Healthcare Resource Use and Direct Costs in Patients with Ankylosing Spondylitis and Psoriatic Arthritis in a Large US Cohort

Jeffrey D. Greenberg, Jacqueline B. Palmer, Yunfeng Li, Vivian Herrera, Yuen Tsang, and Minlei Liao

ABSTRACT. Objective. Direct costs of ankylosing spondylitis (AS) and psoriatic arthritis (PsA) have not been well characterized in the United States. This study assessed healthcare resource use and direct cost of AS and PsA, and identified predictors of all-cause medical and pharmacy costs.

Methods. Adults aged ≥ 18 with a diagnosis of AS and PsA were identified in the MarketScan databases between October 1, 2011, and September 30, 2012. Patients were continuously enrolled with medical and pharmacy benefits for 12 months before and after the index date (first diagnosis). Baseline demographics and comorbidities were identified. Direct costs included hospitalizations, emergency room and office visits, and pharmacy costs. Multivariable regression was used to determine whether baseline covariates were associated with direct costs.

Results. Patients with AS were younger and mostly men compared with patients with PsA. Hypertension and hyperlipidemia were the most common comorbidities in both cohorts. A higher percentage of patients with PsA used biologics and nonbiologic disease-modifying drugs (61.1% and 52.4%, respectively) compared with patients with AS (52.5% and 21.8%, respectively). Office visits were the most commonly used resource by patients with AS and PsA (~11 visits). Annual direct medical costs [all US dollars, mean (SD)] for patients with AS and PsA were $6514 ($32,982) and $5108 ($22,258), respectively. Prescription drug costs were higher for patients with PsA [$14,174 ($15,821)] compared with patients with AS [$11,214 ($14,249)]. Multivariable regression analysis showed higher all-cause direct costs were associated with biologic use, age, and increased comorbidities in patients with AS or PsA (all $p < 0.05$).

Conclusion. Biologic use, age, and comorbidities were major determinants of all-cause direct costs in patients with AS and PsA. (J Rheumatol First Release December 1 2015; doi:10.3899/jrheum.150540)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS PSORIATIC ARTHRITIS OBSERVATIONAL STUDY
MEDICAL CARE COSTS PRESCRIPTION DRUGS COST ANALYSIS

Ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are part of a family of related inflammatory diseases called spondyloarthritis (SpA) that affect the spine, and in some cases, the peripheral joints and extraarticular regions[1,2,3,4]. In the United States, AS is the most common SpA condition, affecting between 0.1% and 0.5% of the population while PsA is estimated at 0.1%[5]. In addition to arthritic symptoms, patients with AS and PsA often have several comorbid conditions, including metabolic syndrome, cardiovascular (CV) disease, obesity, Type 2 diabetes, hypertriglyceridemia, and cerebrovascular disease[6,7,8,9]. Several treatment options are currently available to manage symptoms and disease progression in patients with AS and PsA, including nonbiologic disease-modifying antirheumatic drugs (nbDMARD)

From the Department of Rheumatology, New York University School of Medicine, New York, New York; Health Economics and Outcomes Research, and Outcomes Research Methods and Analytics, US Health Economics and Outcomes Research, Novartis Pharmaceuticals Corp., East Hanover; KMK Consulting Inc., Florham Park, New Jersey; Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, Maryland, USA.

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J.D. Greenberg, MD, MPH, New York University Hospital for Joint Disease, and Department of Rheumatology, New York University School of Medicine; J.B. Palmer, PharmD, Health Economics and Outcomes Research, Novartis; Y. Li, PhD, Outcomes Research Methods and Analytics, US Health Economics & Outcomes Research, Novartis; V. Herrera, PharmD, Health Economics and Outcomes Research, Novartis; Y. Tsang, PharmD, Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy; M. Liao, MA, KMK Consulting Inc.

Address correspondence to Dr. J.D. Greenberg, Department of Rheumatology, New York University Hospital for Joint Diseases, 301 East 17th St., Suite 1410, New York, New York 10003, USA. E-mail: JGreenberg@corrona.org

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and biologic agents (e.g., tumor necrosis factor-α inhibitors)[10,11,12,13,14].

A clear understanding of the financial burden related to the provision of patient care is challenged by the paucity of published economic data in the United States[15,16,17,18]. To date, few US studies have assessed healthcare use and direct costs of AS or PsA[15,16,17]. Studies conducted in the mid- to late 1990s estimated that the direct costs (medical and treatment costs, US dollars) per patient with PsA were $3638; for AS, these costs ranged from $2674 to $4571[15,16]. In 1997, the overall direct costs for patients with PsA exceeded $10 million[18]. The majority of these costs were attributed to pharmacy costs, functional disabilities, and comorbidities[15,16,17].

