasis (PsO) is a chronic inflammatory skin disease that affects approximately 2–4% of the general US population, characterized by skin itching, pain, and scaling [1, 2]. Studies report that up to half of patients with PsO display musculoskeletal (MSK) symptoms, including joint pain, swelling, tenderness, and inflammation [3–6]. Inadequate PsO disease

management can exacerbate MSK manifestations, leading to increased disease burden [4]. MSK symptoms often precede a diagnosis of psoriatic arthritis (PsA) [4, 7–9]. PsO is significantly associated with PsA; up to 30% of patients with PsO develop comorbid PsA [2, 10, 11]. Frequently, PsO precedes PsA by 10 years [12–14], and many patients with PsA are undiagnosed or underdiagnosed by dermatologists [10]. Patients with PsO can experience pre-PsA MSK symptoms prior to PsA diagnosis, leading to pain and physical disability [15, 16]; however, presence of MSK symptoms in patients newly diagnosed with PsO remains unknown.

PsA, a progressive inflammatory arthropathy, is heterogeneous in clinical presentation and affects multiple aspects of the MSK system. PsA clinical manifestations include peripheral arthritis, enthesitis, dactylitis, nail disease, skin disease, and axial involvement, which can lead to irreversible structural damage, loss of function, and reduced quality of life [5, 15, 17, 18]. Currently, there are no definitive biomarkers or diagnostic tests for PsA, and it is challenging to identify because its symptoms mimic those of other rheumatic diseases [19, 20]. Prompt PsA diagnosis is imperative; a diagnostic delay of 6 months from PsA symptom onset can lead to significantly more radiographic joint damage, worse physical function, and inadequate treatment response [16]. Patients with PsA often experience average diagnostic delays up to 5 years [14, 19, 21], which leads to inadequate patient care [22, 23].

Healthcare providers who evaluate patients with PsO can screen for PsA and reduce diagnostic delays; patients with PsO exemplify a readily identifiable population at risk for disease progression. Despite receiving treatment for PsO, patients often still experience substantial MSK symptom burden, which may be underdiagnosed or undiagnosed [4, 9, 24]. A knowledge gap exists regarding the prevalence and timing of MSK symptoms that may predict a PsA diagnosis; closing this gap could address the unmet need of improving diagnosis timing and treatment response.

This study describes the incidence and burden of MSK symptoms among patients with

newly diagnosed PsO and identifies associations between MSK symptoms and a diagnosis of PsA using claims data from a large database. We assessed prevalence and evidence of MSK symptoms at baseline through 60 months from the time of PsO diagnosis to understand the progressive impact of MSK symptoms.

## METHODS

### Study Design and Population

In this exploratory, retrospective study using the Optum Research Database, a large administrative claims database, we identified patients who had a diagnosis of PsO between 1 January 2008 and 28 February 2019 (Fig. S1). The study consisted of three periods (Fig. S2): (1) a 12-month period prior to diagnosis of PsO (baseline); (2) the date of the first claim with a diagnosis of PsO (index date); and (3) a follow-up period starting the day after the index date with a duration of  $\geq 12$  months. The follow-up period ended when the event of interest (e.g., MSK symptom diagnosis) occurred, when the patient disenrolled from the health plan, or the end of the study period was reached.

Eligible patients were aged  $\geq 18$  years at the date of the first claim with a diagnosis of PsO (index date) using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 696.1 and the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes L40.0, L40.1, L40.2, L40.3, L40.3, L40.8, and L40.9; had commercial insurance coverage or were enrolled in Medicare Advantage Part D with  $\geq 2$  claims for PsO on unique dates; and had continuous enrollment with medical and pharmacy coverage for  $\geq 12$  months before (baseline period) and following the index date.

Exclusion criteria included  $\geq 1$  claim for PsO during the baseline period and having unknown/missing demographic information. For incidence of PsA and predictors of PsA diagnosis, patients with  $\geq 1$  claim for PsA diagnosis (ICD-9-CM: 696.0; ICD-10-CM: L40.50, L40.51, L40.52, L40.53, and L40.59) in

any position during the baseline period were excluded.

Administrative claims data from 1 January 2007 to 29 February 2020 were included to capture a 12-month baseline period and a  $\geq 12$ -month follow-up period beyond the identification period. A random 10% sample of patients in the Optum Research Database aged  $\geq 18$  years as of 1 January 2019, with continuous enrollment with medical and pharmacy coverage from 1 January 2019 to 31 December 2019, was included as a representative control cohort. Because the current study used only deidentified patient records and did not involve the collection, use, or transmittal of individually identifiable data, institutional review board approval was not required to conduct this study. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