As physicians and payers examine the cost-effectiveness and assess the growing treatment options associated with AS and PsA, a more accurate understanding of the healthcare resource use and costs is needed because most US studies were published more than 12 years ago[15,16]. In the last 10 years, only 1 US study examined healthcare use in AS and none addressed PsA in a broad general population of patients with commercial healthcare or private Medicare supplemental coverage[16]. Similarly, only a limited number of US studies reviewed direct costs in patients with PsA or AS[15,16,17]. Biologics became available after 2002, which significantly influences the inferences drawn from studies performed before their widespread use[15,16]. The development of newer biologic agents has contributed to the treatment resources for patients with AS and PsA[19]. However, only limited data exist on the effect of these new medications on overall medical costs[17], and the effect of comorbidities on overall medical costs of AS and PsA is poorly understood.

Using a retrospective administrative claims database, our present study was designed to enhance the understanding of the current economic effect on these patient populations in the United States. To our knowledge, this is the first published study within the last decade to evaluate the healthcare resource use and all-cause direct costs associated with AS and PsA. Our objective was to fill the current US knowledge gap descriptively and to report the healthcare resource use and direct costs and predictors of costs for patients with AS and PsA from a payer perspective.

MATERIALS AND METHODS

Data source. We conducted a retrospective observational claims analysis to assess healthcare use and direct costs associated with AS and PsA using administrative data derived from 2 Truven Health Analytics MarketScan Research databases: the Commercial Claims and Encounters Database, and the Medicare Supplemental and Coordination of Benefits Database. These represent the health services of dependents and retired workers in the United States with primary or Medicare supplemental coverage through private employer-sponsored insured health plans. Healthcare is provided under a variety of fee-for-service (FFS), point-of-service (POS), or capitated health plans. Types of health plans included health maintenance organization (HMO) and POS or comprehensive plans[20]. Detailed cost, use, and outcomes data for healthcare services performed in both inpatient and outpatient settings were collected. Unique enrollee identifiers link medical claims to outpatient prescription drug claims and person-level enrollment data. Database constructs included information on patient demographics (age, sex, employment status, geographic location), healthcare use, costs (payment), and comprehensive prescription drug data[20]. All study data were accessed in compliance with the Health Insurance Portability and Accountability Act of 1996. Because MarketScan databases contain deidentified patient data, informed consent or institutional review board approval were not required.

Sample selection and patient population. A diagnosis of AS or PsA was identified using the International Classification of Diseases, 9th ed, Clinical Modification (ICD-9-CM) codes 720.0 (AS) and 696.0 (PsA)[21]. The study period was from October 1, 2010, to September 30, 2013. Patients with AS or PsA aged ≥ 18 years with at least 2 inpatient and/or outpatient ICD-9-CM claims for AS or PsA between October 1, 2011, and September 30, 2012 (identification period) were included in the analysis (Figure 1). Claims had to be on different dates during the identification period. The index date was defined as the first reported ICD-9-CM claim with any diagnosis of AS or PsA during the identification period. One index date per patient was designated for each condition. Patients were required to be continuously enrolled with medical and pharmacy benefits in the 12 months before and after the index date. Patients with a non–rule-out rheumatoid arthritis diagnosis (ICD-9 code, 714.x) 12 months before and after the index date were excluded

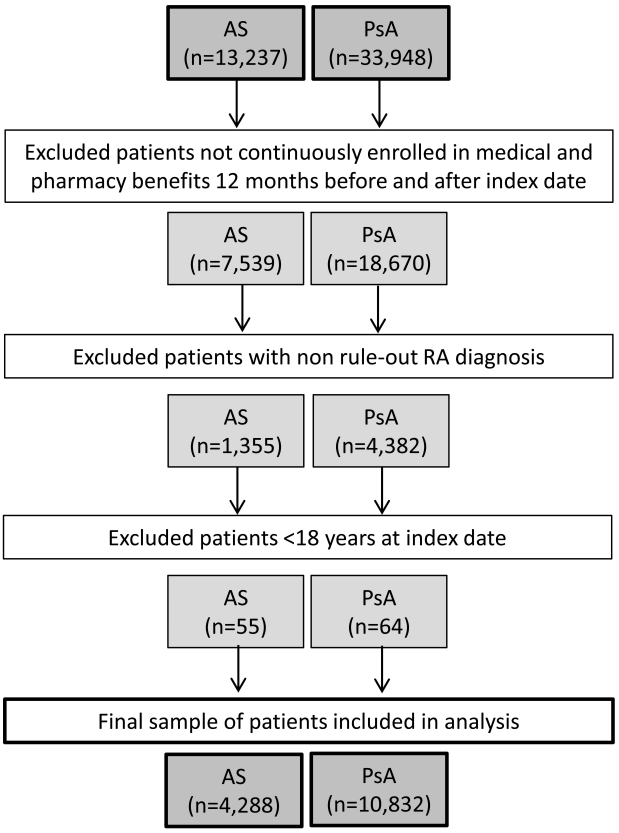

Figure 1. Patient selection flowchart. Patients with ≥ 2 claims for AS or PsA diagnoses identified between October 1, 2011, and September 30, 2012. The index date was the date of the first diagnosis during the identification period. One index date per patient was designated for AS and PsA. For example, a patient included in the PsA cohort could have 2 of the same diagnosis claims (e.g., the AS cohort had to have 2 ICD-9-CM claims of AS). Data source: MarketScan Commercial and Medicare Supplemental databases, 2010-2013 (http://truvenhealth.com/your-healthcare-focus/analytic-research/marketscan-research-databases). AS: ankylosing spondylitis; PsA: psoriatic arthritis; RA: rheumatoid arthritis; ICD-9-CM: International Classification of Diseases, 9th ed, Clinical Modification.

to reduce the potential for misdiagnosis. Demographic and clinical characteristics were obtained during the preindex period (i.e., the fixed 12-mo period before the patient identification period). All-cause direct costs and healthcare resource use were estimated during the 12-month followup period following the index date.

Explanatory variables. Demographic categorical variables included sex, geographic region (Northeast, North Central, South, West), and insurance type (HMO and POS capitation, FFS). Age was molded as a categorical variable to allow for a nonlinear relationship between age and cost and was represented as age 18–34, 35–44, 45–54, 55–64, and ≥ 65 years. Clinical variables evaluated during the preindex period included a measure of comorbidities. The Elixhauser Comorbidity Index (ECI) score was used to measure the burden of comorbid conditions not directly related to AS or PsA. ECI distinguishes 30 comorbid conditions identified using ICD-9-CM codes from complications by considering only secondary diagnoses unrelated to the primary diagnosis[22]. The mean ECI score for each condition and the proportion of patients reporting 0, 1, 2, 3, or 4+ comorbidities were determined. In addition, selected AS- and PsA-related comorbidities (i.e., Type 2 diabetes, hypertension, hyperlipidemia, and ischemic heart disease) were measured based on the Chronic Conditions Warehouse (CCW) algorithm[23].

Outcome measures. The study outcome measures were all-cause healthcare resource use and direct costs reported during the 12-month followup period. Healthcare resource use included hospitalization (inpatient visits), office, and emergency room (ER) visits, and biologic and nbDMARD use among users with at least 1 resource use. Direct costs included plan-paid medical expenditures for hospitalization (inpatient), office, and ER visits, and prescription costs for biologics and nbDMARD. Capitated costs with a value of 0 or 1 for managed care payers were assigned a value using the FFS median cost. All costs were adjusted to 2013 US dollars using the Consumer Price Index. Biologic drugs considered in the analysis were infliximab[24], adalimumab[25], golimumab[26], etanercept[27], certolizumab[28], rituximab[29], tocilizumab[30], abatacept[31], and ustekinumab[32]. nbDMARD included were hydroxychloroquine sulfate[33], leflunomide[34], methotrexate[35], sulfasalazine[36], azathioprine[37], penicillamine[38], and cyclosporine[39].

Statistical analysis. Descriptive summary statistics were performed for all demographics and disease characteristics; these included count and percentages for categorical variables and mean and SD for continuous variables. Mean (SD) and median (interquartile range) were reported for all-cause healthcare use and direct costs. A multivariable generalized linear model (GLM) with γ distribution and log link function was used to identify potential predictors associated with direct costs[40], which included medical and pharmacy costs. The explanatory variables in the multivariable GLM included age, sex, region, insurance plan, ECI score, and baseline biologic use.

The same patient selection process as described in Figure 1 was applied to the multivariable analysis for the definitions of AS and PsA. Patients with missing region (n = 42 for AS, < 1%; n = 125 for PsA, < 1%), missing insurance type (n = 157 for AS, < 3%; n = 425 for PsA, < 4%), or zero outcome (n = 11 for AS, < 1%; n = 5 for PsA, < 1%) were excluded from the multivariate analysis. Coefficient estimates were the exponentials of the original estimates. A coefficient of > 1.0 indicates higher cost and < 1.0 indicates lower costs for a given variable compared with the specified reference. The coefficient indicates cost increases or decreases in a continuous manner compared with the reference group. Standard error and confidence limits were adjusted accordingly. The prespecified significance level for statistical comparisons was $p < 0.05$. All statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc.).