### Study Variables

Primary outcomes were incidence of comorbid PsA diagnosis ( $\geq 1$  claim with a diagnosis code in any position for PsA), prevalence of MSK symptoms other than PsA [identified with  $\geq 1$  claim of diagnosis code for arthralgia, myalgia, tendonitis, fasciitis, arthritis, joint stiffness, back pain, enthesitis, synovitis, fatigue (unspecified chronic fatigue, other malaise and fatigue, and other fatigue), and nail dystrophy (specified/unspecified disease of the nail)], and evidence of MSK symptoms collected at baseline and assessed in 12-month intervals through 60 months among patients with continuous enrollment. Evidence of MSK symptoms included diagnosis codes ( $\geq 1$  claim with a diagnosis code in any position for an MSK symptom), prescription medication [ $\geq 3$  consecutive months of treatment with prescription pain medications (nonsteroidal anti-inflammatory drugs, benzodiazepines, opioids, centrally acting skeletal-muscle relaxants, and systemic glucocorticoids)], procedure and/or assessment [ $\geq 1$  claim with Current Procedural Terminology, Healthcare Common Procedure Coding System (HCPCS), diagnosis, procedure, or revenue code for joint imaging, chiropractic or

osteopathic treatment, or physical therapy], MSK-related healthcare resource utilization [(HCRU)  $\geq 1$  claim for a healthcare visit to a rheumatologist, orthopedist, chiropractor, physical therapist, osteopath, podiatrist, or sports medicine practitioner], or ambulatory assist device ( $\geq 1$  claim with a HCPCS code for an ambulatory assist device).

Data collected at baseline included patient demographics (age, sex, insurance status), clinical characteristics [follow-up length, Charlson Comorbidity Index (CCI) score (predicts 10-year mortality for patients with comorbid diseases; categorized by severity) [25]], comorbid conditions, [which included the top Agency for Healthcare Research and Quality (AHRQ) clinical classifications categories; other connective tissue disease defined as AHRQ category 211.XX; enthesopathies; disorders of synovium, tendon, and bursa; and disorders of muscle, ligaments, and fasciae], and comorbid inflammatory conditions.

### Data Analysis

Patient demographics and clinical characteristics were analyzed descriptively, stratified by baseline comorbid PsA status, and presented as frequencies (%) for categorical variables and means with standard deviations (SDs) for continuous variables. Pearson  $\chi^2$  tests were used for binary measures, and two-sample *t*-tests were used for continuous variables. Cox proportional hazards regression modeling was used to determine the relationship between select covariates and PsA diagnosis among patients with PsO only (i.e., without a claim for PsA in any position during the 12-month baseline period). Predictors of interest included baseline demographic characteristics, MSK symptoms, evidence of MSK symptoms, and clinical characteristics (Quan–Charlson comorbidity score, AHRQ comorbidity conditions, and a flag for any inflammatory comorbid condition). *P* values  $< 0.05$  were considered statistically significant for all analyses.

## RESULTS

### Patient Demographics and Clinical Characteristics

Overall, 116,203 patients newly diagnosed with PsO were included, of whom 110,118 (94.8%) did not have comorbid PsA at baseline (Table 1). The mean (SD) follow-up period for all patients was 1423.8 (917.5) days. Patients with only PsO had a mean (SD) age of 53.7 (16.4) years. Approximately half of patients with only PsO were female (53.0%), and most had commercial insurance (73.7%).

High proportions of patients with only PsO had non-MSK comorbid conditions, including other skin disorders (45.5%), disorders of lipid metabolism (42.9%), and hypertension (42.2%) (Table 1). Over one-third of patients with only PsO (38.4%) had any inflammatory conditions; patients also experienced osteoarthritis (16.6%) and fibromyalgia (4.5%).

Patients with PsO and baseline PsA had demographic characteristics similar to those with PsO only. PsO patients with baseline PsA also had significantly high prevalence of other comorbid conditions and inflammatory conditions at baseline. Compared with patients with PsO only, those with PsO and baseline PsA had a higher prevalence of non-traumatic joint disorders, conditions relating to back problems, and other connective tissue disorders (Table 1).

### MSK Symptoms at Baseline among Patients with PsO

A total of 47.1% of patients diagnosed with only PsO experienced any MSK symptoms at baseline (Fig. 1). Arthralgia (22.7%), back pain (20.8%), and fatigue (14.8%) were among the most frequent individual MSK symptoms in these patients. At baseline, 59.4% of patients with only PsO had any evidence of MSK symptoms, 38.4% had an MSK-related procedure and/or assessment, and 32.9% had an HCRU.

### MSK Symptom Prevalence and Evidence of MSK-Related Resource Utilization among Patients with PsO at 12 and 60 months of Follow-up

At 12 months, 48.2% of patients with only PsO had any MSK symptom; the most prevalent were arthralgia (24.4%), back pain (21.7%), and fatigue (15.1%) (Fig. 2). Prevalence of all MSK symptoms increased in patients at 24-, 36-, and 48-month follow-ups (Table S1). At 60 months, the proportion of patients with PsO only who experienced any MSK symptom increased to 82.1%, and prevalence of all individual MSK symptoms increased (Fig. 2). The most common MSK symptoms were arthralgia (55.9%), back pain (47.8%), and fatigue (39.9%).