RESULTS

Patient selection. Patients with at least 2 ICD-9-CM claims for an AS or PsA diagnosis were identified in the MarketScan Research database between October 1, 2011, and September 30, 2012. The patient selection process and the number of patients with AS (n = 4288) and PsA (n = 10,832) after applying the inclusion and exclusion criteria are illustrated in Figure 1.

Baseline patient characteristics. Baseline demographics and disease characteristics are presented in Table 1. The mean (SD) age of patients with PsA was 51.9 years (11.8) and for AS was 49.1 years (13.4). The AS cohort had a greater percentage of men than women (64.3%). In the PsA cohort, the distribution of men and women was about 50%. Patients with AS had a slightly greater number of comorbidities (mean ECI score of 1.9) compared with patients with PsA (mean ECI score of 1.2). The percentage of patients with AS with an ECI score ≥ 2 was 48.9% compared with 31.7% for the PsA cohort. The AS cohort had the highest percentage of patients with an ECI score of ≥ 4 (13.2% for AS vs 7.4% for PsA). The distribution of the evaluated comorbid conditions was similar across both cohorts; hypertension was the most common comorbidity identified using the CCW chronic

Table 1. Baseline demographic and disease characteristics of patients with AS and PsA. Values are n (%) unless otherwise specified.

Characteristics	AS, n = 4288	PsA, n = 10,832
Age, yrs, mean (SD)	49.1 (13.4)	51.9 (11.8)
Age, yrs		
18–34	649 (15.1)	822 (7.6)
35–44	906 (21.1)	1986 (18.3)
45–54	1199 (28.0)	3353 (31.0)
55–64	1101 (25.7)	3470 (32.0)
≥ 65	433 (10.1)	1201 (11.1)
Sex		
Male	2758 (64.3)	5475 (50.5)
Female	1530 (35.7)	5357 (49.5)
US region		
Northeast	611 (14.2)	1972 (18.2)
North Central	947 (22.1)	2673 (24.7)
South	1443 (33.7)	4053 (37.4)
West	1245 (29.0)	2009 (18.5)
Unknown	42 (1.0)	125 (1.2)
Health insurance		
FFS	3438 (80.2)	8749 (80.8)
HMO and POS capitation	693 (16.2)	1658 (15.3)
Missing/unknown	157 (3.7)	425 (3.9)
ECI score, mean (SD)	1.9 (1.6)	1.2 (1.5)
ECI score		
0	495 (11.5)	4397 (40.6)
1	1698 (39.5)	2997 (27.7)
2	1034 (24.1)	1809 (16.7)
3	497 (11.6)	828 (7.6)
4+	564 (13.2)	801 (7.4)
Comorbidities*		
Type 2 diabetes	528 (12.3)	1773 (16.4)
Hypertension	1263 (29.5)	3534 (32.6)
Hyperlipidemia	888 (20.7)	2647 (24.4)
Ischemic heart disease	281 (6.6)	723 (6.7)
Any of the above	1826 (42.6)	5329 (49.2)

* Identification was based on non-rule-out diagnoses. AS: ankylosing spondylitis; PsA: psoriatic arthritis; FFS: fee for service; HMO: health maintenance organization; POS: point of service; ECI: Elixhauser Comorbidity Index.

condition codes, followed by hyperlipidemia, Type 2 diabetes, and ischemic heart disease (Table 1).

All-cause healthcare resource use: 12-month followup. Unadjusted all-cause healthcare resource use for patients with AS and PsA in the 12-month followup period is summarized in Table 2. Patients with PsA had a lower percentage of hospitalizations (9.4%) compared with patients with AS (11.1%). About 1 in 5 patients with AS or PsA visited the ER during the followup year (22.0% and 20.4%, respectively). Office visits were the most commonly used healthcare resource for both patient groups. More than half of all patients used biologics (52.5% and 61.1%, respectively), and the use of nbDMARD was lower in patients with AS (21.8%) than in those with PsA (52.4%).

Patients in both cohorts who used at least 1 healthcare resource per year had few inpatient/outpatient visits during the followup period (Table 2), and had about 1 hospitalization and 11 office visits per year: 6.6 (9.6) and 10.8 (7.7) for AS and 5.5 (7.1) and 10.7 (7.0) for PsA, respectively. The percentage of patients with AS and PsA who used biologics was similar (52.5% and 61.1%, respectively). The mean number of biologic prescriptions used per year was also similar for patients with AS [7.2 (SD 3.8)] and PsA [7.3 (SD 3.8)]. A lower percentage of patients with AS (21.8%) used nbDMARD than patients with PsA (52.4%). The mean number of nbDMARD prescriptions per year was lower in patients with AS [5.3 (SD 4.2)] than in patients with PsA [6.5 (SD 4.6)].