Similar findings were seen for proportions of patients who experienced evidence of MSK symptoms at 12- and 60-month follow-ups (Fig. 3). At 12 months, 60.9% of patients had any evidence of MSK symptoms, followed by procedure and/or assessment (40.9%), and MSK-related HCRU (36.0%). A comparison of prevalence of MSK symptoms and evidence of MSK symptoms (MSK-related procedure and/or assessment and use of an ambulatory assist device) at 12-month follow-up between patients with PsO and a representative control cohort of patients enrolled in the Optum Research Database is presented in Fig. S3. The proportion of patients with evidence of an MSK symptom increased each year to 89.0% at 60 months, with most patients experiencing MSK-related procedures and/or assessments and MSK-related HCRU (75.7% and 66.8%, respectively) (Table S1; Fig. 3).

The use of advanced therapeutics for PsA or PsO differed significantly among patients with PsO, stratified by baseline comorbid PsA ( $P < 0.001$ ) (Table S2). Overall, 53.4% of patients with both PsO and PsA received  $\geq 1$  advanced therapy indicated for PsO and PsA compared with 10.9% of patients with only PsO. Regarding the use of conventional therapeutics, cyclosporine use was minimal among patients with PsO only (0.6%) and comorbid PsA (0.7%), although usage of methotrexate was greater among patients with comorbid PsA

**Table 1** Demographics and clinical characteristics in patients with PsO stratified by baseline comorbid PsA

Characteristic <sup>b</sup>	All patients (N = 116,203)	Patients with PsO only <sup>a</sup> (n = 110,118)	Patients with PsO and PsA (n = 6085)
Age, mean (SD), years	53.7 (16.2)	53.7 (16.4)	53.8 (13.3)
Female sex	61,487 (52.9)	58,382 (53.0)	3105 (51.0)
<i>Insurance status</i>			
Commercial	85,766 (73.8)	81,142 (73.7)	4624 (76.0)
Medicare	30,437 (26.2)	28,976 (26.3)	1461 (24.0)
Length of follow-up, mean (SD), days	1423.8 (917.5)	1424.7 (918.0)	1407.5 (908.6)
CCI score (0–5), mean (SD)	0.66 (1.3)	0.65 (1.3)	0.88 (1.3)
<i>CCI category</i>			
0	79,944 (68.8)	76,692 (69.7)	3252 (53.4)
1	16,522 (14.2)	15,014 (13.6)	1508 (24.8)
2	10,136 (8.7)	9435 (8.6)	701 (11.5)
3	4436 (3.8)	4112 (3.7)	324 (5.3)
4	2342 (2.0)	2187 (2.0)	155 (2.6)
≥ 5	2823 (2.4)	2678 (2.4)	145 (2.4)
<i>Comorbid conditions<sup>c</sup></i>			
Other skin disorders	52,262 (45.0)	50,094 (45.5)	2168 (35.6)
Disorders of lipid metabolism	50,055 (43.1)	47,285 (42.9)	2770 (45.5)
Hypertension	49,353 (42.3)	46,483 (42.2)	2870 (47.2)
Immunizations and screening for infectious diseases	41,244 (35.5)	38,664 (35.1)	2580 (42.4)
Non-traumatic joint disorders	40,271 (34.7)	36,021 (32.7)	4250 (69.8)
Other connective tissue disorders	39,117 (33.7)	35,971 (32.7)	3146 (51.7)
Respiratory infections	36,712 (31.6)	34,626 (31.4)	2086 (34.3)
Eye disorders	35,820 (30.8)	33,913 (30.8)	1907 (31.3)
Conditions related to back problems (including spondylosis and intervertebral disc disorders)	31,954 (27.5)	29,572 (26.9)	2382 (39.2)
Heart conditions	31,242 (26.9)	29,441 (26.7)	1801 (29.6)
Benign neoplasms	28,726 (24.7)	27,415 (24.9)	1311 (21.5)
Urinary system diseases	28,555 (24.6)	26,929 (24.5)	1626 (26.7)
Diabetes mellitus without complication	26,466 (22.8)	24,983 (22.7)	1483 (24.4)
Other lower respiratory disease	26,400 (22.7)	24,794 (22.5)	1606 (26.4)
Other nutritional, endocrine, or metabolic disorders	25,875 (22.3)	24,266 (22.0)	1609 (26.4)
<i>Comorbid inflammatory conditions<sup>d</sup></i>			

**Table 1** continued

Characteristic <sup>b</sup>	All patients ( <i>N</i> = 116,203)	Patients with PsO only <sup>a</sup> ( <i>n</i> = 110,118)	Patients with PsO and PsA ( <i>n</i> = 6085)
Any comorbid inflammatory condition	45,876 (39.5)	42,300 (38.4)	3576 (58.8)
Fibromyalgia	5719 (4.9)	4991 (4.5)	728 (12.0)
Osteoarthritis	20,320 (17.5)	18,244 (16.6)	2076 (34.1)

CCI Charlson Comorbidity Index, PsA psoriatic arthritis, PsO psoriasis, SD standard deviation

<sup>a</sup>PsO-only cohort defined as patients without a claim for PsA diagnosis (ICD-9-CM: 696.0; ICD-10-CM: L40.50, L40.51, L40.52, L40.53, and L40.59) in any position during the 12-month baseline period

<sup>b</sup>Data presented as *n* (%) unless otherwise stated

<sup>c</sup>Comorbid conditions occurring in  $\geq 20\%$  of patients

<sup>d</sup>Comorbid inflammatory conditions occurring in  $\geq 10\%$  of patients

(37.7%) compared with patients with PsO only (7.2%).