All-cause direct costs: 12-month followup. The unadjusted annual all-cause direct costs for AS and PsA during the 12-month followup period are summarized in Table 3 and Figure 2. Patients with PsA had an unadjusted mean (SD) medical cost of $5108 ($22,258), which was lower than for patients with AS [$6514 ($32,982); Figure 2]. Hospitalization costs were at least 2-fold higher than office and ER visits for both cohorts. PsA was associated with a lower mean (SD) hospitalization compared with AS [$3064 ($17,444) vs $4185 ($26,503)], and office [$1458 ($2097) vs $1571 ($2242)] and ER visit costs [$586 ($2717) vs $758 ($4237)].

Unadjusted mean (SD) prescription drug costs were higher in patients with PsA [$14,174 ($15,821)] compared with patients with AS [$11,214 ($14,249)] during the 12-month followup (Figure 2). Costs for biologics were responsible for most of the prescription drug totals. Patients with PsA incurred higher mean (SD) costs associated with biologics compared with AS [$14,061 ($15,593) vs $11,162 ($14,021)]. The cost of nbDMARD was less than $150 for both cohorts.

All-cause direct costs of AS and PsA. A multivariable analysis was performed to determine whether baseline covariates were associated with all-cause direct costs (medical and pharmacy costs) for AS and PsA during the 12-month followup period. The adjusted coefficient estimate and significance values for each cost predictor are presented in Table 4. After controlling for baseline characteristics, patients with AS aged 18–64 years had 18–30% higher directs costs compared with patients with AS ≥ 65 years ($p < 0.05$; Table 4). Patients with PsA aged 18–34, 45–54, and 55–64 years had 9–18% higher direct costs than patients with PsA aged ≥ 65 years ($p < 0.05$). However, patients with PsA aged 35–44 years had similar direct costs to those aged ≥ 65 years. No differences were observed between men compared with women in regard to direct costs in either group. Patients with an ECI score of ≥ 4 had direct costs twice as high for both AS (coefficient estimate 2.12, 95% CI 1.81–2.48) and PsA (1.95, 95% CI 1.78–2.13) compared with patients with an ECI score of 0 (all $p < 0.001$). The mean direct costs were about 3 times as high among patients with baseline biologic use compared with those without biologic use for both cohorts (2.82, 95% CI 2.61–3.05 for patients with AS; 3.12, 95% CI 2.98–3.25 for patients with PsA; both $p < 0.001$).

Table 2. All-cause healthcare resource use for patients with AS and PsA: 12-month followup.

Resource Use	AS, n = 4288		PsA, n = 10,832	
Patients, n (%)				
Hospitalizations*	476 (11.1)		1017 (9.4)	
ER visits	945 (22.0)		2212 (20.4)	
Office visits	4274 (99.7)		10,816 (99.9)	
Biologics use	2252 (52.5)		6621 (61.1)	
nbDMARD use	936 (21.8)		5675 (52.4)	
Use†	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Hospitalizations*	6.6 (9.6)	4.0 (5.0)	5.5 (7.1)	3.0 (4.0)
ER visits	2.0 (2.2)	1.0 (1.0)	1.8 (1.7)	1.0 (1.0)
Office visits	10.8 (7.7)	9.0 (9.0)	10.7 (7.0)	9.0 (7.0)
Biologics use	7.2 (3.8)	7.0 (7.0)	7.3 (3.8)	7.0 (7.0)
nbDMARD use	5.3 (4.2)	4.0 (5.0)	6.5 (4.6)	5.0 (6.0)

* Hospitalizations refer to inpatient visits. † The values for medical resource information indicate the number of uses on different dates per year among users with at least 1 resource use, and drug use (e.g., biologic, nbDMARD) is defined as the number of prescriptions per year among users. AS: ankylosing spondylitis; PsA: psoriatic arthritis; ER: emergency room; nbDMARD: nonbiologic disease-modifying antirheumatic drug; IQR: interquartile range.

Table 3. Unadjusted all-cause direct costs for patients with AS and PsA: 12-month followup.

Resource Use	AS, n = 4288		PsA, n = 10,832	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Medical costs, US$*				
Hospitalizations	$4185 ($26,503)	$0 (0)	$3064 ($17,444)	$0 (0)
ER visits	$758 ($4237)	$0 (0)	$586 ($2717)	$0 (0)
Office visits	$1571 ($2242)	$1008 ($1183)	$1458 ($2097)	$1020 ($1024)
Prescription drug costs, US$†				
Biologics use	$11,162 ($14,021)	$3016 ($22,690)	$14,061 ($15,593)	$12,541 ($24,446)
nbDMARD use	$52 ($228)	$0 (0)	$113 ($228)	$12 ($143)

* Medical costs were calculated as hospitalization costs plus ER and office visit costs in US dollars. † Prescription drug costs were calculated as biologics plus oral drug costs in US dollars. AS: ankylosing spondylitis; PsA: psoriatic arthritis; IQR: interquartile range; ER: emergency room; nbDMARD: nonbiologic disease-modifying antirheumatic drug.

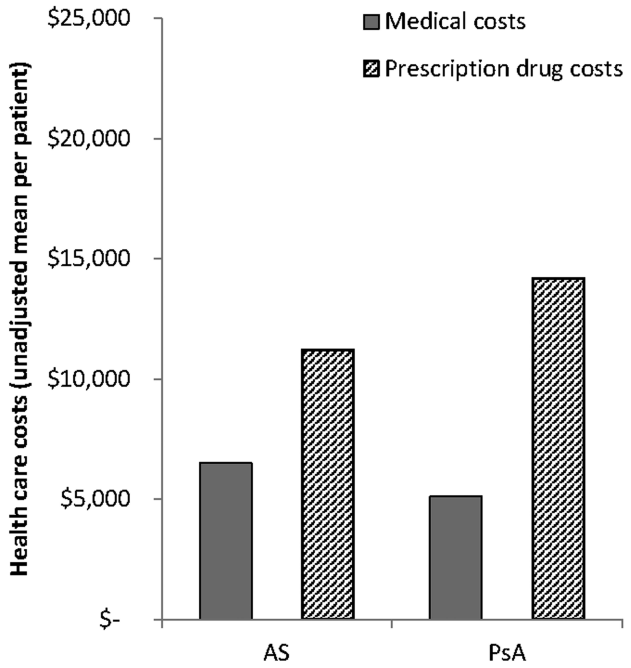

Figure 2. Mean all-cause direct costs during the 12-month followup period. Medical costs were calculated as hospitalization costs plus emergency room and office visit costs in US dollars. Prescription drug costs were calculated as biologics plus oral drug costs in US dollars. AS: ankylosing spondylitis; PsA: psoriatic arthritis.

DISCUSSION

To our knowledge, ours is the first study within the past 10 years to describe the all-cause healthcare resource use and direct costs incurred by patients with AS and PsA. In both cohorts, the most commonly used healthcare resource per year was office visits (11 office visits per yr), and the use of biologics was greater than nbDMARD in both cohorts. Use of biologics was similar in patients with PsA and AS. The use of nbDMARD was lower in patients with AS than those with PsA, possibly indicating the limited oral treatment options available for this condition. Patients with PsA had lower direct medical costs ($5108) than those with AS ($6514), and prescription drug costs were about $2000 higher for patients with PsA ($14,174). In the multivariable analysis, use of biologics was the major driver for the high prescription drug cost. Higher all-cause direct costs were associated with younger age and higher number of comorbidities.

To our knowledge, in the United States to date, all-cause healthcare resource use has only been investigated in 1 prior study for AS and in no studies for PsA in a broad population of insured patients, similar to that of our study. Ward performed a prospective longitudinal study that evaluated the total direct costs of AS and characterized the predictors of high total costs in patients with AS (n = 241)[16]. They found that, for patients with AS, healthcare use was low after the 1-year followup: 3% of patients had a hospitalization, an average of 7 office visits (i.e., rheumatology visits, other doctor visits, chiropractor visits, and physical/occupational therapy visits), and no ER visits[16]. Similar to the Ward study, our study showed that office visits were the most common resource used by patients with AS, with an average of 11 per year[16]. Our study found a slightly higher proportion of patients with AS having hospitalizations (11%), and of those, the average number of hospitalizations was ~7. The reason for these differences is not entirely clear, but may reflect differences between patient populations, comorbidities, types of health insurance, AS disease severity, and changes in healthcare practices since 2002[7,8,9]. The study by Singh and Strand evaluated the healthcare use of veterans with AS and PsA in the Veterans Integrated Service Network-13 using a postal survey[41]. However, comparing the findings of the 2 studies with ours is challenging because of the differences in populations analyzed and methodology.

Several studies assessed the all-cause direct costs for AS and PsA[15,16]. Williams and Meyers estimated the direct costs using claims data (MedStat MarketScan database) for 1999 to 2000. The average annual per patient cost for medical resources and prescription drugs was $4500 for patients with AS and $3600 for patients with PsA[15]. Ward also evaluated total direct cost for AS using patient-reported information

Table 4. Predictors of all-cause direct costs after adjusting for baseline characteristics*. Direct costs were calculated as the sum of all-cause medical and pharmacy costs. Outcomes were predicted using a generalized linear model with γ distribution and log link function.