#### Timing of MSK symptom occurrence and PsA diagnosis among patients with only PsO

Patients with only PsO had a median [95% confidence interval (CI)] time to occurrence of MSK symptoms of 659.0 (651.0–666.0) days (Fig. S4). Median (95% CI) time to evidence of MSK symptoms was 438.0 (433.0–442.0) days.

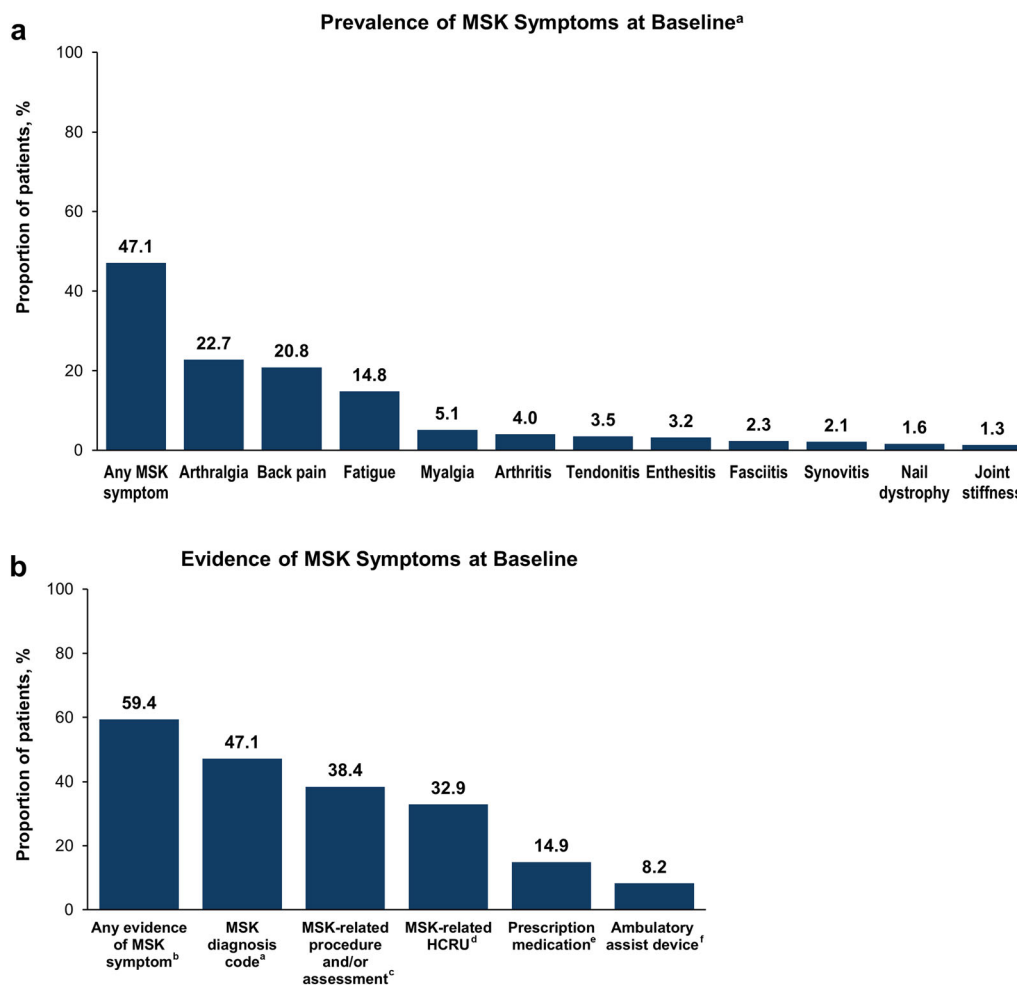
In the overall PsO-only cohort with  $\geq 1$  MSK symptom, the cumulative PsA rates at 1 year, 2 years, and 5 years following index diagnosis were 5.2%, 7.5%, and 12.3%, respectively. In the PsO-only cohort with or without baseline MSK symptoms, the corresponding percentages were 3.7%, 5.6%, and 9.7%, respectively (Table S3).

#### Predictors of PsA Diagnosis among the PsO-Only Cohort

Patient age at PsO diagnosis was significantly associated [hazard ratio (HR) [95% CI]] with increased likelihood of a PsA diagnosis, as seen among patients aged 30–39 years (1.32 [1.19–1.46]), 40–49 years (1.54 [1.40–1.70]), and 50–59 years (1.36 [1.23–1.50]) versus those aged

18 to 29 years (all  $P < 0.001$ ) (Fig. 4). A significant positive association (HR [95% CI]) was also observed between baseline CCI scores of 3 and a PsA diagnosis (1.17 [1.04–1.31];  $P = 0.009$ ) versus a CCI score of 0. Additionally, presence vs absence of baseline MSK symptoms was significantly associated (HR [95% CI]) with increased hazard of a PsA diagnosis, including arthralgia (1.48 [1.41–1.57];  $P < 0.001$ ), myalgia (1.14 [1.05–1.24];  $P = 0.001$ ), tendonitis (1.33 [1.21–1.45];  $P < 0.001$ ), fasciitis (1.18 [1.05–1.32];  $P = 0.005$ ), arthritis (1.97 [1.82–2.12];  $P < 0.001$ ), fatigue (1.13 [1.07–1.19];  $P < 0.001$ ), and nail dystrophy (1.20 [1.03–1.41];  $P = 0.024$ ). Similarly increased hazard (HR (95% CI)) of receiving a diagnosis of PsA was also seen among patients who had baseline evidence of MSK symptoms such as prescription pain medications (1.40 [1.32–1.48];  $P < 0.001$ ) and MSK-related procedures, assessment, and/or HCRU (1.28 [1.21–1.35];  $P < 0.001$ ).

Several factors were associated with decreased hazard of a PsA diagnosis (HR [95% CI]), including an age of  $\geq 70$  years (0.64 [0.57–0.73];  $P < 0.001$ ) versus an age of 18–29 years; male versus female sex (0.95 [0.91–0.99];  $P < 0.028$ ); baseline presence versus absence of other skin disorders such as atopic dermatitis, eczema, and contact dermatitis (0.87 [0.84–0.91];  $P < 0.001$ ); and use versus non-use



**Fig. 1** Proportions of patients with only PsO with **a** prevalence and **b** evidence of MSK symptoms at baseline. *HCPCS* Healthcare Common Procedure Coding System, *HCRU* healthcare resource utilization, *MSK* musculoskeletal, *PsO* psoriasis. <sup>a</sup>MSK symptoms were identified from diagnosis codes on medical claims; patients with  $\geq 1$  claim with a diagnosis code in any position were identified. <sup>b</sup>Patients were identified by diagnosis code, prescription medication, procedures/assessments, HCRU, or ambulatory assist device. <sup>c</sup>One or more claims with Current

Procedural Terminology, HCPCS, diagnosis, procedure or revenue code for joint imaging, chiropractic or osteopathic treatment, or physical therapy. <sup>d</sup>One or more claims for a healthcare visit to a rheumatologist, orthopedist, chiropractor, physical therapist, osteopath, podiatrist, or sports medicine practitioner. <sup>e</sup>Three or more consecutive months of treatment with prescription medications for pain. <sup>f</sup>One or more claims with an HCPCS code for an ambulatory assist device

of an ambulatory assist device at baseline (0.60 [0.55–0.65];  $P < 0.001$ ).

## DISCUSSION

In this retrospective study, patients diagnosed with PsO and followed for  $\geq 12$  months had increased prevalence and evidence of MSK

symptoms over time and experienced MSK-related HCRU before diagnosis of MSK symptoms. Among patients with only PsO (i.e., without a diagnosis of PsA at baseline), 3.7%, 5.6%, and 9.7% of patients were diagnosed with PsA at 1, 3, and 5 years, respectively, with a median time to development of PsA of 1.2 years; these rates are similar to those previously reported by our



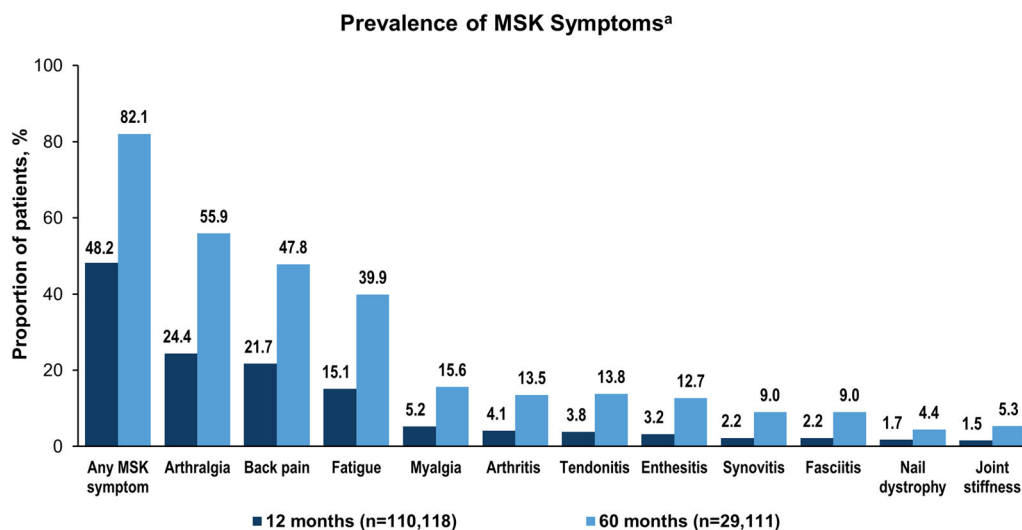
group and others [24, 26–29]. Patient factors such as ages 30–59 years, presence of baseline evidence of MSK symptoms, or baseline inflammatory comorbid conditions were significantly associated with increased hazard of a PsA diagnosis.