Predictor	AS, n = 4078, Coefficient Estimate (95% CI)**	p	PsA, n = 10,277, Coefficient Estimate (95% CI)**	p
Age, yrs, reference ≥ 65 yrs				
18–34	1.28 (1.09–1.50)	< 0.01	1.18 (1.07–1.31)	< 0.01
35–44	1.18 (1.02–1.36)	< 0.05	1.07 (0.98–1.16)	NS
45–54	1.20 (1.05–1.38)	< 0.01	1.09 (1.01–1.18)	< 0.05
55–64	1.30 (1.13–1.50)	< 0.001	1.14 (1.06–1.22)	< 0.001
Sex, reference = female				
Male	1.02 (0.94–1.10)	NS	1.03 (0.99–1.07)	NS
Region in the US, reference = West				
Northeast	0.98 (0.86–1.11)	NS	1.03 (0.96–1.11)	NS
North Central	1.01 (0.90–1.12)	NS	0.88 (0.83–0.94)	< 0.001
South	0.88 (0.80–0.97)	< 0.05	0.93 (0.87–0.98)	< 0.05
Insurance plan*, reference = HMO and POS capitation				
FFS	0.91 (0.82–1.10)	≥ 0.05	1.04 (0.98–1.10)	NS
Baseline ECI score, reference = 0				
1	0.99 (0.87–1.13)	NS	1.09 (1.04–1.15)	< 0.01
2	1.25 (1.09–1.44)	< 0.01	1.21 (1.13–1.28)	< 0.001
3	1.26 (1.07–1.48)	< 0.01	1.37 (1.25–1.49)	< 0.001
4	2.12 (1.81–2.48)	< 0.001	1.95 (1.78–2.13)	< 0.001
Baseline biologics use, reference = patients with no biologic use	2.82 (2.61–3.05)	< 0.001	3.12 (2.98–3.25)	< 0.001

* Patients with missing region (n = 42 for AS, < 1%; n = 125 for PsA, < 1%), missing insurance type (n = 157 for AS, < 3%; n = 425 for PsA, < 4%), or zero outcome (n = 11 for AS, < 1%; n = 5 for PsA, < 1%) were excluded from the multivariate analysis. ** Coefficient estimates were the exponentials of the original estimates. A coefficient of > 1.0 indicates higher cost and < 1.0 indicates lower costs for a given variable compared with the specified "reference." AS: ankylosing spondylitis; PsA: psoriatic arthritis; FFS: fee for service; ECI: Elixhauser Comorbidity Index; NS: not significant; HMO: health maintenance organization; POS: point of service.

gathered through a questionnaire[16]. Researchers found that the average annual direct cost for patients with AS was $2700, including inpatient/outpatient visits, medications, assistive devices, travel to visits, and diagnostic testing. Considering both medical and pharmacy costs, the direct costs in our study were estimated to be $17,728 for patients with AS and $19,282 for patients with PsA. Even after adjusting for inflation, the direct costs for AS and PsA reported in the previous studies[15,16] were considerably lower than in our study. One explanation for these differences is how these conditions are now treated and possibly the addition of biologic use in the last decade[42,43]. Study design variables likely affected the findings.

A longitudinal study by Zhu, *et al*[17] examined medication use and healthcare costs in patients with PsA who had initiated treatment with a biologic, either as monotherapy or adjunctive therapy with a conventional nbDMARD using the Truven Health Analytics MarketScan database. Investigators determined that the total all-cause and PsA disease-specific direct costs (i.e., inpatient, outpatient, ER, and pharmacy costs that contained a PsA diagnosis code) were $26,535 and $17,764, respectively[17]. In our study, total all-cause cost for PsA was $19,282. The difference between our findings and those of Zhu, *et al* may reflect differences in the population because they used a biologic-naive group (excluding patients with biologic claims within 6 mos). Compared with the studies by Williams and Meyers[15] and Ward[16], the costs for PsA and AS in our study and those in Zhu, *et al*[17] suggest that the overall direct cost of managing and treating patients with AS or PsA has markedly increased since 2002.