This study provides a comprehensive assessment of MSK symptom prevalence among patients with newly diagnosed PsO followed up for an extended period. Similar analyses assessed MSK symptoms in patients with PsO prior to receiving a PsA diagnosis [4, 29–32]; a prospective cohort study using medical records and patient survey data reported that 23% and 21.5% of patients with PsO experienced baseline arthralgia and back pain, respectively [4]. Another prospective cohort study of patient survey and medical records for patients with PsO found that 41% and 35% of patients reported baseline arthralgia and nail disease, respectively [31]. Additional studies demonstrated through ultrasonography that subclinical enthesial abnormalities are present in asymptomatic patients with PsO, which may serve as another predictor for the development of PsA [29, 32]. However, these studies focused on patients with established PsO, with mean disease durations of as high as 15.8 and 20.1 years [4, 31]. Our analysis is unique in

assessing the progression of MSK burden from patients with a new PsO diagnosis as the index date.

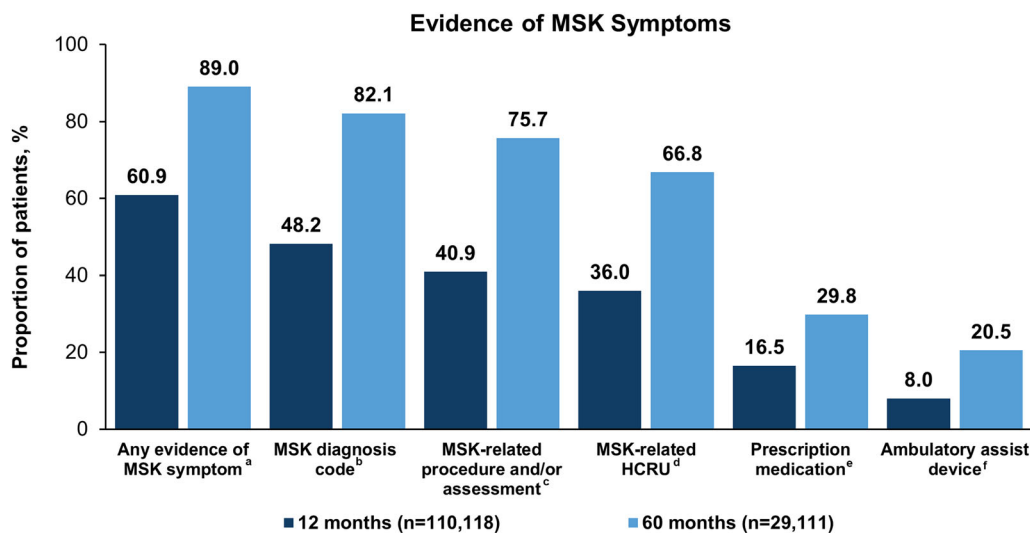
Approximately half of patients in our study experienced MSK symptoms at diagnosis. By 60 months, most patients experienced MSK-related burden, indicating their PsO was not well controlled, and they may need additional intervention or care. Patients with PsO and comorbid PsA at baseline continued to face MSK burdens at potentially higher rates than patients with PsO only, even though these patients also had high rates of advanced therapy utilization throughout follow-up, suggesting that new MSK symptoms continued to develop, and existing symptoms were exacerbated. Furthermore, this study data was collected from 2007 to 2020, when the treatment landscape for PsO and PsA changed considerably. The development and approval of new therapeutics for these indications during this time frame included some agents reported to affect the occurrence of PsA in patients with PsO; future analyses should be conducted to assess the impact of newer treatments on the prevalence of MSK symptoms and diagnosis of comorbid PsA.

Our study demonstrates characteristics of patients with only PsO that may predict a future



**Fig. 2** Proportions of patients with only PsO with MSK symptoms at 12- and 60-month follow-up. *MSK* musculoskeletal, *PsO* psoriasis. <sup>a</sup>MSK symptoms were identified

from diagnosis codes on medical claims; patients with  $\geq 1$  claim with a diagnosis code in any position were identified

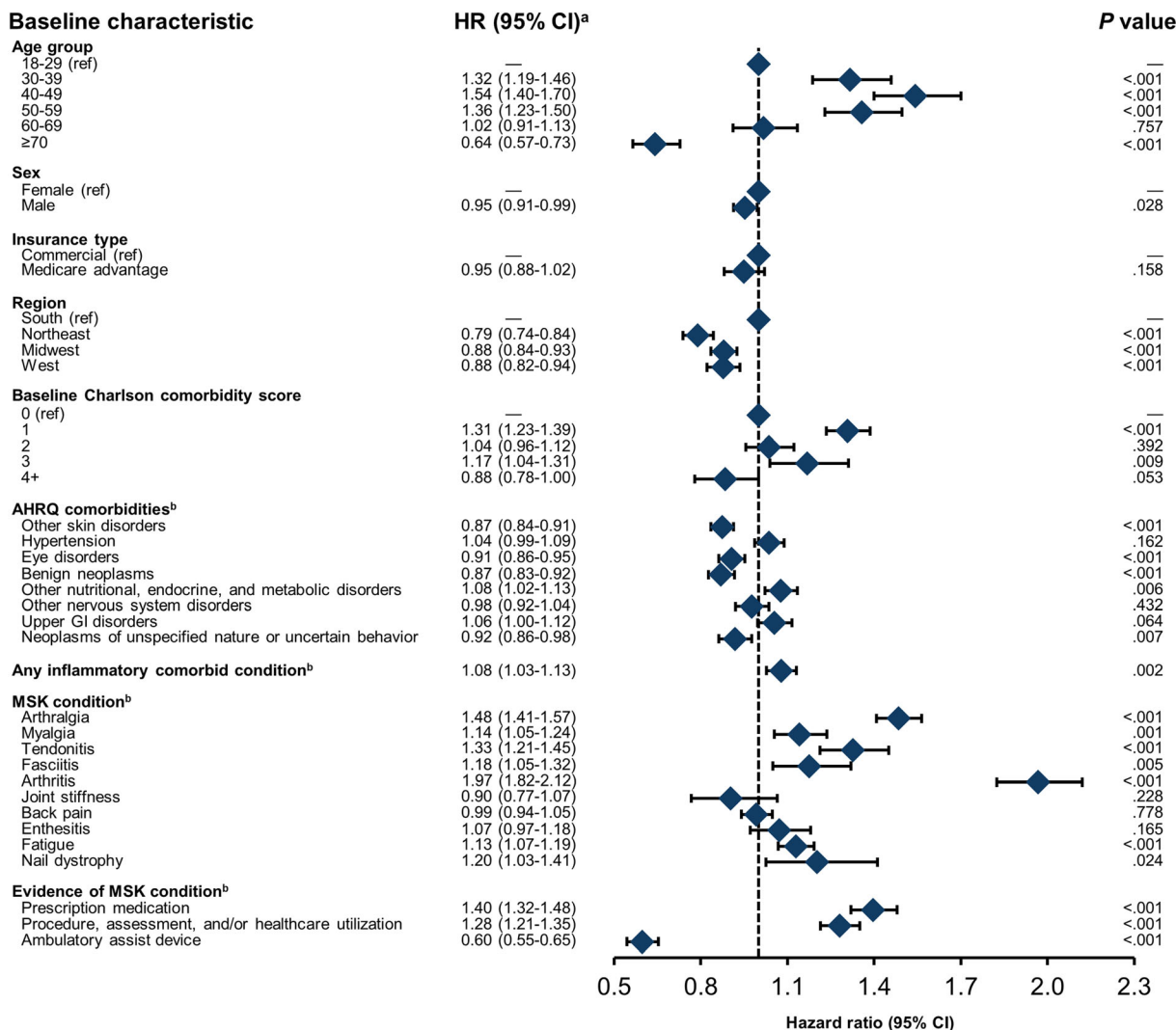


**Fig. 3** Proportions of patients with only PsO with evidence of MSK-related resource utilization at 12- and 60-month follow-up. *HCPCS* Healthcare Common Procedure Coding System, *HCRU* healthcare resource utilization, *MSK* musculoskeletal, *PsO* psoriasis. <sup>a</sup>Patients were identified by diagnosis code, prescription medication, procedures/assessments, healthcare resource utilization, or ambulatory assist device. <sup>b</sup>MSK symptoms were identified from diagnosis codes on medical claims; patients with  $\geq 1$  claim with a diagnosis code in any position were identified.

<sup>c</sup>One or more claims with Current Procedural Terminology, HCPCS, diagnosis, procedure or revenue code for joint imaging, chiropractic or osteopathic treatment, or physical therapy. <sup>d</sup>One or more claims for a healthcare visit to a rheumatologist, orthopedist, chiropractor, physical therapist, osteopath, podiatrist, or sports medicine practitioner. <sup>e</sup>Three or more consecutive months of treatment with prescription medications for pain. <sup>f</sup>One or more claims with an HCPCS code for an ambulatory assist device