Similar to our study, previous studies have found that pharmacy cost was 1 of the largest contributors to expenses in patients with AS or PsA. Ward noted that medication costs accounted for the greatest proportion of direct costs in patients with AS (42%)[16]. Zhu, *et al* reported that pharmacy costs in patients with PsA receiving biologic therapy accounted for 54% of total all-cause expenditures[17]. The results of these 2 studies are consistent with our observation that pharmacy costs made up > 50% of the medical plus prescription cost in patients with AS or PsA. Zhu, *et al* found that all-cause and PsA-specific 1-year pharmacy costs were $14,315 and $11,981, respectively[17]. We found that pharmacy costs (biologic and nbDMARD) in the 1-year followup period were $14,174 for the PsA cohort. The difference in values between the studies may reflect differences in study design and the pharmacy costs that were

included in the analyses. For example, Zhu, *et al* evaluated costs for all medications, including drugs administered during inpatient and outpatient visits, as well as medications with an associated PsA code for their evaluation of PsA-associated costs[17]. In our study, we included only costs of biologics and nbDMARD.

The primary driver of higher direct costs for AS and PsA patients in our study was baseline biologic use; other drivers were age and the number of comorbidities, as reflected by the ECI score. The number of comorbid conditions was not associated with high total costs, which may reflect the different methods used to evaluate the presence of comorbidities (i.e., ECI score vs patient questionnaire). Additional studies are necessary to assess the effect of comorbid conditions on the all-cause healthcare costs of AS and PsA. Despite the high costs associated with biologics, they are effective and recommended for certain patients with PsA or AS whose first-line therapy fails[44,45]. Our findings also suggest the need for patients treated with biologics to be carefully managed to maximize the benefit of these therapies relative to the costs.

AS and PsA are associated with a number of comorbid conditions, which along with the primary disease, can greatly affect a patient's quality of life (QoL)[44,46]. The main treatment goals are to maximize QoL and physical function by not only controlling the signs and symptoms of the disease, but by minimizing comorbidities[43]. Some comorbidities may be related to the inflammation associated with these diseases; inflammatory joint disease is known to be involved in CV and non-CV morbidity in patients with PsA[47]. Other factors, such as CV risk factors, higher ratio of total cholesterol to high-density lipoprotein cholesterol, and smoking, may influence the presence of comorbidities[48].

Our study had a few shortcomings that should be acknowledged. Our study population was restricted to individuals with commercial healthcare coverage or private Medicare supplemental coverage and may not be generalizable to all patients with AS or PsA within the United States[21]. Patients with AS or PsA who have severe functional impairment and are not able to work may not have been represented, leading to an underestimation of costs. Because we used a retrospective approach, our study was limited to patients who were diagnosed clinically; however, patients with undiagnosed AS or PsA may have sought medical attention and incurred additional healthcare resource use and costs. Diagnoses recorded on claims may be coded incorrectly or not coded at all, thereby potentially introducing measurement error in ICD-9-CM–based variables. Administrative claims data were not collected for research purposes, and the diagnostic coding on administrative claims was recorded by physicians to support reimbursement. Thus, data may not be detailed enough to provide a clinically precise description of patients. Therefore, the effect of disease severity and other descriptive variables (e.g., smoking status) on costs and cost drivers was not assessed. Our multivariate analysis revealed a multicollinearity issue between ECI and AS- and PsA-related comorbidities because of the ECI containing AS- and PsA-associated comorbidities. Consequently, we chose not to evaluate the individual AS- and PsA-related comorbidities in the multivariable analysis in our study because they do not reflect the overall comorbidity burden for these 2 diseases. Instead, we used the ECI and CCW to provide a more comprehensive evaluation of the comorbidity burden.

With regard to adjusting for baseline characteristics, our adjustments may not fully account for all comorbidities present in patients with AS or PsA, or the relationship between comorbid conditions within the same patient. Another study is required to assess the economic burden of comorbidities related to AS and PsA. We also did not evaluate the cost of the use of nonsteroidal antiinflammatory drugs (NSAID), analgesics, or physical therapy visits. NSAID are recommended as first-line therapy for patients with both AS and PsA[10,49,50,51,52] and are commonly used to treat both diseases. However, there was no cost or use information in the databases used in our study for NSAID because most are over-the-counter medications. Because the preferred societal perspective of cost is most comprehensive, a limitation of our study is that only costs from the payer's perspective were included. We did not account for indirect costs of the disease such as work productivity. Future studies should be designed to assess the effect of these variables on the direct costs of AS and PsA.

Our findings contribute to the literature on the economic burden associated with the classically defined SpA conditions of AS or PsA. We evaluated the all-cause direct costs and predictors of higher costs for AS and PsA. The most influential predictors of direct costs were the use of biologics, age, and the presence of comorbid conditions. The significant effect that biologics had on overall direct costs indicates the need to better understand the relationships among treatment outcomes, use of medical resources, and real-world biologic use. Future studies should focus on examining the effect of these relationships on disease symptoms, patient QoL, and total healthcare costs.

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