PsA diagnosis. Previous studies have reported that the presence of MSK symptoms is associated with development of PsA. Eder et al., described above, suggested that among patients with PsO, female sex, baseline arthralgia, and high stiffness scores were strong predictors for PsA development [4]. A meta-analysis of four prospective cohort studies reported patients with PsO with arthralgia experienced an increased risk of developing PsA [33]. Similar to prior studies, our results showed that the presence of MSK symptoms, such as arthralgia, tendonitis, and arthritis, was significantly associated with increased risk of PsA diagnosis. Furthermore, this study identified additional factors associated with PsA diagnosis, including age (30–59 years), certain comorbidities including other skin disorders, eye disorders, and benign neoplasms, and evidence of MSK conditions prior to PsO diagnosis (prescription pain medication use and HCRU). Patients and clinicians alike should be aware of these symptoms

and factors as potential signs of subclinical PsA or predictors of PsA development among patients with PsO. Our observation that non-traumatic joint disorders, conditions relating to back problems, and other connective tissue disorders at baseline occurred more frequently among patients with a PsA diagnosis highlights the importance of vigilance among clinicians regarding the development of MSK symptoms, even those not apparently related to psoriatic disease. Although approximately 20% of patients were  $\geq 70$  years of age, older age was associated with decreased risk of PsA development. This is consistent with previous studies showing decline in incidence of PsA among patients aged  $\geq 60$  years, which may be attributed to increased comorbidity burden in aging populations that could mask or obfuscate a diagnosis of PsA [34, 35]. Our results corroborate available data regarding MSK symptoms as predictors for PsA diagnosis and highlight the importance of early patient monitoring during



**Fig. 4** Proportional hazards model of PsA diagnosis among patients with only PsO. *AHRQ* Agency for Healthcare Research and Quality, *GI* gastrointestinal, *MSK* musculoskeletal, *PsA* psoriatic arthritis, *PsO* psoriasis, *ref* reference, *CI* confidence interval, *HR* hazard ratio. <sup>a</sup>Covariates in the model included demographic characteristics (age group, sex, insurance type, and geographic region). MSK symptoms were defined using diagnostic codes (arthralgia, myalgia, tendonitis,

fasciitis, arthritis, joint stiffness, back pain, enthesitis, fatigue, and nail dystrophy), evidence of MSK symptoms (prescription medication; procedure, assessment, and/or healthcare utilization; and ambulatory assist device), and clinical characteristics (Quan–Charlson comorbidity score, AHRQ comorbidity conditions, and a flag for any inflammatory comorbid condition). <sup>b</sup>HRs are for the comorbidity/condition versus the absence

subclinical phases of PsA to identify patients with PsA earlier to reduce diagnostic delays.

This analysis should be interpreted within the context of the study limitations. Patients were required to be enrolled in commercial or Medicare Advantage health plans, a requirement that may not reflect the general

population of patients with PsO and limits the generalizability of findings. Data were derived from patient medical claims, which do not include detailed information on clinical characteristics (i.e., disease severity) or information about time between onset of symptoms and diagnosis of PsO. Furthermore, medical claims

lack validation and are therefore subject to underreporting or incorrect coding and diagnosis. To minimize the impact of this limitation, patients were required to have a prespecified number of PsO-specific claims. Despite excluding patients with a PsA diagnosis from baseline, it is still possible that some physicians may have coded for PsO only in patients who had both PsO and PsA, leading to overestimation of MSK conditions at baseline. Likewise, the potential for presence of osteoarthritis or fibromyalgia could serve as confounders for experiencing MSK symptoms. In addition, patients were not necessarily evaluated or managed by a rheumatologist following development of MSK symptoms, and it may be possible that some patients with MSK symptoms did have PsA without having a diagnosis code for it at baseline. Imaging analyses including X-ray, MRI, and ultrasound were not included in this analysis and could provide additional evidence for transition to PsA in future studies. Some study outcomes (e.g., prescription medication use and HCRU) cannot be attributed to a specific symptom; however, results still provide useful information about MSK-related burden and may set the foundation for future studies using diagnosis codes (e.g., predictive modeling). Finally, no direct comparison was made between MSK symptoms in the groups studied here versus those present in a control group of patients without PsO or PsO and PsA.

## CONCLUSION

In this exploratory study, patients with PsO had increased prevalence rates and evidence of MSK symptoms through 60 months. Diagnosis of PsA was significantly associated with patient age, prescription pain medication, arthritis, and arthralgia. Our results suggest that patients with MSK symptoms should be screened for PsA to prevent diagnostic and treatment delays, and that physicians should be asking their patients with PsO about any MSK complaints during follow-up visits. Furthermore, these findings highlight an opportunity for primary care providers and dermatologists to collaborate with

rheumatologists in the management and care of patients with PsO who have MSK complaints.

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**Data Availability.** The data underlying this article are available in the article and in its online supplementary material.

## Declarations

**Conflict of Interest.** Joseph F. Merola is a consultant and/or investigator for Amgen, Arcutis, Bristol Myers Squibb, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Sanofi, Regeneron, Sun Pharma, Biogen, Pfizer, and LEO Pharma. Dhaval Patil and Antton Egana are employees of Novartis Pharmaceuticals Corporation. Andrea Steffens and Noah S. Webb are employees of Optum. Alice B. Gottlieb has received honoraria as an advisory board member and consultant for Amgen, AnaptysBio, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Dice Therapeutics, Eli Lilly, Janssen, Novartis, Sanofi, UCB, and Xbiotech, and has received research/

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